



POLICY PACKAGE TO COMBAT ANTIMICROBIAL RESISTANCE

- 1. COMMIT TO A COMPREHENSIVE, FINANCED NATIONAL PLAN WITH ACCOUNTABILITY AND CIVIL SOCIETY ENGAGEMENT**
- 2. STRENGTHEN SURVEILLANCE AND LABORATORY CAPACITY**
- 3. ENSURE UNINTERRUPTED ACCESS TO ESSENTIAL MEDICINES OF ASSURED QUALITY**
- 4. REGULATE AND PROMOTE RATIONAL USE OF MEDICINES, INCLUDING IN ANIMAL HUSBANDRY, AND ENSURE PROPER PATIENT CARE**
- 5. ENHANCE INFECTION PREVENTION AND CONTROL (IPC)**
- 6. FOSTER INNOVATIONS AND RESEARCH & DEVELOPMENT FOR NEW TOOLS**

1. COMMIT TO A COMPREHENSIVE, FINANCED NATIONAL PLAN WITH ACCOUNTABILITY AND CIVIL SOCIETY ENGAGEMENT

A MASTER PLAN TO COMBAT ANTIMICROBIAL RESISTANCE

WHY IS A COMPREHENSIVE NATIONAL PLAN ESSENTIAL FOR COMBATING ANTIMICROBIAL RESISTANCE?

The factors which favour the emergence and spread of resistant microbes, and the measures needed to combat antimicrobial resistance (AMR), are well known. A comprehensive plan brings all the elements together so that everyone can do more to make a difference:

- > Policy-makers and planners in government must provide the legal framework and strategy that people need to work together effectively to combat AMR and its public health consequences.
- > Civil society and patients' groups can raise awareness of the issues, and demand action by policy-makers and all stakeholders. Everyone can play a part by using prescribed medicines correctly.
- > Practitioners and prescribers need to combine appropriate prescription of antimicrobials with clear, accurate and understandable advice to patients. Veterinarians should resist pressures to use antibiotics as growth promoters and for disease prevention in livestock.
- > Pharmacists and dispensers must ensure that antimicrobials are safe: obtained from an approved source and stored properly, and supplied in line with prescriptions.
- > Providers, institution managers, and communities should apply infection control measures to prevent the emergence and spread of AMR.
- > The diagnostic and pharmaceutical industry, through research and development, will need to produce the tools needed to better prevent and detect disease, identify AMR earlier, and develop new antimicrobials needed to replace those that have become ineffective.

CHALLENGES TO OVERCOME

- > **Limited public awareness and government commitment:** media attention focuses on individual outbreaks but gives little attention to the wider threat of AMR. It is therefore not a priority of national governments or linked to the achievement of the health-related Millennium Development Goals. Despite their potential to influence policy too few nongovernmental, donor and health advocacy agencies have recognized the threat of AMR.
- > **Fragmentation of effort:** specific activities to combat AMR are taken forward by individual programmes, institutions and regulatory bodies, but too often in the absence of an overall strategy; without an adequate budget; and with no accountability for results.
- > **Perverse incentives** contribute to AMR, through the unregulated marketing of antimicrobials, their use for growth promotion in livestock, or profit-seeking prescribing of antibiotics in human health care. Where legal frameworks exist they are rarely accompanied by effective sanctions.
- > **The voiceless are the worst affected:** poor people are among those who are at greatest risk of infections and those most likely to lack access to quality services and suffer severe illness. They usually lack information or opportunity to demand or become involved in actions to combat AMR.

THE ROLE OF GOVERNMENT

A concerted attack on AMR requires leadership, advocacy, and resources. Governments therefore have a special role. The national 'Master Plan' should set out what has to be done, how and by whom.

A. PROVIDE STEWARDSHIP AND COORDINATION:

AMR is a threat to health which requires a multi-sectoral response. Stewardship by government is therefore key to success. In practice,

stewardship starts with the legal, policy and regulatory framework that covers all aspects of drug supply and use. It also means bringing together departments across government, along with the private and non-governmental organizations in ways that ensure concerted action.

- 1) Establish a national intersectoral government steering committee mandated to forge a partnership with all stakeholders.
- 2) Ensure that the committee is supported by a secretariat with the resources, skills and authority required to coordinate action across government.
- 3) Develop a national AMR action plan, based on a needs assessment, with a clear strategy and prioritized annual targets for all six elements of the policy package; integrate the plan into the national health plan and other relevant sectoral plans.
- 4) Ensure that adequate resources are earmarked for capacity building at all levels within the national plan.
- 5) Set up a monitoring framework, with measurable indicators of action, and report annually against these indicators.

B. COST PLANS AND MOBILIZE RESOURCES

All stakeholders – including ministries of finance – must recognize the urgency of the threat if they are to contribute to a national effort. A realistic assessment of costs to meet needs, as well as estimates of the potential savings from reducing AMR, will help in mobilizing resources.

- 1) Estimate the cost of all elements of the national AMR plan, develop a complete budget, and integrate it into the national health budget and other relevant budgets.
- 2) Mobilize human and financial resources to support the plan through regular budget allocations, mainstreaming of activities within core programmatic and management systems and within other priority health initiatives.

C. BUILD PARTNERSHIPS WITH CIVIL SOCIETY

If people – especially patients, civil society and consumer groups – fully understand the problem and are enabled to engage, they can help drive progress.

- 1) Involve civil society representatives in a formal arrangement for the development of AMR policy, membership of coordinating bodies or alliances, and monitoring actions to combat AMR.
- 2) Hold regular public information and discussion meetings, and assign roles and responsibilities in joint activities and partnerships with patient organizations, consumer groups and other public interest groups.
- 3) Educate consumers about the efficacy, safety, quality and correct (rational) use of medicines.
- 4) Encourage capacity-building in civil society organizations so that they can participate in and benefit from educational and collaborative activities.

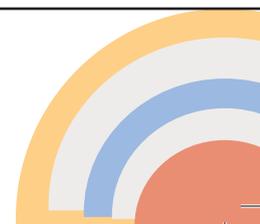
Examples of national coordination for AMR response

Thailand has developed a draft national AMR containment policy and a committee to promote appropriate use of antimicrobials. The policy covers: standardization of testing by microbiology laboratories, human resources development, antibiotic systems in hospitals, ethical guidelines for drug dispensing and prescribing, antimicrobial resistance surveillance and monitoring, antimicrobial use in livestock, and other issues. An antibiotic formulary was also developed and a surveillance network established as well as a campaign on antibiotic use in community hospitals. Using resources from a national health promotion fund, a special three-year project began under leadership of the Chulalongkorn University to strengthen surveillance, communications, advocacy, partnering and knowledge sharing.

The US Government has an Interagency Task Force on Antimicrobial Resistance to plan and coordinate federal government activities. The Task Force has three co-chairs: the US Centers for Disease Control and Prevention, Food and Drug Administration, and National Institutes of Health. Seven other US federal agencies also participate: Agency for Healthcare Research and Quality, Centers for Medicare and Medicaid Services, Department of Agriculture, Department of Defense, Veterans Administration, Environmental Protection Agency, and Healthcare Resources and Services Administration. A first Public Health Action Plan to Combat Antimicrobial Resistance was released in 2001 and has been subsequently updated. Main elements of the Plan include reducing inappropriate antimicrobial use, reducing the spread of antimicrobial resistant microorganisms in institutions, communities, and agriculture; encouraging the development of new anti-infection products, vaccines and adjunct therapies; and supporting basic research on antimicrobial resistance.

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2. STRENGTHEN SURVEILLANCE AND LABORATORY CAPACITY

Surveillance involves the systematic collection and analysis of health-related data, and reporting the findings to those who will use them in decision-making on public health issues.

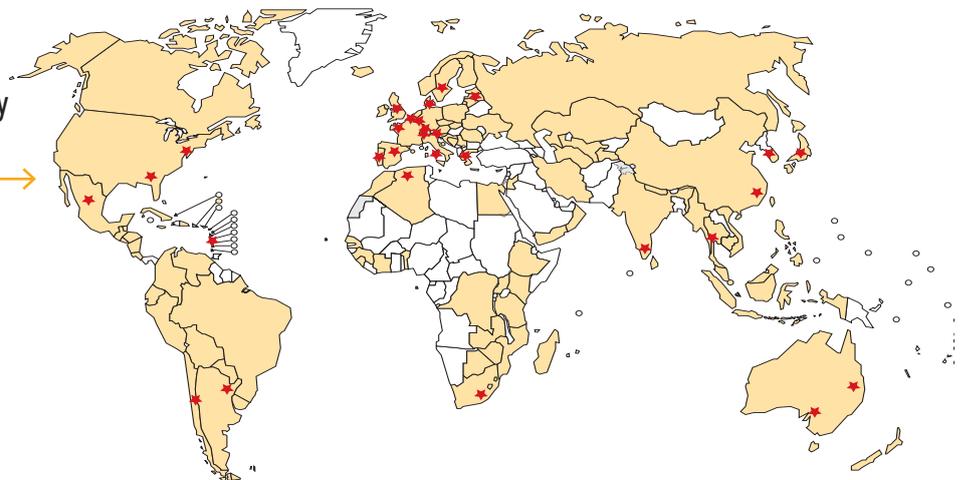
WHY IS SURVEILLANCE NECESSARY TO COMBAT ANTIMICROBIAL RESISTANCE?

Surveillance is needed:

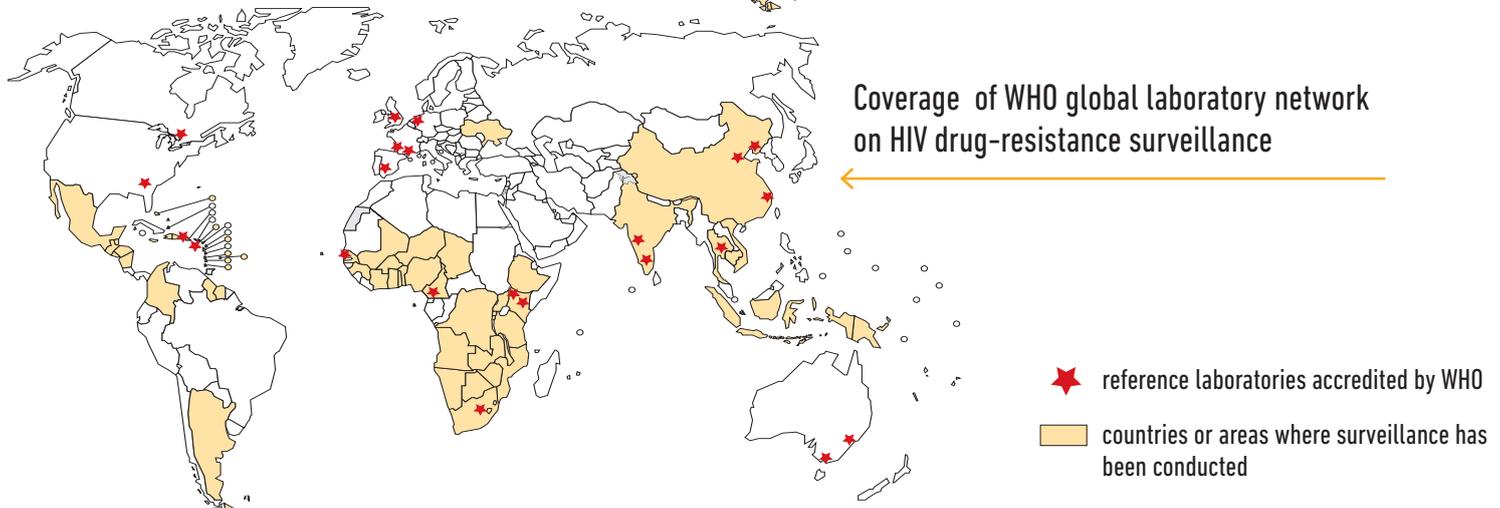
- > to detect resistant microorganisms, follow their spread among people and geographic areas, and enable outbreaks of diseases caused by drug-resistant infections to be notified and investigated promptly;
- > to enable correct decisions to be taken about treatment of patients, and to prevent and control the spread of infection;
- > to guide policy recommendations and to monitor how well the measures taken to combat antimicrobial resistance (AMR) are working;
- > to track the use and misuse of antimicrobial medicines, so that the public health consequences can be assessed.

Examples of functioning global drug resistance surveillance networks

Coverage of WHO global laboratory network on M/XDR-TB surveillance



Coverage of WHO global laboratory network on HIV drug-resistance surveillance



★ reference laboratories accredited by WHO
 ◻ countries or areas where surveillance has been conducted

POLICY PACKAGE TO COMBAT ANTIMICROBIAL DRUG RESISTANCE

COMBAT DRUG RESISTANCE
No action today, no cure tomorrow



CHALLENGES TO OVERCOME

- > **Shortage of competent laboratories:** AMR surveillance depends on microbiology laboratories which can accurately identify resistant microorganisms. Low-income countries generally lack such laboratories, and where laboratories exist, the means to check the reliability of their work are often lacking.
- > **Poor infrastructure and data management:** poor data management prevents routine monitoring and reliable data collection to measure the extent of AMR.
- > **Variation in methods:** without standard protocols for measuring resistance, data cannot be shared and compared between laboratories and countries.
- > **Low coverage of surveillance:** a number of global databases and regional networks for specific diseases hold data related to AMR, but the data are patchy, with many gaps.
- > **Lack of intersectoral cooperation:** the impact on human health of using antibiotics as growth promoters and for disease prevention in food-producing animals is unclear. It cannot be assessed without better collaboration for surveillance of AMR in bacteria from humans, food products and animals.
- > **Inadequate international collaboration:** more extensive international collaboration on AMR surveillance is needed so that information can be shared to provide an early warning of new or unusual outbreaks of drug-resistant infections.

CORE ACTIONS

A. ESTABLISH AMR SURVEILLANCE AND MONITORING SYSTEMS

- 1) Consolidate AMR surveillance, using the right epidemiological methods (including sample-based surveys, sentinel site surveillance and routine surveillance).
- 2) Apply standardized protocols to assess AMR consistently over time and across geographical areas.
- 3) Adapt available model information systems and software for AMR surveillance (e.g. WHONET) and ensure that data flows from hospitals and other health-care facilities to the national level, so that laboratory results and clinical information can be linked.

- 4) Establish systems for recording the use of antimicrobial medicines in hospitals and other health-care facilities and in the community, and link these findings to AMR surveillance data.
- 5) Set up quality assurance systems, including monitoring and supervision of laboratories, continuing education for staff, and verification of the AMR data collected.
- 6) Integrate systems for AMR surveillance between public health services, veterinary services and food safety authorities, including health facilities and congregate settings¹.
- 7) Ensure that surveillance data are analysed and reported promptly on a regular basis; and that the data are used to inform national medicines policy and standard treatment guidelines, to promote the rational use of medicines, and in infection control.

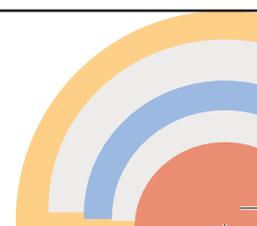
B. BUILD LABORATORY CAPACITY FOR RAPID AND RELIABLE DIAGNOSTIC TESTING

- 1) Designate reference microbiology laboratories to carry out reliable diagnostic testing, with strengthening of the laboratories as necessary.
- 2) Ensure that laboratory data are recorded and reported promptly to prescribers, infection control programmes and national health authorities.
- 3) Establish quality assurance systems and supervision to ensure the reliability of laboratory results.
- 4) Extend access to the best AMR diagnostic methods, including rapid molecular techniques.

C. ENGAGE IN REGIONAL AND GLOBAL SURVEILLANCE NETWORKS

- 1) Share the national surveillance data on AMR and antimicrobial use promptly.
- 2) Support and participate in regional networks and reference laboratories for surveillance of AMR.
- 3) Promote standard reporting and dissemination of information at regional and global levels.

¹ For the purposes of this document, congregate settings refer to a mix of settings that range from correctional facilities and military barracks, to homeless shelters, refugee camps, dormitories and long-term facilities.



3. ENSURE UNINTERRUPTED ACCESS TO ESSENTIAL MEDICINES OF ASSURED QUALITY

The quality and regular supply of medicines is crucial for the treatment of patients and for the prevention and control of antimicrobial resistance. The use of substandard antimicrobial medicines results in prolonged infections and the emergence of resistant microbes.

WHY IS ACCESS TO QUALITY-ASSURED ESSENTIAL MEDICINES NECESSARY FOR COMBATING ANTIMICROBIAL RESISTANCE?

- > Antimicrobial medicines containing less than the specified amount of the active substance contribute to antimicrobial resistance (AMR) because infections persist and resistant microbes are able to grow and survive the treatment. The quality of medicines has to be controlled through national drug regulations.
- > Irregularity of supplies and limited access to affordable, quality-assured medicines are barriers to effective treatment. Faced with problems of availability or affordability, patients often take incomplete courses of treatment or seek alternatives that could include substandard or counterfeit medicines. In these situations the risk of AMR is increased due to suboptimal dosage.

CHALLENGES TO OVERCOME

- > **Lack of systems to assure quality:** many countries do not have adequate systems to assure the quality of essential medicines.
- > **Gaps in legislation for drug regulation:** without comprehensive legislation to support drug regulation, some areas of pharmaceutical activity may not be covered by the regulations.
- > **Poor implementation of drug regulations:** inadequate infrastructure, fragmented drug regulatory functions and a lack of

overall accountability lead to lapses in implementation and to duplication of efforts.

- > **Absence of regulatory tools:** without regulatory tools, such as documented operating procedures, erratic application of legislation and lack of transparency of law enforcement will result.
- > **Inadequate planning and resources:** poor availability of essential medicines in the public sector is often due to lack of resources or under-budgeting, and inefficiencies and wastage can result from inadequate planning, managing and monitoring the supply of medicines.
- > **Insufficient financial control:** lack of price controls, non-transparent price mark-ups, lack of competition, and taxes and tariffs on medicines all tend to raise prices and lower access to essential medicines.
- > **Deficient management of procurement and distribution:** poor estimation of needs, uneven distribution, misuse, lack of effective coordination, and poor storage conditions throughout the distribution system lead to wastage and jeopardize quality.

Countries which have successfully tackled these problems have done so through a series of core actions (see below) guided by well-defined national medicines policy.

CORE ACTIONS

A. REINFORCE THE SYSTEM FOR SUPPLY OF ESSENTIAL MEDICINES

- 1) Set up a national body to coordinate: (a) the development and regular updating of an Essential Medicines List based on national standard treatment guidelines, (b) setting priorities for supplying essential medicines in the public and private sectors, and (c) targeted quality assurance and reimbursement schemes.
- 2) Improve the forecasting of quantities needed in the country based on accurate national data, and ensure adequate and timely ordering, procurement and distribution of essential medicines.
- 3) Ensure sufficient public financing for essential medicines; review the impact of current health care financing on access to essential medicines; and introduce broad-based insurance schemes to cover essential medicines.¹
- 4) Formulate pricing policies, including those on relevant tax and mark-ups, in collaboration with authorities in ministries of finance, trade and commerce; encourage higher margins for affordable generic medicines and lower margins for expensive brand-name medicines.
- 5) Institute adequately resourced mechanisms to monitor prices of medicines, with participation of civil society and consumer groups.

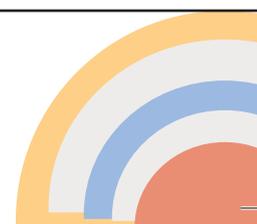
B. ASSURE THE QUALITY OF DRUGS ACCORDING TO INTERNATIONAL STANDARDS

- 1) Structure the drug regulatory authority (DRA) as an independent central coordinating body in the ministry of health with overall responsibility and accountability for all aspects of drug regulation, involving other relevant ministries where necessary; and ensure that its functions are separated from those of drug supply and management to avoid conflicts of interest.
- 2) Review and revise relevant legislation to ensure that the DRA has an adequate legal basis and functions effectively to cover all activities associated with manufacture, importation, distribution, dispensing and promotion; and rectify regulatory gaps by modifying existing legislation or introducing new legislation.
- 3) Develop standards and documented guidelines to be used as tools for applying all drug regulatory functions; and make these guidelines publicly available to ensure transparency of the regulatory process.
- 4) Set up programmes on staff development to provide appropriate training and qualification of personnel engaged in drug regulation.
- 5) Establish mechanisms for systematic monitoring of the regulatory process.
- 6) Ensure that medicines available in the public and private sectors have been registered by the DRA.

¹ *The World Health Report – Health systems financing: the path to universal coverage*. Geneva, World Health Organization, 2010 (WHO/IER/WHR/10.1).

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4. REGULATE AND PROMOTE RATIONAL USE OF MEDICINES, INCLUDING IN ANIMAL HUSBANDRY, AND ENSURE PROPER PATIENT CARE

How antimicrobial medicines are used has an important impact on the emergence and spread of resistant microbes. The correct (rational) use of antimicrobials minimizes the threat of resistance and helps to prolong the useful lifespan of these drugs.

WHY IS RATIONAL USE OF MEDICINES ESSENTIAL FOR COMBATING ANTIMICROBIAL RESISTANCE?

- > Irrational use (misuse) of antimicrobial medicines is a major driver of antimicrobial resistance (AMR).
- > Antimicrobials are misused when taken for too short or too long a period, at too low a dosage, at substandard potency, or for the wrong disease. Both under-use and over-use favour the development of AMR.

Only 50% of people with malaria receive the recommended first-line antimalarial medicine.

Only 50–70% of people with pneumonia are treated with appropriate antibiotics.

Up to 60% of people with viral upper respiratory tract infection receive antibiotics inappropriately.

CHALLENGES TO OVERCOME

- > **Insufficient training for prescribers and dispensers:** inadequate knowledge of health-care providers leads to improper prescription and dispensing practices; these are major factors responsible for the misuse of medicines worldwide.
- > **Lack of legislation and enforcement:** lack of appropriate legislation and/or poor enforcement fosters the indiscriminate use of antimicrobials; for example, unauthorized dispensing of antimicrobials encourages harmful self-medication.

- > **Accessibility of updated information:** even relatively well-trained prescribers may lack the up-to-date information needed to make correct decisions on which medicines to prescribe.
- > **Absence of data and guidelines:** lack of surveillance data and updated treatment guidelines can result in the inappropriate prescription of antimicrobials or the prescription of older antimicrobials that are no longer effective; conversely, excessive and unnecessary use of newer antimicrobial medicines may occur.
- > **Poor application of guidelines:** even when proper treatment guidelines are available, they are not always followed because of ineffective dissemination and lack of relevant training and supervision.
- > **Perverse incentives:** pressure by patients as well as economic incentives, such as profits from both prescribing and dispensing, can stimulate unnecessary prescription of antimicrobial medicines.
- > **Inappropriate promotion:** pharmaceutical promotion focused on increasing sales irrespective of the effects on health often leads to irrational use of antimicrobials.

Countries which have successfully tackled these problems have done so through a series of core actions (see over) guided by a well-defined national medicines policy.

CORE ACTIONS

A. PROMOTE AND ENFORCE STANDARD TREATMENT GUIDELINES

- 1) Develop standard treatment guidelines (STGs) in collaboration with professional societies, medical and paramedical teaching institutions; regularly update and promote the use of the guidelines; and encourage inclusion of the guidelines in basic medical and paramedical curricula.
- 2) Engage professional societies and teaching institutions to provide problem-based training on rational use of medicines linked to STGs and the Essential Medicines List (EML), to establish good prescribing habits.
- 3) Review and revise regulations for professional licensing to link regular participation in continuous education activities with registration requirements.
- 4) Require hospitals and other health-care facilities to establish committees to develop and update institutional drug formularies and STGs, provide training and continuous education, and establish a system for audit and review.
- 5) Work with health-care institutions to ensure the availability of programmes on antimicrobial stewardship and good diagnostic capacity, to promote appropriate antimicrobial prescribing.
- 6) Establish surveillance systems on antimicrobial resistance to provide essential information for maintaining and regular updating of STGs, and monitor trends in antimicrobial usage.

B. ENFORCE PRESCRIPTION-ONLY USE OF ANTIMICROBIALS

- 1) Establish an effective licensing scheme for pharmacies and other outlets where medicines are sold.
- 2) Limit the availability of antimicrobials to prescription-only categories.
- 3) Link prescription-only categories to regulations regarding sale, supply and dispensing.
- 4) Prohibit the prescription and sale of single drug treatments for cases for which the recommended treatment is a combination of drugs.

C. PROMOTE EDUCATION ON ANTIMICROBIAL MEDICINES AND THEIR USE

- 1) Provide independent and unbiased information about medicines for health personnel and for consumers as a function of the ministry of health, with dedicated budgets for this purpose.
- 2) Implement systems to ensure compliance with STGs as an integral part of treatment programmes and monitor the emergence of resistance to antimicrobial medicines.
- 3) Train prescribers and dispensers to educate patients on how to use antimicrobial medicines correctly and the importance of following exactly (adherence to) the prescribed treatment.
- 4) Arrange targeted public education campaigns; introduce the correct use of medicines in health education components of school curricula and adult education programmes; and engage the media in awareness campaigns.
- 5) Actively involve consumers, patients and their organizations in education efforts.

D. REDUCE ANTIMICROBIAL USE IN FOOD-PRODUCING ANIMALS

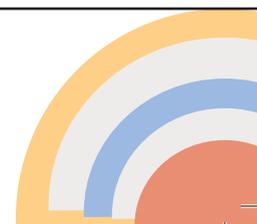
(see separate briefing note - 4D)

E. WORK TO REDUCE FINANCIAL INCENTIVES THAT ENCOURAGE IRRATIONAL USE OF MEDICINES

- 1) Examine the incentive structures that exist locally, and identify factors that influence prescribing and dispensing practices; develop policies to reduce financial incentives for providers, such as separating the functions of prescribing and dispensing, and ensure that the policies are implemented, monitored and enforced.
- 2) Educate prescribers on factors which may influence their prescribing habits.
- 3) Review the methods of payment and reimbursement; and structure charges and reimbursements according to the EML and STGs, to promote more rational use of medicines.
- 4) Introduce regulations which address all aspects of the promotion of pharmaceuticals; ensure that advertisements contain only information that was approved when the product was registered.
- 5) Monitor activities that promote medicines to ensure that they accord with government regulations.

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4D. REDUCE USE OF ANTIMICROBIALS IN FOOD-PRODUCING ANIMALS

Antibiotics are widely used in healthy food-producing animals to promote growth and prevent disease. This practice favours the emergence and spread of resistant bacteria in both animal and human populations.

WHY ADDRESSING THE USE OF ANTIMICROBIALS IN FOOD-PRODUCING ANIMALS?

- > The routine use of antimicrobials in vast numbers of healthy animals is likely to result in the emergence and spread of antimicrobial-resistant bacteria, and cause resistant infections in animals and humans.
- > Resistant microorganisms carried by food-producing animals can spread to humans through consumption of contaminated food, from direct contact with animals, or by environmental spread, for example in contaminated water.
- > The genes coding for antimicrobial resistance can be transferred from microbes carried by animals to microbes that cause disease in humans.

- > Food animals and foods of animal origin are traded worldwide; as a result, antimicrobial resistance (AMR) affecting the food supply of one country becomes a potential problem for other countries.

CHALLENGES TO OVERCOME

- > **Lack of information:** data on the occurrence of resistance and on antimicrobial use in animals are essential for risk analysis and to assess the effectiveness of control measures. However, few countries have systems to monitor antimicrobial resistance and even fewer have systems to monitor the use of antimicrobials in animals.
- > **Lack of standardized data collection:** the data collected are often difficult to interpret and compare because the methods used to obtain them are not standardized.

Examples

The use of a glycopeptide (avoparcin) as a growth promoter in food animals in Europe resulted in the development of vancomycin-resistant *Enterococci* (VRE) in the commensal flora of food animals, on meat from these animals and in the commensal flora of healthy humans, despite the limited use of glycopeptides such as vancomycin only in hospitalized patients. A subsequent ban on the use of avoparcin in food animals in the European Union reduced the occurrence of VRE in animals and its presence in the general population.

The use of fluoroquinolones (e.g. enrofloxacin) in food-producing animals has resulted in the development of ciprofloxacin-resistant *Salmonella*, *Campylobacter* and *Escherichia coli*, which have caused human infections that proved difficult to treat. In several instances, such bacteria have spread worldwide through travel and food trade.

- > **Lack of intersectoral collaboration:** without coordinated AMR surveillance in bacteria from humans, food and animals it is difficult to assess the public health impact of antimicrobial use in food-producing animals and to take corrective measures.
- > **Inadequate training:** lack of training on appropriate use of antimicrobial agents in food-producing animals, and insufficient understanding of their potential contribution to AMR in humans, are common among farmers, veterinary prescribers and dispensers.
- > **Perverse incentives:** the unnecessary use of antimicrobials is often encouraged by financial incentives, such as achieving sales profits by veterinarians, or perceived benefits, such as promoting the growth of food-producing animals.
- > **Gaps in legal and regulatory controls:** insufficient legislation and regulation to restrict the approved use of licensed antimicrobials, and to control the supply of antimicrobials, facilitates the excessive use of antibiotics.

CORE ACTIONS

A. PROVIDE NATIONAL LEADERSHIP AND PROMOTE INTERSECTORAL COLLABORATION

- 1) Establish a formal mechanism of interaction between the Ministry of Health and other relevant ministries and authorities to address the issue of AMR in the agricultural sector.
- 2) Include agricultural and veterinary authorities in the national intersectoral steering committee on AMR.

B. CREATE AND ENFORCE AN ENABLING REGULATORY FRAMEWORK

- 1) Establish a regulatory framework for authorization and control of the quality of veterinary medicines.
- 2) Introduce pre-licensing safety evaluation of antimicrobials for veterinary use, with consideration of potential resistance to drugs used in human medicine.
- 3) Terminate non-therapeutic use of antimicrobials, such as the use of antimicrobials as growth promoters.
- 4) Restrict or eliminate the use in food-producing animals of antimicrobials identified as critically important in human medicine, especially the use of fluoroquinolones, and third- and fourth-generation cephalosporins.
- 5) Require obligatory prescriptions for all antimicrobials used for disease control in food-producing animals.

C. STRENGTHEN SURVEILLANCE AND MONITORING

- 1) Create national systems to monitor antimicrobial usage in food-producing animals.
- 2) Develop national integrated surveillance programmes to monitor current and emerging AMR patterns (including quantitative susceptibility data for zoonotic pathogens and indicator bacteria). Surveillance should involve close collaboration between public health, veterinary and food laboratories.
- 3) Set up a multidisciplinary task force involving authorities in public health, veterinary medicine and food safety to act on the surveillance data for identification of trends, assessment of risks and timely implementation of focused interventions.
- 4) Engage in the development and adoption of standardized protocols to facilitate global harmonization in surveillance of antimicrobial usage in humans and animals, and of antimicrobial resistance.

D. PROMOTE EDUCATION AND TRAINING ON ANTIMICROBIAL USE IN FOOD-PRODUCING ANIMALS

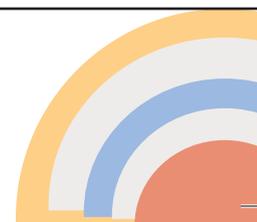
- 1) Develop and implement national guidelines on prudent use of antimicrobials in food-producing animals, with multidisciplinary involvement, taking into consideration antimicrobials categorized as critically important for human medicine.
- 2) Provide training for veterinarians and farmers on the use of these guidelines; and implement auditing and feedback to veterinarians and agricultural producers to improve compliance.
- 3) Develop and implement education strategies that emphasize the importance and benefits of prudent use principles, and provide relevant information on AMR to producers, stakeholders and the public.
- 4) Facilitate implementation of the Codex Alimentarius and OIE (World Organisation for Animal Health) guidelines related to antimicrobial resistance.

E. REDUCE THE NEED FOR ANTIMICROBIALS THROUGH BETTER ANIMAL HUSBANDRY

- 1) Introduce measures to improve animal health, and reduce the need for antimicrobial treatment, including application of effective vaccines.
- 2) Improve health management for food animal production by ensuring good hygiene practices and compliance with good farming practices.

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5. ENHANCE INFECTION PREVENTION AND CONTROL

Measures to ensure good hygiene are the basis for preventing the spread of infections and for bringing disease outbreaks under control. The need for antimicrobials is reduced by good infection control practices.

WHY ARE PREVENTION AND CONTROL OF INFECTION ESSENTIAL FOR COMBATING ANTIMICROBIAL RESISTANCE?

- > Poor infection control in any setting can greatly increase the spread of drug-resistant infections, especially during outbreaks of disease.
- > Effective infection prevention and control (IPC) practices are particularly important for reducing the risk of infection associated with health care that entails the use of antimicrobials.
- > When alternative antimicrobial treatment options are not available, IPC measures are critical for containing the spread of antimicrobial resistance (AMR).
- > Infections caused by resistant microorganisms often fail to respond to standard treatments, resulting in prolonged illness and hospitalization, and increased costs.

CHALLENGES TO OVERCOME

- > **Hospital infections:** hospitalized patients constitute one of the main reservoirs of antimicrobial-resistant microorganisms. Due to their compromised health status and need for medical interventions, these patients are at high risk of acquiring resistant infections that result from frequent use of antimicrobials.
- > **Infection of health-care staff:** health-care workers may also be at increased risk of acquiring resistant infections that lead to further spread of AMR.
- > **Infections beyond health care facilities:** transmission of drug-resistant infections can occur in other health-care facilities and congregate settings.¹ Patients who are carriers of

resistant microorganisms act as a source of infection for others within congregate and community settings.

- > **Lack of responsibility and accountability:** there is often no clearly defined responsibility for leading IPC efforts within ministries of health or other governmental organizations at the national and regional levels. Leadership is needed to guide actions on containment of AMR, implementing Standard Precautions,² and rational use of medicines across the spectrum of health-care facilities and in congregate and community settings.
- > **Deficient IPC support in congregate settings:** regulations and reporting systems to support IPC are frequently lacking in congregate settings that are not directly under the authority of the ministry of health.

CORE ACTIONS

WHO has defined core elements for IPC programmes involved in health care, some of which may also be applicable to congregate and community settings. Some governments have moved actively to establish IPC support structures within and beyond health facilities.

¹ For the purposes of this document, congregate settings refer to a mix of settings that range from correctional facilities and military barracks, to homeless shelters, refugee camps, dormitories and long-term facilities.

² *Standard precautions in health care: aide-memoire*. Geneva, World Health Organization, 2007 (also available at <http://www.who.int/csr/resources/publications/standardprecautions/en/index.html>; accessed January 2011).

A. ENSURE AVAILABILITY OF IPC PROGRAMMES ACROSS THE SPECTRUM OF HEALTH CARE, WITH CORE ELEMENTS INCLUDING:

- > A formal organizational structure to facilitate proper development and management of IPC policies and strategies;
- > Infection control strategies and guidelines, including strategies and guidelines for AMR;
- > Training of health-care providers in the principles and practices of IPC;
- > Appropriate environment (including the facilities and environmental designs) for application of IPC principles and practices;
- > Laboratory and diagnostic support services to inform antimicrobial prescribing, and accurate and timely detection of resistant microorganisms;
- > Surveillance systems to enable rapid detection and containment of emerging drug-resistant microorganisms;
- > Monitoring and evaluation framework to enable timely adaptation of IPC strategies;
- > Links with public health, other services and societal bodies to facilitate communication.

B. FOSTER BASIC IPC STANDARDS IN CONGREGATE SETTINGS

- 1) Assess the facilities for risks of infection transmission and design IPC strategies accordingly.

- 2) Ensure an appropriate environment to permit the application of good hygiene practices, adequate ventilation and engineering controls, hand-washing facilities and avoidance of overcrowding.
- 3) Ensure timely identification of infected individuals; establish proper and timely case management.
- 4) Include congregate settings in national, provincial or state surveillance systems.
- 5) Educate care providers and residents of congregate settings.
- 6) Ensure complete vaccination coverage in congregate settings.

C. PROMOTE STANDARD IPC MEASURES AND PROVIDE EDUCATION ON IPC IN THE COMMUNITY SETTING

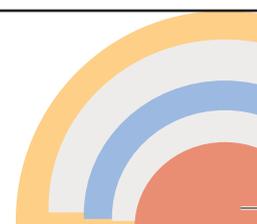
- 1) Provide public education on good hygiene practices to ensure that all understand the importance of hand and respiratory hygiene.
- 2) Collaborate with public health personnel, civil society and community organizations regarding education on good hygiene practices.
- 3) Foster appropriate IPC principles and practices in the community setting.
- 4) Strengthen vaccination programmes to reduce the burden of infectious diseases.

Selected IPC practices for prevention of emergence and spread of antimicrobial-resistant microorganisms

- Hand hygiene
- Patient placement
- Barrier precautions
- Aseptic practices
- Appropriate antimicrobial usage
- Sterilization and disinfection
- Environmental hygiene and waste management
- Facility environmental design for appropriate IPC practices

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6. FOSTER INNOVATIONS AND RESEARCH AND DEVELOPMENT FOR NEW TOOLS

Efforts to avoid the emergence and spread of antimicrobial resistance will prolong the useful life of antimicrobial medicines, but inevitably their effective lifespan will be limited. New medicines and other tools to control infections will still be needed in the future.

WHY ARE MORE RESEARCH AND NEW PRODUCT DEVELOPMENT ESSENTIAL TO COMBAT ANTIMICROBIAL RESISTANCE?

- > The microbes that cause infectious diseases are able to adapt to the antimicrobial medicines used for treatment. With exposure to an antimicrobial, particularly if it is not used correctly, resistant microorganisms will emerge. These resistant organisms can survive and proliferate, causing persistent infection which may spread to others. This process gradually erodes the efficacy of the drug and ultimately it become useless.
- > For some diseases, resistance can be slowed down by using a combination of antimicrobials, to avoid exposure of microbes to one single drug. But despite such measures, the emergence of resistance cannot be entirely prevented.
- > Therefore, there is a pressing need for new products to be brought to market for the prevention, diagnosis and treatment of infectious diseases.

CHALLENGES TO OVERCOME

- > **Insufficient operational research:** research to identify the main factors that contribute to the emergence and spread of antimicrobial resistance (AMR) is lacking in most countries.

- > **Lack of incentives to develop new tools:** few new antibiotics have been brought to market in recent years, largely due to increasing competition within the pharmaceutical industry and the perceived poor financial attractiveness of the market. Even where new public–private research and development (R&D) partnerships exist, the pipeline for new infectious disease diagnostics, drugs and vaccines is still too small.
- > **Delays in access to new tools:** some recently developed diagnostics and medicines have been slow to reach intended users due to delays in regulatory review, limited financing and weak logistics. Furthermore, decisions on priority distribution of supplies when resources are limited may not always favour those most in need, often the health facilities and patients in the poorest communities.

CORE ACTIONS

A. IMPROVE THE USE OF CURRENT DIAGNOSTICS AND ANTIMICROBIALS

- 1) Pursue operational research on local use and misuse of antibiotics and other antimicrobials and on the effectiveness of the relevant regulations.
- 2) Assess how to improve access to diagnostic testing in order to better equip health providers and patients in making decisions on the use of antimicrobials.

B. CREATE INCENTIVES FOR NEW PRODUCT DEVELOPMENT

- 1) Advocate for global and national commitments to develop diagnostics, drugs and vaccines for infectious diseases, and share information on the national costs of inaction.
- 2) Offer “push” incentives to encourage researchers and financing partners by reducing the inherent risks in the initial phases of R&D; such incentives could include government financing for basic research and clinical trials, prioritizing investment in anti-infection research, and providing R&D tax credits.
- 3) Offer “pull” incentives to offset the risks of a limited or volatile market, such as advance market commitments, prizes for research breakthroughs or finished products, and patent buyouts to accelerate affordable access in countries and communities most in need.

C. ENABLE RAPID REGULATORY PROCESSES FOR NEW TOOLS AND EQUITABLE ACCESS

- 1) Eliminate regulatory bottlenecks to facilitate rapid review and licensure of new diagnostics, drugs and vaccines.
- 2) Prepare plans for rapid procurement and distribution of new products, with special attention to overcoming constraints to access by the poorest regions, communities and at-risk groups.
- 3) Monitor access to new products and the results of uptake and use.

The antimicrobial research & development pipeline

- 1 Drug research and development is expensive and time-consuming. The average cost per each new drug that is developed is estimated to be US\$ 800 million to 1.7 billion.
- 2 There is a decrease in discovery research efforts and in antibacterial trials, reflecting a diminishing industry focus on antibacterial drug research and development.
- 3 There are few antibacterial agents in the pipeline. A study in 2004 showed that only 6 out of 506 drugs in development by 15 large pharmaceutical companies and 7 major biotechnology companies were antibiotics.
- 4 A report from the European Centre for Disease Prevention and Control and European Medicines Agency in 2009 showed that there are only two new antimicrobials under development, both being in the early stages when the failure rates are high.
- 5 There is also a decrease in diversity of new antibiotics. Most of the antibacterial agents that entered the market were modifications of existing molecules.
- 6 In 2008, a study of antibiotic development covering small firms as well as big pharmaceutical companies revealed that only 15 antibiotics out of 167 under development had a new mechanism of action.
- 7 A growing number of pharmaceutical companies are withdrawing from the market of antibiotic development, and the trend has accelerated since 2000. Eight of the 15 major pharmaceutical companies that once had antibiotic discovery programmes have left the field, and two others have reduced their efforts.

¹ A useful source on related issues: *The Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPPOA)* can be accessed at http://who.int/phi/implementation/phi_globstat_action/en/

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