

# Combating Antimicrobial Resistance in the Philippines

## Introduction

Infectious diseases kill millions of people around the world, 95% of them live in resource-constrained areas. In the 1940s, the discovery of antimicrobials revolutionized man's ability to treat infectious diseases through these life-saving drugs. However, the emergence of antimicrobial resistance (AMR) decreased the effectiveness of these drugs.

AMR is simply the ability of microbes, to grow in the presence of a chemical, or a drug, that would normally kill it or inhibit its growth. Though AMR is a natural occurrence in microbes which happens as an adaptation to external threats, humans have definitely hastened it.

Antimicrobial resistance has serious health and economic consequences such as increased mortality, prolonged illness, increased cost of health care, and damage to trade. In the World Health Organization Day in 2011, the following facts on antimicrobial were reported:

- About 440,000 new cases of multi-drug resistant TB (MDR-TB)<sup>1</sup> emerge annually, causing at least 150 000 deaths.
- Extensively drug-resistant (XDR-TB)<sup>2</sup> has been reported in 64 countries to date.

<sup>1</sup>MDR is resistance to Rifampicin and Isoniazid.

<sup>2</sup>XDR is MDR plus resistance to any member of the quinolone family and at least to any of the second-line anti-TB injectables (such as kanamycin, capreomycin or amikacin).

- There is widespread drug resistance in malaria-endemic countries to antimalarials: chloroquine, sulfadoxine-pyrimethamine, as well as artemisinin.
- There is a high percentage of hospital-acquired infections (HAI) caused by highly resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococci*.
- Ciprofloxacin is the only antibiotic currently recommended for managing bloody diarrhea due to the resistance of *Shigella* organisms to other previously effective antibiotics.
- Multi-drug resistance of *Neisseria gonorrhoeae* including to the "last-line" oral cephalosporins, is increasing in prevalence worldwide.

## Status of Antimicrobial Resistance in the Philippines

The most dreaded New Delhi Metallo-beta-lactamase (NDM-1) was identified in the *Escherichia coli* isolated from the urine of a 33- year old female in March 2011. Its presence indicates resistance to broad-spectrum antibiotics, which were previously reserved for drug-resistant bacteria.

Many of the causative bacterial pathogens of infections in the ten (10) leading causes of morbidity in the country have also acquired multiple drug resistance. As far as the MDR-TB is concerned, the Philippines ranks 6<sup>th</sup> (i.e. after China, India, Russia, Pakistan, and South Africa) among 27 identified countries. MDR-TB among new cases in the Philippines was found to be at 4%, and 20.9 % for previously treated cases.

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The Antibiotic Resistance Surveillance Program (ARSP) found VERY ALARMING RATES of resistance among various pathogens. For *Escherichia coli* and *Klebsiella* spp, extended spectrum beta-lactamase enzyme has been found rendering them resistant to many antibiotics. Multi-drug resistant strains have already been identified in *Pseudomonas aeruginosa* and *Acinetobacter* spp. *Streptococcus pneumoniae*, a causative agent of acute respiratory infections (ARI), showed increased resistance to penicillin at 4% (95%CI: 1.9-9) in 2011 compared to 0% in 2010.

There are other two VERY ALARMING developments in AMR in the Philippines. One is the steady increase in the resistance rates of *Staphylococcus aureus*, thus increase in the prevalence of methicillin-resistant *Staphylococcus aureus* which is also an important cause of HAI as well as community associated infections. Second is the high resistance rates of *Neisseria gonorrhoeae* to ciprofloxacin (77%), ofloxacin (70%), and tetracycline (58%).

### **Factors driving Antimicrobial Resistance in the Philippines**

Underlying factors that drive AMR consists of:

- inadequate national commitment to a comprehensive and coordinated response, ill-defined accountability and insufficient engagement of all stakeholders;
- weak or absent surveillance and monitoring systems;
- inadequate systems to ensure quality and uninterrupted supply of medicines;

- inappropriate and irrational use of medicines, including in veterinary use;
- poor infection prevention and control practices;
- depleted arsenals of diagnostics, medicines and vaccines as well as insufficient research and development of new products.

### **Combating Antimicrobial Resistance**

In the 2011 World Health Day, the World Health Organization (WHO) promoted the six-point policy package to fight antimicrobial resistance.

**Table 1. Elements of the WHO six-point policy package for AMR**

Policy Areas
(1) Committing to develop a master plan to combat antimicrobial resistance
(2) Strengthening surveillance and laboratory capacity
(3) Ensuring uninterrupted access to essential medicines of assured quality
(4) Promoting rational use of medicines in patient care and animal husbandry
(5) Enhancing infection prevention and control
(6) Fostering innovations and research to develop new tools and drugs

**There is no comprehensive well-funded national plan that prioritizes actions that are needed to address the growing AMR problem in the country.**

The readiness of a country in addressing the AMR issue can be reflected through three important factors: (1) availability of a comprehensive and sustainable national plan; (2) presence of an established national

coordinating body; and, (3) existence of policies that serve as guides or frameworks for action.

The most significant observation is the absence of a specific law that would provide a clear direction and action against AMR in both humans and animals. Although the Philippines has developed a number of policies, these are mainly geared towards selected areas of response to AMR, namely, surveillance, laboratory capacity and drug accessibility and quality. Furthermore, the objective of majority of these policies is limited to ensuring the accessibility and quality of antimicrobials, thus, there are guidelines that cover drug procurement, registration, availability, quality and establishment of coordinating bodies like the Food and Drug Administration (FDA) which monitor compliance to these policies. In the midst of all the laws and related policies, an imbalance is still evident in terms of the areas of focus.

While there are many direct or indirect AMR-related activities conducted by government and nongovernment institutions, these initiatives are widely dispersed and fragmented, without a comprehensive road map being used as a guide. There is also a question of the sustainability (e.g. financial stability) of these actions as integration and aligning of activities among AMR stakeholders towards a common goal of combating the AMR problem still needs to be established.

**Information on the AMR problem from surveillance and laboratory activities is limited in scope,**

**inadequately managed and incompletely utilized.**

The data available for AMR as reported by the ARSP are from the program's 22 sentinel sites from all over the country, and the National Tuberculosis Research Laboratory (NTRL). These data all come from human cases, without any correlation with those from the animal health sector. In animals, antimicrobials are used as part of treatment for specific diseases or as food additives. It is a fact that horizontal spread of AMR can occur from humans to animals and animals to humans. Likewise, results of studies done in academic institutions on AMR are not incorporated in the overall review of AMR in the Philippines. The inadequate integration of AMR data could mean that what is currently being reported is just the tip of the iceberg. This may be due to the fact that there is no legal mandate that identifies responsible agency to oversee and implement a comprehensive AMR surveillance in the country, in both humans and animals.

It also appears that there is no correlation of laboratory-based data with clinical data or antibiotic use surveillance in the status quo, limiting the utility of existing data. This is a manifestation of lack of knowledge on how surveillance data can be used, despite the availability of existing model information systems such as WHONET. It is also not clear what is the extent of external quality assurance system (EQAS) implementation, particularly in ensuring the reliability of laboratory results in laboratories outside the existing ARSP.

### **Monitoring and evaluation of the supply and quality of antimicrobials is weak.**

A national drug policy modelled from the WHO framework has been existing in the Philippines since 1988, known as the Philippine National Drug Policy (PNDP). It focuses on improving accessibility of essential medicines by bringing down their costs, as well as ensuring the safety, efficacy, and usefulness of pharmaceutical products through quality control. However, this policy failed to anchor generic medicines into the local market making essential medicines still not accessible due to their high cost.

Together with the RA 9502 (Universally Accessible Cheaper and Quality Medicines Act of 2008), the 2011 Philippine Medicines Policy (PMP) aims to upgrade the PNDP in order to ensure equitable availability and affordability of safe, efficacious and quality medicines in a health system in order to achieve better health outcomes for the Filipino people. The lead office in the implementation, monitoring and evaluation of this policy is the DOH – National Center for Pharmaceutical Access and Management (NCPAM) in coordination with other stakeholders.

After the passing of RA 9711 (Food and Drug Administration Act of 2009), the capacity of the FDA is hoped to be strengthened in the regulatory enforcement of the quality of all essential medicines for human and animal health, including addressing counterfeit medicines in order to fight antimicrobial resistance. Without

adequate staffing and funding, FDA will lose its ability to track the circulation of drugs within the country and have little capacity to enforce drug quality standards. There is also a need to develop and/or update Standard Treatment Guidelines (STGs) for patient care and animal health. The Essential Medicines List must not remain only as a basis for procurement of drugs by the government but should serve as a powerful tool to prevent and contain AMR.

Moreover, there is a need to improve the dissemination of AMR scientific evidences generated through research in animals and humans for greater audience reach. This is necessary in order to translate the results into useful action, either, through the development of a technology, product or policy.

### **Prescribers, dispensers and consumers have inadequate knowledge, inappropriate attitudes and practices on antimicrobial use.**

The expertise of drug providers and dispensers, as well as patients' level of awareness, varies greatly. Limited surveys on doctors' prescribing habits show that pharmaceutical products are being prescribed inappropriately. Literature shows that antimicrobials account for a big slice of the total drug expenditures in the Philippines, representing the largest of any therapeutic group of drugs. However, information on their use on a national level has always been found to be limited. At best, conclusions can be inferred only from trends noted in tertiary training hospitals in Metro Manila. In one study, as much as

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two-thirds of the physician respondents acknowledged giving antimicrobials that they do not think were warranted at that time (Mary and Lopez, 2009). The most common STG non-adherence committed is the irrational prescription of broad-spectrum antibiotics and prolonged duration of chemoprophylaxis. These issues in humans are compounded by the extensive use of antimicrobials in animal husbandry as growth enhancers and prophylactic agents.

In relation to the pervasive practice of self-medication, the purchase of antimicrobials without doctor's prescription should not happen as they are categorized as prescription medicines. In certain occasions, the pharmacists who are supposed to educate the consumers are in fact acting as prescribers of antimicrobials. In some instances, there are drugstores operating without the supervision of pharmacist, leaving all the dispensing duties to pharmacy assistants who most likely have no adequate training on medicines and in counselling patients.

Patients and caregivers generally consider antibiotics to be relatively risk-free and are often not troubled by considerations of under treatment or development of resistant organisms. Widespread self-treatment often with the least effective agent in an incorrect dosage is considered a major factor in the development of bacterial resistance. There is a popular local practice of recycling prescriptions for recurring symptoms. Prescription sharing between friends and neighbours also happens.

There is as much underuse as there is overuse. Community purchases are often times made without prescriptions. There is significant relationship between the unit cost of drugs and patient compliance, proving that the socioeconomic status of the patient remains to be a cause of therapy problem. There is still a widespread lack of patient awareness that drug regimens should be completed, as exemplified by the common practice of discontinuing the treatment once symptoms subside. Financial constraints, the cultural concept of "hiyang", discontinuation of antibiotic upon relief of symptoms and the allocation for other forms of treatment are the top factors reducing patient's ability to purchase full course.

### **There is poor implementation of infection prevention and control measures in healthcare settings and communities.**

Effective infection prevention and control (IPC) is a major deterrent to the spread of AMR. IPC is not limited to the healthcare facilities, but it also includes the community down to the individual households. The country, through its different agencies (e.g. DOH and DA) has already made standards and guidelines to promote IPC in healthcare facilities. In addition, there are also professional organizations which are focused on promoting IPC in healthcare facilities (e.g. Philippine Hospital Infection Control Society). Education materials and other information dissemination tools are available for communities, especially with the program on Healthy Settings that is

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primarily about the promotion of health that necessarily includes sanitation, in places like schools and workplaces.

Though the framework for IPC is already in place, the standards, guidelines and various measures are not properly disseminated, or not strictly enforced. This may have stemmed from the lack of awareness about the implications and importance of effective IPC, lack of expertise, and lack of dedicated personnel in healthcare facilities across the country. Considering also that poor adherence to STGs results in irrational use of antibiotics, AMR surveillance is not one of the major functions of IPC programs in the hospitals. In most instances, AMR surveillance is not conducted.

### **The country has limited capacity to develop new antimicrobial drugs and diagnostic products.**

Research has always been an integral component of development. It is through this endeavor that new products and technologies arise that will provide concrete evidence on the need for improvements. The country has done a number of basic research in its quest for new antimicrobials. However, these activities are not sufficient since they have not evolved and resulted in the production of new drugs. Majority are student-initiated, preliminary screening tests with very limited funding. In the absence of a monitoring mechanism, even promising results are not pursued for completion or follow-through. In addition, there is minimal operational research on the

development of new antimicrobials and diagnostic tools in the Philippines.

### **Conclusion**

The country situation analysis clearly showed that combating antimicrobial resistance in the country would involve addressing three groups of problems: (1) need for strengthening existing efforts and systems (i.e. surveillance, laboratory, monitoring and evaluation of programs), (2) creation of new policies, guidelines and (3) fragmentation of efforts, initiatives and activities across stakeholders.

### **Recommendations**

With all the issues and gaps identified in the fight against antimicrobial resistance in the country, it is evident that the primary action that has to be taken is the creation of a duly constituted or designated body that would create a comprehensive national AMR plan and consolidate all existing and future efforts into one integrated AMR program. The plan would serve as the guide and template for activities to be implemented, enhanced and strengthened by the different stakeholders.

For the plan to become effective in preventing new emergence of antimicrobial resistance and limiting its spread, it should contain the following important provisions on sustainability, information dissemination, training and education and monitoring and evaluation of implementation of policies, guidelines and activities.

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### ***Sustainability***

1. Adequate financing should be in place in order to support the AMR program and sustain the involvement of stakeholders especially those who are most affected by AMR.
2. Adequate support should be made available for regulatory institutions in order to ensure equitable availability and affordability of safe, efficacious and quality medicines for patient care and veterinary use, as well as ethical practice of medical and veterinary practitioners.

### ***Information Dissemination, Training and Education***

1. Directed, evidence-based large scale and sustained campaigns and interventions for healthcare professionals and patients should be carried out to ensure rational and responsible use of medicines.
2. There should be a concerted and active effort towards research and development of innovative approaches for effective antimicrobials and diagnostics.

### ***Monitoring and Evaluation***

1. The surveillance system for AMR and antimicrobial use should be strengthened such that data from current surveillance programs and research in both human and veterinary health are linked, translated for

practical use, and utilized to guide AMR interventions.

2. A set of standards that would ensure rigorous and transparent procedures for testing, monitoring and reporting the quality, safety and efficacy of drugs and diagnostics should be in place and strictly implemented.
3. The existing essential medicines list should be made relevant based on up-to-date Standard Treatment Guidelines or Clinical Practice Guidelines with full consideration and inclusion of those for animal health conditions.
4. Infection prevention and control should be properly institutionalized, strictly implemented, monitored and evaluated in all hospitals, veterinary facilities and other health care settings.

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