Thailand's First One Health Report

on Antimicrobial Consumption and Antimicrobial Resistance in 2017

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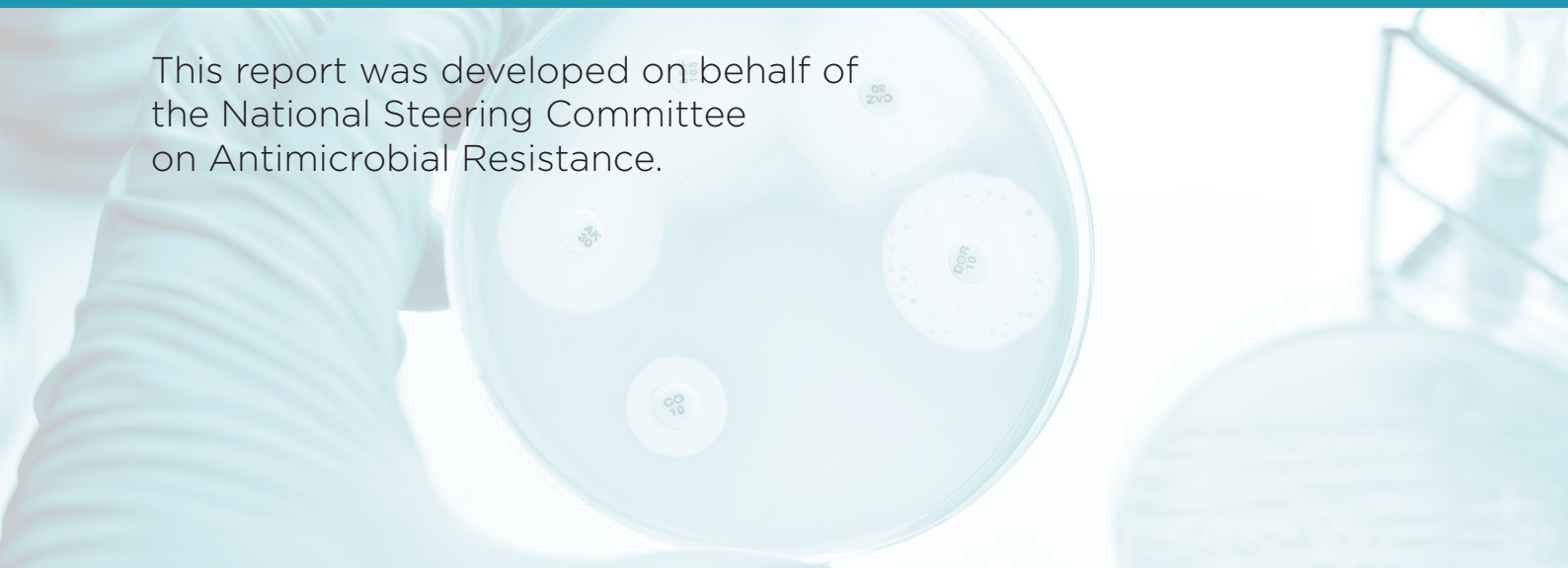
This report was developed on behalf of
the National Steering Committee
on Antimicrobial Resistance.



Thailand's First One Health Report
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Foreword

On behalf of the National Steering Committee on Antimicrobial Resistance, I welcome the publication of Thailand's First One Health Report on Antimicrobial Consumption and Antimicrobial Resistance.

The Committee monitors and oversees the implementation of Thailand's first National Strategic Plan on Antimicrobial Resistance 2017 - 2021 (NSP-AMR), which was endorsed by the Cabinet in August 2016. The development of this report was one of the responses to the strategic objectives of the NSP-AMR. This report was produced through a collaborative process involving professionals working in the human and animal health sectors in Thailand.

The development of this first report is guided by two principles: the 'One Health' approach which recognizes the interconnectivity across human, animal and environmental health; and the 'Triangle that Moves the Mountain' concept which emphasizes the importance of resolving complex intersectoral issues through policy engagement and social movement guided by evidence.

This first report provides baseline data in 2017 for the monitoring of NSP-AMR (2017-2021) goals; which makes the commitment to reduce morbidity attributable to antimicrobial resistance by 50.0%; reduce antimicrobial consumption in the human sector by 20.0% and in the animal sector by 30.0%; and increase the proportion of the population shown to have a predefined basic level of knowledge and awareness of antimicrobial resistance by 20.0%, all by 2021.

We also expect that in future reports, data on consumption in humans and animals will allow for assessment of the relationship between antibiotic consumption and resistance in both sectors.

We thank the members of the Thai working group on Health Policy and Systems Research on Antimicrobial Resistance (HPSR-AMR) and the International Health Policy Program, Ministry of Public Health, Thailand for their contribution to the development of this report, in particular the authors of each chapter.

We fully believe that cross-sectoral cooperation based on the One Health approach can effectively address AMR.

Dr. Paisarn Dunkum
Secretary-General of Food and Drug Administration
On behalf of the National Steering Committee on Antimicrobial Resistance

Contents

Abbreviations and Acronyms

AI	Active ingredient
ACFS	Agricultural Commodity and Food Standards
AMC	Antimicrobial consumption
AMR	Antimicrobial resistance
AMU	Antimicrobial use
API	Active pharmaceutical ingredient
ASP	Antimicrobial Stewardship Programs
AST	Antimicrobial susceptibility testing
ATC	Anatomical Therapeutic Chemical
Aw	Average weight at the time of treatment
BSI	Bloodstream infection
CIA	Critically important antimicrobials
CLSI	Clinical and Laboratory Standards Institute
CRE	Carbapenem-resistant *Enterobacteriaceae*
CRPA	Carbapenem-resistant *P. aeruginosa*
CSF	Cerebrospinal fluid
DDD	Defined Daily Dose
DID	Defined Daily Dose per 1,000 inhabitants per day
DLD	Department of Livestock Development
DOF	Department of Fisheries
EAs	Enumeration areas
ECV	Epidemiological cut-off value
EFSA	European Food Safety Authority
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
ESBLs	Extended-spectrum beta-lactamases
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FAO	Food and Agriculture Organization
FDA	Food and Drug Administration
GI	Gastrointestinal
HPSR-AMR	Health Policy and Systems Research on Antimicrobial Resistance
HWS	Health and Welfare Survey
I	Intermediate
IHPP	International Health Policy Program
IPC	Infection prevention and control
ISO	International Organization for Standardization
JEE	Joint External Evaluation of International Health Regulations (IHR) 2005
Kg	Kilogram
MDR	Multidrug resistance
MIC	Minimum inhibitory concentration
MOPH	Ministry of Public Health
MRCNS	Methicillin-resistant coagulase-negative *Staphylococcus* spp.
MRSA	Methicillin-resistant *Staphylococcus aureus*
NARST	National Antimicrobial Resistance Surveillance Center, Thailand
NWT	Non wild-type

NSO	National Statistical Office
NSP-AMR	National Strategic Plan on Antimicrobial Resistance
OIE	World Organization for Animal Health, or Office International des Epizooties
PCU	Population Correction Unit
PLO	Provincial Livestock office
R	Resistant
S	Susceptible
SAC	Surveillance on Antimicrobial Consumption
SDD	Susceptible-dose dependent
STIs	Sexually Transmitted Infections
UTI	Urinary tract infection
VRE	Vancomycin-resistant *Enterococcus*
WHO	World Health Organization
WT	Wild type

Glossary

Antimicrobial consumption (AMC)

Antimicrobial consumption is the quantity of consumption of antimicrobial drugs, which is measured at the national level as the quantity of its production plus imports minus the quantity of its exports. AMC is expressed as the number of Defined Daily Doses (DDDs) per 1,000 inhabitants per day for human antimicrobials, and milligram per Population Correction Unit, modified by Thailand ($mg/PCU_{Thailand}$) for food-producing animals.

Antimicrobial resistance (AMR)

AMR is the ability of microbes (e.g. bacteria, viruses and fungi) to grow or survive even after exposure to antimicrobial agents at concentrations that are normally sufficient to inhibit or kill that particular strain of organism. In this report, AMR predominantly means AMR in bacteria.

Antituberculous drug

Antituberculous drugs in Thailand Surveillance of Antimicrobial Consumption (Thailand SAC) are drugs used solely for treatment of tuberculosis; however, this may or may not include certain groups of drugs such as macrolides, fluoroquinolones and ansamycins due to their other indications for non-mycobacterial infections.

Antimicrobial agent

Antimicrobial agents have antimicrobial properties or the ability to inhibit growth or metabolic processes in microbes (e.g. bacteria, viruses and fungi). They are obtained from living organisms or through synthesis. In this report, antimicrobial medicines predominantly mean antimicrobial medicines with bactericidal properties, including those with the ability to stop bacterial growth; except in the human antimicrobial consumption chapter in which antimicrobial agent means antibiotics, antituberculous, antimalarial, antivirus and antifungal medicines.

Antibiotics

Antibiotics are antimicrobial medicines with bactericidal properties, (including those with the ability to stop bacterial growth), obtained from living organisms or through synthesis. Examples include penicillin, amoxicillin, tetracycline, norfloxacin and azithromycin. The terms microbicide (microbe killer), antibacterial medicines and antibiotics are used interchangeably.

Bacteria

Bacteria are one of the major groups of microorganisms or microbes, some of which can infect and cause disease in humans and animals. A range of descriptive terms are used. Bacteria cultivated in a laboratory are referred to as isolates, those capable of causing disease are referred to as pathogens (pathogens that are transmissible between animals and humans are zoonotic), and those that are normally resident on or in humans or animals without causing disease are referred to as commensals or colonizers.

Critically Important Antimicrobials (CIA)

In this report, Critically Important Antimicrobials refer to the list of CIA for human medicine defined by the World Health Organization [1]. 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.

One Health

A concept promoting a 'whole of society' approach to attain optimal health for people and animals, and healthy environment.

Surveillance

Surveillance means a continuing process of collecting, collating and analyzing data and communicating information to all relevant actors. It involves the generation and timely provision of information that can inform appropriate decision-making and action.

Susceptible

A category defined by a breakpoint that implies that isolates with an minimum inhibitory concentration (MIC) at or below or zone diameters at or above the susceptible breakpoint are inhibited by the usually achievable concentrations of antimicrobial agent when the dosage recommended to treat the site of infection is used, resulting in likely clinical efficacy.

Susceptible-dose dependent (SDD)

A category defined by a breakpoint that implies that susceptibility of an isolate is dependent on the dosing regimen that is used in the patient. In order to achieve levels that are likely to be clinically effective against isolates for which the susceptibility testing results are in the SDD category, it is necessary to use a dosing regimen (i.e., higher doses, more frequent doses, or both) that results in higher drug exposure than the dose that was used to establish the susceptible breakpoint.

Intermediate

A category defined by a breakpoint that includes isolates with minimum inhibitory concentrations (MICs) or zone diameters within the intermediate range that approach usually attainable blood and tissue levels and for which response rates may be lower than for susceptible isolates. The intermediate category implies clinical efficacy in body sites where the drugs are physiologically concentrated or when a higher than normal dosage of a drug can be used.

Resistant

A category defined by a breakpoint that implies that isolates with an minimum inhibitory concentration (MIC) at or above or zone diameters at or below the resistant breakpoint are not inhibited by the usually achievable concentrations of the agent with normal dosage schedules and/or that demonstrate MICs or zone diameters that fall in the range in which specific microbial resistance mechanisms are likely, and clinical efficacy of the agent against the isolate has not been reliably shown in treatment studies.

Non-susceptible

A category used for isolates for which only a susceptible breakpoint is designated because of the absence or rare occurrence of resistant strains. Isolates for which the antimicrobial agent minimum inhibitory concentrations (MICs) are above or zone diameters below the value indicated for the susceptible breakpoint should be reported as non-susceptible.

Summary

This One Health report is Thailand's first cross-sectoral report which combines antimicrobial consumption (AMC) and antimicrobial resistance (AMR) in humans and food-producing animals.

This report provides better understandings of the current situation of AMC and AMR rates in humans and food-producing animals in Thailand, which will contribute to strengthening national policies on optimizing antimicrobial use (AMU) and address AMR. The main findings of the report are presented below.

Antimicrobial consumption

Antimicrobial consumption in humans

(Source: Food and Drug Administration, Ministry of Public Health)

Overall human antimicrobial consumption

Consumption (DDD)	Human population (inhabitants) in 2017	Consumption (DDD/1,000 inhabitants/day; DID)
1,807,944,443	72,438,300	68.4

Consumption of core and optional antimicrobial classes

For the core antimicrobial class, other beta-lactams ranked first, followed by beta-lactams and penicillins and tetracyclines. The top-three core antimicrobials were ceftriaxone, amoxicillin and tetracycline.

Among antimicrobials in the optional class, antivirals intended for systemic infections were consumed most, along with antimycotics used for systemic infections and antituberculous drugs ranked second and third, respectively. The three most-consumed antimicrobials in the group were ketoconazole, efavirenz and lamivudine.

Consumption of Critically Important Antimicrobials (CIA)

More than half of total antibacterial consumption was in the CIA category, and more than half of consumption in the CIA category belonged to the highest priority group as defined by WHO. The top-three most-consumed antimicrobial groups in the CIA category included cephalosporins (3rd, 4th and 5th generations), aminopenicillins and quinolones. According to substance in the highest priority CIA, ceftriaxone was consumed most, followed by norfloxacin and roxithromycin.

Antimicrobial consumption in food-producing animals

(Source: Food and Drug Administration, Ministry of Public Health)

Overall food-producing animal antimicrobial consumption

Consumption (tonne of API)	Animal population in 2017 (kg of $PCU_{Thailand}$)	Consumption (mg/$PCU_{Thailand}$)
3,690.3	6,618,137,577.6	557.6

Of the total national AMC in food-producing animals, antimicrobials for systemic use (QJ01) ranked highest, followed by those indicated for intestinal use. The third- and fourth-ranked antimicrobials were used for intra-mammary and intrauterine use.

Consumption of each antimicrobial class

The most commonly consumed antibiotics were penicillins, mainly comprising of amoxicillin, followed by tetracyclines and other antibacterials including halquinol, bacitracin and bambermycin.

Consumption by dosage form and route of administration

Over half of veterinary antimicrobial consumption was consumed in the form of medicated premix, mainly consisting of halquinol, chlortetracycline and tiamulin. The second- and third-ranked most-consumed dosage forms were oral powder and oral solutions respectively.

More than half of consumption from injectable antimicrobials was from the consumption of three drugs: gentamicin, amoxicillin and oxytetracycline. For intramammary products, the majority of consumption came from cloxacillin and ampicillin.

Consumption of Critically Important Antimicrobials

For the highest priority CIA, macrolides were consumed most, mainly from tilmicosin and tylosin. The second-ranked CIA was colistin, followed by enrofloxacin.

For high priority CIA, aminopenicillins had the highest ranked consumption, with amoxicillin used as the major drug. This was followed by aminoglycosides, mainly from gentamicin and neomycin.

Antimicrobial resistance

Antimicrobial resistance in humans

(Source: Department of Medical Sciences, and Department of Disease Control, Ministry of Public Health)

Gram-negative bacteria

AMR in bacterial isolates from humans has been increasing in Thailand, especially in Gram-negative bacteria. In 2017, there were high numbers of *Acinetobacter calcoaceticus-baumannii* complex, *Pseudomonas aeruginosa* and *Enterobacteriaceae* that were resistant to carbapenems.

Gram-positive bacteria

In 2017, the resistance rate of methicillin-resistant coagulase-negative *Staphylococcus* spp. was higher than methicillin-resistant *Staphylococcus aureus* (MRSA).

In 2017, 8.8% of *Enterococcus faecium* from all specimens were vancomycin-resistant.

In 2017, the rates of penicillin and ceftriaxone resistance in *Streptococcus pneumoniae* from meningitis isolates were higher than those in non-meningitis isolates.

Other antimicrobial resistant bacteria

In 2017, there was an inereasing rate of fluoroquinolone resistance in Non-typhoidal *Salmonella* spp.

In 2017, all of *Neisseria gonorrhoeae* isolates were still susceptible to ceftriaxone and cefixime. One isolate was detected with a high azithromycin Minimum Inhibitory Concentration (MIC) of 2 mg/L.

Antimicrobial resistance in food-producing animals

(Source: Department of Livestock Development, Ministry of Agriculture and Cooperatives)

Salmonella spp. and *Escherichia coli*

In 2017, the most frequent resistance to antimicrobials commonly used in veterinary medicine were found in ampicillin, sulfamethoxazole, tetracycline and trimethoprim.

Campylobacter spp.

There was evidence that all tested antimicrobials including ciprofloxacin, tetracycline, streptomycin, erythromycin and gentamicin that exhibited resistance, had a lower resistance rate in chicken than in pigs.

Enterococcus spp.

Fewer than 5.0% of isolates were resistant to vancomycin, linezolid and teicoplanin as these drugs were not used in the animal sector.

Knowledge and awareness of antibiotic use and antimicrobial resistance

Knowledge and awareness of antibiotic use and antimicrobial resistance

(Source: National Statistical Office, Ministry of Digital Economy and Society)

- An AMU module was integrated into the Health and Welfare Survey in 2017, covering 27,762 Thai adults (age >15 years) who had self-responded to the module.
- About 7.9% of respondents had received antibiotics in the last month. The majority (70.3%) obtained antibiotics from health facilities, both private and public sectors at all levels.
- Flu symptoms were the most common reason (27.0%) people gave for taking antibiotics and were therefore wrongly used.
- A low level of antibiotics literacy among Thai people is reflected in the fact that only 2.6% of Thai adults gave correct answers to all six statements about antibiotics.
- Public information on the proper use of antibiotics and awareness of AMR was poorly available; only 17.8% of Thai adults had received information about proper use of antibiotics and AMR in the last 12 months.
- Almost two-thirds of respondents were not aware that antibiotics are used in food-producing animals.

1 INTRODUCTION

1. Introduction

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1.1 Problems

Antimicrobial resistance (AMR) is one of the greatest health threats of the 21st century and causes approximately 700,000 annual deaths globally [2]. It has been estimated that failure to address AMR today will result in up to 10 million annual deaths and US$ 100 trillion economic losses by 2050. The highest impact will be in Asian and African regions, accounting for 4.7 and 4.2 million deaths, respectively [3].

Lack of effective Infection Prevention and Control (IPC) measures and failure to curb and optimize antimicrobial use (AMU), in particular the reserved group of highest priority Critically Important Antimicrobials (CIA) as defined by the World Health Organization (WHO) [1] in human and animal sectors, are key drivers for the emergence and spread of AMR. Unfortunately, evidence indicates that antimicrobial consumption (AMC) is on the rise worldwide, with a 36.0% increase between 2000 and 2010 [4].

Cephalosporins and broad-spectrum penicillins are the most frequently used antibiotics, representing 55.0% of worldwide consumption. There is also alarming evidence of increased global use of carbapenems and polymyxins, by 45.0% and by 13.0% respectively; these are two last-resort classes of antibiotics to combat highly resistant bacteria [4].

An equally important area is antibiotic use in companion animals, agriculture and aquaculture. Additionally, poor hygienic practices in meat production-supply chains could induce the emergence and spread of resistant bacteria among animals, farm workers, meat products, the environment and consumers. A recent study estimates that global use of antimicrobials in livestock will increase by 67.0% (from 63,000 to 106,000 tonnes) over the next 10 years [5]. While AMU is on the rise and AMR is increasing, the pipeline of effective antimicrobials is running dry. This situation will eventually lead to a post-antibiotic era and a potential catastrophe for modern medicine; a situation where modern medical techniques that rely on the effectiveness of antibiotics such as organ transplantation and chemotherapy, become impossible and surgical operations cannot be performed because of the risk of untreatable infections [6].

In addressing AMR issues, Thailand has various systems, policies and initiatives in place. Although all AMR data in both human and animal sectors exist, they are not systematically combined and fully used to guide clinical management and decisions by veterinarians in the food animal production sector.

Therefore, in this report, we respond to the need for comprehensive information. This is the first Thailand report which combines data on AMC and AMR under the One Health approach. The data in the report will contribute to formulating national antimicrobial policies in order to support and encourage prudent AMU, ultimately resulting in the mitigation of AMR problems.

1.2 National Strategic Plan on Antimicrobial Resistance 2017-2021

The National Strategic Plan on Antimicrobial Resistance (2017-2021) (NSP-AMR) is the first Thai strategy which addresses AMR specifically. It was developed by the AMR Coordination and Integration Committee, which is a multi-sectoral committee under the Public Health Ministerial Order. The Committee is chaired by the Deputy Permanent Secretary and its secretariat consists of representatives from the Ministry of Public Health, the Ministry of Agriculture and Cooperatives, and universities.

The process to develop the NSP-AMR took 16 months (May 2015 - August 2016) and was based on full participation and engagement by multiple stakeholders through a series of public hearings and a National Health Assembly resolution [7]. The Cabinet endorsed the NSP-AMR on 17 August 2016, entrusting the legality of cross-sectoral actions.

The NSP-AMR aims to reduce morbidity, mortality and economic impacts due to AMR. The strategy sets five goals to be achieved by 2021. These are: 50.0% reduction of AMR morbidity; 20.0% reduction of antimicrobial consumption in humans; 30.0% reduction of antimicrobial consumption in animals; 20.0% increase in public knowledge on AMR and awareness of appropriate use of antimicrobials; and improvement of the capacity of the national AMR management system to level 4 as defined by the WHO Joint External Evaluation Tool (JEE) of International Health Regulations 2005 [8]. The details of NSP-AMR are summarized in Box 1.

To achieve these five goals, the NSP-AMR consists of six strategic actions (see Box 1). Strategic actions one to five cover key areas to resolve AMR whereas strategic action six aims to develop governance mechanisms to implement and sustain AMR actions in accordance with the NSP-AMR.

Box 1. Summary of NSP-AMR (2017-2021)

Vision: Reduction of mortality, morbidity and economic impacts from AMR

Mission: Establish policies and national multi-sectoral mechanisms which support an effective and sustained AMR management system

Goals:
1. 50.0% reduction in AMR morbidity
2. 20.0% reduction in antimicrobial consumption in humans
3. 30.0% reduction in antimicrobials consumption in animals
4. 20.0% increase in public knowledge on AMR and awareness of appropriate use of antimicrobials
5. Capacity of the national AMR management system is increased to level 4 as measured by WHO's Joint External Evaluation Tool (JEE) for International Health Regulations (2005)

Strategies:
1. AMR surveillance system using 'One Health' approach
2. Regulation of antimicrobial distribution
3. Infection prevention and control and antimicrobial stewardship in humans
4. AMR prevention and control and antimicrobial stewardship in agriculture and companion animals
5. Public knowledge on AMR and awareness of appropriate use of antimicrobials
6. Governance mechanisms to implement and sustain AMR actions

1.3 Scope report

The report covers:

a) AMC in humans and food-producing animals;
b) AMR in humans and food-producing animals; and
c) Public knowledge on AMU and AMR.

The scope of antimicrobials for human consumption includes antivirals, antifungals, antiprotozoals, antimalarials and drugs for treatment of tuberculosis according to WHO recommendations. We also apply the World Organization for Animal Health (OIE) recommendation on the scope of AMC in food-producing animals for monitoring purposes.

1.4 One Health Surveillance Information

In Thailand, data on AMC and AMR from the human and animal sectors are jointly collated at the national level. Data are assembled from various channels and there is currently no central depository for inter-sectoral data.

AMC data in humans and animals

As shown in Figure 1, pharmaceutical operators, who are mandated by law to report volumes of import and local production, need to login to PROLOG SYSTEM and prepare an annual report to submit to the Food Drug Administration (FDA) by March 31 of the following year. Then, a responsible and authorized pharmacist of the pharmaceutical company submits the report to the Thai FDA via a web portal. After FDA officers have reviewed the report based on its completeness and identification of any irregularities, the result is fed back to the pharmaceutical company to notify it of further actions needed before final acceptance by the FDA. If there are no comments for corrections or amendments, the report will be accepted by the FDA without amendments. If some errors need to be rectified, the report will be cancelled and the pharmaceutical operator has to re-submit the revised annual report within a specified period of time. Failure to do so will result in legal sanction by the FDA.

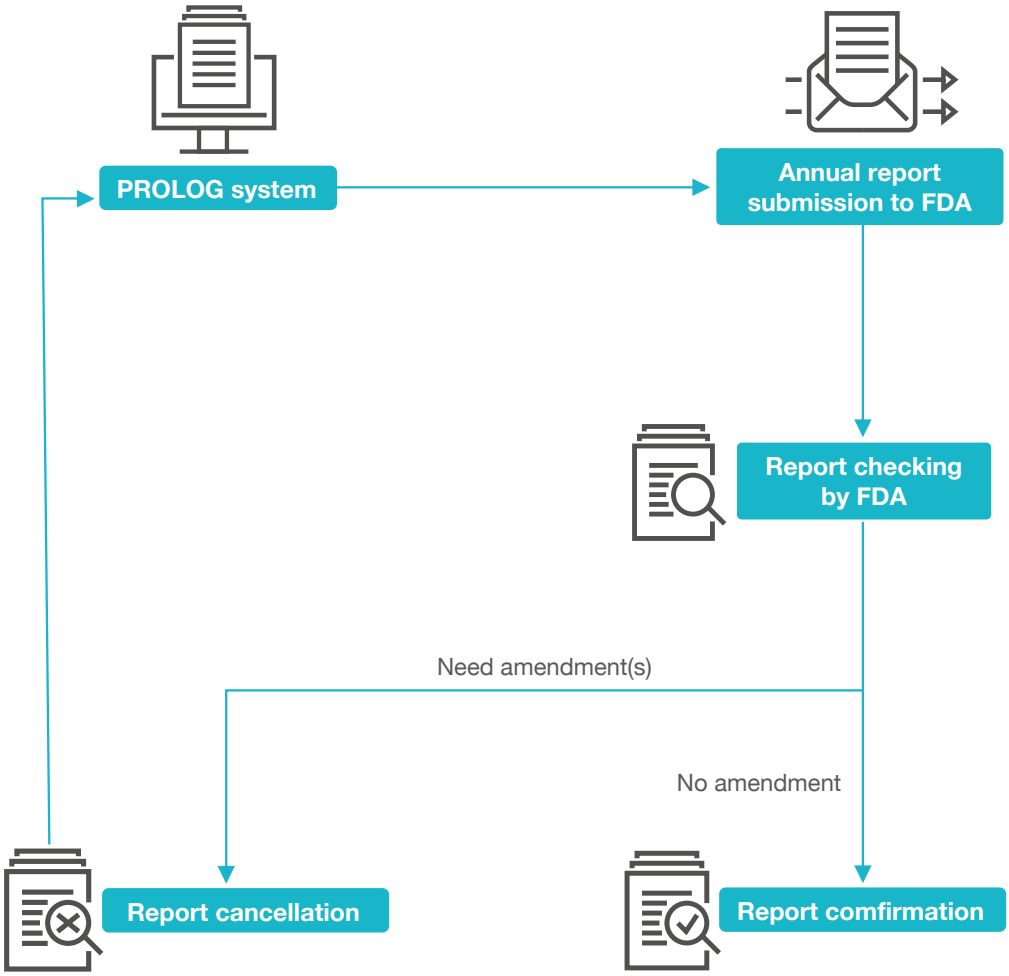

Figure 1. Source and Flow of Information on Consumption

AMR data in humans

Laboratory-based human AMR data were submitted by participating public and private hospitals nationwide to the National Antimicrobial Resistance Surveillance Center, Thailand (NARST), National Institute of Health, Department of Medical Sciences, The Ministry of Public Health, Thailand. The NARST was established in 1998 and was designated as a WHO Collaborating Center in 2005.

Hospitals in the NARST system have limited numbers of patients with gonococcal infection as they either sought care from specialized Sexually Transmitted Infections (STIs) centers or healthcare facilities in private sector. The data on gonococcal AMR in this report were collected from Bangrak STIs center, Silom Community Clinic @TropMed and three other Regional Office of Disease Prevention and Control under the Department of Disease Control, Ministry of Public Health, Thailand.

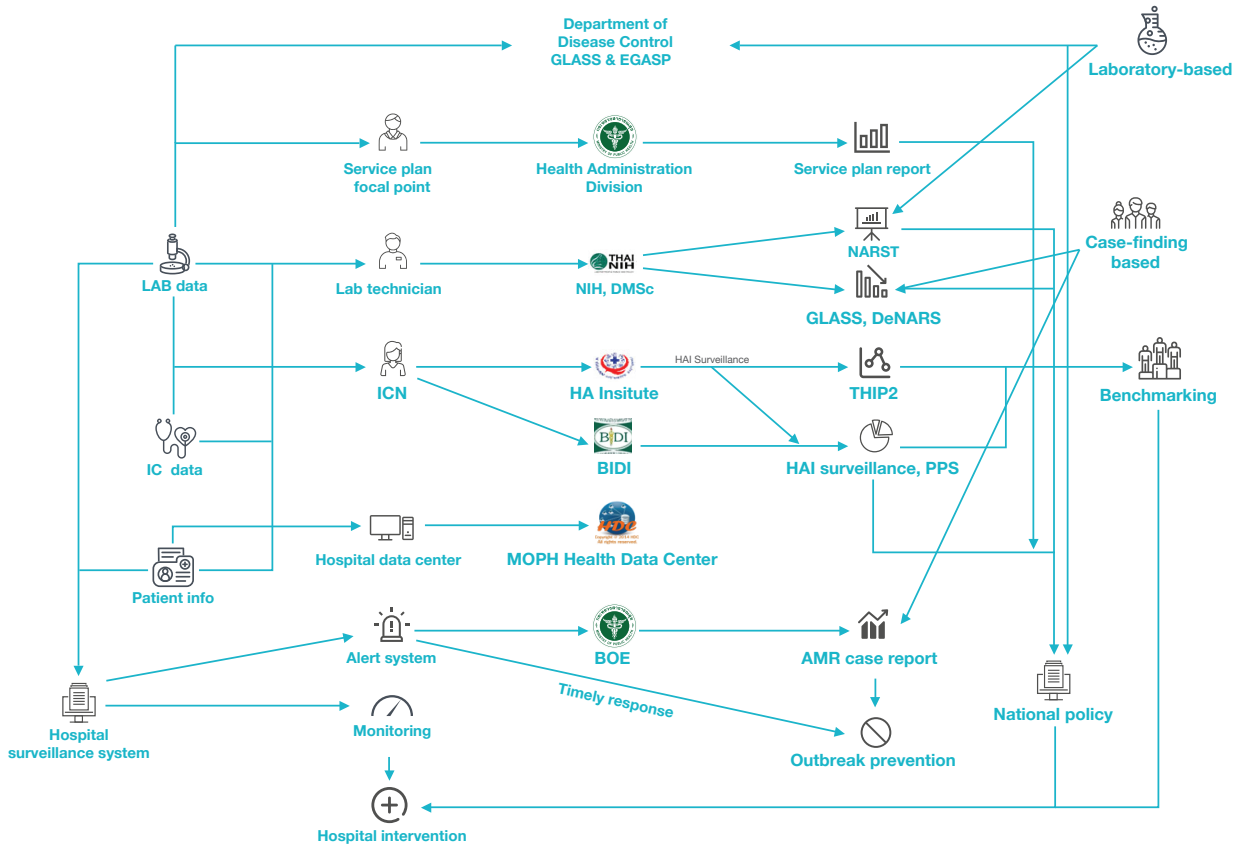

Figure 2. Sources and flow of information on AMR in humans

AMR data in food-producing animals

The national surveillance of AMR in food-producing animals has been conducted in broiler chicken and pigs as the majority of the livestock production in Thailand. This surveillance was conducted across the food-chain from slaughterhouse (cecum and meat) to retail products (meat). After the samples were obtained from all over the country in 2017, they were transported to the Department of Livestock Development (DLD) laboratories. The target bacteria of AMR surveillance included zoonotic bacteria (*Salmonella* spp. and *Campylobater* spp.) and indicator bacteria (*Enterococcus* spp. and *Escherichia coli*). Antimicrobial susceptibility testing (AST) was performed based on the Clinical and Laboratory Standards Institute (CLSI), ISO 20776-1, and the European Committee on Antimicrobial Susceptibility Testing (EUCAST). The tested antimicrobials were as follows: Polymyxins (colistin), Fluoroquinolones (ciprofloxacin), 3rd Cephalosporins (cefotaxime and ceftazidime), Carbapenems (meropenem) and other antibiotic groups used in livestock.

Public knowledge on antibiotic use and AMR

The special module on knowledge and antibiotic use by the general public was designed by IHPP and integrated into the biennial national Health and Welfare Survey (HWS), conducted by the National Statistical Office (NSO) [9]. The survey module applies a structured interview questionnaire to assess the one-month prevalence of antibiotic use, knowledge and sources of information about antibiotics. The survey was conducted by the NSO in March 2017.

1.5 Populations

Human and animal populations

The numbers of humans and animals have been collected and verified by various relevant stakeholders to ensure the accuracy as national estimates. On the basis of populations which are potentially exposed to antimicrobials, the figure of each particular population was used as a denominator to calculate the amount of national AMC.

1.5.1 Human population

The mid-year population in Thailand including both Thai citizens and migrants was estimated to be approximately 72,438,300 (Table 1).

Table 1. Human population

	Male	Female	Total
Citizen	33,664,899	35,372,614	69,037,513
Migrant	3,400,787		3,400,787
Total			**72,438,300**

*World Bank, World Development Indicator 2017 [10]

1.5.2 Animal population

1.5.2.1 Food-producing animal population

The number of food-producing animals was collected and verified with cooperation between the Department of Livestock Development (DLD), Department of Fisheries (DOF), private sector and other relevant stakeholders. For terrestrial food-producing animals, the data were collected and verified from three sources: livestock population surveys by regional DLD offices, data records from the E-movement system monitored by DLD and large-scale producers.

Table 2 shows the average weight of some animals at the time of treatment (Aw); certain species were not available in the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) as there are no such animals raised in ESVAC countries. Consequently, these missing figures were estimated based on the standing weight (Table 2) [11]. The population correction unit (PCU) is used as a denominator for AMC in animals and is calculated by applying ESVAC methodology.

Regarding aquatic animal population, the data were collected from surveys by the Development Policy and Strategy Division, DOF; however, actual figures were officially published in the following year and are inconsistent with the projected figures in the latest report [11]. The species included in the report were fish and shrimp, which are the main production of Thai aquaculture (Table 2). The figures of aquatic animals are shown in kilogram (kg) of biomass. As emphasized by ESVAC, PCU is assumed to be a surrogate for the animal population at risk of being exposed to antimicrobials [12].

Table 2. Food-producing animal population

Animal category	Aw (kg)	Number of animals	Biomass (tonnes)	$PCU_{Thailand}$ (kg)
Terrestrial animals				
Pigs				
Breeding pigs	240**	1,029,281		247,027,440.0
Fattening pigs	65**	18,411,401		1,196,741,065.0
Poultry				
Broiler breeders	4*	18,100,000		72,400,000.0
Broilers	1**	1,594,494,720		1,594,494,720.0
Layer breeders	2*	719,900		1,439,800.0
Laying hens	2*	55,643,971		111,287,942.0
Pullets	1.5*	50,247,469		75,371,203.5
Broiler duck breeders	3.5*	321,300		1,124,550.0
Integrated broiler ducks	3.3*	32,130,000		106,029,000.0
Free-market broiler ducks	3.3*	25,077,362		82,755,294.6
Integrated layer ducks	2.5*	6,507,447		16,268,617.5
Free-market layer ducks	2.5*	9,847,138		24,617,845.0
Cattle				
Dairy cows	425**	245,505		104,339,625.0
Dry cows	425*	273,279		116,143,575.0
Beef cows	425**	4,876,228		2,072,396,900.0
Aquatic animals				
Coastal aquatic animals			382,400	382,400,000.0
Fresh aquatic animals			413,300	413,300,000.0
Total $PCU_{Thailand}$				**6,618,137,577.6**

*Thailand SAC 2017 [11]

**ESVAC 2017 [13]

1.5.2.2 Companion animal population

The number of companion animals could not be accurately estimated. Although companion animals are estimated to have lower AMC than terrestrial food-producing animals, the HPSR-AMR Working Group plans to collect data on the companion animal population to fill gaps under the One Health approach. Studies have shown a majority of antibiotics consumed by companion animals are registered as human antibiotics through off-label use.

1.6 Critically Important Antimicrobials (CIA)

WHO 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 [1]. WHO criteria for including 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.
2. The antimicrobial class is used to treat infections in people caused by either: 1) bacteria that may be transmitted to humans from non-human sources; or 2) bacteria that may acquire resistant genes from non-human sources.

Three prioritization criteria are used to 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 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 high proportion of use in patients with serious infections in health-care settings, since use may favour 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.

The Highest and High Priority CIA were fully applied in this report (Table 3).

Table 3. Antimicrobial classes in WHO Critically Important Antimicrobials

Categorization	Antimicrobial class
Highest Priority CIA	Cephalosporins (3rd, 4th and 5th generation)
	Glycopeptides and lipoglycopeptides
	Macrolides and ketolides
	Polymyxins
	Quinolones
High Priority CIA	Aminoglycosides
	Ansamycins
	Carbapenems and other penems
	Glycylcyclines
	Lipopeptides
	Monobactams
	Oxazolidinones
	Penicillins (antipseudomonal)
	Penicillins (aminopenicillins)
	Penicillins (aminopenicillins with beta-lactamase inhibitors)
	Phosphonic acid derivatives
	Drug used solely to treat tuberculosis or other mycobacterial diseases

ANTIMICROBIAL CONSUMPTION

2.1 Antimicrobial consumption in humans

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Food and Drug Administration, Ministry of Public Health

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Key summary

Overall human antimicrobial consumption

Consumption (DDD)	Human population (inhabitants)	Consumption (DDD/1,000 inhabitants/day; DID)
1,807,944,443	72,438,300	68.4

Consumption of core and optional antimicrobial classes

For the core class, other beta-lactams ranked first, followed by beta-lactams and penicillins and tetracyclines. The top three core antimicrobials were ceftriaxone, amoxicillin and tetracycline.

Among antimicrobials in the optional class, antivirals intended for systemic infections were consumed most, along with antimycotics used for systemic infections and antituberculous drugs, which ranked second and third respectively. The three most-consumed antimicrobials in the group were ketoconazole, efavirenz and lamivudine.

Consumption of critically important antimicrobials in humans

More than half of total antibacterial consumption was in the CIA category and more than half of consumption in the CIA category belonged to the highest priority group as defined by WHO. The three most-consumed antimicrobial groups in the CIA category included cephalosporins (3rd and 4th generation), aminopenicillins and quinolones. By substance in the highest priority CIA, ceftriaxone was consumed most, followed by norfloxacin and roxithromycin.

2.1.1 General

In Thailand, most human antimicrobials are classified as dangerous drugs, which means they must be dispensed only by a licensed pharmacist. Only a few important antibiotics are classified as special controlled drugs, which require a prescription from a licensed physician to be dispensed.

According to the NSP-AMR, Goal 2 is to reduce human antimicrobial consumption by 20.0% in 2021. In order to make the goal measurable, the method of monitoring human AMC is of substantial importance and is one of the reasons that the Thailand Surveillance on Antimicrobial Consumption (Thailand SAC) was developed. Aside from measuring progress towards the national goal, the data are useful for both health professionals and policymakers. The consumption data can help assess the effects of policy implementation, law enforcement, antimicrobial stewardship programmes (ASP) and other relevant interventions. With some improvements in methodology and data granularity, such information can be used at national, regional and local levels to tackle AMR problems in efficient and practical ways.

2.1.2 Data Sources

According to the Drug Act B.E. 2510 (1967) Section 85, all pharmaceutical manufacturers and importers are required by Thai FDA to submit an annual report, which consists of their total production and/or import volumes of registered products by 31 March of the following year [14]. The data were then electronically retrieved after 31 March 2018 for analysis. In an effort to identify actual domestic consumption in the scheme of Thailand's drug distribution, manufacturers and importers, although not mandated by law, were requested to submit their total export volume, so it could be subtracted from the total consumption [15].

To validate the data integrity of the annual reports, Thai FDA officers and the HPSR-AMR working group checked the input data to identify outliers, especially in dosage form, strength of product and amount of active pharmaceutical ingredient(s). Additionally, to ensure the quality of the annual reports, the HPSR-AMR working group developed a tool to assess the quality of data provided by pharmaceutical operators. The purpose was to verify the quality of the data, assess the system that generates the data, and develop a System Assessment Protocol (SAP) and Data Verification Protocol (DVP) to improve both the data and system which produces these data-selected pharmaceutical operators [12].

For human antimicrobials, the Thailand SAC covered the core and optional classes of antimicrobials recommended by WHO (Table 4) [16]. The data were analyzed using the amount of active pharmaceutical ingredients (AI) in Defined Daily Doses (DDD) as a nominator and the mid-year human population as a denominator, ultimately resulting in DDD/1,000 inhabitants/day (DID) [17]. Additionally, the consumption of CIA was based on the latest version of the list [1].

Table 4. The core and optional classes of target human antimicrobials by WHO

Target human antimicrobials	ATC code
1. Core class	
• Antibacterials for systemic use	J01
• Antibiotics for alimentary tract	A07AA
• Nitroimidazole derivatives	P01AB
2. Optional class	
• Antimycotics for systemic use	J02
• Antifungals for systemic use	D01BA
• Antivirals for systemic use	J05
• Drugs for treatment of tuberculosis	J04A
• Antimalarials	P01B

2.1.3 Results

1. Overall consumption of human antimicrobials

Overall, the national consumption of human antimicrobials was 68.4 DDD/1,000 inhabitants/day. Of total target human consumption, antibacterials indicated for systemic use (J01) ranked highest at 46.4 DID, accounting for 67.9%. The second and third most consumed antimicrobials were antivirals intended for systemic use (J05) and antimycotics for systemic use (J02) at 13.0 and 4.2 DID, contributing to 19.0% and 6.2%, respectively (Figure 3).

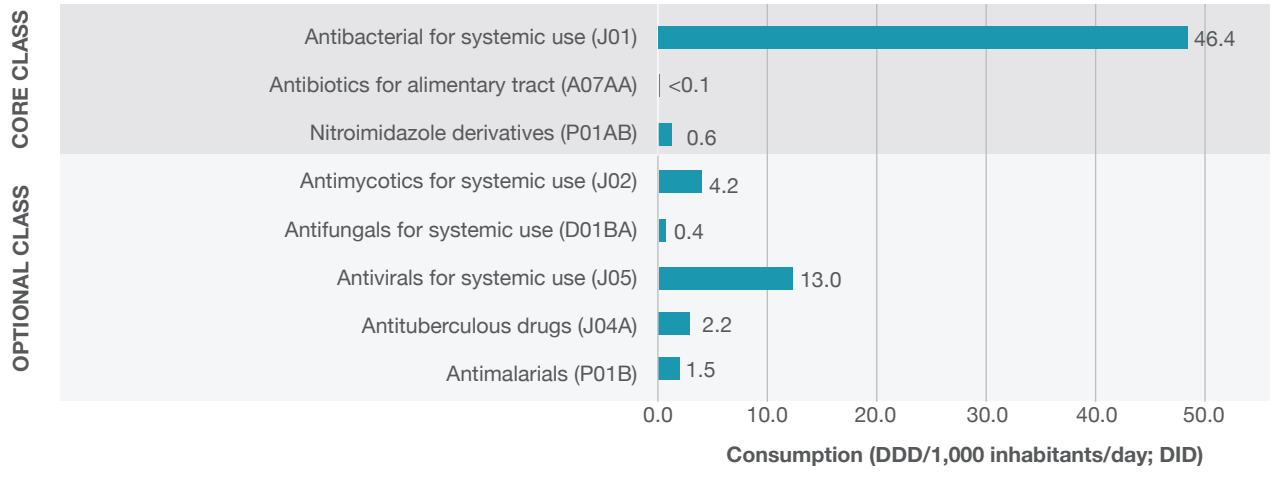

Figure 3. Consumption of human antimicrobials, classified by scope of WHO and ATC code (DID)

2. Core class breakdown

The majority of the core set was antimicrobials for systemic use at 46.4 DID (98.7%) (Figure 3). Of the antimicrobials for systemic use, other beta-lactams (J01D) ranked first at 15.9 DID (34.2%), followed by beta-lactams and penicillins (J01C) at 15.4 DID (33.1%) and tetracyclines (J01A) with a DID of 5.9 (12.7%) (Figure 4). The top-three antimicrobials used for systemic infections were ceftriaxone (13.5 DID, 29.2%), amoxicillin (10.0 DID, 21.6%), and tetracycline (3.4 DID, 7.4%) (Table A1).

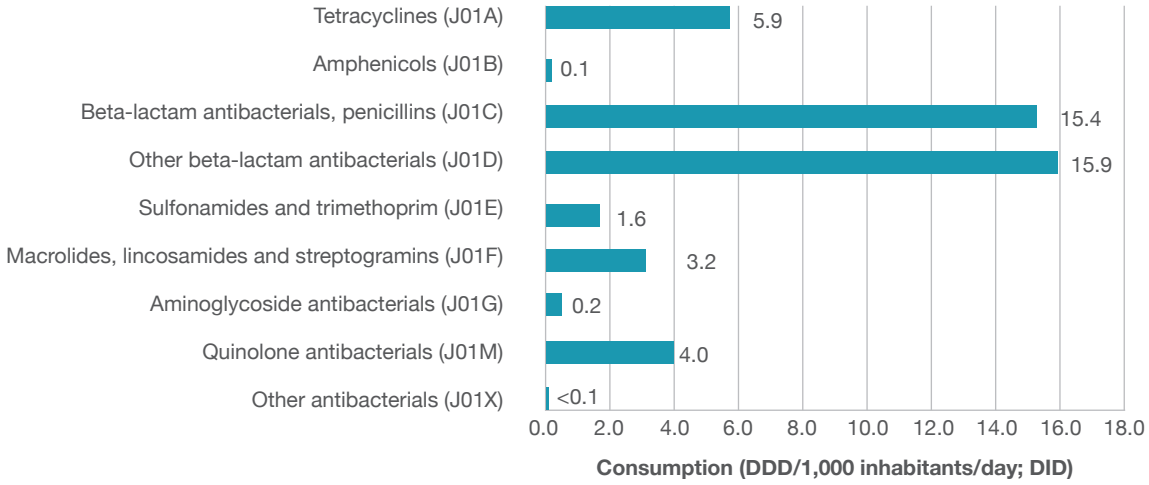

Figure 4. Consumption of human antimicrobials indicated for systemic use, classified by ATC level 3 (DID)

For the first-ranked group, three common antimicrobials were ceftriaxone at 13.5 DID (85.4%), followed by ceftazidime at 0.9 DID (5.9%) and cephalexin at 0.6 DID (3.8%). For the following group, the top-three antimicrobials included amoxicillin at 10.0 DID (65.0%), amoxicillin and enzyme inhibitor at 1.7 DID (11.1%), and ampicillin at 1.4 DID (9.2%). Regarding the third-ranked group, the top-three tetracyclines most used for systemic infection were tetracycline at 3.4 DID (58.3%), doxycycline at 2.4 DID (40.7%), and chlortetracycline at 0.1 DID (0.9%) (Table A1).

As the second-ranked core class, the nitroimidazoles used were only metronidazole (0.6 DID) and tinidazole (<0.1 DID) (Table A2). For the last core class, antibiotics used solely for alimentary tract treatment included neomycin and nystatin at a DID of 0.1 each (Table A2).

3. Optional class breakdown

Among the consumption of the optional antimicrobial classes, the most-consumed antivirals for systemic infections (J05) was 13.0 DID (61.0%), followed by antimycotics used for systemic infections (J02) at 4.2 DID (19.8%) and antituberculous drugs (J04A) at 2.2 DID (10.4%) (Figure 3). In the optional classes, the three antimicrobials most consumed were ketoconazole at 3.7 DID (17.2%), followed by two antivirals, efavirenz at 3.1 DID (14.4%) and lamivudine at 2.7 DID (12.8%) (Tables A3 and A4).

For antivirals indicated for systemic use, the top-three most-consumed drugs included efavirenz (3.1 DID, 23.7%), lamivudine (2.7 DID, 20.9%) and tenofovir disoproxil (2.2 DID, 16.6%) (Figure 5).

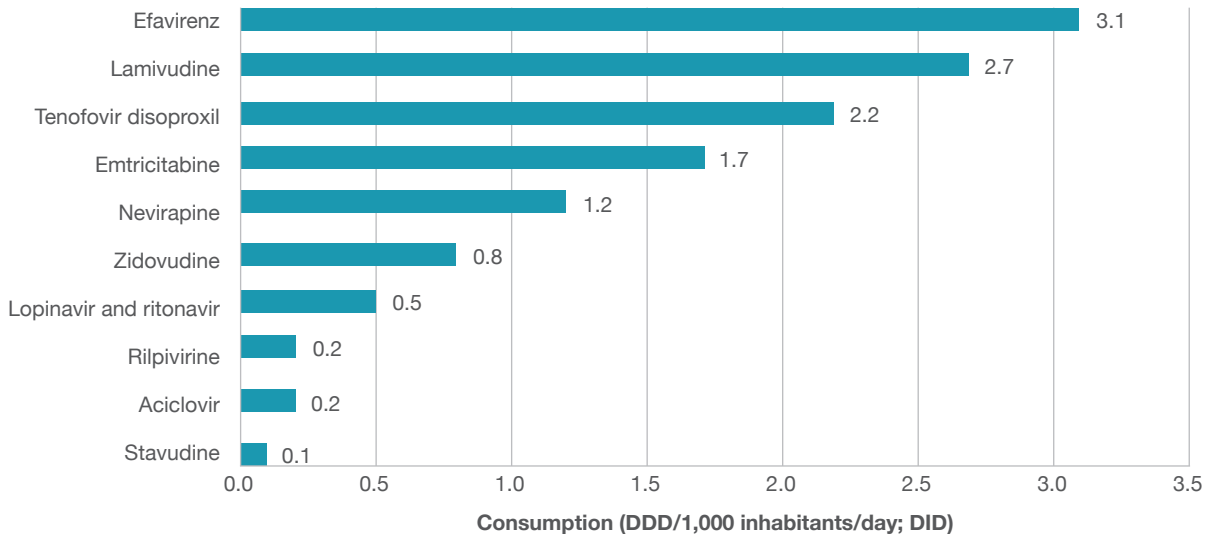

Figure 5. Consumption of top-ten antivirals indicated for systemic use classified by ATC level 5 (DID)

The second most-used antibiotics in the optional class were antimycotics intended for systemic use including fluconazole at 0.3 DID (7.6%) and itraconazole at 0.2 DID (5.4%), in addition to the first-ranked ketoconazole (Table A4). For the remaining antimycotics and antifungals, each was consumed at <0.1 DID (Table A4).

With regard to drugs used to treat mycotuberculosis, isoniazid was consumed most at 0.9 DID (40.1%), followed by rifampicin (0.8 DID, 36.5%) and pyrazinamide (0.3 DID, 11.7%) (Figure 6) (Table A5).

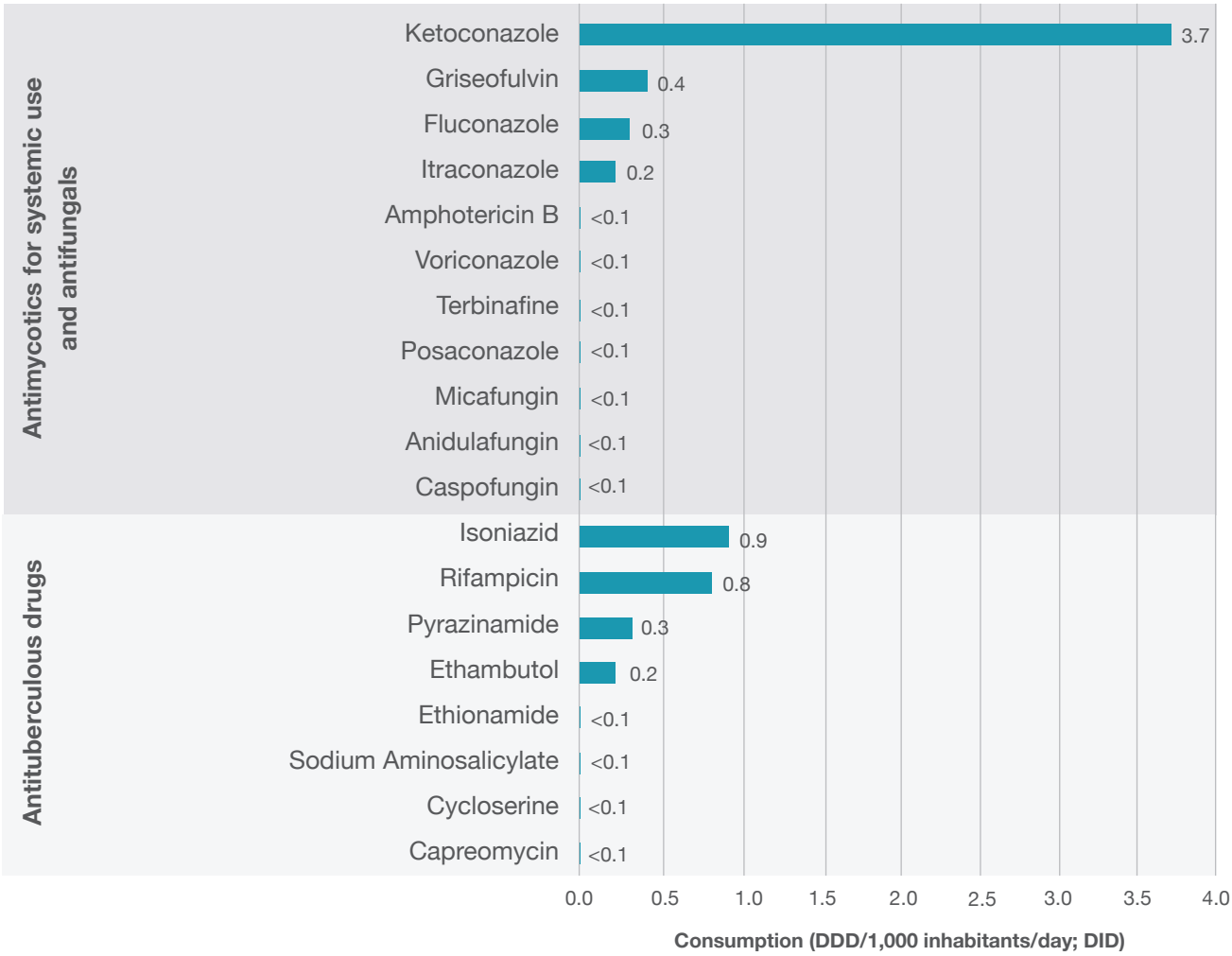

Figure 6. Consumption of antimycotics and antifungals indicated for systemic use including antituberculous drugs, classified by ATC level 5 (DID)

For antimalarial drugs, the three most-consumed drugs were chloroquine at 0.7 DID (50.3%), pyrimethamine at 0.5 DID (32.7%) and hydroxychloroquine at 0.2 DID (12.9%) (Table A6).

4. Consumption of CIA

Among all antimicrobials consumed in humans, the consumption of CIA was 37.2 DID (54.4%). Moreover, over half of CIA consumption was highest priority CIA at 21.5 DID (31.5%), with high priority antimicrobials accounting for 15.7 DID (23.0%) (Figure 7). The top-three most consumed groups of antimicrobials in CIA were cephalosporins (3rd and 4th generation) at 14.9 DID (39.9%), aminopenicillins at 11.4 DID (30.7%), and quinolones at 4.0 DID (10.9%) (Figure 8).

Among the highest priority CIA, ceftriaxone was the most-consumed antibiotic at 13.5 DID (63.0%), followed by norfloxacin at 2.0 DID (9.4%) and roxithromycin at 1.5 DID (7.0%) (Figure 9). For the high priority CIA, the three most-consumed antimicrobials were amoxicillin at 10.0 DID (63.7%), amoxicillin and enzyme inhibitor at 1.7 DID (10.9%), and ampicillin at 1.4 DID (9.0%) (Figure 9).

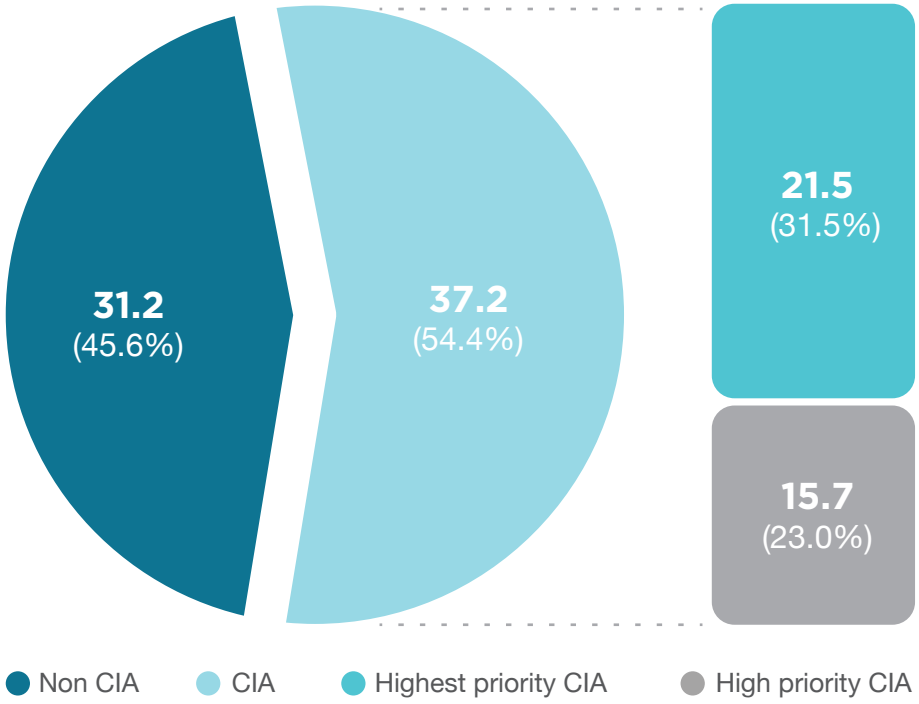

Figure 7. Proportional consumption of critically important antimicrobials to non-CIA in humans (DID)

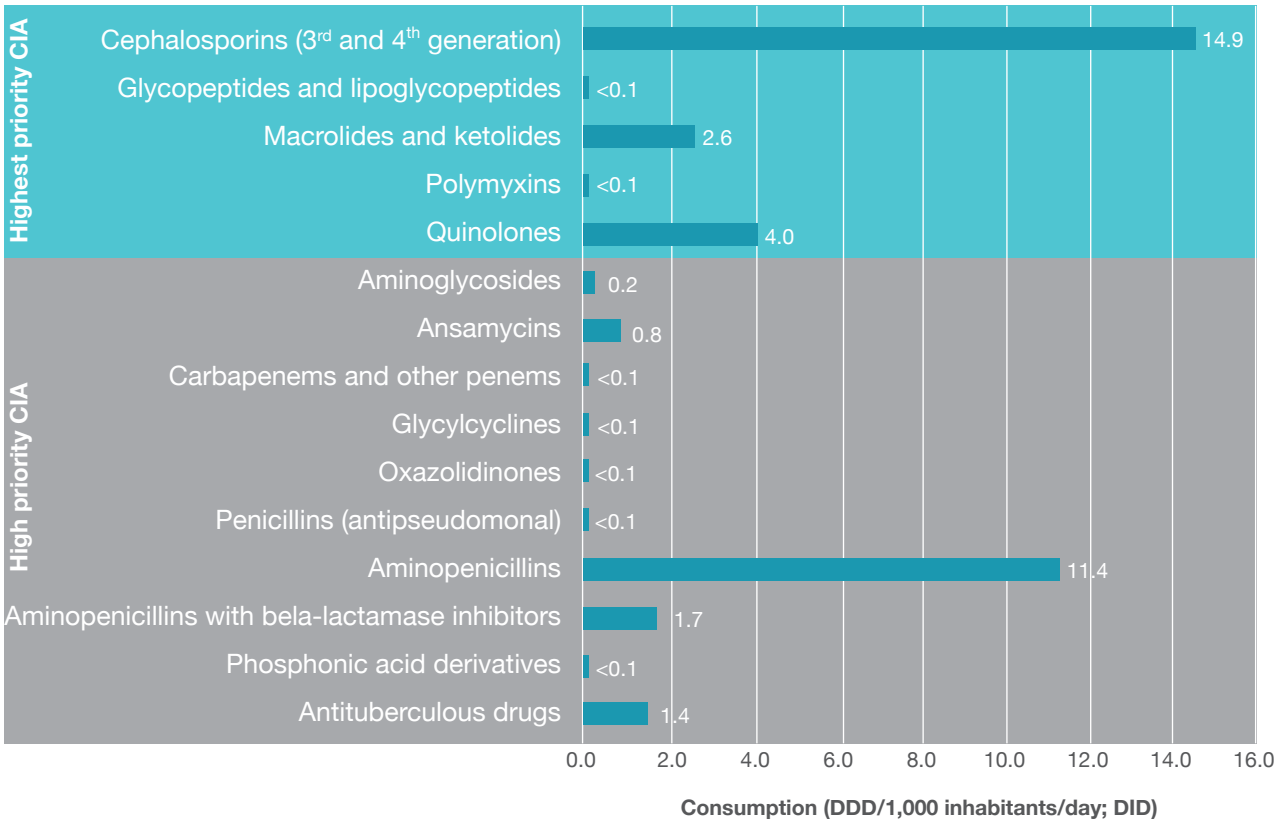

Figure 8. Consumption of WHO critically important antimicrobials classified by class of antimicrobials (DID)

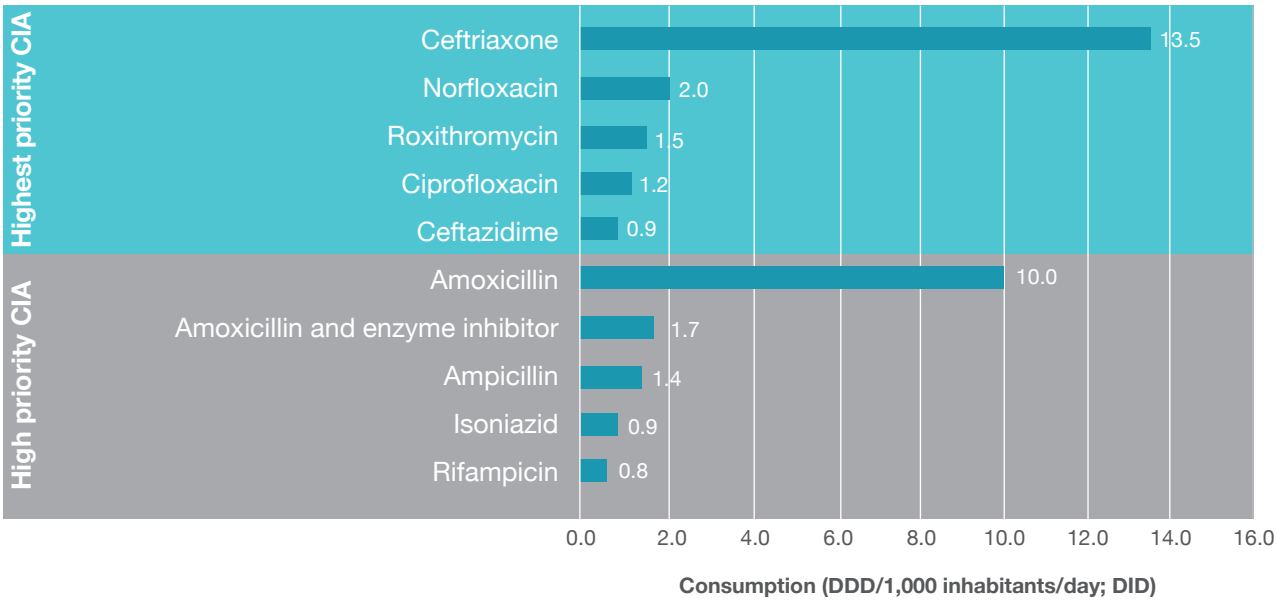

Figure 9. Consumption of WHO critically important antimicrobials, classified by ATC level 5 (DID)

2.1.4 Limitation

In terms of the data source, the regulations do not make it compulsory for pharmaceutical operators to declare exported antimicrobials, so not all pharmaceutical manufacturers and importers submitted export data to the FDA. Consequently, the report of human AMC could be overestimated from including the exported antimicrobials. Moreover, unlike the European Surveillance of Antimicrobial Consumption Network (ESAC-Net), relying on manufacture and importation data has an inevitable disadvantage that the accuracy of the data could be influenced by the number of unconsumed products in stock. However, in an efficient pharmaceutical market, it can be assumed that the stock level should be more or less constant over a year. As a result, the total domestic consumption of human antimicrobials can be still estimated.

Aside from these limitations, the current approach cannot capture illegal medicine products and the monitoring efforts need an on-site regular verification of data integrity and quality. Lastly, but most importantly, the consumption of antimicrobials identified by the Thailand SAC cannot be directly compared with antimicrobial consumption in other countries due to differences in human epidemiology, disease burden and clinical management and use of antimicrobials.

2.1.5 Prospect

In order to capture data of better antimicrobial consumption, all pharmaceutical operators are required to report export volumes with Thai-FDA-verified data from other sources such as ports of entry and air, land and sea borders. In doing so, it not only increases the accuracy of the data, but also prevents illegal importation and smuggling along borders. The disadvantage of using total manufacture and import data is that it cannot provide information on how many drugs are actually used; therefore, reported sales are the most accurate data source, for which law amendments through legislative processes are needed. For the ultimate goal, systems to gather data on antimicrobial use at hospitals, primary healthcare providers and the retail sector should be further developed, as this data can actually reflect real consumption of antimicrobials and help to identify AMR policy direction. However, implementation requires a good drug-dispensing system aligned with reliable information systems such as host-to-host services or other timely and internal validation systems.

2.1.6 Acknowledgments

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2.2 Antimicrobial consumption in food-producing animals

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Food and Drug Administration, Ministry of Public Health

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Key summary

Overall food-producing animal antimicrobial consumption

Consumption (tonne of API)	Animal population (kg of $PCU_{Thailand}$)	Consumption (mg/$PCU_{Thailand}$)
3,690.3	6,618,137,577.6	557.6

Of the total national AMC in food-producing animals, antimicrobials for systemic use (QJ01) ranked highest, followed by those indicated for intestinal use. The third- and fourth-ranked antimicrobials were used for intra-mammary and intrauterine use.

Consumption of each antimicrobial class

Of the major antibiotics used in food-producing animals, the most-consumed antibiotics were penicillins, mainly comprising of amoxicillin, followed by tetracyclines and other antibacterials, the latter of which were from three drugs: halquinol, bacitracin and bambermycin.

Consumption by dosage form and route of administration

Over half of veterinary antimicrobial consumption was consumed in the form of medicated premix, mainly consisting of halquinol, chlortetracycline and tiamulin. The second- and third-ranked most-consumed dosage forms were oral powder and oral solutions, respectively.

More than half of consumption from injectable antimicrobials was from the consumption of three drugs: gentamicin, amoxicillin and oxytetracycline. For intramammary products, the majority of consumption came from cloxacillin and ampicillin.

Consumption of CIA

For the highest priority CIA, macrolides were consumed most, mainly from tilmicosin and tylosin. The second-ranked human CIA used in animals was polymyxins (colistin), followed by fluoroquinolones with enrofloxacin as a main drug.

For high priority CIA, aminopenicillins had the highest ranked consumption in the animal sector, with amoxicillin used as the same major drug. This was followed by aminoglycosides, mainly from gentamicin and neomycin.

2.2.1 General

Unlike human medicines, all veterinary medicines including antimicrobials are classified as dangerous drugs, which means they must be dispensed only by a licensed pharmacist or veterinarian. However, only some are classified as specially controlled drugs, including antibacterials (premix for medicated stuff), quinolones and derivatives (all dosage forms), cephalosporins (all dosage forms), macrolides (all dosage forms), and polymyxins (all dosage forms).

Goal 3 in the NSP-AMR 2017-2021 is to reduce antimicrobial consumption in animals by 30.0% by 2021. The monitoring and evaluation framework is of substantial importance to measure progress towards the goal, and helps develop the Thailand SAC. Consumption data from the Thailand SAC are also useful for health professionals and policymakers as it can help assess the effects of policy implementation, law enforcement, ASP and other relevant interventions. With some improvements in methodology and data granularity, this information can be used not only at national, but also at local and regional levels as well to tackle AMR problems in an efficient and practical way.

2.2.2 Data Sources

All pharmaceutical manufacturers and importers are required by the FDA to submit an annual report of total production and/or importation volumes of registered veterinary medicinal products by 31 March of the following year. The data are then electronically retrieved for analysis. In an effort to identify actual domestic consumption, manufacturers and importers, were requested to voluntarily submit their total export volume to enable subtraction from total consumption. The validation process was conducted at the same time as that for human medicines because some human pharmaceutical companies also produced animal drugs.

For veterinary target antimicrobials, the Thailand SAC kept the list of target antimicrobials in line with the World Organisation for Animal Health (OIE) and ESVAC (Table 5) [18, 19]. The consumption of human CIAs used in animals was also based on the latest version of the list [1].

Table 5. The scope of target antimicrobials intended for use in animals (mainly food-producing animals)

Target human antimicrobials	ATC code
1. Antimicrobial agents for intestinal use	
• Antibiotics	QA07AA
• Sulfonamides	QA07AB
• Other intestinal antiinfectives	QA07AX
2. Antimicrobial agents for intrauterine use	
• Antibiotics	QG01AA, QG01BA
• Sulfonamides	QG01AE, QG01BE
• Antibacterials	QG51AA
• Antiinfectives for intrauterine use	QG51AG
3. Antimicrobial agents for systemic use	QJ01
4. Antimicrobial agents for intramammary use	QJ51

2.2.3 Results

1. Overall veterinary antimicrobial consumption

The total national consumption of antimicrobials for humans and animals includes the amount of manufactured and imported antimicrobials for use in food-producing animals and covers all pharmaceutical dose forms except oral tablets and capsules due to their main use in companion animals. Among the total consumption of antimicrobials in food-producing animals, antimicrobials indicated for systemic use (QJ01) ranked highest with an mg/$PCU_{Thailand}$ of 441.7, accounting for 79.2%. Following the antimicrobial agents for systemic use, the second most-consumed antimicrobials were those for intestinal use (115.8 mg/$PCU_{Thailand}$, 20.8%), the majority of which came from other intestinal anti-infectives (QA07AX) (73.7 mg/$PCU_{Thailand}$). The third-ranked antimicrobials in veterinary consumption were derived from antimicrobials used for intramammary infections with <0.1 mg/$PCU_{Thailand}$ (<0.1%) (Figure 10).

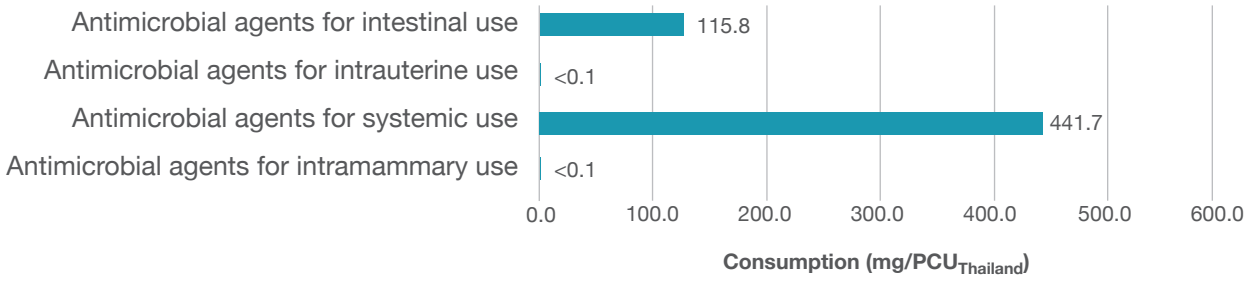

Figure 10. Consumption of target veterinary antimicrobials (mg/$PCU_{Thailand}$)

As shown in Figure 11, of the antimicrobials used for systemic infections (QJ01), beta-lactams (QJ01C and QJ01D) were consumed most, accounting for 150.9 mg/$PCU_{Thailand}$ (34.2%). The most-consumed beta-lactam was amoxicillin with an mg/$PCU_{Thailand}$ of 147.5 (Table A8). The second-ranked antimicrobial consumptions in this group was tetracyclines (QJ01A) with an mg/$PCU_{Thailand}$ of 107.5 (24.3%), mainly from chlortetracycline and doxycycline with an mg/$PCU_{Thailand}$ of 57.2 and 38.9, respectively. This was followed by a combination of macrolides and lincosamides (QJ01F) with 55.1 mg/$PCU_{Thailand}$ (12.5%). More than 70.0% of consumption in this group came from two macrolide antibacterials - tilmicosin and tylosin - with an mg/$PCU_{Thailand}$ of 22.3 and 18.8, respectively.

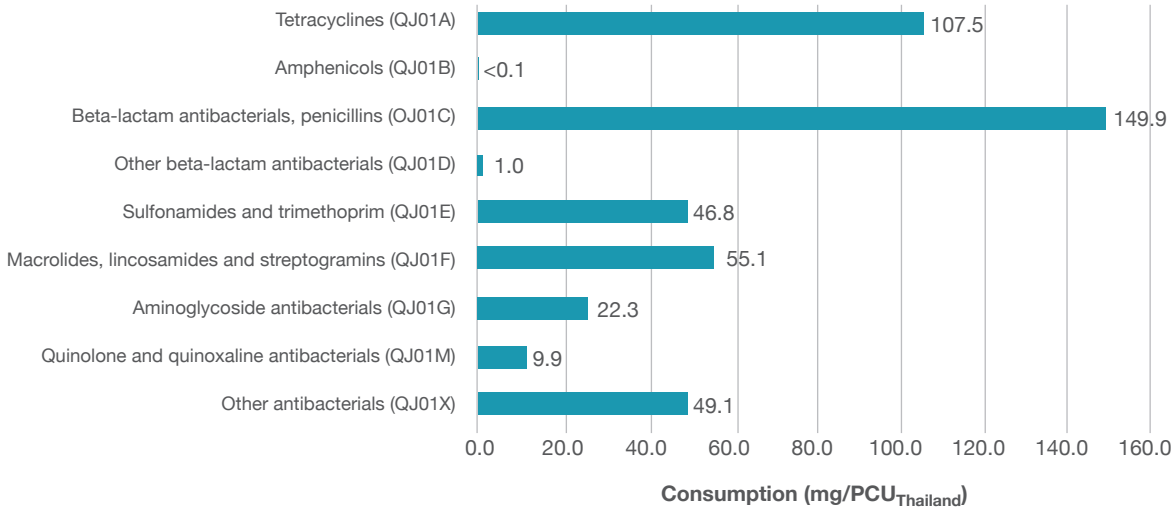

Figure 11. Consumption of veterinary antimicrobials indicated for systemic use (QJ01) (mg/$PCU_{Thailand}$)

For antimicrobials used for gastrointestinal infections (QA07AX), halquinol was used most at an mg/$PCU_{Thailand}$ of 73.7 (Table A9). This was followed by colistin and bacitracin, with an mg/$PCU_{Thailand}$ of 24.6 and 10.5, respectively. The third-ranked antimicrobials in the scope belonged to antimicrobials intended for intramammary infections, mainly from cloxacillin (<0.1 mg/$PCU_{Thailand}$) and ampicillin (<0.1 mg/$PCU_{Thailand}$) (Table A10).

2. Veterinary antimicrobial consumption

a. Antimicrobial class

For the class of antimicrobials in Figure 12, penicillins were consumed the most (26.9%), mainly amoxicillin with 147.5 mg/$PCU_{Thailand}$ in the form of premix. The second rank of antimicrobial consumption belonged to tetracyclines, accounting for 19.3%. Over half of the consumed tetracyclines were from chlortetracycline, mainly in the form of premix as well. Unlike the same trend in the first two ranks as those indicated for systemic use, the third-ranked antimicrobials were the group of other antibacterials. This group consisted of three antimicrobials mainly used in feed: halquinol (73.7 mg/$PCU_{Thailand}$), bacitracin (10.5 mg/$PCU_{Thailand}$) and bambermycin (0.3 mg/$PCU_{Thailand}$) (Table A11).

For antimicrobials used more in animals than in humans, sulfonamides and trimethoprim contributed to 8.4% of total veterinary consumption, mainly from sulfadimidine (35.4 mg/$PCU_{Thailand}$) in the form of a combination product and as suspension for use in drinking water. The other group of antimicrobials used mainly in the veterinary field was pleuromutilins, accounting for 8.1%. Most of the pleuromutilins was from tiamulin (45.4 mg/$PCU_{Thailand}$) mainly in the form of premix (Table A11).

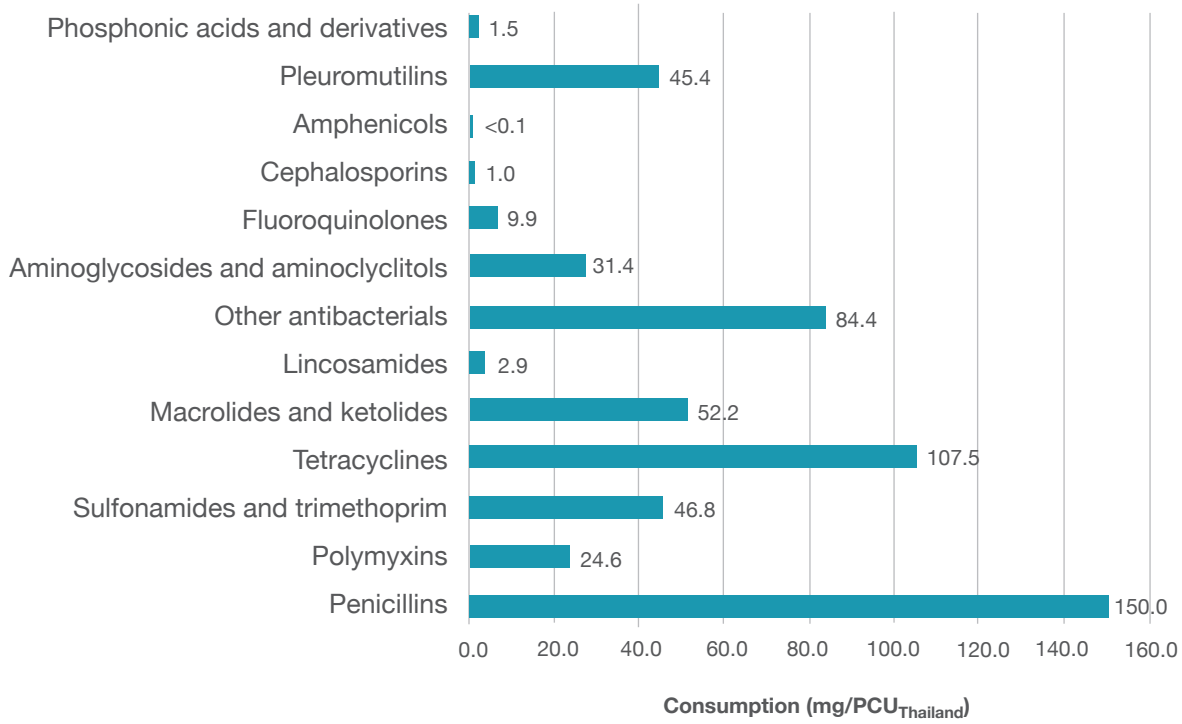

Figure 12. Consumption of veterinary antimicrobials classified by drug class (mg/$PCU_{Thailand}$)

b. Dosage form and route of administration breakdown

When grouped by pharmaceutical dose form, more than half of veterinary antimicrobials were in the form of premix (Figure 13). The three major antimicrobials used as premix were halquinol (24.3%), chlortetracycline (18.7%) and tiamulin (14.1%) (Figure 14) (Table A11). The second most-used dose form was oral powder, the majority of which came from amoxicillin used as powder for drinking water (108.1 mg/$PCU_{Thailand}$, 65.7%). The third-ranked most-consumed dose form was oral solution, most of which came from sulfadimidine used in drinking water (34.3 mg/$PCU_{Thailand}$, 65.6%).

For injectable products, more than half of consumption was from gentamicin (19.6 mg/$PCU_{Thailand}$), followed by amoxicillin (4.3 mg/$PCU_{Thailand}$, 11.5%) and oxytetracycline (4.2 mg/$PCU_{Thailand}$, 11.3%). The consumption of antimicrobials for intramammary use mainly came from cloxacillin (<0.1 mg/$PCU_{Thailand}$, 41.0%) and ampicillin (<0.1 mg/$PCU_{Thailand}$, 40.7%). Other dose forms included intrauterine suspension, oral paste and vaginal tablet, accounting only for <0.1 mg/$PCU_{Thailand}$ (<0.1%) (Figure 13).

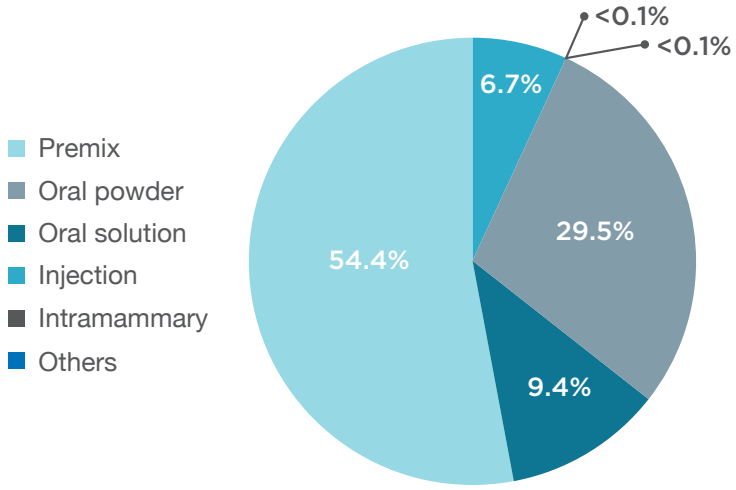

Figure 13. Consumption of veterinary antimicrobials, classified by pharmaceutical dosage form

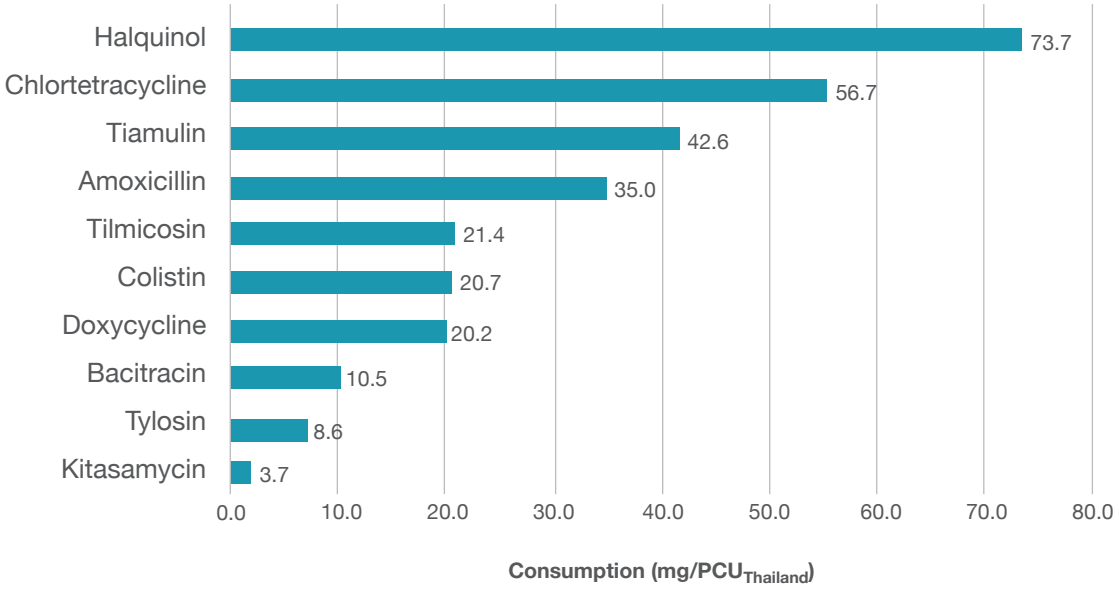

Figure 14. Consumption of top ten veterinary antimicrobials used as premix (mg/PCU$_{Thailand}$)

3. Consumption of CIA

Similar to human antimicrobials, almost half of veterinary domestic consumption was human CIAs. However, unlike human consumption patterns, two-thirds of the CIA consumption in animals came from antimicrobials in the high priority group (Figure 15). Moreover, the profile of CIA in each priority group used in animals was different to that of human consumption.

Regarding the highest priority CIA (Figure 16), the top-three major CIA consumption in animals were from macrolides, polymyxins and quinolones. However, for this priority in humans, the top-three classes were cephalosporins (3^{th} and 4^{th} generation), quinolones and macrolides. For the first rank, the main consumption of macrolides in animals came from tilmicosin (22.3 mg/$PCU_{Thailand}$, 42.8%) and tylosin (18.8 mg/$PCU_{Thailand}$, 35.9%), but in humans the majority of macrolide consumption was from roxithromycin at 1.5 DID, (58.1%) and azithromycin at 0.5 DID (20.5%) (Tables A7 and A12). Ranked second in animal consumption of highest priority CIA, polymyxins were solely from colistin; however, compared in tonnes of active pharmaceutical ingredient (API), the animal consumption of colistin, which was mainly used in the form of premix, was more than human consumption of colistin (Figure 17). As the third-ranked CIA used in animals, quinolones were consumed mainly from enrofloxacin (9.9 mg/$PCU_{Thailand}$, 99.4%) as a single product for oral solution while most-consumed quinolones in humans came from norfloxacin at 2.0 DID (50.1%) and ciprofloxacin at 1.2 DID (30.4%). Ranked first in human consumption but fourth in animal consumption, third- and fourth-generation cephalosporins were consumed by the animal sector mainly from cefquinome (0.8 mg/$PCU_{Thailand}$, 77.9%) and ceftiofur (0.2 mg/$PCU_{Thailand}$, 22.0%) as an injectable form, while humans consumed more than 90.0% in an injectable form of ceftriaxone (Tables A7 and A12).

With respect to CIA in the high priority category, both human and animal sectors consumed penicillins, but the animal sector consumed more than humans. More than 99.0% of aminopenicillins in animals came from amoxicillin while consumption in humans was from amoxicillin at 10.0 DID (87.6%) and ampicillin at 1.4 DID (12.4%). In contrast with sole aminopenicillins, the combination of aminopenicillins with beta-lactamase inhibitors was consumed more in humans than in animals, and both of the sectors' consumption mainly came from amoxicillin combinations (Figure 16). Exclusive to the human sector, the least-consumed penicillins were antipseudomonal penicillins, solely from piperacillin in combination with beta-lactamase inhibitors. As the second-ranked CIA in this priority, the major consumption of aminoglycosides was derived from gentamicin (19.6 mg/$PCU_{Thailand}$, 66.9%) and neomycin (6.9 mg/$PCU_{Thailand}$, 23.6%) (Table A12). However, consumed more by animals, human aminoglycosides were primarily consumed from gentamicin and kanamycin at 0.2 DID (65.1%) and <0.1 DID (14.0%), respectively (Table A7).

Another group of high priority CIA were phosphoric acids and their derivatives consumed solely from fosfomycin and more in the animal sectors as premix for medicated feed (Table A7).

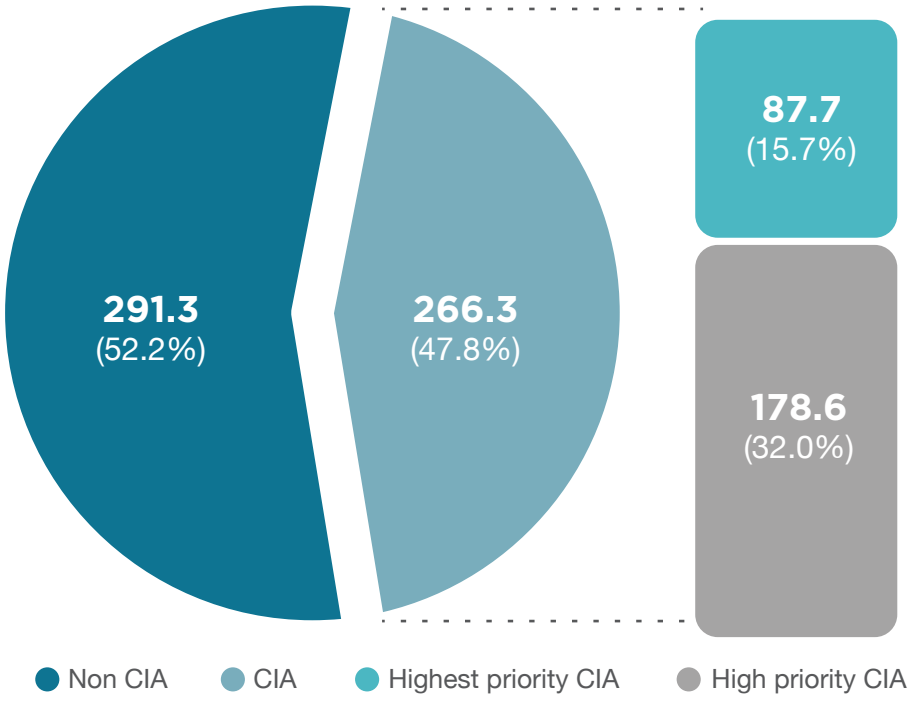

Figure 15. Proportional consumption of WHO critically important antimicrobials (CIA) to non CIA in animals (mg/PCU$_{Thailand}$)

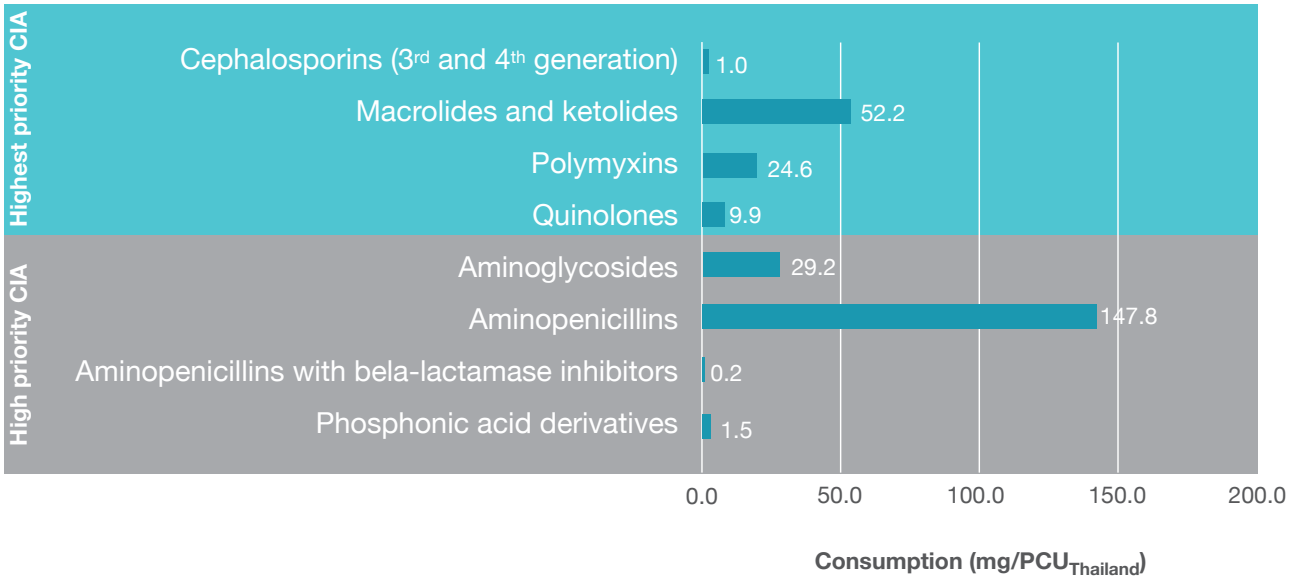

Figure 16. Consumption of critically important antimicrobial in food-producing animals, classified by class of antimicrobials (mg/PCU$_{Thailand}$)

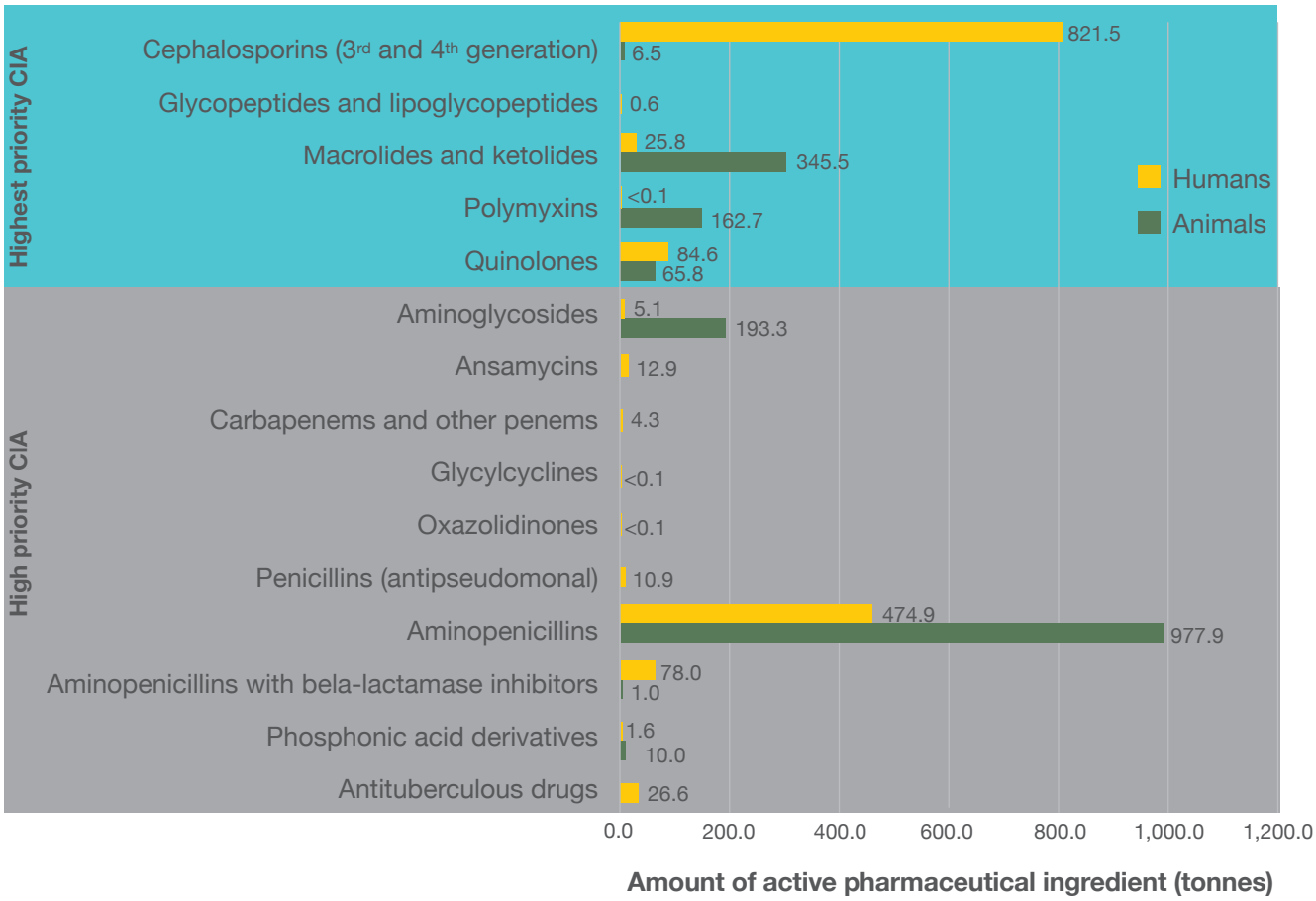

Figure 17. Comparison of WHO critically important antimicrobial consumption, expressed as tonne of active pharmaceutical ingredient in human and animal sectors

2.2.4 Limitation

Despite the efforts made by Thailand FDA so far, the law did not require pharmaceutical operators to submit data on export volumes, and it could not be assumed that all pharmaceutical manufacturers and importers had submitted this data to the FDA. So, the same limitations existed as those faced when measuring human AMC. Also, the consumption of veterinary antimicrobials could not be compared to those of other countries due to differences in animal epidemiology, burdens of disease and farm and clinical management practices. Additionally, aggregated data does not allow consumption data to be broken down into key animal species, so that it was not possible to identify which animal species has extensively used antimicrobials and where specific policies need to be implemented.

2.2.5 Prospect

Similar to human consumption, the veterinary consumption data cannot provide exact information on the extent to which drugs have been used annually; therefore, consumption data would be more accurate if it covered all of the export data. This coverage requires legislative amendments for pharmaceutical operators to comply with. In the future development of the Thailand SAC, animal sectors need to be classified by species in order to provide a more accurate picture of which antimicrobials are used for which animal species. In doing so, it requires, however, collaboration between other authorities such as the Department of Livestock Development, the Department of Fisheries, and other relevant sectors.

2.2.6 Acknowledgments

Thailand SAC is locally initiated and established. It receives financial supports from various partners, in particular the World Health Organization South-East Asia, the United States Agency for International Development, the Food and Agriculture Organization of the United Nations (FAO), and WHO-CCS.

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2.3 Antimicrobial consumption in companion animals

In the Fiscal Year (FY) 2021, the HPSR-AMR plans to conduct research on system analysis of AMU in companion animals and to conduct a pilot surveillance in Thailand. Based on these results, the routine monitoring of AMU in companion animals will be launched in FY2022.

ANTIMICROBIAL RESISTANCE

3.1 Antimicrobial resistance in humans

Data source
National Antimicrobial Resistance Surveillance Center Thailand (NARST),
National Institute of Health, Department of Medical Sciences, Ministry of Public Health,
Department of Disease Control, Ministry of Public Health, Thailand

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Key summary

Gram-negative bacteria

AMR in bacterial isolates from humans has been increasing continuously, especially in gram-negative bacteria (compared with the 2000 data) [20]. High number of carbapenem resistant *Acinetobacter calcoaceticus-baumannii* complex, *Pseudomonas aeruginosa* and *Enterobacteriaceae* were observed in 2017.

Gram-positive bacteria

The resistance rate of methicillin-resistant coagulase-negative *Staphylococcus* spp. (53.2%) was higher than methicillin-resistant *Staphylococcus aureus* (MRSA) (9.6%).

Of all isolates of *Enterococcus faecium*, 8.8% were vancomycin-resistant.

The rates of penicillin and ceftriaxone resistance in *Streptococcus pneumoniae* from meningitis isolates were higher than non-meningitis isolates.

Other antimicrobial resistant bacteria

There was a rising rate of fluoroquinolone resistance in Non-typhoidal *Salmonella* spp.

All of *Neisseria gonorrhoeae* isolates were still susceptible to ceftriaxone and cefixime. One isolate was detected with a high azithromycin MIC of 2 mg/L.

3.1.1 General

AMR is a threat to human health and a cause of public concern since it leaves clinicians with few therapeutic options to treat bacterial infection leading to high morbidity and high mortality. This report presents the data from 2017 surveillance, which contains the AMR data of the major antimicrobial-resistant bacteria as recommended by Thailand's NSP-AMR 2017-2021. It aims to analyze data, the findings of which can hopefully be applied in clinical setting. The scope of this report will therefore encompass data of gram-negative, gram-positive and other bacteria associated with AMR problems in Thailand.

3.1.2 Data Sources

AMR data were collected from 74 hospitals over the country during 2017 and were provided by the National Antimicrobial Resistance Surveillance Center, Thailand (NARST), National Institute of Health, Department of Medical Sciences, Ministry of Public Health, Thailand. Most of isolates were selected from all specimens, e.g. blood, urine, and sputum unless otherwise specified.

Surveillance of AMR of gonococci was performed by Bangrak STIs center, Silom Community Clinic @TropMed and 3 centers of The Office of Disease Prevention and Control. These data on AMR in *Neisseria gonorrhoeae* were then provided by the Department of Disease Control, Ministry of Public Health, Thailand.

Data on antimicrobial resistance and MIC values in 2017 were interpreted according to CLSI susceptibility breakpoints 2017.

3.1.3 Results

1. Gram-negative bacteria

1.1 *Acinetobacter calcoaceticus-baumannii* complex

Acinetobacter baumannii (A. baumannii) is gram-negative, non-glucose fermenter bacteria that usually associated with hospital-acquired infection especially in critically ill patients. Multidrug-resistant *A. baumannii* (MDR- *A. baumannii*) has been increasing significantly over the past 15 years especially in carbapenem-resistant *A. baumannii* (CRAB) which is a serious threat to healthcare in Thailand [20]. Due to limited capacity, not all laboratories can identify the bacteria to species level, so it was reported as *Acinetobacter calcoaceticus-baumannii* complex. Therefore, in this report, susceptibility data are presented as those of *Acinetobacter calcoaceticus-baumannii* complex unless a specific aspect is considered, such as carbapenem-resistance, of which data were specified as *A. baumannii.* For *A. calcoaceticus-baumannii* complex, the proportion of CRAB was high around 70.0% (Table 6). The resistance to ampicillin/sulbactam appeared as high as CRAB which was 60.3% (Figure 18).

Table 6. Percentage of antimicrobial resistance in *Acinetobacter calcoaceticus-baumannii* complex in 2017

Antimicrobials	Percentage of resistance (n)
Penicillins	
- Ampicillin/sulbactam	69.8 (10,260)
- Piperacillin/tazobactam	72.8 (27,671)
Cephalosporins	
- Cefotaxime	97.2 (15,358)
- Ceftriaxone	96.7 (17,457)
- Ceftazidime	70.6 (31,795)
- Cefepime	69.3 (2,529)
Carbapenems	
- Imipenem	70.4 (23,171)
- Meropenem	69.8 (32,077)
Fluoroquinolones	
- Ciprofloxacin	70.3 (28,942)
- Levofloxacin	71.5 (15,544)
Aminoglycosides	
- Amikacin	52.1 (33,074)
- Gentamicin	62.3 (29,227)
Miscellaneous	
- Colistin*	0.3 (961)
- Sulfamethoxazole/trimethoprim	59.9 (26,275)
- Tetracycline	83.5 (242)

*Interpreting by minimum inhibitory concentration test (MIC)

Total number of isolates = 37,465

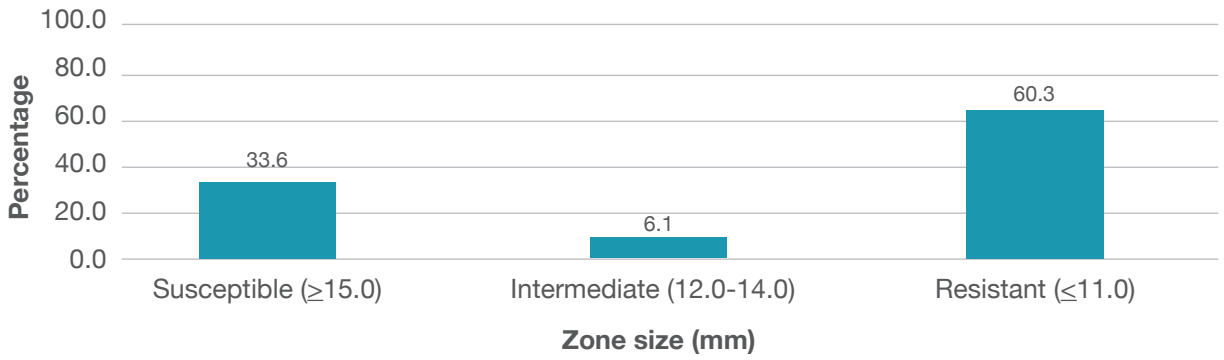

Figure 18. Percentage of susceptible, intermediate and resistance to ampicillin/sulbactam among *Acinetobacter calcoaceticus-baumannii* complex, 2017 (number of isolates = 11,895)

Resistance to colistin was rare and 99.7% of *Acinetobacter calcoaceticus-baumannii* complex remained susceptible to colistin. The colistin minimum inhibitory concentration 50 (MIC_{50}) and 90 (MIC_{90}) from seven hospitals in Thailand were less than 1 mg/L and 1.5 mg/L, respectively (Figure 19).

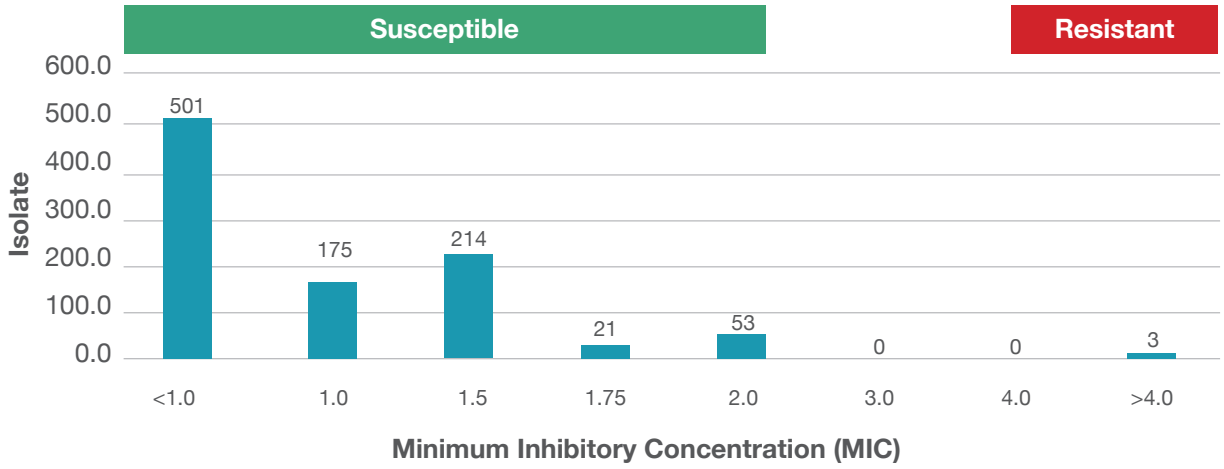

Figure 19. MIC distribution of colistin for *Acinetobacter calcoaceticus-baumannii* complex in 2017 (number of isolates = 967)

1.2 *Pseudomonas aeruginosa (P. aeruginosa)*

P. aeruginosa is gram-negative bacteria that are intrinsically resistant to many antimicrobial agents and has a propensity to become more resistant to active antimicrobial agents via several mechanisms of drug resistance. In recent years, *P. aeruginosa* was identified as a major pathogen causing nosocomial infections and posing trouble for public health.

Table 7. Percentage of antimicrobial resistance in *Pseudomonas aeruginosa* in 2017

Antimicrobials	Percentage of resistance (n)
Penicillins	
- Piperacillin/tazobactam	17.9 (27,651)
Cephalosporins	
- Ceftazidime	18.2 (31,266)
- Cefepime	13.5 (4,764)
Carbapenems	
- Imipenem	19.6 (23,297)
- Meropenem	19.4 (29,240)
Fluoroquinolones	
- Ciprofloxacin	15.3 (28,363)
- Levofloxacin	17.9 (11,981)
- Norfloxacin	38.6 (3,214)
- Ofloxacin	15.5 (1,359)
Aminoglycosides	
- Amikacin	9.7 (30,963)
- Gentamicin	14.8 (28,421)
- Netilmicin	11.7 (6,514)
Miscellaneous	
- Colistin*	0.5 (409)

*Interpreting by minimum inhibitory concentration test (MIC)

Total number of isolates = 34,987

In 2017, 19.4% and 19.6% of *P. aeruginosa* were resistant to meropenem and imipenem, respectively (Table 7). Surprisingly, among these carbapenem-resistant *P. aeruginosa* (CRPA), those remained susceptible to ceftazidime, cefepime and piperacillin/tazobactam at 37.6%, 10.1% and 36.8%, respectively (Figure 20).

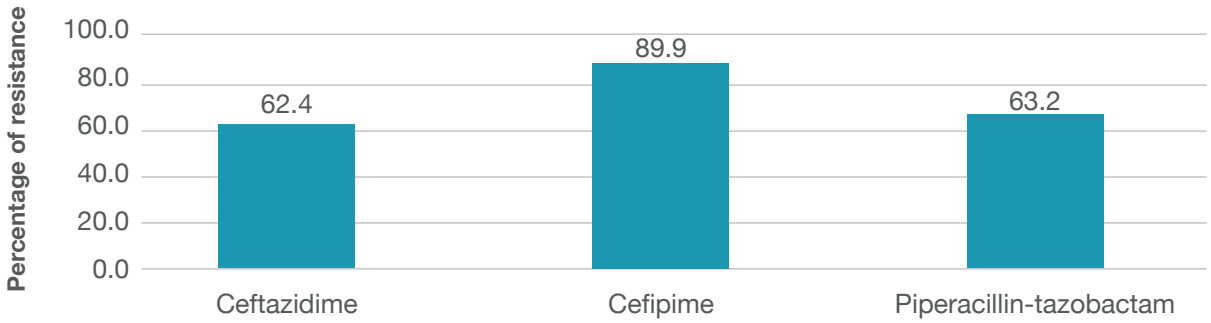

Figure 20. Percentage of antimicrobial resistance among carbapenem-resistant *Pseudomonas aeruginosa* in 2017 (Number of isolates = 9,774)

The presence of *P. aeruginosa* with a higher carbapenem resistance rate than other antibiotics might be related to increased use of carbapenems. Consequently, carbapenems might not be the best choice for *P. aeruginosa*. In addition, CRPA also showed a discordance in susceptibility between meropenem and imipenem. A total of 9.8% of CRPA isolates were susceptible to meropenem but were intermediate or resistant to imipenem, and 6.8% were exactly the opposite (Table 8). These findings can probably be explained by saying that *P. aeruginosa* has multiple resistant mechanisms e.g. efflux pumps or loss of porin as reported elsewhere [21].

Table 8. Percentage of imipenem and meropenem resistance among carbapenem-resistant *Pseudomonas aeruginosa* in 2017

Antimicrobials	Percentage of resistance (n)
Carbapenem	24.1% (9,774)
• Imipenem only	9.8% (955)
• Meropenem only	6.8% (662)
• Imipenem and Meropenem	62.1% (6,068)

Total number of isolates = 40,590

The proportion of colistin-resistant *P. aeruginosa* remained low at 0.5%. Data from seven hospitals in Thailand, MIC_{50} and MIC_{90} for colistin found less than 1.0 mg/L and 1.5 mg/L, respectively (Figure 21).

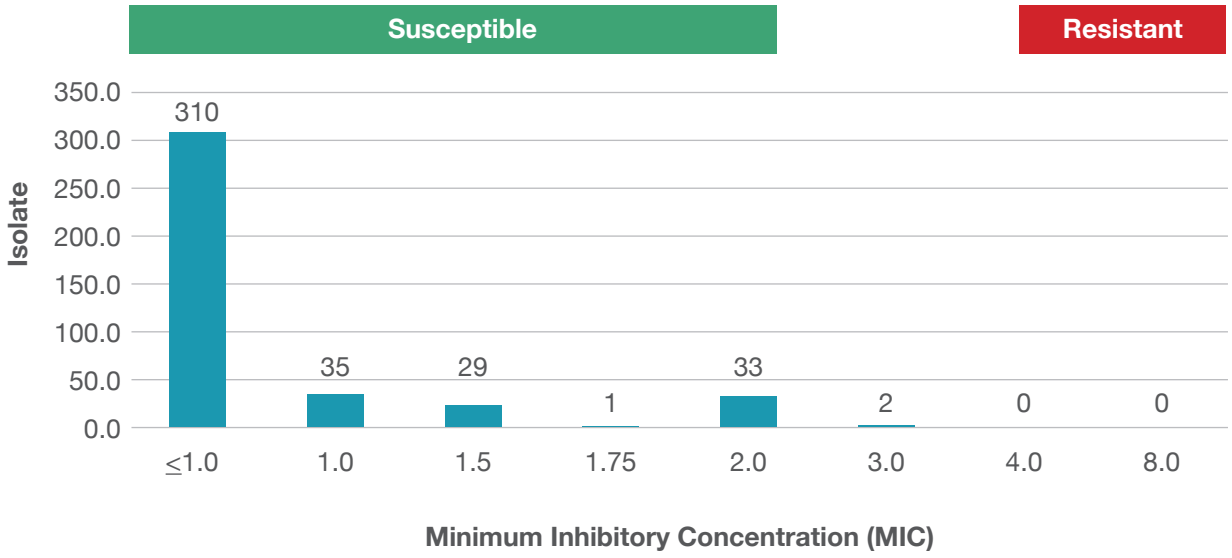

Figure 21. MIC distribution of colistin for *Pseudomonas aeruginosa*, 2017 (number of isolates = 410)

1.3 *Escherichia coli (E. coli)*

E. coli is gram-negative bacteria that is categorized as a member of the *Enterobacteriaceae* family. *E. coli* is a common pathogen that causes community- and hospital-acquired infections such as bloodstream infections (BSI), pneumonia, urinary tract infections (UTI), etc. Third-generation cephalosporins-resistant *Enterobacteriaceae* or extended-spectrum beta-lactamase (ESBLs)-producing *Enterobacteriaceae* has raised concerns over the past decade. There are also ESBLs-producing *Enterobacteriaceae* in community settings in many countries including Thailand. This resistance leads to increased use of carbapenems and eventually leads to carbapenem-resistant *Enterobacteriaceae* (CRE). Accordingly, it is necessary to monitor community-acquired resistant organisms [22].

The percentage of ceftriaxone- and ceftazidime-resistant *E. coli* were 44.0% and 36.0%, respectively. For fluoroquinolone resistance, 52.0% and 51.8% of *E. coli* were resistant to ciprofloxacin and levofloxacin, respectively (Table 9).

Additionally, carbapenem-sparing antibiotics might be alternative agents used for the treatment of third-generation cephalosporins-resistant *Enterobacteriaceae*. For example, cefepime can be given with higher doses if the susceptibility of isolates is in the susceptible-dose dependent (SDD) category. In 2017, 12.4% of *E. coli* were in the cefepime SDD category and 58.5% of the organism were susceptible to cefepime.

Resistant rates of *E. coli* were 2.4%, 2.6% and 2.8% for meropenem, imipenem and ertapenem, respectively. Although these may seem to be low, it is in fact an alarm to indicate a serious AMR problem since these organisms were fully susceptible to all carbapenems in past decades. The data are shown in Table 9.

Table 9. Percentage of antimicrobial resistance in *Escherichia coli*, 2017

Antimicrobials	Percentage of resistance (n)
Penicillins	
- Ampicillin	86.7 (52,360)
- Ampicillin/sulbactam	43.9 (14,915)
- Amoxicillin/clavulanic acid	33.6 (54,705)
- Piperacillin/tazobactam	8.5 (45,229)
Cephalosporins	
- Cefazolin	67.9 (15,913)
- Cefazolin (U)	49.9 (14,836)
- Cefuroxime sodium (PARENTERAL)	47.8 (20,529)
- Cefuroxime sodium (ORAL)	64.2 (676)
- Cefoperazone/sulbactam	10.3 (39,918)
- Cefotaxime	46.2 (54,558)
- Ceftriaxone	44.0 (47,405)
- Ceftazidime	36.0 (64,148)
- Cefepime	40.0 (9,677)
- Cefoxitin	12.3 (21,223)
Carbapenems	
- Ertapenem	2.8 (6,795)
- Imipenem	2.6 (46,313)
- Meropenem	2.4 (55,564)

Antimicrobials	Percentage of resistance (n)
Fluoroquinolones	
- Ciprofloxacin	52.0 (56,661)
- Levofloxacin	50.8 (18,855)
- Ofloxacin	53.1 (7,941)
Aminoglycosides	
- Amikacin	1.5 (61,338)
- Gentamicin	34.3 (61,815)
- Netilmicin	5.2 (11,956)
Miscellaneous	
- Chloramphenicol	23.6 (780)
- Fosfomycin (U)	1.9 (10,296)
- Nitrofurantoin (U)	6.9 (3,214)
- Sulfamethoxazole/trimethoprim	58.4 (58,448)
- Tetracycline	71.8 (5,073)

U = Urine, Urine Catheter, Urine Clean-Voided

Total number of isolates = 74,233

Regarding antimicrobial resistance of *E. coli* isolated from urine, cefazolin was used as a surrogate for oral antimicrobial agents susceptibilities e.g. cefaclor, cefdinir, cefpodoxime, cefuroxime, cephalexin, etc. The percentage of cefazolin resistance was around 50.0% in urinary *E. coli* isolates, therefore, in selected cases, these agents may be viable alternatives to other broad-spectrum agents for uncomplicated urinary tract infections due to *E. coli* (Figure 22).

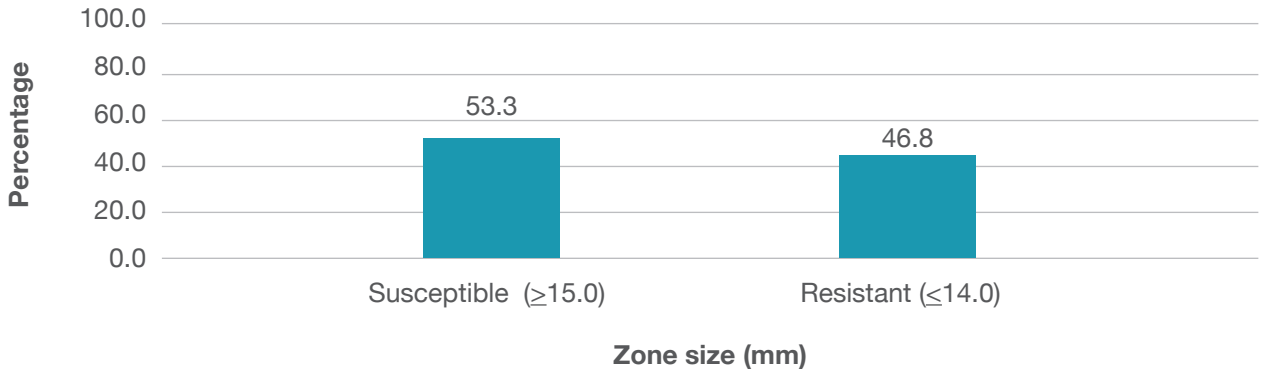

Figure 22. Percentage of susceptible and resistance to cefazolin among urinary isolates of *Escherichia coli*, 2017 (number of isolates = 31,838)

According to the epidemiological cut-off value (ECV) breakpoint of colistin from the Clinical and Laboratory Standards Institute (CLSI) in 2017, a small number of *E. coli* isolates from four hospitals in Thailand showed the colistin MIC ≤ 2 mg/L which were defined as wild-type (Figure 23).

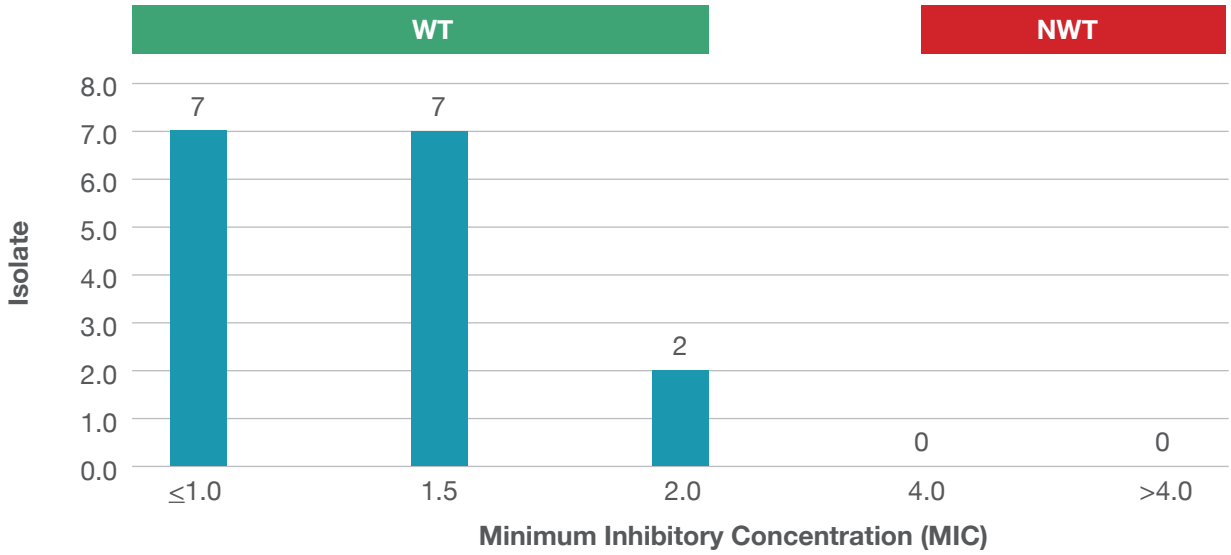

Figure 23. MIC distribution of colistin for *Escherichia coli*, 2017 (number of isolates = 16)

1.4 *Klebsiella pneumoniae* (*K. pneumoniae*)

K. pneumoniae is another member of *Enterobacteriaceae* family. This pathogen is a common cause of various infectious diseases. In Thailand, the rate of carbapenem-resistance has dramatically increased among *K. pneumoniae* and infections caused by this type of resistance are difficult to treat. Increasing resistance in *K. pneumonia* is therefore another challenge in antimicrobial therapy.

Table 10. Percentage of antimicrobial resistance in *Klebsiella pneumoniae*, 2017

Antimicrobials	Percentage of resistance (n)
Penicillins	
- Ampicillin/sulbactam	45.1 (9,857)
- Amoxicillin/clavulanic acid	38.5 (40,752)
- Piperacillin/tazobactam	27.2 (31,444)
Cephalosporins	
- Cefazolin	52.0 (15,505)
- Cefazolin (U)	65.4 (4,001)
- Cefuroxime sodium (PARENTERAL)	46.6 (15,964)
- Cefuroxime sodium (ORAL)	52.5 (505)
- Cefoperazone/sulbactam	25.9 (29,780)
- Cefotaxime	43.6 (40,646)
- Ceftriaxone	42.1 (34,733)
- Ceftazidime	40.6 (46,641)
- Cefepime	33.0 (6,014)
- Cefoxitin	14.9 (16,777)
Carbapenems	
- Ertapenem	11.1 (4,007)
- Imipenem	10.2 (33,180)
- Meropenem	10.1 (41,043)

Antimicrobials	Percentage of resistance (n)
Fluoroquinolones	
- Nalidixic acid (U)	56.7 (240)
- Ciprofloxacin	37.2 (42,293)
- Levofloxacin	26.6 (15,148)
- Norfloxacin (U)	49.8 (8,434)
- Ofloxacin	31.5 (4,221)
Aminoglycosides	
- Amikacin	5.5 (44,951)
- Gentamicin	19.3 (44,574)
- Netilmicin	11.0 (10,178)
Miscellaneous	
- Chloramphenicol	30.1 (754)
- Nitrofurantoin (U)	47.2 (818)
- Sulfamethoxazole/trimethoprim	42.6 (41,802)
- Tetracycline	38.2 (3,107)

U = Urine, Urine Catheter, Urine Clean-Voided

Total number of isolates = 52,906

The proportion of ceftriaxone- and ceftazidime-resistant *K. pneumoniae* were 42.1% and 40.6%, respectively. Furthermore, 5.3% of those were susceptible-dose dependent to cefepime. Hence, the rate of third-generation cephalosporins-resistant *K. pneumoniae* were similar to that of *E. coli*. However, the proportion of fluoroquinolone-resistant *K. pneumoniae* were less than *E. coli,* and 37.2% and 26.6% of those were resistant to ciprofloxacin and levofloxacin, respectively (Table 10).

The rising carbapenem-resistant *Enterobacteriaceae* (CRE) rate is a cause for serious concern, since there are a few therapeutic options to combat these organisms. In 2017, 10.1%, 10.2% and 11.1% of the organisms were resistant to meropenem, imipenem and ertapenem, respectively. From these data, carbapenem-resistant *K. pneumoniae* was greater than carbapenem-resistant *E. coli*. The data are shown in Table 10.

The proportion of urinary isolates of *K. pneumoniae* that were susceptible and resistant to cefazolin appeared similar to *E. coli* and 55.8% of those could be treated with oral cephalosporins (Figure 24).

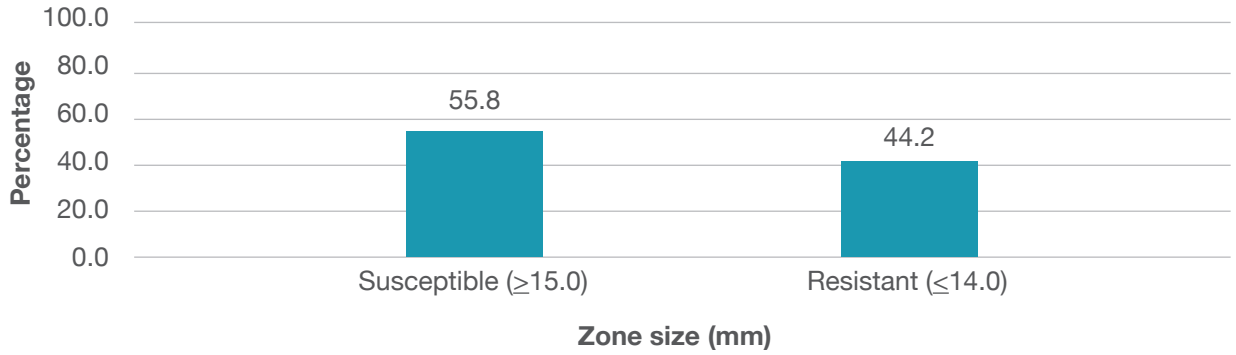

Figure 24. Percentage of susceptible and resistance to cefazolin among urinary isolates of *Klebsiella pneumoniae*, 2017 (number of isolates = 31,838)

In 2017, all *K. pneumoniae* isolates from four hospitals in Thailand remained as wild-type which MIC values were not more than 2 mg/L (Figure 25).

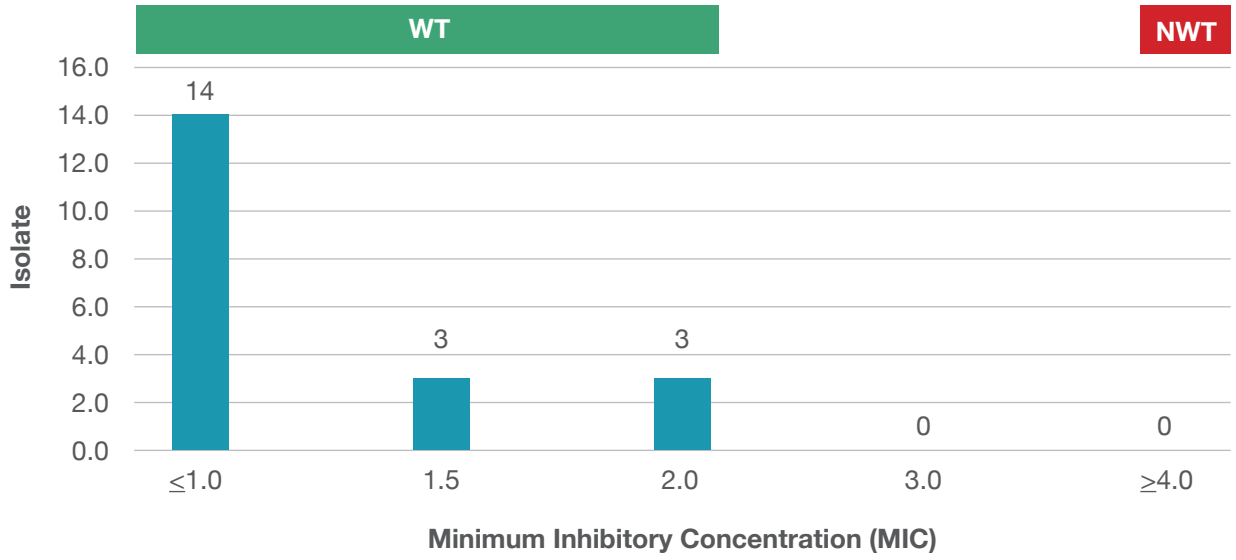

Figure 25. MIC distribution of colistin for *Klebsiella pneumoniae*, 2017 (number of isolates = 20)

1.5 *Enterobacter* spp., *Citrobacter* spp. and *Serratia* spp.

Enterobacter spp., *Citrobacter* spp., and *Serratia* spp., which are gram-negative bacteria, may express high-levels of AmpC-cephalosporinases after being exposed to beta-lactam agents e.g. third-generation cephalosporins and carbapenems; they then become resistant to cephamycin and oxyimino-beta-lactam antibiotics such as ceftriaxone, ceftazidime, cefotaxime, and aztreonam. A large proportion of these bacteria were susceptible to cefepime and piperacillin/tazobactam while almost all of them were susceptible to carbapenems (Table 11).

Table 11. Percentage of antimicrobial resistance in *Enterobacter aerogenes, Enterobacter cloacae, Enterobacter* spp., *Citrobacter freundii* and *Serratia marcescens*, 2017

Antimicrobials	Percentage of resistance in				
	Enterobacter aerogenes, (n) [a]	*Enterobacter cloacae*, (n) [b]	*Enterobacter* spp., (n) [c]	*Citrobacter freundii*, (n) [d]	*Serratia marcescens*, (n) [e]
Penicillins					
- Ampicillin	-	-	93.3 (2,399)	-	-
- Ampicillin/sulbactam	-	-	65.5 (403)	-	-
- Amoxicillin/ clavulanic acid	-	-	86.8 (2,759)	-	-
- Piperacillin/ tazobactam	17.4 (1,463)	17.0 (4,787)	16.0 (1,923)	16.3 (743)	3.0 (630)
Cephalosporins					
- Cefazolin	-	-	92.4 (1,191)	-	-
- Cefazolin (U)	-	-	77.0 (161)		-
- Cefuroxime sodium (PARENTERAL)	-	-	49.3 (535)	-	-
- Cefuroxime sodium (ORAL)	-	-	89.2 (65)	-	-
- Cefoperazone/ sulbactam	12.8 (1,526)	14.2 (4,658)	13.8 (2,140)	14.0 (635)	3.0 (597)
- Cefotaxime	33.8 (2,010)	35.8 (5,810)	36.8 (2,976)	29.9 (952)	9.6 (862)
- Ceftriaxone	29.7 (1,709)	32.4 (5,059)	33.6 (2,410)	29.8 (671)	7.6 (708)
- Ceftazidime	28.0 (2,220)	31.7 (6,925)	27.8 (3,235)	27.8 (1,107)	6.0 (974)
- Cefepime	19.1 (267)	25.6 (906)	25.3 (415)	20.9 (163)	7.0 (171)
- Cefoxitin	-	-	81.7 (763)	-	-

Antimicrobials	Percentage of resistance in				
	Enterobacter aerogenes, (n) [a]	*Enterobacter cloacae*, (n) [b]	*Enterobacter* spp., (n) [c]	*Citrobacter freundii*, (n) [d]	*Serratia marcescens*, (n) [e]
Carbapenems					
- Ertapenem	6.0 (134)	11.7 (521)	5.3 (356)	3.3 (92)	2.4 (82)
- Imipenem	9.1 (1,623)	7.0 (5,254)	11.2 (1,729)	9.7 (826)	1.7 (689)
- Meropenem	4.3 (1,915)	4.3 (5,968)	4.1 (2,470)	5.9 (946)	0.4 (793)
Fluoroquinolones					
- Ciprofloxacin	14.5 (1,972)	19.8 (6,418)	19.7 (2,701)	19.7 (1,016)	5.4 [u] (74)
- Levofloxacin	6.6 (664)	9.5 (2,200)	12.1 (783)	18.4 (277)	2.0 (409)
- Norfloxacin	20.3 (271)	36.8 (1,005)	34.1 (343)	33.6 (283)	1.2 [u] (83)
- Ofloxacin	17.7 (198)	13.8 (529)	13 (531)	13 (77)	1.7 (58)
Aminoglycosides					
- Amikacin	2.3 (2,181)	2.5 (6,695)	3.2 (3,029)	2.1 (1,057)	1.4 (934)
- Gentamicin	13.8 (2,137)	18.0 (6,942)	14.7 (2,686)	15.1 (1,081)	2.5 (952)
- Netilmicin	7.0 (628)	8.6 (1,108)	8.9 (885)	5.1 (117)	0.0 (159)
Miscellaneous					
- Chloramphenicol	-	11.1 (90)	31.0 (113)	-	-
- Nitrofurantoin (U)	46.7 (30)	42.6 (94)	-	-	-
- Sulfamethoxazole/ trimethoprim	20.0 (2,149)	27.9 (6,151)	24.8 (2,960)	27.7 (1,007)	7.2 (842)
- Tetracycline	31.4 (121)	21.9 (406)	31.2 (397)	37.6 (85)	82.5 (57)

U = Urine, Urine Catheter, Urine Clean-Voided

[a] number of isolates = 2,495, [b] number of isolates = 8,067, [c] number of isolates = 3,538, [d] number of isolates = 1,282, [e] number of isolates = 1,220

2. Gram-positive bacteria

2.1 *Staphylococcus aureus (S. aureus)*

S. aureus generally causes skin and soft tissue infections and this pathogen can cause nosocomial infections such as blood-stream infections, infective endocarditis and pneumonia, etc. In Thailand, methicillin-resistant *S. aureus* (MRSA) was typically found in hospital settings, but there were a few case-reports of MRSA from the community. Despite the fact that community-acquired MRSA is very uncommon in Thailand, it remained unclear whether it does currently exist. Therefore, it is necessary to keep this under surveillance.

Table 12. Percentage of antimicrobial resistance in *Staphylococcus aureus* and *Staphylococcus* coagulase negative, 2017

Antimicrobials	Percentage of resistance in *Staphylococcus aureus*, (n) [a]	Percentage of resistance in *Staphylococcus* coagulase negative, (n) [b]
Peniciliins		
- Penicillin	92.0 (12,547)	87.0 (13,732)
- Penicillin*	92.0 (450)	97.5 (770)
- Oxacillin	9.6 (26,584)	53.2 (25,096)
Fluoroquinolones		
- Ciprofloxacin	14.0 (6,983)	37.8 (6,009)
- Ciprofloxacin*	14.0 (278)	41.6 (173)
- Levofloxacin	12.0 (4,788)	37.3 (3,937)
- Norfloxacin (U)	15.2 (705)	48.0 (1,074)
- Ofloxacin	9.8 (663)	37.5 (869)
Aminoglycosides		
- Amikacin	3.7 (1,098)	6.2 (838)
- Gentamicin	7.5 (18,653)	28.0 (15,957)
- Netilmicin	0.0 (121)	6.5 (31)
Glycopeptides		
- Vancomycin	0.1 (1,176)	0.0 (322)

Antimicrobials	Percentage of resistance in *Staphylococcus aureus*, (n) [a]	Percentage of resistance in *Staphylococcus* coagulase negative, (n) [b]
Miscellaneous		
- Chloramphenicol	5.1 (3,233)	9.7 (3,406)
- Clindamycin	14.0 (24,651)	46.8 (23,082)
- Clindamycin*	20.8 (268)	54.5 (165)
- Erythromycin	17.0 (24,990)	57.4 (24,178)
- Erythromycin*	21.3 (268)	61.2 (165)
- Nitrofurantoin (U)	2.1 (47)	6.7 (45)
- Sulfamethoxazole/ Trimethoprim	3.4 (25,483)	33.7 (24,005)
- Tetracycline	42.2 (6,552)	43.9 (5,717)

*Interpreting by minimum inhibitory concentration test

U = Urine, Urine Catheter, Urine Clean-Voided

[a] number of isolates = 31,257, [b] number of isolates = 28,580

The MRSA rate has been decreasing for years. On the contrary, the rate of methicillin-resistant coagulase-negative *Staphylococcus* spp. (MRCNS) has continuously increased. In 2017, the proportion of MRSA among *Staphylococcus aureus* accounted for 9.6%, but the proportion of MRCNS was at 53.2% (Figure 26).

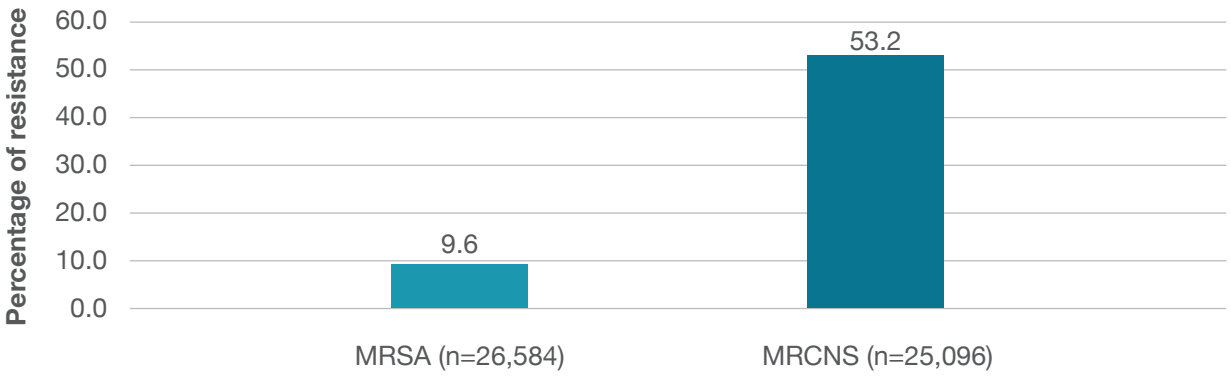

Figure 26. Percentage of methicillin resistance among *Staphylococcus aureus* (MRSA) and *Staphylococcus* coagulase negative (MRCNS), 2017

A total of 99.9% of *S. aureus* and all *Staphylococcus* coagulase negative were still susceptible to vancomycin (Table 12).

2.2 *Enterococcus* spp.

Enterococci are gram-positive bacteria commonly found in the gastrointestinal (GI) tract. It can be a cause of infection such as blood-stream infection, urinary tract infection, skin and soft tissue infection, and intra-abdominal infection. The emergence of Vancomycin-Resistant *Enterococcus* (VRE) has been observed in Thailand, which may reflect suboptimal infection prevention and control practice as well as problems in the use of vancomycin. VRE is another drug-resistant trait that may pose an important health threat to patients in the near future if no action is taken.

The antimicrobial susceptibility of *E. faecalis* showed only 5.2% resistance to ampicillin, but ampicillin-resistant *E. faecium* appeared higher at 90.1%. Furthermore, 8.8% of *E. faecium* isolates were VRE and only 2.3% for *E. faecalis*. Thereby, the ability to identify species of *Enterococcus* spp. is crucial to guiding antimicrobial treatment for enterococcal infections. The data are shown in Table 13.

Table 13. Percentage of antimicrobial resistance in *Enterococcus faecalis, Enterococcus faecium* and *Enterococcus* spp., 2017

Drug	*Enterococcus faecalis,* (n) [a]	*Enterococcus faecium,* (n) [b]	*Enterococcus* spp., (n) [c]
Penicillins			
- Penicillin	30.6 (9,064)	91.1 (4,224)	55.2 (3,659)
- Penicillin*	-	79.3 (87)	-
- Ampicillin	5.2 (12,886)	90.1 (66,970)	37.8 (4,891)
Fluoroquinolones (U)			
- Ciprofloxacin	77.1 (2,094)	96.2 (1,284)	86.3 (512)
- Levofloxacin	64.1 (1,497)	93.2 (789)	77.6 (1,057)
- Norfloxacin	72.2 (5,909)	95.8 (3,506)	77.1 (1,557)
Aminoglycosides			
- Gentamicin 120 mg	45.6 (10,513)	37.6 (5,720)	39.6 (4,033)
Glycopeptides			
- Vancomycin	2.3 (13,253)	8.8 (6,724)	3.2 (5,203)
- Teicoplanin	0.4 (1,872)	15.8 (877)	9.1 (231)

Drug	*Enterococcus faecalis*, (n) [a]	*Enterococcus faecium*, (n) [b]	*Enterococcus* spp., (n) [c]
Miscellaneous			
- Chloramphenicol	30.5 (1,959)	10.7 (822)	-
- Erythromycin	86.1 (2,664)	91.4 (1,087)	78.2 (910)
- Fosfomycin (U)	8.1 (3,200)	-	-
- Nitrofurantoin (U)	2.0 (549)	70.6 (466)	32.2 (102)
- Tetracycline (U)	92.8 (2,658)	96.0 (1,519)	90.9 (1,044)

*Interpreting by minimum inhibitory concentration test

U = Urine, Urine Catheter, Urine Clean-Voided

[a] number of isolates = 14,836, [b] number of isolates = 7,553, [c] number of isolates = 5,461

2.3 *Streptococcus pneumoniae (S. pneumoniae)*

S. pneumoniae is gram-positive bacteria and is the most common cause of various community-acquired infections affecting different organ systems, for instance, pneumonia, sinusitis, otitis media, meningitis, etc. Penicillin non-susceptible *S. pneumoniae* indicates decreased activity of penicillin antibiotics against *S. pneumoniae* because the susceptibility breakpoints for this pathogen are different than if they are obtained from a different body site, i.e., meningeal or non-meningeal.

Table 14. Percentage of antimicrobial resistance in *Streptococcus pneumoniae*, 2017

Antimicrobials	All isolates, (n) [a]	Meningitis, (n)	Non-meningitis, (n)
Beta-lactams			
- Penicillin*	65.8 (371)	50.0 (2)	10.0 (369)
- Cefotaxime*	-	0.0 (11)	0.0 (144)
Fluoroquinolones			
- Levofloxacin	0.9 (1,437)	-	-
- Ofloxacin	0.6 (163)	-	-
Glycopeptides			
- Vancomycin	0.2 (3,217)	-	-

Antimicrobials	All isolates, (n) [a]	Meningitis, (n)	Non-meningitis, (n)
Miscellaneous			
- Chloramphenicol	9.7 (1,356)	-	-
- Clindamycin	30.1 (2,895)	-	-
- Erythromycin	35.6 (3,099)	-	-
- Sulfamethoxazole/ trimethoprim	55.7 (2,650)	-	-
- Tetracycline	72.4 (1,464)	-	-

*Interpreting by minimum inhibitory concentration test

[a] number of isolates = 3,842

The susceptibility breakpoints of penicillin and cefotaxime for *S. pneumoniae* meningitis isolates have a MIC value of ≤0.1 mg/L and ≤0.5 mg/L, respectively. The proportion of *S. pneumoniae* isolates from cerebrospinal fluid (CSF), which were resistant to penicillin and cefotaxime, accounted for 50.0% and 0.0% respectively (Table 14). However, the number of tested isolates was very small.

For non-meningitis cases, the strains with penicillin MIC value ≤2 mg/L susceptible to penicillin and cefotaxime MIC ≤1 mg/L were cefotaxime-susceptible. The data showed that 10.0% and 0.0% of pneumococcal non-meningitis isolates were resistant to penicillin and cefotaxime respectively. The data are shown in Table 14.

3. Other antimicrobial-resistant bacteria

3.1 Non-typhoidal *Salmonella* spp.

Salmonella spp. is gram-negative, non-lactose fermenting bacteria that is a common enteric pathogen. Non-typhoidal *Salmonella* spp. commonly causes food-borne infections, for example, acute gastroenteritis, bloodstream and focal infections, especially in immunocompromised patients.

Table 15. Percentage of antimicrobial resistance in Non-typhoidal *Salmonella* spp. from extraintestinal isolates, 2017

Drug	Percentage of resistance (n)
Penicillins	
- Ampicillin	52.1 (2,197)
Cephalosporins	
- Cefoperazone/sulbactam	0.9 (560)
- Cefotaxime	15.2 (1,622)
- Ceftriaxone	15.1 (1,306)
- Ceftazidime	14.3 (1,143)
Fluoroquinolones	
- Nalidixic acid (U)	51.9 (79)
- Ciprofloxacin	4.6 (1,867)
- Levofloxacin	6.8 (367)
- Ofloxacin	6.4 (157)
Miscellaneous	
- Chloramphenicol	22.7 (432)
- Sulfamethoxazole/trimethoprim	14.3 (2,295)

U = Urine, Urine Catheter, Urine Clean-Voided

Total number of isolates = 2,668

Findings revealed that 14.3% of non-typhoidal *Salmonella* spp. were resistant to co-trimoxazole and 4.6% were resistant to ciprofloxacin defined by disk diffusion method (Table 15). However according to CLSI guidelines, determination of ciprofloxacin MIC by agar or broth dilution is preferred over disk diffusion. Because of the high cost associated with the MIC test, the recommended method has not been able to be carried out in a large number of microbiology laboratories until now. There were 13 isolates performed through MIC, which showed that 23.1% and 30.8% of the isolates were resistant and intermediate-resistant to ciprofloxacin, respectively (Figure 27).

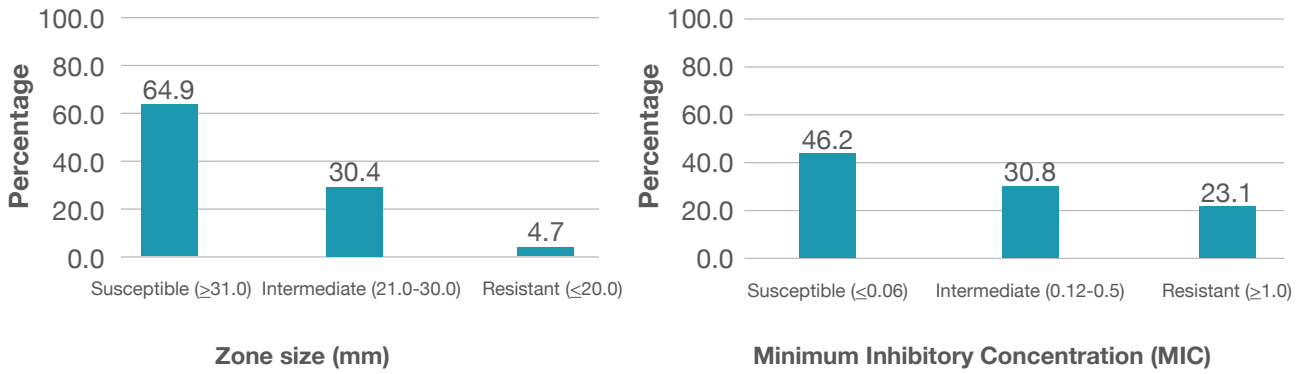

Figure 27. Percentage of susceptible, intermediate and resistance to ciprofloxacin among *Salmonella* spp., 2017

Of total isolates, 15.1% and 14.3% of non-typhoidal *Salmonella* spp. were resistant to ceftriaxone and ceftazidime, respectively. The data are shown in Table 15.

3.2 *Neisseria gonorrhoeae* (*N. gonorrhoeae*)

N. gonorrhoeae is gram-negative cocci bacteria that usually has been reported as common cause of STI. The proportion of antimicrobial resistance in *N. gonorrhoeae* in Thailand showed that none of the isolates were resistant to ceftriaxone and cefixime or gentamicin and spectinomycin. The data are shown in Table 16. In addition, azithromycin-resistant *N. gonorrhoeae* were very rare, and only one strain of those with MIC >1 mg/L had been reported.

Table 16. Percentage of antimicrobial resistance in *Neisseria gonorrhoeae*, 2017

Drug	% resistance, (n) [a]	MIC_{90} (mg/L), (n) [b]
Penicillins		
- Penicillin	99.5 (173)	>32.0 (18)
Cephalosporins		
- Cefixime	0.0 (496)	0.016 (441)
- Ceftriaxone	0.0 (495)	0.008 (484)
Fluoroquinolones		
- Ciprofloxacin	96.8 (462)	8.0 (321)
Aminoglycosides		
- Gentamicin	0.0 (407)	8.0 (407)
- Spectinomycin	0.0 (174)	12.0 (19)
Macrolides		
- Azithromycin	0.2 (441)	0.3 (441)
Miscellaneous		
- Tetracycline	94.1 (10)	24.0 (171)

[a] number of isolates = 506, [b] number of isolates = 485

3.1.4 Limitations

- This report did not identify risk factors linked with baseline characteristics of patients and did not show the distribution of isolates from different hospital levels (primary, secondary or tertiary care). All types of specimen were included in the report. This report did not divide isolates into those from outpatient or inpatient hospital departments including intensive care units.
- Due to the cost of the MIC test, most of the *Staphylococcus aureus* and coagulase-negative *Staphylococcus* spp. isolates were tested by disk diffusion method, instead of the MIC test for vancomycin that is recommended by the CLSI guideline.
- The limited number of *Acinetobacter* spp., *Pseudomonas aeruginosa*, and *Enterobacteriaceae* isolates were tested against colistin to determine MIC.

- A one-year analysis of data was insufficient to draw a conclusion of resistant infectious trends in Thailand.
- The tables in this report were illustrated only the percentage of resistance, while the percentage of intermediate susceptibility are reported as the percentage of resistance, with the exception of Table 15 that shows only percentage of resistance in non-typhoidal *Salmonella*, not including intermediate susceptibility.

3.1.5 Prospects

- Incomplete data from the existing surveillance system reflects insufficiency in resources and knowledgeable laboratory personnel as well as administrative support. If we would like to manage AMR more effectively, support from high-level administration is urgently needed or we could lose the war against these problematic organisms.
- The data regarding trends towards antimicrobial resistance should be observed for several years in order to assess their evolution and situation of antimicrobial resistance problems in Thailand. This will contribute substantially to addressing the problem by implementing effective antimicrobial stewardship policies and infection control programmes.
- Systematically combining data on antimicrobial consumption and antimicrobial resistance at patient, hospital, and community level should be done for further analysis of the correlation between them. This probably reflects the relationship between antimicrobial use and antimicrobial resistance problems.
- Antimicrobial resistance data should be separately analyzed into specimen types and should be stratified by healthcare service sectors, e.g. outpatient, inpatient, intensive care.
- Regional antimicrobial resistance rate should be further analyzed.
- Further analysis of empiric therapy combination by determining in vitro rates of susceptibility to potential antimicrobial combination regimens should be conducted in order to develop empirical antimicrobial treatment guidelines for highly antimicrobial resistant organisms.
- Antimicrobial resistance genes in highly antimicrobial resistant organisms, e.g. CRE or carbapenemase genes in *Enterobacteriaceae* should be identified and reported. This information may be of value in developing treatment guidelines that suggest reasonable therapeutic options from the essential medicines list.
- Data on antimicrobial resistance in viruses, fungi and *Mycobacterium tuberculosis* is planned to be reported in the future.

3.2 Antimicrobial resistance in food-producing animals

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Key summary

Escherichia coli

In 2017, *E. coli* isolates from chicken samples were commonly resistant to ampicillin, sulfamethoxazole and tetracycline. In pigs, *E. coli* isolates were commonly resistant to ampicillin, sulfamethoxazole, tetracycline and trimethoprim. None of the *E. coli* isolates in pig samples were resistant to meropenem.

***Salmonella* spp.**

The high resistance rate of *Salmonella* spp. isolates in pigs and chickens was found in ampicillin, sulfamethoxazole, tetracycline, and trimethoprim. None of the isolates in both chicken and pig samples were resistant to meropenem.

***Campylobacter* spp.**

Campylobacter isolates from chicken cecum samples were commonly resistant to ampicillin, sulfamethoxazole, tetracycline and trimethoprim. In pig cecum samples, *Campylobacter* isolates were commonly resistant to streptomycin and erythromycin.

***Enterococcus* spp.**

Enterococcus isolates from both chicken and pig samples were commonly resistant to erythromycin, tetracycline and streptomycin. The resistance rate to vancomycin was approximately 2.0% in chicken and pig isolates, but none of the isolates were resistant to teicoplanin.

3.2.1 General

In response to the global agenda on AMR and Thailand's NSP-AMR 2017-2021, the Department of Livestock Development is taking clear action. In 2016, ten laboratories under the National Institute of Animal Health (NIAH), Bureau of Quality Control of Livestock Product, and Regional Veterinary Research and Development Center have performed staff training, built laboratory capacities, and implemented standard methods of antimicrobial susceptibility testing (AST) for AMR prior to starting the national surveillance of AMR in 2017.

3.2.2 Data source

The national surveillance of AMR in food-producing animals has been conducted in broiler chicken and pigs, since they are highly consumed in the country. This surveillance was conducted across the food-chain from slaughterhouse (cecum and meat samples) to retail stores (meat samples). In 2017, a total of 5,900 samples were obtained from all over the country. The sample size was calculated based on the World Organisation for Animal Health (OIE)'s Chapter 6.8 of Harmonization of National Antimicrobial Resistance Surveillance and Monitoring Program in 2017 [23]. All samples were transported to and tested at DLD laboratories. The target bacteria of AMR surveillance included zoonotic bacteria (*Salmonella* spp. and *Campylobater* spp.) and indicator bacteria (*Enterococcus* spp. and *Escherichia coli*). AST was performed based on the CLSI, ISO 20776-1, and the European Committee on Antimicrobial Susceptibility Testing (EUCAST). The tested antimicrobials were included as follows:

- Polymyxins (colistin)
- Fluoroquinolones (ciprofloxacin)
- 3rd generation cephalosporins (cefotaxime and ceftazidime)
- Antibiotics which have been banned or are not used in livestock, but were included for surveillance purposes, including carbapenems (meropenem), amphenicols (chloramphenicol), glycopeptides and lipoglycopeptide (vancomycin and teicoplanin), oxazolidinones (linezolid) and glycylcyclines (tigecycline).
- Other antibiotic groups used in livestock including sulfonamides, dihydrofolate reductase inhibitors and combinations (sulfamethoxazole and trimethoprim) and aminoglycosides (gentamicin and streptomycin).

Process of sample collection, microbiological testing, and data analysis is shown in Figure 28.

The responsible agency	1. National Institute of Animal Health 2. Bureau of Quality Control of Livestock Product 3. Regional Veterinary Research and Development Center 4. Division of Animal Feed and Veterinary Products Control	
Target animal	Broiler chickens and pigs	
Target sample and responsible organization	Cecum of broiler chickens and pigs were performed by the National Institute of Animal Health, and Regional Veterinary Research and Development Center.	Chicken and pork were performed by Bureau of Quality Control of Livestock Product, and Regional Veterinary Research and Development Center.
Location	Slaughterhouses	Slaughterhouses and retailers
Target bacterial isolates	*E. coli* *Salmonella* spp. *E. faecium* and *E. faecalis* *C. coli* and *C. jejuni*	*E. coli* *Salmonella* spp.
Antibiotics Susceptibility Testing (AST)	MIC determination: Broth microdilution Conventional method and automated MIC device	
Reference	WHO, OIE, FAO, CLSI, EUCAST and ISO 20776-1	
Drug panel for AST	Cover of all class of antibiotics for testing pathogen reference from CLSI, EUCAST and European Food Safety Authority (EFSA)	

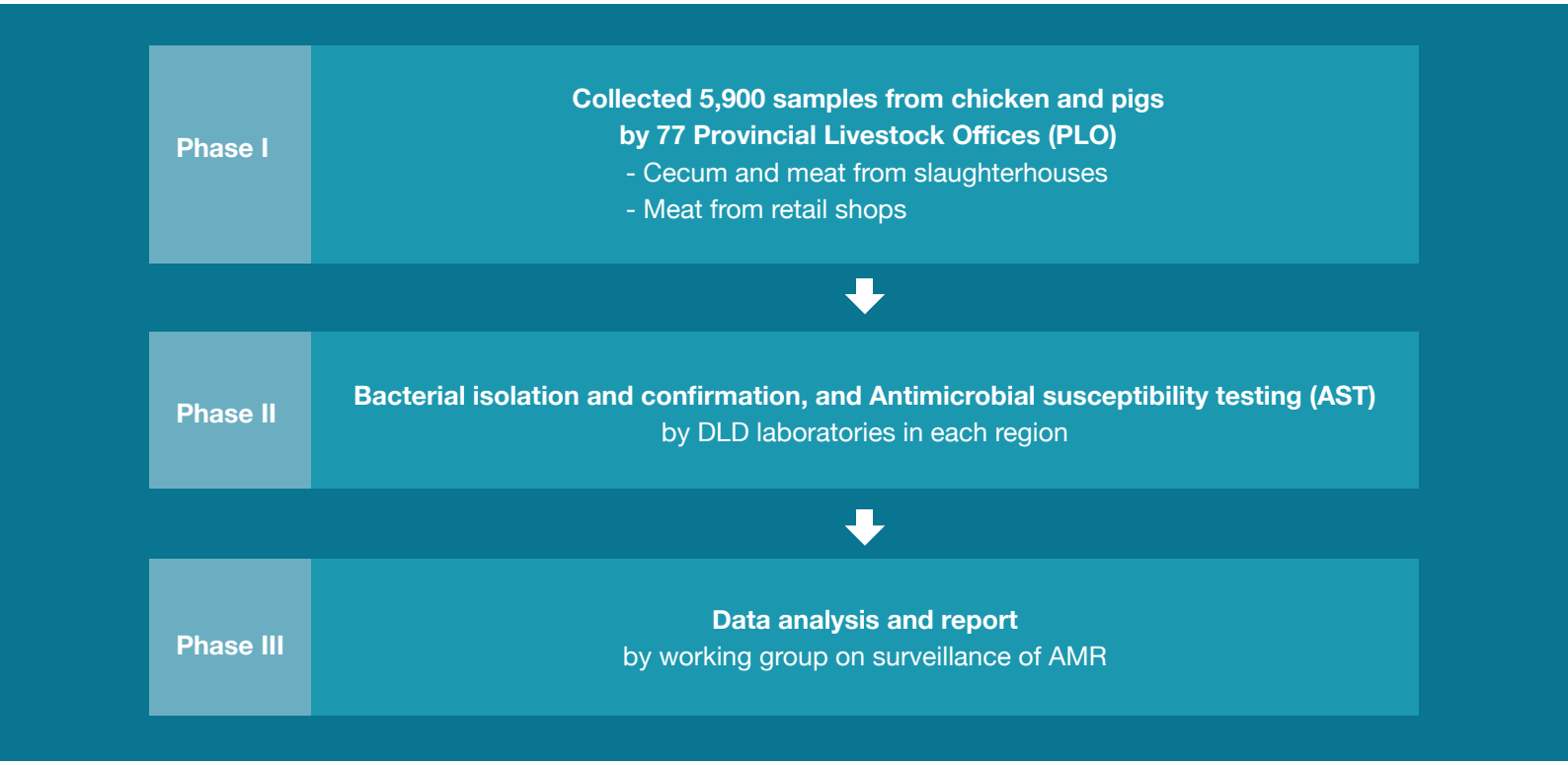

Figure 28. Process of sample collection, microbiological testing, and data analysis

3.2.3 Results

1. *Escherichia coli*

1.1 Chickens

E. coli isolated from cecum and chicken meat samples were resistant to ampicillin, cefotaxime, ceftazidime, chloramphenicol, ciprofloxacin, colistin, gentamicin, meropenem, sulfamethoxazole, tetracycline, tigecycline and trimethoprim. The highest AMR rate in cecum and chicken were found in ampicillin (91.4% and 90.6%), followed by sulfamethoxazole (80.6% and 85.0%) and tetracycline (72.7% and 81.6%), respectively. The AMR rate of *E. coli* isolated from cecum and chicken were 31.0% and 39.3% in chloramphenicol, 30.8% and 46.3% in ciprofloxacin, and 14.5% and 17.4% in colistin, respectively (Figure 29).

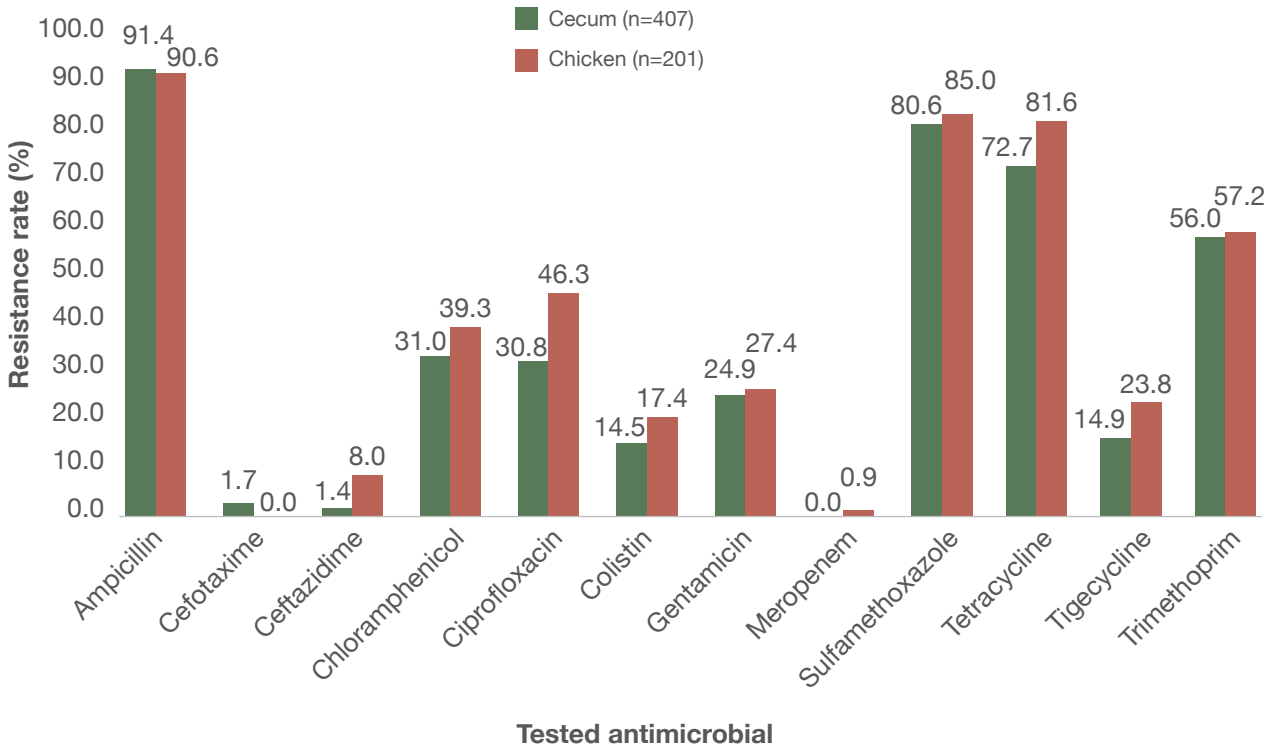

Figure 29. Percentage of antimicrobial-resistant *E. coli* isolated in slaughterhouses (chicken cecum and meat) and retail markets (meat) in 2017 (chicken cecum=407, chicken meat=201)

1.2 Pigs

The cecum and pork samples were commonly resistant to ampicillin, sulfamethoxazole, tetracycline and trimethoprim. The AMR rate of *E. coli* isolates from cecum and pork were 93.0% and 81.0% of ampicillin, 83.3% and 85.6% of sulfamethoxazole, and 71.3% and 80.5% of tetracycline, respectively.

The lower rate of AMR was observed in ceftazidime, cefotaxime, tigecycline and ciprofloxacin. None of the *E. coli* isolates obtained from cecum and pork samples were resistant to meropenem (Figure 30).

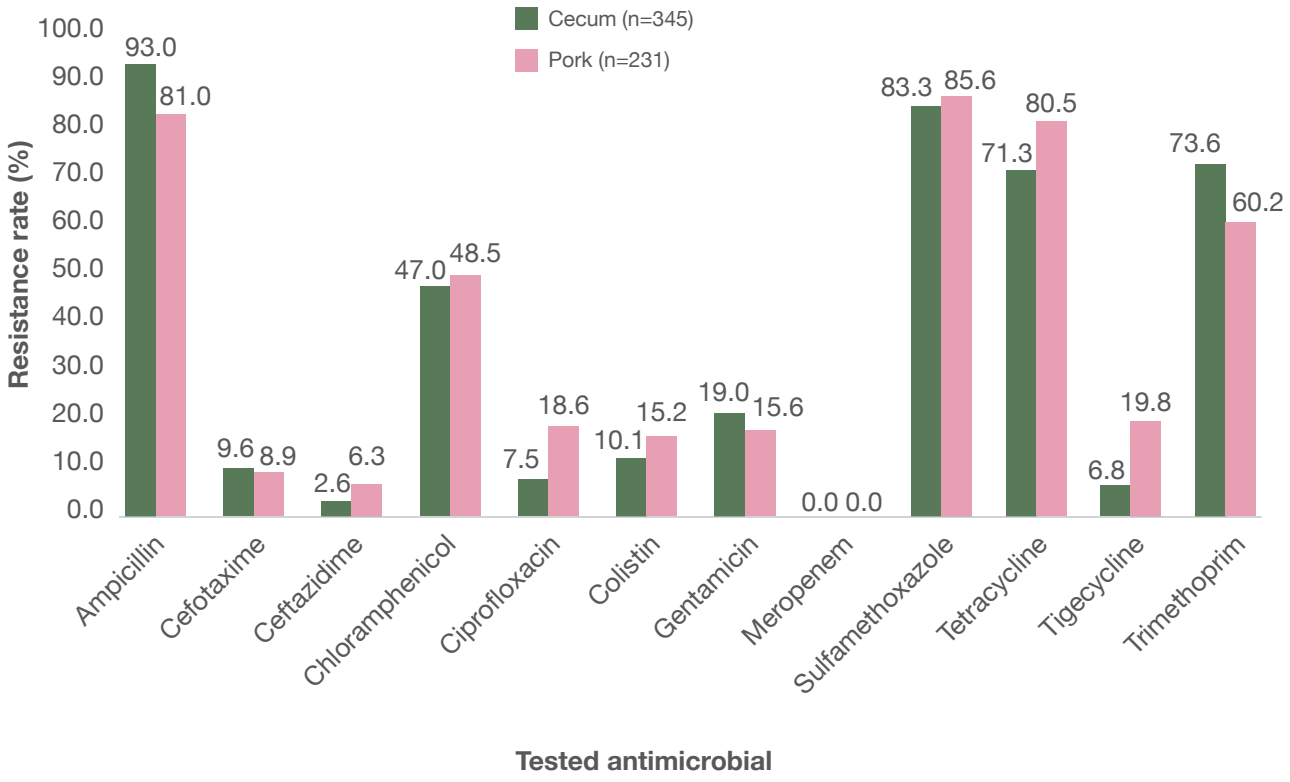

Figure 30. Percentage of antimicrobial-resistant *E. coli* isolated in slaughterhouses (porcine cecum and pork) and retail markets (pork) in 2017 (pig cecum=345, pork meat=231)

2. *Salmonella* spp.

2.1 Chicken

In general, AMR was commonly found in sulfamethoxazole (77.3% in cecum and 81.0% in chicken), ampicillin (78.3% in cecum and 74.1% in chicken), tetracycline (45.6% in cecum and 62.7% in chicken), and trimethoprim (52.3% in cecum and 45.8% in chicken), respectively.

In other antibiotics, AMR rates were detected in ciprofloxacin (22.8% in cecum and 26.5% in chicken), chloramphenicol (17.0% in cecum and 16.9% in chicken), colistin (12.4% in cecum and 19.3% in chicken), and gentamicin (13.9% in cecum and 12.7% in chicken). None of the *Salmonella* spp. isolates obtained from cecum and chicken in 2017 were resistant to meropenem (Figure 31).

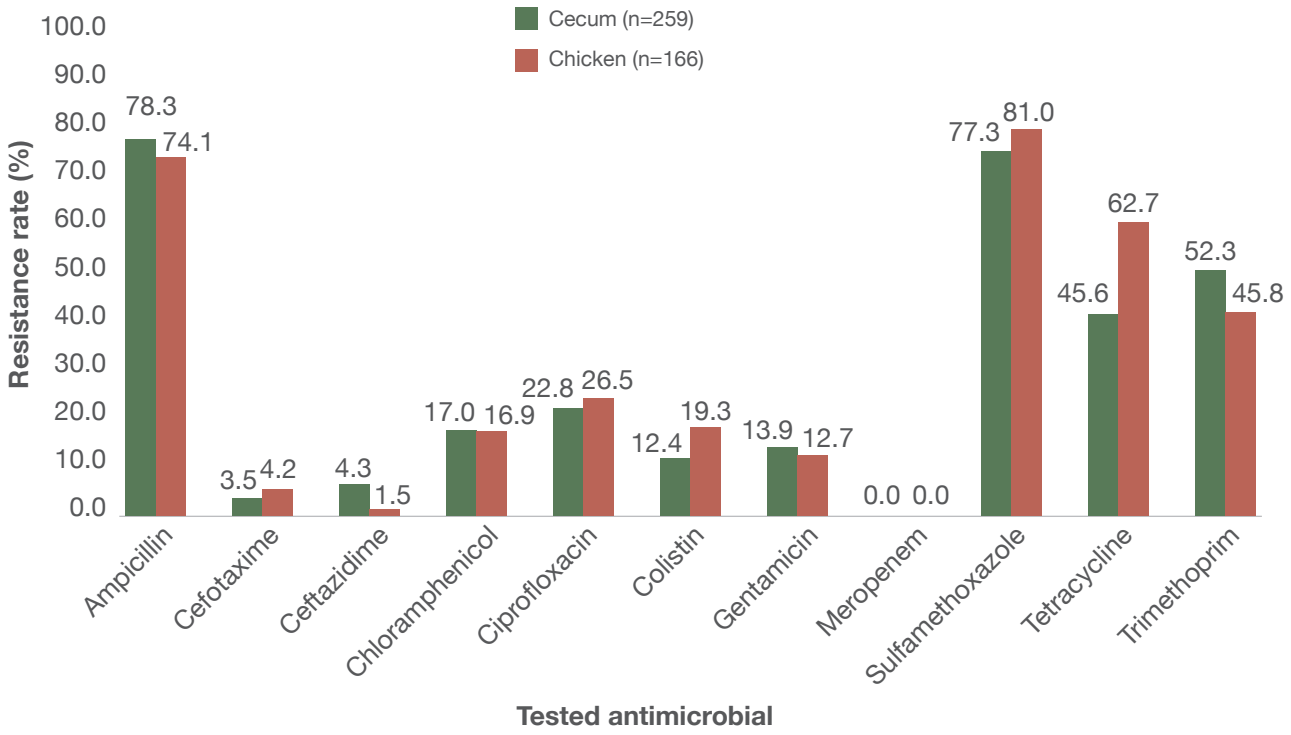

Figure 31. Percentage of antimicrobial-resistant *Salmonella* spp. isolated in slaughterhouses (chicken cecum and meat) and retail markets (meat) in 2017 (chicken cecum=259, chicken meat=166)

2.2 Pigs

AMR was commonly found in ampicillin (84.5% in cecum and 82.9% in pork), sulfamethoxazole (81.2% in cecum and 80.0% in pork), tetracycline (70.2% in cecum and 70.8% in pork), and trimethoprim (55.1% in cecum and 46.7% in pork), respectively.

AMR rates were detected to ceftazidime (34.1% in cecum and 5.4% in pork), chloramphenicol (23.0% in cecum and 23.8% in pork), colistin (15.5% in cecum and 16.3% in pork), and cefotaxime (9.1% in cecum and 7.1% in pork). None of the *Salmonella* spp. isolates obtained from both cecum and pork in 2017 were resistant to meropenem (Figure 32).

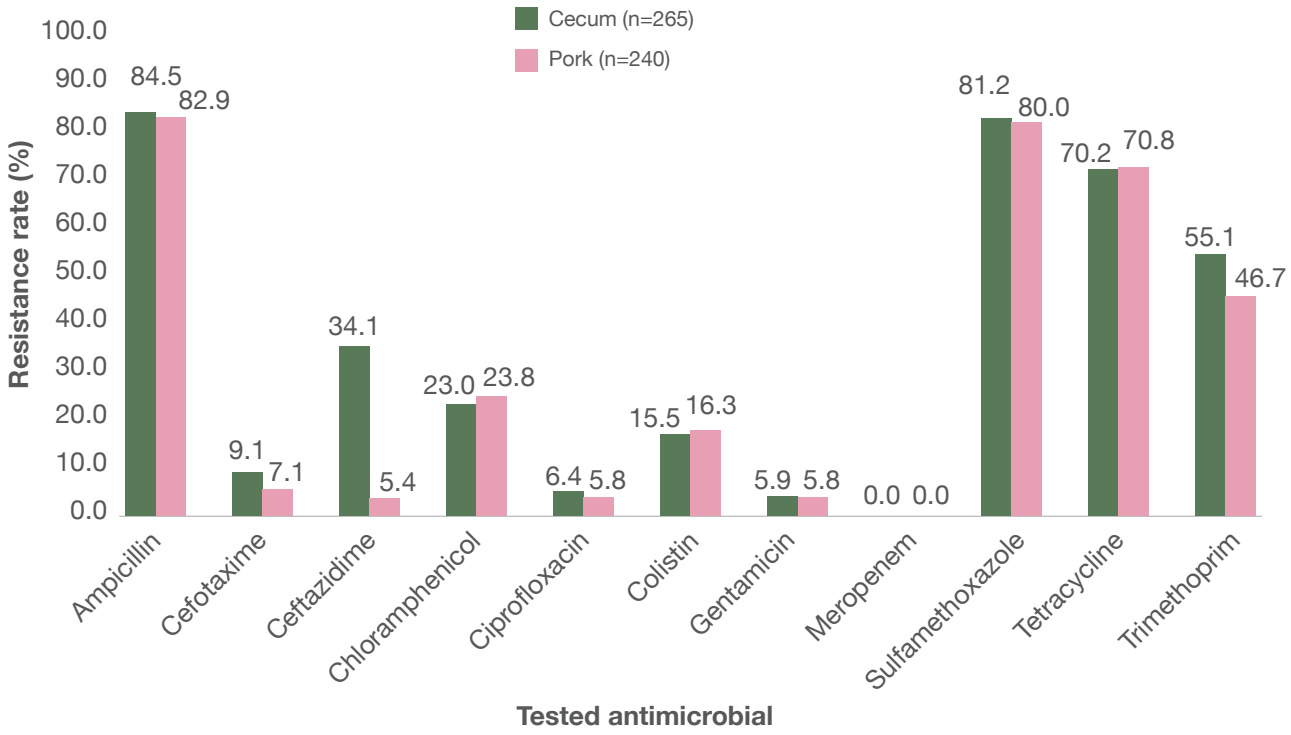

Figure 32. Percentage of antimicrobial-resistant *Salmonella* spp. isolated in slaughterhouses (porcine cecum and pork) and retail markets (pork) in 2017 (pig cecum=265, pork meat=240)

3. *Campylobacter* spp.

3.1 Chicken

Campylobacter isolates from cecum samples in slaughterhouses and retail markets were commonly resistant to ciprofloxacin (39.4%), followed by tetracycline (32.2%), streptomycin (23.6%), and erythromycin (23.1%) (Figure 33).

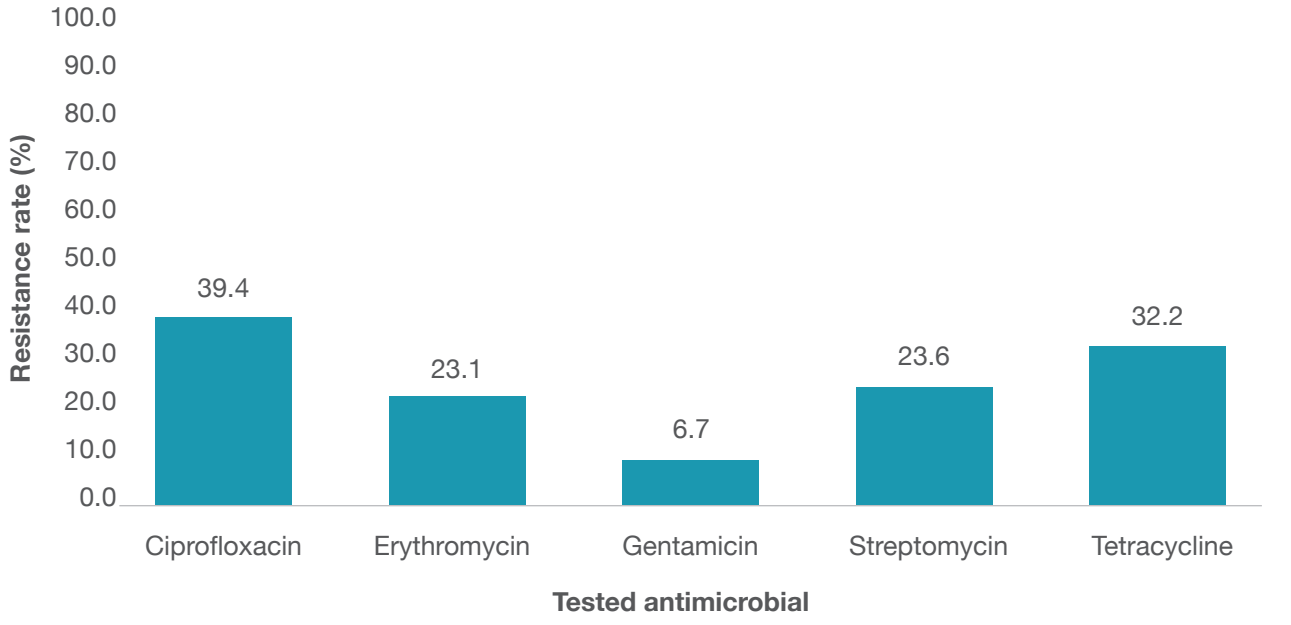

Figure 33. AMR rate of *Campylobacter* spp. isolated from chicken cecum samples (n=208) in 2017

3.2 Pigs

Campylobacter isolates were commonly resistant to streptomycin (61.3%), followed by erythromycin (51.3%), tetracycline (35.3%), and ciprofloxacin (33.3%) (Figure 34).

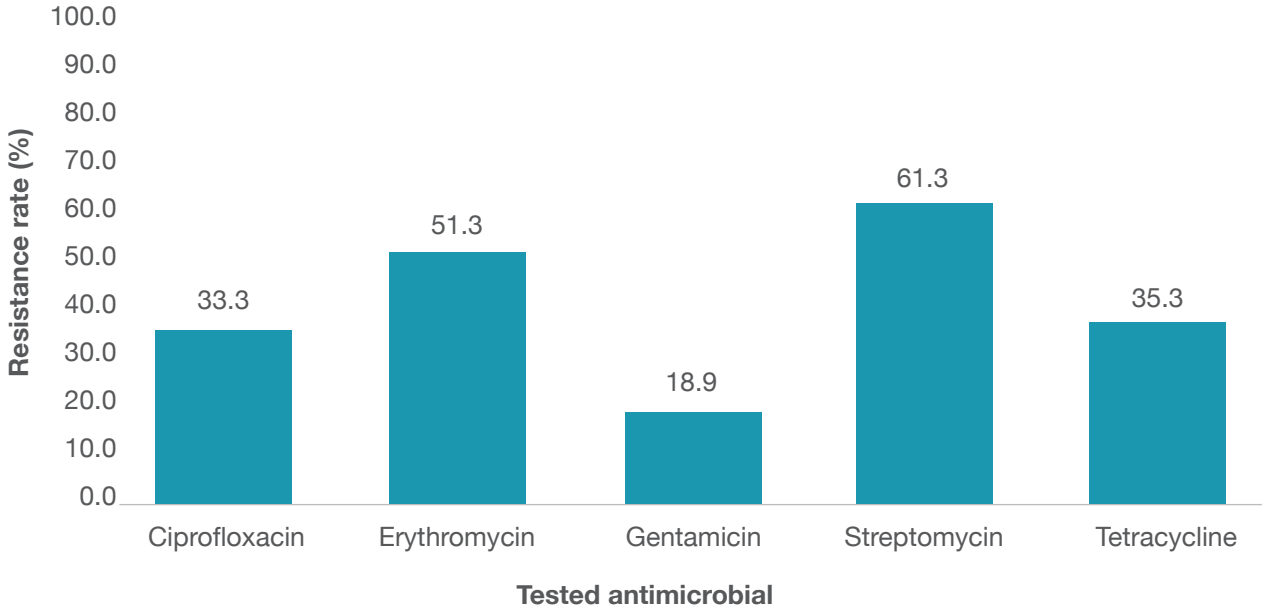

Figure 34. AMR rate of *Campylobacter* spp. isolated from porcine cecum samples (n=150) in 2017

4. *Enterococcus* spp.

4.1 Chicken

Enterococcus isolates were commonly resistant to erythromycin (83.4%), tetracycline (80.0%), and streptomycin (39.8%) (Figure 35).

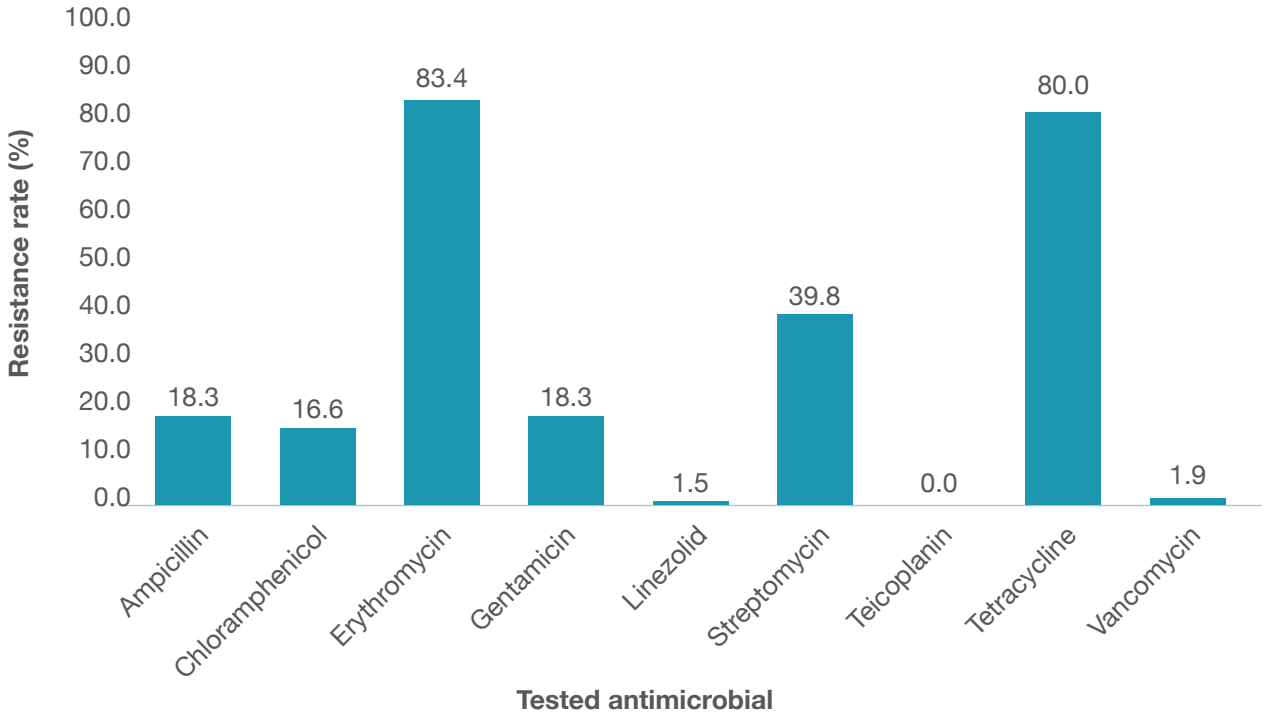

Figure 35. AMR rate of *Enterococcus* spp. isolated from chicken cecum (n=326) samples in 2017

4.2 Pigs

Enterococcus isolates were commonly resistant to erythromycin (72.6%), tetracycline (65.9%), and streptomycin (38.1%) (Figure 36).

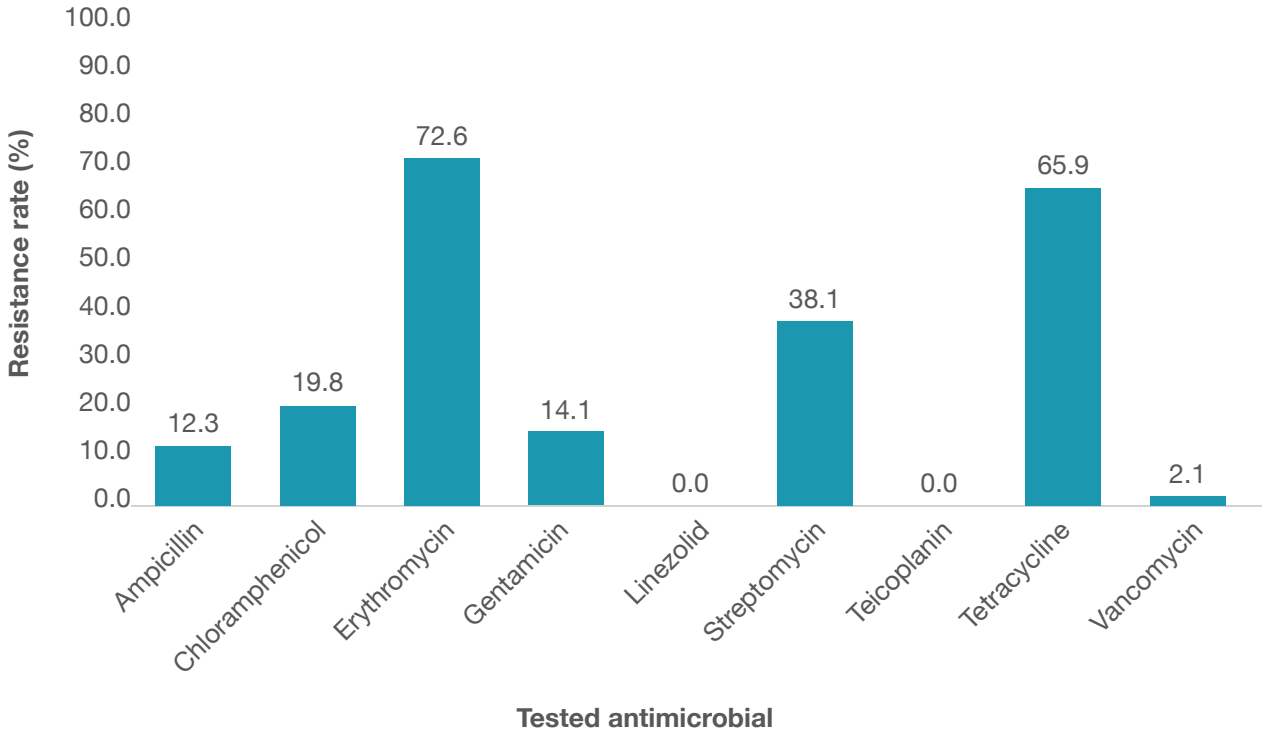

Figure 36. AMR rate of *Enterococcus* spp. isolated from pig cecum (n=212) samples in 2017

3.2.4 Conclusion

In conclusion, the surveillance of AMR in animals indicated that the results of AST reflect the current status of antimicrobial use in livestock. The use of antimicrobials with long history of use tends to be linked to high AMR. Last resort antibiotics, including cephalosporins and colistin, should be restricted use. Since 15.0% resistance to colistin was observed, close investigation should be done. Therefore, the routine surveillance of AMR in chickens and swine are needed in order to monitor how resistant bacteria is spreading among food-producing animals and humans throughout the food chain. Moreover, further study of genotypic resistance that can be transferred between humans and animals is needed to strengthen AMR-response capacity in the country.

In response to AMR, Thailand's National Strategic Plan on AMR 2017-2021 was endorsed by the Thai Cabinet in 2016, with aims to reduce mortality, morbidity and the economic impacts of AMR. The DLD, is the major organization playing a significant role in controlling and regulating the prudent use of antibiotics in animal sector. Its key interventions are listed below.

1. Under the Feed Quality Control Act 2015, the DLD has banned all antibiotics used for growth promoters in food-producing animals.
2. The DLD is the main authority responsible for inspection under the Drug Act and the Feed Quality Control Act. Monitoring the quality of antibiotics helps to ensure high standards.
3. The DLD conducted routine analyses of antibiotic residues in the food chain including in animal feed and livestock products (meat, milk and egg) to trace, assure appropriate use of antibiotics and generate proper duration of withdrawal period in farms.
4. The DLD collaborated with the National Bureau of Agricultural Commodity and Food Standards (ACFS) under the Ministry of Agriculture and Cooperatives involved with standards and policies, which issued a Code of Practice for Control of Use of Veterinary Drugs. This requires multi-sectoral stakeholders, including veterinarians and farmers, to reduce antimicrobial use in farm animals to achieve the goals set out in Thailand's National Strategic Plan on AMR.
5. The DLD is also in the process of drafting a regulation on the control of medicated feed by using prescriptions to regulate the proper use of antibiotic in food-producing animals.

KNOWLEDGE AND AWARENESS OF ANTIBIOTIC USE AND ANTIMICROBIAL RESISTANCE

4. Knowledge and awareness of antibiotic use and antimicrobial resistance

Data source
National Statistical Office, Ministry of Digital Economy and Society

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Key summary

- An antimicrobial use (AMU) module was integrated into the Health and Welfare Survey in 2017, covering 27,762 Thai adults (age >15 years) who had self-responded to the module.
- About 7.9% of respondents had received antibiotics in the last month. The majority (70.3%) obtained antibiotics from health facilities (both private and public sectors at all levels).
- Flu symptoms were the most common reason (27.0%) that people gave for taking antibiotics and were therefore wrongly used.
- A low level of antibiotics literacy among Thai people is reflected in the fact that only 2.6% of Thai adults gave correct answers to all six statements about antibiotics.
- Public information on the proper use of antibiotics and awareness of antimicrobial resistance (AMR) was poorly available; only 17.8% of Thai adults had received information about the proper use of antibiotics and AMR in the last 12 months.
- Almost two-thirds of respondents were not aware that antibiotics are used in food-producing animals.

4.1 General

In order to improve awareness and understanding about AMR as recommended by WHO [24], countries need to develop a sustainable system for monitoring the population's knowledge about antibiotics and awareness of AMR in order to inform effective interventions. In 2015, WHO conducted a multi-country public awareness survey in twelve countries, two from each of the six WHO regions. In the South-East Asia Region, India and Indonesia were two sample countries [25]. A series of special Eurobarometers 338, 445, 478 and a Flash Eurobarometer had been conducted in European countries [26-29]. Other high-income countries have also generated evidence about knowledge and awareness of antibiotic use among the general population [30-32].

The Thailand's NSP-AMR 2017–2021 was endorsed by the cabinet in August 2016 [7]. One of the five goals is to increase public knowledge of antibiotics and awareness on AMR by 20.0% by 2021. In 2017, the National Statistical Office (NSO) and the International Health Policy Program (IHPP) of the Ministry of Public Health, Thailand for the first time jointly developed a module to assess the use of antibiotics, levels of knowledge about antibiotics and sources of information on the appropriate use of antibiotics and AMR among the Thai population. In order to sustain monitoring knowledge about antibiotics in the Thai population, the AMR module was integrated into the Health and Welfare Survey (HWS), an existing health survey established by the NSO since 1974.

In response to the gap in understandings about the use of antibiotics in the population this study aimed to generate baseline evidence on the one-month prevalence of antibiotic use; clinical indications and sources of antibiotics; the levels of knowledge about antibiotics and AMR among the adult Thai population; and factors associated with knowledge and reception of public information about the proper use of antibiotics. This evidence is essential to generate baseline data for monitoring progress in implementing the NSP-AMR.

4.2 Data sources

Development of AMR module

The NSO administered annual Health and Welfare Surveys between 1974-1978, and thereafter every five years between 1981 and 2001. Between 2003 and 2007, the NSO conducted additional annual surveys in order to monitor the impact of Universal Health Coverage on households when it was launched in 2002. More recently, the HWS has been conducted every two years since 2009. Questions asked in a HWS are equally as comprehensive as those in the Demographic and Health Survey, but are superior in terms of flexibility to meet national needs. While maintaining core modules, the HWS accommodates additional modules of policy interest and allows for more frequent rounds of biannual surveys for timely monitoring of policy interventions when needed. The sample size of a HWS allows analysis at the regional level but is not able to provide statistics at the provincial level.

Based on the strong institutional relationship between the NSO and IHPP, a self-administered AMR module consisting of four sections was developed jointly and integrated into the 2017 HWS. See Table 17 for details on questions within the module. The four main sections of the module are as follows: 1) Antibiotics use profiles in the last month, sources of antibiotics and clinical conditions for the use; 2) Antibiotics knowledge, which was assessed using true or false statements and one question; 3) Public information on proper use of antibiotics and AMR in the last 12 months, and the source and impact of this information; 4) Awareness about the use of antibiotics in agriculture and the environment (One Health).

Table 17. AMR module embedded in 2017 HWS

I. USE OF ANTIBIOTICS		
AB1	Have you taken any antibiotics orally such as tablets, powder or syrup in the last month?	Yes/ No/ Don't know
AB2 (IF 'YES' to AB1)	Where did you obtain the last course of antibiotics that you used?	Choices of answer: Health center/ Community hospital/ General or regional hospital/ University hospital/ Other public hospital/ Private hospital/ Private clinic/ Pharmacy/ Grocery store/ Some left over drugs from the previous treatment (your own and others)/ Mobile medical Unit/ Others (Specify)
AB3 (IF YES' to AB1)	What was the reason for last taking the antibiotics that you used? (Multiple answers possible)	Choices of answer: Pneumonia, Bronchitis, Rhinitis and rhinopharyngitis throat, Flu/ Influenza, Sore throat, Cough, Fever, Headache, Diarrhea, Urinary tract infection, Skin or wound infection, Others (Specify), Unknown
II. KNOWLEDGE ABOUT ANTIBIOTICS		
AB4_1	Please tell me whether you think it is true or false. "Antibiotics kill viruses" (The correct answer is a false statement.)	True, False, Don't know
AB4_2	Please tell me whether you think it is true or false. "Antibiotics are effective against colds and flu" (The correct answer is a false statement.)	True, False, Don't know
AB4_3	Please tell me whether you think it is true or false. "Unnecessary use of antibiotics makes them become ineffective" (The correct answer is a true statement.)	True, False, Don't know
AB4_4	Please tell me whether you think it is true or false. "Taking antibiotics often has side-effects such as diarrhoea" (The correct answer is a true statement.)	True, False, Don't know

II. KNOWLEDGE ABOUT ANTIBIOTICS		
AB4_5	Please tell me whether you think it is true or false. "Antibiotics are not equal to anti-inflammatory drugs" (The correct answer is a true statement.)	True, False, Don't know
AB5	When do you think you should stop taking antibiotics once you have begun a course of treatment?	Choices of answer: When your illness is better; When you get full course of antibiotics (from doctor's or health professionals recommendation); Others (Specify); Unknown
III. PUBLIC INFORMATION ABOUT THE PROPER USE OF ANTIBIOTICS AND AMR		
AB6	In the last 12 months, do you remember getting any information about not taking antibiotics unnecessarily, for example for a cold or the flu, or information on antimicrobial resistance?	Yes/ No/ Don't know
AB7 (IF 'YES' to AB6)	From whom did you get this information about not taking antibiotics unnecessarily?	Choices of answer: A doctor told me; A pharmacist told me; Another health professional (e.g. nurse, physical therapist) told me; A family members/ friends told me; I saw it on a TV advertisement; I saw it on the internet/ social media; I saw it on a leaflet/poster; I read it in a newspaper; I saw it on the TV news, I heard it on the radio; Others (Specify); Don't know
AB8 (IF 'YES' to AB6)	Did the information that you received change your views on using antibiotics?	Yes/ No/ Don't know
AB9 (IF 'YES' to AB6)	On the basis of the information you received, how do you now plan to use antibiotics? (Multiple answers possible)	Choices of answer: When you think you need an antibiotic, You will no longer self-medicate with antibiotics, You will no longer taking antibiotics without a prescription from doctor, You will no longer keep left over antibiotics for next time you are ill, Others (Specify), None, Don't know

IV. USE OF ANTIBIOTICS IN AGRICULTURE AND THE ENVIRONMENT (ONE HEALTH)		
AB10	Did you know that sick food animals are treated with antibiotics?	Yes/ No/ Don't know
AB11 (IF 'YES' in AB10)	Did you know that using antibiotics in animals can develop resistance among them?	Yes/ No/ Don't know
AB12	Did you know that using antibiotics to stimulate growth in livestock is banned by Thai government?	Yes/ No/ Don't know

The HWS applied a stratified two-stage sampling. Bangkok Metropolis and provinces constitute strata, with altogether 77 strata. Each stratum is divided into municipal (urban) and non-municipal (rural) areas. In the first stage, sampling enumeration areas (EAs) from urban and rural area used the probability proportional to size based on total household numbers. In the second stage, private households were the sampling units. A new listing of all private households was updated for all sampled EA to serve as the sampling frame. In each sampled EA, a systematic sample of private households was selected.

In the 2017 HWS, a total 27,960 households from 1,990 EAs were identified, where adult members (>15 years old) in these households were surveyed using a self-administered AMR module.

In order to prevent recall bias, we used the past month as reference for the use of antibiotics, and the past year for information about the appropriate use of antibiotics and AMR. Independent parameters were drawn from the core modules of the Health and Welfare Survey, such as wealth quintiles, education, age and gender, urban and rural residents. Integrating an additional AMR module into an existing national representative household survey was a more feasible, cost effective way to monitor knowledge and AMR awareness in the population, as compared to a stand-alone, small-scale survey.

4.3 Results

4.3.1 Use of antibiotics

Of the total interviewed adults, the prevalence of antibiotic use in the last 12 months was 7.9%; while 12.3% of respondents could not confirm whether the medicines they used in the previous month were antibiotics or not. Among the individuals who reported antibiotic use, 50.3% received antibiotics from public health facilities, 20.0% from private health facilities, 26.7% from retail pharmacies and 3.0% from grocery stores.

In Figure 37, we classified self-reported clinical indications for antibiotic use into three groups: treatment of symptoms, treatment of illnesses and unspecified symptoms. Most antibiotics (64.5%) were used to treat symptoms (fever 19.2%, sore throat 16.8%, headache 12.0%, cough 11.3% and diarrhea 5.2%). Antibiotics were also reported for the treatment of illnesses, such as flu (27.0%), skin infection (4.7%) and pharyngitis (4.2%). Interestingly, 17.1% of population answered that they had had other symptoms and diseases, which were unspecified. However, 17.4% of them responded with more than one answer, which were mostly other symptoms and flu.

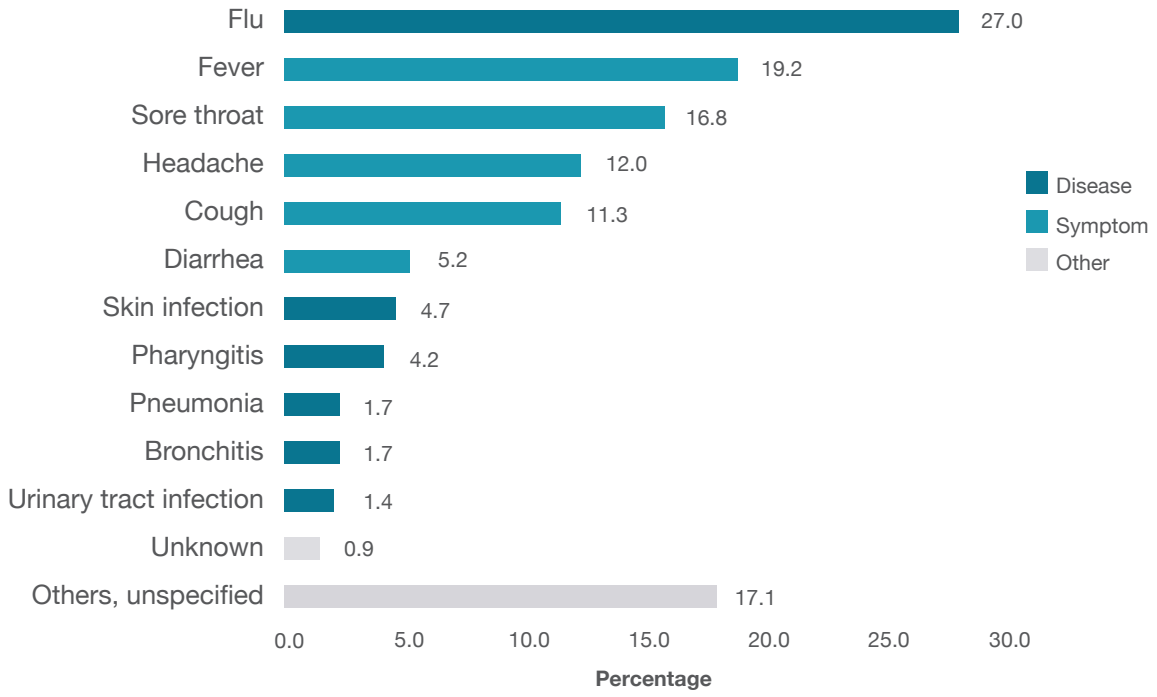

Figure 37. Indication of antibiotic use

Note: that total percentages were more than 100% due to multiple answers.

4.3.2 Antibiotics knowledge

The majority of respondents (63.6%) correctly recognized that unnecessary or inappropriate use of antibiotics can result in ineffective treatment or resistance; 61.7% agreed that they should stop antibiotics after completing a full course of treatment; 42.9% gave the correct answer that antibiotics are not anti-inflammatory drugs. However, half of respondents (52.3%) gave the wrong answer to the statement that antibiotics can cure common cold and flu symptoms and 49.8% of respondents wrongly thought that antibiotics can kill viruses. Almost half of respondents (47.4%) did not know that excessive use of antibiotics can result in side effects such as diarrhea.

Only 2.6% of all adult respondents gave correct answers to all six statements: 8.2% of respondents gave five or more correct answers; less than a quarter of respondents (23.7%) gave four or more correct answers; and less than a half of respondents (46.6%) gave three or more correct answers. Alarmingly, 13.5% of Thai adults gave wrong answers to all six statements (Figure 38).

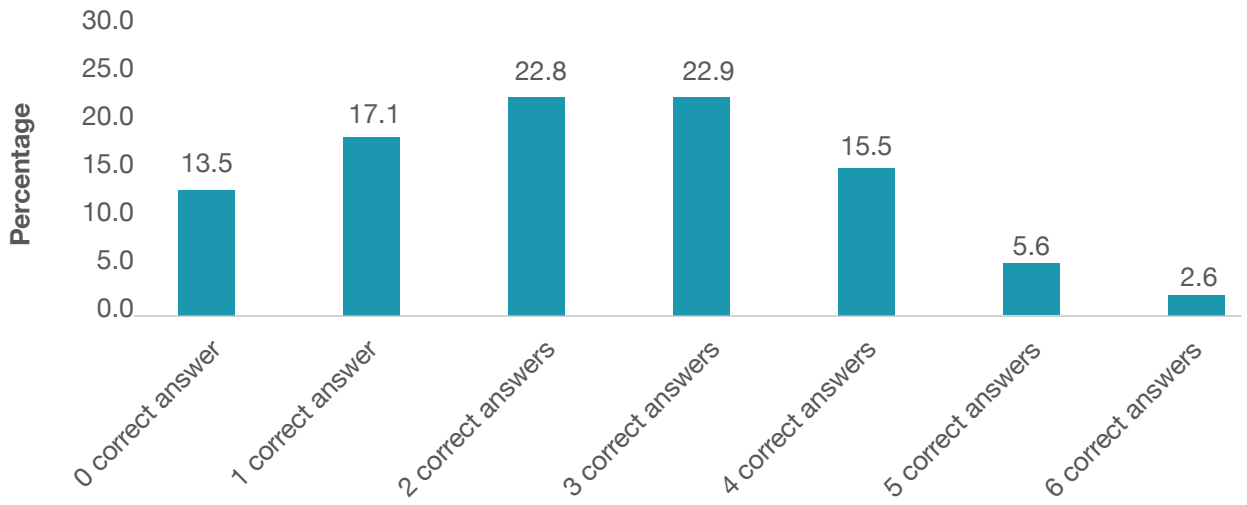

Figure 38. Percentages of respondents who gave correct answers

4.3.3 Public information on proper use of antibiotics and AMR

Only 17.8% of respondents had received information about the appropriate use of antibiotics and AMR in the last 12 months. Three common sources of information were doctors (36.1%), other health professionals (24.8%) and pharmacists (17.7%). Other sources such as television and social media played a minor role contributing 8.3% and 3.5% respectively, while 7.2% of respondents received information from friends and family (Figure 39).

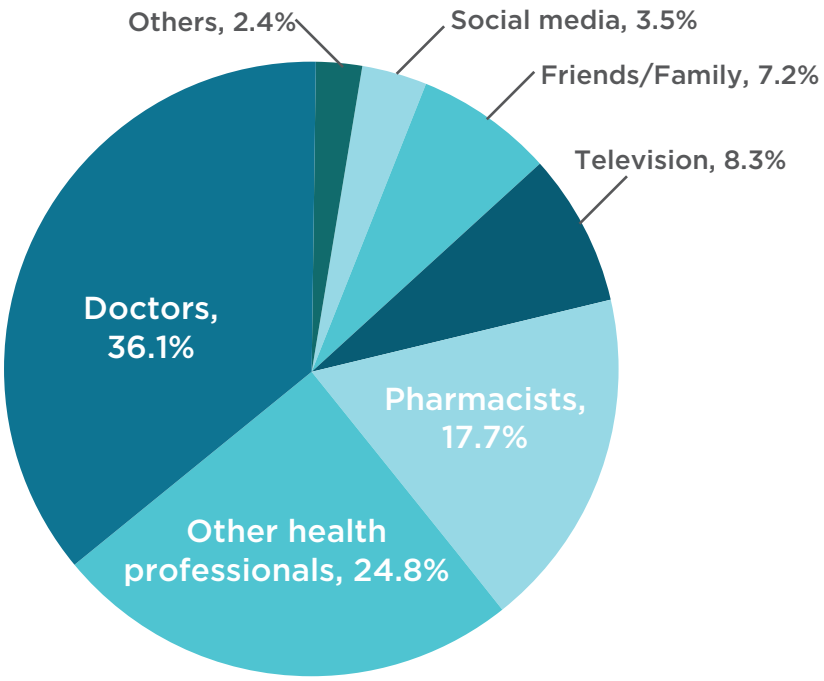

Figure 39. Source of information on antibiotics and AMR in the last 12 months

Note: Others included leaflets, posters, newspapers and radio broadcasting.

4.3.4 Awareness on the use of antibiotics in agriculture and the environment (One Health)

Almost two-thirds of Thai adults (64.7%) were not aware that antibiotics are used in food-producing animals, and 10.7% said that they were not sure. However, 24.6% of respondents were aware that sick food animals are treated with antibiotics. Among those who were aware that sick food animals are treated with antibiotics, 74.0% knew that using antibiotics in animals can lead to antibacterial resistance, 18.5% said that they did not know, and 7.5% said that they were not sure (Figure 40).

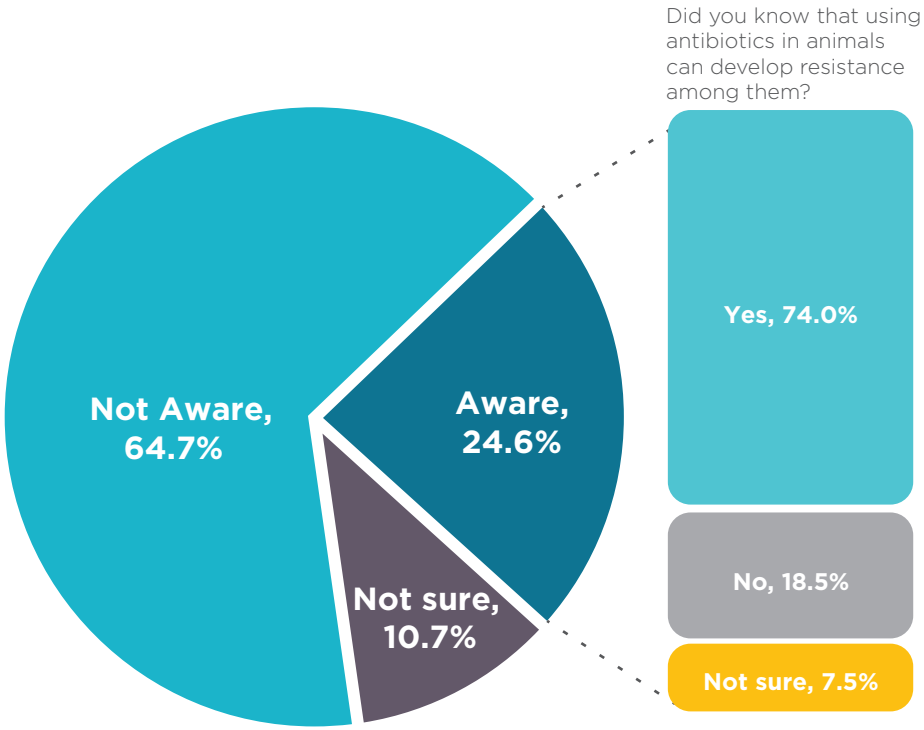

Figure 40. Awareness on the use of antibiotics in food-producing animals

Regarding knowledge of Thailand's ban on the use of antibiotics for animal growth promotion, 68.2% of respondents said they did not know that such a ban existed; 21.1% knew that Thailand has banned the use of antimicrobials as growth promoters in food animals; and 10.7% of respondents said they were not sure.

4.4 Limitations

A few limitations were experienced in this survey. Respondents may have limited understandings about how to differentiate antibiotics from other medicines. This might lead to incorrect responses for the use of antibiotics and affect the findings for the one-month prevalence of antibiotic use. It is important to note that this is a self-reported survey, and this can therefore lead to a degree of bias with respondents providing the answer they believe is expected by NSO interviewers. This bias is prevented by training interviewers properly and providing a field manual. The design of the true and false statements is neutral which also reduces such bias; for example "Antibiotics kill viruses" or "Antibiotics are effective against colds and flu".

4.5 Prospect

- The HWS survey is a fundamental contributing to the monitoring system for levels of knowledge about antibiotics and awareness of AMR in Thai population. It also supports the monitoring and evaluation of the National Strategic Plan on Antimicrobial Resistance (2017-2021) (goal 4: increase public knowledge of antibiotics and awareness on AMR by 20.0% by 2021). It is essential to maintain an AMR module in the HWS survey, which is conducted every two years.
- The low level of antibiotics literacy is also a limitation of self-reported surveys. For example, respondents may not be able to distinguish antibiotics from other medicines, this may lead to an inaccurate response. Learning from the AIDS epidemic, campaigns to increase proper knowledge of antibiotics and awareness of AMR will improve the accuracy of self-reported antibiotic use.
- There is a large gap of public knowledge about the use of antibiotics. The main communication channel is through healthcare professionals, which indicates they are key people in communicating information about the proper use of antibiotics to the public.
- Regulating antibiotic distribution by reclassification of certain items to prescription-only medicines, and effective law enforcement to control antimicrobial distribution and inappropriate use, are recommended.
- Creating effective communication and awareness programmes on antibiotic use and AMR that are tailored for different target audiences, including the general public and agricultural practitioners is also recommended. There is a need to promote better understandings and awareness in the community through a ground-level approach: i.e. school curricula, community-based programmes, public media. Evaluating the cost and effectiveness of these community-based interventions and comparing them with interventions in health facilities and private pharmacies is necessary.
- It is important to close the knowledge gap on AMR in food animals by raising awareness among people, particularly in livestock operators on the ban of antibiotic use for growth promotion. All efforts to educate farmers should be prioritized to ensure antibiotics are used responsibly in food-producing animals.

5

WAY FORWARD

5. Way forward

Author
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5.1 Policy implications

The 2017 national report on AMC presents a strong foundation for policy implementation to optimize antimicrobial consumption in human and animal sectors. In particular, policy should curb and restrict consumption of antibiotics in the CIA group by food-producing animals and strengthen the monitoring of adherence to DLD's ban on the use of antibiotics as growth promoters.

In the human sector there is a need to maximize the use of AMR profiles to guide clinical management and to reclassify CIA groups into prescription-only medicines with strong prescription audits. Further, there is a need to strengthen healthcare facility interventions for infection prevention and control (IPC) in order to prevent morbidities from healthcare-associated infections and AMR. Significant improvements to interventions and adherence to IPC may have immediate and faster impacts on preventing HAI and AMR morbidity than antibiotics stewardship reforms. Similarly, AMR profiles in the food-producing animal sector will guide veterinarians in the management of affected animals though routine laboratory tests of antibiotics susceptibility, which can currently be a challenge. The application of Good Agriculture Practice and improved biosecurity will prevent both infections and the overuse of antibiotics.

Surveillance of resistant pathogens was done by DLD in 2017 through collecting 5,900 samples from slaughterhouses (poultry and swine cecum and meats) and meats on consumer shelves from market. It showed that *E. coli* and *Salmonella* spp. isolates from both chickens and pigs had a high level of resistance to ampicillin, sulfamethoxazole, tetracycline and trimethoprim at about 50.0% of total samples, while had a low level of resistance to colistin and 3rd generation cephalosporins (cefotaxime and ceftazidime). There is a need to continue monitoring adherence to the total ban of use of antibiotics as growth promoters and to strengthen DLD regulation on the use of antibiotics in medicated feed under veterinary prescription.

Although the prevalence of self-medicated antibiotic use in the general public was low, there were some irrational uses of antibiotics such as for flu and common cold symptoms. Almost all self-medicated antibiotics are dispensed through highly qualified sources such as public and private healthcare facilities and licensed private pharmacies. Therefore, the antibiotic-prescribing competencies of healthcare professionals (nurses, doctors and pharmacists) needs to improve as they are the primary change agents for the rational use of self-medicated antibiotics in the general population. Further studies are required to assess antibiotics competencies among these professionals. A review of the curricula of in-service continued professional development to include rational use of antibiotics and AMR awareness is also needed.

5.2 Foundations for sustaining annual reporting on AMC and AMR

Sustaining combined reporting for AMC and AMR requires One Health partners to continue making skilful contributions. The high quality, completeness and accuracy of the mandatory report, including antimicrobial export volumes, is the foundation for the estimate of consumption; this requires the FDA's continue encouragement and enforcement of pharmaceutical operators. Further development requires the FDA's legislative amendment of the Drug Act 2019 enforcing mandatory reporting of sales data by all pharmaceutical operators. Availability of sales data will strengthen accurate estimates, in line with most countries in ESAC-Net and ESVAC.

One missing aspect is to monitor the environmental impact of antibiotics use on livestock farms and in orchards using for the treatment of citrus greening diseases (Huanglongbing) caused by *Candidatus* Liberibacter asiaticus [33]. In the future, the HSPR-AMR working group plan to expand the scope of work to monitor of certain sentinel sites and include data in the national report through an involvement of relevant stakeholders such as Department of Environmental Quality Promotion of the Ministry of Natural Resources and Environment.

Although consumption of antimicrobials in companion animals is likely to be much smaller than in food-producing animals, their closeness to owners can potentially result in a transmission of resistant bacteria from animals to humans. Monitoring the consumption of human antibiotics and AMR in companion animals through research may contribute to how this sector can be scaled up across national monitoring.

6

ANNEXES

6. Annexes

Annex 1 Consumption of antibacterials in humans and animals

Table A1. Consumption of antibacterials intended for systemic use, arranged by ATC level 5 and proportion to overall consumption

ATC level 5	Substance	DDD	DID	Proportion (%)
J01DD04	ceftriaxone	358,039,980.8	13.5	19.8
J01CA04	amoxicillin	264,476,444.8	10.0	14.6
J01AA07	tetracycline	90,604,526.5	3.4	5.0
J01AA02	doxycycline	63,273,150.0	2.4	3.5
J01MA06	norfloxacin	53,589,557.8	2.0	3.0
J01CR02	amoxicillin and enzyme inhibitor	45,041,695.7	1.7	2.5
J01FA06	roxithromycin	39,740,758.3	1.5	2.2
J01CA01	ampicillin	37,498,913.1	1.4	2.1
J01EE01	sulfamethoxazole and trimethoprim	37,191,809.7	1.4	2.1
J01CF01	dicloxacillin	36,532,691.0	1.4	2.0
J01MA02	ciprofloxacin	32,545,392.8	1.2	1.8
J01DD02	ceftazidime	24,593,502.1	0.9	1.4
J01CF02	cloxacillin	18,520,273.8	0.7	1.0
J01DB01	cefalexin	15,727,999.5	0.6	0.9
J01FA10	azithromycin	14,000,706.0	0.5	0.8
J01FF01	clindamycin	12,214,753.9	0.5	0.7
J01FA09	clarithromycin	10,385,778.4	0.4	0.6
J01MA01	ofloxacin	10,309,281.5	0.4	0.6
J01MA12	levofloxacin	9,304,180.5	0.4	0.5
J01DD16	cefditoren	5,659,995.0	0.2	0.3
J01FF02	lincomycin	4,901,463.3	0.2	0.3
J01FA01	erythromycin	4,308,907.3	0.2	0.2
J01EC02	sulfadiazine	4,215,356.9	0.2	0.2
J01GB03	gentamicin	4,058,397.9	0.2	0.2
J01DC04	cefaclor	3,444,666.4	0.1	0.2

ATC level 5	Substance	DDD	DID	Proportion (%)
J01DB04	cefazolin	2,769,748.5	0.1	0.2
J01BA02	thiamphenicol	2,729,245.0	0.1	0.2
J01DC02	cefuroxime	2,642,392.5	<0.1	0.1
J01DD08	cefixime	2,378,975.0	<0.1	0.1
J01CE02	phenoxymethylpenicillin	2,227,484.9	<0.1	0.1
J01DD15	cefdinir	1,426,107.1	<0.1	0.1
J01AA03	chlortetracycline	1,278,150.0	<0.1	<0.1
J01DH02	meropenem	1,123,848.7	<0.1	<0.1
J01CE09	procaine benzylpenicillin	995,010.0	<0.1	<0.1
J01GB04	kanamycin	875,035.7	<0.1	<0.1
J01MA14	moxifloxacin	869,652.0	<0.1	<0.1
J01XD01	metronidazole	866,866.0	<0.1	<0.1
J01CR05	piperacillin and enzyme inhibitor	780,973.4	<0.1	<0.1
J01GA01	streptomycin	520,460.0	<0.1	<0.1
J01DH03	ertapenem	366,415.0	<0.1	<0.1
J01EB02	sulfamethizole	351,146.9	<0.1	<0.1
J01DD01	cefotaxime	341,085.8	<0.1	<0.1
J01DD62	cefoperazone, combinations	327,985.6	<0.1	<0.1
J01GB06	amikacin	290,009.0	<0.1	<0.1
J01XA01	vancomycin	284,142.3	<0.1	<0.1
J01CE01	benzylpenicillin	248,801.9	<0.1	<0.1
J01XX01	fosfomycin	239,014.0	<0.1	<0.1
J01XE01	nitrofurantoin	232,500.0	<0.1	<0.1
J01MA17	prulifloxacin	225,083.3	<0.1	<0.1
J01MA21	sitafloxacin	225,000.0	<0.1	<0.1
J01EB03	sulfadimidine	221,977.5	<0.1	<0.1
J01AA06	oxytetracycline	221,257.0	<0.1	<0.1
J01DH51	imipenem and enzyme inhibitor	212,764.5	<0.1	<0.1
J01ED05	sulfamethoxypyridazine	200,000.0	<0.1	<0.1
J01CR01	ampicillin and enzyme inhibitor	165,746.3	<0.1	<0.1
J01ED07	sulfamerazine	152,768.0	<0.1	<0.1

ATC level 5	Substance	DDD	DID	Proportion (%)
J01BA01	chloramphenicol	129,763.3	<0.1	<0.1
J01DB05	cefadroxil	118,192.0	<0.1	<0.1
J01AA12	tigecycline	110,000.0	<0.1	<0.1
J01CR04	sultamicillin	103,283.0	<0.1	<0.1
J01AA08	minocycline	85,225.0	<0.1	<0.1
J01DH05	biapenem	41,205.0	<0.1	<0.1
J01XB01	colistin	39,705.9	<0.1	<0.1
J01DD12	cefoperazone	36,883.8	<0.1	<0.1
J01DE01	cefepime	26,308.3	<0.1	<0.1
J01DC01	cefoxitin	23,897.8	<0.1	<0.1
J01XX08	linezolid	14,640.0	<0.1	<0.1
J01AA04	lymecycline	10,752.0	<0.1	<0.1
J01CE10	benzathine phenoxymethylpenicillin	10,714.5	<0.1	<0.1
J01XA02	teicoplanin	8,567.5	<0.1	<0.1
J01CG01	sulbactam	7,908.0	<0.1	<0.1
J01GB07	netilmicin	7,243.4	<0.1	<0.1
J01EA01	trimethoprim	6,000.0	<0.1	<0.1
J01DC03	cefamandole	166.7	<0.1	<0.1
J01XX04	spectinomycin	0.7	<0.1	<0.1
	Grand total	**1,226,750,285.3**	**46.4**	**67.9**

Table A2. Consumption of antibiotics for alimentary tract and nitroimidazole derivatives, arranged by ATC level 5 and proportion to overall consumption

ATC level 5	Substance	DDD	DID	Proportion (%)
Antibiotics for alimentary tract				
A07AA01	neomycin	485,295.3	<0.1	<0.1
A07AA02	nystatin	563,359.8	<0.1	<0.1
Grand Total		**1,048,655.1**	**<0.1**	**<0.1**
Nitroimidazole derivatives				
P01AB01	metronidazole	14,474,322.5	0.6	0.8
P01AB02	tinidazole	810,824.5	<0.1	<0.1
Grand total		**15,285,147.0**	**0.6**	**0.8**

Table A3. Consumption of antivirals for systemic use, classified by ATC level 5 and proportion to overall consumption

ATC level 5	Substance	DDD	DID	Proportion (%)
J05AG03	efavirenz	81,536,302.5	3.1	4.5
J05AF05	lamivudine	72,096,324.9	2.7	4.0
J05AF07	tenofovir disoproxil	57,017,735.5	2.2	3.2
J05AF09	emtricitabine	43,908,000.0	1.7	2.4
J05AG01	nevirapine	31,159,440.0	1.2	1.7
J05AF01	zidovudine	21,689,453.7	0.8	1.2
J05AR10	lopinavir and ritonavir	13,640,581.5	0.5	0.8
J05AG05	rilpivirine	4,963,140.0	0.2	0.3
J05AB01	aciclovir	4,355,872.5	0.2	0.2
J05AF04	stavudine	3,963,358.8	0.2	0.2
J05AF06	abacavir	3,015,943.1	0.1	0.2
J05AF10	entecavir	2,285,310.0	<0.1	0.1
J05AE08	atazanavir	1,414,060.0	<0.1	0.1
J05AH02	oseltamivir	1,005,356.0	<0.1	<0.1
J05AF11	telbivudine	607,936.0	<0.1	<0.1
J05AP01	ribavirin	430,164.0	<0.1	<0.1

ATC level 5	Substance	DDD	DID	Proportion (%)
J05AE10	darunavir	367,860.0	<0.1	<0.1
J05AF08	adefovir dipivoxil	362,490.0	<0.1	<0.1
J05AX08	raltegravir	304,530.0	<0.1	<0.1
J05AB11	valaciclovir	93,413.3	-	<0.1
J05AG04	etravirine	91,260.0	-	<0.1
J05AP07	daclatasvir	57,596.0	-	<0.1
J05AF02	didanosine	56,250.0	-	<0.1
J05AX12	dolutegravir	40,500.0	-	<0.1
J05AB06	ganciclovir	29,025.0	-	<0.1
J05AP08	sofosbuvir	28,000.0	-	<0.1
J05AB09	famciclovir	23,803.5	-	<0.1
J05AB14	valganciclovir	22,350.0	-	<0.1
J05AX09	maraviroc	12,720.0	-	<0.1
J05AX05	inosine pranobex	7,400.0	-	<0.1
J05AH01	zanamivir	1.0	-	<0.1
	Grand total	**344,586,177.3**	**13.0**	**19.1**

Table A4. Consumption of antimycotics for systemic use and antifungals for systemic use, arranged by ATC level 5 and proportion to overall consumption

ATC level 5	Substance	DDD	DID	Proportion (%)
Antimycotics for systemic use				
J02AB02	ketoconazole	96,954,490.0	3.7	5.4
J02AC01	fluconazole	8,387,641.8	0.3	0.5
J02AC02	itraconazole	5,995,184.5	0.2	0.3
J02AA01	amphotericin B	265,450.0	<0.1	<0.1
J02AC03	voriconazole	107,902.5	-	<0.1
J02AC04	posaconazole	22,974.0	-	<0.1
J02AX05	micafungin	8,400.0	-	<0.1
J02AX06	anidulafungin	3,600.0	-	<0.1
J02AX04	caspofungin	894.0	-	<0.1
Grand Total		**111,746,536.8**	**4.2**	**6.2**
Antifungals for systemic use				
D01BA01	griseofulvin	10,694,250.0	0.4	0.6
D01BA02	terbinafine	91,042.0	-	<0.1
Grand total		**10,785,292.0**	**0.4**	**0.6**

Table A5. Consumption of antimicrobials solely for treatment of tuberculosis, arranged by ATC level 5 and proportion to overall consumption

ATC level 5	Substance	DDD	DID	Proportion (%)
J04AC01	isoniazid	23,639,337.5	0.9	1.3
J04AB02	rifampicin	21,492,317.5	0.8	1.2
J04AK01	pyrazinamide	6,802,062.3	0.3	0.4
J04AK02	ethambutol	6,175,451.5	0.2	0.3
J04AD03	ethionamide	399,166.7	<0.1	<0.1
J04AA02	sodium aminosalicylate	211,785.7	<0.1	<0.1
J04AB01	cycloserine	5,183.3	-	<0.1
J04AB30	capreomycin	470.0	-	<0.1
	Grand total	**58,725,774.5**	**2.2**	**3.2**

Table A6. Consumption of antimalarials, arranged by ATC level 5 and proportion to overall consumption

ATC level 5	Substance	DDD	DID	Proportion (%)
P01BA01	chloroquine	19,641,209.5	0.7	1.1
P01BD01	pyrimethamine	12,675,010.0	0.5	0.7
P01BA02	hydroxychloroquine	5,057,918.6	0.2	0.3
P01BC01	quinine	1,138,656.9	<0.1	<0.1
P01BA03	primaquine	503,500.0	<0.1	<0.1
P01BA06	amodiaquine	150.0	-	<0.1
P01BC02	mefloquine	128.0	-	<0.1
P01BF01	artemether and lumefantrine	1.7	-	<0.1
	Grand total	**39,016,574.7**	**1.5**	**2.2**

Table A7. Consumption of critically important antimicrobials in humans, arranged by antimicrobial class

Antimicrobial class	Consumption	
	DID	Tonne of API
I. Highest priority		
Cephalosporins (3rd and 4th generation)	**14.9**	**821.5**
• cefdinir	<0.1	0.9
• cefditoren	0.2	2.3
• cefepime	<0.1	0.1
• cefixime	<0.1	1.0
• cefoperazone	<0.1	0.1
• cefoperazone, combinations	<0.1	1.3
• cefotaxime	<0.1	1.4
• ceftazidime	0.9	98.4
• ceftriaxone	13.5	716.1
Glycopeptides	**<0.1**	**0.6**
• teicoplanin	<0.1	<0.1
• vancomycin	<0.1	0.6
Macrolides and ketolides	**2.6**	**25.8**
• azithromycin	0.5	4.2
• clarithromycin	0.4	5.2
• erythromycin	0.2	4.4
• roxithromycin	1.5	11.9
Polymyxins	**<0.1**	**<0.1**
• colistin	<0.1	<0.1
Quinolones	**4.0**	**84.6**
• ciprofloxacin	1.2	32.5
• levofloxacin	0.4	4.7
• moxifloxacin	<0.1	0.3
• norfloxacin	2.0	42.9
• ofloxacin	0.4	4.1
• prulifloxacin	<0.1	0.1
• sitafloxacin	<0.1	<0.1
Subtotal of highest priority CIA	**21.5**	**932.4**

Antimicrobial class	Consumption	
	DID	Tonne of API
II. High priority		
Aminoglycosides	**0.2**	**5.1**
• amikacin	<0.1	0.3
• gentamicin	0.2	1.0
• kanamycin	<0.1	0.9
• neomycin	<0.1	2.4
• netilmicin	<0.1	<0.1
• streptomycin	<0.1	0.5
Ansamycins	**0.8**	**12.9**
• rifampicin	0.8	12.9
Carbapenems and other penems	**<0.1**	**4.3**
• biapenem	<0.1	<0.1
• ertapenem	<0.1	0.4
• imipenem and enzyme inhibitor	<0.1	0.4
• meropenem	<0.1	3.5
Glycylcyclines	**<0.1**	**<0.1**
• tigecycline	<0.1	<0.1
Oxazolidinones	**<0.1**	**<0.1**
• linezolid	<0.1	<0.1
Penicillins (antipseudomonal)	**<0.1**	**10.9**
• piperacillin and enzyme inhibitor	<0.1	10.9
Aminopenicillins	**11.4**	**474.9**
• amoxicillin	10.0	397.5
• ampicillin	1.4	77.2
• sultamicillin	<0.1	0.2
Aminopenicillins with bela-lactamase inhibitors	**1.7**	**78.0**
• amoxicillin and enzyme inhibitor	1.7	77.0
• ampicillin and enzyme inhibitor	<0.1	1.0
Phosphonic acid derivatives	**<0.1**	**1.6**
• fosfomycin	<0.1	1.6

Antimicrobial class	Consumption	
	DID	Tonne of API
Drugs used solely to treat tuberculosis or other mycobacterial diseases	**2.2**	**39.5**
• capreomycin	<0.1	<0.1
• cycloserine	<0.1	<0.1
• ethambutol	0.2	7.4
• ethionamide	<0.1	0.3
• isoniazid	0.9	7.1
• pyrazinamide	0.3	8.9
• rifampicin	0.8	12.9
• sodium aminosalicylate	<0.1	3.0
Subtotal of high priority CIA	**15.7**	**614.4**
Grand total	**37.2**	**1,546.8**

Table A8. Consumption of veterinary antimicrobials for systemic use, arranged by ATC level 5 and proportion to overall consumption

ATC level 5	Substance	Consumption ($mg/PCU_{Thailand}$)	Tonne of API	Proportion (%)
QJ01CA04	amoxicillin	147.5	975.9	26.4
QJ01AA03	chlortetracycline	57.2	378.6	10.3
QJ01XQ01	tiamulin	45.4	300.3	8.1
QJ01AA02	doxycycline	38.9	257.2	7.0
QJ01EQ03	sulfadimidine	35.4	234.2	6.3
QJ01FA91	tilmicosin	22.3	147.8	4.0
QJ01GB03	gentamicin	19.5	129.4	3.5
QJ01FA90	tylosin	18.7	124.1	3.4
QJ01AA06	oxytetracycline	11.4	75.5	2.0
QJ01MA90	enrofloxacin	9.9	65.4	1.8
QJ01EA01	trimethoprim	8.0	53.1	1.4
QJ01FA93	kitasamycin	7.5	49.7	1.3
QJ01FF02	lincomycin	2.9	19.4	0.5
QJ01EQ10	sulfadiazine	2.8	18.5	0.5
QJ01XX04	spectinomycin	2.2	14.8	0.4

ATC level 5	Substance	Consumption (mg/PCU$_{Thailand}$)	Tonne of API	Proportion (%)
QJ01FA92	tylvalosin	2.0	13.0	0.4
QJ01GA90	dihydrostreptomycin	1.8	12.0	0.3
QJ01XX01	fosfomycin	1.5	10.0	0.3
QJ01CE09	procaine benzylpenicillin	1.4	9.0	0.2
QJ01FA01	erythromycin	1.1	7.1	0.2
QJ01DE90	cefquinome	0.8	5.0	0.1
QJ01GB04	kanamycin	0.7	4.8	0.1
QJ01FA07	josamycin	0.5	3.6	<0.1
QJ01CE08	benzathine benzylpenicillin	0.5	3.2	<0.1
QJ01CA01	ampicillin	0.3	1.9	<0.1
QJ01DD90	ceftiofur	0.2	1.4	<0.1
QJ01EQ11	sulfamethoxazole	0.2	1.2	<0.1
QJ01CE02	phenoxymethylpenicillin	0.2	1.1	<0.1
QJ01CR02	amoxicillin and enzyme inhibitor	0.2	1.0	<0.1
QJ01EQ09	sulfadimethoxine	0.1	1.0	<0.1
QJ01GA01	streptomycin	0.1	0.9	<0.1
QJ01EQ17	sulfamerazine	<0.1	0.5	<0.1
QJ01GB90	apramycin	<0.1	0.5	<0.1
QJ01EQ13	sulfadoxine	<0.1	0.5	<0.1
QJ01MA93	marbofloxacin	<0.1	0.3	<0.1
QJ01EQ15	sulfamethoxypyridazine	<0.1	0.2	<0.1
QJ01GB05	neomycin	<0.1	0.2	<0.1
QJ01EQ16	sulfazuinoxaline	<0.1	0.2	<0.1
QJ01FA94	tulathromycin	<0.1	0.1	<0.1
QJ01MA92	danofloxacin	<0.1	<0.1	<0.1
QJ01FA95	gamithromycin	<0.1	<0.1	<0.1
QJ01BA90	florfenicol	<0.1	<0.1	<0.1
QJ01CE01	benzylpenicillin	<0.1	<0.1	<0.1
QJ01AA07	tetracycline	<0.1	<0.1	<0.1
QJ01EQ18	sulfamonomethoxine	<0.1	<0.1	<0.1
QJ01DC02	cefuroxime	<0.1	<0.1	<0.1

ATC level 5	Substance	Consumption (mg/PCU$_{Thailand}$)	Tonne of API	Proportion (%)
QJ01FF01	clindamycin	<0.1	<0.1	<0.1
QJ01EQ07	sulfathiazole	<0.1	<0.1	<0.1
QJ01MA98	sarafloxacin	<0.1	<0.1	<0.1
QJ01DD91	cefovecin	<0.1	<0.1	<0.1
QJ01XQ02	valnemulin	<0.1	<0.1	<0.1
QJ01XX10	bacitracin	<0.1	<0.1	<0.1
QJ01EW19	sulfadimethoxine and ormetoprim	<0.1	<0.1	<0.1
QJ01FA02	spiramycin	<0.1	<0.1	<0.1
QJ01CF06	nafcillin	<0.1	<0.1	<0.1
QJ01CF02	cloxacillin	<0.1	<0.1	<0.1
	Total	**441.7**	**2,923.3**	**79.2**

Table A9. Consumption of veterinary antimicrobials for intestinal use, arranged by ATC level 5 and proportion to overall consumption

ATC level 5	Substance	Consumption (mg/PCU$_{Thailand}$)	Tonne of API	Proportion (%)
QA07AX91	halquinol	73.7	487.5	13.2
QA07AA10	colistin	24.6	162.7	4.4
QA07AA93	bacitracin	10.5	69.3	1.9
QA07AA01	neomycin	6.9	45.5	1.2
QA07AA96	bambermycin	0.3	1.7	<0.1
	Total	**115.8**	**766.7**	**20.8**

Table A10. Consumption of veterinary antimicrobials for intrauterine and intramammary use, arranged by ATC level 5 and proportion to overall consumption

ATC level 5	Substance	Consumption ($mg/PCU_{Thailand}$)	Tonne of API	Proportion (%)
QJ51CF02	cloxacillin	<0.1	0.2	<0.1
QJ51CA01	ampicillin	<0.1	<0.1	<0.1
QJ51DB90	cefalonium	<0.1	<0.1	<0.1
QJ51DB01	cefalexin	<0.1	<0.1	<0.1
QJ51DE90	cefquinome	<0.1	<0.1	<0.1
QJ51AA07	tetracycline	<0.1	<0.1	<0.1
QJ51DB08	cefapirin	<0.1	<0.1	<0.1
QG51AA05	cefapirin	<0.1	<0.1	<0.1
QJ51GB03	gentamicin	<0.1	<0.1	<0.1
	Total	**<0.1**	**0.3**	**<0.1**

Table A11. Consumption of veterinary antimicrobials used as premix, arranged by ATC level 5 and proportion to overall consumption

ATC level 5	Substance	Consumption ($mg/PCU_{Thailand}$)	Tonne of API	Proportion (%)
QA07AX91	halquinol	73.7	487.5	13.2
QJ01AA03	chlortetracycline	56.7	375.5	10.2
QJ01XQ01	tiamulin	42.6	282.0	7.6
QJ01CA04	amoxicillin	35.0	231.6	6.3
QJ01FA91	tilmicosin	21.4	141.4	3.8
QA07AA10	colistin	20.7	136.7	3.7
QJ01AA02	doxycycline	20.2	133.6	3.6
QA07AA93	bacitracin	10.5	69.3	1.9
QJ01FA90	tylosin	8.6	56.8	1.5
QJ01FA93	kitasamycin	3.7	24.4	0.7
QJ01AA06	oxytetracycline	3.6	23.7	0.6
QJ01FF02	lincomycin	1.6	10.5	0.3
QJ01XX01	fosfomycin	1.5	10.0	0.3

ATC level 5	Substance	Consumption ($mg/PCU_{Thailand}$)	Tonne of API	Proportion (%)
QJ01EQ03	sulfadimidine	1.1	7.1	0.2
QJ01EQ10	sulfadiazine	0.9	6.1	0.2
QJ01FA07	josamycin	0.5	3.6	<0.1
QJ01EA01	trimethoprim	0.3	1.9	<0.1
QJ01XX04	spectinomycin	0.3	1.8	<0.1
QA07AA96	bambermycin	0.3	1.7	<0.1
QJ01CE02	phenoxymethylpenicillin	0.2	1.1	<0.1
QJ01EQ17	sulfamerazine	<0.1	0.5	<0.1
QJ01GB90	apramycin	<0.1	0.3	<0.1
QJ01FA01	erythromycin	<0.1	<0.1	<0.1
QJ01MA90	enrofloxacin	<0.1	<0.1	<0.1
QJ01MA98	sarafloxacin	<0.1	<0.1	<0.1
QJ01XQ02	valnemulin	<0.1	<0.1	<0.1
	Total	**303.3**	**2,007.2**	**54.4**

Table A12. Consumption of critically important antimicrobials used in the animal sector, arranged by antimicrobial class

Antimicrobial class	Consumption	
	DID	Tonne of API
I. Highest priority		
Cephalosporins (3rd and 4th generations)	**1.0**	**6.5**
• cefovecin	<0.1	<0.1
• cefquinome	0.8	5.0
• ceftiofur	0.2	1.4
Macrolides and ketolides	**52.2**	**345.5**
• erythromycin	1.1	7.1
• gamithromycin	<0.1	<0.1
• josamycin	0.5	3.6
• kitasamycin	7.5	49.7
• spiramycin	<0.1	<0.1
• tilmicosin	22.3	147.8

Antimicrobial class	Consumption	
	DID	Tonne of API
• tulathromycin	<0.1	0.1
• tylosin	18.7	124.1
• tylvalosin	2.0	13.0
Polymyxins	**24.6**	**162.7**
• colistin	24.6	162.7
Quinolones	**9.9**	**65.8**
• danofloxacin	<0.1	<0.1
• enrofloxacin	9.9	65.4
• marbofloxacin	<0.1	0.3
• sarafloxacin	<0.1	<0.1
II. High priority		
Aminoglycosides	**29.2**	**193.3**
• apramycin	<0.1	0.5
• dihydrostreptomycin	1.8	12.0
• gentamicin	19.5	129.4
• kanamycin	0.7	4.8
• neomycin	6.9	45.7
• streptomycin	0.1	0.9
Aminopenicillins	**147.8**	**977.9**
• amoxicillin	147.5	975.9
• ampicillin	0.3	2.0
Aminopenicillins with beta-lactamase inhibitors	**0.2**	**1.0**
• amoxicillin and enzyme inhibitor	0.2	1.0
Phosphonic acid derivatives	**1.5**	**10.0**
• fosfomycin	1.5	10.0
Grand total	**266.3**	**1,762.7**

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