



# SITUATION ANALYSIS

## Antibiotic Use and Resistance in Vietnam

The GARP- Vietnam National Working Group

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## Foreword

The global problem of antimicrobial resistance is particularly pressing in developing countries, where the infectious disease burden is high and cost constrains the replacement of older antibiotics with newer, more expensive ones. Gastrointestinal, respiratory, sexually transmitted, and nosocomial infections are leading causes of disease and death in the developing world, and management of all these conditions has been critically compromised by the appearance and rapid spread of resistance.

There is little doubt that the more exposure bacteria have to any antibiotic—the greater the “drug pressure”—the more likely it is that resistant strains will arise and spread. Antibiotic drug pressure is the single most important factor promoting development of drug resistance in bacteria. However, reasons for drug pressure are multi-factorial. Although drug resistance is primarily a medical problem, the causes of resistance—at least the pace of escalation—are ecological, epidemiological, socio-cultural and economic. Patients, physicians, veterinarians, clinics and hospitals, and retailers—from large pharmacies to local drug sellers—have little motivation (economic or otherwise) to weigh the negative impact of their use of antibiotics on others, especially those in the future. Standard responses, such as increasing surveillance and launching public information campaigns on the hazards of resistance—while being a necessary part of an overall policy response—may have limited impact on their own. In order to work, policy solutions must alter incentives for patients, physicians, and others in the health care system to act in society’s best interests. Evaluating policy solutions involves understanding infectious diseases in populations. Research on evaluating focused, context-specific policy solutions that are likely to have a significant impact on resistance is a first step. Translating these policy solutions to policy action is the second.

Antibiotic resistance currently does not top any list of national problems. Strategies to control antibiotic resistance should not drain resources from more pressing concerns. Done correctly, controlling antibiotic resistance should be either cost neutral or in fact, be one of the few health interventions that actually save money.

Here we present the situation analysis of antibiotic use and resistance in Vietnam. We used international papers, local papers and reports, and expert interviews to complete this analysis. This report gives insight into interventions that can be targeted to control inappropriate antibiotic use and resistance in Vietnam, while taking care not to diminish access to these, at times lifesaving, drugs.

**Dr. Nguyen Van Kinh**

*Chairman, on behalf of the GARP – Vietnam National Working Group*

## Executive Summary

The Global Antibiotic Resistance Partnership (GARP) aims to address the challenge of antibiotic resistance by developing actionable policy proposals in Vietnam and four other low- and middle-income countries: China, India, Kenya, and South Africa. GARP will develop the evidence base for policy action on antibiotic resistance and identify policy opportunities where research, advocacy, and information have the best chance of slowing the development and spread of resistance.

Since the initiation of *doi moi* reforms in 1986, Vietnam has experienced many positive changes: an increase in incomes and life expectancy, decreased childhood mortality, and improved access to health care and drugs, including antibiotics. Access to antibiotics has brought with it an uninvited but not unexpected guest, antibiotic resistance. Nevertheless, opportunities to conserve the value of antibiotics and improve the outlook for patients are still open.

In 1996, the MoH issued the National Drug Policy, which states, “Antibiotics are very important drugs in treatment, and therefore it is necessary to regulate the prescription, antibiotic use, and antibiotic resistance of most common bacterial pathogens as well as improve laboratory diagnosis.” This policy statement is even more relevant today, in 2010.

## The Global Problem of Antibiotic Resistance

Around the world, bacterial pathogens are becoming ever more resistant to antibiotics. The first-generation antibiotics are already of little use in many circumstances. Newer antibiotics are more expensive, and now even some last-resort antibiotics are losing their effectiveness. Recent evidence is the spread of carbapenem-resistant bacteria (ndm-1) in several countries in Asia and Europe. Like other shared resources, the effectiveness of antibiotics should be viewed as a precious commodity, to be protected and valued, not squandered through unnecessary use. The goal is that antibiotics be used only for bacterial infections that need to be cured by antibiotics.

## Antibiotic Resistance in Vietnam

- Vietnam already experiences high levels of antibiotic resistance. In recent years, individual studies have reported the following:
- Vietnam had the highest prevalence of penicillin-resistant (71.4 percent) and erythromycin-resistant (92.1 percent) *Streptococcus pneumoniae*—a very common cause of respiratory infections—of the 11 countries in the Asian Network for Surveillance of Resistant Pathogens (ANSORP) in 2000–2001.
- 75 percent of pneumococci are resistant to three or more classes of antibiotics.
- 57 percent of the samples of another common bacterial pathogen, *Haemophilus influenzae*, from children in Hanoi were resistant to ampicillin in 2000–2001. Similar rates were found in Nha Trang.

- Bacteria cultured from children with diarrhea are highly resistant. In most cases, oral rehydration therapy is the best treatment for diarrhea, yet one-quarter of children had been given an antibiotic before they got to hospital.
- Resistance is common among gram-negative bacteria (enterobacteriaceae): more than 25 percent of isolates tested in a Ho Chi Minh City hospital were resistant to third-generation cephalosporins in 2000–2001. A study published in 2009 reported that 42 percent of gram-negative bacteria were resistant to ceftazidime, 63 percent to gentamicin, and 74 percent to nalidixic acid in both the hospital and the community.
- Resistance is increasing. In the early 1990s in Ho Chi Minh City, 8 percent of pneumococcus isolates were resistant to penicillin. By 1999–2000, this had risen to 56 percent. Similar trends were seen in northern Vietnam.

Because of the high rates of resistance, many antibiotic regimens recommended in current treatment guidelines are unlikely to be effective. Because infectious diseases remain common in Vietnam, access to effective antibiotics is extremely important. The increasing resistance rates in Vietnam are now jeopardizing the overall effectiveness of antibiotic treatment.

## Drivers of Antibiotic Use and Antibiotic Resistance

The more antibiotics are used, the more antibiotic-resistant organisms will spread. Antibiotics are over-used both in the community—by people buying antibiotics after self-diagnosis or on the advice of a health-care provider—and in the hospital, where antibiotics may substitute for better infection control, broad-spectrum antibiotics may be used instead of narrow-spectrum drugs, and people may be given newer, expensive branded antibiotics instead of less expensive first-line generic products.

Some of the reasons for inappropriately high antibiotic use in Vietnam are discussed below.

### In the Community

**Out-of-pocket health-care expenditures.** User fees at public hospitals, health insurance schemes, the commercialization of the pharmaceutical industry, and the deregulation of the retail trade in drugs have led to significant improvements in the quality and accessibility of health care. However, they have also increased out-of-pocket health expenditures as a proportion of total health expenditures. The high out-of-pocket expenditures encourage people to bypass providers and purchase drugs—including antibiotics—directly, without proper diagnosis. Total drug sales have nearly tripled in value between 2001 and 2008, from USD\$500 million to USD\$1,400 million. No separate figures are available, but antibiotics are among the most widely used drugs, and they are often used inappropriately.

**Purchases without prescription.** Even though prescriptions are legally required, antibiotics (and a wide range of other drugs) can be purchased directly by consumers at pharmacies or drug outlets. Self-diagnosis is not very accurate, but self-treatment is very common. In a community-based study undertaken in 2007, 78 percent of antibiotics taken by the study participants were purchased in private pharmacies without prescriptions. Buying drugs directly is cheaper and faster than going to a practitioner.

**Lack of knowledge about appropriate antibiotic use.** A 2007 study evaluated knowledge about antibiotic use in rural Vietnam. Despite the existence of guidelines, knowledge about antibiotic use was poor, and

health-care providers often dispensed antibiotics inappropriately, for common colds and coughs. The type, dosage, and duration of treatment often did not comply with the guidelines for antibiotic use.

## In Hospitals

**Inadequate infection control and overcrowding.** Good infection control is essential to prevent the further spread of resistant bacteria. Hospitals are overcrowded, however, often with more than one patient in a bed, and waste management is suboptimal.

**Lack of adequate microbiology services.** Most hospitals do not have microbiology laboratories. Existing laboratories operate without requirements for internal and external quality assessments. Well-trained clinical microbiologists to improve laboratory quality are scarce. Data on resistance in Vietnam can therefore not be considered accurate.

**Lack of effective drug and therapeutics committees.** In 1997, the MoH requested that every hospital establish a drug and therapeutics committee to implement guidelines for drug use, give professional advice for rational antibiotic therapy, list the drugs commonly used in the hospital, inform its health-care workers about appropriate drug use, and organize antibiotic drug resistance monitoring and reporting. All central hospitals have such committees, but not all have credentialed pharmacists or microbiologists, and their resources are limited. Most lower-level health-care centers have no drug and therapeutics committees.

## In Agriculture

Antibiotic use is widespread in farm animals and aquaculture for growth promotion and infection prophylaxis and treatment. Pigs and poultry are supplemented with tetracycline and tylosin. Farmed shrimp, crabs, and fish are given quinolones and sulfonamides in concentrations several times higher than recorded in other countries. As a result, antibiotic residues are commonly found in land and sea animals raised in Vietnam, although most levels are within legal limits and most of the residues are of allowed antibiotics.

There are other signs of excessive antibiotic use. One survey showed that raw foods, including meat and shellfish, were contaminated with multidrug-resistant *Salmonella*. *Campylobacter* isolated from chickens has particularly high levels of resistance: 90 percent of isolates are resistant to nalidixic acid, 89 percent to tetracycline, and 82 percent to ciprofloxacin.

## GARP-Vietnam Research

One of the aims of GARP-Vietnam is to fill information gaps, and the GARP-VN National Working Group is currently undertaking several projects:

1. *Creating a senior peer network on antibiotic use and resistance.* Information-sharing channels will be established among several leading hospitals in collaboration with the Drug Administration. Approximately 20 hospitals will submit data to MoH regarding antibiotic use and resistance in their hospitals, and regular reports will be issued.
2. *Assessing the economic burden of resistance.* The most powerful argument for policymakers is

that resistance costs money, whereas antibiotic stewardship may save both money and lives. A study will assess current resistance levels of common bacteria cultured from blood and cerebrospinal fluid. The effect of resistance on the costs of antibiotic treatment will be compared with a baseline of antibiotic treatment before the emergence of resistance.

3. *Assessing the economic incentives for selling antibiotics at community pharmacies.* Questionnaires and direct observations of drug selling will be conducted in 15 rural and 15 urban pharmacies. The profitability of antibiotic sales for pharmacies will be estimated.

## OPPORTUNITIES FOR CONTROLLING ANTIBIOTIC RESISTANCE

Policy option	Action
Antibiotics are prescription only drugs.	Develop national action plan for antibiotic resistance.
Make antibiotics prescription-only	Enforce current law.
Make hospitals' drug and therapeutics committee effective	Enforce requirement for committees, define their functions and standards, and develop audit mechanisms. Give committees tools and guidance on antibiotic stewardship. Provide up-to-date, accurate resistance data.
Establish infection-control committees in hospitals	Give committees sufficient resources to carry out their activities and improve infrastructure. Establish standardized indicators to monitor progress, such as hospital-acquired infection rates by department and hand-washing compliance.
Track national antibiotic resistance	Develop national testing and quality control guidelines. Fund resistance testing, quality control, training, and reporting. Issue annual national report on both antibiotic use and resistance.
Monitor antibiotic use in hospitals	Standardize antibiotic usage indicators to international units (e.g., defined daily dosage per 100 bed-days). Issue annual national report on both antibiotic use and resistance
Develop curriculum for medical and pharmacy schools	Teach and train professionals on antibiotic resistance and appropriate antibiotic use.
Develop treatment guidelines	Ensure timely and evidence-based updates of treatment guidelines for infectious diseases.
Establish pharmacovigilance center	Engage pharmacovigilance center in curbing inappropriate antibiotic prescribing.
Conduct public education campaign	Create awareness and educate Vietnamese public about appropriate and inappropriate antibiotic use.



Set up vaccination programs	Achieve high vaccination coverage for communicable diseases to prevent bacterial infections that require antibiotic treatment.
Enhance laboratory capabilities	Ensure quality laboratory testing. Consider establishing national reference center (center of excellence) for antibiotic resistance testing. Create network for sharing data, guidelines, and expertise.
Curb antibiotic use in agriculture	Enforce current law. Set up national antibiotic use and resistance surveillance system. Issue annual national report on both antibiotic use and resistance. Develop regulations on antibiotic use before harvesting.

Vietnam's many opportunities to control and reverse antibiotic resistance will be fully analyzed in the final GARP-VN report, to be completed in spring 2011. Policy options—some more promising than others—are listed below. The working group will assess these options by estimating their costs, human resource and technical feasibility, time frame for implementation, and likely effects in Vietnam. A short list of the most promising policy options will then be recommended.

This first-situation analysis on antibiotic resistance in Vietnam introduces an important issue to all stakeholders—government, pharmacies, doctors, clinics, nongovernmental agencies, the pharmaceutical industry, and patients. We are all responsible for addressing the problem, and concerted action is needed to maintain the effectiveness of antibiotics while ensuring access to these life-saving drugs.

**On behalf of the National Working Group,  
*Nguyen Van Kinh, chairman***

**Director National Hospital for Tropical Diseases  
*Hanoi, Vietnam***

## I. Basic Health and Economic Indicators

### I.1. Introduction

This overview of the health system in Vietnam provides the context in which to view the situation of antibiotic resistance. It presents information on the background of national health policy, the organization of the healthcare system, and access to healthcare and drugs. National health and demographic indicators are listed, and the burden of major bacterial causes of morbidity and mortality briefly reviewed.

#### I.1.1. Country Profile and Demographic Situation

The Socialist Republic of Vietnam is situated on the Indochina Peninsula, bordering China, Laos, and Cambodia (Figure 1). Vietnam is approximately 331,000 km<sup>2</sup> in area, which is close to the size of Germany.

With a population of more than 88 million, Vietnam is the 13th most populous country in the world, with a population density of approximately 265/km<sup>2</sup>. The median age is a relatively young 27 years, compared to 39–41 years in Europe. Population growth has decreased in the past 20 years, now averaging 1.98 births per woman (Table 1). Approximately 28 percent of the population lives in urban areas, with an annual urbanization rate of 3.1 percent per year.

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Vietnamese children have good access to education, resulting in a literacy rate of 90 percent. By the end of 2005, 81 percent of households in the country had access to electricity. The government aims for 95 percent of all households to have electricity by 2010. In 2010 it is expected that 85 percent of the population will have access to clean water. However, progress on improved sanitation has been slower and the 2010 target of 70 percent is unlikely to be met<sup>2</sup>.

Figure 1: Vietnam



Source: Map provided by OUCRU, made by ArcGIS software

#### I.1.2. Economic Performance and Poverty Incidence.

In the past decade, Vietnam has been one of the world's best performing economies. The real gross

domestic product (GDP) grew an average of 7.3 percent per year and per capita income rose by 6.2 percent per year during 1995-2005. The economy has proven resilient to shocks and negative impacts like SARS and avian influenza. The average annual income per capita rose from 260 USD in 1995 to 835 USD in 2007. At this pace Vietnam is anticipated to achieve an average annual income per capita of 1,000 USD in 2010, making Vietnam a middle income country<sup>3</sup>.

Vietnam is transitioning from a rural to an industrial economy. Between 1995 and 2005, the share of the agricultural sector in the GDP declined from 27 percent to 21 percent, while that of industrial sector rose from 29 percent to 41 percent. In 2007, Vietnam became a member of the World Trade Organization.

Vietnam has also been successful in reducing poverty. The general poverty rate fell from 58.1 percent in 1993 to 22 percent in 2007. The high growth rate and rapid poverty reduction has come with a modest increase in inequality. The incidence of poverty is highest in the remote northern and central highlands and lowest in the southeast and in large urban centers. However, analysis of the density of poverty reveals that most poor people do not live in the poorest districts but in the two lowland deltas, where poverty incidence is intermediate (Figure 2).

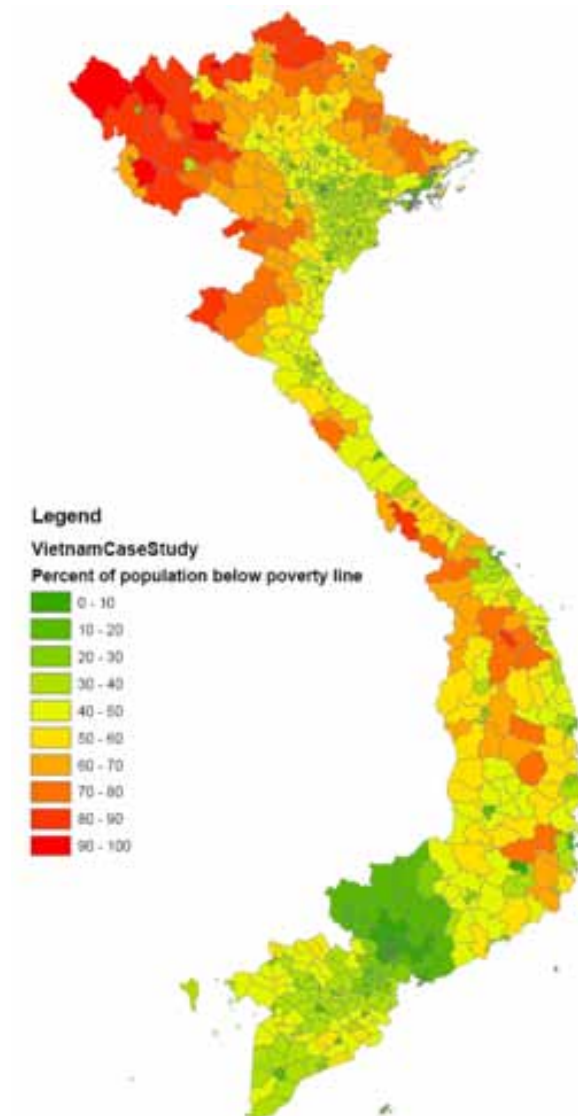
Vietnam has made good progress towards achieving the Millennium Development Goals (MDGs). Five of the ten main MDG targets set for 2015 have already been achieved, including poverty and hunger reduction.

### 1.1.3. Key Health Indicators

Life expectancy is high compared to other developing nations, with current estimates at 69 years for males and 74 years for females, which is similar to that of Brazil and Greece. Overall morbidity and mortality have decreased among vulnerable groups such as women and young children. Under-five child mortality has decreased by more than half, from 58 per 1000 live births in 1990 to 25 per 1,000 live births in 2008<sup>5</sup>. Maternal mortality is relatively low at 150

per 100,000 births in 2005, when compared to some neighboring countries, such as Cambodia where maternal mortality was 540 per 100,000 births in 2004<sup>6</sup>.

**Figure 2: Vietnam poverty map**



Source: Poverty and Food Security Map<sup>4</sup>

Other key indicators of child health include vaccination coverage and malnutrition. The Vietnamese government funds 88 percent of the Expanded Program on Immunization (EPI) recommended vaccines. As a result, 90 percent of Vietnamese children receive the recommended vaccinations, includ-

ing BCG, DPT, HepB, polio, and measles. Vaccination against *Haemophilus influenzae* B (Hib) started in 2009. Vaccination coverage is lower in poorer and remote areas<sup>7</sup>. The pneumococcal vaccine is not scheduled to be introduced through EPI and is currently only available commercially in Vietnam.

Malnutrition is another important health indicator. One of the MDGs was to reduce hunger by half before 2015 and this was achieved before 2006 in Vietnam. Similar to other indicators, malnutrition is more common in the remote areas, where poverty is more prevalent and the ethnic minorities live. The government acknowledges that more should be done to improve living conditions and health in the remote area.

**Table 1: Key development and health indicators Vietnam**

Indicator	Year	Number
Population (millions)	2010	89.57
Pop growth rate (%)	2010	1.096
Urbanization rate (%)	2005-2010	3.1
Life expectancy (male / female)	2010	69/74
GDP per capita (PPP) (US\$)	2009	2,900
Infant mortality rate (per 1000)	2010	21.57
Maternal mortality ratio (per 100,000 live births)	2005	150
Poverty rate (%<1.25\$/d)	2008	14
Access to clean water (%)	2006	92
Access to sanitation (%)	2006	65
Adult literacy rate (%)	2003-2008	90.3

Sources: World Bank, CIA World Factbook, UNICEF Vietnam<sup>6</sup>.

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## 1.2. Structure of the Healthcare System

### 1.2.1. Introduction

Twenty-five years ago, Vietnam's healthcare system was solely supported by the central government and the public sector was the only provider of healthcare services. At that time, drugs were scarce. To make health care more accessible, in 1986 the government began to implement market reforms, including the introduction of user fees at public hospitals, health insurance schemes, the legalization of the pharmaceutical industry, and the deregulation of the retail trade in drugs<sup>10</sup>. Such reforms have transformed the structure of Vietnam's health care into a mixed public-private system, where most drugs are now available at relatively low cost.

### 1.2.2. Organization and Distribution of Healthcare Services

The public healthcare system is divided into four hierarchical levels from central to commune (See Figure 1). Each level comprises several units that are responsible for different aspects of healthcare including treatment, prevention, training, research, and drug distribution. At the national level, the mandate for supervision and coordination, formulation of policies, and mobilization of resources, rests with the Ministry of Health (MoH).

### Facilities

In spite of a rapidly expanding private health-care sector, the public sector remains as the main resource for prevention, research and training. There are 961 large hospitals in Vietnam, of which 41 are national (or central) hospitals, and the remaining are provincial level hospitals. Most national hospitals are located in the capital, Hanoi. At the regional level there are 609 district hospitals and 10,866 community health centers in communes<sup>12</sup>. Commune health centers and regional polyclinics are responsible for

**Figure 3: Health care system<sup>11</sup>**

Level	Ministry of Health	Other government institutes	Private health care
<b>Central</b>	National hospitals Preventive institutes Medical schools Pharmacy schools Health service provision Drug companies	Military hospitals Police Agriculture Post and telecom Traffic and transport	
<b>Provincial</b>	Provincial hospitals Secondary medical school Preventive centers		Private clinics Private pharmacies Private hospitals
<b>District</b>	District hospitals Preventive centers		
<b>Commune</b>	Commune health center Polyclinic (regional)		

Source: Thuan, N.T., Lofgren, C., Lindholm, L. & Chuc, N.T. Choice of healthcare provider following reform in Vietnam. *BMC Health Serv Res* 8, 162 (2008).

primary health care delivery and, except for emergencies, are the first point of contact with the public health care system. These primary care facilities provide preventive and curative services and refer patients to larger centers for advanced diagnostic and therapeutic services. The commune health stations are managed by the District Health Centers.

In 2008, the MoH estimated the average bed occupancy rate across all levels of public hospitals at 128.52 percent across center hospitals and 126.66 percent across provincial hospitals. This rate can increase to over 200 percent in some center hospitals during infectious disease outbreaks. For instance, the bed occupancy rate reached 285 percent in Children’s Hospital Number 1 in Ho Chi Minh City<sup>13</sup>. Overcrowding of public hospitals is one of the major problems across the Vietnamese healthcare system as more patients are seeking both inpatient and outpatient care from public hospitals instead of their local medical stations. A study of 2587 patients carried out from 2001 to 2006 across 6 hospitals in Ho Chi Minh City investigated the reasons for hospital overuse. It turned out that many patients with common

illnesses were going to the outpatient clinics of specialized hospitals (44—85.1 percent) instead of seeking primary health care (67.7 percent). Most of them were transferred from provincial hospitals (85.5 percent) leading to an increase of bed occupancy rate (107.8%—130.0%) and out-patient treatment target (114.4—145 percent). With this workload, a doctor may have to examine 50 to 100 patients per day, making it difficult to ensure adequate quality of care<sup>14</sup>.

Diagnostic testing facilities are limited in regional-level health care centers and often, patients have pay for diagnostic tests. Hospitals usually prefer to provide diagnostics that are profitable, but infectious disease diagnostics are often not profitable because they require expensive equipment and infrastructure. The high work load and lack of diagnostic testing are considered factors leading to the frequent and inappropriate prescribing of antibiotics.

Since the market reforms in 1986, nearly 70 private hospitals, 30,000 private clinics, and 21,600 private pharmacies and distributors have been established<sup>15</sup>. The bed occupancy rate in private hos-

pitals was 67.8 percent in 2006 and 74.7 percent in 2007, according to an inventory of all 731 hospitals in the country conducted by the MoH Medical Service Administration<sup>15</sup>. The number of inpatient visits treated in private hospitals accounted for a relatively small share of total inpatients in all levels of public hospitals; it accounted for 1.9 percent in 2006 and 2.2 percent in 2007<sup>15</sup>.

## Human Resources

There is a shortage of trained staff in the health-care sector with a low nurse-to-doctor ratio, a lack of specialists and trained managers, and many vacancies in rural and remote areas (See Table 2)<sup>16</sup>. Such scarcity of healthcare workers is particularly acute in remote areas compared to big cities. The rate of health care staffs with university degrees is 4.3 doctors per 10,000 inhabitants and 0.2 pharmacists per 10,000 inhabitants in the Mekong delta<sup>17</sup>. In contrast there is a significant presence of such healthcare personnel in the big cities, up to 9 doctors per 10,000 inhabitants<sup>18</sup>. According to the Ministry of Health, in 2009 Vietnam has 1.5 pharmacists per 10,000 inhabitants with 52 percent of such pharmacists concentrated in two big cities (Ho Chi Minh City and Hanoi), intensifying the shortage of well-educated pharmaceutical workforce in remote areas<sup>19</sup>.

**Table 2: Health care work force from 2005-2008<sup>16</sup>**

Categories	2005	2008
<b>Medical staff</b>		
Medical Doctors and higher	48,215	56,208
Assistant doctors	48,059	49,213
Nurses	49,536	67,081
Midwives	17,610	22,943
Technicians	8,771	11,586
Traditional medicine practitioners	293	882
Doctors per 10,000 inhabitant	5.88	6.52

## Pharmaceutical staff

Pharmacist and higher	6,360	10,524
Assistant Pharmacist and 2nd degree technicians	10,424	15,748
Elementary pharmacist	8,298	9,726
Pharmacist per 10,000 inhabitant	0.78	1.22

Source: Health Statistics Yearbook 2008 (Ministry of Health)

## Financing

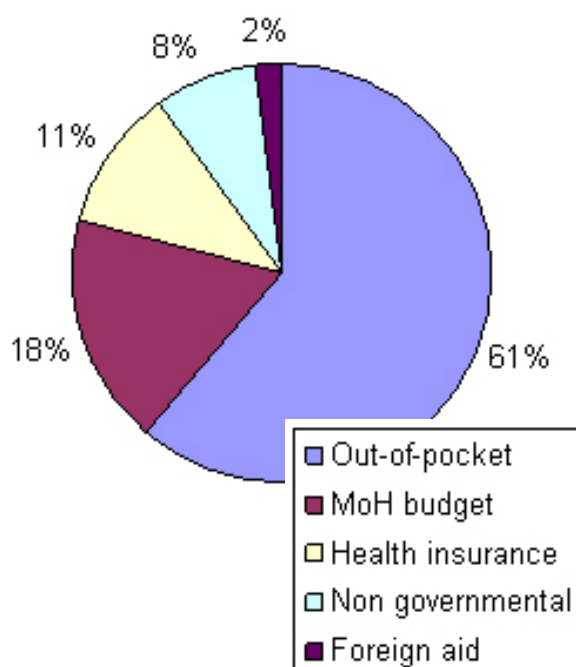
Since the market reforms, the healthcare system has generated multiple funding sources. Due to limited financial resources and the vision to make health care more accessible, the government had decided to implement several measures, including the introduction of user fees at public hospitals, health insurance schemes, legalization of the pharmaceutical industry, and deregulation of the retail trade in drugs<sup>10</sup>. These changes have led to significant improvements in the quality, availability and accessibility of healthcare services in Vietnam. However, such measures have also led to an increase in out-of-pocket health expenditures as a proportion of total health expenditures.

Health spending in Vietnam has increased since the reforms and it accounted for approximately 5-6 percent of GDP in 2005<sup>15</sup>. This is relatively high compared to other countries in the region, such as China, where healthcare spending accounts for 5 percent), and Thailand, where it accounts for 4 percent<sup>20</sup>. The government contributed 31 percent of total health expenditures in 2006, which is low compared to other low- and middle-income countries, which averaged about a 45 percent government share of total health expenditure<sup>15</sup>. For the same year, out-of-pocket expenditures in Vietnam accounted for 61 percent and the remaining 8 percent came from non-government organizations (figure 4)<sup>21</sup>. Out-of-pocket expenditures are significantly higher in Vietnam compared to other developing countries in the region, such as



China (39 percent) and Malaysia (45 percent)<sup>15</sup>.

**Figure 4: Composition of total health expenditure 2006<sup>15</sup>**



Source: Ministry of Health, National Health Accounts 2000-2006 (Hanoi, 2008)

### Health Insurance

By the end of 2007, approximately 42 percent of the total population was covered by health insurance (table 3). The government runs the health insurance system and provides free health insurance (HI) to

vulnerable groups, such as the poor and pensioners. Health insurance covers the cost at a local health station where a person is registered but people need permission to get insured care at a hospital or at a health station outside their own commune<sup>22</sup>. Such health insurance only covers 30 percent to 70 percent of total cost, depending on the level of the hospital.

Since 2005, healthcare has been provided free of charge for children under the age of 6 while health insurance is compulsory for wage earners. The compulsory health insurance premium is about 3 percent of the base salary, of which 1 percent is paid by employee and the remaining 2 percent is paid by the employer<sup>15</sup>. For others, health insurance is voluntary and equivalent to 3 percent of general minimum salary for people who are not salaried. Patients have to pay 20 percent co-payment of health care costs, but the co-payment is eliminated if out-patient care costs less than 100,000 VND per visit and less than 200,000 VND for in-patient care<sup>22</sup>. For high cost medical services, the total amount covered by health insurance cannot exceed 20,000,000 VND<sup>15</sup>. Although health insurance policies have been implemented in some private hospitals, the government covers 64.5 percent of the total health insurance budget<sup>15</sup>.

### 1.2.3. Access to Healthcare and Drugs

Vietnam has a national network of commune-level health stations with at least one medical staff member. Remote areas may have more health stations to reduce travel time as these areas have poor roads and transportation. The poor and those with health

**Table 3: Number of Health Insurance members nationwide, 2005-2007<sup>15</sup>**

		2005		2007	
		Member	%	Member	%
Compulsory	Non-poor	9,154,308	39.8	11,606,569	31.8
	Poor	4,726,324	20.5	15,498,284	42.5
Voluntary		9,133,134	39.7	9,379,349	25.7
Total		23,013,766	100	36,484,742	100

Source: Source: Ministry of Health, National Health Accounts 2000-2006 (Hanoi, 2008)

insurance seek care at commune health centers more regularly than do wealthier citizens. Wealthy households with greater access to government hospitals consume a larger share of health services<sup>23</sup>.

Health seeking behavior has changed since the market reforms, private healthcare facilities provide wealthy citizens with greater access to more and better health services while the poor access medicines via self-medication or private pharmacies. Self-medication is cheaper and less time consuming than consulting a health care provider. According to one study, the average household expenditure per episode of illness is 19,616 VND for self-treatment, 35,206 VND for private providers, and 95,795 VND for public providers. This discrepancy in cost explains the preference for self-medication which results in many cases of inappropriate drug use. Self-treatment with prescription drugs is possible because pharmaceutical regulations prohibiting the sale of many drugs (including antibiotics) without a prescription are not enforced<sup>10</sup>.

### 1.3. Infection Control

A recently updated circular on infection control in healthcare institutions took effect in December 2009<sup>24</sup>. The “Guideline on the Implementation of Infection Control in Health Care Institutions” was developed with technical assistance from WHO. This is an effort of the MoH to improve the national capacity for infection control and to make health-related activities safer for patients, staff, and visitors. The guideline covers both public and private health care facilities and covers various areas of infection control such as hand hygiene, sterilization, standard precaution and isolation, surveillance of hospital acquired infections, environmental cleaning, waste management, food safety, laundry, and corpse handling. An implementation working group has been established to create national operating procedures to implement the guideline. The guideline requires surveillance of hospital-acquired infections in all healthcare facilities. Furthermore, Vietnam has supported the WHO Global Patient Safety Challenge, “Clean Care is

Safer Care” since 2009.

A recent study in northern Vietnam compared the results of two surveys conducted in 2005 and 2007 to study nosocomial infection control across 51 hospitals<sup>25</sup>. It was found that central hospitals in Hanoi showed most improvement while most district hospitals had infection control committees by 2007, but were constrained by limited resources. Local hospitals were not well financed and lacked resources and opportunities for further training. Furthermore, it was noted that several guidelines were outdated and were inappropriate for most hospitals<sup>25</sup>.

Successful implementation of infection control measures is difficult because most hospitals in Vietnam are old and overcrowded and the staffs have high workloads. Bed occupancy rates can exceed 100 percent which means more than one person occupies a hospital bed. This occurs regularly during communicable disease outbreaks like cholera, dengue, or influenza. Furthermore, the family is essential in taking care of the patient by bringing food, feeding, and cleaning, leading to even more crowded conditions.

A study was conducted to observe hand hygiene compliance among healthcare workers in 29 clinical departments, including surgery, obstetrics, and emergency at 1 center hospital and 8 provincial hospitals in North Vietnam. Forty percent of the workers were aware of the basics of hand hygiene but the overall compliance was only 13.4 percent, with 17.7 percent compliance in center hospitals and 10.7 percent compliance in provincial hospitals<sup>27</sup>. Another study conducted at several hospitals in north Vietnam the standard of hand washing facilities was low, with a lack of availability of cleaning products such as water, soap, and wipes<sup>27</sup>. This study also pointed out that about one-third of the hospitals in the study met the standard requirement for hand washing stations<sup>27</sup>. According to a study conducted by WHO, less than 40 percent of patient rooms have a hand washing sink<sup>28</sup>.

Proper waste management is a major problem in Vietnamese hospitals. A study conducted in 12 hospitals across northern Vietnam in 2006 revealed that hospital waste water was discharged directly into the



rice fields<sup>29</sup>. Other findings were that hospital waste was dumped beside streams and hospital grounds also displayed poor sanitary conditions with inappropriate disposal of used syringes<sup>30</sup>. It was reported that hospitals in Ho Chi Minh City are discharging about 14,000 cubic meters of untreated wastewater into public sewers and rivers every day<sup>31</sup>.

## 1.4. Burden of Disease

Vietnam has a relatively high burden of infectious diseases, including a large portion of bacterial diseases, potentially treatable with antibiotics. This section reviews the burden of disease in Vietnam and addresses the main bacterial agents of common hospital and community-acquired infections.

### 1.4.1. National Indicators

Mortality is an important indicator for measuring a country's health and development. While deaths from infectious diseases are still relatively common, Vietnam is also beginning to experience higher rates of death from cardiovascular disease, a sign of a transitional economy and population<sup>32</sup>.

**Table 4: Top five causes of mortality in Vietnam<sup>12</sup>**

Cause of mortality	Incidence (per 100,000 inhabitants)
Intracranial injury (traumatic brain injury)	2.53
Human Immunodeficiency Virus (HIV)	2.43
Pneumonia	2.34
Intracerebral hemorrhage	1.27
Transport accident	1.10
Acute myocardial infarction	0.85

Source: Health Statistics Yearbook 2008 (Ministry of Health)

### 1.4.2. Burden of Bacterial Diseases

Infectious diseases remain common in Vietnam, but data are not collected routinely documenting either morbidity or mortality. Most data are derived from site-specific, hospital-based studies but the majority of illnesses and deaths occur outside these hospitals. Nevertheless, even such limited data from hospital based studies provide insight into the impact and epidemiology of bacterial diseases requiring antibiotic treatment.

#### Burden of Vaccine Preventable Diseases

Recent estimates from UNICEF suggest that *Streptococcus pneumoniae* accounts for more than half of all childhood deaths due to pneumonia each year worldwide. The estimated incidence rate of invasive pneumococcal disease (IPD) was 48.7 per 100,000 children during 2005-2006 in Khanh Hoa Province<sup>33</sup>. Of the total enrolled children, 69 percent were hospitalized for pneumococcal pneumonia and 11 percent for pneumococcal meningitis<sup>33</sup>. *S. pneumoniae* (35.8 percent) was the most commonly isolated bacteria from children under 5 years of age admitted with acute respiratory infections to Saint Paul hospital in Hanoi during 2003<sup>34</sup>. There is no ongoing population-based surveillance for IPD and there are no plans to introduce pneumococcal vaccine in Vietnam.

Prior to the introduction of routine childhood immunization with conjugate *Haemophilus influenzae type b* (Hib) vaccine, it was estimated that there were 600,000 deaths due to Hib infection worldwide each year<sup>35</sup>. In Vietnam, there were at least 5,107 hospitalizations with *H. influenzae* pneumonia per year among children under 5 years of age prior to introduction of vaccines<sup>36</sup>. A study showed that Hib has the second highest incidence rate (22.9 per 100,000) of invasive bacterial disease among children under the age of 5<sup>33</sup>. The age group-specific incidence rate for Hib disease was highest among infants (87.9 per 100,000 infants) and among children aged 2 years (32.9 per 100,000 children)<sup>33</sup>.

An epidemiological study of Hib-associated invasive meningitis in Hanoi during 2000-2002 found

that the estimated incidence of Hib meningitis was 12 per 100,000 among children under the age of 5 years and 26 per 100,000 among children under the age of 2 years<sup>36</sup>. Meningitis due to Hib infection in children less than 2 years of age accounted for 88-94 percent of total bacterial meningitis in children under 5 years of age<sup>35</sup>. A study conducted on children with meningitis admitted to the National Hospital of Pediatrics between 2001 and 2005 showed that 24 percent (129/529) of the cerebrospinal fluid (CSF) (from spinal taps) samples were Hib positive by culture, of which 59.7 percent (77/129) were resistant to amoxicillin<sup>37</sup>. The incidence of Hib disease reported in this study was 22.9 cases per 100,000 children, higher than the reported incidence of 12 (in Hanoi) to 18 (in Vietnam overall) per 100,000 in two other analyses<sup>33</sup>. It is expected that the recent introduction of the Hib vaccine will significantly reduced the incidence of this invasive disease in children.

*Salmonella typhi* was commonly cultured from the blood from febrile patients, but now vaccination and improved sanitation has reduced the burden of *S.typhi* drastically. Vietnam has adopted the Vi polysaccharide vaccine against typhoid fever in high-incidence areas, for children aged 3 to 10 years<sup>38</sup>.

## Meningitis

In Vietnamese children the causes of bacterial meningitis are mainly *H. influenzae* and *S. pneumoniae* as described above. In adults, *Streptococcus suis* is the most common cause of bacterial meningitis, accounting for 26 percent of all culture positive meningitis<sup>39</sup>. *S. suis* is a pig bacterium that is transmitted to humans when processing or eating uncooked pig products. Other important pathogens are *S. pneumoniae* (11.1 percent), *N. meningitidis* (2.4 percent), *Klebsiella* spp. (2.7 percent), *E. coli* (1.8 percent), and *S. aureus* (0.7 percent) and *Haemophilus influenzae* (0.9 percent)<sup>39</sup>. Ceftriaxone is used for the empiric treatment of meningitis in Vietnam. Nearly all—50/55 (90.9 percent) of *S. pneumoniae* isolates—are susceptible to ceftriaxone, with the remaining 5/55 (9.1 percent) having intermediate resistance<sup>40</sup>.

## Bacteremia

In one central general hospital in Hanoi, 8 percent of all blood cultures submitted for testing were positive for bacteremia in 2009<sup>41</sup>. The most common cultured micro-organisms were *K. pneumoniae* (18.3 percent), *E. coli* (17.6 percent), *Staphylococcus aureus* (11.9 percent), *Pseudomonas aeruginosa* (5.9 percent) and *Acinetobacter baumannii* (4.4 percent). The rates of antibiotic resistance were: ESBL positive *K. pneumoniae*, 16.2 percent; ESBL positive *E. coli*, 21.5 percent<sup>41</sup>; and vancomycin intermediate *S. aureus* (VISA), 4 percent<sup>42</sup>. The common pathogens from blood culture from an infectious disease hospital in Hanoi between 2008 to 2009 were *E. coli* (19.3 percent), *K. pneumoniae* (15.2 percent), *S. aureus* (13.8 percent), and *S. suis* (9.7percent)<sup>43</sup>. In Ho Chi Minh City, the most commonly cultured bacteria from blood were *E. coli*, *S. typhi*, *Klebsiella pneumoniae* and *Streptococcus* spp<sup>44</sup>. Other important pathogens cultured from blood samples in Vietnam are *Burkholderia pseudomallei* (cause of melioidosis) and the fungi *Penicillium marneffeii* and *Cryptococcus neoformans* in HIV patients.

## Acute Respiratory Infections (ARIs)

In Vietnam, ARIs are among the largest contributors to the burden of infectious disease and pneumonia is the second most common cause of death from infections. Commune health stations report that ARIs are the most common diagnosis at their facilities and the most common reason for prescribing antibiotics<sup>45</sup>. Most cases of ARI are caused by viruses, including rhinovirus, RS virus, influenza, and others [Unpublished laboratory data OUCRU]. Bacterial respiratory pathogens include *S. pneumoniae*, *K. pneumoniae*, *H. influenzae*, *Moraxella catarhalis*, and *S. aureus*. Unlike developed countries, *K. pneumoniae* is a common cause of severe community-acquired pneumonia among adults In Vietnam [Unpublished laboratory data OUCRU-NHTD].

## Diarrheal Diseases

The burden of diarrheal disease in Vietnam has

decreased with improved living standards, especially access to clean water and sanitation. Despite this, there have been regular cholera outbreaks in North Vietnam since 2007<sup>46</sup>. From March 2001 to April 2002, 587 children who came to a hospital in Hanoi with diarrhea were tested for diarrheal pathogens<sup>47</sup>. Of the children who visited the hospital, 67.3 percent were diagnosed with at least one viral or bacterial pathogen, including rotavirus (47 percent), diarrheagenic *E. coli* (23 percent), *Shigella* spp (5 percent), and enterotoxigenic *Bacteroides fragilis* (7 percent). No *Salmonella* spp or *Vibrio cholerae* were isolated. A large percentage of *E. coli* and *Shigella* spp were resistant to ampicillin, chloramphenicol, and trimethoprim/sulfamethoxazole (co-trimoxazole). *E. coli* isolates were highly resistant to antibiotics: 86.4 percent were resistant to ampicillin (AMP), 77.2 percent were resistant to chloramphenicol (CHL), and 88.3 percent were resistant to trimethoprim/sulfamethoxazole (SXT), respectively. Nearly 89 percent of the *Shigella* strains were resistant to trimethoprim/sulfamethoxazole, 75 percent were resistant to ampicillin, and 53.6 percent were resistant to chloramphenicol<sup>47</sup>. The children presented with fever (43.6 percent), vomiting (53.8 percent), and dehydration (82.6 percent). 162 out of 587 (27.6 percent) children had been given antibiotics even before seeking hospital care. Most of the children in this study were from poor households living in unhygienic conditions<sup>47</sup>.

### Sexually Transmitted Infections (STI)

After the first HIV case was reported in Vietnam in 1990, the number of reported HIV infections and AIDS cases grew rapidly in all provinces<sup>48</sup>. Cumulative reported data as of 31 December 2008 were 179,735 cases of HIV and 71,119 cases of AIDS<sup>12</sup>. Vietnam's HIV epidemic is still in a concentrated phase with the highest sero-prevalence rate among key populations at higher risk, including injecting drug users (IDUs), female sex workers (FSWs) and men who have sex with men (MSM)<sup>49</sup>. The prevalence rate in the overall population is estimated at 0.53 percent<sup>49</sup>. There have been a total of 15,007 deaths due to AIDS in Vietnam<sup>49</sup>. HIV exists in all 63 provinces/cities, in 96 per-

cent of the 659 districts and in more than two-thirds of the 10,732 wards/communes<sup>49</sup>. Of all reported HIV cases, 78.9 percent are in the age group 20–39, with males accounting for 85.2 percent<sup>49</sup>. The age group of people living with HIV is shifting to younger people and heterosexual transmission is becoming more significant<sup>49</sup>.

In a rural Vietnamese setting in 2007, 37 percent of sexual active women were diagnosed with a STD or reproductive tract infection<sup>50</sup>. Common infections were candidiasis (26 percent), bacterial vaginosis (11 percent), followed by hepatitis B (8.3 percent), *Chlamydia trachomatis* (4.3 percent), *Trichomonas vaginalis* (1 percent), *Neisseria gonorrhoeae* (0.7 percent), and genital warts (0.2 percent)<sup>50</sup>. HIV and syphilis were not detected. Half percent of the STI cases were asymptomatic and diagnosis of Chlamydia was more common among those of high economic status<sup>50</sup>.

### Hospital Acquired Infections (HAIs)

At present there are no national estimates of the rates and burden of HAIs in Vietnam. However, new guidelines from the Ministry of Health will require health facilities to record HAIs.

Several studies on HAIs have been carried out in Vietnam, mainly at Bach Mai and Cho Ray Hospitals. At Bach Mai Hospital, surgical site infections (SSIs) were associated with increased post-operative length of stay and direct costs. The extra hospital stay attributable to SSIs was 8.2 days and the excess direct costs was 110 US\$ per patient<sup>51</sup>.

In a cross-sectional study in 36 hospitals in the north of Vietnam in 2006–2007 including 2 center hospitals, 17 provincial hospitals and 17 district hospitals, it was observed that 553 out of 7,571 (7.8 percent) patients developed HAIs<sup>27</sup>. Most common were pneumonia (41.9 percent), SSIs (27.5 percent), and gastro-intestinal infections (13.1 percent). The most commonly isolated micro-organisms were *Pseudomonas aeruginosa* (31.5 percent), *Acinetobacter baumannii* (23.3 percent), and *Candida* spp (14.4 percent). HAIs were most common in pediatric units, intensive care units and surgical wards<sup>27</sup>.

The prevalence rate of HAIs was low, 5.9 percent, in Bach Mai Hospital during 2006. Of all the infections detected 75 percent were respiratory tract infections, 10 percent were urinary tract infections, and 5 percent were digestive tract infections. Common pathogens were *P. aeruginosa* (28.6 percent), *A. baumannii* (23.8 percent), *K. pneumoniae* (19 percent) and *Candida* spp (14.3 percent)<sup>52</sup>. About half of the patients used antibiotics before an HAI was diagnosed<sup>53</sup>. At Cho Ray Hospital, the most common pathogens causing HAIs were Gram negative bacilli, including: *K. pneumoniae* (25 percent), *P. aeruginosa* (24 percent), *A. baumannii* (18 percent), and *E.coli* (19 percent)<sup>54</sup>. *S. aureus* does not seem to be a common cause of HAIs in Vietnam.

A study conducted in ICUs and departments of surgery and obstetrics in three district general hospitals including Quang Ninh, Hoa Binh, Dien Bien, in 2005 reported the overall rate of HAIs as 17.3 percent<sup>55</sup>. SSIs accounted for 55 percent of total infections, urinary tract infections for 21 percent, and lower respiratory tract infections for 17 percent<sup>55</sup>.

## II. Antibiotic Supply Chain and Management

This section reviews the supply chain and management systems for antibiotics in Vietnam. It provides information pertaining to national policy documents and their relationship with drug supply and distribution, the position of antibiotics in therapeutic guidelines and dispensing regulations, and the current status of pharmaceutical management.

### 2.1. Legal Framework of Antibiotic Dispensing

Several departments of the Ministry of Health (MoH) regulate operations at private and public health care facilities, including pharmacies, and issue drug policies. The Drug Administration is responsible for the registration of drugs, licensing of pharmacies and drugstores, drug circulation permits, drug price policies, import and export, drug distribution, drug quality control, domestic manufacture and monitoring the drug supply chain. The Medical Service Administration is responsible for hospital related activities, including treatment guidelines. This department also regulates and monitors health insurance. The Department of Health Inspection is responsible for checking the prices at all pharmaceutical vendors (both hospital and community pharmacies) and for preventing corruption. In 2006, there were 230 full time health inspectors throughout the country, supplemented by 1000 collaborators who provide particular expertise in specific areas, and 30 personnel at the central level<sup>56</sup>.

In the animal sector, two departments of the Ministry of Agriculture and Rural Development (MARD) relate to antibiotic use. The duties of the Department of Animal Health (DAH) are similar to the Drug Administration of MoH, including: drug registration, import and export, domestic production, quality control and establishing the list of prohibited drugs or drugs with limited use in animal health. The National Agro-Forestry-Fisheries Quality Assurance Depart-

ment (NAFIQAD) is in charge of monitoring antibiotic use in husbandry and aquaculture as well as a national surveillance program of antibiotic residue in animal products.

In 1996, MoH issued the National Drug Policy, which clearly states that: “Antibiotics are very important drugs in treatment, and therefore it is necessary to regulate the prescription, antibiotic use, and antibiotic resistance of most common bacterial pathogens as well as improve the laboratory diagnosis.” At present, only the larger provincial and national hospitals have the capacity to perform bacterial culture, identification, and antibiotic sensitivity testing. Most laboratories have no quality systems in place to allow for reliable microbiologic testing. In the Antimicrobial Sensitivity Testing Study (ASTS), many results were of poor quality and inaccurate.

In 1997, MoH requested that all hospitals establish a Drug and Therapeutics Committee comprising clinical doctors, pharmacists, and microbiologists. The committee is responsible for implementing MoH guidelines related to drug use, giving professional advice for rational antibiotic therapy, and establishing lists of commonly used drugs in their hospitals. Certain “reserved” antibiotics, like meropenem would theoretically only be dispensed after consultation with this committee. Another duty of the committee is to inform local healthcare workers about appropriate drug use and to organize antibiotic drug resistance monitoring and reporting. At present, all central hospitals have a Drug and Therapeutics Committee. Most lower-level healthcare centers do not have Drug and Therapeutics Committee due to several reasons such as lack of a credentialed pharmacist and microbiologist for the Committee. In line with the role of the Drug and Therapeutics Committee, a more recent instruction from MoH (Instruction No 05/2004/CT-BYT) requires hospitals to implement local guidelines for rational and safe drug use, monitoring of antibiotic prescription practices, organizing local training programs to improve knowledge of drug use and strengthen hospital pharmacies<sup>57</sup>. The impact of this instruction is not yet known.

The most important law regarding antibiotic use



is the Drug Law of 2005. The goal of this law was to improve appropriate antibiotic use by allowing antibiotics to be dispensed only with a prescription. This law also requires the patient to strictly comply with the prescription, to provide feedback to prescribers, and to report any side-effects. Furthermore, this law prohibits advertisements of prescription-only drugs, including antibiotics. Despite this law, most drug sellers continue to sell antibiotics freely, without a prescription<sup>58</sup>. Currently, there is no sanction for not complying with regulations regarding sales of prescription-only drugs. This may explain why to this moment no pharmacy has been penalized for antibiotic dispensing without prescription. For the outpatient setting, a 2007 law (Regulation No 04/2008/QD-BYT) identifies who is allowed to prescribe. Only doctors working in legal health care centers and as an exception, assistant doctors in remote areas, can be delegated to prescribe. The prescribers are allowed to prescribe after a medical examination and are responsible for their prescription which is valid for five days after it has been issued. This law also states that the prescriber should “not prescribe to satisfy the irrational requirement of the patient.”

Recently, the Regulation of Good Pharmacy Practice, 2007 was issued to improve the quality of pharmacies. Pharmacy standards were already defined for the basic retail drugstore by the Pharmacy Law (2005). Good Pharmacy Practice (GPP) requires pharmacies to have proper facilities (area, drug storage), to monitor drug quality, record drug consumption, and to not sell prescription drugs without a prescription. Furthermore, GPP requires responsible pharmacists to be present in the drugstore for patient consultations and also to provide health information to their clients. Pharmacies without a GPP certificate are only allowed to dispense over-the-counter drugs. MoH requires a GPP certificate for pharmacies that want to dispense prescription-only drugs. However, the deadline for attaining GPP status has not been specified and currently only 5 percent of the pharmacies in Vietnam meet the requirements of GPP standards<sup>59</sup>. MoH provides benefits to encourage pharmacies to comply with GPP standards, including lower tax rates, license to directly import foreign

drugs, sell drugs to the hospitals, and supply drugs for health insurance.

In line with improving drug use in Vietnam, the MoH has set up a national center for drug information and adverse drug reactions monitoring (National DI&ADR Center, Decision 991/QD-BYT, 2009). The goal of this center is to establish a drug information and pharmacovigilance system to ensure drug safety in Vietnam. The center will build drug information databases, including database on pharmacovigilance, consult national competent authorities with information on risk/benefit assessment of marketed medicines, and to provide, consult and disseminate information on drugs and pharmacovigilance issues to health care institutions, health care professionals and the community. This may play an important role in initiating better prescribing practice policies in the health care system.

There are two drug lists in Vietnam, the Essential Drugs list and the Common Used Drugs list. The Essential Drug list states which drugs must be available in health facilities depending on the level of the hospital. Basing on the current Essential Drug list of Vietnam, which is developed from the World Health Organization list, hospitals establish their own Common Used Drug list. Hospitals can modify the Common Used Drugs list as appropriate for their situation, and this list is used to decide on reimbursement by health insurance. The last Common Used Drugs list dates from 2008 and it has 750 drugs with 141 antimicrobials (including antivirals and antiparasitic drugs). Forty-four of the antimicrobials can only be used at the central and provincial level, 16 of these drugs can only be prescribed with approval from the hospital's Drug and Therapeutics Committee. Restricted drugs consist of several 3rd and 4th generation cephalosporins (cefepim, cefoperazon, cefotiam, and ceftriaxon), carbapenems (but not ertapenem), piptazobactam, netilmicin, azithromycin, fluorquinolones (levofloxacin, lomefloxacin, and moxifloxacin), and vancomycin.

## 2.2. Supply Chain

### 2.2.1. Manufacturers

Ninety-three domestic enterprises produce antibiotics in Vietnam, of which 53 meet WHO Good Manufacturing Practices (GMP-WHO) standards while 24 comply with GMP – ASEAN requirements. Most domestic companies repackage several common antibiotics such as beta-lactams, tetracyclin, chloramphenicol, and gentamycin using semi-finished products imported from other countries, mostly China, Singapore and India. Several domestic manufacturers also distribute antibiotics to hospitals or wholesalers (also known as the “pharmaceutical market”) or have their own pharmacies. Four large pharmaceutical companies are that are engaged in production, importation, and distribution of pharmaceuticals have dominated the market. Once owned by the government, these companies have now been equitized with private capital and have become joint-stock companies. In general, the State holds 46.5 percent of legal capital in all joint-stock companies (including non-pharmaceutical companies) while the employees hold 38.1 percent and others hold 15.4 percent stock<sup>60</sup>.

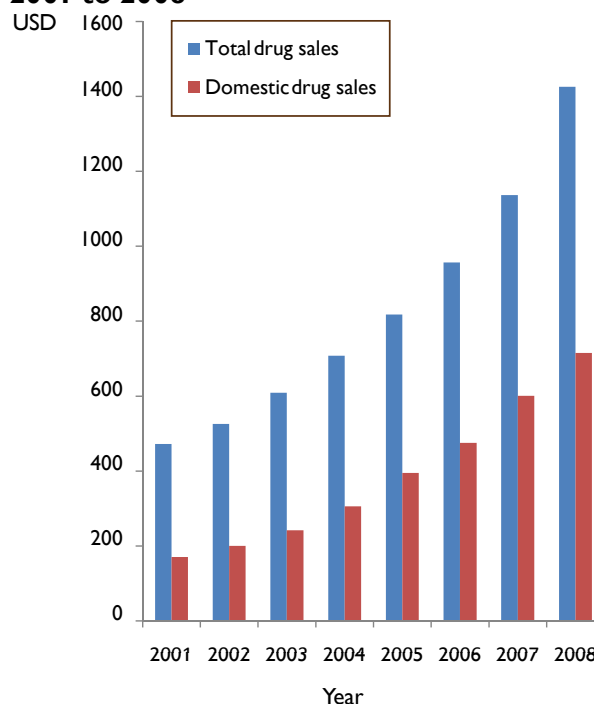
Half of all drugs used in Vietnam were made locally comprise in 2008 (source: MoH). The total value of locally made drugs was US\$715.435 million in 2008, a considerable increase from US\$600.630 million in 2007 (Figure 5, data MoH). MoH has encouraged public healthcare providers to prescribe domestic drugs when possible.

### 2.2.2. Distribution

Distribution of pharmaceuticals in Vietnam takes place through two main channels: treatment (37 percent) and commercial (63 percent)<sup>62</sup>. Sales through hospital pharmacies are considered treatment channels, while sales through private pharmacies are considered commercial. More than 370 foreign and 93 domestic companies supply antibiotics to the Vietnamese market through a complex distribution

system with approximately 800 smaller distributing companies and 39,016 pharmacy outlets (pharmacies, desks, kiosks) in 2008<sup>63</sup>. The management and control of drug price and quality in the supply chain is weak.

**Figure 5: Total and domestic made drug sales in Vietnam (x million USD) from 2001 to 2008<sup>61</sup>**



Source: Drug Administration of Vietnam (Ministry of Health)

There are several “pharmaceutical markets” which are based only in Hanoi and Ho Chi Minh City. These wholesale markets supply drugs to the “pharmaceutical market” of drugstores throughout the whole country.

### 2.2.3. Hospitals

All hospitals have a pharmacy department which is responsible for antibiotic dispensing to both in-patients and out-patients. Each year the pharmacy prepares a list of necessary drugs with the required

amounts, and invites pharmaceutical suppliers to submit bids. A recent inspection by the Drug Administration in 6 hospital pharmacies and 8 pharmacies around the hospitals indicated that nearly 98 percent of the products were sold at lower retail prices at hospital pharmacies than in the retail drugstores<sup>58</sup>. However, in other studies the opposite has been recorded: retail prices in hospitals higher than those of private pharmacies outside. A recent WHO report on medicine prices in Vietnam also states that public sector prices are higher than the private sector<sup>64</sup>.

## 2.2.4. Drugstores

Sick people usually go to one of the 39,000 pharmacies, rather than to a clinic or hospital, in order to save time and money. In such pharmacies, patients describe their symptoms and drug-sellers, with little or no medical training, sell drugs without a prescription<sup>65</sup>. Most patients who buy antibiotics buy them for a short period of approximately 3 days<sup>45</sup>. Antibiotics are often co-sold with vitamin tablets, anti-pyretics, and sometimes steroids [Unpublished data OUCRU-HMU]. According to the law, only a pharmacist with five years experience can own a pharmacy but such pharmacists rent out their license and work elsewhere making it easier for anyone to own a pharmacy.

**Table 5: Prices of some antibiotics at various levels in the distribution system**

Antibiotic	Company	Unit	Hospital	Wholesale price (USD)	Retail price (USD)
Augmentin 625mg (Amoxicillin+Acid Clavulanic)	GSK-England	Tablet	0.58	0.79	0.89
Unasyn (Ampicillin+Sulbactam)	Pfizer-Italy	Vial	3.56	4.26	4.96
Cefalexine 500mg	Traphaco-Vietnam	Tablet	0.025	0.035	0.042
Cefaclor 125mg	Mekofarm-America	Tablet	0.36	0.48	0.55
Cefuroxim 750mg	Rotex-Germany	Vial	2.43	2.81	3.24
Ciprofloxacin 500mg	Bayer-Germany	Tablet	0.67	0.76	0.89

Source: survey of the pharmaceutical market in Hanoi and some drugstores located around Bach Mai hospital

## 2.2.5. Prices at Various Levels in Supply Chain

In a small survey conducted in a pharmaceutical market in Hanoi and some drugstores near Bach Mai hospital, it was found that the retail price of antibiotics is about 15-20 percent higher than the wholesale price (See Table 5). In hospitals, the price of antibiotics is about 15-20 times lower than wholesale price because a fixed-price contract is put in place at the beginning of every year. The lower hospital price applies to in-patients only. Out-patients purchasing antibiotics in the hospital pharmacy pay the retail price of antibiotics along with a fixed mark-up as dictated by MoH regulations (See Table 6)<sup>66</sup>. In the public sector, antibiotics account for 40-50 percent of the total drug costs. Among the 100 highest selling pharmaceutical products in Vietnamese market, 21 were antibiotics in 2002, constituting 29 percent of total value<sup>67</sup>. There are no reliable data available about the total expenditure for antibiotics in Vietnam but a large portion of the profits in drug sales originates from antibiotic sales<sup>68</sup>.

## 2.2.6 Drug Price Control

The Drug Administration (DAV), in coordination with the Ministry of Finance is responsible for imple-



menting and setting drug price controls. This is still developing operational plans. DAV lacks good evidence for setting up a drug price system, hence WHO supports them in gathering the data and to undertake medicines price surveys and component price survey of medicines.

**Table 6. Retail price and government allowed surpluses (mark-ups) for hospital pharmacies**

No	Basic price/ Unit (USD)	Maximum surplus (%)
1	≤ 0.054	20
2	0.054-0.27	15
3	0.27-5.41	10
4	5.41-54.05	7
5	>54.05	5

Source: Health Statistics Yearbook 2008 (Ministry of Health)

The current mechanism of drug price control is not able to achieve the desired objective as the drug prices in Vietnam are higher to international comparators<sup>64</sup>. Currently, DAV collects cost, insurance and freight (CIF) prices of all imported medicines and manufacturers are required to declare wholesale prices before a market authorization (registration) is granted. However, there is no limit to the wholesale prices downstream. The government has no leverage to negotiate on the wholesale prices. The CIF and declared wholesale prices are compared, but even if the wholesale prices are much higher than the CIF, it is still allowed. Hospitals are then required to procure their medicines based on the wholesale prices by a tendering process. But as the wholesale prices are already high, tenders also tend to maximize such wholesale prices, increasing the price even more. Retail prices are determined by the market, but there is

a tendency to sell branded drugs rather than cheaper generics<sup>64</sup>. With the current policy, suppliers can easily justify increase on prices, and government cannot control it. Other countries have a more structured price control mechanism, with strong generic policies, good procurement systems and sing systems leverages (such as health insurance and bulk procurements) to reduce drug prices.

## 2.2.7. Counterfeit Antibiotics

Most counterfeit drugs are sold in markets and drug stores without pharmaceutical license. The volume of fake drugs has decreased and hopefully will continue to do so when pharmacies start to comply with GPP standards and Vietnamese citizens will stop buying from illegal outlets<sup>69</sup>. According to MoH, in 2008, 25 batches of both domestic and imported antibiotics out of total 94 drugs ( 26.6 percent) were recalled from the Vietnamese pharmaceutical market due to low quality<sup>70</sup>. Fake medicines sold in Vietnam are mainly antibiotics: ampicillin, amoxicillin, chloramphenicol, erythromycin, and tetracyclin<sup>69</sup>.

In 2008, large amounts of counterfeit drugs were detected due to increased surveillance activities and improved cooperation between government agencies (Table 7)<sup>71</sup>.

## 2.3. Patterns of Antibiotic Use for Particular Conditions

In collaboration with WHO and UNICEF, MoH has produced national guidelines for treating childhood illnesses, including acute respiratory infections (ARIs), meningitis, diarrhea, influenza, community-acquired pneumoniae, and diarrhea<sup>72</sup>. The 2006 guideline of common infectious diseases by MoH con-

**Table 7: Counterfeit drugs detected through years<sup>70</sup>**

Year	2000	2001	2002	2003	2004	2005	2006	2007	2008
Percentage (%)	0.06	0.05	0.03	0.06	0.06	0.09	0.13	0.17	0.21

Source: Drug Administration of Vietnam-Ministry of Health of Vietnam<sup>71</sup>

tains specific antibiotic treatments (name, dose, duration) for various levels of health facilities, patient characteristics such as symptoms, disease severity, weight and age, and occasionally based on the resistance profile of a detected pathogen<sup>73</sup>. The guideline also provides advice on drug toxicity monitoring (e.g. renal insufficiency with aminoglycosides).

At the community level, the MoH guidelines advise penicillin or amoxicillin for pneumonia of unknown origin. Amoxicillin with clavulanic acid or a second or third generation cephalosporin may be given as an alternative. For suspected atypical pneumonia, the guideline adds a macrolide to the regimen. Considering the resistance rates of *S. pneumoniae* and *H. influenzae* in Vietnam, the recommended use of penicillin or amoxicillin in this guideline may be ineffective<sup>74</sup>. In practice, first generation cephalosporins such as ampicillin or cephalexin are most often given at community health centers. At the hospital level, patients with community-acquired pneumonia are recommended amoxicillin (with or without clavulanic acid) or a second or third generation cephalosporin with a macrolide, following the MoH guideline.

For meningitis, the guideline advises intravenous antibiotics, with ceftriaxon as the first choice. The treatment recommendations differ by age category and the suspected pathogens. The treatment procedures for an important pathogen that causes bacterial meningitis in adults, *Streptococcus suis*, is not yet listed in this guideline. Furthermore, the guideline still recommends intravenous penicillin for pneumococcal meningitis, despite high resistance rates. Also trovafloxacin is listed as a potential treatment for meningitis even though this drug has been banned for many years due to serious liver toxicity. According to the guideline, lower level hospitals are not allowed to administer antibiotics to patients with suspected bacterial meningitis, but must refer the patients to reference hospitals for further diagnosis and treatment<sup>73</sup>.

The Handbook of Integrated Management for Common Childhood Illnesses (MoH, 2006) focuses on guiding mothers on how to care for children at home and when to take them to the hospital. This

handbook summarizes the assessment, classification and treatment of childhood diseases including pneumonia and diarrhea. The guideline recommends cotrimoxazole, amoxicillin, or erythromycin for serious respiratory infections. It also states that children should not be given antibiotics for cough or common cold without signs of pneumonia. For children with severe symptoms a first dose of intramuscular chloramphenicol followed by referral to a larger hospital is recommended.

A study conducted in 2007 has evaluated knowledge about antibiotic use in rural Vietnam. Despite the existence of the guidelines, knowledge about antibiotic use is poor and ARI management by health-care providers often includes antibiotics for common colds and coughs<sup>74</sup>. The study also showed that such antibiotics use does not comply with the type, dosage and duration of treatment recommended in the guidelines<sup>75</sup>.

## 2.4. Inappropriate Antibiotic Use

In the medical and pharmaceutical training curricula, very little time is devoted to antibiotic use, resistance and proper prescription. According to a community-based study undertaken in 1999 78 percent of antibiotics were purchased in private pharmacies without prescriptions. Sixty-seven percent of the participants consulted the pharmacist while 11 percent decided themselves about antibiotic use. Only 27 percent of the pharmacy staff had correct knowledge about antibiotic use and resistance<sup>67</sup>. Despite the regulations and guidelines set for antibiotics, sales of most antibiotics without a prescription is a common practice in Vietnam<sup>75</sup>.

Mothers usually treat sick children without going to a healthcare provider. According to a study in Ba Vi, 82 percent of the children that had at least one symptom of acute respiratory tract infection (ARI) were treated with antibiotics in 1999<sup>67</sup>. The most common antibiotics used were: ampicillin or amoxicillin (86 percent), penicillin (12 percent), erythro-

mycin (5 percent), tetracyclin (4 percent) and streptomycin (2 percent). On average, such drugs were used for about 3 days, but a minimum of 5 days is recommended for antibiotic treatment of bacterial pneumonia. With the increased common use of cephalosporins for more severe diseases, the pattern of antibiotic consumption altered in 2007. Antibiotics dispensed in 2007 were: ampicillin or amoxicillin (49 percent), oral first generation cephalosporins (27 percent), cotrimoxazol (11 percent), macrolides (3 percent), and others (2 percent)<sup>76</sup>.

The reasons for irrational antibiotic prescribing in Vietnam are the same as in other countries: perceived expectations of patients, time constraints, lack of knowledge, lack of diagnostic capability, and financial benefits for the prescriber [ref: GARP 1<sup>st</sup> workshop report]. A major challenge is to identify and modify the incentives for inappropriate prescribing. Furthermore, the high out-of-pocket expenditure in Vietnam forces patients to seek health care in the cheapest way.

## 2.5 Incentive Structure

As reported by the Administration of Medical Services in 2009, antibiotic expenditure generally exceeds 30 percent of total hospital treatment costs, including all drugs and chemicals (data MoH). A large part of the budget is used to purchase third generation cephalosporins (ceftriaxone, cefoperazone), quinolones (levofloxacin) and carbapenem (imipenem). Table 8 highlights the incentives at different levels for antibiotic prescribing and use that were identified during a workshop in 2009 [ref: GARP 1<sup>st</sup> workshop report]. In lower level public hospitals, especially for patients with health insurance, cheaper antibiotics, such as amoxicillin, are used. In private clinics, doctors tend to prescribe “strong” antibiotics such as cephalixin, zinnat, or augmentin. Furthermore, there are financial incentives to prescribe certain, more expensive, antibiotics that companies like to push into the market.

**Table 8: Incentives for antibiotic use**

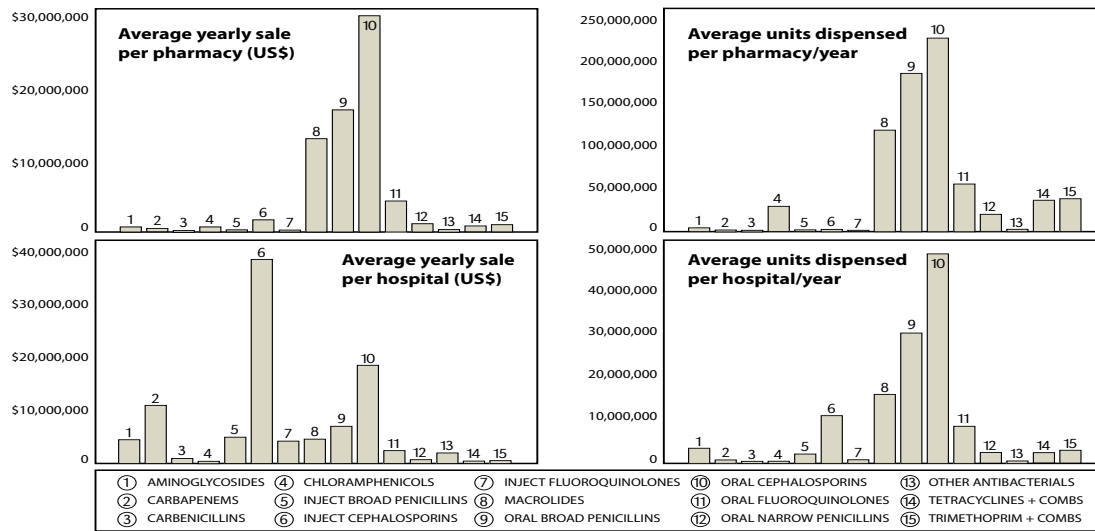
Category	Incentive
Physicians in public sector	Share of antibiotic price, invitations to conferences, gifts Patient expectation May save time
Physicians in private sector	Share of antibiotic price Patient expectation
Clinics	Infrastructural improvements, such as air conditioner, TV, others
Hospitals	Share value of drug procurement contract, infrastructural improvements
Pharmacies/ Drugstore	Promotion programs with discounts Share profits based on antibiotic sales
Patient	Prefer “strong medicine” Better be “safe than sorry”, as there are no diagnostic tests available to rule out bacterial cause of symptoms Self-medication is more convenient and cheaper than going to the doctor

## 2.6 Antibiotic Usage Patterns in Humans

IMS is a commercial organization that tracks sales of the global pharmaceutical market through two main channels in Vietnam: retail pharmacies and hospital pharmacies. The retail pharmacy data presented here show total sales of 439 pharmacies in Vietnam, excluding pharmacies with wholesale activities. The hospital pharmacy data represent total sales of 62 hospitals in 5 cities: Hanoi, HCMC, Hai Phong, Da Nang and Can Tho. The sales data cover the duration of one year: 4th quarter 2008 to 3rd quarter 2009 (IMS data Vietnam 2008-2009).

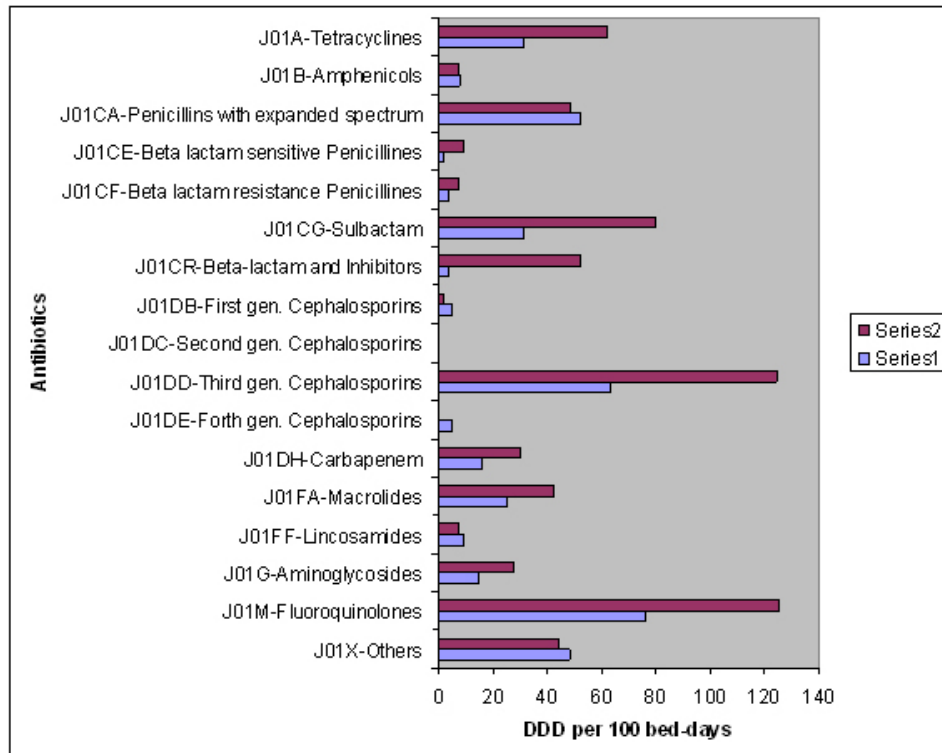
The trend of most commonly sold antibiotics is similar in retail pharmacies and hospital pharmacies (Figure 6). Oral cephalosporins (J01D01) are

**Figure 6: Sales of antibiotics in Vietnam**



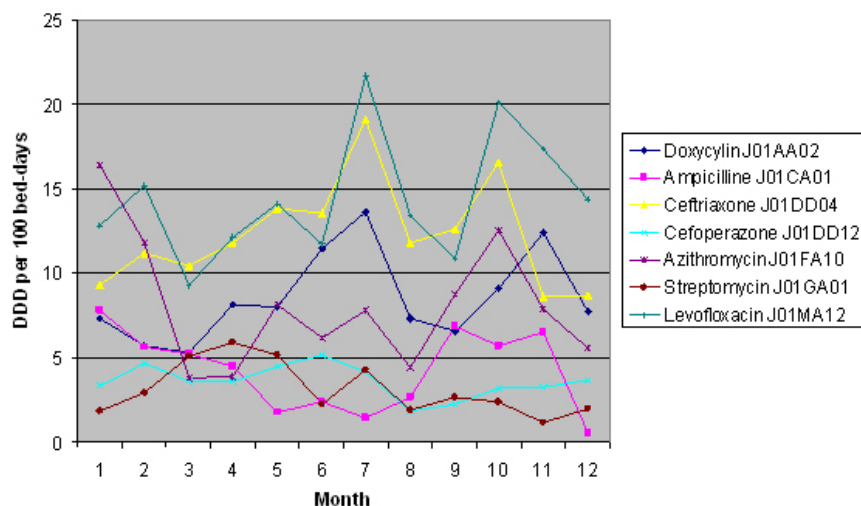
Average sold units in retail pharmacy (top) and hospital (bottom). Average sales data per year in US\$ in retail pharmacy (top) and hospital (bottom) by antibiotic.

**Figure 7: DDD per 100 bed-days of Antibiotics in 2008-2009**



Note: Other antibiotics include Vancomycin, Fosfomycin, Rifampicin, Metronidazole and Tinidazole. DDD = defined daily dose, a standardized

**Figure 8: Monthly DDD per 100 bed-days of 7 highest Abs in 2009**



the most commonly sold antibiotics at all pharmacies, followed by oral broad spectrum penicillins (J01C01), macrolides and fluoroquinolones. The main difference between pharmacies and hospitals is that the bulk injectable antibiotics are commonly sold in hospitals but rarely in retail pharmacies. Therefore, the intravenous antibiotics aminoglycosides and carbapenems are dispensed mainly in hospitals and rarely in retail pharmacies. Older antibiotics, such as chloramphenicol, are sold more in the retail pharmacy and little in the hospital. The sales of polymyxins (e.g. colistin) are negligible in both drug outlets as these drugs are not yet registered in Vietnam for systemic use in drug-resistant infections, even though they are on the common used drugs list.

By sales value, injectable drugs are more costly per unit than oral drugs and represent a higher percentage of the treatment budget. Injectable cephalosporins have the highest sales value in the hospitals, followed by carbapenems. Because of their high price, injectable cephalosporins also account for a substantial part of retail pharmacy sales.

A pilot study at the National Hospital for Tropical Diseases (NHTD) in Hanoi (2008-2009) assessed the antibiotic consumption using defined daily dosages per 100 bed days (DDD/100 bed days) for the 44 kinds of antibiotics used [unpublished data NHTD]. The most commonly used antibiotics in or-

der of DDD /100 bed days in 2009 were levofloxacin (104.73), ceftriaxon (85.93), doxycyclin (62.58), ampicillin ( $\pm$ sulbactam) (48.86 and 45.36, respectively), azithromycin (42.59), imipenem (22.58), cefoperazone (22.14) and streptomycine (21.9; Figure 3). The use of the seven most popular antibiotics increased almost two-fold in 2009 compared to 2008. The use of fluoroquinolones increased from 76.5 to 125.6 DDD/100 bed days and that of third generation cephalosporins from 63.4 and 124.5 DDD/100 bed days. Meropenem use increased about eight-fold in 2009 (7.8 DDD/100 bed days) compared to 2008 (0.9/100 bed days). First and second generation cephalosporins and amphenicols were used little in treatment (See Figure 7). Figure 8 shows that the antibiotic use peaked in the months June, July and November in 2009.

## 2.7. Hospital Antibiotic Expenditure Data

According to the MoH data on hospital drug sales in 2009, antibiotics constituted 36 percent of hospital treatment expenditure (ranging from 3 percent to 89 percent, Table 9). Among 100 randomly selected hospitals, central hospitals spend on average 26 percent (range from 10-45 percent) of their drug budget

on antibiotics. The lowest share of drug budget spent on antibiotics was seen in a psychiatric hospital, with 3 percent and the highest share was found at a pediatric hospital in Ho Chi Minh City, at 89 percent. At the National Hospital for Tropical Diseases (NHTD), a reference center for infectious diseases, 35 percent of the total drug expenditure was on antibiotics. By level, lower level hospitals use more antibiotics than do higher level ones, at 43 percent of drug sales<sup>77</sup>.

**Table 9: Antibiotic expenditure in hospitals in 2009 (data MoH)**

Category	Nr. of hospital	Antibiotic/ Total drug expenditure (percent)	Average (percent)
Center, general hospitals	12	10-45	26
Center, specific hospitals	21	5-89	28
Provincial, general hospitals	52	6-88	43
Provincial, specific hospitals	15	3-66	34

Source: MoH

## 2.8. Antibiotic Resistance Surveillance

Currently there is no active nationwide antibiotic resistance surveillance program in Vietnam. The Swedish International Development Agency (SIDA) and the Ministry of Health supported a resistance surveillance project for 10 years (1996 – 2006) known as the Antimicrobial Sensitivity Testing Study (ASTS). Hospitals from different regions throughout Vietnam participated in ASTS, producing yearly reports. The impact of these reports, and the project as

a whole, is not yet known. A new antibiotic resistance surveillance program is currently being set up by the MoH to collect antibiotic use and antibiotic resistance data from 20 different hospitals with microbiology laboratories.

Available resistance data from several reports and publications are presented below and in Appendix B.

### Streptococcus pneumoniae

In general, penicillin resistance in *S. pneumoniae* is extremely high in Vietnam. A study in Ho Chi Minh city showed that penicillin non-susceptible pneumococcus isolated from blood and CSF increased from 8 percent (1993-1995) to 56 percent (during 1999-2002)<sup>78</sup>. In 2000-2001, Vietnam showed the highest prevalence of penicillin resistance (71.4%) among 11 Asian countries<sup>79</sup>. Resistance rates are 22 times higher in urban children as compared to rural children<sup>80</sup>. Within the Asian Network for Surveillance of Resistant Pathogens (ANSORP), Vietnam had the highest prevalence of penicillin resistance (71.4 percent) and erythromycin resistance (92.1 percent)<sup>79</sup>. Seventy-five percent of pneumococci are resistant to three or more classes of antibiotics<sup>56</sup>. In 2009, most pneumococci were still susceptible to ceftriaxon<sup>44</sup>.

### Haemophilus influenzae Type b (Hib)

Hib isolates cultured from the cerebral spinal fluid collected from children with meningitis in Hanoi (2000-2002) showed that 57 percent were  $\beta$ -lactamase-producers and hence ampicillin-resistant<sup>81</sup>. Similar resistant rates were found in children with acute lower respiratory tract infections in Nha Trang<sup>82</sup>.

### Enterobacteriaceae

In 2004, at a surgical hospital in Ho Chi Minh City 14.7 percent of Gram-negative isolates produced ESBL. Among the ESBL producers, 70 percent were also gentamicin resistant and 72.5 percent ciprofloxacin resistant<sup>83</sup>. In an assessment of the prevalence of



resistance to broad-spectrum cephalosporins among *E. coli*, *K. pneumoniae* and *Proteus mirabilis*, from 2000-2001 in Ho Chi Minh city, it was found that over 25 percent were resistant to third generation cephalosporins and 16 percent were resistant to cefoperazone<sup>84</sup>. Another study in Ho Chi Minh city reported that 42 percent of studied enterobacteriaceae were resistant to ceftazidime, 63 percent were resistant to gentamicin and 74 percent to nalidixic acid. These high resistance rates were also found in healthy individuals in community setting<sup>85</sup>.

## Shigella

High resistance rates are also found in shigella isolated from stool: trimethoprim-sulfamethoxazole (81 percent), tetracycline (74 percent), ampicillin (53 percent), ciprofloxacin (10 percent), and ceftriaxone (5 percent)<sup>86</sup>. More than 75 percent are resistant to more than one drug<sup>87</sup>. In another study carried out in south Vietnam (2006-2008), it was seen that 15.3 percent were ceftriaxone resistant<sup>88</sup>.

## Salmonella typhi

In Vietnam, the proportion of multidrug resistant *S. typhi* strains remained high at 50 percent in 2004. Nalidixic acid resistance increased in 12 years from 4 percent to 97 percent in 2005<sup>89</sup>. Another study confirmed that more than 80 percent of *S.typhi* isolates were resistant to nalidixic acid<sup>90</sup>.

## 2.9. Antibiotic Use in Agricultural Animals and Plants

### 2.9.1 Evidence of Use

A large number of pharmaceutical products are used in animals, including antibiotics, vitamins and anti-parasitic drugs. Antibiotics are the most common registered drugs (70 percent of all drugs) used in animals<sup>91</sup>. Seventy-seven percent of all drugs used in animals are produced locally and 23 percent are

imported. No data are available on antibiotic use in agriculture, but it is known to be widespread. The Dutch government estimated that 700 grams of antibiotics per ton of fish are used in Vietnam which is seven times higher than other nations [Report from the Food Administration, Netherlands, 2009, code VWA/BuR/2009/13186]. Eleven groups of antibiotics are used in agriculture, including antibiotics that are also used to treat human infectious diseases. Antibiotics used in animals are:  $\beta$ -lactams, aminoglycosides, macrolides, tetracyclin, (fluoro)quinolones, phenicols, polymyxins (colistin), pleuromutilins, lincosamides, sulfamides, diaminopyrimidine (trimethoprim)<sup>91</sup>.

Antibiotics are used in all breeding, both land-based and aquaculture, even though such use is not supported by the Ministry of Agriculture. The antibiotics used are: tylosin (16 percent), amoxicillin (12 percent), gentamicin (9 percent) enrofloxacin (7 percent), penicillin (6 percent), lincomycin (6 percent), tiamulin (6 percent), colistin (5 percent), streptomycin (5 percent), norfloxacin (5 percent), tetracyclin (4 percent), ampicillin (4 percent) and florphenicol (3 percent). Forty-four percent of antibiotic selection and dosage is decided upon by the breeder, based on their experience. Thirty-three percent follow the prescription of veterinarians and 17 percent follow recommendations from a supplier or manufacturer. Farmers often do not comply with regulations that require them to stop antibiotic use before harvesting their products<sup>91</sup>.

In a surveillance study conducted at 30 pig farms and 30 chicken farms in Hung Yen and Ha Tay provinces, 60 percent of pig-derived products and 70 percent of chicken-derived products were found to be contaminated with tetracyclins or tylosins<sup>91</sup>. A few tested samples exceeded permissible concentrations. Antibiotic contamination was prevalent in 55 pig farms across Dong Nai and Binh Duong provinces, 52 percent of tested samples contained tylosin, 41 percent tetracyclin, 7 percent oxytetracyclin and 2 percent chlortetracyclin. Some samples contained antibiotic levels above acceptable limits<sup>91</sup>.

The National Agro-Forestry-Fisheries Quality

Assurance Department (NAFQAD) produces yearly reports on residues found in farmed fish, complying with international regulations for export. This report states that limited antibiotic residues have been detected in aquaculture including: quinolones and sulfonamides, which are widely used in aquaculture. Most of residues were within acceptable limits but quinolones were sometimes found at 18 times the allowed limit<sup>92</sup>. Residues of banned antibiotics are rarely detected, suggesting that export rules provide incentives for better use of antibiotics. However, one survey found chloramphenicol contamination in a large proportion of water samples, indicating that this banned drug is still being used<sup>91</sup>. See appendix C (Table 12).

### 2.9.2 Reasons/Incentives for Antibiotic Use in Agriculture

In agriculture, including aquaculture, antibiotics are used extensively as growth promoters, or for prophylaxis and treatment. According to the National Office of Animal Health (NOAH, 2001), antibiotic growth promoters are used to “help growing animals digest their food more efficiently, get maximum benefit from it and allow them to develop into strong and healthy individuals”<sup>93</sup>. Pigs and poultry are supplemented with antibiotics such as tetracyclin and tylosin<sup>91</sup>. Shrimps, crabs and fish are given quinolones and sulfonamides<sup>92</sup>.

Regulation of antibiotic use in animals has increased and certain antibiotics have been banned since Vietnam became a member of World Trade Organization in 2007. According to government regulations, when residues of banned antibiotics exceed the slowed limits, farms will be prohibited from harvesting, processing and exporting products until NAFIQAD confirms compliance. Table 10 lists some of the incentives for using antibiotics in agriculture.

**Table 10: Incentives for using antibiotics in agriculture**

Incentives	
For use	Non-use
-Growth promotion (more product for little additional costs)	-Alternative methods for achieving product's high quality
-Assumption that quality of product improves	-Reduce pressure for antibiotic resistance in both animal and human
-Increase export turn-over	-Comply with the rules of USA and EU market
-Control zoonotic pathogens	-Do not need to monitor residue of antibiotics
-Save money	-Concern for health

### 2.9.3 Antibiotic Resistance in Food Industry

Food-borne diseases are an important cause of morbidity and mortality worldwide. Food contamination with antibiotic-resistant bacteria can be a major threat to public health. In a study conducted to determine the prevalence of *Salmonella* spp and *E. coli* in raw foods commonly sold in the market in Ho Chi Minh City (2004), contamination was common: 60.8 percent of meat and 18 percent of shellfish were contaminated with *Salmonella* and more than 90 percent of all food sources contained *E. coli*. Multiresistant *Salmonella* were isolated from all food types<sup>94, 95</sup>. In Bac Ninh province, all campylobacter isolates from chickens were found to be resistant to cephalothin, 90 percent to nalidixic acid, 89 percent to tetracyclin, and 82 percent to ciprofloxacin<sup>96</sup>. Twenty-one percent of food items collected from the Mekong Delta were examined for antimicrobial resistance to 10 antibiotics, and 21 percent were resistant to at least one<sup>97</sup>.



### III. Preliminary Assessment, Policy and Research Options

#### 3.1. Preliminary Assessment

The increasing availability, affordability and accessibility of antibiotics since the market reforms in Vietnam has likely contributed to better outcomes for infectious diseases but has also resulted in widespread unnecessary use. Limited knowledge among consumers, drug sellers and pharmacists about the value and risks of antibiotics is part of the problem. There are also incentives to selling and buying antibiotics which might pose future societal risks. Sellers gain financial benefits while patients derive immediate personal perceived benefit from antibiotic use. Even within the health care sector limited knowledge of appropriate indications for antibiotic treatment and, lack of infrastructure for laboratory confirmation for bacterial cause of infection lead to widespread, often inappropriate use. Regulations that control access to antibiotics enforcement have become ineffective due to the lack of capacity and effective penalties.

There is a high prevalence of antibiotic resistant bacteria in Vietnam. This is almost certainly a consequence of the high levels of antibiotic use, much of which is inappropriate. Whilst antibiotic use in animals is widespread, the role this plays in resistance levels in human pathogens remains unclear in Vietnam and other countries. As a consequence of the high rates of resistance, many antibiotic regimens advised in current treatment guidelines are unlikely to be effective. Although very hard to quantify, the profile of antibiotic resistance observed in Vietnam undoubtedly causes negative health and economic impacts.

**Table II: Threats and opportunities in controlling antibiotic resistance**

Opportunities	Threats
<b>Community</b> More welfare Better communication (internet and mobile phones widely available) Higher demand for better health care	<b>Community</b> More convenient to go to pharmacy Poor knowledge Poor access to accurate information
<b>Pharmacy</b> Changes in curriculum pharmacy schools GPP initiative Pharmacovigilance center	<b>Pharmacy</b> Incentive to dispense Poor knowledge Poor access to good information Little time spent on antibiotics and resistance during training
<b>Medical system</b> Changes in curriculum medical schools Increased access to diagnostics Infection control initiatives Willingness to improve Lab enhancement programs	<b>Medical system</b> Incentive to prescribe Little funding for surveillance Poor quality resistance testing Poor knowledge Poor access to good information Out-dated guidelines Little time spent in medical schools on antibiotics and resistance

#### 3.2. Policy Analysis

The need for policies to control the use of antibiotics is clearly recognized by the political and medical leadership of Vietnam, and there are many examples of legislation and initiatives designed to limit unnecessary antibiotic use (see table 12). However, judged against their intended goal, these policies have not been effective. Over the counter sales of antibiotics for minor illnesses is extremely common, antibiotic

use in hospitals is high, and resistance rates are increasing. Despite numerous policy initiatives, there is no doubt that antibiotic resistance is a serious and growing problem for Vietnam.

The majority of policy initiatives tried to date can be categorized as regulation, while the drug and health care markets have experienced considerable de-regulation. The regulations to improve antibiotic use and infection control are not enforced and it is important to understand what the barriers are for effective enforcement (e.g., insufficient funding, lack of expertise, human resources, and financial incentives). It is also important to foresee the financial consequences to sellers and reduced access to health care for the population should such regulations be enforced.

The de-regulation of the healthcare sector may have neutralized legislation to control antibiotic use. Also the high individual out-of-pocket expenditure may have increased consumers demand to the service they want and weakened the power of the State to influence the health care market. Policies to reduce out-of pocket expenditure through health insurance may reduce the ability of individual consumers to shape the health care market and might therefore be important in revitalizing the influence of the State.

Policy instruments other than direct legislation and regulation do exist. For example, an effective self-regulating trade association with codes of practice could be an effective tool for controlling antibiotics use. Economic instruments such as drug subsidies that have largely been targeted at increasing drug affordability might also be employed to restrict access. For example, tiered taxation of broad-spectrum agents, or, conversely, subsidies only for a restricted range of antibiotics could be put in place.

Information, education and example can also be powerful tools to change antibiotic use behaviors. Publicity and marketing techniques might be used to change consumer and supplier attitudes. Influential leaders within the medical and pharmaceutical professions might catalyze change by setting public examples of best practice. Stronger product labeling on prescription-only medicines might be effective in

highlighting the potential side effects for individuals and for society from the misuse of antibiotics.

These and other policy options need careful consideration for their feasibility, affordability and possible adverse impacts. This will be the subject of the next phase of the GARP-Vietnam agenda.

### 3.3. Research Opportunities

It is clear that antibiotic consumption and resistance levels are too high in Vietnam. However, the available information is not well collated and communicated, and a 'strong voice' advocating for action against inappropriate antibiotic use is needed. The absence of data on the health and economic burden resulting from antibiotic resistance limits the strengths of arguments for strong action. Better quantification and mapping of the incentive structure for antibiotic prescribing would support the design for more effective interventions.

Based on the situation analysis and the key information gaps identified, three projects are proposed:

1. Creating a senior peer network on antibiotic use and resistance: To establish information sharing channels among several prestigious hospitals including Bach Mai, NHTD, HTD and Cho Ray in collaboration with the Drug Administration and National DI&ADR Center to produce regular reports on AB use and resistance. Up-to-date guidelines would be made available through this network and other relevant documents.
2. Burden of resistance study: To categorize the feature of common pathogens in several selected hospitals and assess burden of bacterial resistance. The most powerful argument to convince policy makers is to show that resistance costs money and antibiotic stewardship will save money and lives. Therefore, studies need to be under-

**Table 12: List of current policies in Vietnam on antibiotic use and resistance and comments**

<b>Policy option</b>	<b>Action</b>
Antibiotics are prescription only drugs.	Develop national action plan for antibiotic resistance.
Make antibiotics prescription-only	Enforce current law.
Make hospitals' drug and therapeutics committee effective	Enforce requirement for committees, define their functions and standards, and develop audit mechanisms. Give committees tools and guidance on antibiotic stewardship. Provide up-to-date, accurate resistance data.
Establish infection-control committees in hospitals	Give committees sufficient resources to carry out their activities and improve infrastructure. Establish standardized indicators to monitor progress, such as hospital-acquired infection rates by department and hand-washing compliance.
Track national antibiotic resistance	Develop national testing and quality control guidelines. Fund resistance testing, quality control, training, and reporting. Issue annual national report on both antibiotic use and resistance.
Monitor antibiotic use in hospitals	Standardize antibiotic usage indicators to international units (e.g., defined daily dosage per 100 bed-days). Issue annual national report on both antibiotic use and resistance
Develop curriculum for medical and pharmacy schools	Teach and train professionals on antibiotic resistance and appropriate antibiotic use.
Develop treatment guidelines	Ensure timely and evidence-based updates of treatment guidelines for infectious diseases.
Establish pharmacovigilance center	Engage pharmacovigilance center in curbing inappropriate antibiotic prescribing.
Conduct public education campaign	Create awareness and educate Vietnamese public about appropriate and inappropriate antibiotic use.
Set up vaccination programs	Achieve high vaccination coverage for communicable diseases to prevent bacterial infections that require antibiotic treatment.
Enhance laboratory capabilities	Ensure quality laboratory testing. Consider establishing national reference center (center of excellence) for antibiotic resistance testing. Create network for sharing data, guidelines, and expertise.
Curb antibiotic use in agriculture	Enforce current law. Set up national antibiotic use and resistance surveillance system. Issue annual national report on both antibiotic use and resistance. Develop regulations on antibiotic use before harvesting.

taken to assess the burden of resistance in Vietnam.

**Proposed Study:** assess bacterial resistance of the 5 most common pathogens in blood, CSF, and respiratory tract and assess whether treatment guidelines are appropriate. Assess the difference in price of drugs that could and should be used according to treatment guidelines and what it would cost to treat the patient with specified resistance profiles.

3. Economic incentive structure for selling antibiotics at community retail pharmacies and in private clinics. To be successful in changing antibiotic prescribing/dispensing behavior, we have to understand the incentive structure. As high profits are made with antibiotic sales, a lot of money will be lost if antibiotics can only be sold when prescribed/dispensed appropriately. How can these incentives be changed?

**Proposed Study:** assess antibiotic income of pharmacies by observing current sales. With stakeholder meetings and focus group discussions with (assistant) pharmacists to find out what drives them to dispense antibiotics other than profits. Assess what incentives/knowledge they may need to do otherwise.

Other gaps that were identified are listed below. The current grant will not be able to cover the following projects.

1. The highest volume of antibiotics used in Vietnam is probably not in humans but animals. It is essential to have this information to be able to develop control policies.

**Proposed Study:** assess antibiotic use in different farms: pig, chicken, and fish/shrimp and correlate this to resistance in humans, animals and meat sold on market.

2. It is clear that the curriculum/training of doctors and pharmacists is insufficient.

**Proposed Study:** Assess and compare with other

countries, the number of hours spent in professional training curricular by doctors and pharmacists on antibiotics, and the content of such curriculum. What do doctors and pharmacists really know about antibiotics?

3. The most important stakeholder in antibiotic use is the patient: do they really want an antibiotic? If yes, why? Do they know what an antibiotic is? We would like to note here that the Vietnamese word for infection is 'viem'. Viem also means inflammation whether caused by a pathogen or not. What information will they need to be convinced not to use an antibiotic?

**Proposed Study:** community surveys and focus group discussions.

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## Appendix A

### Antibiotic resistance data in Vietnam: Hospital level

Surveillance of four most common Gram negative pathogens in both general and specific national hospitals including *E. coli*, *K. pneumoniae*, *P. aeruginosa* and *A. baumannii* showed relatively high prevalence of antibiotic resistance. The prevalence of ESBL in *E. coli* and *K. pneumoniae* in 2005 was about 34 percent for both bacteria. In Bach Mai hospital, the rates of *K. pneumoniae* and *E. coli* increased from 20 percent in 2005 to 34 percent in 2008, and from 18 percent in 2005 to 42 percent in 2008, respectively (See Table 13)<sup>42</sup>.

**Table 13: Rate of E. coli and K. pneumoniae producing ESBL in some hospitals**

Location	K. pneumoniae	E. coli
ASTS program - MOH (2004)	23.7 (n = 485)	7.7 (n = 548)
Cho Ray hospital (2005)	61.7 (87/141)	51.6 (145/281)
Viet Duc hospital (2005)	39.3 (55/140)	34.2 (66/193)
Binh Dinh hospital (2005)	19.6 (29/148)	36.2 (51/141)
Viet Tiep hospital (2005)	25.7 (09/35)	36.1 (22/61)
Bach Mai hospital (2005)	20.1 (37/184)	18.5 (28/151)
Bach Mai hospital (2006)	28.7 (99/347)	21.5 (77/359)
Bach Mai hospital (2007)	32.5 (105/323)	41.2 (136/330)
Bach Mai hospital (2008)	33.6 (85/253)	42.2 (97/231)

Source: GARP 1st workshop report<sup>42</sup>

Two common nosocomial pathogens, *P. aeruginosa* and *A. baumannii*, were assessed for carbapenem resistance in 2008. Twenty percent of *P. aeruginosa* strains and almost 50 percent of *A. baumannii* strains were carbapenem resistant (See table 14)<sup>42</sup>.

**Table 14: Rate Carbapenem resistance of P. aeruginosa and A. baumannii in 6 hospitals in 2008**

Drug	P. aeruginosa (%)	A. baumannii (%)
Meropenem	18	46.2
Imipenem	25	47.1

Source: GARP 1st workshop report<sup>42</sup>

To investigate the prevalence of *S. aureus* which is one of the most common Gram-positive organisms with reduced susceptibility to vancomycin among methicillin-resistant *S. aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA) strains in Vietnam, a total of 200 clinical isolates of MSSA and MRSA collected from 2 national general hospitals in 2008 were assessed by Vancomycin MIC test. The result showed the emergence of vancomycin-intermediate *S. aureus* and/or vancomycin-resistant *S. aureus* among both MSSA and MRSA, averaging 3 percent of MSSA and 5 percent of MRSA strains (See Table 15)<sup>42</sup>.

#### ASTS data

The ASTS program studied antimicrobial resistance in common bacteria isolated from in-patients and out-patients admitted to 22 hospitals nationwide from 1988 to 2004. Included pathogens were *S. aureus*, *E. coli*, *Salmonella*, *Shigella*, *Enterobacteriaceae*, *S. pyogenes*, *S. pneumoniae*, *H. influenzae*, *Enterococcus*, *Klebsiella pneumoniae*, *P. aeruginosa*, and *A. baumannii*. As there exist inconsistencies in the data, the resistance rates are not presented.

**Table 15: Vancomycin MIC distributions of Staphylococcus aureus strains in Bach Mai and Cho Ray hospitals - 2008**

	<b>Strain</b>	<b>N</b>	<b>Mean</b>	<b>SD</b>	<b>Geometric mean</b>	<b>% VSSA (MIC<math>\leq</math> 2mg/L) (%)</b>
<b>Total</b>	<i>S. aureus</i>	200	1.63	0.41	1.57	96
	MSSA	100	1.55	0.44	1.47	97
	MRSA	100	1.72	0.36	1.67	95
<b>Bach Mai hospital</b>	<i>S. aureus</i>	100	1.47	0.43	1.39	100
	MSSA	57	1.34	0.42	1.27	100
	MRSA	42	1.63	0.39	1.57	100
<b>Cho Ray hospital</b>	<i>S. aureus</i>	100	1.80	0.32	1.77	92
	MSSA	43	1.81	0.31	1.79	93
	MRSA	57	1.78	0.33	1.75	91

Source: GARP 1st workshop report<sup>42</sup>

Note: MSSA : Methicillin susceptible *S. Aureus* ; MRSA :Methicillin resistant *S. aureus*

## Appendix B

**Table 16: Antibiotic residue in aquaculture**

		2007		2008		2009	
		Product (%)	Water (%)	Product (%)	Water (%)	Product (%)	Water (%)
Banned Antibiotics	Chloramphenicol	0.9000	19	0.5	14.430	no data	2 samples
	Semicarbazide	0.7000		0.4		0.002	
	Malachite Green	0.3000		0.3		no data	
Limited Use Antibiotics	Tetracyclin	0.0038		0.000		no data	
	Sulfonamide	0.0035 (exceed limit: 0.0017)		1.460		no data	
	Quinolone	0.1250		0.120		0.011	
	Enrofloxacin / Ciprofloxacin	0.1163 (exceed limit: 0.007)		0.094		0.09 (exceed limit: 0.009)	
	Trimethoprim	0.0004		1.850		no data	

Source: GARP 1st workshop report<sup>91</sup>