

Rapid Assessment of the Regulatory Measures in Combating Antimicrobial Resistance (AMR) in the ASEAN Region



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The ASEAN Secretariat
Jakarta

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ACRONYMS & ABBREVIATIONS

ALD	ASEAN Leaders' Declaration
AMC	Antimicrobial Consumption
AMR	Antimicrobial Resistance
AMS	ASEAN Member States
AMU	Antimicrobial Utilization/use
AWGPD	ASEAN Working Group on Pharmaceutical Development
CME	Continuous Medical Education
DLD	Department of Livestock Development
FAO	Food and Agriculture Organization
FEC	Formulary Executive Council
FDA	Food and Drug Administration
ICAMR	Inter-Agency Committee on AMR
ISPA	Imipenem-Sensitive Pseudomonas Aeruginosa
MCR -1	Mobilized Colistin Resistance-1 gene
MOH	Ministry of Health
MOPH	Ministry of Public Health
MSOM	Malaysian Statistics on Medicines
NAG	National Antibiotic Guideline
NARC	National Antimicrobial Resistance Committee
NHSO	National Health Security Office
OIE	World Organisation for Animal Health
P4P	Pay-for-Performance
RAT	Rapid Assessment Tool
RDU	Rational Drug Use
REGOVP	Registration Guideline of Veterinary Products
STG	Standard Treatment Guideline
Thai-SAC	Thai Surveillance of Antimicrobial Consumption
VRE	Vancomycin-Resistant Enterococci
WHO	World Health Organization

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BACKGROUND

ASEAN was established in 1967 with the aim of narrowing the development gap among the member states by creating a community that is founded on regional cooperation and social economic integration. It also envisions the promotion of regional growth, peace and harmonization among the member states through assisting each other in economic, social, cultural, technical, scientific and administrative matters.

Antimicrobials are employed to manage infectious diseases, however, the wide and indiscriminate use of these agents contribute to the emergence of resistant pathogens which have become the major causes of morbidity and mortality. Antimicrobial Resistance (AMR) is considered a threat to the treatment and control of infections. It costs money, affects livelihood and can severely impede the trade and economy. As a result, the World Health Organization (WHO), World Organisation for Animal Health (OIE), and Food and Agriculture Organization of the United Nations (FAO) have organized a tripartite collaboration to take collective actions to minimize the emergence and spread of AMR.

At ASEAN level, the ASEAN Working Group on Pharmaceutical Development (AWGPD) has collaborated to organize activities on rational use of medicines, including antimicrobial agents. Since the year 2011, annual workshops on rational use of antimicrobial agents were organized among ASEAN countries. Apparently there is no detailed inventory of what legislations most countries have and actually do to control use and sale of antimicrobials in human and veterinary sectors and this led the discussion of conducting a Rapid Assessment Tool (RAT) in combating AMR in the 29th AWGPD meeting. Subsequent to that, concept note and questionnaire were developed and survey conducted in 2017 among ASEAN Member States (AMS).

In response to this global public health threat, all the AMSs are one with developing the ASEAN Leaders' Declaration (ALD) to combat AMR which has been adopted in November 2017. The ALD has provisions related to the strengthening of regulatory systems and supply chain management to ensure equitable, timely and sustainable access to safe, efficacious, affordable and quality antimicrobials across all sectors.

STUDY OBJECTIVES AND METHODS

Study Objectives

This study aims to provide an understanding of the current regulatory mechanisms on antimicrobials that are implemented in the ASEAN Member States (AMS) by addressing the following specific objective:

- to collate information on regulatory measures practiced in ASEAN countries to control and monitor the use and sale of antimicrobials, both as active ingredients and finished pharmaceutical products, for human and animal consumption.

Methodology

This is a descriptive study using a cross-sectional design summarizing individual country data on the following regulatory measures to control and monitor the use and sale of antimicrobials for both human and animal sectors:

1. Registration and licensing of products.
2. Legislations and guidelines for sale of antimicrobials.
3. Monitoring and surveillance activities.

These are the three main domains included in the questionnaire used in the study (Annex A). The survey was conducted over a period of two months from January to March 2017. The tool was disseminated to focal points of all 10 ASEAN Member States through email (i.e. Ministry of Health, Food and Drug Administration) in coordination with the ASEAN Secretariat. Submission of completed questionnaires was also done electronically.

Data from the accomplished questionnaires of individual member states were collated and extracted and then entered into a database using Microsoft Excel 2013 spreadsheet. The summary of results was presented through tables and graphs. Categorical data (i.e. “yes” or “no” questions) were analyzed and presented as frequencies, whereas numerical and qualitative responses were reported as enumerated by country respondents.

RESULTS

A total of 10 ASEAN Member States participated in the rapid assessment, namely Brunei Darussalam, Cambodia, Indonesia, Lao PDR, Malaysia, Myanmar, Philippines, Singapore, Thailand and Viet Nam.

Registration of Products

All AMSs have an existing organization for the regulatory control of antimicrobials for human use which are listed below (Table 1). Cambodia did not specify the name of the responsible agency in their country.

Table 1. List of organizations responsible for the regulation of antimicrobials for human use

Country	Regulatory Agency
Brunei Darussalam	Brunei Darussalam Medicines Control Authority (facilitated by the Department of Pharmaceutical Services, Ministry of Health)
Indonesia	National Agency of Drug and Food Control
Lao PDR	Food and Drug Department
Malaysia	National Pharmaceutical Regulatory Agency
Myanmar	Myanmar Food and Drug Board of Authority
Philippines	Food and Drug Administration
Singapore	Health Sciences Authority
Thailand	Food and Drug Administration, Ministry of Public Health
Viet Nam	Ministry of Health

Only Indonesia, Malaysia, Philippines, and Thailand have an established system for the registration of antimicrobials employed in animal husbandry (Table 2). Unlike its regulatory agency for human use, Indonesia handles the veterinary products under the Directorate General of Livestock and Animal Health Services, Ministry of Agriculture. The Philippines on the other hand, has the Food and Drug Administration (FDA) in coordination with the Bureau of Animal Industry which is an office under the Department of Agriculture. The agencies controlling the antimicrobials for human and animal use are the same in Malaysia and Thailand. Singapore requires the registration of all products intended for human use regardless if these are subsequently used for veterinary purposes. While Cambodia and Myanmar were not able to determine the existence of the organization

responsible of regulating antimicrobials for veterinary use, Lao PDR and Viet Nam did not state whether they have such an agency.

Table 2. List of organizations responsible for the regulation of antimicrobials for veterinary use

Country	Regulatory Agency
Indonesia	Directorate General of Livestock and Animal Health Services, Ministry of Agriculture
Malaysia	National Pharmaceutical Regulatory Agency
Philippines	Food and Drug Administration and Bureau of Animal Industry, Department of Agriculture
Thailand	Food and Drug Administration, Ministry of Public Health

Licensing of Pharmaceutical Companies

All AMSs except Viet Nam has given feedback on the processes involving the licensing of pharmaceutical companies in their respective nations. The authority that licenses importers, manufacturers and wholesalers of drug products for human use are identified below (Table 3).

Table 3. List of authorities that licenses drug establishments in the human health sector

Country	Regulatory Agency
Brunei Darussalam	Brunei Darussalam Medicines Control Authority facilitated by the Department of Pharmaceutical Services, Ministry of Health
Cambodia	Department of Drug and Food
Indonesia	Indonesia Agency Drug and Food Control
Lao PDR	Food and Drug Department
Malaysia	National Pharmaceutical Regulatory Agency; Pharmacy Enforcement Division, Ministry of Health
Myanmar	Food and Drug Administration
Philippines	Food and Drug Administration
Singapore	Health Sciences Authority
Thailand	Food and Drug Administration, Ministry of Public Health
Viet Nam	Ministry of Health; Provincial Department of Health

As regards the counterpart agencies for the animal industry, six (6) AMSs have identified their respective licensing authorities for veterinary drug importers, manufacturers and

wholesalers (Table 4). The regulation of veterinary drug establishments in Indonesia is handled by the Ministry of Agriculture while in Brunei Darussalam and Malaysia, the same organizations govern the licensing of drug establishments in both human and animal health sectors. The Animal and Veterinary Service of the National Parks Board, Singapore, plans to regulate veterinary drug importers and wholesalers through licensing in the future.

Table 4. List of authorities that licenses drug establishments in the veterinary sector

Country	Regulatory Agency
Brunei Darussalam	Department of Pharmaceutical Services, Ministry of Health
Indonesia	Directorate General of Livestock and Animal Health Services, Ministry of Agriculture
Malaysia	National Pharmaceutical Regulatory Agency; Pharmacy Enforcement Division, Ministry of Health
Philippines	Food and Drug Administration and Bureau of Animal Industry, Department of Agriculture
Singapore	National Parks Board/Animal and Veterinary Service, Ministry of National Development
Thailand	Food and Drug Administration, Ministry of Public Health

Brunei Darussalam, Indonesia, Lao PDR, Malaysia, Myanmar, Philippines, Singapore and Thailand responded that they have a system in place to monitor counterfeit products. In Indonesia, the National Food Agency and Drug Control is the authority monitoring counterfeit medicines. Of the eight AMSSs, only Lao PDR, Myanmar and Philippines have recorded incidence of counterfeit antimicrobial products in the market. There have been cases of fake amoxicillin and gentamicin in the Philippines. Lao PDR and Myanmar on the other hand did not specify the counterfeit antimicrobials involved.

Legislations and Guidelines for Sale of Antimicrobials (Human Use)

Eight (8) out of the ten ASEAN Member States have existing legislation that requires antimicrobials to be supplied only on a prescription. These are Brunei Darussalam, Indonesia, Lao PDR, Malaysia, Myanmar, Philippines, Singapore and Viet Nam, all of which enforces the legislation within the country except for Viet Nam. Indonesia has a drug classification system in place to increase the safety, accuracy as well as secured distribution of drugs. Based on Pharmaceutical Control and Law of Prescription's Drug (State No. 419, 22 December 1949), antimicrobials are categorized as "Gevaarlijk" in Indonesia, which means that its use is dangerous if not based on a doctor's prescription. In Thailand, antimicrobials are listed under two classes: prescription drugs and pharmacist-dispensed drugs. The antimicrobial classification is made by the FDA with an advisory from the National Drug Committee under the Drug Act. Myanmar, though is having an existing legislation, acknowledged that their country has a weak implementation of the policy.

Even though there were policies in place to prevent dispensing of antimicrobials without prescription, Lao PDR, Philippines and Viet Nam admitted that the practice is rampant in their country. In the Philippines, some antimicrobials can be bought without prescription in community pharmacies and night market; however, stringent measures by the FDA lessen the selling of antimicrobials without prescription. Viet Nam and Myanmar also confirmed that antimicrobials are being sold without prescription in community pharmacies and night market, and sometimes in medical halls. Indonesia, on the other hand, have a mandatory list wherein antimicrobials listed can be provided by pharmacists without a prescription based on their competency and scientific judgement.

Lao PDR, Malaysia, Myanmar, Philippines, Singapore and Thailand are among those countries wherein legal sale and supply of antimicrobials by authorized dispenser or pharmacist or dispensing doctor require recording as stated by the law. The responsible agencies that perform the enforcement of the law were summarized in Table 5.

Table 5. Responsible agencies per country that ensure the enforcement of the law related to the recording of the legal sale and supply of antimicrobials

Country	Responsible Agency
Lao PDR	Food and Drug Department Bureau of Food and Drug Inspection
Malaysia	Pharmacy Enforcement Division, MOH
Myanmar	Food and Drug Administration (FDA)
Philippines	Food and Drug Administration
Singapore	Health Sciences Authority
Thailand	FDA in collaboration with the Provincial Health Offices
Indonesia	Director General for Directorate General of Pharmaceutical and Medical Devices, Ministry of Health is the responsible agency that regulates pharmaceutical wholesalers only

However, antimicrobials cannot be bought via internet in the following countries: Cambodia, Indonesia, Lao PDR, Malaysia, Myanmar, Philippines, Singapore and Thailand. Thailand, under the Drug Act 1967 and its amendments, prohibits the sale of antimicrobials and other drugs via the internet.

Standard Treatment Guidelines and National Antibiotic Guidelines

There are available Standard Treatment Guidelines (STGs) related to infectious diseases in almost all AMS except for Cambodia. Tuberculosis, HIV/AIDS, imipenem-sensitive *Pseudomonas aeruginosa* (ISPA), malaria, dengue fever, leprosy, frambusia and filaria are the infectious diseases being monitored in Indonesia. In Thailand, within the last five years, the national STGs on infectious diseases such as tuberculosis, HIV/AIDS, malaria, dengue, hepatitis, ebola, zika, MERs-CoV, Avian influenza and some other infectious diseases

were developed. Lao PDR, Malaysia and Myanmar have monitoring process in place on adherence to STGs, such as through the Drug Therapeutics Committee in health facilities of Lao PDR, Infection and Prevention Control Audit in Malaysia and specific medical societies and programs in Myanmar. Philippines, Cambodia, Brunei Darussalam and Viet Nam have no mechanism of monitoring for STGs.

Table 6 summarizes the AMS with National Antibiotic Guidelines, its current edition, frequency of updates and monitoring.

Table 6. AMS with National Antibiotic Guidelines

Country	Current Edition	Frequency of Updates	Remarks
Brunei Darussalam	N/A	N/A	There is a national hospital antibiotic guidelines for public hospitals and antibiotic guidelines published in 2016 for a specific private hospital.
Cambodia	N/A	N/A	No antibiotic guidelines implemented at the national level.
Indonesia	2016	Annually	Directorate of Pharmaceutical Services has been conducting Monitoring and Evaluation on the use/implementation of the National Formulary in health care facilities since 2016. In Indonesia, there is also Ministerial Decree No. 2406/2016 about General Guidelines of Antibiotics Usage.
Lao PDR	N/A	N/A	No antibiotic guidelines implemented at the national level. Only the presence of standard treatment guidelines which were updated less than 5 years ago. It is one of the indicators in the Rational Use of Drugs.
Malaysia	2014	<5 years	Antibiotic Point Prevalence Survey started in 2015 for compliance monitoring.
Myanmar	N/A	N/A	No antibiotic guidelines implemented at the national level. Guidelines from specific medical societies are available which are updated through regular Continuous Medical Education (CME).
Philippines	2017	N/A	The National Antibiotic Guideline is being implemented in both public and private hospitals, covering major infectious diseases in the country. *Antibiotic Point Prevalence Survey using the WHO tool was conducted in 2018.

Country	Current Edition	Frequency of Updates	Remarks
Singapore	N/A	N/A	No antibiotic guidelines implemented at the national level.
Thailand	Not specified	N/A	There are some antibiotic guidelines implemented at the national level. The rates of antibiotic prescriptions of upper respiratory infections and acute diarrhoea are monitored at the national level.
Viet Nam	2015	<3 years	Still on the process of developing a monitoring scheme to ensure compliance to the guidelines.

National Formulary

The presence of a national formulary at the different health care levels is presented in Table 7. Seven (7) AMS, namely Brunei Darussalam, Indonesia, Lao PDR, Malaysia, Philippines, Singapore, and Thailand, have a mechanism to control formulary listing of new antimicrobial agents.

Table 7. Presence of a formulary at different levels of care

	Primary	Secondary and Tertiary
Public	Brunei Darussalam, Indonesia, Lao PDR, Malaysia, Myanmar, Philippines, Singapore, Thailand	Brunei Darussalam, Indonesia, Lao PDR, Malaysia, Myanmar, Philippines, Singapore, Thailand, Viet Nam
Private	Indonesia, Philippines, Thailand	Indonesia, Philippines, Thailand

At the public sector in Brunei Darussalam, new antibiotics are listed after evaluation by the Drug and Therapeutics Committee and endorsed for listing into Standard List by Drug Advisory Committee. In Indonesia, new antimicrobial agents shall be deliberated within the National Committee of National Formulary, Ministry of Health and then listed as addendum. The Formulary of Lao PDR is based on the Essential Medicines List. Malaysia, on the other hand, has a Ministry of Health Drug Formulary Review Committee. The Philippines has the Formulary Executive Council (FEC) guiding the Department of Health in listing essential drugs including vaccines and antibiotics in the national formulary. Singapore also has a national committee which evaluates the cost effectiveness of the drug before listing it into the standard drug list for public healthcare institutions. Lastly, in Thailand, all new medicines including new antimicrobials need to be monitored under the Safety Monitoring Program for their safety profile. The Subcommittee of National List of Essential Medicines (NLEM) will review if the medicines are to be listed in the NLEM and the Thai National Formulary serves as a guideline on appropriate use of the medicines listed in NLEM. Myanmar is yet to develop their National Committee.

Distribution of Antimicrobial Samples

Policies are implemented to control the distribution and use of sample antimicrobial products in Brunei Darussalam, Malaysia, Philippines, Singapore and Thailand. Samples are not allowed in Brunei Darussalam. Malaysia and Singapore have their own directives towards the public sector only. In the Philippines, the distribution of antibiotic samples to patients and physicians are not allowed in both public and private healthcare facilities in accordance with the *Implementing Guidelines on the Promotion and Marketing of Prescription Pharmaceutical Products and Medical Devices*. In Thailand, the National Committee on Pharmaceutical System Development issued the National Code of Conduct for Ethical Pharmaceutical Promotion that covers all types of medicines including antimicrobials. The guideline recommends that there should be management mechanisms to manage and distribute any samples in every health facility.

Direct interaction of representatives from the pharmaceutical companies and healthcare professionals are being monitored in Indonesia, Malaysia, Philippines and Thailand. In Brunei Darussalam, there is no formal policy but there are directives or reminders to all professionals regarding their responsibilities when meeting with pharmaceutical representatives.

Legislations and Guidelines for Sale of Antimicrobials (Animal Use)

Table 8 summarizes the availability of policies on the use and supply of antimicrobials in the veterinary sector of each AMS.

In Brunei Darussalam, these antimicrobial groups are prohibited to be used in livestock animals: chloramphenicol, nitrofurantoin compound (e.g. nitrofurazone), nitroimidazole compound (e.g. metronidazole), fluoroquinolones and glycopeptide.

Indonesia has been implementing Law No. 18/2009 Husbandry and Animal Health for the prohibition for sale of antimicrobials as growth promoters and its restrictions for use. According to Indonesia, the direct supply of antimicrobial agents from importers/manufacturers/wholesalers to farmers is not allowed without the intervention of a veterinary doctor; however, it happens in practice.

Registration Guideline of Veterinary Products (REGOVP) regulates the registration of antimicrobials and other veterinary drugs for treatment of animals in Malaysia. The guidelines are primarily drawn up in accordance to the legal requirements of the Sale of Drugs Act 1952 and the Control of Drugs and Cosmetics Regulations 1984.

The Philippines has no written policy in the prohibition of use of antimicrobials as growth promoters in animals but there are Administrative Orders issued prohibiting the use of chloramphenicol, furazolidone and carbadox in food animals.

Singapore prohibits the use of antimicrobials for growth promotion in food-producing animals through Directives issued under the Animals and Birds (Licensing of Farm) Rules.

Furthermore, an import permit is required for import of animal feed. The feed must not contain prohibited substances or any materials/mixtures which the composition and content is unknown. Certain medically important antimicrobials are not allowed for use in food-producing animals to preserve their effectiveness for human medicine, and there are maximum permitted residue levels for drugs.

In 2005, Thailand FDA disallowed antimicrobials to be registered under the growth promoter indication. In 2006, the use of antimicrobials as growth promoters was banned in poultry by the Ministry of Agriculture and Cooperatives (MOAC). Then, in 2015, MOAC issued a regulation to prohibit all antimicrobials to be used as growth promoters. The treatment of animal disease and use of veterinary drugs including antimicrobial on farm shall be under supervision of veterinarian. The veterinarian shall practice according to the Veterinary Profession Act B.E. 2545 (2002) and its amendments and the requirement of TAS 9023 of Thai Agricultural Standard on Good Practices for Control of the Use of Veterinary Drugs that is certified by the Department of Livestock Development (DLD). Importation of feeds and premixes containing antimicrobials is regulated by DLD and FDA, respectively. Also the Animal Feed Quality Control Act 2015 prohibits the use of the following antimicrobials in animal feeds: nitrofurans, nitroimidazoles, chloramphenicol, avoparcin, carbadox and olaquinox. In 2018, MOAC issued a regulation to control medicated feed under the Animal Feed Quality Control Act 2015.

Table 8. Summary of the availability of policies on the use and supply of antimicrobials in the veterinary sector

Country	BRN	KHM	IDN	LAO	MYS	MMR	PHL	SGP	THA	VNM
Prohibition for sale of antimicrobials as growth promoters	Y	UNK	Y	UNK	N	UNK	Y	N	Y	Y
Prescription-only provision of antimicrobial treatment	Y	UNK	Y	UNK	Y	UNK	Y	N	Y	UNK
Importation of feeds with antimicrobials without license	N	UNK	N	UNK	N	UNK	N	N	N	UNK
Direct Supply of antimicrobial agents from importers/manufacturers/wholesalers to farmers without the intervention of a veterinary doctor	N	UNK	N	UNK	N	UNK	N	N	N	UNK
Antimicrobial restrictions	Y	UNK	Y	UNK	Y	UNK	Y	Y	Y	UNK
Monitoring of Sales of antimicrobials:										
Food animals	Y	UNK	N	UNK	Y	UNK	N	Y	Y	N
Companion/Pet Animals?	N	UNK	N	UNK	Y	UNK	N	Y	N	N

*Y- Yes; N- No; UNK- Unknown or No answer.

Brunei Darussalam, Singapore, Malaysia and Thailand monitor the sales of antimicrobials in food animals. Only Malaysia and Singapore monitor the sales of antimicrobials in companion animals. The Division of Livestock and Veterinary Services and Department of Agriculture and Agrifood in Brunei Darussalam, Pharmaceutical Services Division, MOH in Malaysia and the Department of Livestock Development in Thailand are the agencies authorized to monitor the sales of antimicrobials in food and companion animals.

All the AMS were asked if data for national sales of veterinary antimicrobial be collected. Brunei Darussalam, Philippines, Singapore and Thailand, all were optimistic in collecting the national data. Brunei Darussalam can collect data based on the importation data of the country. Thailand can collect both production and importation data of veterinary medicines. In Philippines, however, a written policy or guideline must be issued on this matter but compliance from concerned drug companies may take time. In Singapore, sales of veterinary antimicrobials are collated as part of an annual World Organisation for Animal Health (OIE) survey, which can be segregated by food animals or companion animals.

Legislations and Guidelines for Sale of Antimicrobials (Human and Animal Use)

The marketing of antimicrobial products been regulated for human and animal husbandry in Indonesia, Malaysia, Brunei Darussalam, Philippines and Thailand. In Indonesia, there is a regulation that all prescription drugs must not be advertised which was stated on the Pharmaceutical Control and Law of Prescription's Drug (State No. 419, 22 December 1949).

There is also a mechanism for inter-sectoral coordination and harmonization of regulatory policies on the use of antimicrobials between the human health and animal health sectors in the following countries: Brunei Darussalam, Indonesia, Malaysia, Myanmar, Philippines, Singapore and Thailand.

The agencies that are responsible for this coordination are the Department of Pharmaceutical Services, Ministry of Health, together with the Division of Livestock and Veterinary Services, Department of Agriculture and Agrifood in Brunei Darussalam; Indonesia's Ministry of Health and Ministry of Agriculture; National Antimicrobial Resistance Committee (NARC) composed of Ministry of Health and Ministry of Agriculture and Medical Development Division of Malaysia as the secretariat; Ministry of Health and Sports and the Ministry of Agriculture, Livestock and irrigation in Myanmar; the Philippine Inter-Agency Committee on AMR (ICAMR) composed of the Department of Health, Department of Agriculture, Department of Trade and Industry, Department of Science and Technology and Department of the Interior and Local Government; Ministry of Health, Animal and Veterinary Service of the National Parks Board, Singapore Food Agency, National Environment Agency and PUB, Singapore's national water agency, in Singapore; and the Bureau of Drug Control, Food and Drug Administration, Ministry of Public Health and the Division of Animal Feed and Veterinary Products Control, Department of Livestock Development, Ministry of Agriculture and Cooperatives in Thailand.

Monitoring and Surveillance Activities (Human Use)

Surveillance on Antimicrobial Utilization

Only Brunei Darussalam, Lao PDR, Malaysia, Singapore, Thailand and Viet Nam have a surveillance program on antimicrobial utilization (AMU). In Brunei Darussalam, data are obtained from dispensary records of government health facilities. The same is true in Singapore where national monitoring is done across public hospitals. In Thailand, the National Health Security Office (NHSO) responsible for the Universal Health Coverage monitors the rates of antibiotic prescriptions in hospitals for specific conditions, e.g., upper respiratory infection and acute diarrhea. For antimicrobial consumption at the national level, the Food and Drug Administration (FDA) with relevant partners is developing the Thai Surveillance of Antimicrobial Consumption (Thai-SAC) System, which will monitor national trends on both human and animal antimicrobial consumption. In Malaysia, data on antimicrobial consumption can be obtained from Malaysian Statistics on Medicines (MSOM). The Philippines participated in the WHO global efforts to establish antimicrobial consumption (AMC) surveillance systems and methodology using national sales and procurement data of antibiotics and shall make AMC surveillance routine as part of monitoring drug resistance in the human sector.

Table 9. AMU Surveillance in Humans

Country	Responsible Unit	Level of Monitoring			Frequency
		Local	State/ Regional	National	
Brunei Darussalam	Ministry of Health- Department of Pharmaceutical Services (mainly only usage data compilation by pharmacy)	✓	✓	✓	Annually
Lao PDR	Healthcare Department and Food and Drug Department				-
Malaysia	Ministry of Health- Pharmaceutical Services Division	✓	✓	✓	Annually
Singapore	Ministry of Health- National Antimicrobial Resistance Control Committee			✓	Half-yearly

Country	Responsible Unit	Level of Monitoring			Frequency
		Local	State/ Regional	National	
Thailand	National Health Security Office (NHSO) responsible for the Universal Health Coverage	✓	✓	✓	-
Viet Nam	a. Ministry of Health-Medical Services Administration, National AMR Unit (National Level) b. Provincial Medical Service Department (Local level)	✓		✓	-

Malaysia and Thailand routinely discuss the AMU surveillance data at the local, regional and national levels, while in Singapore these are discussed at the local and national levels. Brunei Darussalam remarked that at the moment, utilization data is only used for procurement purposes by the Pharmacy Services but in the future, there is a plan to link it with antimicrobial resistance data. In Indonesia, although there is no surveillance program, AMU is discussed locally at hospital level. Although the Philippines has yet to establish its system, AMU surveillance data collection and analysis is consistently discussed at the local, regional and national levels.

Surveillance on Antimicrobial Resistance

Six AMS (i.e., Malaysia, Myanmar, Philippines, Singapore, Thailand and Viet Nam) have antimicrobial resistance (AMR) surveillance program (Table 10).

Table 10. AMR Surveillance in Humans

Country	Responsible Unit	Level of Monitoring			Frequency
		Local	State/ Regional	National	
Malaysia	Institute of Medical Research	✓	✓	✓	Annually
Philippines	Antimicrobial Resistance Surveillance Program (ARSP) of the Research Institute for Tropical Medicines (RITM)			✓	-

Country	Responsible Unit	Level of Monitoring			Frequency
		Local	State/ Regional	National	
Singapore	Ministry of Health- National Antimicrobial Resistance Control Committee	✓		✓	Half-yearly
Thailand	National Antimicrobial Resistance Surveillance, Thailand (NARST) ¹ , Department of Medical Sciences (DMSc), Ministry of Public Health	✓	✓	✓	Quarterly
Viet Nam	a. Ministry of Health- Medical Services Administration, National AMR Unit (national Level) b. 16 hospitals and all general hospital in the provinces (regional and local levels)	✓	✓	✓	-

Among the six AMSs, Malaysia, Myanmar, Philippines and Thailand discuss the AMR surveillance data at all three levels, while Singapore conducts the discussion at local and national levels. In Thailand, the AMR surveillance data at all levels are publicly available on the NARST website and are usually used during policy discussion.

In terms of information dissemination on emerging patterns of AMR, only Myanmar issues public health alerts at the national level through health education, media talks and symposium.

On the other hand, to control the usage of antimicrobials following the emergence of AMR, Myanmar follows the medical society guidelines while Singapore implements the Antibiotic Stewardship Program in public hospitals. The Philippines has likewise started to train all Level 3 hospitals in the development of an antimicrobial stewardship program in their own facilities, which shall also be conducted in 2018 among Levels 1 and 2 hospitals, as well as primary healthcare facilities.

¹ NARST also serves as a WHO Collaborating Center for AMR Surveillance and Training at the Southeast Asian Region, and it is also part of the Global Antimicrobial Surveillance System (GLASS).

Antimicrobial Stewardship Program

Seven out of the 10 AMS (Brunei Darussalam, Indonesia, Malaysia, Philippines, Singapore, Thailand and Viet Nam) have restriction policy for the prescribing and use of antimicrobials in health facilities. Majority use their national formulary/national standard drug list/essential medicines list as basis to restrict the use of antimicrobials. In Thailand, antimicrobials classified as Class D in the EML are subject to close monitoring for their usage. Table 11 lists the antimicrobials with high level of restriction at the different levels of healthcare in Brunei Darussalam, Malaysia, Philippines, Singapore and Thailand.

Table 11. Antimicrobials with high level of restriction at different levels of healthcare

Country	Antimicrobials with High Level of Restriction	
	Primary Care	Secondary and Tertiary Care
Brunei Darussalam	Depending on the class of antimicrobials; some of these are restricted to be used by specialist/consultant only.	Depending on the class of antimicrobials; some of these are restricted to be used by specialist/consultant only.
Malaysia	Co-amoxiclav, Cefuroxime (in government sector only started in 2015 & annually monitoring).	Polymyxins, Carbapenems
Philippines	IV antifungals (all except fluconazole), aztreonam, carbapenems (all), fourth generation cephalosporins (all), colistin, linezolid, vancomycin.	IV antifungals (all except fluconazole), aztreonam, carbapenems (all), fourth generation cephalosporins (all), colistin, linezolid, vancomycin.
Singapore	-	Carbapenems, polymyxins, linezolid, moxifloxacin.
Thailand	-	Broad-spectrum antimicrobials especially third/fourth generations of cephalosporin, cabapenems and colistin.

Indonesia, Malaysia, Philippines, Singapore, Thailand and Viet Nam said that antimicrobial stewardship program is in place in their country. Indonesia and Philippines practice antimicrobial stewardship in public and private secondary and tertiary healthcare facilities. Malaysia and Thailand implement the antimicrobial stewardship program in all public healthcare facilities, i.e., primary to tertiary healthcare. In Singapore, antimicrobial stewardship is only applied in secondary and tertiary public healthcare facilities, while in Viet Nam, it is practiced in both public and private healthcare facilities.

Monitoring and Surveillance Activities (Animal Use)

Residual Antimicrobial

Six AMS (Brunei Darussalam, Indonesia, Malaysia, Philippines, Singapore and Thailand) reported that they monitor residual antimicrobial levels in food stock, in particular they all test the antimicrobial levels in meat. No country, however, tests antimicrobial levels on specimens obtained from animals before slaughter.

Antimicrobial Use

None of the AMS has a surveillance program to monitor the use of antimicrobials in animals. In Indonesia, the guidelines were already drafted in 2016 and a pilot project was started in the early part of 2017. Singapore has a national program to ensure that poultry and coastal fish farms keep a record of antibiotic usage for farms accredited under schemes akin to Good Animal Husbandry Practices. In Thailand, the current program is in the development process under the Thai-SAC system.

Antimicrobial Resistance

Indonesia, Malaysia, Thailand and Singapore have a surveillance program in place to monitor the resistance of antimicrobials in animals (Table 12). In the Philippines, the Animal Disease Diagnosis and Reference Laboratory and Animal Health Division of the Bureau of Animal Industry together with the National Meat Inspection Service is doing a pilot surveillance in Regions III and IV-A. In Thailand, the Department of Livestock Development's laboratory network is responsible for monitoring AMR surveillance in food animals. Singapore, through the Singapore Food Agency and the Animal and Veterinary Service of the National Parks Board, has a surveillance program to monitor resistance in food products of animal origin and clinical samples from food animals.

Table 12. AMR Surveillance in Animals

Country	Responsible Unit	Level of Monitoring			Frequency
		Local	State/ Regional	National	
Indonesia	Veterinary Regional Lab and National Quality Control Laboratorium and Certification for animal product			✓	-
Malaysia	Department of Veterinary Services	✓			Specific time

Country	Responsible Unit	Level of Monitoring			Frequency
		Local	State/ Regional	National	
Singapore	Singapore Food Agency and the Animal and Veterinary Service of the National Parks Board			✓	Routine
Thailand	Department of Livestock Development (DLD laboratory network among central and regional laboratories)			✓	

DISCUSSIONS AND CONCLUSIONS

There is now ample evidence on the scenario of existing regulatory measures among the AMS in combating antimicrobial resistance. Overall, most of AMS have established system to control use and sale of antimicrobials for human use compared to animal husbandry.

Human Use

All of antimicrobial products were registered before taking into the market and pharmaceutical companies were licensed in order to import, manufacture and sale antimicrobial for human use. Although there is a system in place to monitor counterfeit product, there is still incidence of counterfeit antimicrobial products in the market in some countries.

Legislation that requires antimicrobials to be supplied only on a prescription are being enforced in almost all AMS countries but antimicrobial products being sold without prescription is still rampant whereby it can be found at community pharmacy, drug store, night market and also medical halls. In half of AMS countries, recording of sale and supply of antimicrobials by dispenser or pharmacist or dispensing doctor is not stated in the law. Laws must be tightened up to ensure that sale of antimicrobials is adequately controlled.

Almost all countries reported the absence of a guideline for the prescribing of antimicrobials at national level but availability of Standard Treatment Guidelines (STG) for infectious diseases is seen sufficient to guide the prescribers to prescribe antimicrobials rationally. Other than STG, drug formulary is also available in most public hospital and primary care facilities. Any antimicrobial guideline available should be adopted by facilities in both public and private facilities to standardize prescribing practice in these sectors.

Half of AMS have a policy to control the distribution and use of antimicrobial sample in facilities as well as the direct interaction of representative from pharmaceutical companies and healthcare professionals. This practice need to be well-controlled in order to support the responsible use of antimicrobial and to pro-long their effectiveness.

Established surveillance program to monitor antimicrobial resistance and antimicrobial utilization can be seen in most AMS but antimicrobial use data was not discussed routinely as compared to antimicrobial resistance data. Data from these two surveillances are important to provide situational analysis of antimicrobial resistance and utilization so that necessary intervention at national level could be implemented. Emergence of antimicrobial resistance detected by AMR surveillance should trigger issuance of public health alerts. However, almost all AMS do not issue public health alerts at the national level and no protocol applied to control antimicrobial usage.

Antimicrobial Stewardship program has been recognized as an effective program to promote prudent use of antimicrobials and is in place and practiced by public facilities in most AMS. This program should be expanded to all facilities including those in the private sector.

Animal Use

Some countries allow the incorporation of some antimicrobials into animal feed as growth promoter or for other non-therapeutic purposes. This can be seen also in most AMS which do not prohibit the use of antimicrobial agents as growth promoter.

Legislation on supply of antimicrobial for animal treatment only by prescription from veterinarian should be enforced to control and ensure the judicious use in animal. Currently, less than half of AMS have that provision in their law.

More than half AMS restricted antimicrobial use in veterinary sector. Among these countries, not all impose the restriction in their law, some of them only indicate in guideline, administrative order and policy.

Surveillance system of AMR and AMC in animal is still lacking and need to be strengthened. For example, majority of AMS do not monitor AMR in animal and no AMS has a surveillance program to monitor the use of antimicrobials in animal. National data on the sale of veterinary antimicrobials is also limited due to lack of monitoring on sale of antimicrobials in food animals and also companion or pet animals. Furthermore, most AMS monitor the residual antimicrobial levels in food stock by testing antimicrobial levels in meat only but none of the AMS test antimicrobial level on specimen obtained from animal before slaughtered.

Human and Animal Use

In response to One Health approach, AMR activities in most AMS involve an inter- sectoral coordination and harmonization regulatory policies on the use of antimicrobial between human health and animal health.

Further discussion is needed at ASEAN level to formulate strategies such as standardizing practices and promote better regulation on the use and sale of antimicrobials toward reducing the risk of AMR.



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