กรมควบคุมโรค
Department of Disease Control

Antimicrobial Resistance Surveillance and Investigation Guidelines

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Introduction

Thailand applies the International Health Regulations of 2005 (IHR 2005). These are regulations between the member states of the World Health Organization that stipulate for the member states to have plans in place for dealing with antimicrobial resistance to strengthen epidemiological and laboratory surveillance on the national level, referring to international agreements on the development of surveillance standards with consideration to preliminarily existing standards and improvements of alternative medical treatment guidelines and collaboration in sustainable antimicrobial drug development.

The guidelines for surveilling and investigating antimicrobial resistance were prepared for nurses charged with controlling contagious diseases in hospitals, epidemiological personnel, and lab personnel to ensure that the personnel in the antimicrobial resistance surveillance network can successfully detect abnormalities and respond to and report on patient cases of antimicrobial resistance, in addition to having personnel in the antimicrobial resistance surveillance network to monitor patients who contracted diseases with antimicrobial resistance in order to effectively investigate antibiotic-resistant disease and write investigation reports.

Antibiotic-resistant disease surveillance work requires the collaboration of epidemiological surveillance networks, with disease investigation guidelines obtained from experience leading to the success of the implementation of these guidelines through excellent cooperation among executives, academics, and work groups from the Department of Disease Control and local agencies with the hope that the antibiotic-resistant disease surveillance guidelines will benefit persons involved in disease prevention and control.

The Authors

July 2021.

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Introduction

Introduction

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Definition of Antimicrobial Resistance

"Antimicrobial resistance" in this manual means bacteria resistance to drugs that suppress or destroy bacteria.

Types of Antimicrobial Drug Resistance

There are 2 types of antimicrobial resistance as follows:

1. Intrinsic Antimicrobial Resistance – This means antimicrobial resistance arising out of the specific characteristics of the bacteria that contain no components targeted for the activation of some types of antimicrobial drugs from the start. For example, *Escherichia coli* is always resistant to Vancomycin even if *E. coli* has had no prior contact with Vancomycin. This type of antimicrobial resistance makes it unnecessary to test the sensitivity of *E. coli* to Vancomycin, since it can be expected that *E. coli* will always resist Vancomycin, and Vancomycin will not be used to treat diseases caused by *E. coli*.

2. Acquired Antimicrobial Resistance – This means microbial resistance by bacteria that were sensitive to an antimicrobial in the past but mutated into an antimicrobial-resistant bacterial strain after exposure to the antimicrobial to which the bacteria used to be sensitive. For example, most *E. coli* are sensitive to Ceftriaxone, but after *E. coli* comes into contact with Ceftriaxone or another type of antimicrobial (such as Fluoroquinolones), the *E. coli* will develop until it becomes resistant to Ceftriaxone. This type of antimicrobial resistance occurs as a result of several mechanisms, for example, when bacteria develop enzymes that destroy the antimicrobial when bacteria modify the activation targets of the antimicrobial such that the antimicrobial cannot be activated and when bacteria expel the antimicrobial from their cells.

Antimicrobial resistance in bacteria in this manual means acquired antimicrobial resistance, with the infectious diseases arising from the antimicrobial-resistant bacteria being 1 of the 5 emerging infectious diseases.

Acquired antimicrobial resistance is divided into 3 types as follows:

1. Multidrug-Resistance (MDR) – This means resistance to at least 1 out of 3 types of antimicrobial drugs used to treat infections caused by the bacteria in question.

2. Extensive Drug Resistance (XDR) – This means resistance to at least 1 antimicrobial drug out of all drugs, except for 1-2 antimicrobial drugs used to treat infections caused by the bacteria in question.

3. Pandrug-Resistance (PDR) – This means resistance to all types of antimicrobial drugs out of all drugs used to treat infections caused by the bacteria in question.

An example of antimicrobial resistance by *Acinetobacter baumannii* with reference to the antimicrobial drug classes and each antimicrobial drug in the antimicrobial drug classes used to treat *A. baumannii* infections is shown in Table 1.1.

MDR *A. baumannii* means *A. baumannii* resistant to Ceftazidime, Ciprofloxacin and Amikacin but still responsive to Meropenem, Colistin and Tigecycline.

XDR *A. baumanni* means *A. baumannii* resistant to Ceftazidime, Ampicillin-Sulbactam, Meropenem, Ciprofloxacin, Amikacin and Cotrimoxazole but still responsive to Colistin and Tigecycline.

PDR *A. baumannii* means *A. baumannii* resistant to all types of antimicrobial drugs in the antimicrobial drug classes in the table.

In practice, classification of antimicrobial resistance in *A. baumannii* is as follows: *A. baumannii* that is still sensitive to Meropenem is usually MDR, while *A. baumannii* resistant to Meropenem but responsive to Colistin is usually XDR, and *A. baumannii* resistant to Meropenem and Colistin is usually PDR.

TABLE 1. Classification of Antimicrobial Drugs in Each Antimicrobial Drug Class.

Antimicrobial Drug Class	Antimicrobial Drug in Each Antimicrobial Drug Class
Extended-Spectrum Cephalosporins	Cefotaxime, Ceftriaxone, Ceftazidime, Cefepime
Beta-Lactams + Beta-Lactamase Inhibitors	Amoxicillin-Clavulanate, Ampicillin-Sulbactam, Piperacillin-Tazobactam
Carbapenems	Ertapenem, Imipenem, Meropenem, Doripenem
Fluoroquinolones	Norfloxacin, Ofloxacin, Levofloxacin, Ciprofloxacin
Aminoglycosides	Gentamicin, Tobramycin, Amikacin, Netilmicin
Folate Pathway Inhibitors	Cotrimoxazole
Tetracyclines	Tetracycline, Doxycycline, Minocycline, Tigecycline
Polymyxins	Colistin, Polymyxin B

Significance of Antimicrobial Drug Resistance

Antimicrobial drug resistance is a major cause of illness and death in the world's population. In Thailand, over 100,000 patient cases of antimicrobial-resistant infections occur each year, with over 30,000 patient deaths caused by antimicrobial-resistant infections and resource losses due to antimicrobial-resistant infections amounting to over 40,000 million baht or about 1% of the gross domestic product (GDP).

Occurrence of Antimicrobial Resistance

Antimicrobial resistance can occur as a result of 2 mechanisms as follows:

1. Development of Antimicrobial-Resistant Strains

In normal people or patients who contracted infections not caused by bacteria (such as influenza patients whose infections are caused by a virus) who are needlessly prescribed antibiotics, the antimicrobials they received can cause their normal florae residing in their gut (such as *Escherichia coli*) and in their oral cavity (such as *Streptococcus* spp.) and on the skin (such as *Staphylococcus aureus*) to mutate to become resistant to the antimicrobial drug or drugs and reside in the body without displaying any symptoms before potentially causing antimicrobial-resistant infections later on.

In patients with bacterial infections (such as urinary tract infections caused by *E. coli*) who are administered appropriate antimicrobial drugs (drug type, drug dose, drug administration, and duration), the disease-causing bacteria are destroyed, but the antimicrobials might cause some local bacterial florae in the body to mutate into strains resistant to the antimicrobial drug or drugs and reside in the body without displaying any symptoms before potentially causing antimicrobial-resistant infections later on.

In patients with bacterial infections who are administered antimicrobials inappropriately (drug type, drug dose, drug administration, and duration), the patients often do not recover or die from their bacterial infections, and the antimicrobial drugs administered might cause the disease-causing bacteria to mutate into a strain resistant to the antimicrobial drug or drugs, leading to antimicrobial-resistant infections. In addition, the antimicrobial drug might cause the local bacterial florae in the body to mutate and become strains resistant to the antimicrobial drug or drugs and reside in the body without displaying any symptoms before potentially causing antimicrobial-resistant infections later on.

Furthermore, for antimicrobial drugs that normal persons or patients are administered for the treatment or prevention of diseases, normal persons and patients might already be exposed to antimicrobial drug residues in their food (especially animal meats/organs from animals administered antimicrobials during their growing process). These antimicrobial residues can cause the local bacteria florae in the body to mutate and become strains resistant to the antimicrobial drug or drugs and reside in the body without displaying any symptoms before potentially causing antimicrobial-resistant infections later on.

2. Exposure to Antimicrobial-Resistant Infections

Normal persons or patients living in communities exposed to food or an environment contaminated with antimicrobial-resistant bacteria can acquire antimicrobial-resistant bacteria that reside in the body without displaying any symptoms before potentially causing antimicrobial-resistant infections later on.

In public health personnel in hospitals who are exposed to antimicrobial-resistant bacteria from patients with antimicrobial-resistant bacteria or patients with antimicrobial-resistant infections in their bodies or from the hospital environment, which is a common source of accumulation of antimicrobial-resistant bacteria during their work in providing care to hospital patients, the public health personnel can acquire antimicrobial-resistant bacteria that reside in their body without displaying any systems before potentially causing antimicrobial-resistant infections later on.

In hospital patients who are exposed to antimicrobial-resistant bacteria from their food, environment, medical supplies/devices or public health personnel carrying antimicrobial-resistant bacteria in or on their bodies (especially from the hands of public health personnel), the patients can acquire antimicrobial-resistant bacteria that reside in their body without displaying any symptoms before potentially causing antimicrobial-resistant infections later on.

Spread of Antimicrobial Resistance

Normal persons, public health personnel and patients carrying antimicrobial-resistant bacteria can spread antimicrobial-resistant bacteria from themselves to other persons through close contact with such persons. Otherwise, the antimicrobial-resistant bacteria residing in or on the bodies of these people (such as the hands, fecal matter, urine and saliva) might contaminate food, beverages and the environment, and when any person is exposed to food, beverage or an environment containing the antimicrobial-resistant bacteria, the person might acquire the antimicrobial-resistant bacteria that reside in their bodies without displaying any symptoms before potentially causing antimicrobial-resistant infections later on.

The development and spread of antimicrobial-resistant bacteria above are related to people, animals, food and the environment in the One Health pattern.

Diagnosis of Antimicrobial Resistance in People

Antimicrobial-resistant bacteria can be found in persons who display no clinical symptoms of infection (carriers of antimicrobial-resistant bacteria) and in persons with clinical symptoms of infection (patients).

Diagnosis of antimicrobial resistance in persons with no displayed clinical symptoms of infection requires testing for antimicrobial resistance in a microbiological laboratory by using samples collected from said persons such as by collecting fecal samples to test for gram-negative bacteria resistant to Ceftriaxone or creation of extended-spectrum beta-lactamase (ESBL) and collection of nasal cavity samples to test *S. aureus* for Methicillin-resistant *S. aureus* (MRSA).

Meanwhile, diagnosis of antimicrobial resistance in patients with antimicrobial-resistant infections might rely on information encountered such as patients' lack of response to antimicrobial treatments for disease-causing bacterial infections that should be responsive to the antimicrobials in question (for example, when patients with acute pyelonephritis commonly caused by *E. coli* are administered Ceftriaxone for 2 days but experienced no improvements in their symptoms).

Such cases suggest that the disease-causing bacteria are resistant to antimicrobials. However, a conclusive diagnosis of antimicrobial resistance in the bacteria requires testing for antimicrobial -resistant bacteria and testing of the encountered bacteria's responsiveness to antimicrobials in a microbiological laboratory based on samples collected from the patients.

Therefore, diagnosis and surveillance of antimicrobial resistance require testing to find the antimicrobial-resistant bacteria and testing of the bacteria's responsiveness to antimicrobials in a microbiological laboratory based on samples collected from the carriers of antimicrobial-resistant bacteria and patients with antimicrobial-resistant infections.

The methods for surveillance of antimicrobial resistance and investigation of antimicrobial resistance are discussed in later chapters.

Prevention and Control of Antimicrobial Resistance

Prevention and control of antimicrobial resistance rely upon guidelines consistent with the occurrence and spread of antimicrobial resistance discussed above such as elimination of the creation of antimicrobial-resistant bacteria, elimination of exposure to antimicrobial-resistant bacteria and elimination of the spread of antimicrobial-resistant bacteria as follows:

1. Control and Prevention of Antimicrobial Resistance in Communities

1.1. Elimination of Creation of Antimicrobial-Resistant Bacteria

Use antimicrobials in an appropriate and responsible manner, i.e., only use antimicrobials as necessary.

1.2. Elimination of Exposure to Antimicrobial-Resistant Bacteria

Engage in appropriate personal hygiene behaviors (such as by eating clean food and water and washing hands before eating and after contact with things potentially contaminated with germs); use appropriate personal protective equipment such as gloves, face masks, goggles, etc.; and avoid contact with people, animals and environments contaminated with antimicrobial-resistant bacteria.

1.3. Elimination of the Spread of Antimicrobial-Resistant Bacteria

Engage in appropriate personal hygiene behaviors (such as by washing hands before touching things shared with other persons and after contact with things potentially contaminated with germs, including fecal matter in the toilet). In addition, if antimicrobial-resistant bacteria or antimicrobial-resistant infections are present, wash hands before touching food and other people; avoid close contact with other people; and use appropriate personal protective equipment such as gloves, face masks, goggles, etc.

2. Control and Prevention of Antimicrobial Resistance in Hospitals

2.1. Elimination of Creation of Antimicrobial-Resistant Bacteria

Appropriately and responsibly use antimicrobials, that is by only using antimicrobials as required.

2.2 Elimination of Exposure to Antimicrobial-Resistant Bacteria

Public health personnel strictly wash hands after coming into contact with patients and contaminated environments and use appropriate personal protective equipment such as gloves before coming into contact with patients and contaminated environments.

Patients eat clean food and beverages without coming into contact with contaminants and wash hands after coming into contact with contaminants.

2.3. Elimination of the Spread of Antimicrobial-Resistant Bacteria

Public health personnel should wash their hands and use appropriate personal protective equipment such as by wearing gloves before touching patients and strictly isolating patients carrying antimicrobial-resistant bacteria or antimicrobial-resistant infections.

Patients carrying antimicrobial-resistant bacteria or antimicrobial-resistant infections should wash hands before touching other people and wash hands after touching other people or any environment contaminated with germs and should wear appropriate personal protective equipment such as gloves, face masks, goggles, etc.

Thus, in order to ensure the success of antimicrobial-resistance surveillance and investigations according to the objectives set by the Department of Disease Control, Ministry of Public Health, in the 2021 fiscal year a project was launched to develop network personnel on the district and central levels to monitor and investigate for antimicrobial resistance and to ensure that the personnel in the antimicrobial resistance surveillance network can detect abnormalities and respond to outbreaks among patients with antimicrobial-resistant infections and report on them in a timely manner and also to ensure that personnel in the antimicrobial resistance monitoring network can monitor patients with antimicrobial-resistant infections and investigate antimicrobial -resistant infectious diseases and report on disease investigations effectively to ensure integration in the work of related agencies such that it is carried out in an orderly, effective and efficient fashion.

As such, the Department of Epidemiology has created guidelines on antimicrobial resistance surveillance and investigation for nurses in charge of controlling infectious disease in hospitals, epidemiological personnel, and laboratory staff to ensure their understanding of the roles and duties of hospitals in the antimicrobial resistance surveillance and investigation system for the benefit of persons involved in their uses in disease control and prevention.

The contents of this article were extracted and copied from the "Mid-plan Phase Progress Report: Implementation of the Strategic Plan on Dealing with Antimicrobial Resistance in Thailand, B.E. 2560-2564 (2017-2021)".

Efforts to Resolve Antimicrobial Resistance under the Strategic Plan on Dealing with Antimicrobial Resistance in Thailand, B.E. 2560 – 2565 (2017 – 2022)

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Thailand long has had in place work plans to solve the problem of antimicrobial resistance (AMR), but past efforts suffered from a key weakness, and that is that agencies operate separately without unity and without applying the One Health approach to solve the AMR problem, which is a major problem broadly affecting people, animals, plants, food and the environment, not to mention the national and global economies.

The effort to resolve antimicrobial resistance under the Strategic Plan on Dealing with Antimicrobial Resistance in Thailand, B.E. 2560-2565 (2017-2022)[1] started with raising the issue of AMR to the national policy level. For this, the Antimicrobial Resistance Policy Committee functioned as the central administrative mechanism on the national level to facilitate multi-sectoral collaboration to resolve the issue of antimicrobial resistance in an integrative manner according to the One Health approach. Furthermore, there exists a collaborative plan between the Thai government and the World Health Organization on antimicrobial resistance of 2017-2021 (WHO Country Cooperation Strategy Program on AMR: CCS-AMR program) for providing budgetary support for the development of a system for monitoring and assessment and academic information support for implementing the Strategic Plan on Dealing with Antimicrobial Resistance in Thailand. Accordingly, the overview of the strategic plan is shown in Table 1.

TABLE 1. National Strategic Plan on Dealing with Antimicrobial Resistance in Thailand, B.E. 2560-2565 (2017-2022)

Objectives

1. 50% reduction in illnesses caused by antimicrobial-resistant bacteria.
2. 20% reduction in the use of antimicrobials in humans.
3. 30% reduction in the use of antimicrobials in animals.
4. 20% increased knowledge about antimicrobial resistance and awareness about the appropriate use of antimicrobials.
5. Antimicrobial resistance management system performance according to international criteria on a level of at least 4.

1 The Antimicrobial Resistance Management Strategies Sub-committee at Meeting No. 1/2564 on 24 March 2021 passed a resolution in approval of extending the timeframe of the Strategic Plan on Dealing with Antimicrobial Resistance in Thailand, B.E. 2560-2564 (2017-2021), up to year 2022 for the new plan to be developed to have a timeframe that is consistent with national strategies. Thus, this current plan is the "Strategic Plan on Dealing with Antimicrobial Resistance in Thailand, B.E. 2560 – 2565 (2017 – 22022)".

Strategies

1. Surveil antimicrobial resistance according to the One Health approach.
2. Control the overall spread of antimicrobial resistance in the country.
3. Prevent and control infections in medical facilities and supervise and oversee the appropriate use of antimicrobials.
4. Prevent and control antimicrobial resistance and control and supervise the appropriate use of antimicrobials in the agricultural and animal husbandry sectors.
5. Promote knowledge of antimicrobial resistance and awareness of the appropriate use of antimicrobials in the population.
6. Manage and develop policy-level mechanisms for implementing antimicrobial resistance efforts in a sustainable manner.

The purpose of this article is to present the overview of efforts under the Strategic Plan on Dealing with Antimicrobial Resistance in Thailand. The contents of this article were extracted and copied from the Half-Plan Phase Progress Report: Implementation of the Strategic Plan on Dealing with Antimicrobial Resistance in Thailand, B.E. 2560-2564 (2017-2021)".

National Level Structures and Mechanisms for Implementing the Strategic Plan

The implementation of the strategic plan relies on 2 structures and mechanisms, namely, policy and administrative mechanisms through the "National Antimicrobial Resistance Policy Committee", which the Prime Minister assigned the Deputy Prime Minister to be its chairman. This committee has multi-sectoral components, including human, animal, food and environmental health components from multiple agencies such as the government, the private sector, professional organizations and the general public. Accordingly, the committee has appointed 5 subcommittees under its supervision in order to supervise and oversee different aspects of the strategy, namely, 1) the Strategic Subcommittee on Dealing with Antimicrobial Resistance; 2) the Subcommittee on Development of an Antimicrobial Resistance Monitoring System according to the One Health Approach; 3) the Subcommittee on Reducing Impacts from Antimicrobial Resistance in Medical Facilities; 4) the Subcommittee on Dealing with Antimicrobial Resistance in the Agricultural and Animal Husbandry Sectors; and 5) the Subcommittee on Promoting and Raising Awareness in Antimicrobial Resistance and Appropriate Use of Antimicrobial Resistance in the Public. Furthermore, there is also a "Work Committee on Antimicrobial Resistance Effort Coordination and Integration" composed of a team of committee secretary generals, sub-committees and related experts that functions to plan activities and monitor work through horizontal coordination across different strategies to ensure effectiveness in resolving the country's AMR problem according to the One Health approach, and there is also an academic mechanism, wherein the government has approved the "WHO Country Cooperation Program for Thailand on Antimicrobial Resistance", which is a scientific platform for providing academic information support and for facilitating the implementation the strategic plan with greater effectiveness.

Development of Strategic Plan Monitoring and Evaluation Systems

In the implementation of work under the strategic plan, monitoring and evaluation systems are being developed in tandems, such as the development of a system for monitoring the amount of antimicrobial consumption in people and animals in Thailand and the creation of questions about antimicrobial resistance in Thailand's health and welfare surveys by the National Statistical Office of Thailand.

Furthermore, the performance of Thailand's systems for dealing with antimicrobial resistance is also being evaluated by the Joint External Evaluation Tool for International Health Regulation 2005 of the World Health Organization, by which it was found in 2017 that Thailand's performance in antimicrobial resistance management is at a medium level (Levels 2-4), distributed as follows: good performance in antimicrobial resistance detection (Level 4), medium performance in the monitoring of diseases caused by antimicrobial resistance (Level 3), medium performance in hospital infection prevention and control work plans (Level 3) and fair performance in supervision and oversight of antimicrobial use (Level 2).

In 2019, a report by the Global Health Security Index, which was prepared by an agency in the United States, ranked the health security performance of various countries worldwide, and AMR management performance was set as one of the indicators of health security. Accordingly, the antimicrobial resistance management performance evaluation results showed that Thailand scored 75 out of 100 points total (with the global average at 42.4), thus ranking Thailand as the 22nd country out of 195 countries in terms of readiness for dealing with antimicrobial resistance.

Progress in the Implementation of Each Strategy

Strategy 1. Surveil antimicrobial resistance according to the One Health approach. Significant changes occurred in 3 aspects as follows: (1) the development of a collaborative framework between agencies in monitoring antimicrobial resistance according to the One Health approach, which includes antimicrobial residues, to lead to the design and creation of consistent systems and successful use of monitoring results in supervising and overseeing efforts in each sector; (2) start of exchanges of information about consumption of antimicrobials and antimicrobial resistance according to the One Health approach through the creation of antimicrobial consumption and antibiotic resistance reports in humans and animal meats in Thailand; and (3) development of new and necessary information systems and enhancement of the capabilities of existing systems in terms of human health, public health, animal health and the environment.

Strategy 2. Control the overall spread of antimicrobial resistance in the country. Significant changes have occurred in 3 areas as follows: (1) revocation of registration of inappropriate antimicrobials such as oral colistin and reclassification of anti-tuberculosis and injected antimicrobials as special controlled drugs (in line with Phase 1 of the Plan for Reclassifying Antimicrobials for Humans, B.E. 2561-2563 (2018-2020), with current activities taking place in Phase 2 to review and reclassify oral antimicrobials; (2) classification of medicated premix

antimicrobials in animal feed to be special controlled drugs and clearly separating the control of said drugs and medicated feeds from each other and designating quinolones, cephalosporins, macrolides and polymyxins, that are used in animals, to become special controlled drugs; and (3) development of the Thailand Surveillance of Antimicrobial Consumption system (Thailand SAC) to monitor the situation of consumption of human and animal antimicrobials.

Strategy 3. Prevent and control infections in medical facilities and supervise and oversee the appropriate use of antimicrobials. significant changes have occurred in 3 areas as follows: (1) approval by the national antimicrobial Resistance Policy Committee for policy-level guidelines on dealing with antimicrobial resistance in medical facilities and hospital-level framework and national-level collaboration framework for integrated AMR management in hospitals (IAM); (2) implementation by the Ministry of Public Health in 2018 of the IAM framework in 125 hospitals under its administration and launching of a pilot project in all government hospitals and 52 private hospitals for piloting the IAM framework; and (3) commencement of the development of tools for evaluating hospital performance under the IAM framework and systems for monitoring and evaluating implementation results.

Strategy 4. Prevent and control antimicrobial resistance and control and supervise the appropriate use of antimicrobials in the agricultural and animal husbandry sectors. Changes have occurred in 4 sectors as follows: (1) In the livestock sector, legal measures and related regulations have been developed, i.e., on the control of medicated feed under the Animal Feed Quality Control Act, B.E. 2558 (2015), for which veterinaries control medicated feed production systems, on promotion and development of slaughterhouse and animal product processing plants under the Control of Animal Slaughter for the Distribution of Meat Act, B.E. 2559 (2016), and international standards, by which 95 pig and chicken farms have already been certified today nationwide, and the Raised Without Antibiotics (RWA) safe livestock production systems project, by which 66 pig farms have been certified nationwide, which represent about 100,000 pigs in the project, with project expansion ongoing to include egg chicken farming. (2) In the fishing industry, practice guidelines have been created on the appropriate use of antimicrobials in aquaculture; fishery academics and farmers received training in the reasonable use of antimicrobials in aquaculture; and personnel received development in legal oversight, health management for aquatic animals and disease prevention in aquatic animals in line with biosafety principles. (3) In the crop farming sector, a study has been conducted into the situation, impacts and residues of antimicrobials resulting from the use of antimicrobials in the prevention of greening disease in citrus and promotion of utilization of physical measures (such as removal and replanting of citrus) in place of use of antimicrobials in the management of greening disease in citrus. Finally, (4) in the pet sector, a project was launched for the promotion of reasonable use of drugs in animal hospitals, and a manual has been developed on the principles of the use of antimicrobials in pets.

Strategy 5. Promote knowledge in antimicrobial resistance and awareness on appropriate use of antimicrobials in the population. Significant changes occurred in 3 areas as follows: (1) existence of a structure for coordinating the implementation of national strategies covering the public, health promotion and civil society sectors along with the development of the action plan and communication plan for promoting knowledge in antimicrobial resistance and awareness on use of antimicrobials in the public in the period from 2019-2021; (2) presence of evaluation and monitoring of knowledge and awareness on the appropriate use of antimicrobials in the population to provide a national overview through health and welfare surveys in 2017 to provide knowledge into Thailand's situation in this area; and (3) agencies have in place strategies for more consistently and systematically providing knowledge to the population such as by the use of personal media strategies (ground war) to include knowledge about this issue into the curriculum and activities of village health volunteers who number over one million people nationwide and the use of main media strategies (air war) and social media and television campaigns that can be accessed by the population nationwide.

Strategy 6. Manage and develop policy-level mechanisms for implementing antimicrobial resistance efforts in a sustainable manner. Significant changes occurred in 3 areas as follows: (1) enhancement of Thailand's AMR work to become political policies with the National Antimicrobial Resistance Policy Committee and establishment sub-committees functioning as national-level mechanisms to facilitate the joint work of various ministries and agencies; (2) joint work between ministries and agencies under the One Health approach to drive the strategic plan and create a core team to coordinate the strategy to resolve problems and support work in the country and Thailand's international role on the issue of antimicrobial resistance; and (3) presence of a work plan under the strategy of cooperation between the Thai government and the World Health Organization on antimicrobial resistance to having a key scientific platform for providing academic information support and system development for monitoring the implementation of the strategic plan.

Conclusion

The implementation of Thailand's strategic plans in managing antimicrobial resistance gives priority to resolving the key weaknesses in the AMR effort of Thailand in the past by starting with raising the issue of antimicrobial resistance to become political policies to facilitate the collaborative work of ministries and different agencies under the One Health approach, followed by the development of national-level mechanisms to drive the 1st to the 6th strategies and the establishment of a multitude of work processes among various agencies to be consistent in the same direction in addition to giving importance to investment to develop new and essential systems and enhance the capabilities of existing systems in order to drive and evaluate long-term national AMR results to ensure that the national AMR management system is sustainable, established on secure academic foundations, can provide essential information for policy decisions and effectively support the implementation of strategic plans.

Chapter 2

Integration of Antimicrobial Resistance Surveillance

Integration of Antimicrobial Resistance Surveillance

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Whenever antibiotics are used, resistant bacteria will eventually develop and spread. This happens in both people and animals. These drug-resistant bacteria spread from people to animals, animals to animals, people to animals and animals to people. They contaminate waterways when fecal matters or wastes from humans or animals enter these waterways. They can also be found frequently in foods produced from animals fed antibiotics, and slaughter processes and distribution networks lead to cross-contamination involving multiple food products where drug-resistant bacteria can be found.

As such, surveillance of antimicrobial resistance according to the One Health Approach is divided into surveillance of antimicrobial resistance in humans, surveillance of antimicrobial resistance in animals and antimicrobial resistance in the environment. Principally, these are as follows:

1. Surveillance of antimicrobial resistance in humans focuses on surveillance of antimicrobial resistance in hospitals for the most part, and patients seeking hospital treatment are the ones to receive testing.
    1.1 Laboratory-based antimicrobial resistance surveillance:
        1.1.1 Antibiogram.
        1.1.2 Susceptibility test.
        1.1.3 Unusual AMR data.
    1.2 Epidemiological antimicrobial resistance surveillance:
        1.2.1 Surveillance of persons with drug-resistant infections.
        1.2.2 Surveillance by patient identification.
        1.2.3 Surveillance of patients with important drug-resistant infections.
2. Surveillance of antimicrobial resistance in animals:
    2.1 Surveillance of antimicrobial resistance in economic animals, aquatic animals and pets.
    2.2 Surveillance of antimicrobial resistance in animal products.
    2.3 Surveillance of antimicrobial resistance in the environment.
3. Surveillance of antimicrobial resistance in the environment.

Antimicrobial-Resistant Bacteria in the Surveillance Network

Antimicrobial resistance occurs as a result of the following key factors: 1) mutation by microbial subsequent to exposure to an incomplete dose or duration of antibiotics according to treatment regimens that leads to genetic changes in favor of antimicrobial resistance to facilitate the continued survival of the microbial; and 2) receipt of genetic materials by bacteria from another bacteria and production of antimicrobial-resistant genetic materials within the self. Because the resistance of microbial to a type of antibiotic can lead to drug resistance in all related drug groups, it causes a diminishment in treatment options for diseases, and increased prevalence of drug resistance impacts human and animal health in the form of ineffective treatment by use of existing antibiotics, the need to use different, stronger medications, longer hospital treatment durations and increased mortality from infection. Furthermore, antimicrobial resistance can spread to human and animal populations through food, water and the environment, and this spread is influenced by trade, travel and movements of people and animals, by which resistant bacteria can be encountered in food animals and food products designated by humans for consumption.

Surveillance of Antimicrobial Resistance

Antimicrobial resistance is a complex problem requiring multi-sectoral guidelines according to the One Health Approach that covers human health, land animals, aquatic animals, plants, food production, animal feed and the environment with the aim of facilitating communication and collaborative work in the implementation of work plans, policies, laws and research that will realize better objective outcomes. Accordingly, the situation of antimicrobial resistance is determined through surveillance of antimicrobial resistance, which is ***"a process to collect, analyze, interpret and distribute data related to the nature of change in antimicrobial resistance"*** that affects humans, animals, plants and the environment **systematically and continuously** with the purpose of providing guidelines on the appropriate use of medications in hospitals and that provides benefits in detecting the spread of antimicrobial-resistant bacteria, planning, decision-making, policy-making and development of measures for preventing and controlling the problem of antimicrobial resistance.

Surveillance of antimicrobial resistance according to the One Health approach is divided into surveillance of antimicrobial resistance in humans, surveillance of antimicrobial resistance in animals, and surveillance of antimicrobial resistance in the environment. That being said, antimicrobial resistance surveillance in humans is primarily the **surveillance of antimicrobial resistance in hospitals where bacteria are present,** and the types and integration of antimicrobial resistance surveillance will be discussed in the next section.

Antimicrobial-Resistant Bacteria Important to Public Health

Antimicrobial resistance surveillance has its primary basis in the evaluation of the weaknesses of living beings to produce guidelines for clinical management. As a result, it is necessary to also consider the careful use of medications to ensure that information specification will not produce excessive impacts on the laboratory setting. Therefore, we recommend the number of antimicrobial drugs submitted for responsiveness testing for the purpose of surveillance to be three or four drugs at most, and this should occur through coordination with laboratories participating in the project, and for different antimicrobials necessary for different groups of organisms (e.g., gram-positive and gram-negative) in the selection of such representatives, it is necessary to evaluate antimicrobials recommended for prevention by chemotherapy in the same manner as for treatment.

Food- and Water-borne Diseases

Food and water-borne diseases are threats to the health of the population in some parts of the world. In many cases, the use of antimicrobials is not necessary. However, for the case of shigellosis and Shigella dysenteriae, antimicrobial treatment is beneficial, and in many resource-lacking environments, the frequency of *Shigella dysenteriae*'s resistance to ampicillin and cotrimoxazole has risen to a high level. Therefore, knowledge about drug resistance models is enormously beneficial in treatment recommendations. However, for patients who seek hospital treatment, large numbers receive antimicrobial treatments before other treatments, which can lead to an excessively high evaluation of antimicrobial resistance.

Respiratory Diseases

Acute respiratory diseases are a major cause of illness and death worldwide, especially in children, and antimicrobials are used in most of the treatments for these diseases. Due to a fairly high total number of patients with pneumonia on the national or regional level, periodic surveillance systems are possible, and samples are collected from some of these patients. This type of surveillance system offers many benefits. For example, it makes it possible to limit sample collection to take place during seasons of high disease incidences and shortens the random sampling duration, which makes transportation easier and preserves the enthusiasm of data collectors, and only a small part of the key medical facilities in the country needs to be involved. For as long as these represent the overall population/cases, the number of medical personnel requiring additional training for sample collection can be reduced along with the risk from changes in the random sampling method changes. Accordingly, a smaller number facilitates more stable collaboration between primary health centers participating in a project and the coordinating center, which is beneficial when subsequently sampling guardians (such as in subsequent years),

wherein samples are obtained continuously from patients who receive treatment in medical facilities and follow case definitions. In children, according to the criteria of the WHO, a napkin is used to wipe the nasal cavity instead of collecting phlegm. *Streptococcus pneumoniae and Haemophilus influenzae* are important diseases that can be isolated from phlegm samples since they are the most commonly encountered and relevant bacteria.

Sexually Transmitted Infections

Most countries already have activities for surveillance of sexually-transmitted infections. Clinics for sexually-transmitted infections (STIs) might send samples to a national reference laboratory for diagnostic testing. The existing system for transporting test samples from STI clinics to laboratories and for sending results and interpretations back to clinics can be used for surveillance of antimicrobial resistance in gonorrhea in *Neisseria gonorrhoeae.* For surveillance antimicrobial resistance in *Neisseria gonorrhoeae* in gonococci, a continuously improved surveillance system is proposed by the use of clinically-collected samples, and the participating STI clinics will use the same case definitions. For example, for the first time, the patient does not receive treatment at their penises or white discharges occur with NRL responsiveness testing, actions will be taken to deal with all *N. gonorrhoeae* isolated that match the case definitions. Accordingly, the surveillance center that is participating should function as a representative in estimating the frequency of the drug-resistant strain on the national or regional level. In addition, the sampling duration is considered based on the number of samples submitted and the number of participating laboratories for each country or region. The NRL will choose the antimicrobial substance for responsiveness testing depending on the local distribution of drug resistance in gonococci and the recommended antimicrobials for treatment in the table, by which tetracycline, penicillin, third-generation cephalosporin and ciprofloxacin are recommended for use.

Integrated AMR management is a hospital-level framework for resolving the issue of antimicrobial drug resistance in an integrated manner. Its key principles are as follows:

1. Drug resistance is considered a hospital-level problem that every party involved must work together as a team to deal with while having in place clear management mechanisms and hospital-level effectiveness.

2. It is important for resolving antimicrobial resistance in a systematic manner while being a leading organization to which hospital executives must give major importance.

3. Every party wants to succeed together in resolving the problem of antimicrobial resistance in hospitals.

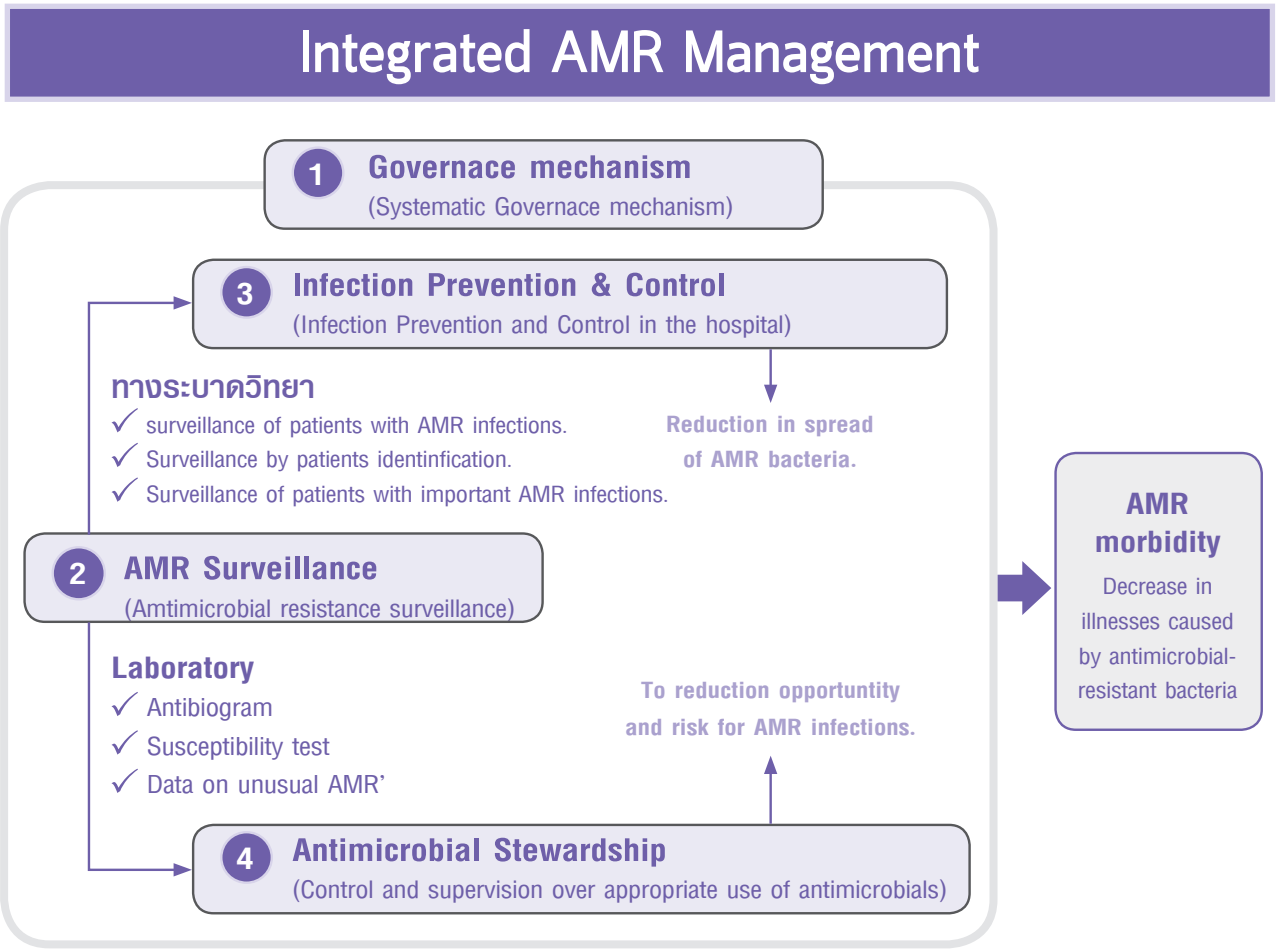

Figure 1. Integrated AMR management.

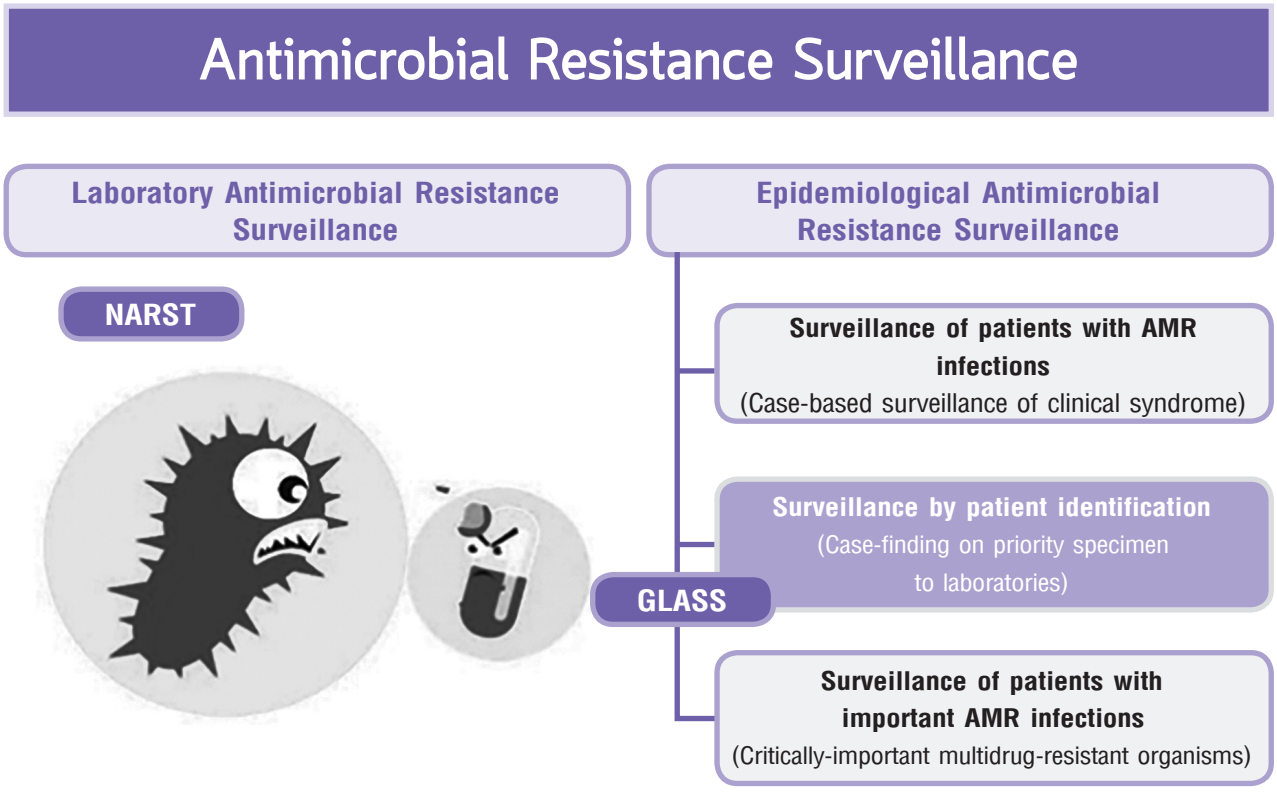

Figure 2. Antimicrobial resistance surveillance.

Critically important multidrug resistant organisms

- Vancomycin-resistant, *Staphylococcus aureus* (VRSA)
- Vancomycin-resistant *Enterococcus* (VRE)
- Colistin-resistant, *Acinetobacter baumannii*
- Colistin-resistant, *Pseudomonas aeruginosa*
- Third generation Cephalosporin-resistant, *Neisseria gonorrhoeae*

Case-based surveillance of clinical syndrome

TABLE 2. Case-based surveillance of clinical syndrome

Organism	Antibiotics
1. ***Acinetobacter baumannii***	- Carbapenem, Colistin
2. ***Pseudomonas aeruginosa***	- Carbapenem, Colistin, Piperacillin, Tazobactam
3. ***Klebsiella pneumoniae***	- Carbapenem, Colistin, 3rd generation Cephalosporin
4. ***Enterococcus***	- Vancomycin
5. ***Staphylococcus aureus***	- Methicillin, Vancomycin
6. ***Streptococcus pneumoniae***	- Penicillin, Ceftriaxone หรือ Cefotaxime, Erythromycin, Fluoroquinolone
7. ***Escherichia coli***	- Carbapenem, Colistin, Fluoroquinolone, 3rd generation Cephalosporin
8. ***Salmonella* spp.**	- Colistin, Fluoroquinolone, 3rd generation Cephalosporin

TABLE 3 Classification by symptoms of each type of antimicrobial-resistant infection.

Clinical syndrome/ presentation	Recommended case definition	Appropriate specimen	Optimal sampling location and surveillance type	Key pathogens
Acute diarrhoea	Clinical: Diarrhoeal illness with visible blood in stool Lab: Isolation of *Shigella dysenteriae* from stool	Faeces	Primary health care facility Sentinel	*Shigella dysenteriae*
Pneumonia	Clinical: Febrile illness with purulent productive cough; rapid breathing in children Lab: Isolation of *Streptococcus pneumoniae* or *Haemophilus influenzae* from sputum or blood	Sputum, blood (nasopharyngeal swabs may be used in children)	Primary health care facility Sentinel	*Streptococcus pneumoniae, Haemophilus influenzae*

Clinical syndrome/ presentation	Recommended case definition	Appropriate specimen	Optimal sampling location and surveillance type	Key pathogens
Bacteraemia/ septicaemia	Clinical: Sudden onset of fever; +/- petechial haemorrhages, purpuric rash, or rose spots Lab: Isolation of pathogen from blood	Blood	Hospital Continuous	*Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus, Salmonella* Typhi, *Escherichia coli*
Meningitis	Clinical: Sudden onset of fever with neck stiffness or altered consciousness or other meningeal sign Lab: Isolation of pathogen from CSF (+/- from blood) or positive antigen test or Gram-negative diplococci present in centrifuged deposit of CSF	CSF, blood	Hospital Continuous	*Neisseria meningitidis, Streptococcus pneumoniae, Haemophilus influenzae*
Urethral/vaginal discharge	Clinical: Urethral or vaginal discharge Lab: Gram-negative intracellular diplococci confirmed on culture as *Neisseria gonorrhoeae*	Urethral/vaginal swab	STI clinic Sentinel	*Neisseria gonorrhoeae*
Urinary tract infection (UTI)	Clinical: Frequency and dysuria or fever in presence of indwelling catheter or other focus of infection Lab: Isolation of *Escherichia coli* from urine in significant numbers (or blood)	Urine (midstream or catheter specimen)	Primary health care facility Sentinel	*Escherichia coli*
Surgical wound infection	Clinical: Pus in wound +/- fever Lab: *Staphylococcus aureus* or *Streptococcus pyogenes* isolated on culture	Pus or wound swab	Hospital Continuous	*Staphylococcus aureus*

Clinical syndrome/ presentation	Recommended case definition	Appropriate specimen	Optimal sampling location and surveillance type	Key pathogens
Hospital-acquired UTI, septicaemia, pneumonia	Clinical: see above Lab: Isolation of *Staphylococcus aureus*, *E. coli*, *Pseudomonas aeruginosa* or *Klebsiella pneumoniae*	Urine, blood, sputum, pus from any infected site	Hospital Continuous	*Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae*

TABLE 4 Drugs for testing the responsiveness model of each type of pathogen.

Key pathogens	Antimicrobials to be tested for surveillance purposes
Shigella dysenteriae	Ampicillin, chloramphenicol, co-trimoxazole, nalidixic acid
Streptococcus pneumoniae	Oxacillin, ampicillin, erythromycin, chloramphenicol, co-trimoxazole
Haemophilus influenzae	Ampicillin, erythromycin, chloramphenicol, co-trimoxazole
Staphylococcus aureus	Penicillin, oxacillin
Salmonella typhi	Ampicillin, chloramphenicol, co-trimoxazole, ceftriaxone, ciprofloxacin
Escherichia coli	Ampicillin, co-trimoxazole, gentamicin
Neisseria meningitidis	Penicillin, chloramphenicol
Neisseria gonorrhoeae	Penicillin, tetracycline, ceftriaxone, ciprofloxacin
Pseudomonas aeruginosa *Klebsiella pneumoniae*	Gentamicin, ceftazidime

SUMMARY OF ANTIMICROBIALS FOR ANTIMICROBIAL RESISTANCE SURVEILLANCE TESTING

TABLE 5 Summary of antimicrobials for testing antimicrobial resistance surveillance.

Drug Type	Importance
Tetracycline	Representative of members of this group, except minocycline
Chloramphenicol	Results may be extrapolated to thiamphenicol
Ampicillin	Representative of broad spectrum penicillins susceptible to beta-lactamase
Benzyl penicillin	Tests susceptibility to all beta-lactamase-susceptible penicillins
Oxacillin	Representative of the whole group of beta-lactamase-resistant penicillins

Drug Type	Importance
Ceftriaxone; ceftazidime	Representatives of third generation cephalosporins
Co-trimoxazole	Representative of trimethoprim alone and in combination with sulphonamide
Erythromycin	May be used to indicate susceptibility to certain other macrolides (azithromycin, clarithromycin)
Gentamicin	Should be used for primary testing of susceptibility to other aminoglycosides
Nalidixic acid	Quinolone resistance
Ciprofloxacin	Fluoroquinolone resistance

Ranking of Importance of Antimicrobial-Resistant Bacteria

For public health purposes, it is not possible to observe all types of bacterial resistance on the same level. The World Health Organization has named seven resistant disease-causing pathogens, namely, *E. coli, K. pneumoniae, S. aureus, S. pneumoniae, Salmonella* spp.*, Shigella* spp. *and N. gonorrheae* as the order of importance for surveillance, and a CDC report specified 18 pathogens as public health problems in the United States and sorted drug-resistant pathogens related to the need for urgent public health actions in order to combat diseases. Each country might have its own set of important disease-causing pathogens. However, focusing on an agreed-upon order of importance of bacteria with a specific form of drug resistance can help ensure confidence that the data required for facilitating global collaboration in preventing and controlling antibiotic resistance can be integrated in a sustainable manner.

Improved detection of resistant bacteria can be achieved through enhancements and expansion of existing surveillance systems that monitor resistance in healthcare settings (such as the National Healthcare Safety Network [NHSN]), in agricultural settings (such as the National Antimicrobial Resistance Surveillance System [NARMS]), and across healthcare and community settings (such as the Emerging Infections Program [EIP]). Enhancements include providing incentives for healthcare-facility reporting, advancing automatic capture of electronic data from healthcare facilities and clinical laboratories, including more diverse patient and community venues as reporting sites, and expanding the sampling of bacterial specimens from agricultural settings. Taken together, improvements to NHSN, EIP, and NARMS will enhance detection of emerging threats in humans and animals, speed outbreak response, and identify populations at greatest medical risk. Moreover, experience with NHSN has shown that reporting also leads to better prevention (Goal 1), because hospitals and state and local health departments use NHSN data to guide local action to interrupt the spread of resistant infections.

Important Antimicrobials of the World Health Organization

In this report, Critically Important Antimicrobials refer to the list of CIA for human medicine defined by the World Health Organization. It ranks medically important antimicrobials for risk management of antimicrobial resistance due to non-human use. It was developed for cautious use in mitigating the human health risks associated with antimicrobial use (AMU) in both humans and food-producing animals. TheWHO has produced a list of Critically Important Antimicrobials for Human Medicine since 2005 and the latest updated WHO CIA list was announced in 2018. The CIA list is prioritized to address AMR and promote the prudent use of antimicrobials in both human and veterinary medicine.

The WHO criteria for inclusion of antimicrobial substances in the CIA list require that two parameters are fulfilled:

1. The antimicrobial class is the sole, or one of limited available therapies, to treat serious bacterial infections in humans.
    - a1 : Sole or one limited treatment method for treating severe bacterial infections in people.
    - a2 : For treatment of bacteria-caused infections that (1) can be transmitted by non-human sources or (2) by resistant genes from non-human sources.
2. Antimicrobials for treating infections in humans from: 1) bacteria that might be transmitted to humans from non-human sources; or 2) bacteria that might have received resistant genes from non-human sources.
    - a1 : Used to treat a large number of people with infections for which limited antimicrobials are available
    - a2 : Used with high frequency in human medicine or in certain high risk groups
    - a3 : Used to treat human infections for which an extensive evidence exists on the transmission of resistant-bacteria or genes from non-human sources

Three prioritization criteria are used to further categorize antimicrobial substances in the CIA list into two sub-groups of Highest Priority CIA and High Priority CIA:

1. High absolute number of people, or a high proportion of use in patients with serious infections in healthcare settings affected by bacterial diseases for which the antimicrobial class is the sole or one of few alternatives to treat serious infections in humans.
2. High frequency of use of the antimicrobial class for any indication in human medicine, or a high proportion of use in patients with serious infections in healthcare settings, since users may favor the selection of resistance in both settings.
3. The antimicrobial class is used to treat infections in people for whom there is evidence of transmission of resistant bacteria (e.g. non-typhoidal *Salmonella* and *Campylobacter* spp.) or resistance genes (high for *E. coli and Enterococcus* spp.) from non-human sources.

- Cephalosporins (3rd, 4th and 5th generation)
- Glycopeptides and lipoglycopeptides
- Macrolides and ketolides
- Polymyxins
- Quinolones

Quinolones

Quinolones are known to select for quinolone-resistant *Salmonella* spp. and *E. coli* in animals. At the same time, quinolones are one of the few available therapies for serious *Salmonella* spp. and *E. coli* infections. Given the high incidence of human disease due to *Salmonella* spp. and *E. coli*, the absolute number of serious cases is substantial.

Cephalosporins (3rd and higher generation)

Cephalosporins (3rd and higher generation) are known to select for cephalosporin-resistant *Salmonella* spp. and *E. coli* in animals. At the same time, 3rd and higher-generation cephalosporins are one of the few available therapies for serious *Salmonella* spp. and *E. coli* infections in humans, particularly in children. Given the high incidence of human disease due to *Salmonella* spp. and *E. coli*, the absolute number of serious cases is substantial.

Macrolides and Ketolides are known to select for macrolide-resistant Campylobacter spp. in animals, especially *Campylobacter jejuni* in poultry. At the same time, macrolides are one of few available therapies for serious *Campylobacter* infections, particularly in children, for whom quinolones are not recommended for treatment. Given the high incidence of human disease due to *Campylobacter* spp., especially *Campylobacter jejuni*, the absolute number of serious cases is substantial.

Campylobacter jejuni has a definite number of severe cases. Glycopeptides are known to select for glycopeptide-resistant *Enterococcus* spp. in food animals (e.g., when avoparcin was used as a growth promoter, vancomycin-resistant enterococci (VRE) developed in food animals and were transmitted to people). At the same time, glycopeptides are one of the few available therapies for serious enterococcal infections. Given the high number of cases, the previously documented occurrence of transmission of VRE to people from food animals, and the very serious consequences of treatment failures in such cases, glycopeptides are classified as being of the highest priority.

Polymyxins (e.g. colistin) are known to select for plasmid-mediated polymyxin-resistant *E. coli* in food animals. At the same time, intravenous polymyxins are one of few available therapies for serious Enterobactericeae and *Pseudomonas aeruginosa* multi-resistant infections in people in healthcare settings in many countries, especially in seriously ill patients in critical care. Given the high incidence of human disease due to Enterobactericiae, the absolute number of serious cases where colistin is needed can be considered substantial.

TABLE 6 List of drug-resistant bacteria and list of 9 antimicrobials used as national-level warning signals.

Organism	Antibiotics
1. *Acinetobacter baumannii*	- Carbapenem, Colistin
2. *Pseudomonas aeruginosa*	- Carbapenem, Colistin
3. *Klebsiella pneumoniae*	- Carbapenem, Colistin, 3rd generation Cephalosporin
4. *Enterococcus*	- Vancomycin

Organism	Antibiotics
5. *Staphylococcus aureus*	- Methicillin (MRSA), Vancomycin
6. *Streptococcus pneumoniae*	- Penicillin, Ceftriaxone หรือ Cefotaxime
7. *Escherichia coli*	- Carbapenem, Colistin, Fluoroquinolone, 3rd generation Cephalosporin
8. *Salmonella* spp.	- Colistin, Fluoroquinolone, 3rd generation Cephalosporin
9. *Neisseria gonorrhoeae*	- Cefixime

The 7 important drug-resistant pathogens advised by the World Health Organization include *E. coli, K. pneumoniae, S. aureus, S. pneumoniae, Salmonella* spp., *Shigella* spp. และ *N. gonorrheae*

TABLE 7 Examples of important antimicrobials used as national warning signals.

Drug Class	Drug
Polymyxins	Colistin
Carbapenems	Doripenem, Ertapenem, Imipenem ·≈– Meropenem
3rd Generation Cephalosporins	Ceftriaxone, Cefixime, Ceftazidime ·≈– Cefotaxime
Fluoroquinolones	Ciprofloxacin, Norfloxacin, Ofloxacin ·≈– Levofloxacin
Beta-lactamase inhibitor combination	Amoxicillin-Clavulanic acid ·≈–Piperacillin-Tazobactam

Remarks: The list of pathogens and drugs are subject to changes according to the situation.

One Health, Environment and Antimicrobial Resistance

Whenever antibiotics are used, resistant bacteria will eventually develop and spread. This happens in both people and animals. These drug-resistant bacteria spread from people to animals, animals to animals, people to animals and animals to people. They contaminate waterways when fecal matters or wastes from humans or animals enter these waterways. They can also be found frequently in foods produced from animals fed antibiotics, and slaughter processes and distribution networks lead to cross-contamination involving multiple food products where drug-resistant bacteria can be found.

Widespread use of antimicrobials in every sector (humans and agriculture) means that these drugs are often found in the environment, especially water sources and the soil where bacteria can be subsequently exposed to them in low concentrations. Antibiotics are often used in raising aquatic animals and in crops (such as gentamicin and streptomycin for spraying on apple fruits), and so it is easier for antibiotic residues to contaminate water resources.

Laboratory-based Antimicrobial Resistance Surveillance

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Drug resistance is a public health problem of global significance because disease-causing bacteria today have adapted to the point of becoming resistant to nearly every type of antimicrobial drug. It is believed that, if no actions are taken, the world will enter the post-antibiotic era, that is, an era where there are no antibiotics. Accordingly, in this chapter, the drug resistance of problematic bacteria does not include tuberculosis-causing bacteria but includes all other types of drug-resistant bacteria that cause infection risk in surgeries or treatment of cancer patients or patients with immunodeficiencies and that contribute to greater mortality due to infectious diseases.

National Antimicrobial Resistance Surveillance Center, Thailand: (NARST)

In 1997, the Department of Medical Sciences established the National Antimicrobial Resistance Surveillance Center. Over 28 hospitals applied to join the network within the first 28 years, and work in the initial stages received financing from the World Health Organization. Then in 2005, the Ministry of Public Health established the Antimicrobial Surveillance Program Management Committee with the Director-General of the Department of Medical Sciences serving as its chairman, and the National Antimicrobial Resistance Surveillance Center at the time had 60 more hospitals joining the network, and the center has been operated with the budget of the Department of Medical Sciences ever since. Its functions are as follows[1]:

1. Gather, analyze and disseminate information on the testing of responsiveness of disease-causing bacteria to antimicrobials for the creation of an antibiogram (a national-level model for the responsiveness to microbial of each type of pathogen, university health network (UHOSNET)) and hospitals, including the monitoring of the size of the problem and the situation of antimicrobial resistance in bacteria on the national level and the level of the health regions of the Ministry of Public Health.

2. Function as a development and performance-enhancing center in bacteria type classification and testing of the antibiotic responsiveness of pathogens by diagnostic laboratories nationwide to ensure a uniform standard.

3. To function as a center for supporting technical standards for medical microbiological laboratories and knowledge about drug-resistant bacteria for diagnostic laboratories for surveillance and reporting of drug resistance in hospitals, including detection of new drug-resistant genes and pathogens.

The work of the National Antimicrobial Resistance Surveillance Center is aimed at acquiring a laboratory-based antimicrobial resistance surveillance system, beginning with the following activities:[2]

1. Creation of an Antimicrobial Resistance Surveillance System

The establishment of an antimicrobial resistance surveillance system requires hospitals to apply to be members of the surveillance system network to submit data obtained from patient sample testing and analysis in their regular work. These must be hospitals with medical microbiological laboratories tasked with testing and analyzing patient samples and recording test results meticulously and accurately. In addition, the surveillance network should be made up of hospitals that are different such as government hospitals under and not under the supervision of the Ministry of Public Health, private hospitals and university hospitals, and they should be from different localities to ensure data diversity and produce a national overview with the broadest coverage.

2. Data Collection and Analysis for Dissemination

Minimum Inhibition Concentration: MIC) Hospital laboratories in the cooperation network send data continuously every 3 months to the National Antimicrobial Resistance Surveillance Center through the AMR Lab Information Sharing System (ALISS). The data will contain test results on the type of pathogenic bacteria and test results on the responsiveness of the pathogens to antimicrobials, including patient data such as hospital number (HN), sex, age, lab number, location type (such as IPD, OPD, and ICU ward), patient sample type, bacteria type and sensitivity testing (diameter of the drug suppression zone or minimum inhibition concentration (MIC). The aforementioned data are analyzed by using the WHONET program of the World Health Organization (a program that can be downloaded for use at no charge and that is continuously updated by the World Health Organization) to show the trend of each drug-resistant pathogen (Figure 3) to assess the effectiveness of the practice guidelines for preventing and controlling drug-resistant infections and setting national drug resistance management policies, followed by the creation of an antibiogram (Figure 4) that helps doctors choose drugs more accurately for treatment and that provides data for supervising and controlling antimicrobial use (antimicrobial stewardship) to reduce unnecessary use of broad-spectrum antibiotics. In addition to the data obtained from the surveillance network, the surveillance network also continuously requests for data support on pathogens that cause *Neisseria gonorrhoeae* from the Bang Rak Group on sexually-transmitted infections under the Department of Disease Control, since the pathogens belong to the group the World Health Organization proposed to be included in the national drug-resistance surveillance system. Accordingly, data on the responsiveness to antimicrobials by gonorrhea are analyzed and presented in a histogram to show the trend of drug resistance based on the MIC value and then published along with other data on the website, http://narst.dmsc.moph.go.th.

Furthermore, the surveillance center also provides support in providing confirmation tests of drug-resistant pathogens sent by the network in order to detect both drug-resistant pathogens and genes that are national problems and new diseases, by which the latter are reported to the Bureau of Epidemiology under the Department of Disease Control for local coordination and commencement of an investigation.

3. Enhancement of Capabilities in Testing Antimicrobial-resistant Pathogens in Network Laboratories

Data published by the surveillance network are used for many benefits as mentioned above. Therefore, the quality and reliability of data are highly important. As such, the surveillance center organizes operation meetings to exchange problems and review test methods and support knowledge and information on new drug-resistant pathogens to ensure that they remain up-to-date continuously every year. Furthermore, a manual and standard for testing for disease-causing pathogens and safety have been made (Figure 5.) and published for microbiological activities inside and outside the network for use to accompany work according to international standards. Furthermore, external quality assessment (EQA) is conducted to assess the performance of drug-resistant bacteria twice annually along with the use of orientation to improve hospitals with sub-par EQA scores (85%).

Figure 2.1. Percentage of the bacteria *Klebsiella pneumoniae, Enterobacter cloacae, Pseudomonas aeruginosa* and *Acinetobacter* spp. that are resistant to imipenem carbapenems from 2000 to 2020.

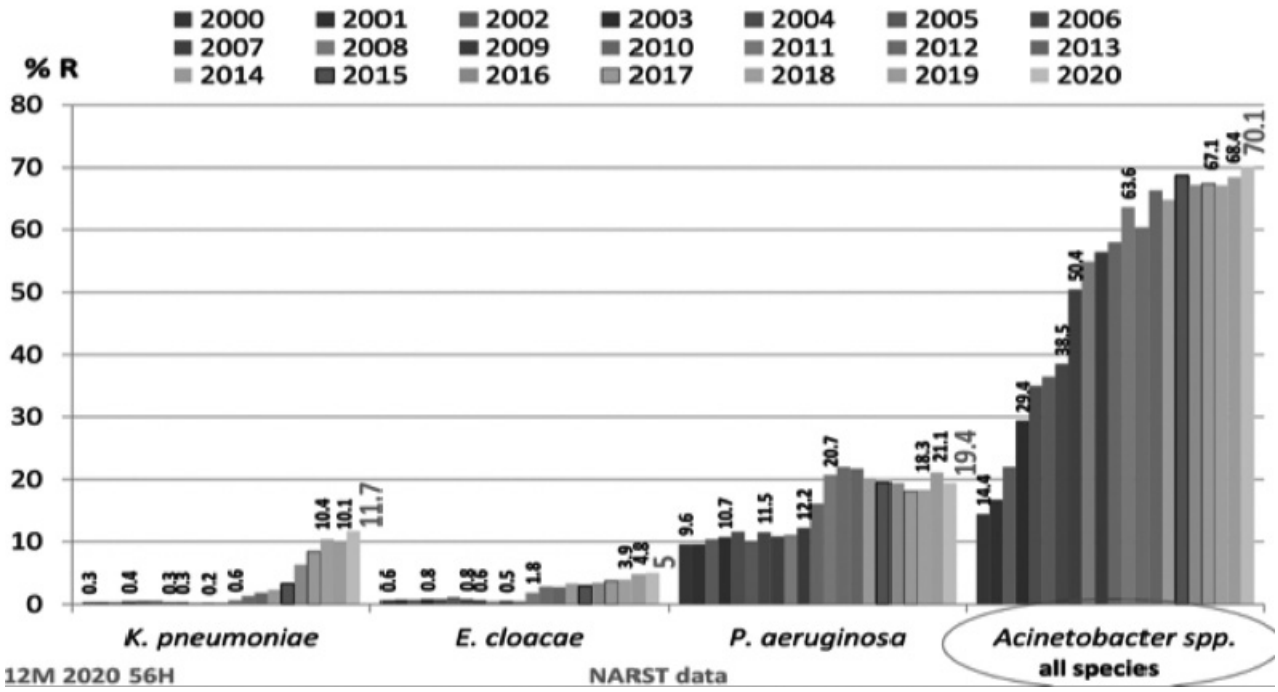

Figure 2.2. Antibiogram showing percentages and responsiveness to antimicrobials by pathogenic bacteria.

Percentage of susceptible Organisms Isolated From All Specimen,

Organism	TOTAL ISOLATES	BETA - LACTAMS																
		PENICILLIN	PENICILLIN BY MIC	AMPICILLIN	AMOXICILLIN/ CLAVULANIC ACID	AMPICILLIN / SULBACTAM	PIPERACILLIN / TAZOBACTAM	CEFAZOLIN (A)	CEFAZOLIN (U)	CEFUROXIME SODIUM (parenteral)	CEFUROXIME SODIUM (Oral)	CEFOPERAZONE/ SULBACTAM	CEFOTAXIME	CEFTAZIDIME	CEFTRIAXONE	CEFEPIME	OXACILLIN	CEFOXITIN
Acinetobacter calcoaceticus-baumannii complex	19,830			R	R	27 (5938)	25.4 (17928)						9.4 (11767)	25.2 (18645)	9.7 (11858)	25.4 (3237)		
(ICU)	4,547			R	R	13.2 (1148)	16.3 (4183)						4.8 (2743)	16.1 (4435)	4.5 (3065)	13.6 (1645)		
(inpatient)	10,237			R	R	23.7 (2667)	24.4 (6345)						8.3 (6222)	24.1 (19007)	8.6 (6534)	23.1 (3218)		
(outpatient)	692			R	R	53.5 (155)	51.7 (525)						22.1 (439)	52 (679)	27.1 (387)	53.1 (292)		
Acinetobacter spp.	1,185					71.9 (398)	74 (1058)						42.6 (847)	47.2 (1141)	45.5 (807)	66.9 (472)		
Aeromonas hydrophila	495						86 (315)			84.1 (69)			83 (305)	88.9 (332)	83.1 (355)	98 (153)		26.5 (162)
Burkholderia cepacia complex	509			R	R	R								84.1 (502)				
Burkholderia mallei	6													- *				
Burkholderia pseudomallei	718				97.2 * (214)									98.9 * (274)				

Figure 2.3. Manual and standards for disease testing and safety.

Surveillance by Identification of Patients with Antimicrobial-resistant Infection (Case-finding based on priority specimen to laboratory)

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The problem of antimicrobial resistance has been causing continuously increasing losses in public health and the economy worldwide. As a result, in 2015, the World Health Organization announced the 5-item Global Action Plan on Antimicrobial Resistance (GAP) and established the Global Antimicrobial Resistance Surveillance System (GLASS) to support GAP in 2 items, namely, support of knowledge through surveillance systems and research in antimicrobial resistance. As such, the purpose of the GLASS system is to provide guidelines for use as guidelines for the establishment of an antimicrobial surveillance system to assess the situation of antimicrobial resistance and the size of drug resistance worldwide, including detection and reporting of new antimicrobial-resistant pathogens, communication of action plan guidelines for targeted prevention and control and assessment of action plan effectiveness. In addition, data can also be used to compare the sizes of problems and drug resistance situations in various regions worldwide, since the GLASS system specifies the criteria for collection analysis format for data in a single platform, whereby the World Health Organization has announced for members to participate in the implementation of the GLASS system through the publication of the Global Antimicrobial Resistance System: Manual for Early Implementation in the same year.[3]

Thailand, as a member country of the World Health Organization, has sent a letter stating its intention to participate in the implementation of the GLASS system in 2017. Accordingly, the Ministry of Public Health has assigned the Department of Medical Sciences to represent the country in the country's work and coordination relating to the GLASS system and has begun sending data to the World Health Organization's GLASS system as of 2017. The activities that have taken place are as follows: [4]

1. Construction of a surveillance network. The GLASS surveillance system searches for patient cases with antimicrobial-resistant infections (case-finding based on priority specimen to laboratory), making it necessary to have additional patient data from laboratory data. Therefore, the hospital network of the GLASS system requires a team made up of infection control nurses (ICNs) and doctors working in an integrative manner with fairly good effectiveness with the medical microbiological laboratory team. Furthermore, information technology personnel are required to provide assistance in connecting patient data from hospital databases with medical microbiological test results. Accordingly, in the future, the AMR Lab Information Sharing System (ALISS) will help make this connection more convenient.

2. Collection, Selection and Preparation of Data for Submission to the World Health Organization

The laboratories of network hospitals cooperate by sending data for 12 months (January to December) to the National Antimicrobial Resistance Surveillance Center, by which the data consist of 1) the number of patients receiving a diagnosis at the network hospital; and 2) the number of patients ordered for medical microbiological laboratory testing, whether for gram-positive or gram-negative bacteria, and results on the responsiveness or non-responsiveness to the intended drugs for the specified specimens.

TABLE 7. Patient Information.
- Patient information is as follows:

1	Hospital name/code	For use in sorting duplicate data and not for submission to the World Health Organization.
2	Patient ID.	
3	Hospital number	For use in sorting duplicate data and not for submission to the World Health Organization.
4	Admission number	
5	First name	
6	Last name	
7	Gender	
8	Age	
9	Date of birth	
10	Admission date	
11	CI/HAI/ Unknown	ICN doctor's considerations according to the GLASS system definitions.
12	Organism	
13	Lab number	For use in sorting duplicate data and not for submission to the World Health Organization.
14	Specimen type	
15	Specimen collection date	
16	Antibiotic (R, I, S)	

The medical microbiological laboratory data of the GLASS system specify the types of specimens and the disease-causing pathogens under surveillance as shown in TABLE 8. Furthermore, they also specify the types of antimicrobials used to test the drug responsiveness of pathogens as shown in TABLE 9.

TABLE 8. Specification of specimen types and surveilled pathogens.

Specimen type	Pathogens
Blood	*E. coli*, *K. pneumoniae*, *A. baumannii*, *S. aureus*, *S. pneumoniae*, *Salmonella* spp.
Urine	*E. coli*, *K. pneumoniae*
Stool	*Salmonella* spp. และ *Shigella* spp.
Urethral, cervical และ throat swab	*N. gonorrhoeae*

TABLE 9. Specification of the types of antimicrobials used to test drug responsiveness of pathogens

Pathogens	Antibiotics
E. coli	Co-trimoxazole, Ciprofloxacin or levofloxacin, Ceftriaxone or cefotaxime and ceftazidime, Cefepime, Imipenem, meropenem, ertapenem or doripenem, Colistin, Ampicillin
K. pneumoniae	Co-trimoxazole, Ciprofloxacin or levofloxacin, Ceftriaxone or cefotaxime and ceftazidime, Cefepime, Imipenem, meropenem, ertapenem or doripenem, Colistin
A. baumannii	Tigecycline or minocycline, Gentamicin and amikacin, Imipenem, meropenem or doripenem, Colistin
S. aureus	Cefoxitin
S. pneumoniae	Oxacilline, Penicillin G, Co-trimoxazole, Ceftriaxone or cefotaxim
Salmonella spp.	Ciprofloxacin or levofloxacin, Ceftriaxone or cefotaxime and ceftazidime, Imipenem, meropenem, ertapenem or doripenem
Shigella spp.	Ciprofloxacin or levofloxacin, Ceftriaxone or cefotaxime and ceftazidime, Azithromycin
N. gonorrhoeae	Cefxime, Ceftriaxone, Azithromycin, Spectinomycin, Ciprofloxacin, Gentamicin

Definitions in the GLASS System

1. HAI (Hospital Acquired Infection)

This means sample collection from patients recovering in hospital for > 2 calendar days or patients recovering in hospital for < 2 calendar days but transferred from a hospital in which they were previously hospitalized for > 2 calendar days.

2. CI (Community Infection)

This means sample collection from patients recovering in hospital for < 2 calendar days or outpatients.

Removal of Duplicate Data

Duplicate data means data sets that match in all 4 of the following pieces of data:

1. Patient ID or national identification card number.
2. Specimen type or sample type.
3. Pathogens or types of disease-causing bacteria.

4. Origin of infection or HAI or CI. If unknown or not applicable, the program will compute by subtracting the admission date from the sample collection date or enter unknown if there is no data for computation. After using the WHONET GLASS program to gather data received from all hospitals in the network, the program will issue a command to delete duplicate data before preparing the data in the next step.

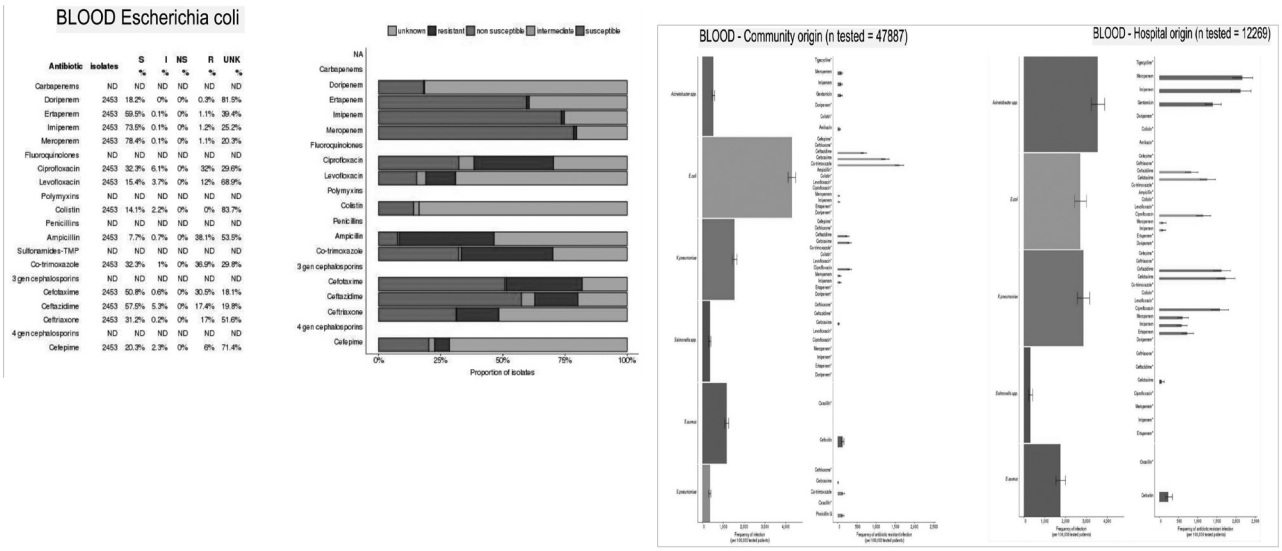
Data Preparation

When data from all hospitals in the network are gathered, they will be deemed as Thailand's national data and will be made into 2 data files by using the WHONET GLASS program, namely, a RIS file and a sample file according to the manual before being uploaded onto the GLASS website.

Data Dissemination

The World Health Organization will analyze and publish data on the website, https://www.who.int/glass/en/

Figure 6. Pictures published on the World Health Organization's website



Antimicrobial-Resistant Infection Patient Surveillance Guidelines (case-based surveillance of clinical syndromes)

Surveillance of Antimicrobial Resistance in Human Health and Public Health

Surveillance of antimicrobial-resistant infections is a major component in the management of antimicrobial-resistant pathogens, and good antimicrobial resistance surveillance can help discover disease outbreaks in a timely manner to enable swift actions to control disease infections from spreading to other persons, in addition to providing data about the sizes and significance of problems in antimicrobial-resistant infections that can be utilized in resolving antimicrobial-resistant infections in the hospital setting and provide data on the efficacy of infection prevention and control in hospitals

There are 2 main types of surveillance of antimicrobial resistance in hospitals and communities as follows:

1. Laboratory-based surveillance of antimicrobial resistance based on data systems based on hospital laboratories (laboratory-based surveillance system). The data obtained can be used to benefit antimicrobial stewardship, because 3 types of data are provided as follows:

1.1 Hospital antibiogram data. This indicates the responsiveness of pathogens to antimicrobials used in the hospital setting. This data is useful in the selection of antimicrobials for empirical treatments and is beneficial in the selection of antimicrobials for inclusion in hospital medication lists.

1.2 Susceptibility test data for antimicrobial resistance. This data is obtained from culturing pathogens found from the submitted specimens of each patient and is beneficial in the selection of antimicrobials for treating the infections experienced by each patient.

1.3 Unusual AMR data. This data is data on antimicrobial-resistant pathogens never previously encountered in hospitals. Accordingly, medical technicians, microbiologists and microbiological laboratory personnel play major roles in the surveillance of this type.

2. Epidemiological surveillance based on data of patients with drug-resistant infections (case-based surveillance system). This is a method of surveillance that starts from the moment patients exhibit symptoms and display symptoms with laboratory test results indicating drug-resistant infection. This type of surveillance is useful for treatment and infection prevention and control work in hospitals (IPC) and should be

implemented in the form of prospective active surveillance, i.e., to surveil patients while they are still in the hospital in order to obtain data for use in preventing, controlling and resolving problems in a timely manner. This type of surveillance is sub-divided into 3 additional types as follows:

2.1 Surveillance of patients with drug-resistant infections (case-based surveillance of clinical syndromes. Currently, this is implemented in every hospital in the form of surveillance of patients with drug-resistant infections according to the HAI surveillance system and is meant to provide situational awareness, outbreak detection and early warning to allow appropriate selection of infection prevention and control measures.

2.2 Surveillance by patient identification (case-findings based on priority specimens sent routinely to laboratories for clinical purposes). This is a method of surveillance according to the guidelines of the World Health Organization (GLASS: Global AMR Surveillance System) that enhances effectiveness in the surveillance and detection of drug-resistant infections in hospitals and can be used to assess antimicrobial resistance burden and distribution trend of drug-resistant infections caused by hospital or community infections. It can also be used to assess the effectiveness of infection prevention and control measures in hospitals.

2.3 Surveillance of patients with important drug-resistant infections (critically-important multidrug-resistant organisms). This is the surveillance of patients found to have important infections or infections not frequently encountered in hospital settings. When these infections are found, a warning must be issued within the hospital and they must be reported to the Bureau of Epidemiology. Accordingly, epidemiological personnel and infectious diseases control nurses and microbiological laboratory personnel plays major roles in this type of surveillance.

Purpose of Surveillance of Antimicrobial-Resistant Infection Patients

The surveillance system for patients found with antimicrobial-resistant pathogens includes data collection, analysis and reporting on the situation of important antimicrobial-resistant pathogens from the national hospital surveillance network. Its purposes are as follows:

1. Development of a case-based surveillance system for patients with antimicrobial-resistant infections (case-based surveillance of clinical syndromes).
2. Situational and trend reports on the hospital, provincial, regional and national levels to raise awareness in communities, hospitals and the nation.

Surveillance of Patients with Antimicrobial-resistant Infections (case-based surveillance of clinical syndromes)

This is the surveillance of patients with antimicrobial-resistant infections and starts from when patients come to seek hospital treatment in either the outpatient or inpatient department of the hospital. Its order of practice for infection surveillance is as follows:

1. Inspect to determine whether or not an infection has occurred by relying on the following information:

- Fever (body temperature greater than 38 degrees Celsius).

- Other symptoms based on the organ with infection, such as coughing, burning sensation during urination or urinary obstruction, diarrhea, skin inflammation and redness, pus discharges, headache, listlessness, etc.

- For the case of infection in children younger than 1 year, this consist of fever (rectally -measured body temperature of 38 degrees Celsius or higher) or coldness of the body (rectally -measured body temperature of under 37 degrees Celsius), respiratory arrest, bradycardia, listlessness, vomiting, etc.

- Laboratory test results such as abnormally high or low white blood cell count, gram staining, pathogen culture, x-ray imagery, ultrasound, MRI, immunological test, molecular test results, etc.

2. If an infection is encountered, determine which organ is infected by relying on the criteria or definitions for infection in each of the body's organs according to international standards. Otherwise, in cases where the infection has occurred in the hospital setting, use the hospital infection diagnosis manual of the Bamrasnaradura Infectious Diseases Institute, Department of Disease Control, Ministry of Public Health.

3. Determine the disease-causing pathogen. Interpret test results to determine whether or not the pathogens discovered are indeed disease-causing. Do so by relying on the diagnostic criteria for disease-causing pathogens. Otherwise, if the case fits no criteria, rely on knowledge about various disease-causing pathogens in the body's organs, local florae and pathogenic contamination. In cases where the pathogen is suspected to be disease-causing or caused by contamination, consult a medical doctor or a microbiological laboratory.

4. Patient classification by source of contact is divided as follows:

- Community-acquired infection (CAI). This is an infection present from the first moment of admission. It is an infection found on the first date the patient displays symptoms or displayed symptoms or when test results provide a diagnosis of components of infection (date of event) and takes place from before the date of hospital admission to the 2nd day after hospital admission (hospital day 1-2).

- Hospital-acquired infection or hospital-associated infection (HAI). This is an infection present on the first date on which the patient has symptoms, displayed symptoms or diagnostic test results that are components of infection (date of event) after the 3rd day after hospital admission (hospital day 3). In cases where the patient was referred from another hospital, use the same diagnostic criteria as for infection from other hospitals or infection from one's own hospital.

Bacteria Infections and Antimicrobials in the Surveillance System

There are 8 important types of drug-resistant bacteria requiring surveillance as follows:

1. *Acinetobacter baumannii,* which is resistant to carbapenem or colistin.

2. *Pseudomonas aeruginosa,* which is resistant to antipseudomonal penicillin (piperacillin/tazobactam) or carbapenem or colistin.

3. *Klebsiella pneumoniae*, which is resistant to extended-spectrum cephalosporin (ceftriaxone or cefotaxime) or carbapenem (CRE) or colistin.

4. *Escherichia coli,* which is resistant to colistin or carbapenem (CRE) or fluoroquinolone (ciprofloxacin) or extended-spectrum cephalosporin (ceftriaxone or cefotaxime).

5. *Staphylococcus aureus,* which is resistant to methicillin (MRSA) or vancomycin (VISA and VRSA).

6. *Salmonella* spp., which is resistant to colistin or fluoroquinolone (ciprofloxacin) or extended-spectrum cephalosporin (ceftriaxone or cefotaxime).

7. *Enterococcus faecium,* which is resistant to vancomycin (VRE).

8. *Streptococcus pneumoniae,* which is resistant to penicillin (ampicillin) or macrolide (erythromycin) or extended-spectrum cephalosporin (ceftriaxone or cefotaxime).

Acinetobacter baumannii resistant to carbapenem or colistin.

Mostly, this is present in the form of hospital infections. There are many drug resistance mechanisms and possibly multiple mechanisms will be present at the same time. The pathogen can survive in the environment, especially in hospital environments, for extended periods of time of several months. *A. baumannii* can multiply in the vicinity of wash basins, floors and patient beds in hospitals, and an outbreak can occur in the absence of a sufficiently adequate isolation precaution system. Due to the above, *A. baumannii* is a major cause of infection in the hospital setting.

The risk factors for *A. baumannii* infections in the hospital setting include long hospitalization time, treatment in the intensive care unit, use of a respirator, presence of a body catheter, previous history of receiving cephalosporins, aminoglycosides and imipenem, immunodeficiencies, etc. Common sites of infection include pneumonia, bacteremia, urinary tract infection, post-neurosurgery infection and intraabdominal infection.

Currently, it has been found that *A. baumannii* is resistant to multiple antimicrobials, especially carbapenems. Data from the National Antimicrobial Resistance Surveillance Center (NARST), Thai National Institute of Health, Department of Medical Sciences, from January to June 2020 found that *A. baumannii* has a rate of resistance to carbapenems as high as 72.5% and 3.4% resistance to colistin. Furthermore, data from the IPC and AMR Surveillance Program of the Bamrasnaradura Infectious Diseases Institute reveal that, for HAIs from *A. baumannii*, the rate of resistance was as high as 76% for to carbapenems and as high as 4.2% for colistin, thus making it more complicated to choose antimicrobials to treat *A. baumannii* infections and increasing mortality.

***Pseudomonas aeruginosa resistant to* Antipseudomonal penicillin (piperacillin/tazobactam) or carbapenem or colistin**

P. aeruginosa can survive extensively in the hospital environment such as catheters, surgical instruments, respirator tubes, disinfection solutions, etc., thus making it a leading cause of hospital-acquired infections. The pathogen has multiple drug resistance mechanisms and many mechanisms might be present simultaneously. The factors correlated with antimicrobial-resistant *P. aeruginosa* infections include immunodeficiencies, presence of structural lung disease solid tumor, use of respiratory, use of intravenous catheter, and prior use of fluoroquinolones, antipseudomonal ß-lactam and aminoglycosides, prior history of colonization by drug-resistant *P. aeruginosa,* etc. The important sites of infection in the hospital setting include pneumonia, bacteremia, urinary tract infection, wound infection and burn wound infection

Data from NARST from January to June 2020 reveals that *P. aeruginosa* has a rate of resistance to carbapenems of 21.5% and a rate of resistance to colistin of 3.9%, while IPC and AMR Surveillance Program data from the Bamrasnaradura Infectious Diseases Institute reveals that, for HAIs by *P. aeruginosa*, the resistance rate was 28.7% for carbapenem and 1.7% for colistin.

***Klebsiella pneumoniae resistant to* extended-spectrum cephalosporin (ceftriaxone or cefotaxime) or carbapenem (CRE) or colistin**

K. pneumoniae can cause infection to multiple systems within the body, whether in the form of CAI or HAI. Common sites of infection include pneumonia. It can cause significant pulmonary inflammation, necrosis and viscous mucus and with mucous and bloody discharges. Lobar pneumonia also commonly occurs as well as intraabdominal abscesses such as liver abscesses, bacteremia, urinary tract infection and biliary tract infection. Infection also occurs more frequently in patients with diabetes or cancer, patients taking immunosuppressant drugs, patients who consume alcohol or patients with liver or kidney failure.

Data from NARST from January to June 2020 found *K. pneumoniae* to have a rate of resistance of 50% for extended-spectrum cephalosporins, 42% for ceftazidime and 10.5% for carbapenems. Furthermore, data from the IPC and AMR Surveillance Program of the Bamrasnaradura Infectious Diseases Institute revealed that, for the HAI rate from *K. pneumoniae,* the rate of resistance was as high as 64% for extended-spectrum cephalosporins and 32% for carbapenems.

***Escherichia coli* resistant to colistin or carbapenem (CRE) or fluoroquinolone (ciprofloxacin) or extended-spectrum cephalosporin (ceftriaxone or cefotaxime)**

E. coli is an intestinal flora that can cause infection in multiple systems of the body, whether CAI or HAI. Common sites of infection include urinary tract infection, bacteremia, biliary tract infection, pneumonia and wound infection, and some strains such as enterotoxigenic *E. coli* (ETEC) and enteroinvasive *E. coli* (EIEC) can cause diarrhea. For common risk factors for infection, this infection is found with greater prevalence in patients taking immunosuppressant drugs and elderly patients. Drug resistance can occur from exposure to drug resistant genetic materials from other bacteria or after exposure to ceftriaxone or fluoroquinolone.

Data from NARST from January to June 2020 reveals that *E. coli* was resistant to extended -spectrum cephalosporins and had 50% resistance to cefotaxime, 40% resistance to ceftazidime

and 2.8% resistance to carbapenems. Meanwhile, data from the IPC and AMR Surveillance Program of the ของสถาบันบำราศนราดูรพบ reveals that, for HAI from *E. coli,* the resistance rate was as high as 57% for extended-spectrum cephalosporin and as high as 15.3% for carbapenems

In the treatment of these gram-negative bacterial infections, it is potentially necessary to use a high dose of medication and multiple antimicrobial drugs together, along with other treatments aside from critically-important antimicrobials such as abscess drainage, removal of necrotic tissue, etc.

Staphylococcus aureus resistant to methicillin or Methicillin resistance _Staphylococcus aureus_ (MRSA) or vancomycin (VISA and VRSA)

S. aureus can reside in people without causing any disease (colonization) by residing in the anterior region of the nasal cavity, in addition to the armpits, groin, female genitalia, and anal region. The fact that the pathogen can reside in people without causing any disease and occasionally contaminate the skin, especially on the hands, is a major factor for the persistence and outbreaks of drug-resistant pathogens, especially MRSA.

Most MRSA infections in Thailand are HAI cases and are often linked to the use of catheters such as catheter-associated bloodstream infections and ventilator-associated pneumonia or linked to surgery such as surgical site infection, prosthetic joint infection and prosthetic heart valve infection. Furthermore, it can also cause infection at other sites such as cellulitis, necrotizing fasciitis, bacteremia, pneumonia, urinary tract infection, septic arthritis, osteomyelitis, orbital cellulitis, endophthalmitis, epidural abscess, etc.

Data from the IPC and AMR Surveillance Program of the Bamrasnaradura Infectious Diseases Institute reveals that the rate of HAI infection from MRSA was as high as 14%, while data from NARST revealed 8.4% for the same.

For vancomycin intermediate *S. aureas* (VISA), the vancomycin resistance mechanism is that the pathogen can excessively generate its cell wall, causing its cell wall to thicken and for drugs to be unable to penetrate. Meanwhile, for vancomycin-resistant *S. aureus* (VRSA), this is caused by exposure to the vanA genes from *Enterococci* spp., which changes the structure of the cell wall such that vancomycin cannot attach to targets. The vanA gene can be passed on and lead to significant treatment problems. Thus, whenever VISA is encountered, the case is MRSA, and when the MIC value to vancomycin is 4-8 micrograms/milliliter, it is necessary to perform confirmatory tests and report and use strict measures to control the spread of the disease, especially if the VRSA is encountered (MIC greater than 16 micrograms/liter).

Salmonella spp.

This pathogen is transmitted by intake of food or beverages contaminated with *S*. Typhi and *S*. Paratyphi, which cause enteric fever and high fevers lasting in excess of 1-2 weeks, general abdominal pain, constipation in the early stages, rashes, nausea and vomiting and diarrhea. Meanwhile, *Salmonella* non-Typhi can cause gastroenteritis and primary bacteremia, and infection can be found in various organs following blood infection such as endocarditis, endovascular infection, bone and joint infection, etc.

Patients in the risk group for severe infection include those with HIV infection, steroid use, malignancy, chronic renal or liver disease, DM, elderly status or infant status.

Data from NARST from January to June 2020 reveals that, for *Salmonella* non-Typhi, resistance was as high as 31% to fluoroquinolones and as high as 10-12% to extended-spectrum cephalosporins, and there is a higher rate of multiple-drug resistance in some serotypes.

***Enterococcus faecium* ดื้อต่อยา vancomycin (VRE)**

Vancomycin-resistant enterococci (VRE) is *Enterococcus* spp. resistant to vancomycin. Mostly, this is *E. faecium.* Data from NARST in 2020 reveals that about 1% of *E. faecalis* is VRE and that about 10% of *E. faecium* is VRE.

This group of pathogens is local intestinal flora and is a frequent cause of hospital-acquired infections. Common infection sites include urinary tract infection, intraabdominal infection and bacteremia, and complications can lead to infective endocarditis. Important risk factors include being elderly, having undergone surgery and use of broad-spectrum antimicrobials

Enterococcus spp., especially VRE in urine culture, mostly matches the colonization type. Thus, observation should be the key principle for determining whether or not actual infection is taking place and whether or not treatment is needed.

***Streptococcus pneumoniae* resistant to penicillin (ampicillin) or macrolide (erythromycin) or extended-spectrum cephalosporin (ceftriaxone or cefotaxime)**

S. pneumoniae causes infections with a variety of clinical representations from asymptomatic colonization to severe infection. Factors related to infection include abnormalities of antibodies, complements, phagocytes and spleen abnormalities, HIV infection, alcoholism, cirrhosis, DM, chronic kidney disease and being elderly.

Most infections are CAIs and cause diseases such as otitis media, acute purulent sinusitis, acute exacerbation of chronic bronchitis and pneumonia, with major complications potentially including parapneumonic effusion or empyema, meningitis and bacteremia.

Data from NARST from January to June 2020 reveals increased resistance of *S. pneumoniae* to penicillin (ampicillin) or macrolide (erythromycin) or extended-spectrum cephalosporins (ceftriaxone or cefoxime).

IPC & AMR Surveillance Program

This program gathers data on infections and drug resistance in the hospital setting and is a collaborative effort between the Bamrasnaradura Infectious Diseases Institute, Clinical Research Collaboration Network and local hospitals within the areas under the responsibility of disease control and prevention offices in 12 regions and the Institute for Urban Disease Control and Prevention that started in 2016 with the purpose of developing a system for collecting information about infections in the hospital setting to serve as an information hub on hospital-acquired infections in Thailand and to serve as a leader in the effort to develop work systems for effectively preventing and controlling infections in the hospital setting and public health service centers on every level. In 2018, the scope

of surveillance was expanded to cover antimicrobial-resistant pathogens with data collection covering about 600 hospitals for the purpose of developing and improving an HAI and AMR surveillance system.

Accordingly, whenever a hospital-acquired infection occurs, the nurses tasked with infection prevention and control in the hospital will make a record in the IPC & AMR Surveillance Program and record the disease-causing pathogen as well as the drug-resistant pathogen. However, because the IPC & AMR Surveillance Program currently largely focus on hospital-acquired infections, there is a lack of data on CAIs.

Usage Procedure

1. Log into the website www.bamras.thaimedresnet.org and sign into the system by using the hospital's username and password.

2. The infectious diseases database contains data divided into 3 parts:

2.1 Name of patient ward, patient department, status of patient ward (open or closed).

2.2 Monthly patient information. Enter data in 3 parts as follows:

2.2.1 Number of days of catheterization such as number of days in bed rest, number of days wearing a urinary catheter, spinal drain, central line, IV line; number of days on respiratory, number of surgeries, number of infections, number of infected patients, percentage of hospital-acquired infections and rate of hospital-acquired infections.

2.2.2 Information on infection patients such as HN, age, sex, date of symptom discovery, site of infection, bacteria culture (in cases where specimens were submitted for culture), type of specimens sent for testing, date of submission for culture, pathogens discovered, results on specific drug resistance for 9 target pathogens, test results on specific drug resistance in target drugs and record of either sense intermediate or resistance drug resistance test results.e

2.2.3 Patient discharge status.

2.3 Reporting

2.3.1 Control chart showing the rate of infection by site, such as ventilator-associated pneumonia (VAP), catheter-associated urinary tract infection (CAUTI), catheter-associated blood stream infection (CABSI) and surgical site infection (SSI).

2.3.2 Graph showing infection with data on the site of infection and disease-causing pathogen.

2.3.3 Graph showing disease-causing pathogens for which up to 5 different disease-causing pathogens can be selected for comparison.

2.3.4 Submission of Excel file data and descriptive data.

Guidelines for Reporting Patients with Critically – important Antimicrobial-Resistant Infections

AIDS, Tuberculosis and Sexually-transmitted Infections Surveillance System Development Group
In collaboration with the International Health Regulations Collaboration and Coordination Work Group

Background and Objectives

According to the framework of the 20-year national strategic plan on public health, strategy for excellence and service excellence, health service plans are to be developed along with a project for preventing and controlling antimicrobial resistance (AMR), including the Strategic Plan on Dealing with Antimicrobial Resistance in Thailand, B.E. 2560-2564 (2017-2021), and the Rational Drug Use (RDU) program. These are to be implemented according to the indicators for guaranteeing government performance: percentage of hospitals with RDU and percentage of hospitals with an integrated antimicrobial resistance management system. Furthermore, Thailand is required to follow the International Health Regulations 2005 along with the framework and goals under The Global Health Security Agenda (GHSA), which strives to solve the problem of antimicrobial resistance with the Bureau of Epidemiology functioning as the International Health Regulation National Focal Point (IHR Focal Point).

Thus, in order to achieve integrated management of antimicrobial resistance, and reduce the number of infected cases and deaths from critically-important antimicrobial-resistant infections, a national antimicrobial resistance surveillance and response system has been established to detect incidences of antimicrobial-resistant disease outbreaks in a timely manner and achieve the goals of the Global Health Security Agenda (GHSA) and the Strategic Plan on Dealing with Antimicrobial Resistance in Thailand, B.E. 2560-2564 (2017-2021). The development of the antimicrobial-resistant infection surveillance and response system by the Bureau of Epidemiology under the Department of Disease Control is meant to strengthen detection and responses of the antimicrobial resistance monitoring network from the epidemiological network, laboratory network, hospital infection prevention and control network, patient care and treatment network, the Food and Drug Administration, and surveillance point hospital network for increased effectiveness.

Purpose

The patient surveillance system detects antimicrobial resistance, collects data, analyzes and reports on the situation of important antimicrobial-resistant infections from the national hospital surveillance network according to the definitions and infections described in this manual for the following purposes:

Primary Purposes

1. Development of a surveillance system for critically-important multidrug-resistant organisms by reporting on individual patient cases.

2. Reporting the situation and trend on the hospital, provincial, regional and national levels to raise awareness in communities, hospitals and the country.

Secondary Purposes

1. Development of knowledge on the antimicrobial-resistant infection surveillance system through case-based surveillance and changing the patient surveillance data standards in Thailand.

2. Development of knowledge related to the spread of antimicrobial-resistant infections in hospitals and communities.

3. Assessment of the feasibility in the use of a form for reporting antimicrobial-resistant patients by the Bamrasnaradura Infectious Diseases Institute (BIDI platform) for surveilling and issuing warnings of outbreaks or consideration of shared platforms in agencies under the Ministry of Public Health by coordinating collaboration among the Thai National Institute of Health, Ministry of Public Health, Department of Medical Sciences, Bamrasnaradura Infectious Diseases Institute, Bureau of Epidemiology, Department of Disease Control and related agencies such as the Department of Medical Services, The Healthcare Accreditation Institute, etc. in order to propose guidelines for the development of a platform for monitoring, integrating and processing data in the future.

1. Work of the Antimicrobial-Resistance Surveillance System

1.1. Surveillance Areas

The hospital-based surveillance system relies on data from laboratories and medical records of patients seeking treatment. The Bureau of Epidemiology coordinates with the Public Health Research Institute and the Bamrasnaradura Infectious Diseases Institute to jointly develop surveillance guidelines, with region-level offices of disease prevention and control tasked with coordinating, supervising and overseeing surveillance work and public health offices tasked with monitoring and coordinating local surveillance work. Additionally, the nurses' network for preventing and controlling infectious diseases in hospitals and the laboratory surveillance network have joined together to develop surveillance guidelines to determine the

feasibility of expanding surveillance of patients with antimicrobial-resistant infections in hospitals on every level and to jointly identify problems and obstacles to ensure effective future surveillance work.

1.2 Surveillance Units

From 2019 to 2020, hospitals under the Office of the Permanent Secretary of Public Health, government medical facilities, private medical facilities and laboratory networks worked together to develop a model for surveilling patients with antimicrobial-resistant infections, and they serve as the key agencies for data collection. In addition, every hospital, whether in the public or private sector, helped jointly develop a model warning network for patients with severe antimicrobial-resistant infections and served together as data collection agencies.

1.3 Study Population

1) The population in the areas under the responsibility of hospitals or the population outside of areas under the responsibility of hospitals where patients seek hospital treatment.

2) Patients who seek hospital treatment, whether in hospital outpatient or inpatient wards.

3) Patients who fit the definition for surveillance according to the "Hospital Infection Diagnosis Manual of the Bamrasnaradura Infectious Diseases Institute, Department of Disease Control, Ministry of Public Health" or patients whose bacteria culture and antibiotic responsiveness testing revealed the presence of specified items of antimicrobial-resistant pathogens.

4) All patients already reported in the system are monitored from the date of report of the conclusion of treatment and/or knowledge of treatment outcome or monitoring of treatment outcome up to 1 month after the report.

1.4 Definition of Surveillance

Patient Types

In the classification of patients diagnosed with antimicrobial-resistant pathogens in any of the items sent for testing, the first task to perform is to inspect whether an infection is ongoing by relying on the following information: fever (body temperature of 38 degrees Celsius or more) and other symptoms such as coughing, diarrhea, pus, etc., and for infections in children younger than 1 year, these consist of fever (rectally-measured body temperature below 37 degrees Celsius), respiratory arrest, bradycardia, listlessness, vomiting, etc., along with an unusually high white blood cell count (> 12,000 cell/mm^3), and examples of other laboratory results include gram staining, germ culture, x-ray imagery, ultrasound and immunological test results, etc. If an infection is present, a state which organ is infected and the infection-causing disease. This information is used to identify the incubation period of the infection. Next, classify patients as **infected/cases** according to the criteria or definition for infection for each of the body's organs according to international standards, and in cases where there is limited data or conflict on whether or not

infection is present, the treating physician will render an opinion to ultimately determine whether or not an infection is present. If there are no symptoms and displayed symptoms of infection according to the aforementioned definition, then the treating physician and related persons are to classify based on the discovery of the infection what the cause of infection is. A cause may be **colonized** or **contaminated**, and, if a conclusion cannot be drawn or the available evidence is unclear, classify the patient as **unspecified**. Do so by using the classification numbers as follows:

TABLE 10. Variables for classifying patients by type of infection.

Code Diag_class	Definition
1	Infected/case
2	Colonized
3	Contaminated
4	Unspecified

Patient Classification by Source of Infection

The classification by source of infection starts with classifying the date of start of illness/ presence of symptoms and displayed symptoms, date of patient sample collection and laboratory results to determine whether the patient has an ongoing infection. If the patient is indeed diagnosed with an infection under the surveillance system, or a case has been encountered, track down the source of infection to determine whether it occurred through hospital contact (healthcare -associated infection) or community contact. In cases where germ culture and antibiotic resistance testing reveal the presence of surveilled antimicrobial-resistant pathogens, but the diagnosis is colonization or contamination, it is not necessary to classify the patient as a patient (case), and it is not necessary to classify the source of contact with the pathogens. In analysis, present this part according to basic proportions and with incident, density to allow isolation of the discovered areas only and do not use it to analyze and classify details in the same manner as the patient (cases). Accordingly, pathogen contact can be classified and defined as follows:

1. Patient Contact/Infection in Hospital Settings (Healthcare-associated Infections: HAI/ Nosocomial Infections: NI)

1.1 HAI means patient discovered with the surveilled antimicrobial-resistant pathogens, with the counted time from the date of access to treatment in the inpatient ward of a hospital up to the date of laboratory result confirmation at > 2 calendar days.

1.2 HAI refer means patient discovered with the surveilled antimicrobial-resistant pathogens, with the counted time from the date of access to treatment in the inpatient ward of a hospital to the date of laboratory result confirmation at < 2 calendar days, but the patient was referred from an initial hospital in which the patient was hospitalized for treatment for at least 2 days.

2. Patient contact/infections in communities (community infections: CI) means cases where the patient has come into contact with or contracted infection from the community and then shows signs or symptoms of infection before receiving treatment at a medical facility or whose time from the first date of admission to the time of display of signs or symptoms of infection after seeking hospital treatment as counted from the first date of admission was less than 2 calendar days.

3. Patients with infection from the moment of admission (**present on admission**: POA) means cases of infection where the date of event (DOE) occurs in the time period from before hospital admission to the date of hospital admission on the 2nd day, which is not considered cases of hospital infections (hospital day 1-2). In these cases, it is not possible to determine from where the patient contracted the infection.

Other Important Variables Collected

- General information of patients that includes the first name, last name, sex, age, nationality and address information.
- Clinical information and medical diagnosis.
- Information on patient type classification according to patient/contact definitions.
- Information on antimicrobial-resistant pathogens/laboratory information.
- Information on medical treatment outcomes.

TABLE 11. Classification of exposure time relative to date of event.

Hospital day	Date of Event Assignment for RIT	Classification
2 days before hospitalization.	Hospital Day 1	POA
1 day before hospitalization.	Hospital Day 1	
1	Hospital Day 1	
2	Hospital Day 2	
3	Hospital Day 3	HAI
4	Hospital Day 4	
5	Hospital Day 5	

TABLE 12. Variable classification by source of exposure.

Code expose class	Definition
1	HAI
2	HAI refer
3	CI
4	POA

Bacteria and Antimicrobials in the Antimicrobial-resistant Infection Surveillance System

The critically-important antimicrobial-resistant pathogens (critically-important MDRO surveillance) are as follows:

1) Vancomycin-resistant, *Staphylococcus aureus* (VRSA)

2) Vancomycin-resistant Enterococcus (VRE)

3) Colistin-resistant, *Acinetobacter baumannii*

4) Colistin-resistant, *Pseudomonas aeruginosa*

5) Third generation Cephalosporin-resistant, *Neisseria gonorrhoeae*

6) Other newly discovered severe drug-resistant infections are severe or drug-resistant pathogens never before discovered to be resistant to multiple or all antibiotics.

Remarks: Other severe drug-resistant pathogens mean antibiotic-resistant bacteria that have a high likelihood of severe transmission or high capability for drug resistance and severity at all sites of infection and all specimen types sent for testing.

Surveillance Procedures

1.1 Data Collection

1) Use the AMR-1 report form to gather data from individual patients.

2) Submit specific patient data every 7 days by using the AMR-1 individual patient report form to the web page at http://203.157.15.62 that belongs to the Bureau of Epidemiology. Then the Bureau of Epidemiology verifies accuracy, sorts and analyzes the data on the provincial, regional and national levels and presents them on the patient surveillance website every month.

3) Data Reporting Procedure

Step 1. At the microbiological laboratory, laboratory diagnosis is performed upon discovery of a pathogen belonging to an important group according to the aforementioned list and antimicrobial responsiveness testing reveals that the pathogen is resistant to specified antimicrobials.

Step 2. The relevant patient must be reported to the treating physician and/or related persons for consideration.

Step 3. The treating physician evaluates the patient and diagnoses that the patient or deceased person carries/carried antimicrobial-resistant infection or classifies the patient as a colonized/contaminated/POA (unspecified) case.

Step 4. The hospital infection prevention and control work section or nurses in charge of controlling infections in the hospital setting or epidemiological officials collect data according to the AMR-1 individual patient report form (Appendix 1).

Step 5. The AMR-1 form is reported to a provincial-level situation awareness team (SAT) or http://203.157.15.62 by taking photographs or scanning the AMR-1 form directly unloadable via the website. Each hospital will use a 5-digit hospital code according to the code in the RorNgor.506 report form.

Step 6. The provincial level SAT team will verify the completeness and accuracy of the data in the AMR-1 individual patient report form and then send the data and upload the AMR-1 form into the epidemiological news monitoring program according to the procedure.

Step 7. The region-level surveillance coordination team receives and verifies the data, sorts the data, performs analysis and assesses the situation. If an outbreak is discovered, inform the central SAT team to send outbreak news to related agencies to conduct an investigation and restrict the outbreak.

Step 8. The central surveillance coordination team receives and verifies the data, sorts the data, performs analysis and assesses the situation to send news of the outbreak to related agencies for investigation and restriction of the outbreak.

Step 9. The antimicrobial resistance surveillance coordination team receives and verifies the data, sorts the data, performs analysis and assesses the situation to report the situation on the website http://203.157.15.62 and performs the weekly situational assessment. If an outbreak is discovered, an outbreak is likely or the pathogen is extremely dangerous, a report will be made to a team of experts for consideration of conducting a joint disease investigation with the relevant local hospitals.

Remarks:

"Team of experts" mean consultants and committees on surveillance of patients with antimicrobial-resistant infections, teams for preventing and controlling infections in the hospital setting, the Bamrasnaradura Infectious Diseases Institute, laboratory analysis teams, the Public Health Thai National Institute of Health, the Department of Medical Services, epidemiological teams under the Bureau of Epidemiology and specialists.

1.2 Data Sorting and Presentation

Computer software is used to perform analysis to assess the situation of surveillance and the situation of patient treatment. For the duration of the analysis, results are presented to provide knowledge about the situation weekly or at least once monthly or at required time periods, given data readiness.

1.3 Data Analysis and Interpretation

Surveillance data can be used to perform analysis to provide knowledge into the epidemiological situation and the trend of incidences of disease of pathogens to provide knowledge about the following:

- The prevalence of patients with antimicrobial-resistant infections reported on a monthly, quarterly and annual basis.
- Number of patients sorted by type of exposure to pathogens.

1.4 Dissemination of Surveillance Results

The Bureau of Epidemiology in collaboration with the Bamrasnaradura Infectious Diseases Institute and the Department of Medical Sciences summarizes results under their responsibility according to specified monthly, quarterly and annual time periods and disseminates information and news among various agencies for data uses and joint creation of an integrated surveillance database for mutual benefits.

Publications on the website of the Bureau of Epidemiology include data on national-level figures and percentages, region-level items and monthly hospital publications and related journal publications, including the Weekly Epidemiology Surveillance Report (WESR) of the Bureau of Epidemiology, quarterly reports and the Annual Epidemiology Surveillance Report (AESR).

1.5 Surveillance Network

This consist of a network of agencies providing data support for integrated surveillance.

- Outpatient/Inpatient Departments

Collaboration and coordination in the collection of data on patients discovered with antimicrobial-resistant pathogens. Upon discovery of microbiological test results that indicate the presence of antimicrobial-resistant pathogens in a patient, register with the hospital infection prevention and control work section/epidemiological work section.

- Microbiological Laboratory

Gather data on lab analysis results. Upon discovery of pathogens in submitted specimens, state the type of the bacteria pathogens under surveillance and the test results on the responsiveness of the antimicrobial-resistant pathogens requiring surveillance by doing so in collaboration with the hospital infection prevention and control work section and the epidemiological work section to manage the data.

- Hospital Infection Prevention and Control Work

Gather patient data submitted for lab analysis and discovery of bacteria under surveillance and test results on the responsiveness of the antimicrobial-resistant pathogens requiring surveillance by working in collaboration with the microbiological laboratory work section and epidemiological work section in data management.

- Epidemiological Work

Gather and analyze patient data from lab analysis showing the discovery of the pathogenic bacteria under surveillance and the test results on the responsiveness of the antimicrobial-resistant pathogens requiring surveillance by working in collaboration with the microbiological laboratory work section and epidemiological work section in data management.

- Hospital Level

This consists of surveillance units functioning in providing medical treatments and diagnoses to patients and reporting patients through surveillance units by reporting data to the region-level data center (contracting unit of purchase: CUP) to report to the surveillance network under the Bureau of Epidemiology at least once weekly. Personnel who perform work in tasks related to infection prevention and control in the hospital setting coordinate cooperation with microbiological laboratory personnel, personnel performing disease surveillance duties and other related agencies.

- Provincial Level

Provincial public health offices serve as the network's provincial-level centers for surveillance and have duties in participating in disease control investigations in collaboration with the epidemiological work section and hospital infection prevention and control work section and to supervise and support academic work and make use of data by receiving data once monthly from the website of the Bureau of Epidemiology and then preparing disease situational reports for presentation to executives.

- Region Level

Disease prevention and control offices function as the central network for region-level surveillance and have duties in participating in investigations and disease control in collaboration with the epidemiological work section and hospital infection prevention and control and infection work section to supervise and support academic work activities and make use of data by receiving data once monthly from the website of the Bureau of Epidemiology before preparing disease situational reports for presenting to executives.

- National Level

Bureau of Epidemiology

The Ministry of Public Health through the Bureau of Epidemiology under the Department of Disease Control serves as an agency tasked with overseeing policies and setting in place work standards in disease surveillance, prevention and control and developing courses and providing work training in surveillance and investigating patients with antimicrobial-resistant infections to personnel such as doctors and nurses. Furthermore, in collaboration with the antimicrobial-resistant surveillance center, the Public Health Scientific Research Institute, Department of Medical Services and the Bamrasnaradura Infectious Diseases Institute under the Department of Disease Control and related agencies, the ministry engages in collaboration to develop academic work and research technologies that can reflect the situation of antimicrobial-resistant infections in patients as well as the problems, severity and trends of the current situation to keep up with situational changes and to integrate database work to enable shared utilization to ensure effective data for use in appropriate disease prevention and control.

Bamrasnaradura Infectious Diseases Institute

The Ministry of Public Health through the Bamrasnaradura Infectious Diseases Institute under the Department of Disease Control functions as the agency tasked with supervising policies and setting in place working standards for surveillance and prevention and control of infections in the hospital setting, developing courses and providing work training on the prevention and control of infections in the hospital setting to personnel such as doctors, pharmacists, nurses, including institute directors and the Secretary-General of the Infection Prevention and Control Commission on the national level under the instructions of the Minister of Public Health. Furthermore, the ministry also provides academic support and researches technologies that can reflect the situation of infections in the hospital setting along with the problems and severity of diseases from the current situation. Accordingly, the Bamrasnaradura Infectious Diseases Institute coordinates cooperation with related agencies and integrates work and databases to ensure shared utilization and effective availability of data for appropriate use in disease prevention and control.

National Antimicrobial Resistance Surveillance Center, Thai National Institute of Health, Department of Medical Sciences

This agency is tasked with the development of microbiological laboratory standards and quality certification for laboratories in support of academic and technological efforts in antimicrobial resistance surveillance, including coordination of national and international level efforts to promote and develop standards for testing, analysis and overall national assessments.

Appendix 3. Data Analysis

Reported numbers of patients are divided into infection patients (cases) and two groups of patients in whom pathogens have been encountered namely, colonization and contamination groups, and patients with unspecified infection status.

Sample Analysis Guidelines

- Analyze samples according to target organisms.
- Analyze samples according to specimen type.
- Analyze number of patients by patient type.

In analysis, analyze by individual pathogens.

Frequency of Antimicrobial-Resistant Patients by Person

- Total number of patients by counting patient-first isolation (de-duplication).
- Total number of patients by pathogen (organism type) and by specimen type).
- Ratio between males and females.
- Number of patients by occupation/nationality.
- Number of proportion of patients by age group as follows:

Age Group
Birth30- days
31 days90- days
91 days–4 years
14–5 years
19–15 years
39–20 years
59–40 years
60 years and up

- Number of patients by the source of disease (HAI, HAI refer, CI, POA).
- Frequency by site of infection.
- Frequency of samples (specimens).
- Treatment status (as of date of receipt of lab report and 3 months follow-up to monitor whether the treatment outcome is recovery or death).

Frequency of Antimicrobial-Resistant Infection Patients by Time (Time Trend)

- By week or by month or by year.

Frequency of Antimicrobial-Resistant Infection Patients by Place

- Current address.
- Patient department, e.g., emergency (EME), outpatient department (OPD), intensive care unit (ICU), sub-ICU.
- Patient wards in medical facilities, e.g., obstetrics, surgery, internal medicine, pediatric, etc.

Chapter 3

Investigation of Antimicrobial Resistance in Hospitals

Investigation of Antimicrobial Resistance in Hospitals

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Outbreaks and infections of antimicrobial-resistant pathogens in hospitals are increasing due to factors present today, where multidrug-resistant bacteria (MDR) and pandrug-resistant bacteria (PDR) have been found. These developments led to increased outbreaks of infectious diseases in the hospital setting. Accordingly, control of these problems requires effective measures to prevent and control the spread of drug-resistant pathogens in hospitals and correct measures for investigating and controlling outbreaks.[7]

Purpose of Outbreak Investigations

Investigations are meant to study the details of infection and unusually high spread of disease in the same places and times based on the epidemiological principle of identifying the source of infection, the population at risk and mode of transmission, which lead to outbreaks, in order to seek guidelines for controlling infections and transmission until they subside in a timely manner and to implement measures for preventing future outbreaks.[8]

Outbreak Detection in Hospitals

Outbreaks of drug-resistant pathogens in hospitals can be detected by the following methods:[9]

1. Surveillance system. Hospitals must have in place an effective system for surveilling and gathering data on target drug-resistant pathogens in hospitals and swiftly report abnormalities to the persons concerned.

2. Medical personnel. These must possess knowledge about the problem and situation of drug resistance in the hospital setting as well as their roles in collaborating when drug-resistant outbreaks occur in agencies under their responsibility.

3. Laboratories:

- These need to have criteria in place for diagnosing drug-resistant pathogens present in laboratories according to international standards.
- These need to have in place a system for communication and reporting laboratory test results in cases of encounters with abnormal drug-resistant pathogens.
- These need to prepare reports on the responsiveness of pathogens to antimicrobials as well as the changes in pathogens found in hospitals while periodically reporting to the persons concerned.

Outbreak Investigation Procedure

Upon discovery of patients with an abnormally high number of drug-resistant infections in the hospital setting or suspicion of an outbreak, an investigation should be conducted according to the following key steps:[10]

1. Verify diagnosis
2. Confirm existence of an epidemic
3. Find other patients (active case finding)
4. Investigate the epidemic by time, place, and person
5. Formulate hypothesis
6. Test hypothesis
7. Recommend control measures
8. Report disease investigation results

1. Verify diagnosis.

Upon suspicion of an epidemic, the investigator must verify data about the occurrence of the disease primarily based on the symptoms and displayed symptoms of patients together along with laboratory test results in order to confirm the diagnosis on which types of disease or infection occurred in the patients in order to to provide guidelines for correctly and appropriately preparing for disease investigation. Information for confirming disease diagnosis can be obtained from the following:[11]

- Medical record
- Laboratory findings
- Clinical examination
- Consultation with the care givers

2. Confirm existence of an epidemic.

The investigator should evaluate multiple sources of information to determine whether or not an epidemic has indeed occurred, such as information from infectious diseases surveillance in the hospital setting, laboratory data, especially pathogen culture results and test results on the responsiveness of pathogens to antimicrobials, along with data from the various related agencies of the hospital that are connected to the abnormally high prevalence of infection in specific sites or encounters of infection caused by the same drug-resistant pathogens in multiple patients at the same time in order to accompany consideration on whether or not an epidemic has occurred.

The criteria for confirming that an epidemic has occurred and that the epidemic has to be investigated are as follows:

- Discovery of an unusual increase in the number of infections in patients due to the same pathogens over the same time period, and, when compared to past infection rates, the increase exceeded the mean by +2 S.D.
- Discovery of 2 or more patients with the same type of infection and epidemiological linkage.
- Discovery of a single patient where the infection occurred due to a previously-undiscovered pathogen in the hospital.

In the step to confirm whether or not an epidemic has occurred, pseudo-outbreaks might be encountered, that is, the discovery of the same type of pathogens in multiple patients without any connection to the symptoms and displayed symptoms of patients.

Pseudo-outbreaks can occur due to the following:

1) Medical personnel, e.g., incorrect diagnoses or lack of sorting of patient data between community-acquired and hospital-acquired infections.

2) Laboratories, e.g.,

- Contamination from specimen collection and submission and contamination during testing.
- Use of incorrect methods and techniques for analysis and reporting on pathogens.
- Development of testing and analysis techniques with a different specificity from before.

3) Surveillance system, e.g., changes in the disease surveillance system and development of a reporting system.

3. Find other patients (active case finding)

Drug-resistant pathogens can be found in patients in forms that cause disease (infection) and that increase in numbers in the body without any symptoms (colonization). Therefore, in conducting an epidemiological investigation, it is necessary to search for additional patient cases to determine the scope of the disease and the size of the problem requiring epidemiological control.

In the search for additional patients to determine which patients are involved in the epidemic, it is necessary to establish a case definition for each epidemic clearly as a tool for identifying other patient cases in a manner most consistently matching with facts without the inclusion of any patients from other causes in the investigation.

The establishment of case definitions must cover the symptoms and displayed symptoms of patients and specific laboratory tests or other test results, including the places involved during the epidemic, such as patient wards, surgery rooms, chemotherapy wards, intensive care units, etc. Case definitions must also be sensitive enough to cover patients with few symptoms in order to control the disease successfully but not be so sensitive that unrelated patients are included in the epidemiological investigation.[12]

Established case definitions can be divided into the following:

1. Confirmed cases, meaning patients with clear symptoms/displayed symptoms and confirmed laboratory test results.
2. Probable cases, meaning patients with clear symptoms/displayed symptoms.
3. Possible cases, meaning patients with fairly unclear symptoms/displayed symptoms.

Example of the Establishment of a Case Definition

From the investigation of an outbreak of carbapenem-resistant *Acinetobacter* spp. in the medical intensive care unit of a hospital, the established case definition for the epidemiological investigation is as follows: Patients who received more than 2 days of treatment in the medical intensive care unit with laboratory test results from the site of infection or proactive surveillance showing presence of carbapenem-resistant *Acinetobacter* spp. In both infection and colonization forms from January to March 2021.

4. Investigate the epidemic by time, place and person.

Use collected data to distribute patient characteristics and determine the frequency by time and place to learn the clear nature of the epidemic and set a more precise hypothesis about the epidemic.

4.1 Distribute patient characteristics by collecting data about each patient covering the demographic data of patients such as sex, age, date of access to treatment, illness condition, existing diseases at the time of illness, symptoms and displayed symptoms, history of surgery, catheterization in the body for treatment, etc. Then use the data to perform line listing to improve data consideration convenience. Showing the rate of illness in each group (attack rate) can help provide an image of patients vulnerable to infection, which can be used in considerations for analytical epidemiological studies and setting of a hypothesis about the epidemic.

Figure 7. Example of use of line listing to show the characteristics of patients in a drug-resistant infection outbreak in an infant patient ward.

Characteristics of outbreak-related *S. marcescens* isolates and clinical data of patients.

Patient no.	Gender	Gestational age (weeks)	Weight at birth (g)	Age at infection or colonization (days)	Source of infection or colonization	PFGE genotype	PCR genotype
1	Male	27	1,030	34	Rectal swab	A	A'
2	Female	27	1,030	39	Throat swab	A	A'
3[a]	Female	32	1,700	9	Rectal swab	A	A'
4	Male	30	1,325	57	Throat swab	A	A'
5[a]	Female	32	1,920	9	Rectal swab	A	A'
6[b]	Male	30	1,720	5	Blood	B	B'
7[b]	Female	31	1,780	16	Blood	B	B'
8[b]	Female	34	1,650	6	Blood	B	B'
9	Male	30	1,720	6	Throat swab	B	B'
10[c]	Female	37	2,700	49	Nose swab	B	B'
11	Female	32	1,650	25	Rectal swab	B	B'
12	Female	32	1,650	25	Throat swab	B	B'
13	Male	29	1,550	42	Throat swab	B	B'
14	Female	32	1,780	15	Eye swab	B	B'
15	Female	30	805	38	Eye swab	B	B'

[a] patients 3 and 5 are twins; [b] patients with septicemia; [c] isolate from pediatric intensive care unit

Source:Steppberger K, Walter S, Claros MC, Spencker FB, Kiess W, Rodloff AC & Vogtmann C. Nosocomial outbreak of Serratia marcescens in a neonatal intensive care unit. Infect Control Hosp Epidemiol. 2002;23(8):457–61.

4.2 Distribution of the characteristics of the epidemic by time. Determine the relationship of the number of patients with the time of illness to produce guidelines for learning about the period of exposure to the disease, and present the patient time data in an epidemic curve to see the nature of the epidemic.

- Common/point source outbreak: The outbreak was caused by patients being exposed to disease pathogens from the same source.
- Propagated source outbreak: The outbreak was caused by the spread of pathogens from multiple sources.

Figure 8. Example of patient outbreak data by use of epidemic curves.

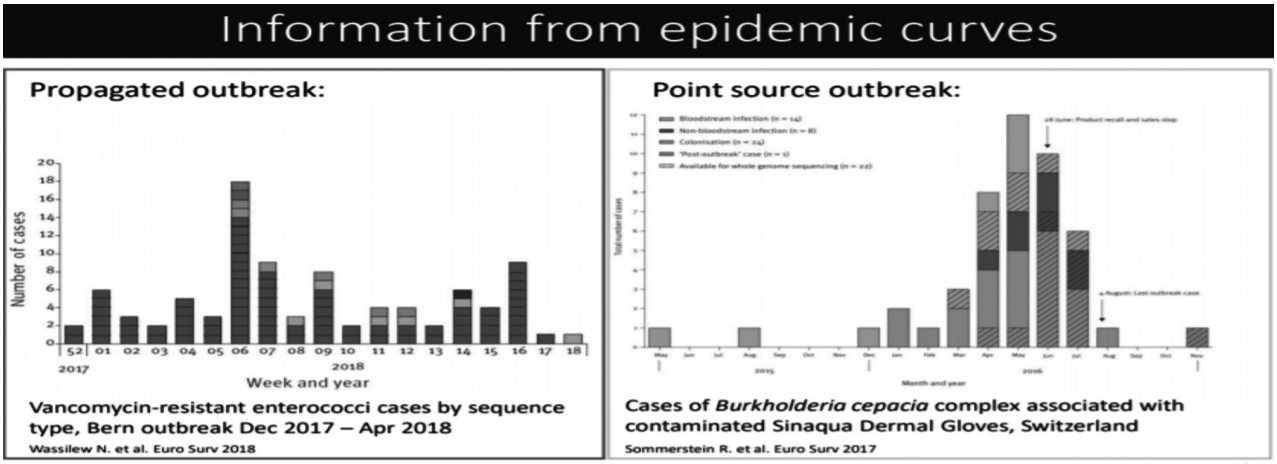
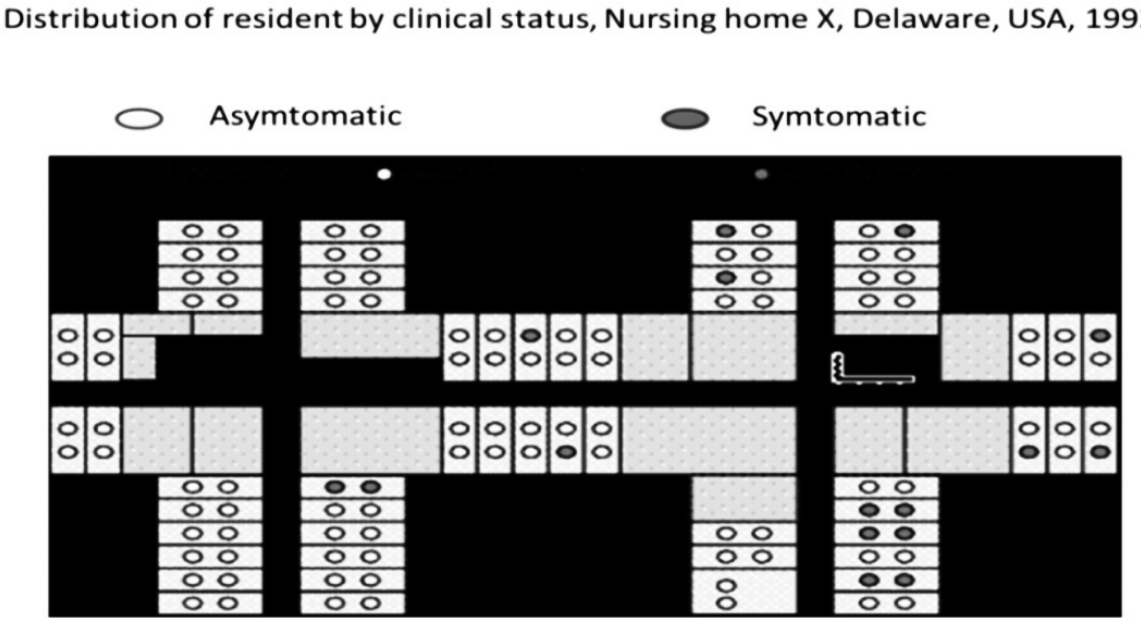


Figure 9. Example of showing patient outbreak data by use of a spot map.



Source: Lazareck L. Choosing an appropriate type of map. From: Field Epidemiology Manual Wiki. A set of online resources for professionals working in intervention epidemiology, public health microbiology and infection control and hospital hygiene

5. Formulate hypothesis.

The epidemiological data collected by time, place and person will show the nature of the epidemic on what the patients or risk groups are, the source of the disease and its methods of propagation, including the factors contributing to propagation. In addition, the investigator must observe the environment and the behaviors of personnel working in the agencies where there is an ongoing outbreak and seek expert opinion to make use of the data in setting a hypothesis and confidently proving the suspected cause of the epidemic.

Examples of hypothesis-setting:

- Use of respirators causes drug-resistant infections.
- Intravenous intake of food has led to the occurrence of nosocomial bacteremia.

6. Test hypothesis.

The investigator should collect samples suspected to be the source of the pathogens in the epidemic such as by collecting rectal swabs, throat swabs and serum from patients or by collecting specimens from the environment such as water, secretions, nutrients, etc. expected to be related to the disease in patients and then send them for microbiological laboratory testing to produce more accurate data for supporting the hypothesis. As for considerations on where to collect samples from and which methods to use for testing, the mutual options of the disease investigation team and the laboratory should be sought.

For hypothesis testing, common statistical techniques are used as follows:

- Chi-Square test Case-controlled study: Study of the rate of illness in patients with factors suspected to be causes of disease (cases) and patients without such factors (control) to determine whether the two groups have statistically-significant differences. In doing so, Chi-square is used.
- Cohort study: Factors suspected to be causes of infection are studied by determining the risk value for infection in patients with and without infection by using a "relative risk" score or "odds ratio" and a 95% confidence interval.

7. Recommend control measures.

An important component of the investigation into antimicrobial resistance in the hospital setting is for it to be conducted every time alongside the implementation of measures for preventing and controlling the spread of drug-resistant pathogens. Furthermore, after conducting an epidemiological investigation to the extent of successfully identifying the cause of the epidemic, source of the disease and method of propagation, the investigator should summarize the details about the epidemic and the specific epidemic control measures in order to cause the epidemic to quickly subside and prevent the same epidemic from occurring again.

Examples of measures used for controlling drug-resistant epidemics:

- Relevant persons washing hands.
- Appropriately cleaning and disinfecting medical equipment and the environment.
- Patient isolation.
- Inquiring about patient's past history.
- Considering of closing down patient wards as necessary.

8. Report disease investigation results.

Summarize activities and details discovered from disease investigation, comprising the following:

- Cause of the epidemic.
- Discovered the source of the pathogens. Sometimes, an epidemiological investigation cannot determine the cause. In such cases, state so in the report.
- State the nature of transmission of infection.
- State the high-risk contact persons among the patients.
- Risk factors for the onset of disease.
- Implemented disease control measures.
- Present situation after disease surveillance and control.

Preliminary Report Writing for Antimicrobial-resistant Infections

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Bureau of Epidemiology

In epidemiological investigations into diseases or public health problems, regardless of whether they are infectious or non-infectious diseases, the writing of epidemiological investigation reports is an important step in the disease investigation process, as it presents the stories of the events that have transpired as well as the activities that occurred to the relevant persons from the executive level to the levels of other persons in charge and facilitates actions to be taken according to the agencies responsible for disease prevention and control. Therefore, disease investigators must pay attention to the writing of investigation reports.

The writing of disease investigation reports is meant to inform that actions have started to be taken to control an epidemic. Disease investigation reports also are work records and summaries of disease investigation processes. Accordingly, they state the hypothesis of causes, the feasibility of diseases or disease transmission and prove of feasibility hypothesis in addition to stating the strengths and weaknesses of disease investigations and stating disease investigation methods and disease control measures, which are a presentation of past work performance. For the benefits of writing disease investigation reports, disease investigation reports can be used in legal issues, and report-writing provides good opportunities for disease investigation officials to review and potentially correct mistakes. As errors in disease investigation reports often raise new questions, additional research or studies occur. Importantly, disease investigation reports can also be used as good teaching media by other readers, who can learn from reading past reports before developing them in dealing with diseases.

Epidemiological investigation reports are divided into 2 main types, namely, executive reports and full reports. In the writing of investigation reports for antimicrobial resistance in the hospital setting, the focus is placed on writing only the executive reports, whereby executive reports are preliminary reports.

In the writing of disease investigation reports, in cases of antimicrobial resistance in the hospital setting, emphasis is placed on making reports to present to public health work executives in the form of situation reports. The investigation results on the diseases that have occurred provide important data for disease investigation reporting for presentation to executives comprising the background and investigation results with emphasis on the key issues discovered from disease investigation and the details of disease investigation and disease control activities already performed, including results of disease control and prevention activities, epidemics that occurred and their trends, a summary of priorities and urgencies and recommendations for

consideration of future action. Accordingly, the writing of disease investigation reports should summarize the key issues before preparing a report daily. In addition, to prevent issues from being left out, local officials can be sought for inquiries right away, and then a report should be made immediately after the end of the disease investigation to ensure complete recall of the investigation details. [28]

The components for writing executive investigation reports are as follows:

1. Background. This part states the background of the disease investigation such as how the disease was detected, its significance and the need for disease investigation, including the date and time of the incident and personnel or agencies reporting to agencies or personnel jointly involved in disease control investigation work from the start to the end of the investigation under the Department of Disease Control and according to disease investigation and control objectives. The purpose of disease control investigations includes confirmation of diagnosis and epidemics, descriptions of epidemic events by time, place and person, identification of epidemiological risk factors and presentation of control measures for preventing the spread of antimicrobial-resistant infections.

2. Investigation results. This part shows that the results obtained from the investigation conform to the objectives set by the disease investigation team, by which the data used to write the disease investigation results follow the epidemiological investigation steps for antimicrobial resistance epidemics in the hospital setting. The data in this area describe the details of persons, time and places.

For case-specific disease investigations, the data to be used for report writing are the important information about the patient. These consist of **the demographic data of the patients** such as the first name-last name, sex, age, nationality, address during illness, occupation, chronic diseases, patient status (recovering/recovered/deceased, by which specify the date of death); **clinical data** such as the start date of illness, symptoms/displayed symptoms, first date of access to treatment, department, patient ward, initial diagnosis, diagnosis on the date of specimen submission, date of hospital admission; **laboratory data** that specify specimen types, collection sites, collection dates and result dates; and **the discovered pathogens** by diagnosing infection (infection/colonization/contamination). Accordingly, if an infection diagnosis is encountered, the source of contact with the disease and laboratory test results are to be stated along with the laboratory test results by specifying the type of bacteria and specimen type based on the collection site. Accordingly, if multiple infections are present, it might be necessary to create a table to attach to accompany the report, depending on the discretion of the report author. [29]

For cluster investigations, the data are often sorted, analyzed and presented by distributing according to the nature of the disease and might be presented in chart format or graph format as deemed fitting. In addition, it will be necessary to show the rate of infection in each patient group vulnerable to infection, and for the propagated source outbreak, show the sign of patient data in the epidemic by using the epidemic curve or by distributing the frequency of the outbreak

by location to determine the correlation between the number of sick patients and facilities where diseases occur, in order to show the distribution of the disease in epidemic areas, which might be showable as a spot map or area map.[29]

Searches for other patients (active case finding). This requires the establishment of a clear epidemiological definition for use as a tool for searching for devices belonging to other patients to obtain results that match with facts and provide the greatest coverage.

Environmental survey results – This is the description of environmental characteristics and samples.

Use the epidemiological criteria and seek and identify the source of infection and specify the population at risk and mode of transmission as well as specify the causes of the epidemic (risk factors) to seek guidelines for controlling infection and reducing the spread in a timely manner and to implement measures without causing additional epidemics.

3. Disease control activities already performed. Specify the details of disease control activities already performed (prevention and control interventions) such as destruction of the source of disease, patient treatment, provision of health education and specimen collection for testing, contact case tracking and continuous surveillance. If multiple agencies are involved, state the agencies and how the activities carried out affected disease control as well as who the person in charge was.

4. Situation of the epidemic and outbreak trends. Based on data obtained by investigation on the efficacy of already implemented disease control activities, use data obtained to analyze the trend of the epidemic situation such as whether or not patient numbers will increase, whether the situation is hard to control or whether the epidemic will subside. In any case, if the trend of the epidemic cannot be determined due to the absence of sufficient information, the reason for that being so should also be stated, since the aforementioned information is important to the specification of policies by public health executives in issuing instructions or providing work support.

5. Summarization of key issues and public health urgencies. Data obtained from epidemiological investigations provide situational summaries and can be used to state the problems and impacts on health in addition to telling whether or not new infections/situation outbreaks have occurred or if the outbreaks are those of already well-known diseases/situations, along with whether or not the problem has to be urgently resolved, with consideration to other impacts such as economic impacts, social impacts and tourism impacts.

6. Recommendations for further action. Propose disease control and prevention guidelines that should be implemented regardless of whether the measures are existing ones that require continuation or new measures that are specific to given situations. Furthermore, when other agencies are involved, also clearly state the issues requiring coordination and the persons in charge.

Chapter 4

Antimicrobial-Resistant Infection Prevention and Control in Hospitals

Antimicrobial-Resistant Infection Prevention and Control in Hospitals

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Introduction

Over the past few years, we have been facing new communicable disease epidemics that threaten the rest of the world as well as Thailand. In the past several decades, these diseases have caused both health burdens and negative economic and social impacts, regardless of whether these diseases are SARS, avian influenza, Middle East Respiratory Syndrome, or many other new diseases that we have never known before that have just now started revealing themselves. Most recently, an ongoing problem that is receiving special monitoring is infection by the Coronavirus 2019 (COVID-19), which is a coronavirus strain whose patient cases first began to be reported in December 2019 in the city of Wuhan, Hubei Province, and by 8 January 2020, the first patient case of this disease was reported in Thailand. At the present, there are reports of widespread human-to-human infection, and since December 2019 the World Health Organization has received reports of over 171,010,497 confirmed cases and 3,556,328 deaths, and 153,107,960 recovered and discharged cases. For Thailand, there have been 159,792 cumulative cases, 108,345 recovered cases, and 1,031 deaths (data as of 31 May 2021 at 12:00 pm), with new patient cases being encountered in prisons and periodically-provided government quarantine facilities. Accordingly, Thailand has implemented appropriate strategies and processes to prevent and control infections such as by developing knowledge and skills on the use of patient screening and isolation precautions, use of personal protective equipment (PPE), use of environmental and engineering management measures, and laboratory operation with firm adherence to biosafety principles to give operators work confidence and facilitate the prevention of the spread of pathogens in the hospital setting among family clusters and close-contact clusters.

Guideline for Isolation Precautions in Hospitals

The Center for Disease Control and Prevention of the United States and controlled infectious diseases hospitals under the advisory committee of the World Health Organization recommended prevention of the spread of antimicrobials and patient isolation by use of standard precautions in every patient, including measures

for preventing disease transmission and patient isolation and other practices in the same manner as for MERs and COVID-19. In addition, the World Health Organization has recommended droplet precautions to be used along with contact precautions. Nevertheless, airborne transmission can occur in patients with pneumonia or significant coughing or when activities/procedures that are ongoing cause small airborne aerosols such as when inserting-removing respirators, mucus suction, mucus collection, medication spray application, etc.

Therefore, the World Health Organization and the United States Center for Disease Control (US-CDC) provided guidance on the use of airborne precautions to prevent the spread, and the details of the management guidelines for preventing the spread of pathogens in medical facilities are shown in TABLE 13.

TABLE 13. Management guidelines for preventing the spread of pathogens in medical facilities.

Contact Guidelines	Touch	Vapor	Air	Prevention in Patients with Weakened Immune System
Patient Isolation Method	Single room (if available)	Single room	Negative-pressure air isolation room	Single room
Protective Equipment for Medical Personnel	Gloves, gowns, aprons, goggles, masks, shoes	Face masks, gloves, gowns, goggles	N-95 face masks	Sanitary masks
Prevention Measures for Patients	None	Face masks	Face masks	Face masks

The measures for patient isolation and preventing the spread of pathogens in medical facilities (isolation precautions)[14] according to epidemiological considerations are divided into two broad practices, namely, standard precautions and transmission-based precautions.

Transmission-based Precautions

There are many pathogens that are causes of infections in medical facilities, whether they are bacteria, viruses, molds, parasites or prions. These pathogens can spread in medical facilities through 3 components as follows:

1. The source of the disease-causing pathogens. Pathogens in medical facilities often occur from human sources of disease such as patients, nurses, workers, and visitors. These people might be symptomatic or asymptomatic or might be in the incubation stage of the disease or in a stage of active growth and division without any displayed symptoms (colonization).

2. People who are sensitive to infection. A major factor for infection in people is an individual's sensitivity to infection. Each person's responses differ after exposure to pathogens. While some people might display no symptoms at all, others might display severe symptoms and eventually die. Personal factors include the following:

- Excessively high or low age.
- Being on immunosuppressant drugs.
- Having pre-existing diseases that increase sensitivity to contracting microbial infections.
- Having gone through surgery.
- Exposure to radiation therapy often causes weakened immunity in the skin and organs.
- Having various devices inserted into the body such as body catheters that creates channels for pathogens to enter the body easily.

3. Mode of Transmission. Pathogens in medical facilities can spread by 3 modes, namely, contact, droplets, and airborne modes. A single pathogenic microbe can spread by more than 1 channel. Therefore, in controlling the spread of pathogens in medical facilities, it is necessary to understand the mechanisms for preventing the spread of the pathogens as follows:[13]

3.1 Contract transmissions are transmissions of pathogens by contact, and it is divided into three types as follows:

3.1.1 Direct contact. This is the spread of pathogens from person to person or from a disease-carrying environment to people by direct contact or by contact with vapors from nasal discharges or saliva such as exposure to pathogens through open wounds or blood or bodily secretions of patients, etc.

3.1.2 Indirect contact. This is the spread of pathogens from the source of the disease or patient via a medium, which mostly is in the form of objects, items, materials, or devices, to another person, such as the spread of pathogens from shared use of devices or use after improper sterilization after use with a patient or spread of pathogens through the hands of health personnel that was not washed after contamination with pathogens.

3.2 Droplet transmissions. This is the spread of pathogens via vapors from nasal discharges and saliva with sizes exceeding 5 microns. Mostly, the range of dispersion is no more than 0.30 meters away from the source, but it can be as far as 1.80 meters in some cases, depending on the severity and method of dispersion, droplet density, and environmental factors such as temperature and humidity. Examples of these include respiratory diseases caused by an adenovirus (adenovirus, respiratory), bronchiolitis, bronchitis, croup or acute laryngeal and tracheal inflammation, epiglottitis, mycoplasma pneumoniae, pneumonia, plague-pneumonia, rubella, mumps, pertussis, influenza, meningitis, viral meningitis, meningococcal infection, etc.[15] Furthermore, it was found that some respiratory infections such as influenza (Moser, Bende, Margolis, Noble, Kendal & Ritter, 1979) and some gastrointestinal viral infections such as rotavirus (Chadwick & McCann, 1994) can also be transmitted by aerosol at a distance in excess of 0.30 meters in enclosed spaces such as patient accommodations and hotel accommodations. This shows that these pathogens can survive suspended in the air and be carried over distances when aided by the wind. In addition,

for SARS-CoV, although the primary modes of transmission of these pathogens are contact and droplets, the pathogens can be spread far when persons engage in activities that cause small vapors (aerosol transmission) in enclosed spaces.[26]

3.3 Airborne transmissions. These occur as a result of disease-producing aerosol contaminated with pathogens. The sizes of the aerosol are less than 5 microns, and the aerosol can remain suspended in the air for extended periods of time. As a result, when the air containing the pathogens is inhaled, infectious diseases can occur. Because these microbes are very small, they can be spread farther than 3 feet away from the source and can remain suspended and be carried by wind and air for hours or days depending on environmental factors such as movements within the room and especially airflow, which can cause these pathogens to spread farther. Pathogens that can be transmitted airborne include pulmonary tuberculosis (TB), extra-pulmonary tuberculosis that produces bodily secretions, measles, chickenpox, disseminated herpes zoster and disseminated herpes simplex, severe acute respiratory syndrome (SARS), Middle East Respiratory Syndrome (MERS) and avian influenza. Thus, in addition to needing measures to prevent airborne transmissions, it is also necessary to follow contact precautions.

Pathogens can also be spread by disease-carrying animals such as flies, cockroaches, mosquitos, and rats. These animals can cause pathogens to be spread in medical facilities, especially in the cafeteria and patient wards, provided no strict cleaning practices take place. Accordingly, foods contaminated by the pathogens carried by these animals can cause diseases in consumers. Furthermore, microbes transmitted by air can be encountered in the environment, such as spores of the fungus *Aspergillosis* spp. that can be found in the environment, and cause immunodeficient patients to contract infections from them.[27]

The key principles for preventing and controlling the spread of disease in medical facilities include the 3 following principles:

1) Administrative controls in medical facilities. These are the most important foundational measures for reducing the risk of disease transmission in public health service facilities.

2) Environmental controls. These have secondary importance to preventing infections in medical facilities.

3) Use of personal protective equipment (respiratory-protection controls). It was found that, following the presence of the 2 above control measures, the environment of medical facilities will be less contaminated with air-transmitted diseases.

Patient Isolation Guidelines for Preventing the Spread of Pathogens in Medical Facilities

The administrative teams of medical facilities should ensure confidence in the services they provide by applying the principles for preventing the transmission of pathogens by specifying them as hospital policies and including them in the objectives of their organization's patient care safety system. Furthermore, they should provide service support in terms of financial resources and human resources to facilitate efforts to control infectious diseases, and medical facilities should provide education and training about how to prevent the transmission of work-specific pathogens to public health teams as part of their orientation before work and periodically and consistently provide additional modern information. Moreover, they should provide document recommendations for patients and service recipients about how to clean hands and how to behave when coughing or sneezing (respiratory hygiene/cough etiquette practices) and patient isolation practices (transmission-based precautions).

The principles for preventing infections and controlling pathogen transmissions in medical facilities (isolation precautions)[13] mean practices to prevent infections in patient care and controlling the transmission of pathogens from patients to other patients, personnel, relatives and the environment around the hospital by use of various measures such as patient screening and isolation measures and use of personal protective equipment appropriate to the mode of transmission, comprising the following:

1. Standard precautions. This means measures used on every patient seeking service in medical facilities with the basic consideration of the fact that every patient might be infected with a disease that can be transmitted by blood and all forms of bodily secretions, without consideration to patient disease diagnosis or infection status and to use these measures as the preliminary practice to prevent the transmission of pathogens from patients to medical personnel, regardless of whether the source and mode of transmission of the pathogens is known. These practices are to be applied to blood and all bodily secretions aside from sweat, regardless of whether or not the secretions contain blood, and cover contact with skin-bearing wounds and tissues according to the following key components:

1.1 Hand hygiene. During patient care, avoid contact with the surfaces of objects located close to patients in order to avoid hands from being contaminated with environmental pathogens and to prevent pathogens from being transmitted from contaminated hands to the environment. Studies found that pathogens can survive for extended periods in the environment depending on the type of pathogen such as the following:

- Parainfluenza virus can survive for up to 10 hours on smooth surfaces and up to 6 hours on clothing.
- Noroviruses can survive up to 12 days on carpets.
- Hepatitis B virus can survive for up to 7 days on electrocardiogram electrodes.
- *Clostridium difficile* can survive up to 5 months on the floor.
- Methicillin-resistant *Staphylococcus aureus* (MRSA) can survive up to 9 weeks on dry floors and up to 2 days on laminated plastic surfaces.
- Vancomycin-resistant enterococcus (VRE) can survive up to about 2 months on counter surfaces.
- *Acinetobactre baumannii* can survive up to 4 months on dry surfaces.

Therefore, cleaning the hands is the most important method for preventing the spread of disease pathogens and for reducing infections in medical facilities[16], since the spread of a large number of pathogens occurs from the contaminated hands of personnel. Accordingly, clearly dirty hands can be cleaned by using soap with water or by using sterilizing solutions mixed with clean water. Otherwise, if the hands are not clearly dirty, then they can be cleaned by applying alcohol on the hands, except for situations where the hands are at risk of exposure to spores such as *C. difficile* or *Bacillus anthracis*, in which case wash the hands with water and soap or sterilizing soap, since alcohol, chlorhexidine, iodophore, and other sterilizing solutions cannot destroy the spores of these pathogens. In addition, the hands have to be cleaned in the following 5 important activities: 1) before contacting patients, 2) before performing a clean or sterile procedure, 3) after contacting the bodily secretions or dirty contaminants of patients, 4) after contacting patients, and 5) after contacting the environment around patients. Moreover, the hands should be cleaned before and after the removal of all types of personal protective equipment.

1.2 Use of personal protective equipment. Personal protective equipment should be worn when engaging in patient care activities that have indicators that contact might be necessary with the pathogen-carrying droplets, secretions, blood, or fluids of patients, and caution must be exercised to prevent contamination of clothing and skin when removing personal protective equipment. Accordingly, the appropriate practices are as follows:[22]

1.2.1 Gloves. Wear gloves every time whenever the hands have wounds or are expected to come into contact with blood or secretions or become contaminated by pathogens and immediately remove gloves after completing activities. Also do not wear the same pair of gloves to care for more than 1 patient and replace the gloves when changing activities with the same patient if the hands have come into contact with contaminants.

1.2.2 Protective gowns. Wear clean protective gowns to protect the skin and clothing from contamination when performing procedures and activities with patients that might lead to contamination by blood or the bodily secretions of patients, which might spatter on to the body, and wear 1 gown per patient per occasion and immediately remove the gown after use.

1.2.3 Face masks. For the wearing of face masks, they can be divided by use as follows:

- Masks covering the mouth and nose with air filtration (surgical masks). These are used for preventing large droplets and airborne vapors and are recommended to be worn in persons with weakened immunity or who have the potential to spread pathogens.
- Masks covering the mouth and nose with particle filtration (respiratory protective masks). These are divided into the following types:

1) Pathogen-filtrating masks can filter out pathogens contaminating small vapors suspended in the air with effectiveness in screening pathogens up to 3 microns in size. Medical personnel is advised to wear these masks when there is the risk of exposure to pathogens mixed with small airborne vapors of mucus (airborne transmission). The masks are further divided into different types such as N95, N99, N100, R95, R99, and R100.

2) Pathogen- and toxin-filtrating type. These masks can filter out pathogen-bearing aerosol and prevent toxins suspended in the air. They can filter out pathogens as small as 1-5 microns and are made up of a special type of filters (HEPA filters) such as P95, P99, and P100 filters.

3) Pathogen-filtration masks that cover the nose and have respiratory with an exhalation valve. These masks can filter out diseases mixed in aerosol and contain respiratory with an exhalation valve. The respiratory with exhalation valve will open when exhaling to expel air and will close when inhaling. The inhaled air will pass through an air filter such as the N95 filter.[15]

TABLE 14 Filtration Effectiveness of N95 Face Masks

Remarks	N means mouth-nose mask that cannot filter out oil vapors. R means mouth-nose mask that can partially filter out oil vapors. P means mouth-nose mask that can effectively filter out oil vapors.
N95 R95 and P95 N99 R99 and P99 N100 R100 and P100	95% filtration effectiveness. 99% filtration effectiveness. 99.97% filtration effectiveness.

1.2.4 Goggles. These are used when it is expected that patient blood or secretions or droplets will spatter into the eyes of medical personnel such as during mucus suction, surgery, child delivery, wound stitching, abscess lancing, dentistry work, spinal fluid extraction post endoscopy, etc.

1.2.5 Face shields. These are used when it is expected that patient blood or secretions will spatter onto the face or eyes of the operator from the front and sides. These, however, cannot prevent airborne pathogens.

1.2.6 Caps. These are used to prevent transmission from dandruff and hair of medical personnel to patients and can help prevent patient blood and bodily secretions from spattering onto the hair such as during child delivery, surgery, dental drilling, etc.

1.2.7 Aprons (CPE). Aprons are used to prevent the spattering of blood and bodily secretions from patients or water is used to wash contaminated devices.

1.2.8 Boots. These are used to protect against the blood and bodily secretions of patients with oozing pus or that might come into contact with the feet or legs of medical personnel such as during transportation/movement of waste, bathroom cleaning, child delivery, surgery, and washing of instruments, etc.[25]

1.3 Respiratory hygiene/cough etiquette. Knowledge should be provided to medical personnel, patients and relatives about respiratory hygiene/cough etiquette. Accordingly, toilet paper or napkins should be used to cover the mouth and nose rather than hands, or else secretions, mucous vapors and saliva might come into contact with the hands and spread from the hands. If possible, places should be arranged specifically for accommodating patients with respiratory infections, with these places located at least 30 centimeters away from other persons. Importantly, hands should be washed after contact with droplets, mucus and saliva after coughing and sneezing, and toilet paper should be discarded in lidded waste bins and sanitizing fluids should be provided for cleaning the hands and face masks.

1.4 Patient placement. Make considerations based on the likelihood of transmission of pathogens. Place patients with high transmission risk in isolation rooms or have patients with the same infections be placed in the same rooms (cohort rooms).

1.5 Patient-care equipment and instruments/devices. For those that might be contaminated by pathogens from the patients' bodies, exercise caution when holding or handling equipment contaminated with blood, fluids or secretions to prevent contact with the skin, tissues and clothing and to prevent infection from spreading to other patients and the environment. Furthermore, reusable equipment must be cleaned and sterilized to be free of germs before use, and single-use equipment must be stored for proper disposal. In addition, wear personal protective equipment such as gloves and gowns according to the expected level of contamination when needing to come into contact with clearly dirty equipment and tools. The method for reducing pathogens present on medical equipment depends on the desired pathogen reduction objective for ensuring safety in the equipment, tools and devices used in medical facilities. Accordingly,

many methods can be used to reduce the number of pathogens present on the surfaces of living organisms and equipment, tools and devices as follows:

1.5.1 Cleaning. This is the best method for reducing pathogens. It is easy and cost-saving, and when done correctly, it can eliminate most pathogens. Therefore, cleaning is the first procedure to follow in the process to reduce pathogens.

1.5.2 Disinfection. This means the destruction of most forms of infection, except for bacterial spores.

1.5.3 Sterilization. This means the total eradication of pathogens, including bacterial spores. Because there are many methods for disinfection/sterilization of medical equipment, in order to appropriately disinfect/sterilize each piece of equipment, it is necessary to first correctly categorize the equipment used by agencies. Accordingly, there are 3 categories of medical devices as follows:

- Critical items. These are equipment and instruments used with patients and that involve puncturing or penetration of tissue or piercing/insertion into the body or blood vessels. They include needles, surgical instruments and catheters for various organs such as urinary catheters, etc. These pieces of equipment must always be sterilized.

- Semi-critical items. These are equipment and instruments used in patients and that come into contact with the body's flesh or tissues or skin bearing injuries or scratches, such as respirators and anesthesiologic instruments. These instruments should be subjected to a high level of disinfection.

- Non-critical items. These are equipment and devices used in patients in a way that involves contact with normal skin without injuries or scratches and include blood pressure monitors, kidney trays and enema containers. These pieces of equipment should be subjected to cleaning or a low level of disinfection.

1.6 Care of the environment. The surfaces of environments potentially contaminated by pathogens should be appropriately cleaned, including surfaces close to daily patients, such as beds, bed barriers, bed tables and areas in patient units. Cloths dipped in disinfectants capable of killing environmental pathogens should be used for regular cleaning, followed by wiping with a dry cloth every day. Furthermore, frequently touched surfaces such as door knobs and bathroom floors should be cleaned more frequently than other areas, and electronic devices frequently used with patients should be cleaned frequently, such as blood pressure monitors and oxygen saturation measurement devices, and wastes should be managed appropriately, especially in regards to the sorting of ordinary and contaminated wastes. Accordingly, wastes should be sorted at the point of service and a system should be in place for assessing waste sorting. If contamination by secretions such as patient blood or fecal matter is present, splash over the area by using disinfecting agents

such as 0.5% sodium hypochlorite (5,000 ppm), leaving the area for 10-15 minutes and then wipe the area clean by using water mixed with detergent followed by clean water and then drying as normal.

1.7 Textiles and laundry. Exercise caution when coming into contact with and moving fabric contaminated with blood or secretions from the bodies of patients. Hold them in a manner that causes the least amount of rippling to avoid dispersion, and wash fabrics contaminated with blood or patient secretions twice by using regular water first in order to eliminate dirty stains up to a level and then proceed to the laundry process by using detergent at the appropriate proportion. This process is divided into 2 cases as follows:

1.7.1 If the fabric is contaminated with sweat and dead skin, wash normally by first washing with regular water and then washing with an appropriate amount of detergent at temperatures of 60-70 degrees Celsius for 10 minutes or 71 degrees Celsius for 3 minutes. Then spin for 1 hour and then dry in a dryer for 30 minutes before removing the fabric from the dryer to send to the folding service section.

1.7.2 For washing infected fabric, wash by using regular water twice first and then wash by using an appropriate amount of detergent with the water temperature at 71 degrees Celsius for 25 minutes to kill both bacteria and viruses. If the washing machine's temperature cannot be adjusted, soak the fabric in 0.5% hypochlorite solution (5,000 ppm) for 30 minutes before normal washing.

1.8 Safe injection practices. Work accidents affect both service providers and service users. Even though accidents that occur do not always cause infection, e.g., in the case of glass cuts and being punctured by sterile needles, these occurrences nevertheless cause injuries that increase the risk of infection should there be a contract with blood or bodily secretions from infected persons before the wounds have healed. Furthermore, if the accidents are caused by equipment that increases the risk of infection, the emotional state of workers who experience such accidents will naturally be significantly negatively impacted.

2. **Transmission-based precautions.** These are ways for patients whose modes of transmission are known or who have the risk of illness from various new diseases and ways to prevent the spread of pathogens according to contact mechanisms in addition to patient care.[20]

2.1 Contact precautions are used as practice principles for patients who are known or suspected to have an infection or who show evidence of symptoms that indicate risk for transmission of pathogens by direct and indirect contact. Accordingly, the practice principles are as follows:

2.1.1 Providing beds/rooms for patients. Patients should be placed in isolation rooms. Otherwise, patients with the same infection should be placed in the same rooms.

2.1.2 Hand-cleaning. The hands should be cleaned correctly during contact with each patient. It is recommended to avoid contact with patients and patients' belongings.

2.1.3 Wearing personal protective equipment. Medical personnel must wash their hands before putting on gloves when having to come into contact with patients or blood or fluids of patients or surfaces and items near patients. Gowns should be worn when having to directly come into contact with patients or floor or wall surfaces or instruments located close to patients and that might be contaminated, and personal protective equipment should be removed before leaving patient rooms. Additionally, the hands should be cleaned after coming into contact with each type of personal protective equipment.

2.1.4 Patient movement. Only move patients as required, and while moving patients, exercise precautions to prevent transmission of pathogens to other patients. Ensure that the body of the patient with infection or with disease-causing pathogens is thoroughly covered, and communicate to ensure that patients quickly receive services to reduce the risk of transmission of pathogens to other persons and the environment.

2.1.5 Instruments and equipment used in patient care. Exercise caution in picking up and touching the instruments and equipment used with patients by following standard precautions and using disposable instruments separately for each patient. In addition, for equipment to be used with other patients, always clean and disinfect the equipment properly before use with other patients.

2.1.6 Cleaning up the environment. Perform cleaning at least once daily, especially in areas of frequent contact such as bed barriers, door knobs, etc. Medical personnel must advise patients and relatives on how to behave before patient visits, and contact precautions are to be halted when the symptoms and displayed symptoms of patients disappear. Otherwise, follow the guidelines for the pathogens in question.[21]

2.2 Droplet precautions. Use these as practice principles for patients who are known or suspected to have infections that can be transmitted by droplets with sizes greater than 5 microns that are caused by persons carrying diseases or persons who cough, sneeze or speak. Examples of the such disease include diphtheria, pertussis, *Mycoplasma pneumoniae, Haemophillus influenzae type b, Neisseria meningitidis,* pneumonic plague, *Streptococcus pharyngitis,* pneumonia, scarlet fever and adenovirus, influenza, mumps, parvovirus B, rubella, etc. Accordingly, the practice principles are as follows:[24]

2.2.1 Patient room/bed placements. Place patients in isolation rooms and close all doors every time after entering-exiting patient rooms. If no isolation rooms are available, arrange for patients displaying significant symptoms of coughing and mucus to first stay in isolation rooms and place patients with the same disease infections to stay in the same rooms. However, if no isolation rooms are available, and it is necessary to have these patients stay together with other patients,

arrange the beds to be spaced more than 30 centimeters apart with good ventilation and effective airflow control. In addition, avoid placing patients in the same room as other patients with a high risk of infection, such as patients with immunodeficiencies, etc.

2.2.2 Hand cleaning. The hands have to be cleaned properly when contacting each patient in the same room.

2.2.3 Wearing of personal protective equipment. Medical personnel who enter patient rooms or who provide care to patients must wear surgical masks that cover the face and nose, except for when performing procedures that cause dispersion or require close patient contacts, in which case wear face masks covering the face and nose with N95 or N100 filters, e.g., when spraying medications, inserting-removing respirators, phlegm suction, etc. For the part of patients, use cloth or paper to cover their mouths and noses while coughing and sneezing, and have them wear face masks that cover their mouths and noses and provide air filtration at all times when other persons are present in the room, except for when eating or brushing teeth.

2.2.4 Patient movements. Only move patients as necessary. If it is necessary to move patients outside of the room, have patients wear face masks covering their mouths and noses with air filtration at all times, and inform the destination agency in advance to prepare to receive patients and to prevent transmission. Furthermore, follow the respiration/sneezing etiquette when required and always seek guidance from medical personnel on appropriate behaviors when visiting patients. Unless necessary, visits should be avoided while infection can be transmitted, or else make sure to limit visitations. The droplet precautions can be discontinued when the symptoms and displayed symptoms of infection in patients disappear. Additionally, after patient discharge, open the windows to ventilate air and require cleaners to wear personal protective equipment such as air filtration face masks, gowns and gloves and prioritize wiping and cleaning of horizontal surfaces. For surfaces of materials and equipment located close to the patient, wipe by using 70% alcohol, and for ordinary surfaces, clean by using water mixed with detergent.

2.3 Airborne precautions. These are practice measures for patients known or suspected to be infected with diseases with a potential airborne human-to-human mode of transmission such as tuberculosis, measles, chickenpox, shingles, etc. Accordingly, the practice principles are as follows:[23]

2.3.1 Patient room placements. Rooms should be negative pressure isolation rooms with 6-12 air ventilation cycles per hour with filtration of air to be removed from the rooms. For ordinary isolation rooms, isolate patients in isolation rooms with good air ventilation, and specify the direction of airflow and always close the door after entering or leaving the patient's room, and avoid swinging fans. Also prepare containers to hold waste with waste bags to hold secretions for discarding in infectious waste bins that feature tightly sealed lids. In cases where

no isolation rooms are available, place patients with the same infection in the same area (cohort area) by arranging patient beds to be located in an area with good ventilation such as the edges of windows. These areas should also be downwind, and the patient area should be as confined as possible. In addition, in cases where there is an outbreak or a large number of patients such that the aforementioned measures are needed, have the patients be placed in the same room as other patients who have the same infection. Also, use temporary methods to facilitate air ventilation such as air suction fans to construct a negative-pressure environment in the patient holding area, and ventilate air directly to the outside and away from people or subject all air to HEPA (high efficiency particulate) filters before releasing it to the outside, and hang an airborne precautions sign in front of the patient isolation room or bed throughout the entire duration of the transmissible stage of the disease outbreak.

2.3.2 Limit visits or only allow visits after the disease transmission phase or with the approval of the treating doctor. Accordingly, visitors must always obtain guidance from medical personnel in advance concerning appropriate practices for patient visits, and the number of visitors should also be limited, with no children, elderly people and immunodeficient people allowed to visit, etc.

2.3.3 Wearing of personal protective equipment. Personnel are required to wear respiration protection devices with high filtration effectiveness such as N95 when visiting patient rooms, and patients should use cloth or paper to cover their mouths and noses when coughing or sneezing and should wear air filtration face masks that cover their mouths and noses (surgical masks) at all times when others are present in the room, except when eating and brushing the teeth.

2.3.4 Patient placement. Restrict the movement of patients. If it is medically necessary to move patients out of a room, while moving the patient should be required to wear a face mask that covers the mouth and nose with air filtration (surgical mask) at all times, and the agency to accept and provide continued care for the patient should be informed in advance in order to set a clear service schedule and prepare for receiving the patient in order to prevent disease transmission. In addition, also follow the respiratory hygiene/cough etiquette practices, and for patients with signs of skin diseases caused by chicken pox, smallpox or tuberculosis, close the sites of the disease to prevent dispersion and contact with the contagious disease from the site of infection. The airborne precautions can be discontinued according to the recommendations for each type of disease, and other practice measures are to be used as appropriate such as in the prevention of tuberculosis transmission[17] and environmental measures[18]. Furthermore, after patient discharge, if the patient was in a negative pressure room, leave the system on for approximately 35 minutes before entering the room to clean, as shown in the table below. Accordingly, persons performing cleaning are required to wear all personal protective equipment such as face masks capable of filtering particulate matter, gowns and gloves, and the room's working system

should be turned on at all times during cleaning. After cleaning is completed, continue leaving the room's system on for an additional 35 minutes before accommodating a new patient. However, if the isolation room lacks a pressure adjustment system, open all windows to ventilate for about 60 minutes before performing cleaning, and persons performing cleaning must wear personal protective equipment such as particulate filtration face masks, gowns and gloves and thoroughly clean the room and open the windows to ventilate for at least 60 minutes. In addition to the aforementioned practice principles, there are also practices for protective environmental management for immunocompromised patients such as blood cancer patients, patients undergoing chemotherapy, immunodeficient patients, etc. These patients are often sensitive to different infections depending on the severity and duration of their immunosuppression. In general, patients have a high risk of infection from bacteria, fungi, parasites and viruses caused by pathogens present in the body and outside the body, and past studies found that isolating these patients in high-efficiency particulate matter filters (HEPA) filters cannot decrease the rate of infection in these patients.[19]

This is because infections in these patients often occur due to their own pathogens (endogenous flora), and when personnel fails to clean their hands or to use pathogen-free instruments, infections can occur in these patients. As such, in the care of these patients, the following practices[25] should be followed:

1) Control the environment. The air entering the patient's room should be filtered by using central or point-of-use high-efficiency particulate (HEPA) filters that can exclude 99.97% of particulate matter with a diameter $\geq$ 0.3 microns. In addition, cause airflow to be directed past the patient's bed and to flow out the other side. The room's air should also have negative pressure relative to outside air, with air cycling at least 12 times per hour.

2) Reduce dust by using non-porous surfaces and flooring materials that can be scrubbed and wiped. When dust is encountered, wipe by using a wet/damp cloth.

3) Avoid using mats along pathways and inside the patient's room.

4) Do not allow fresh and dry flowers and potted plants from being placed inside the patient's room.

5) Restrict the movements of the patient and have the patient leave the room for diagnoses and other activities.

Key Measures for Preventing and Controlling Antimicrobial Resistance in Communities

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The key measures for preventing and controlling antimicrobial resistance in communities are that the community population should have awareness and knowledge and appropriately modify their behaviors related to causing antimicrobial resistance, exposure to antimicrobial-resistant pathogens and spreading of antimicrobial -resistant pathogens and monitoring and assessment of the population's knowledge and behaviors about causing antimicrobial resistance, exposure to antimicrobial-resistant pathogens and spreading of antimicrobial-resistant pathogens.

The measures for promoting the community population to have awareness, knowledge, and appropriate behavior modification about causing antimicrobial-resistant pathogens, exposure to antimicrobial-resistant pathogens, and spreading of antimicrobial-resistant pathogens must be multifaceted measures. The measures previously tested in pilot communities that were found to be effective were the use of information obtained from interviews/questionnaires of the community population as guidelines for developing the development of measures and the use of these measures in the target population within the community through reliance upon village health volunteers (VHVs) who use the training they receive to effectively and extensively communicate with the population belonging to the households under the care of each VHV by using a variety of communication methods to allow the community population to have appropriate awareness, knowledge and behavior modification related to causing antimicrobial-resistant pathogens, exposure to antimicrobial-resistant pathogens and spreading of antimicrobial-resistant pathogens as follows:

1. Antimicrobials are drugs for destroying bacteria only and cannot be used to eliminate other pathogens such as viruses that cause influenza.

2. Antimicrobials are not anti-inflammatory drugs as most people mistake them to be.

3. Antimicrobials cannot treat pain or inflammation not caused by bacterial infection.

4. Antimicrobials are classified as "dangerous drugs" by the Food and Drug Administration under the Ministry of Public Health. As such, antimicrobials can be used primarily in medical facilities. Although many antimicrobials are sold in drug stores, these antimicrobials must be prescribed by pharmacists only, and the sale of antimicrobials by grocery stores and retail stores is illegal.

5. Many commonly encountered community diseases such as influenza, acute dysentery, and ordinary fresh wounds caused by accidents can often recover on their own through general care without the need to use antimicrobials.

6. Avoid buying antimicrobials (what most people often call anti-inflammatory drugs) from stores, retailers, or drug stores for personal use.

7. Avoid requesting for public health personnel to prescribe antimicrobials when seeking services at a medical facility.

8. Use antimicrobials fully according to their specified doses and durations recommended by physicians, if the use of antimicrobials is necessary.

9. Do not allow other persons to use one's own antimicrobials.

10. Do not store leftover or expired antimicrobials for use in the next treatment.

11. Do not dispose of leftover antimicrobials or expired antimicrobials as ordinary trash, in the toilet, or in natural water sources, because said antimicrobials might cause pathogens in the environment to mutate and develop into antimicrobial-resistant pathogens. Accordingly, leftover or expired antimicrobials should be returned to the hospital according to the guidance of the Food and Drug Administration under the Ministry of Public Health for their destruction.

12. Use of antimicrobials, especially inappropriate use of antimicrobials, can cause pathogenic bacteria and bacteria living in the body to mutate into antimicrobial-resistant pathogens that reside in the body without causing any symptoms and that later causes antimicrobial-resistant infections.

13. Avoid eating food that contains antimicrobial residues such as meats from animals grown by use of antimicrobials, because antimicrobial residues in food can cause pathogenic bacteria and bacteria present in the body to mutate into antimicrobial-resistant strains in the body without displaying any symptoms and then subsequently cause antimicrobial-resistant infections.

14. Avoid eating foods and being in environments contaminated with antimicrobial-resistant pathogens, since the antimicrobial-resistant pathogens that are exposed to might then reside in the body without displaying any symptoms before subsequently causing antimicrobial-resistant infections.

15. Persons carrying antimicrobial-resistant pathogens in their bodies without displaying any symptoms and patients with active antimicrobial-resistant infections can spread antimicrobial -resistant pathogens to other persons, food, beverages, and the environment.

16. Treatment of antimicrobial-resistant infections is difficult, and the mortality risk is high in patients with antimicrobial-resistant infections.

17. People should exhibit appropriate personal hygiene behaviors such as by eating food and drinking beverages that are clean, cleanly washing hands before eating and before coming into contact with things that are shared with other persons and after contact with pathogenic contaminants and fecal matter in the toilet, in addition to using appropriate personal protective equipment such as gloves, face masks, goggles, etc. and avoiding contact with pathogen-carrying people, animals and environments.

The surveillance of the effectiveness of measures to promote the community population with appropriate awareness, knowledge, and behavior modification related to causing antimicrobial -resistant pathogens, exposure to antimicrobial-resistant pathogens, and spreading of antimicrobial -resistant pathogens, should occur before and after the use of the aforementioned measures. The easiest method to assess the effectiveness of the aforementioned measures is to use results from interviews/questionnaires from the community population before and after the use of the aforementioned measures in order to make comparisons. However, this method has a key limitation and that is that this assessment method primarily relies on the population's perceptions, which, although may facilitate the assessment of the people's awareness, is often inaccurate and unreliable when used to assess the knowledge and behaviors of the population. Accordingly, other, more suitable methods for assessing people's knowledge and behaviors include knowledge tests and serious surveillance of the people's behaviors, which is difficult and requires a lot of time and resources. However, an assessment method that has been tested in pilot communities and that has been found to be easier and an actual holistic assessment of the desired behaviors is the assessment of the rate of important antimicrobial-resistant infection rates in the community, such as gram-negative bacteria that are resistant to Ceftriaxone or that produce extended-spectrum beta-lactamase (ESBL) that can be isolated from the feces of community members. This is because the rate of infection of these antimicrobial-resistant pathogens within the community will be high if the community people have a low level of awareness, knowledge, and behaviors related to causing antimicrobial-resistant pathogens, exposure to antimicrobial-resistant pathogens and spreading of antimicrobial-resistant pathogens, and the rate of infection of these antimicrobial-resistant pathogens will be low or lower if the community population has an appropriate level of awareness, knowledge, and behaviors about causing antimicrobial-resistant pathogens, exposure to antimicrobial-resistant pathogens and spreading of antimicrobial-resistant pathogens.

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Appendix A

Appendix A

- **AMR–1 Form for Laboratory Reporting of Individual Patient Cases with Important Antimicrobial-Resistant Infections**
- **AMR–2 Form for Laboratory Reporting of Individual Patient Cases with Critically-Important Antimicrobial-Resistant Infections**
- **Guidelines for Reporting Critically-important Antimicrobial-Resistant Infection Cases**

ภาคผนวก ข

คำสั่งแต่งตั้งคณะทำงานแนวทางการเฝ้าระวังและสอบสวนเชื้อดื้อยาต้านจุลชีพ

AMR–1 Form for Laboratory Reporting of Individual Patient Cases with Critically-Important Antimicrobial-Resistant Infections

AMR–1 Form for Laboratory Reporting of Individual Patient Cases with Critically-Important Antimicrobial-Resistant Infections		ID No. _ _ - _ _ _ _
1. Hospital/Medical Facility:	2. HN:	3. AN:
General Information		
4. First-Last Name:		
5. Sex: ☐ Male ☐ Female	6. Age: ……..… Years ……..… Months ……..… Days	
7. Nationality: ☐ Thai ☐ Myanmar ☐ Cambodian ☐ Laotian ☐ Chinese ☐ Other Specify……..……..……..		
8. Address during Illness (if known) House No. ……..…. Village/Building ……. Lane…… Road …… Sub-district ……..District ……..…… Province …..……		
Clinical Information		
9. First Date of Illness: dd / mm / yy	10. First Date of Admission for Treatment: dd / mm / yy	
11. Department:	12. Patient Ward:	
13. Initial Diagnosis:		
14. Diagnosis on Date of Specimen Submission		
15. Whether referred from another hospital:	16. Date of First Admission to Hospital: dd / mm / yy	
Laboratory Information		
17. Specimen Type:	18. Collection Site:	
19. Specimen Collection Date: dd / mm / yy	20. Result Date: dd / mm / yy	
21. Pathogens Discovered		
☐ Vancomycin-resistant, *Staphylococcus aureus* (VRSA)	☐ Colistin-resistant, *Acinetobacter baumannii*	
☐ Vancomycin-resistant, *Enterococcus* spp. (VRE)	☐ Colistin-resistant, *Pseudomonas aeruginosa*	
☐ 3rd gen. Cephalosporins-resistant, *Neisseria gonorrhoea*e	☐ Other Specify……	
22. Infection Diagnosis: ☐ Infection ☐ Colonization ☐ Contamination		
23. If diagnosis is Infection, please classify the source of contact: ☐ HAI ☐ HAI refer ☐ CI ☐ Present On Admission		

Laboratory Test Results for Discovery of Other Critically-important Drug-resistant Pathogens from Specimens or Other MDROs

No.	Type of Drug-Resistant Pathogen (Bacteria)	Specimen Type	Collection Site

24. Patient Status: ☐ Ongoing treatment ☐ Recovered ☐ Deceased Date of Death: dd / m / yy		
Reported by:	Position:	
Workplace:	Telephone:	Report Date: dd / m / yy

AMR–2 Form for Laboratory Reporting of Individual Patient Cases with Critically-Important Antimicrobial-Resistant Infections

AMR–2 Form for Laboratory Reporting of Individual Patient Cases with Critically-Important Antimicrobial-Resistant Infections (For laboratories that accept specimens for testing or do not treat patients)	ID No. _ _ - _ _ _ _

1. Hospital/Medical Facility/Laboratory (testing):

General Information

2. First-Last Name:		5. Lab ID:	
3. Sex: ☐ Male ☐ Female	4. Age: …… Years …… Months …… Days	6. HN:	7. AN:

8. Address during Illness (if known) House No. ……..…. Village/Building ……. Lane……
Road …… Sub-district ……..District ……..…… Province …..……

Laboratory Information

9. Hospital/Medical Facility (that submitted for testing):

10. Specimen Type:	11. Collection Site:	
12. Specimen Collection Date: dd / mm / yy	13. Specimen Receipt Date: dd / mm / yy	14. Result Date: dd / mm / yy

15. Pathogens Discovered

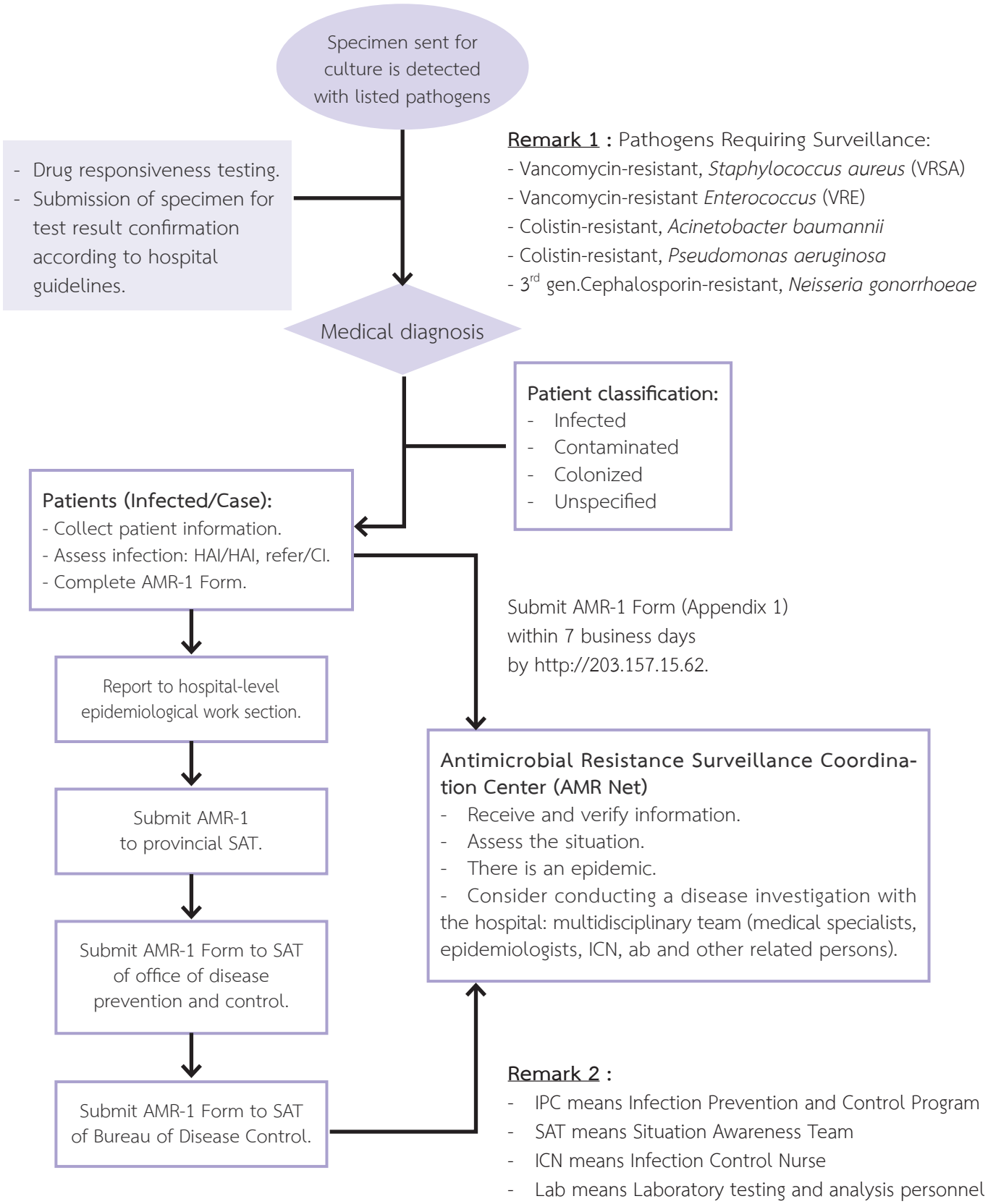
☐ Vancomycin-resistant, *Staphylococcus aureus* (VRSA)
☐ Vancomycin-resistant, *Enterococcus* spp. (VRE)
☐ 3rd gen. Cephalosporins-resistant, *Neisseria gonorrhoea*e
☐ Colistin-resistant, *Acinetobacter baumannii*
☐ Colistin-resistant, *Pseudomonas aeruginosa*
☐ Other. Specify……

Laboratory Test Results for Discovery of Other Critically-important Drug-resistant Pathogens from Specimens or Other MDROs

No.	Type of Drug-Resistant Pathogen (Bacteria)	Specimen Type	Collection Site

Reported by:	Position:	
Workplace:	Telephone:	Telephone:

Guidelines for Reporting Critically-important Antimicrobial-Resistant Infection Cases



คำสั่งกรมควบคุมโรค

ที่ ๙๑๘ /๒๕๖๔

เรื่อง แต่งตั้งคณะทำงานแนวทางการเฝ้าระวังและสอบสวนเชื้อดื้อยาต้านจุลชีพ

ด้วยกรมควบคุมโรค โดยกองระบาดวิทยา ได้จัดทำโครงการการพัฒนาบุคลากรเครือข่ายระดับเขตและส่วนกลางเพื่อการเฝ้าระวังและสอบสวนเชื้อดื้อยาต้านจุลชีพ โดยการพัฒนาบุคลากรเพื่อการเฝ้าระวังและตอบสนองต่อการระบาดตามแผนยุทธศาสตร์การจัดการเชื้อดื้อยาต้านจุลชีพประเทศ พ.ศ. ๒๕๖๐ - ๒๕๖๔ ซึ่งเป็นไปตามข้อตกลงของกฎอนามัยระหว่างประเทศ และ Global Health Security Agenda (GHSA)

เพื่อให้การพิจารณากรอบเนื้อหา ทบทวนเอกสาร และจัดทำแนวทางการเฝ้าระวังและสอบสวนเชื้อดื้อยาต้านจุลชีพ ให้เป็นไปด้วยความเรียบร้อยและมีประสิทธิภาพ อาศัยอำนาจตามความในมาตรา ๓๒ แห่งพระราชบัญญัติระเบียบบริหารราชการแผ่นดิน พ.ศ. ๒๕๓๔ แก้ไขเพิ่มเติมโดยพระราชบัญญัติระเบียบบริหารราชการแผ่นดิน (ฉบับที่ ๕) พ.ศ. ๒๕๔๕ กรมควบคุมโรค จึงแต่งตั้งคณะทำงานแนวทางการเฝ้าระวังและสอบสวนเชื้อดื้อยาต้านจุลชีพ โดยมีองค์ประกอบ หน้าที่และอำนาจ ดังนี้

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๑.๒๕ นางสาวเพ็ญศิริ ยะหัวดง นักวิชาการสาธารณสุขปฏิบัติการ กองระบาดวิทยา กรมควบคุมโรค	คณะทำงาน
๑.๒๖ นางพัชริดา หงษ์จันทร์ นักวิชาการสาธารณสุขปฏิบัติการ กองระบาดวิทยา กรมควบคุมโรค	คณะทำงาน
๑.๒๗ นางสาวอรพรรณ กันยะมี นักวิชาการสาธารณสุขปฏิบัติการ กองระบาดวิทยา กรมควบคุมโรค	คณะทำงาน
๑.๒๘ นางสาวปิวรา บุญวิเศษ นักวิชาการสาธารณสุขปฏิบัติการ กองระบาดวิทยา กรมควบคุมโรค	คณะทำงาน
๑.๒๙ นางสาวณฐวดี ศรีวรรณยศ นักวิชาการสาธารณสุขปฏิบัติการ กองระบาดวิทยา กรมควบคุมโรค	คณะทำงาน
๑.๓๐ นายอรรถวิทย์ วัชรธรรมรักษ์ ผู้ประสานงานโครงการ กองระบาดวิทยา กรมควบคุมโรค	คณะทำงาน
๑.๓๑ นายรุ่งโรจน์ ใจยงค์ นักวิชาการสาธารณสุขปฏิบัติการ กองระบาดวิทยา กรมควบคุมโรค	คณะทำงาน และเลขานุการ

๒.หน้าที่...

๒. หน้าที่และอำนาจ

๒.๑ จัดทำกรอบเนื้อหาแนวทางการเฝ้าระวังและสอบสวนผู้ป่วยติดเชื้อดื้อยาต้านจุลชีพ

๒.๒ จัดทำแนวทางการเฝ้าระวังและสอบสวนผู้ป่วยติดเชื้อดื้อยาต้านจุลชีพ

๒.๓ ปฏิบัติงานอื่น ๆ ตามที่ได้รับมอบหมาย

ทั้งนี้ ตั้งแต่บัดนี้เป็นต้นไป

สั่ง ณ วันที่ ๘ มิถุนายน พ.ศ. ๒๕๖๔

(นายโอภาส การย์กวินพงศ์)
อธิบดีกรมควบคุมโรค

กรมควบคุมโรค
Department of Disease Control