



**Asia-Pacific
Economic Cooperation**

**APEC Guideline
to Tackle Antimicrobial Resistance
in the Asia-Pacific Region**

APEC Health Working Group
October 2014

Produced by
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APEC guideline to tackle antimicrobial resistance in the Asia-Pacific region

Executive Summary

In 2012, APEC leaders declared that they would support the efforts made by our economies to address health issues across sectors, and encourage further concrete steps to strengthen health systems for sustainable development of human resources, economic development and innovative growth in the APEC region (2012 APEC Leaders' Declaration). In 2013, APEC leaders also declared the importance of engagement in capacity building efforts and effective regional and global partnerships across the public and private sectors with the aim of addressing emerging infectious diseases and strengthening public health systems (2013 APEC Leaders' Declaration). Infectious diseases still remain the major threat to public health in the world and global spread of antimicrobial resistance (AMR) in major pathogens is obviously one of the most serious threats to public health and human security. AMR also has a serious impact on economy due to huge increase in healthcare cost for treatment of infections caused by AMR.

Effective control and prevention of AMR can be achieved only by regional and global collaborations including the public and private sectors as mentioned by APEC leaders in 2013 because AMR can spread across borders. For this reason, APEC has been supporting serial projects to set up the future strategies to control and prevent AMR in the region since 2010; "International initiatives to control antimicrobial resistance in the Asia-Pacific region" (HWG 05/2010A), "Enhancing health security in APEC - International campaign program to control antimicrobial resistance in the Asia-Pacific" (S HWG 02 12A), and "Strengthening health security - APEC symposium on strategies to control and prevent antimicrobial resistance" (S HWG 04 12A). The "APEC guideline to tackle antimicrobial resistance in the Asia-Pacific region" is prepared by the Asia Pacific Foundation for Infectious Diseases (APFID) in Korea, which has been performing the previous APEC projects,

in collaboration with APEC economies based on the results of the serial APEC projects since 2010 (HWG 05/2010A, S HWG 02 12A, and S HWG 04 12A) .

“The APEC guideline to tackle antimicrobial resistance in the Asia-Pacific region” is primarily based on the strategic action plan to control and prevent AMR in the Asia-Pacific region from previous APEC projects. The strategic action plan to control AMR consists of six major components that are aimed to achieve effective control and prevention of AMR in the Asia-Pacific region; 1) Surveillance of AMR and antibiotic use, 2) Increased awareness of AMR, 3) Appropriate use of effective antibiotics, 4) Hospital infection prevention and control, 5) Vaccination, and 6) Policies and regulations. The APEC guideline can provide APEC economies with the general concept and the frame of the strategies to address the growing threat of AMR in the region for the first time. Since current problems and issues of AMR and antibiotic uses may vary by economy, implementation of the strategic action plan should be individualized based on local situation.

1. Surveillance of AMR and antibiotic use

- 1.1 The national surveillance system of AMR should be urgently established in every APEC economy that can identify the national status of AMR.
- 1.2 The national surveillance systems for antimicrobial consumption both in patients and in animal husbandry should be established in each economy using the standardized methods.
- 1.3 The microbiology laboratory procedures, data collection, and data reporting should be qualified and standardized.
- 1.4 The international surveillance system(s) in the Asia-Pacific region collecting the data about AMR in APEC economies should be established.

2. Increased awareness of AMR

- 2.1 Appropriate use of current antibiotics can be encouraged by campaigns and educational activities for general public at various levels - hospital, local, regional, or national level.
- 2.2 Campaign 4 developed from the APEC project entitled “Enhancing health security in APEC - International campaign program to control antimicrobial resistance in the Asia-Pacific” can be utilized as a campaign program in the Asia-Pacific region.
- 2.3 Education of healthcare professionals should be continuously implemented. All economies are encouraged to implement antimicrobial stewardship program in the healthcare setting.

3. Appropriate use of effective antibiotics

- 3.1 Appropriate use of effective antibiotics is a key factor to prevent the further emergence of AMR in major pathogens, which includes the appropriate use of current antibiotics as well as the development of novel agents.
- 3.2 Antimicrobial use in food animals should be monitored and controlled by the regulations and guidelines.
- 3.3 Healthcare policies and regulations for control of antibiotic use should be urgently established in some economies in the Asia-Pacific region.
- 3.4 Development of novel antibiotics is critically required to overcome the problems of AMR and international collaboration is essential for the discovery of new antibiotics.

4. Infection prevention and control

- 4.1 Hospital infection control is a basic procedure to prevent the spread of resistant clones in the hospital as well as in the community.
- 4.2 Stringent and rigorous infection control procedures should be implemented in all hospitals.
- 4.3 The microbiology laboratory should provide adequate diagnostic testing to identify nosocomial infections and accurate antimicrobial susceptibility testing.

5. Vaccination

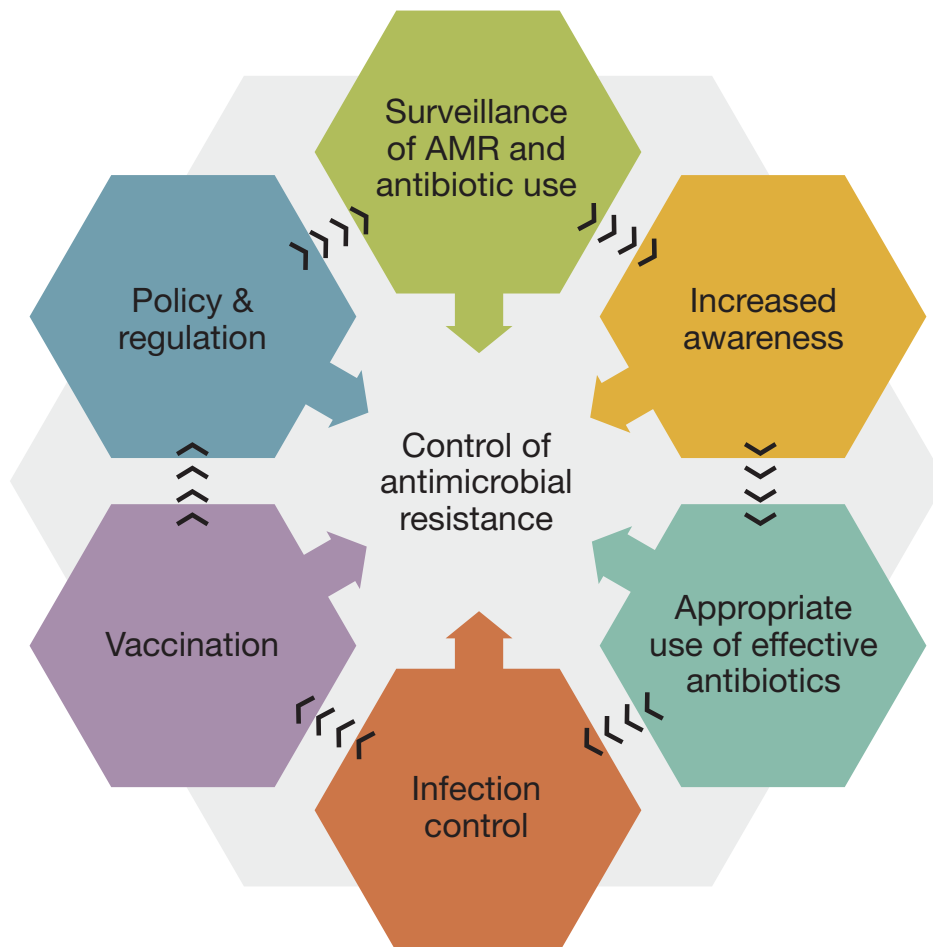
- 5.1 Effective vaccination can reduce the prevalence of AMR in major bacterial pathogens.
- 5.2 National and international efforts should be exerted to increase the awareness of the importance of vaccination both in general public and in healthcare professionals.

6. Policy and regulation

- 6.1 Control and prevention of AMR should be one of the top priorities among national policies and agenda.
- 6.2 Appropriate and relevant governmental regulations, commitment and support are essential for successful control of AMR.

- 6.3 Relevant policies and regulations to control antibiotic abuse are urgently required in many APEC economies, particularly in the Asian region.
- 6.4 Any kind of antibiotics should be purchased based on doctor's prescription and it should be regulated by law in all APEC economies.
- 6.5 Monitoring and regulation to prevent the production and circulation of counterfeit drugs should be implemented in all APEC economies.
- 6.6 Antibiotic uses in animal husbandry should be monitored and regulated by appropriate regulations.

[Six major components of strategic action plan to tackle antimicrobial resistance]



I. Background

1. Global crisis of antimicrobial resistance (AMR)

Infectious diseases are serious healthcare threats despite the remarkable advances in modern medicine. Recent data from the World Health Organization (WHO) showed that infectious diseases are the second most common cause of death worldwide (a total of 24% of deaths worldwide is caused by infectious diseases) (WHO, 2008; http://www.who.int/healthinfo/global_burden_diseases/DthInc_2008.xls). However, treatment of infectious diseases is becoming more difficult due to widespread emergence of AMR in major pathogens, which makes antimicrobials ineffective, resulting in treatment failure, prolonged illness, disability, greater risk of death and economic loss. In addition, treatment failures caused by AMR 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 infection. AMR is a more serious healthcare threat than any single infectious disease because it encompasses all types of infections. Furthermore, due to slowed development of new antimicrobials, very few antimicrobials are left to treat infections caused by multidrug-resistant pathogens. Thus, AMR has become one of the most serious concerns in public health worldwide, especially in the Asian region that showed the highest prevalence of AMR in major pathogens.

Given the growing concern of AMR, WHO released six-point policy brief for 2011 WHO World Health Day (Leung E, 2011) and publication entitled “The evolving threat of antimicrobial resistance: Options for action” in 2012 (WHO, 2012). Also, WHO published the first global report on AMR entitled “Anti-microbial resistance: global report on surveillance” in April 2014, which reveals that this serious threat is no longer a prediction for the future, it is happening right now in every region of the world (WHO, 2014). AMR is not a local problem but an international and global issue because AMR can spread between different economies or continents. The massive increases in trade and human mobility brought about by globalization have enabled the rapid spread of infectious agents, including those that are resistant. Recent outbreak and international spread of antimicrobial resistant bacteria, New Delhi metallo-beta-lactamase-1 (NDM-1) producing *Escherichia coli*, from India to many other region in the world including the UK, Sweden, Austria, Belgium, France, Netherlands, Germany, the United States, Canada, Japan, China, Malaysia, Australia, and Korea could be one of the best examples of transmission of AMR between economies, showing critical impact of AMR on economy and trade in addition to impact on public health (Kumarasamy KK, 2010). Since the global spread of this new “superbug” was partly due to medical tourism, economic activities related to medical tourism and

international travel were seriously affected.

Community pathogens have acquired AMR including penicillin- or macrolide-resistant *Streptococcus pneumoniae*, methicillin-resistant *Staphylococcus aureus* (MRSA), and multidrug-resistant (MDR) enteric pathogens. Not only these community-acquired infections but also nosocomial pathogens such as MRSA or glycopeptide-resistant *S. aureus* (vancomycin-intermediate or resistant *S. aureus*, VISA or VRSA, respectively), glycopeptide-resistant enterococci (vancomycin-resistant enterococci, VRE), extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae, and MDR non-fermenters are also being recognized with increasing frequency around the world. The global emergence and rapid spread of AMR in these community and nosocomial pathogens have become serious clinical concerns. While richer economies, to a large extent, are still able to rely on the latest antimicrobials to treat resistant infections, access to these life-saving drugs is often limited or totally impossible in many parts of the world.

2. Clinical and economic impact of AMR

AMR is not just a healthcare issue, but a very serious threat to international economy and trade. The economic impact of AMR is devastating with huge amount of additional healthcare costs for treatment of antimicrobial resistant infections. The annual health care costs associated with the treatment of antimicrobial resistant infections were estimated to be approximately US\$ 20 billion per year and the annual societal cost exceed US\$ 35 billion in the United States (Leung E, 2011). AMR could also significantly affect the international trade both directly and indirectly. The global trade of food and other agricultural commodities is affected by the regulations to prevent import of the livestock products with antibiotic residues which are due to the use of antibiotics in food animals as growth promoters.

Given the enormous clinical and economic impact of AMR, WHO has identified AMR as one of the greatest threats to human health. The theme of World Health Day 2011 by WHO was AMR with a slogan entitled “Antimicrobial resistance: no action today, no cure tomorrow” (<http://www.who.int/world-health-day/2011/en/index.html>). To combat drug resistance, WHO has mentioned that “antimicrobial resistance and its global spread, threatens the continued effectiveness of many medicines used today to treat the sick, while at the same time it risks jeopardizing important advances being made against major infectious killers” and has called for urgent and concerted actions by the governments, health professionals, industry, civil society, and patients to slow down the spread of drug resistance and limit its impact today to preserve medical advances for future

generations. World Economic Forum also highlighted AMR as a major global risk in their Global Risks Reports both in 2013 and 2014. In the Global Risks 2013 report, they showed AMR endangers not only the health systems but also the social and economic systems in the world (World Economic Forum, 2013). In the Global Risks 2014 report, they highlighted AMR as one of top societal risks confronting the world (World Economic Forum, 2014).

3. Antibiotic use as a driving force

Antibiotics are very important weapons against bacterial infections. However, AMR became a global health problem since the 1990s. Particularly, Asian region is the epicenter of AMR with the highest prevalence rates of AMR in major bacterial pathogens, which are two- or three-times higher than those in the western part of the world. Although the spread of resistant clones is one of main reasons, widespread abuse and misuse of antibiotics is a basic driving force of the emergence of AMR in the Asia-Pacific region.

Although AMR is a serious public health threat in the Asia-Pacific region, there is still a general lack of awareness on AMR. According to many published papers, antibiotics are frequently used for viral infections such as respiratory tract infections although antibiotics are not effective for viral infections (Hulsher MEJL, 2010). According to a study in China, 78% of inpatients were treated with antibiotics and 55% of patients were given more than two different antibiotics (Hu S, 2003). However, only 3.8% of cases were microbiologically evaluated before the use of antibiotics. In a study performed in Indonesia, antibiotics were prescribed in 84% of inpatients but only 21% of cases were considered appropriate use of antibiotics (Hadi U, 2008). According to a study in Korea, prescription rate for upper respiratory tract infection was 55% in primary healthcare clinics in Korea (Kim N, 2005). In Japan, prescription rate for upper respiratory tract infection was 60% and third generation of cephalosporins, macrolides, and fluoroquinolones were prescribed in 46%, 27%, and 16% of patients, respectively (Higashi T, 2009).

Lack of awareness and knowledge on AMR and appropriate use of antibiotics are one of the main reasons for inappropriate use of antibiotics. A survey of knowledge and awareness of antibiotics and AMR by general public over age 20 in Korea revealed that 51% of people thought that antibiotics are effective for common cold although 72% of people responded that AMR is a serious problem in Korea (Song JH, 2010). At the Expert Forum of the APEC project entitled “International initiatives to control antimicrobial resistance in the Asia-Pacific region” (HWG 05/2010A) held on 5 April, 2011 in Seoul, Korea with 50 experts on infectious diseases

and AMR from 13 Asian economies, including China, Hong Kong China, Indonesia, Japan, Korea, Malaysia, the Philippines, Singapore, Chinese Taipei, Thailand, Viet Nam, India, and Sri Lanka, factors associated with antibiotic abuse or misuse were discussed and the results of the survey of infectious disease experts on current status of antimicrobial uses and AMR in Asian economies was also discussed. According to the survey, both general public and medical personnel in the region do not have adequate knowledge on AMR and appropriate use of antibiotics (APEC#211-HT-04.1).

Another important factor associated with antibiotic abuse or misuse is weak and unorganized policies and regulations on antibiotic use in APEC economies. Antibiotics can be purchased without prescription in most Asian economies except Japan, Korea, Malaysia, and Singapore according to experts from APEC economies in the Asian region. In China and Chinese Taipei, although they have policy about separation of prescribing and dispensing antibiotics, antibiotics can be purchased without prescriptions. Over-the-counter (OTC) antibiotics can be purchased in pharmacy, supermarket, internet shopping mall, or alternative medicine clinic in those economies. Also, counterfeit antibiotics are widely used in most APEC economies in the region except Hong Kong China, Japan, Korea, and Singapore although all economies have certain type of regulations to control counterfeit antibiotics. The International Medical Products Anti-counterfeiting Taskforce (IMPACT) of WHO also has reported that counterfeit drugs are used in many economies in the Asian region including Indonesia, the Philippines, China, and India (IMPACT, 2006).

Antibiotics are also used in animals not only for therapeutic purposes but also as a growth promoter in farm animals. When antibiotics are used as a growth promoter, it is usually administered at a low, sub-therapeutic dose that could lead to the development of AMR in microorganisms in food animals. AMR can transfer between animals and humans through food chain or direct contact. Although there have been considerable efforts to limit the use of antibiotics in animals worldwide, antibiotics are still abused or misused in animals in many economies in the Asia-Pacific region, which may contribute to the increase of AMR in the region.

4. Asian region as an epicenter of AMR

Although regional situation of AMR may vary by region or economy, it is evident that Asia is certainly a part of the world in which there are increasing concerns regarding AMR because of a high prevalence of AMR in major bacterial pathogens and relatively poor and weak healthcare infrastructures in many economies. It is expected to be much more detrimental to the economy of Asian region with regard to the magnitude of

the costs and subsequent financial loss. However, in many Asian economies, AMR is still a neglected issue due to lack of awareness. Weak and unorganized policies and regulations in many Asian economies are also contributing to the increase in AMR. Since more than 70% of world population is living in the Asian region, problems of AMR in the region are not just a regional issue but a global problem.

In comparison with western part of the world, geographic variations in the AMR are notable in Asia because of the uneven policies of antimicrobial usage as well as different standards of public hygiene between economies. Based on the published reports, Asian region is evidently an epicenter of AMR in the world with the highest prevalence of AMR in major bacterial pathogens. According to published papers, very high prevalence rates of beta-lactam and macrolide resistance in *S. pneumoniae*, which is the single most important cause of lower respiratory tract infections in both adults and children, were found in Asian economies (Johnson DM, 2006; Song JH, 1999, 2004; Kim SH, 2012). Particularly, erythromycin resistance has remarkably increased in many Asian economies where >70% of clinical isolates were fully resistant. Also, Asian economies like China, Indonesia, Korea, Japan, Thailand and Viet Nam showed very high rates (> 50%) of MRSA, which is the most important cause of hospital-acquired infections such as pneumonia, surgical site infections and bloodstream infection and kills more than 19,000 patients annually in the United States only, suggesting that many Asian economies would have a huge number of deaths due to this infection (Grundmann H, 2006; Song JH, 2011). Carbapenem-resistance rates of *Acinetobacter* spp. and *Pseudomonas aeruginosa* were very high and MDR non-fermenters were highly prevalent in Asian economies (Chung DR, 2011).

Despite many serious events of AMR internationally, there have been few practical efforts to improve the preparedness for control of AMR based on international collaboration to reduce the economic impact as well as public health impact of AMR. Particularly, although AMR is a serious public health threat in the Asian region, where antimicrobial agents are widely abused and misused, it is quite obvious that the lack of awareness of critical situation of AMR prevents Asian economies from preparing comprehensive international strategies for AMR and leads to ineffective responses to AMR in the region. Given its devastating impact on human lives and economy, future strategies should be prepared with multifaceted collaboration among all relevant stakeholders in the Asia-Pacific region and the comprehensive strategies for control and prevention of AMR are urgently required in the region. However, there have been no practical plans or implementations to control this problem based on international and multi-sectoral collaboration in the Asia-Pacific region to date.

Despite the serious problems of AMR in the Asia-Pacific region, many economies in the region do not have

adequate national infrastructure and system to control and prevent the problems. Many Asian economies are sharing the same problem of AMR not only due to poor healthcare infrastructure but also due to the spread of AMR between economies. Therefore, effective control and prevention of AMR in the Asia-Pacific region can be achieved only by effective international collaboration based on strong national initiatives. Urgent issues to be addressed in the region would be to establish effective international collaboration system for surveillance of AMR and evaluation of clinical and economic impact of AMR and to prepare the future strategies for control and prevention of AMR in the region based on these evaluations.

5. APEC's efforts to combat AMR in the Asia-Pacific region

Given the critical impact of AMR in the Asia-Pacific region, APEC has been supporting the international projects to set up the future strategies to control and prevent AMR in the Asia-Pacific region since 2010. The first APEC project on AMR entitled “International initiatives to control antimicrobial resistance in the Asia-Pacific region” (HWG 05/2010A) was proposed by Asia Pacific Foundation for Infectious Diseases (APFID) in collaboration with Asian Network for Surveillance of Resistant Pathogens (ANSORP) and APEC economies with support from Korea Centers for Disease Control and Prevention (CDC), which was approved to get APEC support in December 2010. Main contents of the project were to organize Strategic Focus Group (SFG), consisting of multi-sectoral experts from APEC and external APEC stakeholders, and to hold Expert Forum to discuss the current issues on AMR and to prepare future strategies to control and prevent AMR in the Asia-Pacific region. SFG consists of three groups ; Surveillance group, Future strategy group, and Policy and regulation group. The first Expert Forum was held on 5 April 2011 in Seoul, Korea with participation of 50 experts on infectious diseases and AMR from 11 APEC economies, including China, Hong Kong China, Indonesia, Japan, Korea, Malaysia, the Philippines, Singapore, Chinese Taipei, Thailand, and Viet Nam, and 2 non-APEC economies, including India and Sri Lanka, to discuss the current status and problems of AMR in the Asia-Pacific region. The second Expert Forum was held on 15 October 2011 in Seoul, Korea with participation of 40 experts consisting of infectious disease physician, microbiologist, pharmacist, veterinarian, and healthcare-related governmental officials representing both governmental and non-governmental institutions and organizations from 11 APEC economies, including China, Hong Kong China, Indonesia, Japan, Korea, Malaysia, the Philippines, Singapore, Chinese Taipei, Thailand, and Viet Nam, to discuss the future strategies to control AMR in the Asia-Pacific region. At the second APEC Expert Forum, there was interactive discussion by three breakout groups. Surveillance group discussed the major issues on AMR and antibiotic uses and future plan of national and international surveillance of AMR. Future strategy group discussed the basic scheme of

future strategies to control and prevent AMR. Finally, policy and regulation group discussed national health systems, policies, and regulations regarding antibiotic use and national and international healthcare system to control and prevent AMR.

Based on the results of the first APEC project, consecutive project entitled “Enhancing health security in APEC - International campaign program to control antimicrobial resistance in the Asia-Pacific” (S HWG 02 12A) was approved for funding for Session 2 in 2012, which was to develop strategies, contents and materials for an international campaign program for implementation of the campaign to increase the awareness of AMR as well as to promote the appropriate use of antibiotics in both general public and healthcare professionals in the Asia-Pacific region. The APEC Expert Forum was organized in Seoul, Korea on 9 November 2013 with 30 experts from 9 APEC economies including China, Indonesia, Korea, Malaysia, Peru, the Philippines, Chinese Taipei, Thailand, and Viet Nam and from non-APEC stakeholder - Western Pacific Regional Office of WHO. At the APEC Expert Forum, concept, contents and implementation plan of the international campaign program to increase awareness on AMR and to promote appropriate antibiotic use in the Asia-Pacific region were discussed. Based on the Expert Forum, the international campaign, named as “Campaign 4”, has been developed to increase awareness on AMR and to promote appropriate antibiotic use for general public and healthcare professionals in the Asia-Pacific region. And, the contents and materials for the Campaign 4 were also developed for its implementation in APEC economies.

The third APEC project entitled “Strengthening health security - APEC symposium on strategies to control and prevent antimicrobial resistance” (S HWG 04 12A) was performed to improve understanding and awareness of AMR in healthcare providers, government officials, and other stakeholders in the Asia-Pacific region and to explore solutions to control AMR by organizing an international symposium. The APEC symposium was held on 15 March 2013 in Kuala Lumpur, Malaysia with the theme of “Strategies to control and prevent AMR” with focus on strategies to control AMR including how to implement antimicrobial stewardship in Asian economies, how to control antibiotic abuse and implement policies to control AMR in both human medicine and animal husbandry, and how to evaluate economic impact of AMR.

This APEC guideline to tackle AMR was prepared based on the discussion among SFG consisting multi-sectoral experts from APEC economies and external APEC stakeholders at the first and second Expert Forum of the first APEC project (APEC#211-HT-04.1 and APEC#211-HT-04.2), the Expert Forum of the second APEC project (APEC#213-HT-01.3), and the APEC symposium of the third APEC project (APEC#213-HT-01.2). A

lists of members of the SFG and speakers of the APEC symposium are provided in the Appendix. The purpose of this APEC guideline is to envision and implement the future strategies for prevention and control of AMR in the Asia-Pacific region. Also, through all these efforts and international collaborations endorsed by APEC, the final goals are to prevent and control AMR in the Asia-Pacific region and to strengthen APEC's capacity to respond to public health threat caused by AMR in APEC economies.

II. Strategic action plan to control AMR in the Asia-Pacific region

The strategic action plan to control and prevent AMR in the Asia-Pacific region consists of six major components as in Figure. Surveillance of AMR is the first step to detect and identify the problems of AMR in the region. Increased awareness of AMR through educational and campaign activities is the basic and essential strategy to control AMR which can promote appropriate use of antibiotics. Appropriate use of effective antibiotics is of utmost importance because antibiotic abuse or misuse is the most critical driving force for the emergence of AMR. This includes the appropriate use of current antibiotics and the development of novel antibiotics. Hospital infection prevention and control is also important since it can prevent the spread of resistant clones in the hospitals and in the community. Vaccination can prevent the emergence of infectious diseases as well as can reduce the prevalence of AMR in a certain bacterial pathogen, such as *S. pneumoniae*. Finally, adequate and relevant policies and regulation by governmental system for control of antibiotic uses, prevention of counterfeit drugs, and surveillance of AMR are very crucial for successful control of AMR. The strategic plan should be prioritized according to the local situation of each economy in the Asia-Pacific region.

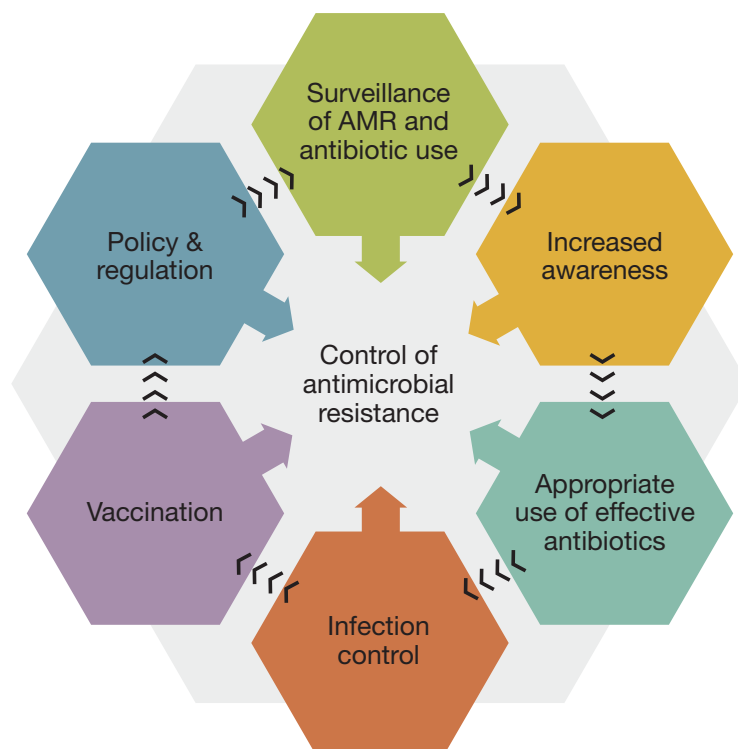


Figure. Six major components of strategic action plan to control antimicrobial resistance

1. Surveillance of AMR and antibiotic use

1.1. Background

AMR is now spreading geographically much faster than at any time in the history. Although AMR is spreading worldwide, most serious situation of AMR is now observed in the Asian region. For effective control of AMR in the region, surveillance of AMR based on international collaborations is critically required. Surveillance of AMR is essential for providing information on the magnitude and trends in AMR. Surveillance of AMR tracks changes in microbial populations, permits the early detection of resistant strains of public health importance, and supports the prompt notification and investigation of outbreaks. Surveillance findings are needed to inform clinical therapy decisions and to guide policy recommendations. Surveillance is needed for monitoring the effect of interventions. The study of AMR can also collect patient demographic data that may be used to determine which pathogens are more prevalent among various patient populations and how AMR is changing among them.

The actions taken on the basis of surveillance data will depend on the level at which the data are being collected and analyzed. A fundamental principle of any communicable disease surveillance program is defining and standardizing laboratory identification methods. These standards should be compatible with other economies to allow international comparison of local data. International collaboration on surveillance may also be of value, to share information as an early warning of new or unusual AMR events. In addition international quality assurance standards can help to overcome the potential difficulties arising from the use of different methods.

Monitoring of antibiotic uses is also very important because inappropriate use of antibiotics is the most basic driving force for the emergence of AMR. Based on the reports from Asian economies, antibiotics are very frequently abused or misused in most economies in Asia not only in patients but also in animal husbandry. Furthermore, counterfeit antibiotics are widely circulated in many Asian economies, which can induce the emergence of AMR due to inadequate dose of antibiotic compound.

1.2. Strategic action plan for surveillance of AMR and antibiotic use

(1) Establishment of national and international surveillance system in the Asia-Pacific region

Surveillance is a key element in the strategy to control and prevent AMR. The most basic unit for the surveillance of AMR is the hospital. Hospital surveillance should be performed according to the standardized

protocols and methods, which are also used for the national surveillance of AMR. National surveillance network should include representative number of hospitals in the APEC economy and surveillance of AMR should be performed based on the standardized protocols and methods.

It is also very important to evaluate the status of AMR at international level because AMR can spread between economies. International surveillance can be performed either by specific surveillance networks or by coalition of existing national surveillance networks of the APEC economies. In order to collate the data from national surveillance networks, it is essential that methods of collecting isolates and in vitro susceptibility tests should be standardized.

i) Methods of national and international surveillance

It may be ideal to have active surveillance which involves collecting and testing bacterial isolates at the reference laboratory since it can provide timely data with more complete information than passive surveillance which collects the existing surveillance data. However, active surveillance is more difficult to perform and resource-intensive. Passive surveillance is more practical and easy to perform, but laboratory of individual institution should be qualified and the protocols have to be standardized. The surveillance for AMR can be comprehensive or sentinel. The right method for national surveillance of each economy should be determined according to the resource situation. At the Expert Forum held on 15 October 2011 in Seoul, Korea, consensus was made to perform passive surveillance for an international surveillance of AMR as a basic scheme with active surveillance program for specific pathogens.

ii) Optimal number of hospitals participating in the national surveillance network

To generate the representative data of AMR, surveillance should include adequate number of hospitals including both moderate-sized/secondary level/provincial hospitals and large/tertiary/national hospitals. Although it is difficult to define the optimal number of hospitals for representative data on AMR of each economy, consensus made at the Expert Forum held on 15 October 2011 in Seoul, Korea was that surveillance should include at least 2 hospitals for each provincial region of each APEC economy.

iii) Role of governmental system and private systems for the national surveillance

National government has primary responsibility to provide financial and technical support for national surveillance systems of AMR. The Center for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), or the Ministry of Health in APEC economies could be a core system for national surveillance system. Non-governmental or private systems such as academic societies, organizations, or companies can support and collaborate with the governmental system.

iv) Methods to share the AMR data in the Asia-Pacific region

Various methods could be utilized to share the data and information about AMR in the region ; publication of the data in the scientific journals, on-line information system. Data reporting system is better to be standardized by using WHONET database system which is used in WHO or other new system which can be developed by APEC economies in the future for this purpose.

v) International systems for surveillance of AMR in Asia

WHO with support of APEC could be the core system for international surveillance of AMR in the Asia-Pacific region. Since many economies in the region are using WHONET system for data management, central coordination of surveillance data by WHO offices could be possible.

vi) Transportation of bacterial strains for international surveillance

International transportation of bacterial strains is regulated by the International Air Transport Association (IATA). Since bacterial strains are potentially hazardous materials, strict procedures including special courier services are essentially required.

(2) Standardization of microbiology test, data collection, and reporting

Economies in the Asia-Pacific region have different levels of microbiology laboratory capacity and may use the different protocols and criteria to identify isolates and to perform antimicrobial susceptibility testing. Therefore, quality assurance and standardization of microbiologic tests are crucial to obtain accurate information on AMR, to monitor AMR trends and to compare AMR in different economies in the Asia-Pacific region. Collection of the data and reporting should also be standardized.

i) Target organisms for surveillance of AMR

Following organisms could be included in the national and international surveillance of AMR: *S. pneumoniae*, *H. influenzae*, *Moraxella* spp., *Salmonella*, *Shigella* spp., *Vibrio cholerae* in community-acquired infections and *S. aureus* (MRSA, VISA, and VRSA), vancomycin-resistant enterococci (VRE), ESBL-producing gram negative bacilli, *Klebsiella pneumoniae* carbapenemase (KPC)-producing organisms, carbapenem-resistant Enterobacteriaceae (CRE), and carbapenem-resistant and MDR non-fermenters such as *P. aeruginosa* and *Acinetobacter* spp.. However, target organisms for national surveillance may vary by APEC economy depending on the local situation.

ii) Standardization of in vitro susceptibility test in APEC economies

Laboratories in most economies in the Asia-Pacific region follow the standards and guidelines of Clinical and Laboratory Standards Institute (CLSI). Disc diffusion method according to CLSI guideline is recommended for basic surveillance method while minimal inhibitory concentration (MIC) testing is also needed depending on the purpose and method of surveillance program.

iii) Standardization of the microbiology laboratories for AMR surveillance

Quality improvement and standardization of the microbiology laboratories in APEC economies is urgently required. In order to achieve this, education and training program in each microbiology lab is basically required. Second, a national External Quality Assurance System (EQAS) should be implemented. Third, national accreditation programs and licensing schemes for laboratories should be established. Finally, on-site audit and monitoring of performances by the microbiology laboratory should be performed by an appropriate agency.

(3) Surveillance of antibiotic consumption in clinical practice

Antibiotic usage is closely associated with the emergence of AMR. To evaluate the status of antibiotic abuse or misuse, data on antibiotic usage should be obtained. However, the nationwide surveillance system of antibiotic consumption has not been established in most economies in the Asia-Pacific region. The standardized methods such as Defined Daily Doses (DDD) defined by the WHO should be utilized for measurement of antibiotics used.

i) Development of effective system to monitor the use of antibiotics

Since APEC economies have varying capabilities in undertaking monitoring of antibiotic use, the standard protocol for surveillance of antibiotic use should be developed based on local situation. CDC or FDA in collaboration with academic organizations can perform the nationwide survey of antibiotic use. Antibiotics that should be monitored include glycopeptides, carbapenems, quinolones, and third generation of cephalosporins although the list of target antibiotics should be determined depending on local situation.

ii) Monitoring the use of counterfeit antibiotics

Counterfeit antibiotics are one of the major contributing factors for the emergence of AMR as well as the cause of treatment failure with fatal outcome in many economies in the Asia-Pacific region. Healthcare authorities should establish the legal control of the production and circulation of counterfeit drugs. Strict regulation of the

quality of antibiotic manufacturing is essentially required with aggressive penalizing production and circulation of counterfeit drugs.

(4) Surveillance of AMR and usage in food animals

Antibiotic abuse in animal husbandry is another important factor for the emergence of AMR in major bacterial pathogens. It is critical to monitor the use of antibiotics in food animals as well as to regulate the use of antibiotics as a growth promoter. Particularly, quinolones and colistin should be monitored among animals because these agents used in food animals could directly impact on the emergence of AMR and subsequent treatment failures in the clinical practice.

Although antibiotics are widely used in food animals in many economies in the Asia-Pacific region, accurate evaluation and measurement of antibiotic uses have not been investigated. In particular, economies in the Asian region should implement the national strategy to control and prevent the use of antibiotics in food animals as well as surveillance of antibiotic consumption in animal husbandry.

2. Increased awareness of AMR

2.1. Background

Despite the critical situation of AMR, this is still a neglected issue in many APEC economies, particularly developing economies. Lack of awareness and knowledge on critical problems of AMR prevents APEC economies to prepare comprehensive strategies to control and prevent the emergence and spread of AMR in the region. Also, it is one of the main reasons for inappropriate use of antibiotics. However, there have been no adequate educational and campaign activities for this issue in most APEC economies, particularly economies in the Asian region. Since AMR emerges due to multiple complex reasons and spreads internationally, future strategies to control and prevent AMR in the region should be based on multi-sectoral and international collaboration. Especially, APEC can contribute to more effective management of AMR in both APEC economies and external APEC stakeholders through APEC's capacity to socialize governments, to attract international attention to the AMR threats, and to share best practices. Therefore, educational and campaign activities to raise awareness on AMR and appropriate antibiotics are urgently needed in the Asia-Pacific region for the control and prevention of AMR based on international collaboration and support by APEC.

2.2. Strategic action plan for increased awareness of AMR

(1) Educational campaigns for general public and healthcare providers

Increased awareness of appropriate use of antibiotics by general public and healthcare providers is very essential to prevention and control of AMR in the Asia-Pacific region. Based on the survey in the Asian region, general public in most Asian economies needs to have more adequate knowledge and information about appropriate use of antibiotics and AMR. Among various measures to provide information on antibiotic use and AMR, educational campaign is one of the most effective ways.

i) National campaign for general public

The governmental systems such as the Ministry of Health, CDC, or FDA should be in charge of the national campaign in collaboration with academic organizations and infectious disease experts. There are many ways to implement the public campaign for general public, but the best way would be to use mass media such as TV or radio. On-line campaigns using the website and social networking service (SNS) are another effective means, while printed materials such as posters, leaflets, and other dedicated materials can be utilized. Although the main key messages of public campaigns should be customized according to local situations of antibiotic use and AMR, messages must be simple and easy to understand.

The CDC in the United States and European CDC have established the Antibiotic Awareness Day in November. Likewise, special campaign days or week can be designated in Asian economies in the future. If the APEC can support the international campaign for appropriate use of antibiotics in the Asian region, it could be more appealing to the governmental authorities who should be leading this activity.

ii) Educational campaign for healthcare professionals

Educational campaign for healthcare professionals who prescribe antibiotics is very important to prevent the abuse or misuse of antibiotics. According to the survey which was conducted for the first Expert Forum of the APEC project entitled “International initiatives to control antimicrobial resistance in the Asia-Pacific region” (HWG 05/2010A) which was held on 5 April 2011 in Seoul, Korea, healthcare professionals in most Asian economies need to have more adequate and correct knowledge of antibiotic use and AMR (APEC#211-HT-04.1). The most basic content of educational campaign for healthcare professionals is the current status of AMR, its implications in the clinical practice, and current situation of antibiotic abuse and misuse. This information should be regularly updated and provided to healthcare professionals. Development of clinical practice guidelines for diagnosis and treatment is crucial. Treatment guidelines should be based on local and national status of AMR. Educational curricula for medical students and trainees are also important. Educational program for healthcare professionals could be prepared by academic organizations.

(2) Campaign 4

APEC supported the project entitled “Enhancing health security in APEC – International campaign program to control antimicrobial resistance in the Asia-Pacific” (S HWG 02 12A) in 2012. The project was aimed to develop campaign strategies and contents and materials of the international campaign program to raise awareness on AMR and to promote appropriate antibiotic use in APEC economies, particularly in the Asian region, to control and prevent AMR and to enhance the health security in the Asia-Pacific region. And, the international campaign, named as “Campaign 4”, has been developed for general public and healthcare professionals in the Asia-Pacific region.

The Campaign 4 can provide a platform of public campaign for APEC economies in the Asia-Pacific region. The contents and materials for Campaign 4 including posters, brochures, leaflets, e-learning programs, a website (www.campaign4.org), video clips as well as educational programs have been developed and these contents and materials in English and local language version can be implemented in the Asia-Pacific region.

3. Appropriate use of effective antibiotics

3.1. Background

There have been strong correlations between the use of antibiotics and the emergence of AMR in major bacterial pathogens. Particularly, antibiotic abuse or misuse is more frequently associated with AMR. Therefore, appropriate use of antibiotics is the first and basic step for prevention and control of AMR. Given the dearth of novel antibiotics in recent decades, appropriate use of current antibiotics is of utmost importance.

With this effort, development of novel antibiotics is also critically required. There are increasing reports of the emergence of extensively drug-resistant (XDR) or pan drug-resistant (PDR) pathogens throughout the world, which underscore the importance of new antibiotics that can be effective against these pathogens.

3.2. Strategic action plan for appropriate use of current antibiotics

(1) Policy and regulations on the use of antibiotics

Given the widespread abuse and misuse of antibiotics in the Asian region, any kind of antibiotics should be purchased based on the doctors’ prescription. Currently, very few economies in the Asia-Pacific region have established the separation of prescribing and dispensing antibiotics. It should be urgently regulated by law.

Counterfeit antibiotics should also be strictly prohibited and regulated by law. Since counterfeit drugs are

widely used in many Asian economies, international collaboration is also urgently required. More detailed strategic action plan will be discussed in the section 6, Policy and regulation.

(2) Antibiotic stewardship

Antibiotic stewardship in the hospitals is essential for appropriate use of antibiotics. Guidelines for antimicrobial treatment and prophylaxis, and hospital antimicrobial formularies should be developed and regularly updated in the hospitals. These should be based on the institutional and national situation of AMR as well as situation of antibiotic use. To strengthen the antibiotic stewardship in the hospitals, monitoring of AMR and use of antibiotics in the hospitals should be conducted.

(3) Restriction of antibiotic use in food animals

Since antibiotic abuse and misuse in the food animals is an important cause of AMR, unnecessary and inappropriate use of antimicrobials for non-therapeutic use in animals should be reduced. According to the list by OIE (World Organization for Animal Health), many antibiotics used in human patients are also used in food animals. Recently, the United States and Korea established a law to ban all antibiotics as a growth promoter in food animals. However, many APEC economies in the Asia-Pacific region do not have any strict law and regulations to restrict antibiotic use in food animals. Therefore, national systems to monitor and regulate antimicrobial usage in food animals should be activated.

3.3. Strategic action plan for development of novel antibiotics

(1) Creating research and development (R&D) infrastructure

Antibiotic pipeline is dried out with scanty new antibiotics during the past 20 years. This problem should be solved through collaboration by political, scientific, and industrial systems on an international basis. Because major pharmaceutical companies are not interested in developing novel class antibiotics due to various reasons, international community and national governments should provide more favorable environment for R&D infrastructure. Financial incentives either push or pull mechanisms should be provided to R&D activities. Regulatory uncertainty should be corrected to facilitate the introduction of new agents. Public-private partnership (PPP) should be established for more effective R&D program. Since many APEC economies in the Asian region do not have capabilities to develop novel antibiotics, international collaboration is absolutely required.

i) Financial incentives

Financial incentives to entice pharmaceutical industry to reengage in antibiotic R&D. Financial incentives (push

and pull mechanisms) are required. Push incentives include research grants, contracts and tax credits, while pull incentives are guaranteed markets, liability protection, patent extension or data exclusivity (IDSA, 2010).

ii) Regulatory certainty

Regulatory uncertainty is one of the major hurdles to new antibiotic development. To activate the antibiotic R&D and the introduction of new antibiotics to the clinical medicine, regulatory process should be simplified and clarified.

iii) Public-private partnership (PPP)

PPP is essential to focus on developing critically needed antibiotics for multidrug-resistant pathogens despite the small size of the market. PPP can contribute to merge antibiotic conservation efforts with new antibiotic R&D efforts.

(2) Novel antibiotics needed most in Asian economies

Based on the current situation of AMR in the Asia-Pacific region, MDR *P. areuginosa* and *A. baumannii*, and CRE should be the primary target pathogens for novel antibiotics. In some economies in the Asian region, XDR or PDR gram-negative pathogens have been increasing which can be treated only by colistin or tigecycline. However, colistin (polymixins) is not available currently in the Philippines, Japan and Indonesia and increasing resistance to colistin is also observed in other economies in Asia. Given the lack of effective antibiotic options against these pathogens, development of new antibiotics are critically required.

4. Infection prevention and control

4.1. Background

Healthcare-associated infections (HAI), often caused by antimicrobial resistant bacteria, are very important cause of increased mortality and morbidity. Hospital infection control is an effective way to curb AMR by preventing the spread of resistant bacteria within the hospital. Hospital infection control is important not only for the control of AMR in the hospital but also to prevent the emergence of AMR in the community because resistant pathogens can spread out from the hospital to the community.

4.2. Strategic action plan for infection prevention and control

(1) Establishing the infection prevention and control program in the hospital

Infection prevention and control program should be a top priority for healthcare facilities. Infection prevention and control in healthcare settings should be enhanced by developing new interventions based on rapid diagnosis, improved understanding of the factors that promote cross-infection, and guidelines for effective infection prevention and control. Infection control professionals and practitioners, continuous support by hospital leadership, and multifaceted education and reinforcement of policies are required for successful hospital infection prevention and control. Adequate resources must be available for prevention and control for nosocomial infections, including expert consultation, laboratory support, monitoring, and data analysis. Written infection prevention and control policies and procedures must be established, implemented, and updated periodically.

(2) Hand hygiene policy

Hand hygiene is the most important way for preventing the spread of antibiotic resistant pathogens in healthcare settings, and appropriate guidelines for hand hygiene should be provided. It is critical that compliance with hand hygiene policy is monitored regularly. Hand hygiene policy should begin with the use of an alcohol-based hand rub before and after any contact with the patients, dealing with body fluids or any soiled materials, removing gloves and changing bedding or linens. The hands should be thoroughly washed with soap and water whenever hands are visibly dirty or contaminated with proteinaceous material or are visibly soiled with blood or other body fluids or when dealing with outbreaks caused by spore-forming bacteria such as *Clostridium difficile*.

In Hong Kong China, the Hand Hygiene Awareness Day was designated on May 5, 2010 to promote hand hygiene and received broad support and participation from both public and healthcare providers. This kind of multifaceted control strategy may be a good way to promote hand hygiene and infection control in the Asian economies.

(3) Reduction of transmission of MDR organisms

MDR organisms are usually defined as microorganisms that are resistant to three or more classes of antimicrobial agents. For infection control purposes, MDR organisms including MRSA, VISA, VRSA, VRE, ESBL-producing Enterobacteriaceae, carbapenem-resistant *A. baumannii*, and carbapenem-resistant *P. aeruginosa* should be monitored and controlled. Successful control of MDR organisms requires multifaceted interventions including improvement in hand hygiene, contact precautions, active surveillance cultures, education, enhanced environmental cleaning, and administrative support.

(4) Hospital accreditation program to reinforce the infection prevention and control

Hospital accreditation program can play a major role to establish the hospital infection prevention and control program in most economies in the Asia-Pacific region. For example, in Korea, hospital infection prevention and control program is one of the top priorities for hospital accreditation by national evaluation agency. This accreditation process has affected many Korean hospitals to establish the adequate hospital infection prevention and control program. The problem is small- to medium-sized hospitals that have limited resources and facilities such as isolation rooms and infection control practitioners. Given the practical issues in this healthcare setting, each APEC economy has to provide adequate support and guides to the hospital infection control program.

5. Vaccination

5.1. Background

With growing burden of AMR worldwide, fewer antibiotic options are left against resistant pathogens. Preventing the occurrence of infection by vaccination would eliminate the need for antibiotic use and the risk of emerging AMR in bacterial pathogens. Currently, vaccines have been developed for various bacterial pathogens including typhoid fever, cholera, tuberculosis, diphtheria, tetanus, pertussis, *S. pneumoniae*, *Haemophilus influenzae* type b and meningococci. Vaccines targeting MDR pathogens such as *S. aureus* or *P. aeruginosa* are also being developed. Among these bacterial vaccines, pneumococcal conjugate vaccine (PCV) is the most representative example of vaccine that can reduce the prevalence of AMR.

Pneumococcal diseases are one of the leading causes of death worldwide with 1.6 million deaths annually. Disease burden of pneumococcal infections has been increasing due to widespread emergence of AMR in *S. pneumoniae*. During the past 3 decades, resistance of pneumococci to beta-lactams, macrolides, and other antibiotic classes has escalated dramatically throughout the world, although it is more severe in the Asian region than in the western part of the world. Pneumococcal infection is also the most common vaccine-preventable disease. In the United States, the 7-valent PCV (PCV7) has resulted in 94% reduction in the incidence of pneumococcal diseases caused by PCV7 serotype strains and 75% reduction in invasive pneumococcal diseases (IPD) regardless of the serotypes. It also reduced the prevalence of AMR in *S. pneumoniae*. These data clearly showed that PCV7 was a very effective vaccine to prevent pneumococcal infections and AMR.

Although PCV7 has decreased the incidence of pneumococcal diseases caused by vaccine serotypes, there was a remarkable increase in the incidence of IPD caused by non-PCV7 serotype strains such as serotype 19A

worldwide. Since serotype 19A is very frequently related to MDR, emergence of serotype 19A is leading to the increased prevalence of MDR. Therefore, a new conjugate vaccine which can cover these non-vaccine serotypes is urgently required. PCV13 that includes 6 additional serotypes including serotype 19A was recently approved and introduced in the United States and some economies in the region. PCV13 is expected to prevent pneumococcal diseases effectively and also to reduce the prevalence of pneumococcal resistance.

5.2. Strategic action plan for vaccination

Given the importance of vaccination to prevent the occurrence of infectious disease and the emergence of AMR, vaccination should be encouraged in APEC economies. PCV is the proven example of bacterial vaccine that can reduce the prevalence of AMR in *S. pneumoniae*. Currently, PCV13 would be the best option for this purpose. Influenza vaccination is also important because it can prevent influenza and the use of antibiotics in the clinical practice.

In order to enhance the awareness of vaccination and compliance in the Asia-Pacific region, education and campaign should be implemented for both general public and healthcare professionals. Also, key messages could be disseminated by mass media, leaflets, symposium and medical training.

6. Policy and regulation

6.1. Background

Control and prevention of AMR should be based on multidisciplinary approach consisting of medical, legal, social, economic and public measures. In this regard, relevant policies and regulations for control of antibiotic uses, surveillance of AMR, evaluation of clinical and economic impact of AMR, and public implementation of interventional measures are very crucial. However, many economies in the Asia-Pacific region are not aware of the current status of AMR and its impact on clinical medicine and socioeconomic damage.

The most important policy to prevent antibiotic abuse or misuse is separation of prescribing from dispensing antibiotics. By the law and regulation, antibiotics can be purchased only by doctor's prescription. However, this law has been implemented only in some economies in the Asian region such as Korea, Japan, Singapore and Malaysia, while antibiotics can be easily purchased as OTC drugs without prescription in many other Asian economies. This is one of the most important reasons for antibiotic abuse in these Asian economies and for increasing emergence of AMR in major pathogens.

Counterfeit antibiotics which contain inadequate concentration of antimicrobial compound are widely circulated in many Asian economies. This is another form of antibiotic abuse and misuse, which can lead to the emergence of AMR. However, in many economies in the Asia-Pacific region, there is minimal control over public access to OTC antibiotics without prescription. Furthermore, an advertisement for antibiotics or public marketing is allowed in the media in some Asian economies.

6.2. Strategic action plans for policy and regulation

(1) Role of government to combat AMR

National government should play a very crucial role to reduce AMR and to lower the HAI in each APEC economy. Government needs to make combating AMR as a “national priority” and to take responsibility to combat AMR for public health. Government should make every effort to establish relevant and effective policies and regulations to reduce AMR.

(2) Legal control of antibiotic supply, distribution, and sales

Legal regulation to prohibit purchase of antibiotics without doctor’s prescription is of utmost importance to prevent antibiotic abuse in APEC economies. It can be possible only based on multidisciplinary approach by the government, medical society, pharmaceutical companies and public health system. Particularly, the role of government is very crucial. Stringent legislative control of antibiotic prescribing and dispensing should be reinforced.

Financial incentives for prescribing drugs including antibiotics should not be allowed by strict legal regulation. Public advertisement of antibiotics also should be banned. The government should regularly monitor the amount of antibiotic use in patients and assess the appropriateness of antibiotic usage in medical institutions. These data should be provided to the medical community and also to the general public.

(3) Development of the healthcare policies for use of antimicrobial agents

Containment of AMR should be the national priority given its impact on clinical medicine and socioeconomic aspect. The national healthcare policies for use of antimicrobial agents should be established by public healthcare authorities or reimbursement agency. The national intersectional antimicrobial stewardship task force could be established including multidisciplinary experts from different academic societies such as infectious disease physicians, infection control professionals, clinical microbiologists, information system specialist, nurses, clinical pharmacists, health care professionals, veterinarians, agriculturalists, pharmaceutical manufacturers, government, media representatives, consumers and other relevant stakeholders. The Task

Force can work with related institutions and academic groups and societies for updating the guidelines of "appropriate use of antibiotics" and "special antibiotic use". Government and academic societies should play the crucial role in the implementation of national policies for the use of antimicrobial agents.

i) Requirements for establishment of the national healthcare guidelines

In order to establish the national healthcare policies, the regulation and guidelines of national health insurance payment such as declaring “Directions for drug-restricted benefits for national health insurance” should be established and updated through collaboration with medical institutions, research institutions, and drug suppliers. It would be helpful to establish the guidelines to restrict antimicrobial usage for upper respiratory tract infections and the costs of antimicrobial agents used in the treatment of ambulatory patients with acute upper respiratory tract infections without evidence of bacterial involvement are not reimbursed. It is also required to establish the guideline to regulate the use of prophylactic antibiotics, which focus on reducing overuse of prophylactic antibiotics during clean and clean-contaminated surgeries

ii) Monitoring and evaluating the compliance of national healthcare guidelines

The compliance and usefulness of the national healthcare guidelines for use of antibiotics can be monitored and evaluated by various ways ; 1) establish the effective and real-time web-based AMR surveillance system, 2) encourage hospitals to establish computer management system for prescription and formulary restrictions, 3) encourage hospital to establish decision support system to optimize the antibiotics, 4) establish the evaluation and audit mechanism through the hospital accreditation program to monitor and evaluate the compliance and usefulness of use of antibiotics

iii) Financial incentives for appropriate use of antibiotics

Financial incentives can be provided to the hospitals for establishment of effective surveillance system of nosocomial infections and AMR, information system, computer management system, computer physician order entry, antimicrobial order forms, or computer decision–support system that can contribute to appropriate use of antibiotics.

iv) Monitoring the use of antibiotics in the clinical practice

The use of antibiotics in the clinical medicine and animal husbandry should be monitored. Hospital uses of antibiotics can be monitored through collaboration with hospitals and also by hospital accreditation program. Whole amount of antibiotics used in each APEC economy can be monitored by sales record of antibiotics by

pharmaceutical companies. Data and information of the amount of antibiotic use and evaluation of the current status of antibiotic use should be provided to the healthcare authorities and medical community.

v) Prohibition of production and circulation of counterfeit drugs

Production and circulation of counterfeit drugs in APEC economies should be strictly prohibited in any circumstances. Any person who manufactures or imports counterfeit drugs should be subject to punishment. Any person who knowingly sells, supplies, dispenses, transports, stores, brokers, transfers or displays with intent to sell counterfeit drugs or prohibited drugs should be punished with imprisonment or fine.

vi) Establishing clinical practice guidelines for appropriate use of antibiotics

The development of guidelines in relation to the appropriate use of antibiotics is an essential part of the strategy. Evidence-based treatment guidelines can lead to more appropriate antimicrobial prescribing by physicians. The use of such guidelines is most effective when combined with supportive interventions such as educational training and supervision programs. The guidelines should be evidence-based to the greatest degree possible and regularly reviewed. It should include both prescribing and non-prescribing antimicrobials and recommend treatment options for each clinical situation. It includes information on the most appropriate antibiotic and information on each antibiotic such as dosage, duration of treatment, effect of alcohol consumption, reactions with other medication, etc.

vii) Restriction of antibiotic usage in food animals

Use of antibiotics as growth promoters in animal husbandry should be monitored and regulated. Use of antibiotics in animal husbandry can be monitored by the random inspection of farms and by monitoring the production quantity and sales volume of antibiotics by pharmaceutical companies. Based on accurate monitoring, antibiotic uses as growth promoters should be strictly prohibited. The best option would be to establish the legal ban of antibiotic use in food animals as in the United States and Korea. Otherwise, effective control of antibiotic use in animal husbandry is practically difficult.

III. Conclusive remark

Given a growing crisis of AMR worldwide, particularly in the Asia-Pacific region, APEC Health Working Group (HWG) has devoted its efforts to tackle AMR by supporting serial APEC projects on AMR proposed and performed by APFID in collaboration with APEC economies and external APEC-stakeholders. This was very crucial because effective prevention and control of AMR can be achieved only by multifaceted international collaborations based on strong national and international initiatives. Based on the serial APEC projects on AMR, the APEC guideline to tackle AMR in the AP region AMR in the Asia-Pacific region has been developed. The APEC guideline includes the six major strategies to control and prevent AMR in the region ; surveillance of AMR and antibiotic use, increased of AMR, appropriate use of effective antibiotics, infection prevention and control, vaccination, and policy and regulation. This guideline can provide APEC economies with the frame of the strategies to address the growing threat of AMR in the region and can contribute to reduce economic and clinical burden of AMR in APEC economies.

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Appendix

Lists of experts and speakers for

- i) the first APEC Expert Forum held on 5 April 2011 in Seoul, Korea of APEC project entitled “International initiatives to control antimicrobial resistance in the Asia-Pacific region” (HWG 05/2010A)

- ii) the second APEC Expert Forum held on 15 October 2011 in Seoul, Korea of APEC project entitled “International initiatives to control antimicrobial resistance in the Asia-Pacific region” (HWG 05/2010A)

- iii) the APEC Expert Forum held on 9 November 2013 in Seoul, Korea of the APEC project entitled “Enhancing health security in APEC - International campaign program to control antimicrobial resistance in the Asia-Pacific” (S HWG 02 12A)

- iv) the APEC symposium held on 15 March 2013 in Kuala Lumpur, Malaysia of the APEC project entitled “Strengthening health security - APEC symposium on strategies to control and prevent antimicrobial resistance” (S HWG 04 12A)

Annex 1. List of participants for the APEC Expert Forum held on 5 April 2011 in Seoul, Korea**APEC economies**

APEC economy	Name	Affiliation
China	Hui Wang	Peking University People's Hospital
	Bin Cao	Beijing Chaoyang Hospital
	Yonghong Yang	Beijing Children's Hospital
	Xuzhuang Shen	Beijing Children's Hospital
	Shaoguang Huang	Ruijin Hospital
	Yuxing Ni	Ruijin Hospital
	Min Lu	Shanghai Children's Hospital, Jiao-Tong University
Hong Kong, China	Thomas So	Princess Margaret Hospital
Indonesia	Latre Buntaran	Children's and Maternity, Harapan Kita Hospital
Japan	Nobuyuki Shimono	Kyushu University Graduate School of Medical Sciences
	Yujiro Uchida	Kyushu University Graduate School of Medical Sciences
	Hiroshige Mikamo	Aichi Medical University Hospital
Korea	Jae-Hoon Song	Samsung Medical Center; Asia Pacific Foundation for Infectious Diseases; Project overseer
	Kyong Ran Peck	Samsung Medical Center
	Doo Ryeon Chung	Samsung Medical Center
	Cheol-In Kang	Samsung Medical Center
	So Hyun Kim	Asia Pacific Foundation for Infectious Diseases
	Kwan Soo Ko	Sungkyunkwan University
	Yae Jean Kim	Samsung Medical Center
Malaysiam	Rohani Md Yasin	Institute for Medical Research
	Christopher Lee	Hospital Sungai Buloh, Jalan Hospital
The Philippines	Celia Carlos	Research Institute for Tropical Medicine

The Philippines	Sonia Sia	Research Institute for Tropical Medicine
Singapore	David Lye	Tan Tock Seng Hospital
	Ban Hock Tan	Singapore General Hospital
Chinese Taipei	Po-Ren Hsueh	National Taiwan University Hospital
	Cheng-Hsun Chiu	Chang Gung Children's Hospital
Thailand	Visanu Thamlikitkul	Siriraj Hospital
	Anan Chongthaleong	Chulalongkorn University Hospital
Viet Nam	Pham Hung Van	University of Medicine and Pharmacy
	Do van Thanh	Bach Mai Hospital
	Tran Van Ngoc	Cho Ray Hospital

Non-APEC economies

Non-APEC economy	Name	Affiliation
India	V. Balaji	Christian Medical College Vellore
	V. Ramasubramanian	Apollo Hospital
Sri Lanka	Jennifer Perera	University of Colombo
	Kushlani Jayatileke	Sri Jayewardenepura Hospital

Annex 2. List of participants for the APEC Expert Forum held on 15 October 2011 in Seoul, Korea

* Working Group - S : Surveillance group, F : Future strategy group, P : Policy & regulation group

APEC economy	Name	Affiliation	Group*
China	Yonghong Xiao	1st Affiliated Hospital of Medical College, Zhjiang University	S
Hong Kong, China	Andrew Wong	Infection Control Branch, Department of Health	P
	Thomas So	Princess Margaret Hospital	F
Indonesia	Amy Rahmadanti	Referral Health Care, Ministry of Health of Indonesia	P
	Engko Sosialine Magdalane	Pharmaceutical Services, Ministry of Health of Indonesia	P
	Iwan Dwiprahasto	Faculty of Medicine, Gadjah Mada University	F
	Lindawati Alimsardjono	University of Airlangga	F
	Usman Chatib Warsa	University of Indonesia	S
Japan	Yuki Uehara	Juntendo University, Graduate School of Medicine	F
Korea	Jae-Hoon Song	Samsung Medical Center; Asia Pacific Foundation for Infectious Diseases; Project overseer	F
	Kyongwon Lee	Yonsei University College of Medicine	S
	Jun-Wook Kwon	Korea Centers for Disease Control and Prevention	P
	Kyong Ran Peck	Samsung Medical Center	F
	Doo Ryeon Chung	Samsung Medical Center	F
	Cheol-In Kang	Samsung Medical Center	P
	Yeong-seon Lee	Korea Centers for Disease Control and Prevention	S
	Sun-hee Park	Korea Centers for Disease Control and Prevention	S
	Hye-Kyoung Park	Korea Centers for Disease Control and Prevention	P
	Kee-tae Jeon	Korea Centers for Disease Control and Prevention	P
	Min-hui Seong	Korea Centers for Disease Control and Prevention	P

Korea	Hyun-sook Koo	Korea Centers for Disease Control and Prevention	P
	Jin-Myung Kim	Ministry of Health and Welfare	P
	So Hyun Kim	Asia Pacific Foundation for Infectious Diseases	S
Malaysia	Christopher Lee	Hospital Sungai Buloh	F
	Norazah Ahmad	Institute for Medical Research	S
The Philippines	Benilda Galvez	Department of Pulmonary Medicine, The Lung Center of the Philippines	F
	Celia Carlos	Research Institute for Tropical Medicine	S
	Lilibeth C. David	National Center for Disease Prevention and Control, Department of Health	P
Singapore	David Lye	Tan Tock Seng Hospital Singapore	F
	Li Yang Hsu	National University Hospital	S
Chinese Taipei	Shu-Hui Tseng	Centers for Disease Control, Department of Health	P
Thailand	Farsai Chanjaruporn	Bureau of Drug Control, Food and Drug Administration	P
	Jurai Wongsawat	Bamrasnaradura Infectious Diseases Institute, Ministry of Public Health	F
	Visanu Thamlikitkul	Siriraj Hospital	F
	Wantana Paveenkittiporn	National Institute of Health, Department of Medical Sciences	S
Viet Nam	Hung Van Pham	University of Medicine and Pharmacy	S
	Nguyen Van Kinh	National Tropical Disease Hospital	F
	Nguyen Viet Hung	Infection control Department, Bach Mai Hospital	S
	Tran Van Ngoc	Cho Ray Hospital	F
	Van Cao	Department of Immuno-Microbiology, Institute of Pasteur	F
APEC	Name	Affiliation	Group*
Health Working Group	Steve Chen	Program Director, APEC HWG Secretariat	P

Annex 3. List of participants for the APEC Expert Forum held on 9 November 2013 in Seoul, Korea**APEC economies**

APEC economy	Name	Designation	Affiliation
China	Wenbao Zhang	Dr.	Division of Medical Service and Nursing, Bureau of Medical Administration and Medical Management, National Health and Family Planning Commission
	Yonghong Xiao	Professor	1st Hospital affiliated to Zhejiang University
	Hui Wang	Professor	Peking University People's Hospital
Indonesia	Wita Nursanthi	Chief	Section Standardization, Sub Directorate Health Referral Services
Korea	Byung-Guk Yang	Director	Korea Centers for Disease Control and Prevention (KCDC), Ministry of Health & Welfare
	Jae-Hoon Song	Project Overseer ; Chairman, APFID; CEO, SMC	Division of Infectious Diseases, Samsung Medical Center, Sungkyunkwan University School of Medicine; Asia Pacific Foundation for Infectious Diseases (APFID)
	Geun-Ryang Bae	Director	Division of Infectious Diseases Surveillance, KCDC, Ministry of Health & Welfare
	Dong-Woo Lee	Chief Medical Research Officer	Division of Infectious Diseases Control, KCDC, Ministry of Health & Welfare
	Hyun-Sook Koo	Senior Researcher	Division of Infectious Diseases Control, KCDC, Ministry of Health & Welfare
	Jin Myung Kim	Assistant Director	Division of Diseases Control Policy, Ministry of Health & Welfare
	Hee Soon Yu	Manager	Quality Assessment, Division 4, Health Insurance Review & Assessment Service (HIRA)
	Doo Ryeon Chung	Professor ; Coordinator, APFID	Division of Infectious Diseases, Samsung Medical Center, Sungkyunkwan University School of Medicine; Asia Pacific Foundation for Infectious Diseases (APFID)
	Cheol-In Kang	Professor	Samsung Medical Center

Korea	So Hyun Kim	Project Manager	Asian Network for Surveillance of Resistant Pathogens (ANSORP), APFID
	Kyungmin Huh	Dr.	Samsung Medical Center
	Young Eun Ha	Dr.	Samsung Medical Center
	Lorena Jeon	Manager	International Initiatives to Control Antimicrobial Resistance (I Care), APFID
	Margaret Key	Market Leader	Burson-Marsteller
	Lirah Lim	Manager	Burson-Marsteller
Malaysia	Norazah Ahmad	Head	Bacteriology Unit, Institute for Medical Research, Ministry of Health
	Rosminah Mohd Din	Deputy Director	Pharmaceutical Services Division, Ministry of Health Malaysia
	Christopher Lee	Head	Medical Department, Hospital Sungai Buloh
Peru	Coralith Garcia	Dr.	Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia (UPCH)
The Philippines	Irene Farinas	Medical Officer IV / Chief Designate	Policy, Planning, Program Development and Research Division, National Center for Pharmaceutical Access and Management (NCPAM), Department of Health (DOH)
Chinese Taipei	Yung-Ching Liu	Director	Taipei Medical University-Shuang Ho Hospital, Ministry of Health and Welfare
Thailand	Visanu Thamlikitkul	Professor	Division of Infectious Diseases and Tropical Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University
	Pinyo Rattanaumpawan	Professor	Division of Infectious Diseases and Tropical Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University
	Adhiratha Boonyasiri	Professor	Division of Infectious Diseases and Tropical Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University
Viet Nam	Cao Hung Thai	Dr.	Department of Health Examination, Ministry of Health
	Doan Mai Phuong	Director	Faculty of Microbiology, Bach Mai Hospital

APEC HWG	Steve Chen	Program Director	APEC Health Working Group Secretariat
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Non-APEC stakeholder

Non-APEC stakeholder	Name	Designation	Affiliation
WHO	Anuj Sharma	Technical Officer	WHO Western Pacific Region

Annex 4. List of speakers for the APEC symposium held on 15 March 2013 in Kuala Lumpur, Malaysia

APEC economies

APEC economy	Name	Affiliation
Australia	Stephen Page	Advanced Veterinary Therapeutics
China	Yonghong Xiao	1st Hospital affiliated to Zhejiang University
Hong Kong, China	Wing Hong Seto	Queen Mary Hospital
Korea	Jae-Hoon Song	Samsung Medical Center; Asia Pacific Foundation for Infectious Diseases; Project overseer
	Doo Ryeon Chung	Samsung Medical Center
	Yong Ho Park	Animal and Plant Quarantine Agency
	Tae-Jin Lee	Seoul National University
Malaysia	Christopher Lee	Hospital Sungai Buloh
	Victor Lim	International Medical University
The Philippines	Celia Carlos	Research Institute for Tropical Medicine
Singapore	Li Yang Hsu	National University Hospital
Chinese Taipei	Shu-Hui Tseng	Centers for Disease Control, Chines Taipei
Thailand	Anucha Apisarnthanarak	Thammasat University Hospital
United States	Sara Cosgrove	Johns Hopkins University
	David Shlaes	Anti-Infectives Consulting

Non-APEC stakeholder

APEC economy	Name	Affiliation
WHO	Hendrik Jan Bekedam	WHO Western Pacific Region
Israel	Yehuda Carmeli	Tel Aviv Sourasky Medical Center
Switzerland	Stephan Harbarth	Hopitaux Universitaires de Geneve

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