World Health Organization

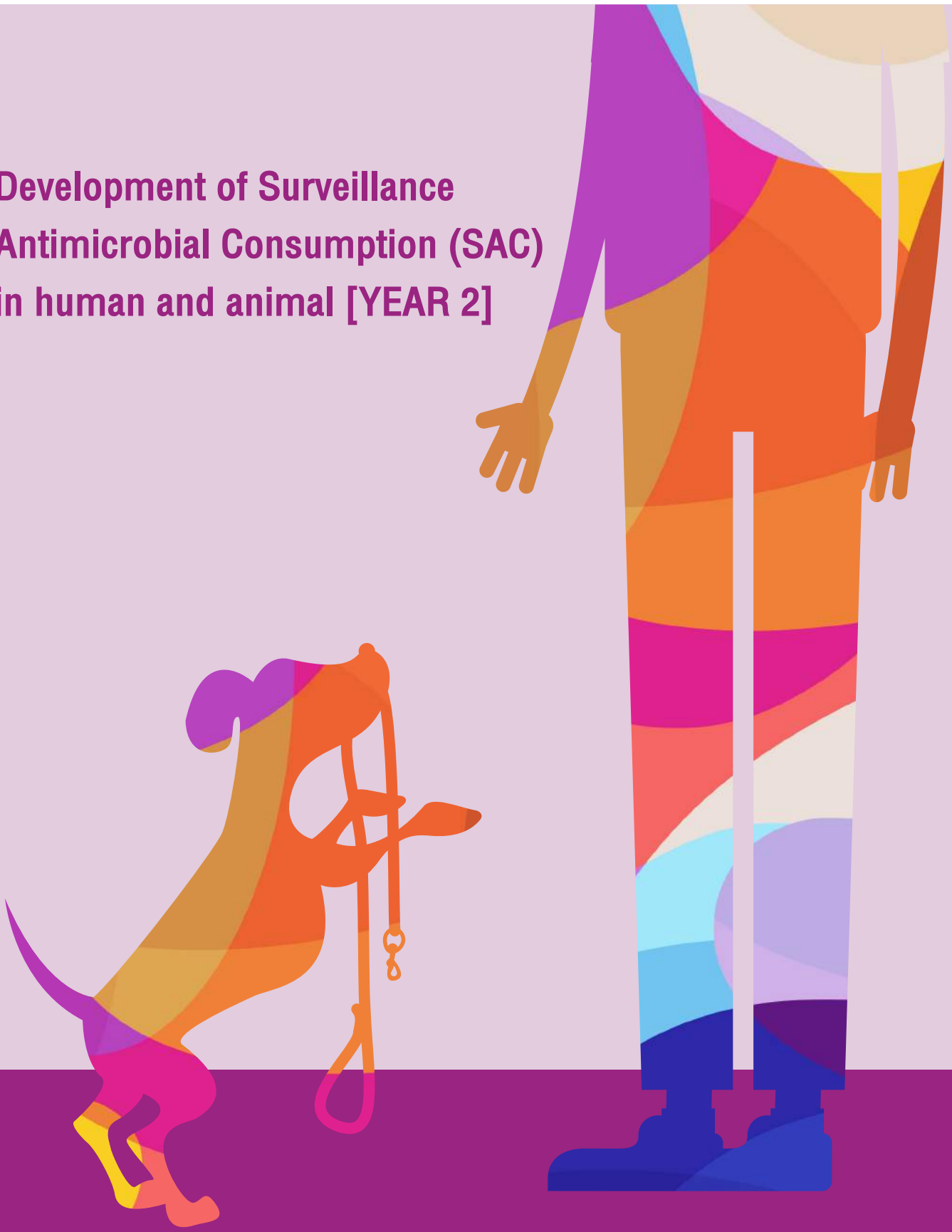
HEALTH SYSTEMS RESEARCH INSTITUTE

ThaiHealth

NHSO National Health Security Office

IHPP Thailand

Development of Surveillance Antimicrobial Consumption (SAC) in human and animal [YEAR 2]



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RTG/WHO COLLABORATIVE PROGRAMME

PROJECT FINAL REPORT

General: A final technical report describing all activities and results of the project should be submitted in the English language on Form No. WHO/RTG-3.5 within ninety days after completion of the Agreement. In cases where the reports are written in the Thai language, the cover sheet and executive summary must be in English. The final report is an important document not only with respect to the project itself, but also to its specific value for progress in health development of the country. This form can be used for research projects and other activities such as training, workshops, conferences, study tours, and meeting attendance/participation.

PART I. COVER SHEET: This cover sheet is self-explanatory as it contains much of the same information found in the Proposal form and must be signed by the responsible officer and the responsible administrative authority (i.e., Division Director or Dean or higher-level officer; president or secretary-general for NGO) of the participating organization.

1. Full Name of Responsible Officer: Viroj Tangcharoensathien

Title: Dr.

2. Full Name of Organization:

International Health Policy Program Foundation

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4. Title of Project:
Development of Surveillance Antimicrobial Consumption (SAC) in humans and animals [YEAR 2]

5. Total Budget (Baht):	**6. Duration:**
5,366,350 THB	**11 Months (July 2018 – May 2019)**

7. Date Agreement Signed: 5 July 2018

8. Funds Received:	**Amount (Baht)**	**Date Received**
Total:	**5,366,350**	**August 2019**

9. Completion Date of Project:
31 May 2019

10. Signatures:

10.1 Responsible Officer:

(Dr.Viroj Tangcharoensathien)

10.2 Responsible Administrative Authority:

(Dr.Sunicha Chanvatik)

11. Date Report Submitted: 15 July 2019

PART II. EXECUTIVE SUMMARY: [This summary should be one to two pages in length and should be treated as a self-contained document highlighting (1) the project objectives, (2) major activities undertaken, and (3) project's results in terms of what has been accomplished with major conclusions and recommendations. It should be written using clear, succinct and specific terms to describe the project's basic elements in such a way that individuals unfamiliar with the project can understand what has been accomplished.]

(1) The project objectives,

Overall objective:

To strengthen the methodological approaches for the sustainable production of the Thailand Surveillance of Antimicrobial Consumption (Thailand-SAC), with improved quality and reliability of annual production and importation data, exclusion of exportation data, including distribution channels and facilitation of public reporting of antimicrobial consumption. This project will also provide information for the National Steering Committee on Antimicrobial Resistance (AMR) chaired by the Deputy Prime Minister.

Specific objectives:

1. To develop an electronic reporting system as required by the Department of Livestock Development (DLD), as part of the ongoing SAC, of veterinary antimicrobial consumption by eight to ten key animal species through the consumption of medicated feed provided by medicated feed manufacturers.
2. To enable effective interoperability among relevant authorities.
3. To develop a tool for the assessment of data integrity of the mandatory annual report to be submitted by pharmaceutical operators (importers and manufacturers).
4. To increase awareness and engagement of policy makers, the general public and stakeholders in addressing challenges in antimicrobial consumption in humans and animals through effective public and policy communications.

(2) Major activities undertaken,

To consolidate and sustain the Thailand-SAC with improved quality and reliability of annual sales data, including that of distribution channels, and by facilitating public reporting on antimicrobial consumption. These activities can be categorized into five components:

Activity 1: Software development which captures data of consumption of different antibiotics through medicated feeds by key animal species which contributes to the detail use profiles by animal species in the Thailand-SAC

This project developed additional software to work in conjunction with the current software program used by the Thai FDA as an annual mandatory reporting platform by pharmaceutical operations which contributes to the Thailand-SAC (both human and animal consumption). This software was developed during year one (2018).

1. Antimicrobial consumption through medicated feeds by key animal species was reported through the annual e-reporting to this software by feed mill manufacturers, as mandated by law, who are and are not members of the Feed Mill Association of Thailand.
2. Developing standard guidelines for information sharing in order to prepare for the readiness of future evolution of a host to host (H2H) system between the Ministry of Public Health, Department of Livestock Development, Ministry of Agriculture and Cooperatives. Manufacturers, exporters and distributors who use their own software of imports and manufacturing Health care providers, retail pharmacy sector which provide services to the end (human) user.

Activity 2: Development of a tool for the DQA of the mandatory annual reports to be submitted by all pharmaceutical operators as mandated by the Drug Act

This activity focused on the development of a tool for data quality assessment (DQA) of the mandatory annual reporting to be submitted by pharmaceutical operators to the Thai FDA. The report contains the total volume and value of import and manufactures of all medicines, including antibiotics, for humans and animals,

by March of the following year. The activity also included applying this tool for the assessment of data quality by selected pharmaceutical operators.

Therefore, the purposes of the tool are to (1) verify the quality of the data, (2) assess IT systems which generate data and reporting, including the mandatory reporting to the Thai FDA, and (3) develop action plans to improve both data quality and systems which produce this data in selected pharmaceutical operators.

Two main tools have been developed: a) System Assessment Protocol (SAP) and b) Data Verification Protocol (DVP).

- The purpose of the SAP is to identify potential challenges to data quality created by the data management and reporting systems at selected manufacturers. The assessment of the data management and reporting systems will take place in two stages: off-site desk review of documentation provided by the operator and on-site follow-up assessments. The outcome of this assessment is the identification of strengths and weaknesses for each functional area throughout the chain of the data management and reporting system.

- The purpose of the DVP is to trace and verify the data, to cross-check the reported results with other primary data sources and spot check if a sample of data has been accurately recorded. Data verification is conducted through in-depth on-site verification at selected manufacturers.

The sites to be visited are purposely selected based on their size and the quality of their reported data. The final data quality audit report will cover the evidence which the audit team collected, identify specific challenges, and provide recommendations to improve data quality and systems. The on-site verification does not aim to produce correcting figures for adjustment of the submitted report by that operator. Instead, it aims to improve the systems of data management, data collection and data reporting.

The researchers felt that improving the integrity of the data systems is the goal of data quality improvement, rather than putting efforts in generating correcting factors (either adjusting up or down) to the submitted report. Also, intensive dialogues between the Thai FDA and pharmaceutical operators on the value of accurate figures in the annual report for the production of the Thailand-SAC is of utmost importance. Another key step in ensuring high data quality is to obtain feedback from the Thai FDA concerning any inaccuracies and/or inconsistencies of the reporting.

Activity 3: Producing the surveillance of antimicrobial consumption report in Thailand, 2017

Data collection from the mandatory annual report of the volume and value (either ex-factory or quoted price) of total annual imports and manufacture of all medicines, including antimicrobials, will be consolidated. The data will be analyzed into DDD (Defined Daily Dose) per 1000 population per day for key antimicrobial classes used in humans. If the data allows (as it is still uncertain if the pharmaceutical operator will voluntarily report the distribution channel, as it is not required by the Drug Act), the report will be broken down into two main channels: hospital and community consumption.

The total report in Kilograms of active ingredient (AI) for animal consumption will be analyzed into mg of AI per Population Correction Unit (PCU) and, if data allows, the average consumption will be broken down by key animal species for 2018.

We will compare time trend with that of consumption between 2017 and 2018 in both human and animal sectors.

Efforts will be made to produce the report in an analytical and comprehensive manner, and where appropriate will benchmark with international peers. The report of the two-year consumption trend will be similar to that which was reported by the Swedish SWEDRES|SVARM report [see https://bit.ly/1GoRf8Q].

Activity 4: Improving the ministerial regulation for strong enforcement

This does not require resources, but the Thai FDA will amend the ministerial regulation which endorses a) the new electronic reporting submission form for all pharmaceutical operators, b) the report itself in electronic format, and c) the requirement of monthly special reports of certain medicines of high risk of abuse for close monitoring in every four months. The electronic reporting submission form covers the distribution channels (if voluntary submission is available), including volume and value of exportation of all medicines

including antimicrobials. The export volume will be deducted from the total import plus total manufacturing in 2018. The adjustment of 2017 has been conducted already.

Activity 5: Consultative meeting with stakeholders

This activity will support all the four activities above through consultation with stakeholders, a follow up meeting among researchers and consistent communication with policy makers.

(3) Project's results in terms of what has been accomplished with major conclusions and recommendations,

The major accomplishments are:

- Development of software for the electronic reporting system used by the DLD, as part of the ongoing development of the Thailand-SAC, with different categories of veterinary antimicrobial consumption using medicated feed which will be categorized by key animal species
- A standard guideline and protocol for information sharing to be ready for the H2H system
- A guideline on the criteria and process of the assessment of data integrity systems of the pharmaceutical operators and the findings of the on-site DQA of a number of pharmaceutical manufacturers
- National report on the Thailand-SAC 2018 covering both human and animal consumption.

Outcome

1. The evidence of antimicrobial consumption in humans and animals through the Thailand-SAC is critical for the government to introduce policies in optimizing consumption through strengthening stewardship in both sectors.

2. A consolidated Thailand-SAC with a fully integrated and functional operating system and effective data linkage between two software programs, one used by the Thai FDA which hosts the Thailand-SAC, and the other used by the DLD, which hosts the consumption by animal species through medicated feeds. The Thailand-SAC can, in the long term, produce a report of consumption by humans and animals similar to the report produced by the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) and the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC), which advance efforts by providing a breakdown of consumption by animal species. Still, there is need for a breakdown of human consumption by the hospital and community sectors. In the future, there may be a need for a methodological development to breakdown human consumption between the two sectors.

3. The development of a multi-sectoral, multi-disciplinary research team, which is the real legacy of WHO (World Health Organization) support; they have shown sustained commitment and will continue to strengthen the Thailand-SAC and ensure policy utilities in responses to AMR threats.

PART III. END-OF-PROJECT STATUS: [This section should provide information regarding (1) the overall history of project implementation, (2) the achievement of project objectives, (3) the final level of resource utilization, and (4) the final delivery of the stated product. It is used as a basis for concluding the end-of-project status and, in some cases, identifying follow-on activities that may be needed to ensure that the benefits of the project are realized to the maximum extent or mechanisms required for dissemination of the technical knowledge to the intended beneficiaries.]

End of project status,

The overall history of project implementation:

- This research received strong cooperation from many in the research network on the overall project implementation including the Thai FDA, DLD, the Thai Feed Mill Association, as well as scholars and many in the private sectors, in order to strengthen information systems and assist in all operations in line with the planned timeline.
- However, the regulatory adjustment by the Thai FDA has required lengthy bureaucratic processes ever since the adoption of the revised drug act (6th edition). The regulatory amendment of the mandatory reporting requirement, which supports the Thailand-SAC, remains slow in making progress. To overcome this, the Thai FDA requested pharmaceutical operators to provide voluntary reports on distribution channels and the value and volume of exports. However, the total sales volume, which is the definitive dataset, has yet to be disclosed in voluntary reporting.

The achievement of project objectives,

The accuracy, correctness, preciseness and detail of the AMR consumption report is a key objective for the 2nd year implementation of the Thailand-SAC with the following achievements,

1. The antibiotics production and distribution reporting program was developed to follow up the antibiotics distribution to animal species as well as to develop the electronic reporting system. As part of the ongoing SAC, veterinary antimicrobial consumption sorted by key animal species was referred with the consumption amount of medicated feed which was reported by the medicated feed manufacturers. The software and program was developed to facilitate various platforms of e-submission using web-based submission, tablet and mobile applications. Officers in feed mill factories will input their data either into a spreadsheet and upload it or by web service, and veterinarians will confirm the data and submit it to the Department of Livestock Development.

Additionally, the program will facilitate the calculation of drug amounts automatically to minimize the human error in inputting data and produce data on antibiotics consumption in DDD in humans and in milligrams of API in animals.

2. The assessment tool for evaluating the accuracy of the annual reports by manufacturers was developed and tested as a tool for the assessment of data integrity.

There were 17 manufacturers of antibiotics that were willing to participate in the program and had gone through on-site DQA. Most of them were purposively selected as large manufacturers where their data integrity has a major positive impact on the accuracy of the mandatory annual reporting. Of these 17 manufacturers, eleven are large sized, four are medium sized, and two are small. Most of them, 14 of 17 manufacturers, have fully computerized systems to assist in the preparation of the mandatory annual reports, and have a designated pharmacist to check and verify the accuracy of the information in the report before final official submission to the Thai FDA.

Of these 17 manufacturers, three (all of them large manufacturers) fully passed all three evaluations (Table 1). When considering the information management systems of all three manufacturers, we found that the computer software systems were linked throughout the production process as well as the preparation of reports to be sent to the Food and Drug Administration's information system. There was full data integrity among these three. In addition, there were interesting good practices in the manufacturer having the highest score. This manufacturer had assigned duties according to the structure of an organization chart, and clearly assigned the primary responsible person to record the information according to the mandatory reporting by the FDA. Senior management could also search for and verify their information with the reports. Also, there is the setting of error in the raw material distribution control system. It is used to determine the remaining amount, which is stored as information that can be checked.

Table 1. Inspection results of System Assessment, Cross-Check, and Spot Check.

Manufacturer size	System Assessment		Cross-Check assessment		Spot Check assessment		Summary of manufacturers that passed all three assessments
	Pass	Fail	Pass	Fail	Pass	Fail	
Large Size	9	2	3	8	10	1	3
Medium Size	3	1	2	2	2	2	0
Small Size	0	2	0	2	2	0	0
	12	**5**	**5**	**12**	**14**	**3**	

When considering manufacturers which failed system assessment (N=5), most of the issues can be improved without increasing financial investment; for example, by determining correct operating procedure or providing operating instructions in written form, or enforcing the proper procedure/process of preparing reports and accounts that are compliant with the law on the annual external audit.

The main reason that the cross-check result failed (N=12) is that the accountant, who prepared the account and the report, had no clear understanding of the guidelines set by the FDA; for example, the position of the data used in the preparation of the report, and the need to make a copy of the drug production account and drug sale account according to the form P.Y. 5. To prevent this simple error, we suggest that the Food and Drug Administration produce a manual for training or briefing of responsible persons and verify if they have accurate understanding of the objective and the parameters required by the annual mandatory report.

3. The guidelines for host (manufacturers) to host (Thai FDA) integration was developed to facilitate the e-submission, verification, operators feedback and official approval by FDA. Direct electronic submission will minimize human error due to huge amounts of reporting. Such a host to host linkage system will transfer reporting parameters from the data base used by the pharmaceutical operators directly to the Thai FDA.

The host to host system can only be realized when all pharmaceutical manufacturers have a reliable IT system and reliable data integrity. See detail in appendix 2.

4. The AMR consumption report of 2017 was published and communicated to relevant stakeholders and provides a comparative baseline for the future year reports. Additionally, it can be utilized to increase awareness and engagement with policy makers, the general public and stakeholders in addressing challenges in antimicrobial consumption in humans and animals; in particular, the critically important antibiotics which must be reserved as a last resort for human use. The 2018 data has yet to be published by the end of 2019.

Consumption of human antimicrobials in Thailand in 2017 was 74.22 DDD/1,000 inhabitants/day. Of these, the antibacterial group (ATC group J01) had the highest consumption (70.39% of total), followed by antivirals (J05) (17.56%) and antifungals (J02) (5.69%). Of the antibacterials for systemic use (ATC group J01), the top three were amoxicillin, at 15.04 DDD/1,000 inhabitants/day, followed by ceftriaxone (13.54 DDD/1,000 inhabitants/day), and tetracycline (3.43 DDD/1,000 inhabitants/day).

The consumption of veterinary antimicrobials by food-producing animals, expressed as mg/PCU Thailand, was 560.08 mg/PCU Thailand. The top three antimicrobials with the highest proportion of veterinary antimicrobial consumption was Penicillins (QJ01C) (26.89%), intestinal anti-infectives (QA07A) (20.78%) and Tetracyclines (QJ01A) (19.28%).

At the ATC vet code level five, the top three were amoxicillin, with the largest consumption of 148.12 mg/PCU Thailand (26.45%), followed by halquinol (73.99 mg/PCU Thailand, 13.21%), and chlortetracycline (57.47 mg/PCU Thailand, 10.26%).

The top ten consumption of veterinary antimicrobial agents in Thailand in 2017 was 485.31 mg/PCU Thailand, or 86.65% of total national consumption by food-producing animals. Policy attention should be given to monitor the appropriate use of antimicrobials in these top ten, which will contribute to optimizing consumption.

In response to calls for rational use of antimicrobials and preservation of critically important antimicrobial items as the last resort, this report puts a special focus on the use of antimicrobial classes listed by WHO (5 th revision (http://who.int/foodsafety/cia/en)) as the highest priority and high priority critically important antimicrobials (CIAs) for human medicine

For the highest priority CIA, it include Cephalosporins (3 rd, 4 th and 5 th generation), Glycopeptides, Macrolides and Ketolides, Polymyxins and Quinolones. The consumption of highest priority CIA was 28.99% of total human antimicrobials and 15.73% of total animal antimicrobials in 2017.
Antimicrobials including both the highest and high priority CIAs were recommended to be preserved for humans as the last resort were used in human.

The findings from this first 2017 national report on antimicrobial consumption in humans and animals should be interpreted with care, given the number of limitations of the database. The mandatory reports by importers and manufacturers are not fully validated for accuracy through on-site verification, and are therefore subject to over- or underreporting due to human errors. Mandatory reporting provides total import and manufacturing where total sales data are not available. Therefore, the Health Policy and Systems Research on Antimicrobial Resistance (HPSR-AMR) team has made an assumption that total annual imports and manufacturing are equal to total annual consumption, assuming the stock is constant in an efficient market. Recognizing these limitations, the Thailand-SAC team is in the process of rectifying these gaps. Some countries produce SAC data by using national prescription data and provide a breakdown by retail sector, primary care and hospital sector for human consumption, and by animal species. Although efforts are being made to improve electronic submissions with more detail requested on distributional channels in humans and by animal species in future SAC reports, Thailand currently has these limitations.

Consumption in 2017 aims for in-country monitoring of optimizing consumption as mandated by NSP-AMR, it cannot benchmark Thailand with other international peers due to differences in a) data sources, b) human and animal epidemiology and disease burden, c) health and legal systems in relation to access to antibiotics and d) food animal production systems and profiles. Any un-careful interpretations lead to unnecessary disputes which are counter-productive and not the objective of Thailand SAC. The detail is attached in appendix 4.

5. The regulatory amendment plan was initiated to enhance the accuracy of AMR consumption amount data in Thailand. The mandatory annual report should include the following additional information:

- Total export amount of antimicrobials which will be used to net out (the Thailand-SAC covers only national consumption).
- Percentage of drug distribution by distributional channels and according to animal species.

Ministerial Regulations and report forms are attached in the appendix.

The final level of resource utilization,

- The proposed budget was fully utilized efficiently.

The final delivery of the stated product,

- Apart of this report, by end of 2019, Thailand SAC will produce 2018 consumption with more accurate data both in human and animal in line with the project deliverables.

PART IV. DATA ON USE OF RESOURCES: [Provide (1) summary disbursement data on all the WHO budget or resources received and expended under the project; and (2) description of any problems or remedies relating to use and/or availability of the budget or resources.]

Budget line (category of expenditure)	Authorized amount as per budget A	Actual Project Expenditure B	Diff. between authorized and actual C =A-B
No 1. Remuneration for Mentor/Researchers	940,500.00	940,500.00	-
1.1 Consultant	247,500.00	247,500.00	-
1.2 Expert researcher	198,000.00	198,000.00	-
1.3 Research assistance	275,000.00	275,000.00	-
1.4 Coordinator	220,000.00	220,000.00	-
No 2. Administrative cost	**182,500.00**	**177,541.54**	**4,958.46**
2.1 Communication cost	5,500.00	9,503.41	(4,003.41)
2.2 Producing and printing the report	5,000.00	8,905.00	(3,905.00)
2.3 Office supplies (stationary, cartridge, paper, etc.)	22,000.00	34,493.86	(12,493.86)
2.4 Translation fee	100,000.00	100,000.00	-
2.5 English editorial	50,000.00	24,639.27	25,360.73
No 3. Operational cost	**3,743,500.00**	**3,747,953.24**	**(4,453.24)**
Activity 1 Developing standard guidelines for information sharing to be ready for host to host system	466,000.00	481,669.45	(15,669.45)
3.1.1 Business flow & Data flow Analysis Researcher to analysis Business flow & Data flow "Senior Professional Level"	50,000.00	50,000.00	-
3.1.2 Convene meeting for Data Standard Setting: Allowance	144,000.00	143,319.45	680.55
3.1.3 Convene meeting for Data Standard Setting: Food and refreshment	72,000.00	32,950.00	39,050.00
3.1.4 Data verification	200,000.00	200,000.00	-
3.1.5.Transportation		35,500.00	(35,500.00)
3.1.6.Transcription fee		4,000.00	(4,000.00)
3.1.7.Souvenir		15,900.00	(15,900.00)
Activity 2 Development of tools for the assessment of data quality by pharmaceutical operators	547,500.00	531,552.50	15,947.50
3.2.1 Develop tools, System Assessment Protocol (SAP) and Data Verification Protocol (DVP)			-
- Review document, convene meeting and write report (60 days) "Senior Professional level"	50,000.00	75,000.00	(25,000.00)
- Air fare ticket	10,000.00	3,967.50	6,032.50
- Perdiem (Area A) Non-local participants	3,000.00		3,000.00
- Perdiem (Area A) local participants	12,000.00	1,500.00	10,500.00
- Food	6,000.00		6,000.00
3.2.2 Pre-testing data collection tools in cooperation with Thai FDA experts to develop the annual reports verification guideline.			-
- Researcher to do pre-testing data collection and writing report of 1 site visits (7 days) "Senior Professional Level" :	87,500.00	87,500.00	-
- Air fare ticket	10,000.00		10,000.00
- Perdiem (Area A) Non-local participants	3,000.00		3,000.00
- Perdiem (Area A) local participants	10,000.00		10,000.00
- Logistic cost (Minivan)	6,000.00		6,000.00
3.2.3 Field data collection in cooperation with Thai FDA experts (10 sites)			-
- Researcher to do pre-testing data collection and writing report of 1 site visits (7 days) "Senior Professional Level".	50,000.00	50,000.00	-
- Perdiem (Area A) Non-local participants	15,000.00	1,500.00	13,500.00
- Perdiem (Area A) Non-local participants	30,000.00	90,200.00	(60,200.00)
- Logistic cost	50,000.00		50,000.00
- Food	25,000.00	27,940.00	(2,940.00)
- Logistic cost (Minivan)	30,000.00	43,945.00	(13,945.00)

3.2.4 Compiling good practices for assuring the report quality in pharmaceutical industry			-
- Researcher to review document, compile data and write report (15 days) “Senior Professional level” :	50,000.00	50,000.00	-
3.2.5 Consolidate all reports to final data quality audit report, identify specific audit findings and recommendations			-
- Consolidation the final report	100,000.00	100,000.00	-
Activity 3 Produce the Surveillance of Antimicrobial Consumption report in Thailand 2014-2017	2,460,000.00	2,460,000.00	-
3.3.1 The reporting system on antimicrobial distribution for medicated feed mill manufacturers.	1,500,000.00	1,500,000.00	-
3.3.2 Data collection management (2 Databases)	160,000.00	160,000.00	-
3.3.3 Data analysis (Human and animals parts)	200,000.00	200,000.00	-
3.3.4 Consolidation of final report of Thailand-SAC 2014-2017 in Thai & English	300,000.00	300,000.00	-
3.3.5 English editorial	50,000.00	50,000.00	-
3.3.6 Book’s info graphic & art design	100,000.00	100,000.00	-
3.3.7 Publication	150,000.00	150,000.00	-
Activitiy 4 Improving the ministerial regulation for strong enforcement	Cost sharing by FDA budget		
Activity 5 Consultative meeting with stakeholders (overall meetings 12 times)	270,000.00	274,731.29	(4,731.29)
3.5.1 Allowance	72,000.00	45,000.00	27,000.00
3.5.2 Travel (Flight tickets cost for participants)	120,000.00	38,638.80	81,361.20
3.5.3 Accommodation	36,000.00	10,610.49	25,389.51
3.5.4 Food and refreshment	36,000.00	103,324.00	(67,324.00)
3.5.5 Producing and printing documents	6,000.00	1,560.00	4,440.00
3.5.6 Transportation		75,598.00	(75,598.00)
No 4. Materials			
No. 5. Institutional fees (not exceeding 10% of total budget, not including No. 4 materials)	4,866,500.00		4,866,500.00
5.1 Institutional fees (10 % of total budget)	486,650.00	486,650.00	-
Total budget	**5,353,150.00**	**5,352,644.78**	**505.22**

PART V. LESSONS LEARNED: [This section should include explanations or recommendations regarding unfinished work and/or suggestions considered useful for future projects or activities]

The Development of Surveillance Antimicrobial Consumption (SAC) in humans and animals [YEAR 2] is essential to strengthen the monitoring system of drug distribution in Thailand and support the implementation of the National Strategic Plan on Antimicrobial Resistance (2560-2564 BC).

1. Key future direction of Thai-SAC development

At the retreat meeting (Rose Garden between 7 and 8 May 2019), where members of the HPSR AMR discussed the future of the Thailand-SAC development, there was a consensus of the following direction and strategies:

1.1 Development of a robust Track & Trace System of antimicrobial consumption

The track & trace system starts from the API import until the finished product usage optimize usage and prevent the irrational usage of untracked antimicrobials.

1.2 Strengthen the data integrity of annual reports and systems for estimating consumption

Accuracy and precision must be enhanced by minimizing double counting, net out the export volume, which contributes to the precision of national consumption and in the long term initiating wholesale data reports (instead of current import and manufacturing volume, which primarily reflects national consumption).

1.3 The PCU unit of the AMR consumption report

Antimicrobial consumption per PCU-Thailand should be maintained and aligned with OIE reporting as well as comparable with the ESAC-Net and ESVAC reporting.

1.4 The development of an antimicrobial usage system in Thailand

Valid antibiotics usage should be collected directly from public and private healthcare services for a detailed breakdown by hospital, primary care facility, as well as by classes of antibiotics, different animal farms (both terrestrial and aquacultural), and data from "iDoctor/Doctor Dog" program obtained from animal clinics and hospitals for use in companion animals. The upcoming software used by the DLD will serve one purpose: the future development of Thailand-SAC subaccount for Pet (Thai-SAC-Pet) which will be able to estimate total consumption in cats and dogs and can be netted out from human consumption (for off label use) and from terrestrial and aquacultural animal consumption.

2. Key technical lessons from the Thai-SAC development

2.1 Data completion and clarification

Before processing data from the database of the FDA toward calculation, the data cleaning and verification is a vital process to improve the data integrity.

Methodology for veterinary consumption calculation

In this study, there were two sources of data, registration database at FDA and mandatory annual reports by pharmaceutical operators. The registration database included essential information on veterinary medicinal products (VMP) by ATC Vet Code level 5, the active pharmaceutical ingredient (API), the amount of API, strength unit and dosage form, . As for annual reports, the type of pack size, pack size, number of packs, and quantity of import or manufacture were compulsorily reported and electronically recorded . Part of the information from both of sources was retrieved .

Prior to the calculation process, the data from both sources were mapped into two single Excel worksheets depending on the type of VMP: single VMP (sVMP), the VMP that contains only one antimicrobial API; or combination (cVMP), the VMP which contains more than one antimicrobial API. Then, the calculation process was performed using Microsoft Excel version 2013. Generally, the steps of calculation were as follows:

1. Check for unit agreement. This step aims to identify the unit agreement between strength unit and pack size in terms of solids (milligram, gram, or kilogram) or liquids formulation (milliliter or liter).
2. Calculate the amount of API using the following formula:

$$Amount\ of\ API = \frac{Strength}{Strength\ unit}\ x\ Quantity\ of\ import\ or\ manufacture$$

3. Adjust unit. In this calculation, the amount of API was calculated and converted into grams.

4. Subtract the amount of APIs from out-of-scope VMP (oVMP) and tablets. Some out-of-scope pharmaceutical dosage forms (dermatological preparations and preparations for sensory organs) needed to be excluded, as these formulations were not applied to terrestrial or aquatic animals. These antimicrobials are primary used by companion animals.

5. Subtract the amount of API which are non-target ATC vet codes. For cVMP which contained non-antimicrobial APIs, they are excluded. For the combined VMP, the amount of each API was estimated separately.

After the process of data preparation had been finished, the estimate were classified and presented into two aspects: the total national API and API by ATC vet code. Furthermore, as both the aspects were originated from the same source of data, the total estimate of national API must have been balanced with combined API by ATC vet code. If any irregularity was detected, they are addressed and rectified to make all sheets balanced.

Validation for human antimicrobials

Method

Validation of the number of DDD as estimated by the working group was conducted independently by two external peer reviewers. The reviewers used STATA 14.0 for calculating the DDDs per uniquely-identified registering of numbers of drugs that were distinguished by two key attributes: (1) level-5 ATC and (2) dosage form plus route of administration (Table 2).

Table 2. Data elements and sources for validating the DDD calculation.

Five data elements	**Three data sources**		
	1. Industry's report	**2. FDA's registration**	**3. WHO's ATC/DDD**
A. Qualification			
1. *Unique identifier*	Register number	Register number	Register number
2. *Attribute 1*	Branded name	Active ingredient(s)	ATC level 5 & variant
3. *Attribute 2*		Dosage form - Oral solid - Oral liquid - Injection	Administration route - Oral (O) - Parenteral (P)
B. Quantification			
4. *Storage type 1 (numeric)*	**Quantity (*Q*)**	**Strength (*S*)**	**Defined daily dose (*DDD*)**
5. *Storage type 2 (string)*	**Unit of Q** - mg., g., units - cap., tab. - ml.	**Unit of S** - mg., g., units - mg./ …cap., …tab. - mg./ …ml.	**Unit of DDD** - mg., g., units - cap., tab.

In addition to the three qualitative elements, data for calculation of the DDD was obtained from three sources, including: 1) industry's report on quantity (Q); 2) FDA's registered strength (S); and 3) WHO's ATC/DDD system, based on the formula: DDDs = Q x S / DDD. Working data were divided into two major subsets; 1) single drugs; and 2) combined drugs.

Each was distinguished by the units of quantity reported, including mg. or g.; capsule or tablet (for oral solid form); and ml. (for oral liquid form). Thirteen registered items of single source with the strength reported in "units (MU)", those with missing data on strength, and those with the data corrected in-between by the FDA were omitted from the validation process.

Finding

A total of 2,316 and 403 registered items of single and combined drugs respectively were subject to the validation. Of the total number of 229, 1,676, and 398 items of single drugs which were reported the quantity in mg or g, capsules or tablets and ml, respectively; there were 14 items which we found discrepancy in the DDD through validation by the external review process.

For the total number of 403 combined drugs, 298 items with assigned DDD figure; only 0, 0, and 2 items of these combined items reported their quantity in mg. or g., capsules or tablets, and ml, respectively which we found DDD discrepancy. Out of 105 items of the combined drugs did not have assigned DDD; then separate DDD of each of the combined drug was estimated; at the first level of ATC; 1 of 11, 28 of 85, and 0 of 9 items were found to have the DDD discrepancy for those reported the quantity in mg or g, capsules or tablets, and ml, respectively.

Out of 75 items of the combined drugs with separate DDD of the second level of ATC; 0 of 10, 9 of 57, and 0 of 8 items were found the DDD discrepancy for those reported the quantity in mg or g, capsules or tablets and ml, respectively.

A total of 24 items of the combined drugs with separate DDD at the third level of ATC reported the quantity in capsules or tablets, of which six items were found to have the DDD discrepancy. For three items with the fourth ATC of combined drugs with separate DDD, all strength data were missing, hence none were validated.

All these discrepancies were rectified by the research team. This work is extremely tedious and time consuming.

2.2 The Development of a tool for the DQA of reports submitted by the pharmaceutical operators

The tool was developed by applying the Data Quality Audit Tool as proposed by USAID 2008[1] together with the methodology applied in conducting routine audit by the Post Marketing, Bureau of Drug Control, Food and Drug Administration. Summary of methods for checking information is classified into 3 sequential components as follows.

1) System assessment, is an assessment of the readiness of the information system established by the manufacturers, using the evaluation form developed by researchers, and the analysis of the flow chart of data as well as the information by interview in order to understand the organizational structure, the training of responsible staffs, manuals that describes the procedure of extracting information from various parts of the work process, data collection, and data verification in the Data collection and Reporting Forms/Tools system as well as the Data Management process. The evaluation is done by the total score of each operator according to the following specified criteria.

- Available and complete (2 points score). Supporting documents were requested for review.
- Available but not complete (1 point score). Supporting documents were requested for review.
- Not available/Only verbal (0 points score).

2) Cross – Check, is the check of the consistency of data from more than one different sources. If an inconsistency is found, the manufacturer must be able to clarify, and to find the cause for traceability. This study examines the following key information.

- Annual report (Accounting Department).
- Sales volumes (Sales Department).
- Stock card which records the finished products at the beginning of the year and the end of the year.

3) Spot – Check is to get one excerpt in the operation procedure in order to randomly check the accuracy of the information whether it is consistent with the figures in the recorded document or not, for example, weighing the raw materials contained in the raw materials warehouse to verify the record in stock cards.

3. The sustainability of the Thai-SAC system

Several enabling factors are identified for a sustainable Thai SAC include:

- The formal working group is set up to proactively drive project with high engagement from all relevant stakeholders.
- The current funding for the project is for R&D; the Thai FDA, hosting the Thailand-SAC needs to plan routine budget to support the sustainability of Thailand SAC in subsequent fiscal years.
- The capacity of working group should be strengthened and include new young talent researchers and staffs for transition from R&D phase into a routine sustainable production of Thailand-SAC.
- The policy communication of the findings is important to optimize consumption in both human and animal sectors.

Appendix 1

(File attachment 1 โครงการพัฒนาระบบติดตามการกระจาย และการใช้ยาต้านจุลชีพในมนุษย์และสัตว์ปีที่ 2)

Appendix 2

(File attachment 2: HOST to HOST)

Appendix 3

(File attachment 3: Assessment of data quality)

Appendix 4

(File attachment 4: Thailand Surveillance of Antimicrobial Consumption (Thailand SAC) in 2017 report)

Appendix 5

(File attachment 5: Regulation)

[1] U.S. Agency for International Development (USAID). (2008). Data Quality Audit Tool. Retrieved from www.theglobalfund.org/documents/.../ME_DataQualityAudit_Tool_en/

Development of Surveillance Antimicrobial Consumption (SAC) in human and animal [YEAR 2]

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