Prevention and containment of antimicrobial resistance

During the past six decades antimicrobial agents have played a critical role in reducing the burden of communicable diseases all over the world. The emergence of resistance and its rapid spread is negating the impact of these drugs, obstructing progress towards achievement of the Millennium Development Goals for HIV, TB and malaria and hindering effective application of modern technologies in mitigating human misery. While appearance of resistance is a continuous phenomenon in microorganisms, its amplification and spread is through an array of practices conducted by human beings. Improper utilization of antimicrobial agents especially in high disease-burden settings and for non-therapeutic use as in the veterinary sector result in strong selection pressure that allows the resistant strain to grow and rapidly replace the susceptible isolates.

Diseases due to resistant organisms take longer to heal, require expensive and at times toxic drugs for longer periods, often making the disease untreatable. The resistant organisms can also move across countries through travel and trade. In that sense, antimicrobial resistance is a global challenge requiring concerted efforts at national and international levels to preserve the available antimicrobial agents. This is possible through treatment policies such as combination therapy, rational prescription, patient adherence, strong regulatory mechanism and educational activities, along with an efficient surveillance system that monitors the emergence and spread of resistance, as well as the utilization of antimicrobial agents.

To facilitate this activity at country level, WHO has developed a strategy that is simple, practical and easy to scale up. The regional strategy aims to give particular attention to interventions involving the introduction of legislation and policies governing the use of antimicrobial agents, establishing laboratory-based networks for surveillance of resistance and ensuring the rational use of these drugs at all levels of health-care settings. The effective implementation of this strategy by various national disease control programmes will lead to
reduction in the morbidity and mortality due to antimicrobial-resistant infection, and preserve the effectiveness of antimicrobial agents in the treatment and prevention of microbial infections.

The High-Level Preparatory (HLP) Meeting held at the Regional Office in New Delhi from 28 June to 1 July 2010 reviewed the working paper and made the following recommendations:

**Actions by Member States**

1. Establish a nationally coordinated, multisectoral alliance against antimicrobial resistance (AMR) with a designated focal point in the Ministry of Health.

2. Strengthen national surveillance mechanisms for AMR.

3. Initiate and sustain awareness and educational activities for prescribers and users of antimicrobials for their rational use.

**Actions by WHO-SEARO**

1. Provide technical support in development of national governance mechanisms and surveillance networks in accordance with the regional strategy on AMR.

2. Facilitate sharing of knowledge and information between and among countries of the SEA Region and with other regions.

3. Develop technical and educational material that can be adapted by Member States.

The working paper and the HLP meeting recommendations based on it are submitted to the Sixty-third Session of the Regional Committee for its consideration. The Committee is also requested to consider the draft resolution on the subject.
Background

1. Communicable diseases continue to be the major public health problem in the South-East Asia (SEA) Region of WHO. Each year, of 14 million deaths that occur in the Region, 6 million (40%) are due to communicable diseases, contributing to 42% of the total disability adjusted life years (DALYs) lost\(^1\). The continuous interplay between complex socio-economic, environmental, and behavioural factors, as well as population movements in an interconnected world provides a milieu conducive to persistence and spread of communicable diseases both within and across borders, thereby threatening international health security. Several disease control programmes have been launched to reduce the burden of these diseases and/or their elimination. One of the most critical factors that will facilitate elimination of these diseases is availability of effective antimicrobial drugs against the causative agents.

2. Apart from public health disease control programmes, infectious diseases exert significant mortality and morbidity as outcomes of acute infectious diseases including diarrhoeal diseases, respiratory infections, sexually transmitted infections, urinary tract infections and wound infections acquired in communities or in hospital settings. Mankind’s fight against these diseases is also largely dependent upon the efficacy of specific antimicrobial agents that, during the past seven decades, saved millions of lives, substantially reduced the burden of diseases and improved the quality and longevity of life. Accordingly, these drugs were called "wonder drugs".

3. Unfortunately in the recent past, the emergence and spread of resistance in several microorganisms have rendered the management of many infectious diseases difficult, using the common anti-infective drugs. Resistance poses a growing threat to the treatment and control of endemic, epidemic-prone as well as pandemic diseases. Resistance in microorganisms costs money, livelihood and lives and threatens to undermine the effectiveness of health delivery programmes. The development of resistance to drugs commonly used to treat malaria, tuberculosis (TB) and human immunodeficiency virus (HIV) infection is of particular concern as it is a huge impediment to achieving the Millennium Development Goals (MDGs) by 2015, towards poverty alleviation and improving the quality of human life all over the world. According to the European Centre for Diseases Control (ECDC), antimicrobial resistance is possibly the single biggest threat facing the world in the area of infectious diseases.

Genesis of resistance

4. The appearance of resistance to antimicrobials in microorganisms is a natural, unstoppable biological phenomenon. It gets amplified or accelerated by a variety of factors and practices that facilitate "selective pressure" of antimicrobial agents. The selection pressure is utmost when antimicrobials are used irrationally in health and veterinary sectors. The microbes that adapt and survive carry genes for resistance, which can be passed on to the next generation of microbes.

5. Resistant bacteria can also pass on their resistance genes to other related bacteria through "conjugation", whereby plasmids carrying the genes jump from one organism to another. Resistance to a single drug can thus spread rapidly through a bacterial population. When antimicrobials are used incorrectly - for too short a time, at too low a dose, at inadequate potency, or for a wrong disease - the possibility that bacteria will adapt and replicate rather than be killed is greatly enhanced.

6. The emergence and spread of antimicrobial resistance are complex problems fuelled by the knowledge, expectations and interactions of prescribers and patients, and by a regulatory environment. Patient compliance with recommended treatment is another major problem. Easy access of antimicrobials in developing countries and myths among communities about their effectiveness in all pyrogenic conditions exert an equally important influence on emergence of resistance.

7. While resistance can and does appear in any setting, hospitals, with a combination of highly susceptible and immunocompromised patients exposed to prolonged antimicrobial use, and cross-infection, have become a hot spot for highly resistant bacterial pathogens.

8. Veterinary prescription of antimicrobials also contributes to the problem of resistance. The largest quantities are used as regular supplements for prophylaxis or growth promotion, thus exposing a large number of animals, irrespective of their health status, to frequently sub-therapeutic concentrations of antimicrobials. Several microorganisms move from animals to humans through the food chain or through direct contact, and carry with them resistance genes.

9. The following are few of the important causes that accelerate the emergence of resistance

   **Prescribers** perceptions regarding patients expectations and demands substantially influence their prescribing habits that are not modulated by standard treatment guidelines nor by any regulatory mechanism that ensures the rational use of drugs. Antimicrobials are prescribed "just to be on the safe side" because of diagnostic uncertainty, lack of prescribers' knowledge regarding optimal diagnostic approaches, lack of opportunity of patient follow-up or fear of possible litigation. Prescription of antimicrobials in hospitals is also frequently irrational. An analysis of the prescribing practices in ten studies from teaching hospitals worldwide showed that 41% to 91% of all antimicrobials prescribed were considered inappropriate.

   **Patients** self-medication, procurement of drugs from pharmacy without prescription, taking antimicrobials for periods shorter than the recommended because of the patient having started to feel better and noncompliance with the dosage and duration of the regimen creates an environment for organisms to adapt rather than be killed.

   The availability of poorly formulated or manufactured, counterfeit or expired antimicrobials that are still sold and used for self-medication and prophylaxis also allows for a sub-optimal impact of the drug on the microorganism thereby enabling it to adapt and develop resistance to the drug.

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3 WHO. Global strategy for containment of antimicrobial resistance. 2001 (WHO, Geneva)
The **veterinary use of antimicrobials** contributes significantly to the problem of antimicrobial resistance. In North America and Europe, an estimated 50% tonnage of all antimicrobial production is used in food-producing animals and poultry. The largest quantities are used as regular supplements for prophylaxis and growth promotion, thus exposing microorganisms continuously to high doses and a big selection environment for resistant microbes. The recent control of antimicrobial usage for growth promotion and mass treatment in the European Union has resulted in reduction in resistance rates, suggesting that a significant selective effect is associated with this use.

Much evidence supports the view that the total consumption of antimicrobials is the critical factor in selecting resistance. Paradoxically, underuse through lack of access, inadequate dosing, poor adherence and substandard antimicrobials may play as important a role as overuse. For these reasons, improving the rational use of antimicrobial agents is a priority if the emergence and spread of resistance are to be controlled.

**Consequences of resistance**

10. The consequences of resistance are severe. Infections caused by resistant microbes fail to respond to treatment, resulting in prolonged illness and greater risk of death. Treatment failures also lead to longer periods of infectivity, which increase the numbers of infected people moving in the community and thus expose the general population to the risk of contracting a resistant strain of a microorganism. Furthermore, patient safety is threatened due to the rapidly-growing pandemic of antimicrobial resistance.

11. When infections become resistant to first-line antimicrobials, treatment has to be switched to second- or third-line drugs, which are nearly always much more expensive and sometimes more toxic as well e.g. the drugs needed to treat multi-drug resistant tuberculosis (MDR-TB) are over 100 times more expensive than the first-line drugs used to treat non-resistant forms. In some countries, the high cost of such replacement drugs is prohibitive, with the result that some of these cases can no longer be treated.

12. The costs associated with antimicrobial resistance are multiple; inadequate or failed treatment of patients leading to morbidity, and mortality is a huge human cost. In addition, the loss of cheaper, older agents for effective therapy and the need to acquire more expensive ones are easily recognized costs. However, this cost pales into insignificance when compared with the cost of the disruption of the delivery of health-care services caused by multiple antibiotic-resistant bacteria including cost of isolation, cross-infection control and cancelled procedures. As this cost is not easily recognized or accounted for, it is frequently forgotten.
Consequences of resistance

- Longer treatment
- Longer duration of illness
- Higher mortality
- Treatment with expensive drugs
- Increased burden on health system
- Negates technological advances in the medical sector
  - Complex surgeries
  - Transplantations and other interventions
- Patient acts as a reservoir of resistant organisms for the community and health-care workers
- Huge impact on economy

Status of antimicrobial resistance in the SEA Region

13. Systematic studies to understand the status of antimicrobial resistance, and its trends, and consumption of antimicrobial agents have been undertaken in the SEA Region. However, the data available from published reports from Member States of the Region provide an insight into the magnitude of the problem of resistance. The information available for selected diseases/organisms is briefly described hereunder:

Tuberculosis

14. The Region suffers disproportionately from the global burden of tuberculosis; 34% of all TB patients are in this Region\(^4\) Resistance to first-line anti-TB drugs has become a concern for national TB control programmes. The population weighted mean of MDR-TB\(^5\) in the Region is 208% (1.9%-3.6%) among new cases and 18.8% (13.3%-24.3%) among previously treated cases. It is estimated that around 150 000 cases of MDR-TB reside in this Region with more than 80% of these being in Bangladesh, India, Indonesia, Myanmar and Thailand.

15. The level of multidrug-resistant TB however remains low (below 3%) reflecting the good quality of TB programmes. The need for preserving the efficacy of first-line antituberculous drugs has been widely felt since drugs used in the management of MDR-TB cases are not only expensive but also toxic.

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\(^5\) MDR-TB = Resistance in mycobacteria to isoniazid and rifampicin.
16. Extensively drug-resistant TB (XDR-TB)\(^6\) has been detected in mycobacteria isolated in Bangladesh, India, Indonesia and Thailand giving another serious dimension to managing resistance in TB.

**HIV and sexually-transmitted infections**

17. Emerging diseases continue to challenge public health as never before. An estimated 3.5 million people are currently living with HIV/AIDS; the Region’s HIV/AIDS burden is next only to sub-Saharan Africa. The generic antiretroviral (ART) drugs produced by the pharmaceutical industry in the Region are contributing greatly to improve the survival rate of patients worldwide and in rendering HIV as a chronic but a manageable condition. Although the response to ART drugs is excellent when they are delivered at health facilities, the emergence of resistance in HIV can destroy the hopes of survival for millions of people living with HIV.

18. There has been a substantial change in the antimicrobial susceptibility of Neisseria gonorrhoeae. Thirty years back, gonorrhoea used to respond effectively to penicillin. Now the resistance to penicillin and fluoroquinolones is widespread across the Region\(^7\).

**Malaria**

19. Resistant malaria has already become a major issue for a population of 400 million living in areas that expose them to a high risk of contracting it. Artemisinin-based combination therapies (ACT) have recently been introduced in virtually all countries in which malaria is endemic, thereby making such drugs the most essential class of antimalarial agents. However, recent data indicate that artemisinin resistance has already emerged along the border between Cambodia and Thailand. Surveillance data from the Thai Ministry of Health indicate that clinical failures of artemisinin-based therapies exist in the Thai–Cambodian border, whereas efficacy with artesunate–mefloquine along the western borders of Thailand remains high.\(^8\)

20. A "global disaster" could happen if malaria parasites worldwide developed resistance against the new artemisinin-based combination therapies (ACTs) that have become the gold standard. Large parts of the world would have no drugs to fall back on, and malaria cases and deaths could soar, erasing the hope that the world might be on the eve of a huge reduction in the disease. Yet, resistance against ACTs is precisely what now seems to be developing in western Cambodia, along the Thai border.\(^9\)

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\(^6\) XDR-TB = MDR-TB + resistance to fluoroquinolones and at least one of the three injectable second-line drugs (capreomycin, kanamycin and amikacin).


Kala-azar

21. Kala-azar is a public health problem in Bangladesh, India and Nepal that is being targeted for elimination using miltefosine. Pentavalent antimonials (SbV) have been successfully used for treatment of kala-azar since the last six decades. Since the 1970s, however, their conventional dosages have failed to achieve the desired results with 60% unresponsiveness being reported with the WHO regimen in Bihar (India). Pentamidine initially used as a second-line drug, acquired resistance (25%) even with prolonged dosage. The newer oral drug, miltefosine is a potent antileishmanial drug with a longer half-life, a property likely to delay resistance. The evolution of resistance to this drug will cause havoc to the regional efforts to combat this disease.

Diarrhoeal diseases

22. Cholera germs have acquired resistance to a number of antimicrobials. The resistance spectrum varies in different locales. In areas around New Delhi (India) extensive resistance to furazolidone, cotrimoxazole and nalidixic acid has been noted, while tetracycline has remained effective. On the other hand, in Bangladesh, tetracycline resistance has been found to be frequent.

Respiratory infections

23. Streptococcus pneumoniae is the most common causative agent of pneumonias in children and adults in Asia. Till the 1980s, almost all isolates of this organism used to be susceptible to penicillin. In 2006, in a hospital in Thailand, almost 69% isolates of this bacterium were found to be penicillin resistant.

Typhoid and paratyphoid fever

24. Typhoid and paratyphoid fever continue to be important causes of illness and death, particularly among children and adolescents in the SEA Region where this disease is associated with poor sanitation and unsafe food and water. Published reports indicate that multidrug-resistant Salmonella typhi are prevalent widely in India and Indonesia. Shortly after the

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emergence of multidrug-resistant Salm. typhi in this Region, case fatality rates approaching 10% (close to 12.8% recorded in pre-antibiotic era) were reported\textsuperscript{14}.

**Wound sepsis due to Staphylococcus aureus**

25. More than 50% isolates of Staphylococcus aureus in hospital settings are now methicillin resistant. In a study undertaken in a 1000 bedded hospital in Thailand, 48% patients with bacteraemia due to resistant Staph. aureus died. Methicillin -resistant Staph. aureus (MRSA) is a major problem in hospital-associated infections in almost all countries in the SEA Region\textsuperscript{15}.

**Nosocomial infections**

26. Multiresistant klebsiellae, Pseudomonas and Acinetobacter species have given new dimensions to the problem of hospital-associated infections. Acinetobacter baumannii has become an important pathogen in intensive care units. It produces a wide range of beta lactamases and has a formidable spectrum of intrinsic resistance mechanisms that can mean that some strains are resistant to almost all known antimicrobial agents. In a study done in Thailand, mortality in admitted patients due to imipenem-resistant Acinetobacter baumannii was 52% as compared to 19% in those who were infected with the sensitive variant\textsuperscript{16}.

**International spread of resistant organisms from the SEA Region**

27. With rapid means of travel, international movement of resistant bacteria occurs frequently. In Canada, the United Kingdom and the United States of America several outbreaks of resistant strains have been reported, with resistant strains originating from different countries\textsuperscript{17} including in the SEA region.

\textsuperscript{15} Tyagi A, Kapil A, Singh P. Incidence of methicillin resistant *Staphylococcus aureus* (MRSA) in pus samples at a tertiary care hospital. JIACM 2008, 9:33-35.
\textsuperscript{17} MacPherson DW, Gushulak BD, Baine WB, Bala S, Gubbins PO et al. Population mobility, globalization and antimicrobial drug resistance. *Emerging Infectious Diseases* 2009, 15:1727-1732.
International spread of resistant organisms from the SEA Region

- Two outbreaks of methicillin resistant Staph. aureus (MRSA) in hospitals in Canada:
  - origin in North India
- MDR Typhoid fever in the United States of America:
  - Origin: six countries (including India)
- MDR Mycobacteria
- Resistant malaria at the Thai-Cambodia border
- Resistance in influenza H1N1 and HIV
- AmpC b lactamase producing enterobacteriaceae from the Indian subcontinent to the United Kingdom
- Salmonella from Thailand to Denmark

Veterinary source of resistant pathogens

28. Several salmonellae were isolated from chicken carcasses imported into Bhutan, 40 of 42 Salmonella enteritidis exhibited resistance to more than 2 drugs\textsuperscript{18}. From clinically healthy cows in Thailand, 68% of isolates of Salmonella enterica were resistant to at least one antimicrobial and 6% were multiresistant\textsuperscript{19}. A spread of multiresistant Salmonella Schwarzengrund from chickens to humans in Thailand and from imported Thai food products to persons in Denmark and the United States has been well documented\textsuperscript{20}.

Role of WHO

29. A World Health Assembly resolution in 1998\textsuperscript{21} had urged Member States to develop measures to encourage appropriate and cost-effective use of antimicrobials; prohibit the dispensing of antimicrobials without the prescription of a qualified health-care professional; improve practices to prevent the spread of infection and thereby the spread of resistant pathogens; strengthen legislation to prevent the manufacture, sale and distribution of counterfeit antimicrobials and the sale of antimicrobials in the informal market; and reduce the use of antimicrobials in food-animal production. This message was reinforced in the World Health

\textsuperscript{18} Ellerbroek L et al Antibiotic resistance in salmonella isolates from imported chicken carcasses in Bhutan and from pig carcasses in Viet Nam. J Food Prot 2010;73:376.
\textsuperscript{20} Aarestrup FM et al. International spread of multidrug-resistant Salmonella Schwarzengrund in food products. Emerging Infectious Diseases 2007; 13:726.
Assembly resolution WHA58.27 in 2005\textsuperscript{22} wherein Member States were encouraged to ensure the development of a coherent, comprehensive and integrated national approach to implementing the strategies for containment of antimicrobial resistance, and to monitor regularly the use of antimicrobial agents and the level of antimicrobial resistance in all relevant sectors.

30. The WHO strategies of all major disease control programmes (HIV, TB, malaria, influenza) do advocate monitoring of drug resistance and suggest appropriate activities. The international movement of resistant strains especially when these are multi- or extensively-resistant can be considered a public health event of international concern (PHEIC) as per the International Health Regulation (IHR 2005).

31. Recognizing the emerging importance of this subject and to enhance its visibility for an early action, “Antimicrobial Resistance” is proposed to be the theme of World Health Day 2011.

**Major issues**

32. Several issues continue to plague the prevention and containment of antimicrobial resistance as well as efforts to preserve the efficacy of antimicrobial drugs to maintain their “wonder” status. Some of these issues are:

- It is a neglected problem with profound impact on health and economy;
- inadequate visibility of this issue at decision-making level in spite of World Health Assembly resolutions;
- absence of a national approach/direction to combat the emerging problem of antimicrobial resistance;
- lack of continuous education among prescribers;
- poor or no systematic surveillance of resistance and consumption of antimicrobial agents;
- ineffective regulatory mechanism;
- lack of economic potential/incentives for pharmaceuticals to invest in development of new drugs;
- abysmal infection control practices;
- absence of community education and awareness; and
- weak or no collaboration between stakeholders.

33. Antimicrobial resistance is a cross-cutting issue that is influenced by several factors. Accordingly, it requires ownership and active participation by several stakeholders, some of

whom are: Ministries of health, animal husbandry and education; national regulatory authority; medical and veterinary professional bodies; medical and veterinary councils; national medical and veterinary research councils; health facilities in public, private and other sectors; international agencies; NGOs; laboratory professionals; and the mass media and community champions. The issue also requires a concerted effort utilizing a rational strategic approach.

Rationale for a strategy

34. Resistance is a biological, behavioural, technical, economic, regulatory and educational problem and requires a comprehensive response. Antimicrobial resistance has been an unrecognized and neglected problem that is not only cross-cutting but also has far-reaching implications as an emerging public health problem with a huge risk to international health security. Newer drugs are being discovered very slowly. Efforts need to be made to slow down or delay the resistance thus preserving the available antimicrobials. A few success stories of reversing resistance through the rational use of antimicrobials are available from the SEA Region. Efforts in this regard therefore need to be scaled up to combat this problem comprehensively.

35. It is essential to develop a regional strategy that is acceptable to multiple stakeholders, is simple and practical, and can be adapted by Member States, and that can act as a powerful tool to prevent the negation of progress made in the field of communicable diseases. The regional strategy aims to give particular attention to interventions involving the introduction of legislation and policies governing the use of antimicrobial agents, establish laboratory-based networks for the surveillance of resistance and ensure the rational use of these drugs at all levels of health-care settings.

36. The strategy recognizes that antimicrobial resistance is a global problem that must be addressed in all countries. No single nation, however effective it is at containing resistance within its borders, can protect itself from the importation of resistant pathogens through travel and trade. Poor prescribing practices in one country now threaten to undermine the potency of vital antimicrobials everywhere. Accordingly, the strategy suggests interventions that can be used to slow the emergence and reduce the spread of resistance in a diverse range of settings.

Guiding Principles

37. The following are the broad principles that have guided the development of a strategic approach:

- Understand emergence and spread of resistance.
- Rationalize the use of available antimicrobial agents.
- Prevent emergence of resistance by reducing selection pressure by appropriate control measures.
- Bring about a change in behaviour of prescribers of antimicrobial agents and communities to ensure their rational use.
• Combat antimicrobial resistance by promoting discovery, development and delivery of new drugs/tools.

• Combat antimicrobial resistance through nationally-coordinated efforts with defined functions for different sectors/programmes.

Regional strategy for prevention and containment of antimicrobial resistance

Goal

38. “To minimize the morbidity and mortality due to antimicrobial-resistant infection and to preserve the effectiveness of antimicrobial agents in the treatment and prevention of microbial infections”.

Objectives

39. The objectives of the regional strategy are to:

• Establish a national alliance for prevention and control of antimicrobial resistance;

• Institute a surveillance system that captures the emergence of resistance, as well as the trends of its spread; and the utilization of antimicrobial agents in different settings;

• Promote the rational use of antimicrobial agents at all levels of health-care and veterinary settings;

• Strengthen infection control measures to reduce the disease burden; and

• Support basic and operational research.

Key strategic elements

a. To establish a national alliance for prevention and control of antimicrobial resistance

40. Concerted and nationally-coordinated efforts are needed to bring together various stakeholders and harness the expertise and resources available within the country in different sectors. A dedicated focal point (unit or individual) in the ministry of health can effectively coordinate antimicrobial resistance-related activities and forge national alliance of relevant programmes, stakeholders from public, private and NGO sectors. For providing guidance and oversight an intersectoral steering committee can be constituted to develop and monitor a national strategic approach towards antimicrobial resistance with consensus of all stakeholders about their specific roles. At the same time the national regulatory mechanism needs to be strengthened.
b. To institute a surveillance system that captures the emergence of resistance, as well as the trends of its spread; and the utilization of antimicrobial agents in different settings

41. Several networks may be operational in the country that generate and collate data on resistance in microorganisms and consumption of antimicrobial agents. These should be activated to support national efforts towards containment of antimicrobial resistance. If such networks are not functional, these must be established. These networks are essential to quantify the disease burden due to resistant organisms as well to understand the emergence of resistance and trends in its spread.

42. These networks can also determine and monitor the use of antimicrobials, assess therapeutic and non-therapeutic use in animals, appraise the impact of promotion of pharmaceuticals and generate and collate data on resistance, use of antimicrobials and the economic impact, which can be communicated to stakeholders for policy formulation and programme development/improvement.

c. To promote the rational use of antimicrobial agents at all levels of health-care and veterinary settings

43. This is the most complex and yet critical objective since it involves strengthening of technical and regulatory requirements along with bringing about a change in the behaviour of prescribers and users. The implementation of this objective shall require development of standard national/local treatment guidelines (STG) advocating evidence-based monotherapy or combination therapy, training of professionals in the use of these STG, ensure the use of STGs through hospital committees and provide an effective curriculum on rational prescription of antimicrobial agents for undergraduate and postgraduate teaching of medical, dental, veterinary and pharmacy students.

44. Given the impact of veterinary use of antimicrobial agents, it will be critical to ban the non-therapeutic use of antimicrobial agents using the IHR Framework, develop standard treatment guidelines for use in the veterinary sector, and train professionals in the use of STGs.

45. In the SEA Region, easy availability of antimicrobial agents over the counter and myths among the communities that all diseases are amenable to this group of drugs demands early and effective interventions in order to educate communities on proper compliance and non-self-medication; prevent over-the-counter availability of antimicrobial drugs; and provide continuous education to pharmacists/chemists in the appropriate use of antimicrobial agents.

d. To strengthen infection prevention and control measures to reduce the disease burden

46. Since all factors that promote or influence communicable diseases also facilitate resistance, efforts made to reduce the disease burden are bound to mitigate the extent of resistance. These activities shall include strengthening of disease control programmes; augmenting infection control practices in hospitals; establishing infection control practices, especially
universal/standard precautions; providing an enabling environment; and ensuring availability of adequate number of trained health-care staff. Promotion of health practices through education and awareness programmes for communities can bring down the disease burden substantially. Furthermore, collaboration with the mass media can yield rich dividends in creating awareness.

e. To promote research in the area of antimicrobial resistance

47. Countries need to promote basic research to ascertain the dynamics of spread and drivers of resistance, understand the mechanism of resistance, and to evaluate the impact on human health of the use of antimicrobials in agriculture and fishery. There is a strong case to support operational research to develop optimum doses and duration of various drugs as monotherapy or in combinations, understand the impact of resistance on illness and economy and to elucidate the behavioural aspects about self-medication and adherence and develop suitable interventions in this regard.

48. The development of new antimicrobial agents or alternatives thereof requires support from government as well as industry-supported research through research grants, public-private partnership (PPP), public contribution to research funding and R&D tax credits; the pay-for-outputs from R&D process, including advance purchase commitments or patent buy-outs and also by reducing the time to gain market entry through fasttrack mechanisms of regulatory approvals.

Implementation mechanism

49. Resistance to antimicrobial agents is a cross-cutting problem, a problem which needs to be tackled through a well-coordinated action. The regional strategy recognizes the need for a wide range of activities that are required to support the control of antimicrobial resistance and the need for commitment from a wide variety of players. It needs to be endorsed by all countries of the SEA Region and will lead to sustained action to combat this problem. Microbes are dynamic organisms and so should be our approach to tackling their resistance to antimicrobial agents. The strategy also recognizes the need for action across a wide range of interests and by many organisations and individuals. Since microorganisms do not recognise geographical boundaries and are increasingly spread through international travel and commerce, it also recognizes the need for the regional Office to play its part by providing appropriate technical support in stepwise implementation of the strategy at national and local levels.

50. The following steps need to be taken to implement this strategy:

- Obtaining national commitment towards prevention and containment of antimicrobial resistance.
- Constitution of an inter-sectoral steering committee with all stakeholders from public and private sectors represented and chaired by a senior policy maker.
- Establishment of a cell and focal point in the ministry of health within the unit responsible for emerging infectious diseases or IHR (2005) to coordinate national
alliance (comprising mainly existing programmes) and empowered to provide evidence-based directives for the rational use of antimicrobial agents and disease prevention and control interventions.

- Constitution of a national expert advisory committee.
- Designation of subgroups in specialized areas.
- Development of public information campaigns.
- Establishment of national surveillance system with mandatory reporting system through efficient and quality laboratory networks and existing surveillance systems.
- Developing and making available various national standards, guidelines for surveillance and treatment, and strengthening regulatory support for their implementation.
- Organize continuing education for professionals and all health-care workers etc. through medical and health-related institutions, and professional bodies.
- Invoking IHR and other national measures to reduce or ban the use of antimicrobials as growth promoters in animals.
- Collation of research findings for conversion into actions.
- Establishment of national forum of multidisciplinary professionals (health, veterinary, agriculture, and fishery etc.) to share information to promote understanding of the impact of the use of antimicrobial agents on human health.
- Collaborate with international agencies for technical support and obtaining information from other countries/sectors. WHO to coordinate information exchange in the SEA Region.
- Regular meetings to review, assess and modify the action plans.

**Monitoring and Evaluation**

51. A strong component of monitoring and evaluation mechanism through alliance utilizing the aforementioned indicators and targets shall be established. National baseline data should be established. The national steering committee shall regularly review the data generated for this purpose and provide guidance for changes, if any, required to achieve the targets.

52. Regional annual reviews should be undertaken through WHO intercountry coordination mechanism and a mid-term assessment made of the strategy.

**Mainstreaming the national response**

53. Given the cross-cutting nature of the problem and complexity of the response, it is essential that every stakeholder has clarity about its role in combating this menace, both within its own mandate as well as for those issues that have a bearing upon activities of other sectors.
Ownership of the strategy by all stakeholders is critical for its moving forward and yielding the desired results.

54. Antimicrobial drug failure may occur for many reasons but it impacts not only patient care and safety but also threatens effective management of infectious diseases globally. A strategic approach is urgently needed to combat this emerging threat.