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วารสารวิชาการสาธารณสุข
สำนักวิชาการสาธารณสุข กระทรวงสาธารณสุข
ปีที่ 29 ฉบับพิเศษ มกราคม - กุมภาพันธ์ 2563

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Introduction

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- Results
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บทบรรณาธิการ **Editorial**

Thai Drug Systems 2020

While medicines play a crucial role in the health systems, they also contribute to the rapidly increasing cost of providing health services. In Thailand, medicine prices, particularly single-source manufacturer or patented drugs are often higher than those in many high-income countries. The World Health Organization estimates that globally up to 40 per cent of medicines are used irrationally. Additionally, the irrational use of medicines creates tremendous side and toxic effects. There is also evidence that differences in health insurance schemes lead to inequitable access to essential medicines.

To achieve the goal of the sustainable Universal Health Coverage – universal access to essential health services and technologies without financial barrier -- a country needs a decent and well managed medicine systems. The systems include how essential medicines are developed, selected, produced/imported, procured, equitably distributed, effectively accessed and rationally used under 'good governance'. Good management of the systems would reduce waste and cost and increase access to essential medicines.

This theme issue, **'Thai Drug Systems 2020'**, of the Journal of Health Science, Ministry of Public Health, Thailand, includes 14 articles describing various components of the Thai drug systems. All articles are extracted from the 14 chapters in the third Thai Drug System Report 2019. The report assessed current situations, and proposed concrete recommendations for development. The Report, since it first edition in 1995, has been well recognized and widely referred to among Thai academics, researchers, and policy advocates. This theme issue, in English, now attempts to meet the interests of the international community

The authors are experts from various 'walk of lives' related to medicines systems, from both public and private sector. They include academics, health professionals, civil society organizations and policy makers. Although the chapters and articles have been extensively reviewed including a few face-to-face consultation meetings, they still have limitations. These include the availability of the required information, the authors' interest to contribute and time constraints.

We thank the Chief Editor of the Journal of Health Science, Dr. Wiwat Rojanapitayakorn, who strongly committed, and dedicated his time and effort for the publication of this theme issue. Special thanks also go

to the editorial team of the report, Dr Vichai Chokevivat, Mr. Sorachai Jamneandamrongkan, Dr. Sripen Tantivess – for their invaluable comments and suggestions. We appreciated all authors' huge efforts and patients in preparing and revising the final chapters and manuscripts in due time.

Finally, we thank the Health Systems Research Institute for its generous financial and management supports and the Thai Food and Drug Administration, the National Health Security Office, universities and all members of the technical committee of the report for their strong technical support.

Dr. Suwit Wibulpolprasert

Chairman of the Technical Committee

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National Drug Policies in Thailand: Evolution and Lessons for the Future

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Abstract Many countries encountered various pharmaceutical problems which challenged them to find long-term solutions to achieve the goal of access to medicines. To address these issues, the World Health Organization suggested that countries generate and implement a National Drug Policy (NDP), and launched guidelines to assist the process of policy development. In most countries, the NDP has similar key objectives of access, quality, and rational use of medicines; but some local specific objectives might differ. This review explores the historical development of NDPs in Thailand using information from both public and not-public sources, analyzes outcomes and challenges, and provide recommendations for further development. The findings show that national drug policies in Thailand were initially developed in 1981 and evolved over time until getting the current NDP in 2017. The NDP development took existing pharmaceutical problems and national strategies of the Royal Government into account in order to create a policy which were sensitive to local situations and national directions. The evolution from the first to the fourth NDP has strengthened its platform to increase continuity and development of special projects and interventions to solve the problems in the drug system. Although NDPs in Thailand have been quite successful, there are stll some strategic inadequacies which require further support and participation from stakeholders and additional resources for implementation. Furthermore, a competent advocacy body and a Secretariat Office should be established to bolster policy coordination and implementation progressively.

***Keywords*: drug system, national drug policy, drug system strategy, reference drug price, targeted list of priority medicines**

Introduction

Right to health is considered as fundamental human right in which medicines are significant elements of for prevention and treatment to maintain people's good health.[1,2] However, many countries are still facing problems in the drug systems such as high cost of medicines, inequitable access, pervasively inappropriate marketing and promotion of pharmaceu-

ticals.[3-5] These issues have made it difficult for countries to fulfill the aim of access to medicines in response to the right to health. The World Health Organization (WHO) recommends that to address some of these pharmaceutical problems countries should develop a national drug policy (NDP) with a committed framework for achieving good access to medicines.[6]

The concept of a national drug policy was initially mentioned in the 28th World Health Assembly in 1975; and in 1986 WHO launched guidelines for member states to develop national drug policy. The NDP guidelines mainly comprise goals and objectives which depend on a country's situation and priorities. Key policy objectives are to improve access, quality, and rational use which require certain components, i.e. selection of essential drugs, quality assurance, and drug financing, in order to meet WHO's recommendations.[6,7]

In Thailand, national drug policies was initiated in 1981 (B.E. 2524); and evolved into the current NDP in 2017 (B.E. 2560) which aims to address the pharmaceutical problems and fully develop national drug systems.[8,9]

The objectives of this article are to present the review of the historical development of NDPs in Thailand and to identify challenges and provide recommendations for further development.

Methods

This qualitative study is a documentary review of the evolution and development of NDPs in Thailand using both public and non-public data. Drug policies and other relevant information were obtained from various sources including academic journals, research reports, minutes of committee and subcommittee meetings, official correspondence, and laws and regulations. All the efforts are aimed to describe the historical development of NDPs, analyze successful outcomes and challenges, and provide some recommendations.

History and Evolution

The development of national drug policies began with situation analysis on pharmaceutical problems e.g. low quantity of local production especially the active ingradients, irrational use of drugs, and high pharmaceutical prices and expenditure. These analysis helped to set goals and strategies of NDPs. There are committee and sub-committees which consist of governmental authorities, independent technical experts and other stakeholders. The sub-committee's tasks are to make recommendations to the committee for decisions to achieve NDPs' goals and objectives. This advisory body and its subordinates mainly are the national committee - National Drug System Development Committee (NDSDC) - and 6 sub-committees for the following purposes of developing on: Drug System Strategies and National Drug Policy, National List of Essential Medicines, Rational Use of Drugs, Pharmaceutical Reference Prices, Pharmaceutical Industry, and Steroid Monitoring System. The Committee's Chair is the Deputy Prime Minister and the Sub-Committees' Chair is the Deputy Permanent Secretary of Ministry of Public Health (MoPH). The secretariat office for the Committee and Sub-committees are mainly the Food and Drug Administration (FDA) and joint secretariat with other government

organizations. To date, there have been 4 NDPs in Thailand which can be separated into 3 significant periods.

The Initiatives of National Drug Policy

National Drug Policy B.E. 2524

The first National Drug Policy formulated and officially imposed in 1981 (B.E. 2524) by Minister of Public Health. It specified 5 projects to implement which included: (1) improving the medicine supply and distribution system, (2) improving drug manufacturing practices, (3) conducting research and development (R&D) of modern and herbal medicines, (4) increasing health professionals' knowledge on essential medicines, and (5) strengthening the drug regulartory system. This policy was implemented and led to limited scope of results, yet it was suit to the national situations and covered systemic problems, particularly the irrational use and waste of medicines. However, some problems – R&D of pharmaceutical raw materials in order to build the capacities and feasibilities for local pharmaceutical production – were mentioned in the NDP but were not a focus of the implementation.[9,10]

National Drug Policy B.E. 2536

This second NDP was launched in 1993 (B.E. 2536) with shrinkages and additions to the previous policy strategies. This NDP inluded roles and responsibilities of various organizations in order to make the policy clearer to implement and for main actors to take actions. The considerable changes of the NDP were to (1) promote and expand NLEMs to private hospitals and settings, (2) investigate the health promotion and preventive potential of herbs and herbal medicinal products, and (3) develop the drug registration and approval system, especially laws and regulations, for fostering consumer protection. The policy performed quite well with accomplishment, for instant developing surveillance and monitoring system for drug safety and adverse effects; stipulating a labeling requirement of generic names' indication; issuing the drug registration guidance for export purposes; developing National List of Essential Medicines (NLEMs) to have sub-categories in order for specialists' and subspecialists' suitable prescription to diseases. However, the policy outcomes showed little progress on the local production of pharmaceutical raw materials, regulations for clinical research and ethical issues, and finding the solution for high cost of drugs. Many of these problems remained, partly because of not having a secretariat office to continuously coordinate and support policy implementation nor policy monitoring and evaluation system.[11,12]

The Changes for Continuity

National Drug Policy B.E. 2554

There was a situation of discontinuous policy during 1993-2011 (B.E. 2536-2554), which was a consequence of the frequent expiration of National Drug Committee's tenure following dissolution of the parliament. Therefore, in 2008, to solve the problem of poliy discontinuity, Regulations of the Office of the Prime Minister on National Drug System Development Committee B.E. 2551 was formulated and approved to allow NDP to be developed by National Drug System Development Committee (NDSDC).[13] Consecutively the third NDP was developed by the NDSDC, and gianed officially approved from the

cabinet of Thailand in 2011.[14]

The third NDP derived from the country's pharmaceutical situation and additinal advocacy: the resolution of the 1st National Health Assembly in 2009 on universal access to medicines and the resolution of the 2nd National Health Assembly in 2010 on ethical issues for drug promotion and alternative and traditional medicines for healthcare services. This led to the situations brought out National Drug System Development Strategy B.E. 2555-2559 with the following strategies: (1) accelerating access to medicines, (2) promoting rational use of drugs (3) developing local pharmaceutical industry (4) improving national regulatory systems.[13] The monitoring in 2017 showed that most strategic indicators were achieved including locally produced generic medicines which had increased to 150 medicines (indicator: 30 medicines), irrational use of antibiotics had decreased by 50 percent. Nevertheless, there were obstacles hindering successful outcomes e.g. lack of staff to undertake responsible tasks for the committee, and inadequate NDP's advocacy power to make changes in drug systems, although they typically had enough capacity to encourage and coordinate stakeholders.[15]

Comprehensive Transformation and Movement

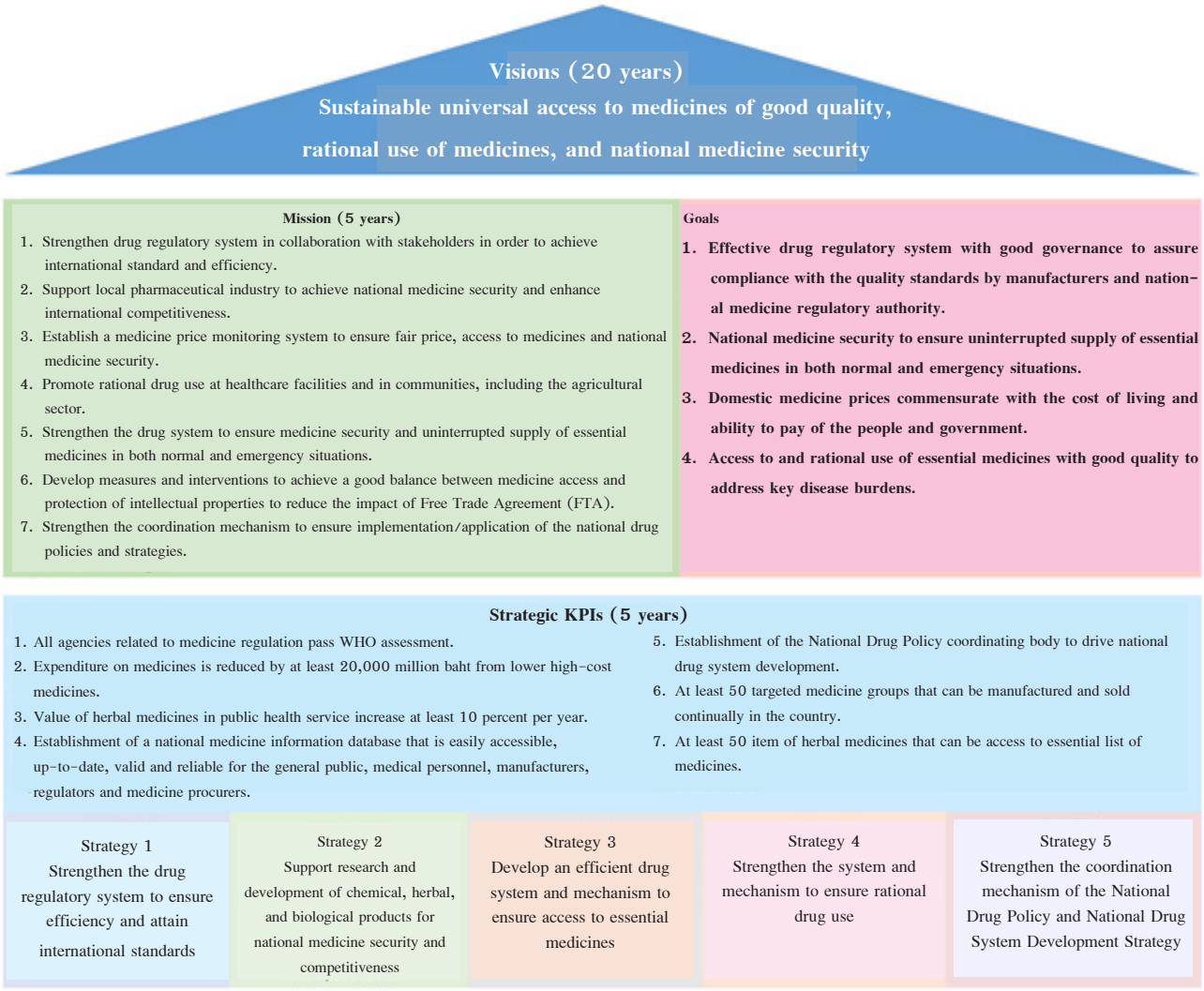
National Drug Policy B.E. 2560-2564

In 2016 the national policy vision, Thailand 4.0, launched by Royal Thai Government aimed to unlock the middle-income country and inequality traps with new economic model.[16,17] Successively, the 20-year Thai National Strategy and the National Master Plan also came into force, and it was mandatory for other local policies and plans to deliberately corresponded with the national vision.[18] In addition, it was necessary in the pharmaceutical context so that policy development could address nsome key challenges. For example, there was a high percentage of pharmaceutical expenditure (41%) from overall health expenditure (100%), percentage of imported medicines (37%) to locally produced medicines (63%) in the NLEM, and antimicrobial resistant as a result of problem from irrational use of drugs in healthcare and agriculture.[19]

These issues were included in the National Drug Policy B.E. 2560-2564 with the principal objectives of increasing the potential of local pharmaceutical industry, controlling pharmaceutical expenditure, reducing pharmaceutical imports, and promoting rational use of drugs, as shown in Figure 1. This NDP was approved in principle by the NDSDC in 2016 (B.E. 2559), not yet officially endorsed by the cabinet,[20] because the government has changed the screening and prioritization process of agendas proposed to the Cabinet for considerations. These Cabinet's processes took longer period of time for official approval of the NDP.[21]

As the NDP was not officially endorsed, the NDSDC had agreeably decided to advocate NDP temporarily with integrated measures on access to medicines, pharmaceutical cost containment, and national integrity and self-reliance which these measures were possible to be implemented successfully by government authorities, including Food and Drug Administration, Department of Medical Sciences, Department of Thai Traditional and Alternative Medicines, and Department of Intellectual Property. Therefore, yearly quick-win projects and interventions were made to help address some key issues.[22,23]

Figure 1 National drug policy and national drug system development



The Quick-Win Projects and Interventions

There are 2 importantly measurable projects: reference prices for public procurement and targeted list of priority medicines.

(1) Reference Prices (RPs) for Public Procurement

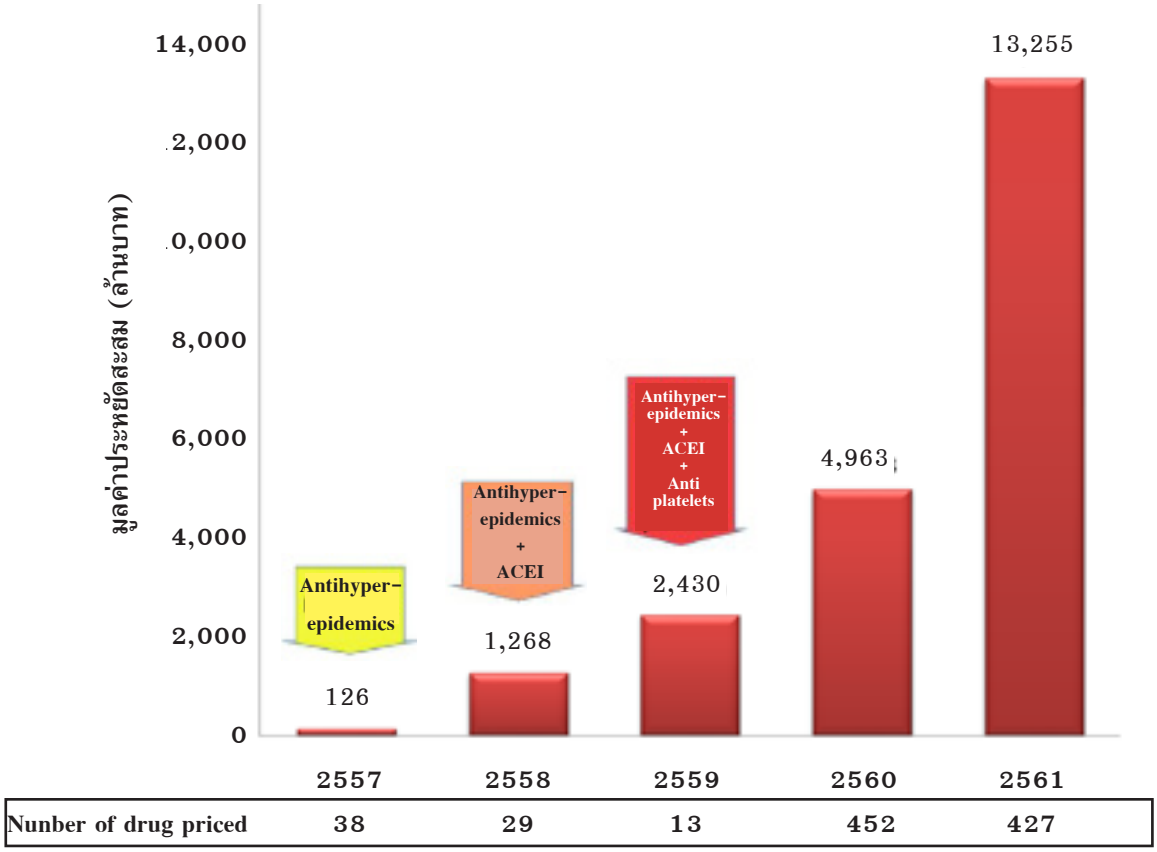
The Reference Prices for Public Procurement had originally been introduced in 2008 by the National Drug System Development Committee (NDSDC), which gave measures for pharmaceutical cost containment in order to save pharmaceutical expenditure as well as increase access to medicines. To implement these measures, the Committee appointed a Reference Pharmaceutical Prices Subcommittee to set the Reference Prices; these were only for NLEM medicines as maximum procurement prices and were set on the calculation basis of "mode".[24] The RPs was forced through the Regulations of the Office of the Prime Minister on Government Procurement B.E. 2535 and later through the Public Procurement and Supplies Administration Act B.E. 2560. It is mandatory that the public hospitals, especially hospitals under MoPH, procure pharmaceuticals and medical products with their prices which were below or equal to the RPs.[25]

Later in 2013 NDSDC improved concepts and main procedures to be more reliable and fair to both hospitals (purchaser) and manufacturers (merchant). Such improvements included: (1) a greater implementation extent of measure – setting RPs for conventional and traditional & herbal medicines both NLEM medicines and non-NLEM medicines, (2) separation of drug groups regarding market competition to employ suitable methods for RPs setting – group 1 is the competitive market and group 2 is the monopoly and oligopoly market, (3) modification of the calculation method from mode to "median", and (4) development of fairness and transparency – including public hearings and appeal procedures to the decisive process of pricing.[24,26]

The reference prices for public procurement is firmly a part of NDP strategy 3: controlling pharmaceutical expenditure and increase access to medicines, and is indirectly a part of NDP strategy 4: promoting the rational use of drugs. The measure has been implemented using new concepts and procedures during 2014–2018 which priced 959 drugs in 10 therapeutic groups. Consequently, a study conducted by the Thai FDA suggests that the government procurement budget for pharmaceuticals saved accumulatively 13,000 million Baht, which mostly derived from antihyperlipidemic drugs and angiotensin converting enzyme inhibitors (ACEIs) at approximately 7,300 and 2,000 million Baht respectively,[26] as shown in Figure 2.

The Reference Prices (RPs) for Public Procurement have purposely been implemented for pharmaceutical

Figure 2 Cumulative budget savings of pharmaceutical reference prices



cost containment during 5 years (2014-2018) with budget saving 13,000 million Baht. However, it is not possible to say that the saving was a unique result of the NDP B.E. 2560-2564, because the evaluation period was 2014-2018 and the NDP (B.E. 2560-2564) was implemented during 2017-2021. Therefore, the result of the RPs measure can partly be claimed for the current NDP of only 2 years during 2017-2018, which saved government procurement budget about 5,200 million Baht.

The RPs measures introduce maximum purchasing prices which means that medicine procurement is now actually purchased at lower prices than the RPs due to the negotiating and bargaining power of hospital purchasers. So, the savings made as a result of the measures (5,200 million Baht) was only a minimum saving on medicine procurement; the saving amount could potentially be higher than that.

(2) Targeted List of Priority Medicines

The national situation of pharmaceutical industry showed that pharmaceutical manufacture had the lowest potential among all other health-related manufacturing industries; in addition, the proportion of local production value to imported value was quite low 1:2. Furthermore, a tendency toward pharmaceutical consumption increased substantially due to the growing ageing society in Thailand and leading to increased demand on medicines for chronic diseases.[27-29]

To narrow the gaps, the Thai Food and Drug Administration (FDA) as the NDSDC's secretariat launched a "Targeted List of Priority Medicines" with integrated inventions.[23] This mainly works to achieve NDP strategy 2, developing and supporting the local pharmaceutical industry for the purposes of domestic consumption and exportation; this could also contribute to increasing access to essential medicines and reinforcing national drug systems more sustainably, in relation to NDP strategy 3.

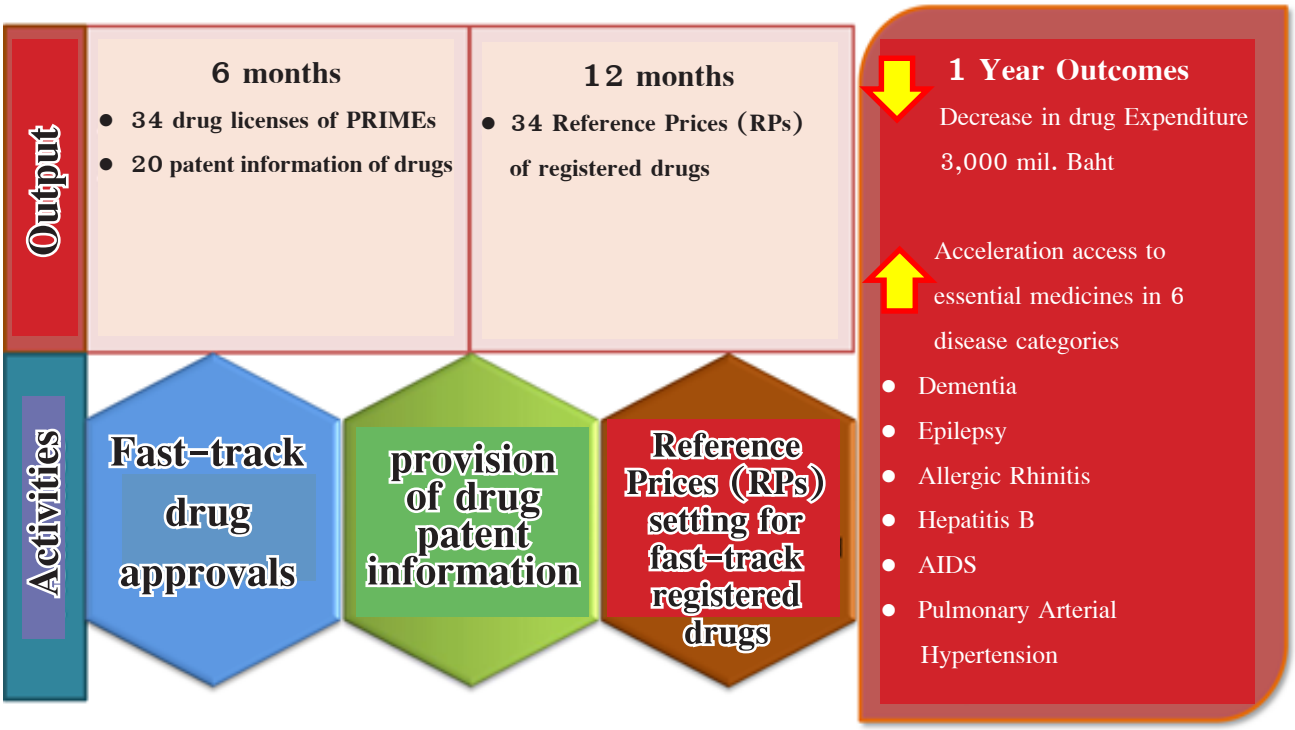
The Targeted List of Priority Medicines (PRIMEs) brought about in 2017 has a list of 144 medicines to support and enhance medicine availability and also increase access to medicines. The PRIMEs were selected mainly based on essential medicines with local unavailability or with a single brand and imported high-cost medicines for which government support were necessarily needed to motivate and incentivize local manufacturers.[23] A prioritization process later matched PRIMEs suitably with integrated inventions, as a matter of fact, each medicine needed different interventions to address their particular problems.

To encourage the availability of generic drugs, the Thai FDA issued 2 announcements putting integrated inventions in place to enhance local production and importation: including (1) provision of drug patent information to local manufacturers to induce their interests on generic production; (2) 50% reduction in registration fee; (3) fast-track drug approvals; and (4) RP setting for fast-track registered drugs.[30,31]

The PRIMEs, with their integrated interventions, had been expected to decrease medicine prices and save the government budget about 3,000 million Baht. It was also expected to increase access to medicines in 6 therapeutic groups: dementia, epilepsy, allergy rhinitis, hepatitis B, AIDS, and pulmonary arterial hypertension (PAH) as shown in the Figure 3.

The actual results after project implementation during 2017-2018 revealed that 102 licenses for generic drugs were approved, and were able to substitute original drugs in 5 therapeutic groups, except

Figure 3 One-year roadmap for targeted list of priority medicines (PRIMEs)



AIDS.[23,32] In addition to expediting drug approvals, the Reference Prices for Public Procurement was a critical intervention to increase access to medicines. Under the PRIMEs project, 29 medicines were priced RPs and surprisingly saved the government procurement budget about 4,400 million Baht, which was higher than expected.[32] Even though the PRIMEs project has not made interventions for all 144 priority medicines (for example, as a result of different problems and situations of each PRIMEs, it provided patent information on only 40 medicines, a reduction in registration fees for 53 medicines and fast-track approvals and RPs setting on 34 medicines), it has completed almost all of its goals in the project first phase.

To date, NDP B.E. 2560-2564 has not been officially evaluated yet, as it was not finished the implementation period of the NDP, despite having an obviously positive performance by saving the government's procurement budget and increasing access to essential medicines.

Discussion

The National Drug Policy in Thailand has evolved significantly over the past 35 years with 4 different versions. The first and the second NDP achieved their goals and objectives mainly solely on improving quality use and increasing access to medicines by developing the surveillance and monitoring system for drug safety and adverse effects, and separating National List of Essential Medicines (NLEMs) to have sub-categories suitably for diseases and special health issues. However, the NDP did not thoroughly solve all pharmaceutical industry-related problems. The NDPs performed well for the situation at that time but it did not deal with the inherent problems of the in-

dustry.

The third NDP (B.E. 2554) considerably changed the NDP platform from a political to a legal platform. The Regulations of the Office of the Prime Minister on National Drug System Development Committee B.E. 2551 were able to formulate the policy more continuously, but still needed official establishment of the cabinet approval. Although this NDP enjoyed many achievements and fulfilled most indicators, according to monitoring and evaluation's results some strategic objectives remained incomplete and unattained. More government support, greater participation of stakeholders and sufficient staff members with professional capabilities were needed for effective NDP implementation.

The latest and current policy, NDP B.E. 2560-2564, has been developed more exclusively and suitably with the country's context in line with both government strategic goals and the drug system itself. Although this NDP has not been approved officially, in 2016 the responsible committee, NDSDC, allowed implementation of the unofficial version because the Cabinet's policy approval required a long time of screening and prioritization process. The Cabinet's approval is essential to policy implementation for stakeholders' participation, particularly other stakeholders and agencies outside MoPH. Therefore, to implement policy temporarily, the integrated measures along with yearly quick-win projects and interventions were undertaken. Projects have included Reference Prices (RPs) for Public Procurement; and Targeted List of Priority Medicines (PRIMEs), which the ultimate purpose was to save government procurement budget; and to motivate availability of generic drugs substituted for original drugs by means of local production respectively. These 2 projects have performed well and delivered the fruitful outcomes of procurement budget saving (5,200 million Baht) and increase patient access to medicines in 5 therapeutic areas.

In conclusion, the national drug policy in Thailand has evolved considerably since 1981. It developed in the beginning as NDP B.E. 2524 to solve the pharmaceutical problems of the lack of timely access to medicines and rational use of drugs, and next as NDP B.E. 2536 to provide consumer protection though the drug registration and approval system. To strengthen continuity of NDP formulation, the Regulations of the Office of the Prime Minister on National Drug System Development Committee B.E. 2551 was launched to facilitate NDP's development continuously which resulted in NDP B.E. 2554. Similar to previous versions, this NDP mostly succeeded in increasing the potential of local pharmaceutical industry, and in promoting the rational use of drugs and in decreasing the irrational use of antibiotics. The current NDP B.E. 2560-2564 was formulated comprehensively by involving national strategies and master plans in addressing local pharmaceutical situations and problems. Presently, the Cabinet has not yet officially endorsed this latest NDP, although the Committee has implemented quick-win projects and interventions, namely Reference Prices (RPs) for Public Procurement and Targeted List of Priority Medicines (PRIMEs).

Overall, Thailand's numerous National Drug Policies have fulfilled their objectives and goals and improved drug systems considerably. The policy would however have achieved more, if the NDSDC set out higher and stronger levels of enforcement to be the

Act (not Regulation) in coordination with various stakeholders. The NDP was generated closely to fit the needs of current national policies, strategies, and master plans to be assured supports from the Royal Thai Government. In addition, to address pharmaceutical problems effectively and in a timely manner there should be a permanent secretariat office officially established in the FDA with sufficient numbers of government officers to coordinate and operate the committee and subcommittees for successful policy implementation.

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บทคัดย่อ: นโยบายแห่งชาติด้านยาของประเทศไทย: วิวัฒนาการและบทเรียนเพื่อการพัฒนา

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หลายประเทศเผชิญกับปัญหามากมายในระบบยาที่จำเป็นต้องแก้ไข เพื่อทำให้ประชาชนสามารถเข้าถึงยาจำเป็นที่มีคุณภาพได้อย่างทั่วถึง โดยองค์การอนามัยโลกได้ให้ข้อเสนอแนะไว้ว่าเพื่อแก้ปัญหาในระบบยา แต่ละประเทศควรจัดทำนโยบายแห่งชาติด้านยา พร้อมทั้งได้จัดทำคู่มือนโยบายแห่งชาติด้านยาเพื่อเป็นแนวทางให้แก่ประเทศต่าง ๆ โดยนโยบายแห่งชาติด้านยาประกอบไปด้วยวัตถุประสงค์หลักสำคัญคือ การเข้าถึงยา ยาที่มีคุณภาพ และการใช้ยาอย่างสมเหตุผล อย่างไรก็ตาม แต่ละประเทศอาจมีวัตถุประสงค์หรือเป้าหมายเพิ่มเติมที่แตกต่างกันออกไปได้ตามบริบทของประเทศ โดยการศึกษานี้เป็นการทบทวนวรรณกรรมและเอกสารที่เกี่ยวข้อง จากฐานข้อมูลที่เผยแพร่และมิได้เผยแพร่เป็นสาธารณะ มีวัตถุประสงค์เพื่อศึกษาการพัฒนานโยบายแห่งชาติด้านยาของประเทศไทยและวิวัฒนาการ รวมถึงวิเคราะห์ผลการดำเนินนโยบายและความท้าทาย และให้ข้อเสนอแนะสำหรับการพัฒนาในอนาคตต่อไป ผลการทบทวนวรรณกรรมพบว่า นโยบายแห่งชาติด้านยาของประเทศไทยริเริ่มพัฒนาครั้งแรกในปี พ.ศ.2524 จนถึงปัจจุบัน นโยบายฯ ได้เริ่มจัดทำโดยการรวบรวมสถานการณ์และสภาพปัญหาในระบบยา และต่อมาได้ผนวกบูรณาการยุทธศาสตร์ชาติและแผนแม่บทแห่งชาติที่รัฐบาลได้ประกาศใช้เข้าในการจัดทำด้วย เพื่อให้ได้นโยบายฯ ที่สอดคล้องและครบถ้วน จากการดำเนินนโยบายแห่งชาติด้านยาของประเทศไทยตั้งแต่ฉบับที่ 1 ถึงฉบับปัจจุบัน พบว่านโยบายแห่งชาติด้านยาของประเทศไทยได้มีวิวัฒนาการและพัฒนาเป็นอย่างมาก ด้วยความพยายามสร้างความต่อเนื่องในการพัฒนานโยบายและจัดทำโครงการหรือมาตรการเพื่อให้สามารถแก้ปัญหาในระบบยาได้อย่างเหมาะสม อย่างไรก็ตาม แม้ว่านโยบายแห่งชาติด้านยาจะบรรลุตัวชี้วัดยุทธศาสตร์ แต่ยังคงมีความท้าทายที่ยังไม่บรรลุ เช่น การขับเคลื่อนสนับสนุนอุตสาหกรรมผลิตยา เพื่อความมั่นคงทางยาของประเทศ ซึ่งจำเป็นต้องได้รับความร่วมมือและมีส่วนร่วมจากภาคส่วนที่เกี่ยวข้อง รวมถึงทรัพยากรจำเป็นที่เพียงพอต่อการขับเคลื่อน นอกจากนี้ควรมีสำนักงานเลขานุการถาวรจัดตั้งขึ้นในสำนักงานคณะกรรมการอาหารและยา และผลักดันให้คณะกรรมการพัฒนาระบบยาแห่งชาติและคณะอนุกรรมการที่เกี่ยวข้องอยู่ภายใต้อำนาจการกำกับดูแลของพระราชบัญญัติยา เพื่อทำให้สามารถดำเนินและประสานขับเคลื่อนนโยบายแห่งชาติด้านยาได้มีประสิทธิภาพและเกิดผลสัมฤทธิ์มากยิ่งขึ้น

คำสำคัญ: **ระบบยา, นโยบายแห่งชาติด้านยา, ยุทธศาสตร์ระบบยา, ราคากลางยา, ยามุ่งเป้า**

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Thailand's Legal Framework Concerning Drugs

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Abstract This study aimed to explore and summarize current landscape of Thailand's laws and regulations concerning drugs and related legal problems. The study was conducted through documentary research and gathering of experts' opinion on key problems and recommendations. On governance of drug system, it was found that there were 39 pieces of associated laws concerning drugs which can be further categorized into 5 categories which are laws on pharmaceutical products control (4 pieces), laws on governance of healthcare professions and service (11 pieces), laws on consumer protection (5 pieces), laws on trade and commerce (10 pieces), and laws on others specific responsibility (9 pieces). On financing of drug system, the laws on trade and commerce have significant bearing on higher national drug expenses. Although Thailand has been implementing the universal health coverage program; but laws on health security is still unable to prevent bankruptcy due to high healthcare cost. On drug research and development and drug manufacturing, the laws on pharmaceutical product control does not have tangible measure promoting domestic drug research and development with the exception of recently passed Herbal Products Act B.E.2562. On drug selection, laws on pharmaceutical product control focuses on registration procedure which emphasizes effectiveness, efficiency, and safety of the product. Selection procedure was established for drugs listed in the National List of Essential Medicines which are then offered through benefit package of all health security funds. On drug procurement, Governmental Procurement and Inventory Management Act B.E. 2560 allows government departments to organize collective bargaining on district/provincial level, which departments under the Ministry of Public Health are particularly receptive to, resulting in reduction in drug expenses. Health security funds also negotiating drug prices on national level to procure essential drugs at reasonable price thus increase accessibility for the patients. On drug distribution, Drugs Act, B.E. 2510 and Health Facility Act, B.E. 2541 allows drug stores and private clinics, in addition to hospitals, to dispense prescription drugs. This alleviates workload and traffic in and to hospitals as patients may bring prescription to those alternative distribution channels. On drug utilization, At present grants preliminary recompense to patients who suffer from improper medical services according to health

security laws and also facilitates litigation for further compensation through consumer protection laws.As a recommendation to enable effective enforcement of laws concerning drug leading to intended result, agenda for rigorous enforcement, passing of new laws in certain issues, amendment to specific details which hinder the development of nation's drug system should be prioritized.

Keywords: **drug, drug system, laws, drug act, laws concerning drug**

Introduction

Drug is one of life's necessities, merit goods and key resource in health care. In B.E. 2556, Thailand's expense on drug is approximately 140,000 million bahts which equates to 24% of health expenditure.[1] Given such importance, efficient drug governance system is essential.

Laws is a system of rules which is imposed on a particular community to regulate rights, duties, and the relationship between its members[2] to maintain order, deliver justice, and protect the public interest according to the need of the state,[3] thus many pieces of laws were passed by the government to regulate drugs throughout their lifecycle.

Thailand has been having problems with high drug expenses, irrational uses and misuse of drug. Nowaday, there are a multitude of new technologies under development that will have a major impact on medical and pharmaceutical industry such as the use of artificial intelligence/machine learning,[4] drug development from biological product, and gene editing.[5] All of these will certainly change drug research and development and also affect the economy, monetary, and fiscal system in the future. For this, laws can be an accelerator or a hindrance to further progress.

From the importance of laws elaborated above, this study was conducted with the aim to explore and summarize current landscape of laws concerning drug, its scope, and enforcement problems that can later be used to establish guidelines for new laws or amendment in benefit for Thailand.

Methodology

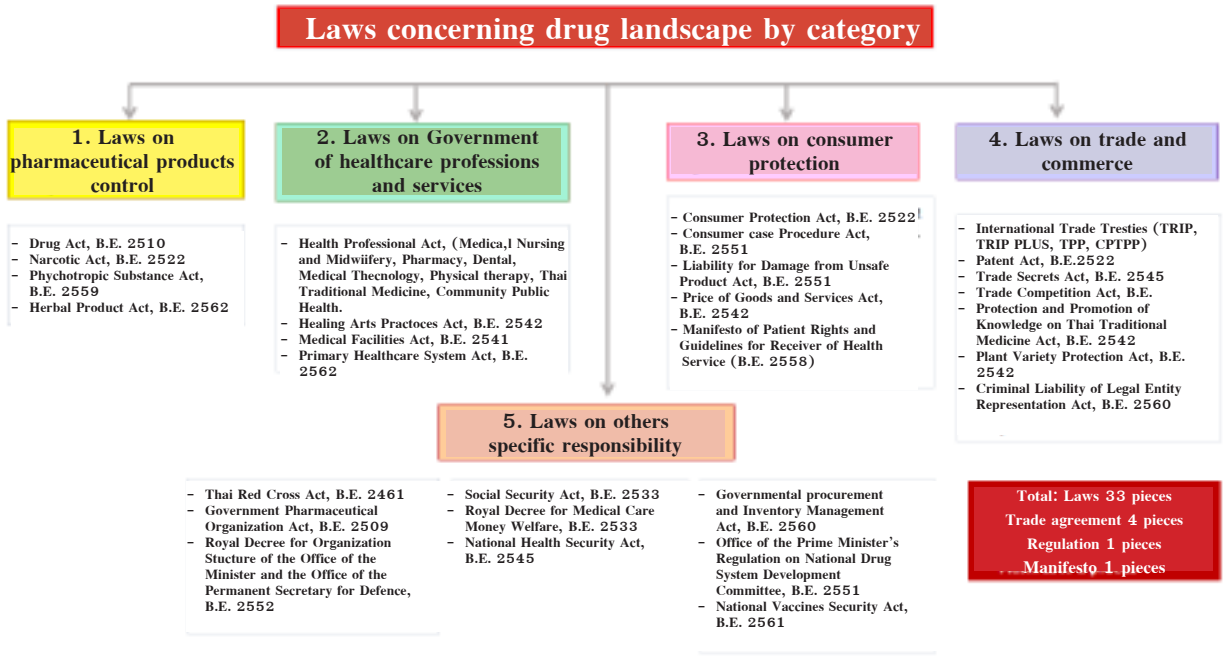
Through documentary research and categorizing laws into categories which are laws on pharmaceutical products control, laws on healthcare professions and services, laws on consumer protection, trade and commerce, and laws on others specific responsibility, these categories of laws were analyzed in different dimensions of drug management system including governance, financing, research & development and manufacturing, selection, procurement, distribution, and utilization. Data and recommendations were also gathered experts' opinions on specific problem.

Results

1. Current landscape of laws concerning drug

All components of drug system are interconnected from the drugs, prescribers, dispensers consumers or patients, to management. The study has found that Thailand have passed laws governing aforementioned components in total of 39 pieces. As shown in Figure 1, there are 4 laws on pharmaceutical products control, 11 on governance of healthcare professions and services, 5 on consumer protection, 10 on trade and commerce (including international treaties),

Figure 1 Lanscape of drug laws category in Thailand



and 9 on others specific responsibility.

1.1 Laws on pharmaceutical products control

Intended purpose of laws in this category is to regulate manufacturing, trading, importing, and possessing of drugs, narcotics, psychotropic substances, and herbal products.

Key laws in this category are Drug Act B.E. 2510,[6] Narcotic Act B.E. 2522,[7] Psychotropic Substance Act B.E. 2559,[8] and Herbal Products Act B.E. 2562.[9]

Laws on pharmaceutical products control category share similar principle focusing on controlling process of manufacturing, importation, sales, and possessing of narcotics and psychotropic substances. They primarily specify power and duty of responsible committees, licencees, and practitioners. They also regulate the application processes for manufacturing/sales/importation permits, drug registration process, categorization, advertising, post-marketing surveillance, and penalties.

While all drugs are regulated under Drug Act B.E. 2510, some drugs are also considered psychotropic substance or narcotic which make them fall under Psychotropic Substance Act B.E. 2559 and Narcotic Act B.E. 2522, respectively. These are laws that must be strictly complied with as they specify a far more severe penalties in comparison to Drug Act B.E. 2510. Activities regarding psychotropic substances and narcotics for medical uses require a permit under associated law in addition to one under Drug Act to proceed further.

In accordance to deregulation of cannabis for medical uses, a Ministry of Public Health's regulation exempts cannabis extracts with Tetrahydrocannabinol (THC) less than 0.01 percent by weight and products which has Cannabidiol (CBD) as main ingredient with THC less than 0.2 percent by weight from falling under schedule 5 narcotic apart from cannabis and hemp.[10] There is also a Narcotics Control Committee's regulation[11] establishing specification for hemp

product which may be exempted from restriction as schedule 5 narcotic.

Problem regarding laws on pharmaceutical products control

1) Almost all laws under this category focus on effectiveness, quality, and safety of the product but lack provision on promotion of research and development in the manufacturing industry, and pricing standard. They also lack provision on businesses' liability to consumer on damage from product use.

2) Previous attempts to solve problem on distribution of dangerous drugs and misuse of drugs were to tighten the control by re-categorizing them to special controlled drug or psychotropic substance which require prescription or can only be used in medical facilities while there is no established common system to issue prescription that is recognized by all dispensers, lessen people access to drugs that may be more effective in their treatment.

3) Current registration regulation is too rigid to adapt to changing context or high technology drug and accommodate new kind of drugs.

4) Since Drug Act passed, the requirement for dispensing channels to always have a pharmacist on premises during operating hours cannot be enforced. After the grace period from B.E. 2522 that ends on 30 September B.E. 2529 which only require pharmacists to be on premises at least during 3 operating hours, there are still operators reporting 3 operating hours while actually operating longer.

5) There is no effective regulation to the growing problem of false or propaganda advertisement of products on mass, and social media which in many cases result in loss of life.

6) There is no effective law enforcement against offenders in psychotropic substance contamination and intentional addition in dietary supplements. Cases include Sibutramine in weight loss products, and Sildenafil in virility supplementsby claiming properties for male enhancement.

1.2 Laws on governance of healthcare professions and services

This category regulates healthcare professionals, practitioners of the healing arts, and service provision on both public and private sectors. Key laws are the following.

1) The 8 healthcare profession acts[12-19] cover each health profession: medical doctors, pharmacists, dentists, nurses and midwives, medical technicians, physical therapists, Thai traditional medicine professionals, and community public health professionals. All acts aim to establish and enforce professionals' practice to comply with the respective standards and ethics, define the scope of each profession. These laws also have provisions on foundation of professional councils and committees, regulation of its members' compliance with ethics enforced through reprimanding, probation, and suspension or revocation of professional license according to given context.

2) Healing Arts Practices Act B.E. 2542[20] governs 7 branches of healing arts which are occupational therapy, communication disorder therapy, cardiovascular technology, radiological technology, clinical psychology, orthotics, and Chinese traditional medicine. Its basis and principles are similar to those of healthcare profession acts.

3) Health Facility Act B.E. 2541[21] regulates standards and operation of health facilities in private sector but in public sector this law will be enforce only about Health facility characteristics and standard

under ministerial regulation.

4) Primary Healthcare System Act B.E. 2562[22] define the scope of primary healthcare services connecting households and communities to secondary and tertiary healthcare services and mandate primary healthcare access as a basic right for the citizens.

Problem regarding laws on healthcare professions and services

1) Healthcare profession acts and actual practice of each profession currently overlap and transgress the scope of other professions in, e.g., diagnosis, drug dispensing, blood sugar level check, blood pressure check. These negligences over adhering to scope of responsibility of each profession can lead to major conflict later between professions.

2) Article 40 of the Constitution of the Kingdom of Thailand states that occupational regulation must be kept to the necessary minimum, any law put into effect must not discriminate against certain group nor intervene in education institution's provision of education which leaves little room for professional councils to carry out their duty in protecting the people without implementing measures that can be considered intervention.

1.3 Laws on consumer protection

This category concerns itself around protection of the citizens in drug related issues and guarantees the rights of consumers receiving healthcare services. Key laws consists of the followings.

1) Consumer Protection Act B.E. 2522[23] defines consumer's rights and protection specifically regarding product labelling, advertisement, contracts, product and service safety. This law also allows Office of the Consumer Protection Board (OBCP) or other non-profit consumer organizations to represent the consumer in a lawsuit.

2) Consumer Case Procedure Act, B.E. 2551[24] prescribes judicial method that facilitates exercising of consumer rights in order to timely alleviate the damage.

3) Liability for Damage from Unsafe Product Act B.E. 2551[25] specifies liability and mandates fair reparation from manufacturer of the unsafe product and related parties to victims suffering damage from its use.

4) Prices of Goods and Services Act B.E. 2552 requires price of products and charge of services[26,27] which include drugs and medical supplies to be clearly displayed and also requires hospitals to declare cost and sale price of drugs, medical supplies, medical services, and other related services.

5) Manifesto of Patient Rights and Guidelines for Receiver of Healthcare Service (B.E. 2558), issued by the Ministry of Public Health and professional councils, guarantees patients' rights such as access healthcare services that is up to the standard, access to one's own medical information, receive second opinions, and data privacy. It also specifies guidelines for patients to follow when receiving service.

1.4 Laws on trade and commerce

This category mostly comprises of international trade treaties, laws and amendments that were passed in accordance with those treaties. They include:

1) Agreements on Trade-Related Aspects of Intellectual Property Rights (TRIPS)[29] and expanded agreements (TRIPS-Plus), Trans-Pacific Partnership (TPP), and Comprehensive and Progressive Trans-Pacific Partnership (CPTPP)[30] which Thailand has an obligation to comply with as a member of the World

Trade Organization. These agreements aspect concerning the protection of intellectual property is the primary factor that impact Thailand's drug system.

2) Patent Act B.E. 2522[31] governs affairs regarding patent for invention covering new inventions, derivatives, and inventions with industrial application. Patents for both product and process are valid for 20 years from application date.

3) Trade Secret Act B.E. 2545[32] defines information that is a trade secret, scope of protection, violation, limitation period, and process of securing registered trade secret by government departments.

4) Trade Competition Act B.E. 2560[33] specifies business governance to ensure free and fair competition, prevent monopolization and unfair trade.

5) Protection and Promotion of Knowledge on Thai Traditional Medicine Act, B.E. 2542[34] protects and promotes Thai traditional medicine and use of herbal products through selection of herbs with economic value and warrant further research to be categorized as controlled herbs.

6) Plant Variety Protection Act, B.E. 2542.[35] promotes conservation and agricultural development of indigenous plant species with participation local communities to create sustainable utilization.

7) Criminal Liability of Legal Entity Representative Act B.E. 2560[36] holds the board, managers, or other people in positions of authority in the operation of a legal entity responsible for violations committed by the entity and be penalized to the sentence imposed by concerning laws.

Problem regarding Patent law

The repeal of compulsory licensing, and other patent-related measures and the dissolution of Drug Patent Committee whose authority covered drug price regulation left Thailand without viable mechanism to oversee drug patents and its holder, effectively conceded complete monopoly to patent holders.

1.5. Laws concerning others specific responsibility

This category may be further divided into those concerning the foundation of drug research and development, and manufacturing organization which include: the Thai Red Cross Act B.E. 2461[37] established the Queen Saovabha Memorial Institute. The Government Pharmaceutical Organization Act B.E. 2509[38] established the Government Pharmaceutical Organization (GPO). The Royal Decree for Organization Structure of the Office of the Minister and the Office of the Permanent Secretary for Defence B.E. 2552[39] founds the Defence Pharmaceutical Factory (DPF).

Those concerning health security which include: Social Security Act B.E. 2533[40] provides security for employees. Royal Decree for Medical Care Money Welfare B.E. 2533[41] provides security for government officials and their family. National Health Security Act B.E. 2545[42] provides security for all citizens who may not be covered under the other two laws.

Others specific responsibility law those concerning drug system include:

1) Governmental Procurement and Inventory Management Act B.E. 2560[43,44] standardizes operational boundary and procedures of procurement and inventory management to promote transparency and fair opportunity to all suppliers. In spite of said goals, The law has its preference on drugs manufactured by the Government Pharmaceutical Organization and Thai Red Cross and drugs . And promote or support

purchasing in Thai Innovative Drug List.

2) Office of the Prime Minister's Regulation on National Drug System Development Committee B.E. 2551[45] establishes national policy on drugs and strategic plan to ensure systematic and effective drug system development, develops maintenance and updating measures and processes for National List of Essential Medicines and corresponding reference prices, and specifies preventative and reactive measures to problems from drug use and drug resistance.

3) National Vaccines Security Act B.E. 2561[46] promotes and supports research and development, manufacturing, and distribution of quality vaccines in adequate quantity for building of immunity in people and animal vectors of human diseases.

Problems regarding laws on others specific responsibility

1. Governmental Procurement and Inventory Management Act dictates government departments to procure drugs manufacturable by the GPO only from the GPO, prevents suppliers in private sector from selling to the government, which is the major portion of the domestic market, even when they can offer a better price, in effect de-incentivize drug manufacturing in the private sector.

2. Growing and continual practice of collective bargaining of drug procurement among hospitals in every regions under the Ministry of Public Health has been driving down drugs' price from domestic manufacturers. This practice might have long-term influence on drug research and development of those manufacturers.

2. Analysis overall laws concerning drug

Table 1 presents the details the interconnectedness of different categories of laws over drug system management from the perspective of governance, financing, research and development, manufacturing, selection, procurement, distribution, and utilization.

From the perspective of governance of drug system, Thailand passed 39 pieces of laws governing all related components of drug system. With 4 pieces on pharmaceutical products control, 11 on healthcare professions and services, 5 on consumer, 10 on trade and commerce (including international trade treaties), 3 on foundation of drug research and development and manufacturing organization, 3 on health security, and 3 on drug system, there requires an integration in application and enforcement of these laws to result in a drug system that can effectively protect the citizens.

On Drug Financing, international trade treaties have down-side effect on financing the drug system where they drive up drug expenses. Even with existing health security funds covering every citizen, citizens still go into bankruptcy from high healthcare expenses for there are still essential treatments that fall outside of the benefit coverage.

On Drug Research and Development and Manufacturing, pharmaceutical products control laws focus primarily on upholding products to international standard and not on promotion of domestic drug research and development. There exist tangible measures in promotion of research and development of herbal products as an alternative to modern medicines in recently passed Herbal Products Act, however they are still being implemented thus Thailand is still depending on foreign entity for imported drug and not self-reliance on the matter.

On Drug Selection, laws focuses on effectiveness, efficiency, and safety of controlled substances in

Table 1 Laws concerning drug analysis framework

Dimention of Drug System Management	1. Laws on Pharmaceutical Product Control	2. Laws on Health Care Professional and Services	3. Laws on Consumer Protection	4. Laws on Trade and Commerce	5. Laws on Others Specific Facilities
Governance	- Drugs Act, B.E. 2510 - Narcotic Act, B.E. 2522 - Psychotropic Substance Act, B.E. 2559 - Herbal Products Act, B.E. 2562	-	- Liability for Damage from Unsafe Product Act, B.E. 2551 - Price of Goods and Services Act, B.E. 2542	- International Trade Treaties (TRIP TRIP PLUS TPP CPTPP) - Patent Act, B.E. 2522 - Protection and Promotion of - Knowledge on Thai Traditional Medicine Act, B.E. 2542 - Plant Variety Protection Act, B.E. 2542 - Criminal Liability of Legal Entity Representative Act, B.E. 2560	- Thai Red Cross Act, B.E. 2461 - Government Pharmaceutical Organization Act, B.E. 2509 - Royal Decree for Organization Structure of the Office of the Minister and the Office of the Permanent Secretary for Defence, B.E. 2552 - Governmental Procurement and Inventory Management Act, B.E. 2560 - Office of the Prime Minister's Regulation on National Drug System Development Committee, B.E. 2551 - National Vaccines Security Act, B.E. 2561
Financing			- Price of Goods and Services Act, B.E. 2542	- International Trade Treaties (TRIP TRIP PLUS TPP CPTPP) - Patent Act, B.E. 2522	- Social Security Act, B.E. 2533 - Royal Decree for Medical Care Money Welfare, B.E. 2533

Table 1 Laws concerning drug analysis framework (cont.)

Dimention of Drug System Management	1. Laws on Pharmaceutical Product Control	2. Laws on Health Care Professional and Services	3. Laws on Consumer Protection	4. Laws on Trade and Commerse	5. Laws on Others Specific Facilities
				- Protection and Promotion of Knowledge on Thai Traditional Medicine Act, B.E. 2542 - Plant Variety Protection Act, B.E. 2542	- National Health Security Act, B.E. 2545
R&D/Manu-facturing	- Drugs Act, B.E. 2510 - Narcotic Act, B.E. 2522 - Psychotropic Substance Act, B.E. 2559 - Herbal Products Act, B.E. 2562			- International Trade Treaties (TRIP TRIP PLUS TPP CPTPP) - Patent Act, B.E. 2522 - Protection and Promotion of Knowledge on Thai Traditional Medicine Act, B.E. 2542 - Plant Variety Protection Act, B.E. 2542	- Thai Red Cross Act, B.E. 2461 - Government Pharmaceutical Organization Act, B.E. 2509 - Royal Decree for Organization Structure of the Office of the Minister and the Office of the Permanent Secretary for Defence, B.E. 2552
Selection	- Drugs Act, B.E. 2510 - Narcotic Act, B.E. 2522 - Psychotropic Substance Act, B.E. 2559 - Herbal Products Act, B.E. 2562	- Health Facility Act, B.E. 2541		- International Trade Treaties (TRIP TRIP PLUS TPP CPTPP) - Patent Act, B.E. 2522 - Protection and Promotion of Knowledge on Thai Traditional Medicine Act, B.E. 2542 - Plant Variety Protection Act, B.E. 2542	- Social Security Act, B.E. 2533 - Royal Decree for Medical Care Money Welfare, B.E. 2533 - National Health Security Act, B.E. 2545 - Office of the Prime Minister's Regulation on National Drug System Development Committee, B.E. 2551

Table 1 Laws concerning drug analysis framework (cont.)

Dimention of Drug System Management	1. Laws on Pharmaceutical Product Control	2. Laws on Health Care Professional and Services	3. Laws on Consumer Protection	4. Laws on Trade and Commerce	5. Laws on Others Specific Facilities
Procurement	- Drugs Act, B.E. 2510 - Narcotic Act, B.E. 2522 - Psychotropic Substance Act, B.E. 2559 - Herbal Products Act, B.E. 2562		- Liability for Damage from Unsafe Product Act, B.E. 2551 - Price of Goods and Services Act, B.E. 2542	- Trade Competition Act, B.E. 2560	- Social Security Act, B.E. 2533 - Royal Decree for Medical Care Money Welfare, B.E. 2533 - National Health Security Act, B.E. 2545 - Governmental Procurement and Inventory Management Act, B.E. 2560 - Office of the Prime Minister's Regulation on National Drug System Development Committee B.E. 2551
Distribution	- Drugs Act, B.E. 2510 - Narcotic Act, B.E. 2522 - Psychotropic Substance Act, B.E. 2559 - Herbal Products Act, B.E. 2562	- Health Facilities Act, B.E. 2541 - Primary Healthcare System Act, B.E. 2562			- Social Security Act, B.E. 2533 - Royal Decree for Medical Care Money Welfare, B.E. 2533 - National Health Security Act, B.E. 2545 - National Vaccines Security Act, B.E. 2561

Table 1 Laws concerning drug analysis framework (cont.)

Dimention of Drug System Management	1. Laws on Pharmaceutical Product Control	2. Laws on Health Care Professional and Services	3. Laws on Consumer Protection	4. Laws on Trade and Commerce	5. Laws on Others Specific Facilities
Utilization	- Drugs Act, B.E. 2510 - Narcotic Act, B.E. 2522 - Psychotropic Substance Act, B.E. 2559 - Herbal Products Act, B.E. 2562	- Health Professional Act (Medical, Nursing and Midwifery, Pharmacy, Dental, Medical Technology, Physical Therapy, Thai Traditional Medicine, Community Public Health) - Healing Arts Practices Act, B.E. 2542 - Health Facilities Act, B.E. 2541 - Primary Healthcare System Act, B.E. 2562	- Consumer Protection Act, B.E. 2522 - Consumer Case Procedure Act, B.E. 2551 - Liability for Damage from Unsafe Product Act, B.E. 2551 - Manifesto of Patient Rights and Guidelines for Receiver of Healthcare Service, B.E. 2558		- Social Security Act, B.E. 2533 - Royal Decree for Medical Care Money Welfare, B.E. 2533 - National Health Security Act, B.E. 2545 - Office of the Prime Minister's Regulation on National Drug System Development Committee, B.E. 2551

registration process but no requirement on cost and sale price. Drug selection process specified by National Drug System Development Committee for the National List of Essential Medicine and other collection used by government departments helps build confidence, to a degree, toward safety and value of drugs in the list to the public.

On Drug Procurement, government departments, especially those of the Ministry of Public Health, have been organizing joint drug procurement at district and provincial levels driving competition between suppliers to lower the price and resulting in lowered drug expenses. Private hospitals also adopt the practice among those in same chain/network. Health security funds, in the same spirit, use collective bargaining power at national level to procure essential drugs at a reasonable price in support of hospitals to provide access to these drugs to the people.

On Drug Distribution, pharmaceutical products control and health facility laws allow drugs to be dispensed through drug stores, hospitals, and private clinics with exception for household remedies which can be sold at any shop. Thailand now have a policy encouraging patients to receive prescribed drugs at drug store with presence of prescription to reduce hospitals' workload. The policy could lead to common prescription system and clearer separation of responsibility between doctors and pharmacists in the future.

On Drug Utilization, the National Drug Committee prioritizes countermeasure drug resistance problem through continual support for RDU hospitals project promoting rational drug use with a goal to become an RDU country. People who suffer from improper healthcare services may, through Health Security Act, acquire preliminary recompense. Those suffering from unsafe products may, through Liability for Damage from Unsafe Products Act and Judicial Method for Consumer Cases Act, sue for reparation.

Discussion and Recommendations

To promote effective enforcement of aforementioned laws concerning drug for the result as intended by laws, the authors would like to present the following considerations.

1. Better enforcement of existing laws

1.1 The policy which allows prescription drugs to be dispensed at drug store with presence of the prescription does not have much utilization in practice as there is the only requirement for prescription on dispensing channel such as drug store but no requirement for the prescription to be issued by doctors when prescription drugs are to be applied to patients thus no actual prescription gets to the hand of pharmacist at drug store. Drug Act should cancel exception that hospitals and medical clinics must not request the drug sale license and give every health care facillities be under force of Drug Act.

1.2 Drug Store is health care services unit that stay closly to the people. Since legislate Drug Act in B.E. 2510 service of drug stores had been separated from state services. Thus Drug stores should be integrated into public service network and national public health system to alleviate the problem of pharmacist shortage in public sector from government downsizing policy, and the overcrowdedness and long wait time in public health facilities.

1.3 Problem of transgression of responsibility scope between healthcare professions, for example, diagnosis, drug dispensing, blood sample collection, and blood pressure check should be rectified through provisions in healthcare profession acts establishing knowledge and skill assessment procedures and common standards to determine if an individual professional may perform those tasks in overlapping area.

1.4 Drugs be classified as dangerous waste. There shoud be separate to prevent the effects to the environment. Thus The Food and Drug Administration should set up a nation-wide system for drug waste management and disposal, detailing the specifics of collection, and disposal procedures.

2. Amendment to existing laws and enactment of new laws

2.1 Amendment or new law should be passed to promote innovation in domestic drug development through development fund which may be a joint venture between the government and private sector amount in proportion to the total market value of manufactured and imported drugs.

2.2 There should be a new law founding a fund for compensate and heal for patient suffered from receiving erroneous or non- standard healthcare services to lessen the amount of direct lawsuit against involving healthcare personnel.

2.3 To solve the problem that drug store is operating without a pharmacist. Office of Food and Drug Committees should be shifted requirement from fixing pharmacist to operate only at the store he/she was registered as operating pharmacist to letting any

pharmacist operates at any store with operating hours clearly declared, the pharmacist is compensated hourly and the store may sell drugs at anytime as long as there is an operating pharmacist on-site.

2.4 Drug Act should be established guidelines for drug sales through the internet and other emerging channels to protect public safety while allowing convenient enabled by new context.

2.5 There should be a standardized requirement for healthcare service providers to itemize the expenses collected from the consumer into cost of drug, professionals' service fee, administrative cost, etc. so that the consumer may gain insight into the expenses and more easily compare services by virtue of their quality and cost.

2.6 To alleviate negative impact of international trade agreements, amendments should be passed on various related legislation, especially the Patent Act, in compliance with TRIP but no more than required. There must be processes for the public to file objection to a patent both before and after the patent is granted. The power to exercise compulsory licensing, which complies with TRIP, must be preserved to protect the country's health security while allowing royalty fee to be negotiated between government department using compulsory licensing and the patent holder or its licensee.

3. Laws that hinder development of drug system

3.1 Article 75 of the Constitution of the Kingdom of Thailand states that the state must not operate business with competitive nature to private sector. So that the missions of the Government Pharmaceutical Organization should be realigned to cooperation with the private sector to advance domestic drug industry. Its responsibility must be collaborate with private sector for pharmaceutical production and reserves and should be clearly defined in terms of amount and scope of drug types, and its privilege in government procurement should be revoked to enable free and fair competition while maintaining drug security.

3.2 The strict procedures implemented by government departments as prescribed by Governmental Procurement and Inventory Management Act to ensure correctness and transparency must be balanced with having enough flexibility to respond to changing situations, for instance, artificial drug shortage from delayed procurement as a result from excessive bureaucracy.

Recommendations for further research

1) Drug price structure and laws for standardized drug price.
2) Ideal laws for drugs from biological products, other new kind of drugs, and compounding pharmacies.
3) Trust building toward generic substitution.
4) Drug security and national self-reliance through research and development of drugs from herbal and biological products.
5) Guidelines for governance of drug sales and advertisement in electronic network.
6) Ramification of Governmental Procurement and Inventory Management Act on domestic drug manufacturing industry and drug system.
7) Method and process of periodic assessment of drug law enforcement effectiveness for amendment recommendation as prescribed in the constitution.

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การศึกษานี้มีวัตถุประสงค์เพื่อทราบถึงสถานการณ์ของกฎหมายที่เกี่ยวกับยา ความสัมพันธ์กับระบบยา และรวมถึงปัญหาการบังคับใช้กฎหมายต่าง ๆ ที่เกี่ยวข้อง วิธีการศึกษาใช้วิธีการทบทวนสืบค้นจากเอกสาร และประชุมกลุ่มย่อยผู้เชี่ยวชาญกรณีประเด็นปัญหา อุปสรรคของกฎหมายที่สำคัญและข้อเสนอแนะ ผลการศึกษา ประเทศไทยมีการออกกฎหมายในการกำกับดูแลในทุกองค์ประกอบที่เกี่ยวข้องกับระบบยา มีกฎหมาย ข้อตกลง ระเบียบ และประกาศที่เกี่ยวข้อง รวมทั้งสิ้น 39 ฉบับ โดยแบ่งได้เป็น 5 กลุ่ม คือกฎหมายที่เกี่ยวกับการควบคุมผลิตภัณฑ์ยา รวม 4 ฉบับ กฎหมายควบคุมการประกอบวิชาชีพด้านสุขภาพและการจัดบริการ รวม 11 ฉบับ กฎหมายที่เกี่ยวกับผู้บริโภค รวม 5 ฉบับ กฎหมายที่เกี่ยวกับการค้า รวม 10 ฉบับและกฎหมายที่เกี่ยวกับองค์กรที่สามและองค์กรอื่น ๆ ที่มีอำนาจหน้าที่เฉพาะ รวม 9 ฉบับ กฎหมายที่เกี่ยวกับการเงินการคลังในระบบยาที่สำคัญ ก็คือกลุ่มกฎหมายเกี่ยวกับการค้าทำให้ประเทศไทยต้องเสียค่าใช้จ่ายด้านยาที่สูง กฎหมายด้านประกันสุขภาพยังไม่สามารถประกันไม่ให้ประชาชนล้มละลายจากการต้องเข้ารับการรักษาพยาบาลที่มีค่าใช้จ่ายสูงมากได้ กฎหมายที่เกี่ยวกับการวิจัยพัฒนาและการผลิตยา กลุ่มกฎหมายเกี่ยวกับผลิตภัณฑ์ส่วนใหญ่ ยังไม่มีมาตรการการส่งเสริมสนับสนุนการผลิตและการวิจัยพัฒนายาในประเทศที่ชัดเจน ยกเว้นกฎหมายผลิตภัณฑ์สมุนไพรที่ออกใหม่ กฎหมายเกี่ยวกับการคัดเลือกยา จะเน้นที่กระบวนการขึ้นทะเบียนยาในกลุ่มกฎหมายเกี่ยวกับผลิตภัณฑ์ซึ่งเน้นเรื่องประสิทธิผล ประสิทธิภาพและความปลอดภัยเป็นหลัก มีกระบวนการคัดเลือกยาเพื่อเข้าสู่บัญชียาหลักแห่งชาติซึ่งทุกกองทุนประกันสุขภาพกำหนดในชุดสิทธิประโยชน์ กฎหมายที่เกี่ยวกับการจัดซื้อและจัดหายา ในส่วนภาครัฐโดยเฉพาะในกระทรวงสาธารณสุข ได้มีการจัดซื้อยาร่วมกันในระดับเขตหรือจังหวัด ซึ่งทำให้สามารถประหยัดงบประมาณค่ายาลงได้มาก และในกองทุนประกันสุขภาพต่าง ๆ ก็มีการใช้ระบบการต่อรองราคายาในระดับประเทศเพื่อให้ได้ยาที่จำเป็นและมีราคาเหมาะสมทำให้ประชาชนเข้าถึงยาได้มากขึ้น กฎหมายที่เกี่ยวกับการกระจายยา กำหนดให้มีช่องทางการกระจายยาคือ ร้านขายยา โรงพยาบาลและคลินิกเอกชน ยกเว้นยาสามัญประจำบ้านสามารถจัดซื้อได้ทั่วไป ปัจจุบันมีนโยบายให้ประชาชนนำใบสั่งยาไปรับยาที่ร้านยาได้ด้วยเพื่อลดความแออัดในโรงพยาบาล ประชาชนจะมีทางเลือกมากขึ้นในการเข้ารับบริการด้านยา กฎหมายที่เกี่ยวกับการใช้ยา ปัจจุบันผู้ได้รับความเสียหายจากการรับบริการทางการแพทย์ สามารถอาศัยกฎหมายด้านการประกันสุขภาพในการขอรับความช่วยเหลือเบื้องต้นเมื่อได้รับความเสียหายจากการรับบริการ และสามารถใช้กลุ่มกฎหมายเกี่ยวกับผู้บริโภคในการฟ้องเรียกร้องความรับผิดและเงินชดเชยความเสียหายได้สะดวกขึ้น ข้อเสนอแนะเพื่อให้กฎหมายที่เกี่ยวกับยามีความสมบูรณ์ สามารถบังคับใช้ได้ตามเจตนารมณ์และมีประสิทธิภาพมากขึ้นจึงควรให้ความสำคัญในประเด็น การให้ความเข้มงวดในการบังคับใช้กฎหมายเดิม การปรับปรุงหรือออกกฎหมายใหม่ในบางประเด็น การแก้ไขรายละเอียดกฎหมายที่เป็นอุปสรรคต่อการพัฒนาระบบยาของประเทศ และรวมถึงการเตรียมการรับผลกระทบที่เกิดจากการออกกฎหมายทางการค้า

คำสำคัญ: **ยา, ระบบยา, กฎหมาย, กฎหมายเกี่ยวกับยา**

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A Review on the Selection of Drugs in Thai Heath Care at National, Pharmaceutical industries and Public Hospital Levels

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Abstract Drug selection of pharmaceutical drugs plays a crucial role in management. We have identified three levels of the drug selection at country, hospital, and pharmaceutical industries. This study aims to describe the history, current situation of each level, and the success and challenges for further improvement. The finding revealed that the main criteria in drug selection are efficacy, safety, and quality for all levels, but the details may be different. Drug registration is an important regulation channel before drugs can be sold in the country. In addition, there is also a mechanism for surveillance and management to fulfill drug shortage and orphan drugs. The selection process of National List of Essential Medicine (NLEM) based on criteria national affordability, cost-effectiveness, and equity. At hospital level, there is the Pharmacy and Therapeutic Committee (PTC) to support effective and efficient medicine management through medicines selection and promoting safe and rational use of medicines but these can vary between hospitals. Pharmaceutical industries' selection is driven by profitability and incentives provided by the government measures related to the targeted medicines, which encourage earlier generic entries either as locally produced or imported drugs. The challenge in the near future for the Thai FDA is the urgent revision of drug registration process according to importance based on risk evaluation. Additionally, information related to drug registration should be made publicly available through a public assessment report to promote transparency and allow other relevant government agencies, such as the Subcommittee on National Essential Medicine and hospitals to use the information for their selection processes.

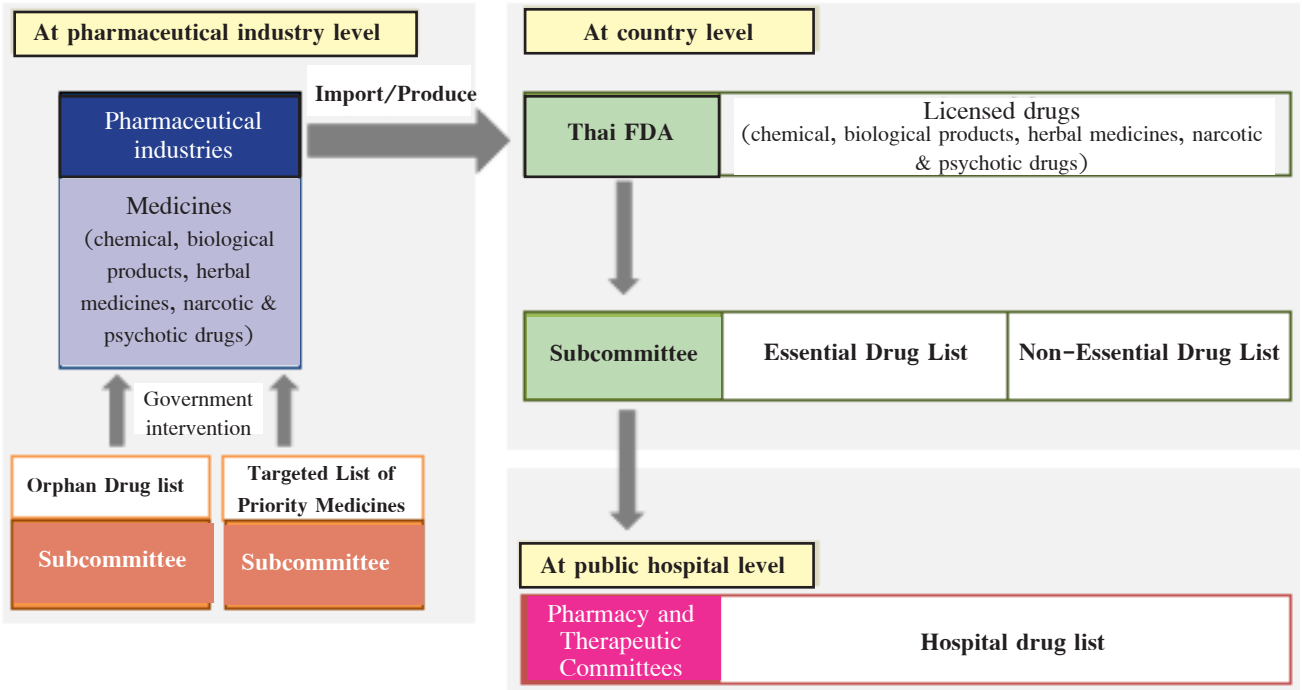
***Keywords*: drug selection, drug registration, national list of essential medicine, orphan drugs, targeted list of priority medicines, Pharmacy and Therapeutic Committee**

Introduction

Pharmaceutical drugs (also referred to as pharmaceutical medicine) play a critical role to cure or prevent disease and improve health, But they can be very harmful when uses inappropriately.[1] Moreover, the production, distribution and dispensing of them also require special knowledge and expertise. Therefore, all aspects of them need an effective system for pharmaceutical management which entails a full cycle of operations beginning with drug selection, procurement, logistics and distribution and finally delivery to end-users.[2,3] Among these processes, the selection of pharmaceutical drugs is the most powerful tool because it has two facets which could contribute to both barriers and facilitates for patient access to medicines.

In Thailand, the framework of pharmaceutical drugs' selection can be divided into three levels (see Figure 1). At country level, public hospital level and pharmaceutical industry level. At the country level, there are two main process: (1) the Drug registration process which the Thai Food and Drug Administration (Thai FDA) under the authority of the Ministry of Public Health is responsible for implementing medicines regulation in order to ensure the efficacy, safety and quality of drugs freely sold in Thailand, and (2) the National List of Essential Medicines (NLEM) which is the pharmaceutical reimbursement list for the three public health schemes namely the Civil Servant Medical Benefit Scheme (CSMBS), the Social Security Scheme (SSS), and the Universal Health Coverage Scheme (UCS).[4] At hospital level, this review focusses only public hospitals. There are the Pharmacy and Therapeutic Committees (PTC) which assess and select the drugs into the hospital formulary.[5] At pharmaceutical industry level, manufacturers and importers play a key role to control the pharmacological products in markets in relation to different benefits and

Figure 1 Flowchart of the drug selection at 3 levels



interests. However, there are government's efforts to intervene the market by implementing policies such as those on the orphan drugs lists and the targeted list of priority medicines (PRIMEs) in order to encourage industries to manufacture or import the relevant drugs. These may possibly align the interest of pharmaceutical industries to meet the needs of patient in situation where the industry may behave otherwise without the appropriate incentive.

This study aims to describe the selection of each of these level, followed by the discussion and conclusion and provides policy recommendations for which would potentially be relevant to the decision makers and stakeholders.

Methods

A document review was conducted on the Thai drug system, drug's situation systems, development of regulatory control system, the NLEM, orphan drugs and drug shortages in Thai contexts. The sources include laws and regulations, published articles from some search engines e.g. Google and domestic databases (up to September 2019), gray literature (i.e., research reports and meeting minutes of the relevant committees and subcommittees, official correspondences) in Thai. Additional information was collected from the manufacturers' interviews and authors' involvement in the policy making process in Thailand as the secretariat of Subcommittee on Orphan Drug, Subcommittee on Development of National List of Essential Medicines and Subcommittee on Pharmaceutical Industry Development. Furthermore, some data were extracted from the database of registered drugs last updated in June 2019.

Results

1. Drug selection at Country level

1.1 Drug Registration

Thailand has a long history of implementing drug regulation for protecting consumer health with the Drug Acts B.E. 2510 and its various revisions and amendments since 1967 including the Drug Act (No. 2) B.E. 2518; (No. 3) B.E. 2522; (No. 4) B.E. 2527; (No. 5) B.E. 2530; and the latest Drug Act (No. 6) B.E.2562.[6] The Bureau of Drug control under the Thai FDA is responsible for implementing medicines regulation which governs the registration of drugs, licensing of drug manufacture, sales, and importation. Medicines are classified into two major groups: modern and traditional drugs which included medicines for both human and animals.[7] However, this article focuses on the modern drugs registration including new drugs, generic drugs and new generic drugs during the period of 1936 to 2019.

A brief historical evolution related drug regulatory is chronologically listed in Table 1 illustrating the evolution of the selection process at the country level has been evolving to align with international standard and to adapt to changes in the trends of medical technology advancement with the aim to increase drug quality. Currently, there are 2,282 medicines (excluding repetition) with approximately 20,000 licenses in the market.

1.2 Selection of essential drugs into the National List of Essential Medicines (NLEM)

After regulatory approval, some of them can be proposed to the NLEM process. The Subcommittee on the NLEM under the National Committee of Drug System Development is responsible agency to develop and update the list regularly The first version of

Table 1 Historical evolution related drug regulatory in Thailand, 1936-2019

Period	Drug regulatory process
Early years (1936 - 1966)[6,8]	The Control of Drug Selling Act, B.E. 2479 (1936) was the first legislative measure implemented dealt with only sale practices. It became illegal unless person did not obtain a license prior to sell drug. After several year, Sale of Drug Act, B.E. 2493 (1950) was promulgated. At that time, the company that manufactured or imported drug only notified the formulas and ingredients to the FDA before producing or importing which later receive drug license.
1967-1978[6,8]	A push for revision new drug emerging from the proliferation of counterfeit medicine. The Drugs Act, B.E. 2510 (1967) was enacted to supersede the previous law covering substantial aspects in drug regulation control. For example, licensing drug registration, pharmaceutical manufacturing and good manufacturing practice, suspending or withdrawn licensing, and selling and advertisement. Only the drug formula which did not include in the pharmacopoeias notified by the Minister was required for registration. Once obtained the certificate of formula registration, the drug may be produced or imported. At that period, the drugs licenses would be renew every 5 years. In 1978, the first Guidelines to Good Manufacturing Practice (GMP) was developed as guided by the World Health Organization (WHO) and then launched it in the same year.
1979-1988[6,8]	According to the third revision of this Act in 1979, it had require all medicines, whether included in the pharmacopoeia or not, to go through the drug registration process. Moreover, it eliminated the specified 5-year validity period of licenses. Thus, it would be valid as long as the license being operate for that manufacturer/importer. As a result, the drugs licensed since 1983 having indefinite period of time. In 1984, the Thai FDA had promoted the local pharmaceutical industries for improv ing standard and later 4 years after, the GMP Certificates were officially granted to manufacturers in 1988.
1989[6,8]	The Thai FDA separated the registration process between those for 'new drugs' and 'generic drugs' and introduced the Safety Monitoring Program (SMP) requiring safety monitoring of approved 'new drugs' to be implemented by the manufacturers/importers and report to the Thai FDA. The new drug category acted as protection for overseas patented drugs which were not previously marketed in the country by preventing generic drug importers and producers from registration process.
1994[6,8]	Bioequivalence data can be submitted for generic drug registration process to show bioequivalence of the submitted generic product to its original counterpart. The bioequivalence study must be conducted after the 2-year SMP was completed or after the originator patent expired (however, this restriction was removed in 2001).
2000[6,8]	The requirement to specify an expiry date on the packages of medicine for human use was introduced which meant that study on drug stability must be conducted to determine the shelf life of that particular drug. Also, the registration process for biologic drugs was separated from chemical drugs. As a result, Ministerial Announcement for Modern Pharmaceutical Manufacturing was issued in 2003, all local pharmaceutical industries were forced to comply with GMP standard of WHO.

Table 1 Historical evolution related drug regulatory in Thailand, 1936-2019 (continued)

Period	Drug regulatory process
2009[6,8,9]	In 2009, the Thai FDA has announced the implementation of ASEAN Harmonization on Pharmaceutical Registration in order to eliminate the technical barriers, The ASEAN members have implemented the ASEAN Common Technical Requirement and Dossier (ACTR/ACTD) on Quality, Safety and Efficacy. The ACTD is a part of the application dossier which includes four parts: (1) administrative data and product Information; (2) quality; (3) nonclinical/safety; and (4) clinical/efficacy. This rules substantially burdened the local manufacturers and generic drug companies to prepare required documents, yet it harmonized the registration procedure of dossiers in almost all parts including: quality, nonclinical/safety, clinical/efficacy, in other ASEAN countries.
2011[8,10]	Ministerial Announcement for Modern Pharmaceutical Manufacturing was issued in 2003, all local pharmaceutical industries were forced to comply with GMP standard and PICs.
2019[11]	The Drug Act of B.E. 2562 (2019) was enacted with its content facilitating the new policy direction which emphasized on research and development. This included the development of services to provide advice and to allow drug registration to initiate during clinical trials. Criteria to approve the manufacture/import of drugs for research use was established as per international standard. Further more, fast track for high priority drugs was introduced to shorten registration process for these drugs, and fees related to drug registration activities was revised in order to allow the Thai FDA to operate in a more effective and timely manner.

the NLEM developed in 1981, adopted the concept of the World Health Organization's Model List of Essential Medicine in order to promote the rational use of medicines.[12,13] There were 370 medicines (excluding duplicates) listings which was served initially as a basis for the medicine supply in the public sector.[13] After Thailand faced the economic crisis in 1998; however, the list was a largely revised and then used as a reimbursement list for the Civil Servants Medical Benefit Scheme (CSMBS) in order to cut down unreasonable expenditure.[12] As a result, the subcommittee appointed the 23 National Expert Panels representing different drug groups to select medicines based on criteria. At that time, the list was classified into five different categories regarding the level of health providers' and prescribers' specialty, as follows:

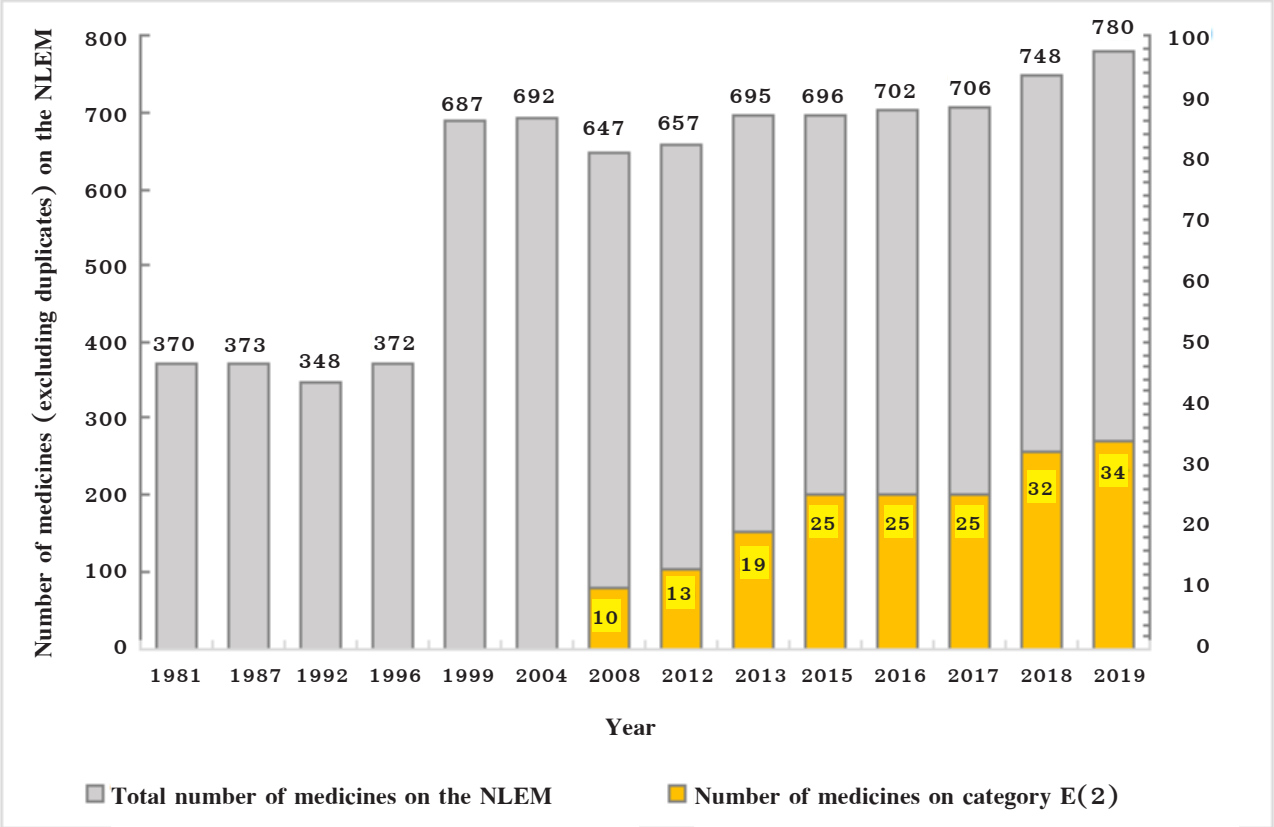
- Category A: Basic medicines for all health facilities, to use as first-line treatment,
- Category B: Alternative, second line medicines of those in Category A,
- Category C: Medicines prescribed only by specialists approved by the hospital director,
- Category D: Medicines used only particular indication and disease, and these drugs will be subjected to Drug Utilization Evaluation (DUE) to ensure proper use,
- Category E: Medicines used for special government projects (e.g., HIV/AIDS, TB drugs).

As a result of strong emphasis of the NLEM after this reform, the number of medicines has significantly increased by almost two folds between 1996 and

1999 (Figure 2).

Since 2004, the NLEM Subcommittee has applied a more evidence-based approach for the revision of NLEM. The application of cost and criteria for comparative evaluation of products in term of "ISafE score" and "Essential Medical Cost Index (EMCI)" have been established. ISafE stands for Information, Safety, ease of use namely patient adherence, frequency of drug administration, and Efficacy of each medicine.[21,22] The medicines with ISafE score (ranging from 0 to 1) above the 50thpercentile in the same group are further assessed for their treatment cost by the NLEM adjusted cost index (Essential Medicine Cost Index; EMCI). EMCI is the treatment cost for a medicine (defined daily dose) divided by the ISafE score. The medicines with low EMCI are likely to be adopted in the NLEM because these medicines are economical and cost-effective.[12] In addition, the selection of drugs into the list became more transparent and participatory by including key stakeholders such as representatives from the three public health insurance schemes, health service providers, and patient groups.[12]

Figure 2 The total number of medicines on the NLEM, 1981 to 2019[13-20]



In 2008, the government was under increasing pressure to include new high-cost drugs into the list, NLEM category E was divided into two subgroups: E(1) is the previous the category E, and E(2) is majorly high-cost medicines for special situation customized for a particular patient.[10-12] There were 10 medicines on the category E(2).[23] After that, the

mechanism for selecting high-cost drugs was introduced by adopting health technology Assessment (HTA), mainly health economic evaluation and budget impact analysis as evidence to support the decision-making process.[24] Within this HTA step, the high-cost medicine was analyzed to determine whether it was cost-effective and affordable. But ultimately, the policy makers' decision also depends on other decision tool such as financial burden of households, social and ethical issues, and program feasibility. These processes have been used since their inceptions to the present day. Currently, there are totally 780 medicines on the NLEM[19] as seen in Figure 2.

The challenges of the next step are the development tool for assessment of cost-effectiveness and appropriate funding mechanisms under the constraints of limited resources to be able to access the high-cost innovative medicine, especially the targeted drug or biological product which are the future trends.

2. Drug selection at public hospital level

According to "Thai Drug Management Manual, 1978", all levels of public hospitals under the jurisdiction of Ministry Of Public Health (MoPH) must establish the Pharmacy and Therapeutic Committees (PTCs).[25] PTCs were designed to: optimize rational use of medicines through establishing restricted drug-use policies and practical guidelines for medical management; evaluate and select medicines for the formulary lists; manage procurement; and ensure adherence to the administrative guidelines. The PTCs consists of a multi-disciplinary panel of experts such as physicians, pharmacists, dentists, nurse and other health care professionals which the number of PTC members varies depending on each healthcare institution.[5,25] The most important functions of the PTCs are drug evaluation and selection based on efficacy, safety, quality and price (or cost-effectiveness). Almost three decades, procurement of medicines into the hospital has been conformed to the Regulations of the Office of the Prime Minister on Procurement B.E. 2535 (1992) and the Regulation of the Office of the Prime Minister on Electronic Procurement B.E. 2549 (2006). The drugs' price seem to be the main selection criterion to make decisions.[26-28] However, the Government Procurement and Supplies Management Act B.E. 2560 (2017) was later enacted with the principles of anti-corruption and transparency on governmental procurement in order to standardize procurement and supplies management, apart from the previous regulations. In accordance with the new Act, the price-performance criteria was required for pharmaceutical procurement via bidder.[29] Each hospital and its PTC set the criteria for compulsory and voluntary factors of decision making. There are two main aspects including the general quality criteria, and the specific quality criteria.[28]

3. Drug Selection at the Pharmaceutical Industry Level

The Thai pharmaceutical industry can be divided into state and private manufacturers. The Government Pharmaceutical Organization (GPO) is the key state pharmaceutical manufacturer while private manufacturers can be further divided into those producing drugs locally or importers. The processes for selecting drugs to bring to the market will vary between these different types of manufacturers.[15]

For local producers, the key considerations are whether the drug is in the NLEM, drugs with high

market values, and high priority drugs, as the unmet pharmaceutical needs and drugs with the potential return on investment at an acceptable level. Importers are mainly multi-national companies (MNCs) and generally import drugs which fulfil unmet health needs including those to treat diseases for which no effective treatment exists in the market or those which increase convenience and adherence for the patients. However, there are government policies related to drug registration, price control and reimbursement policies, which can be a positive or negative influence. Manufacturers take into account all these considerations about which drugs are suitable for market entry. In addition, local companies import branded drugs from abroad for which the selection criteria are somewhat similar to MNCs' practices but may also consider the patent expiration/duration and the ability for a domestic producer to manufacture the drug locally. This information on pharmaceutical industries was taken from excerpts from interviews in July 2019.

For GPO, its main mission is to supply drugs, acquired through production and procurement, in adequate quantities to meet the needs of government hospitals and hence the drugs that would be mainly selected are essential drugs in the NLEM, drugs which are not yet produced locally, and those which support urgent health policies such as vaccines. In addition, there is mission to research and develop new pharmaceutical products and medical supplies to respond to the need and necessity of the Thai society.

Due to the non-perfectly competitive pharmaceutical markets, Thai government has a strong attempt to create incentives for encouraging the new development of safe and effective drugs or bringing new pharmaceuticals into the market. There are two cases of government regulation: (1) The Orphan Drug List's policy; and (2) the Targeted list of priority Medicines' policy in order to organize the highest level of accessible and equitable drug possible and protect public safety.

3.1 The orphan drug list

In Thailand, the orphan drug has been developed siince 1992, initially serving as a basis for temporarily and permanently stock out of drugs needed in the public sector, and approval drug needed but approval and available in other countries. The National Drug Committee appointed the Subcommittee on Orphan Drug which coordinated by the Bureau of Drug Control of the Thai FDA. This Subcommittee's roles and responsibilities are to address the problems and advise proper solutions. The definition of an orphan drug is specified as a drug needed with the problem on drug shortage. After accomplishment, the first Orphan Drug List (1994) was publicly announced with 43 medicines. Later in 2005, more features were added to this definition which included 3 main criteria: (1) drugs were in need for diagnosis, alleviation, treatment, and cure; (2) drugs were in need with any of these causes: a rare disease, a severe disease, a disease can cause prolonged disability, a drug with low consumption and no drug alternatives; (3) drugs with shortage. These criteria based on both the status of rare diseases and drug shortage issues were different to the definition/criteria for orphan drug in other countries such as the US, Canada, Australia and EU. In 2006, Thai FDA has developed a guideline regarding the registration of orphan drugs which was subsequently revised and published in 2013. According to the guideline, some requirements for the assessment of orphan drugs are exempted, particular-

ly if the orphan drugs have been used more than 10 years and its efficacy and safety have been well established. In such cases, the Thai FDA would allow submitting without preclinical or clinical modules. Also, Thai FDA granted the privilege for these drugs in order to create more incentives for manufacturers and importers such as 'fast track' regulatory registration and exemption of drug registration fees including approval and other amendments' fee.[30] At present, the updated list in 2019 is announced with 76 medicines (excluding repetitions).[31] Most of them, both public and private pharmaceutical companies would like to assist with production or importation. However, 29 drugs in this category remained unavailable in the market.[32] Therefore, Thai government has put efforts to increase patients' access to the medicines through tariff policy for orphan drugs' imports. Eventually, there is the Cabinet Resolution in November 2019 stipulated orphan drugs' importation to be entirely exempted from the customs tariff.

3.2 Targeted list of priority Medicines (PRIMEs)

Due to the rise in drug spending, the government introduce an initiative in 2017 called "targeted list of priority medicines (PRIMEs)". Initially, the PRIMEs list included 144 medicines which were the drug needed for public health, sold in either a monopoly or oligopoly and could potentially encounter problems of drug access and security.[33,34] The government encourages the pharmaceutical industries including manufacturers and importers to bring the generic on the PRIMES list into the drug market as soon as possible. The following measures were also implemented to promote the entry of generic substitution to high-cost original drugs:[33]

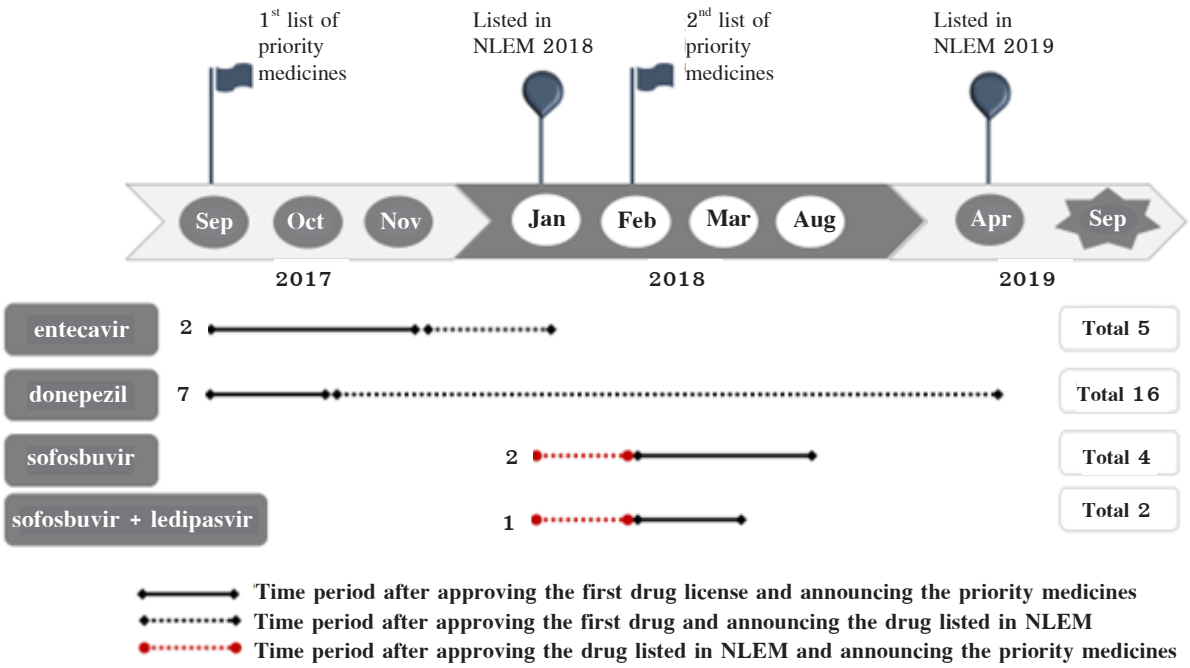
- The reduction of registration fees by 50% as per the Thai FDA announcement on 5th September 2016 and 8 February 2018
- Drug patent information search to provide local manufacturers/importers with the data to develop plans related to the introduction of generic drugs
- Development of reference prices for public procurement.

From these measures that took place between 2017 and 2018, there were 102 registered drugs with 57 manufactured locally and 45 imported from other countries. After announcing the first and second of PRIMEs, the number of registered drugs have all increased and included in the NLEM due to lower costs and budget impact. For example, the number of approved brands for entecavir (treatment of hepatitis B) increased from 2 to 5 registrations, and donepezil (treatment of Alzheimer's disease) increased from 7 to 16 registrations (Figure 3).

Discussion and Conclusion

In this article we have mainly described of the development of drug selection policies at the country level, particularly the process of drug registration and NLEM listing. For the drug selection at the public hospital level, we included only the general guidelines, which provide the direction for hospitals to conduct drug selection. However, in actual practice, this may vary from one hospital to another. Furthermore, it should be noted that information relating to how manufacturers select drugs to bring to market may be highly sensitive and what is presented here gives just a general framework on what was considered during the process. Having said that, we were able to summarize the progress and evolution policy implement-

Figure 3 The four priority medicines during the implemented period between 2017 and 2018



Source: Drug registration database of Bureau of Drug Control, Thai FDA June 2019

ed at the Thai FDA level in terms of the impact on the availability of the orphan drug listed and the targeted list of priority medicines in the market. There was an increase in the registration of generic drugs and subsequent accessibility to Thai population.

It has been illustrated that the selection process at the country level has been evolving to align with international standard and to adapt to changes in the trends of medical technology advancement which aimed to increase drug quality. From the study by Pattanaphesaj J, et al.[35] it was shown that drugs which did not meet the standard as set by the Quality Control Project reduced from 19% in 2003 to 0.8% in 2016 indicating better quality control during manufacturing and drug quality in the market. One of the key reason is the introduction of Good Manufacturing Practice (GMP) in 2003 as one of the requirements for drug producers to comply, leading to the use of stability data in drug manufacturing regulation. Also, bioequivalence study was required to show that generic drugs are as effective in treating diseases compared to its original counterpart, and therefore, the prescribers can use these generic drugs with confidence. However, there are key challenges in the drug registration process as following:

1) Drug definition which the regulatory pathway can be improved to international standard by reducing complexity in the criteria and guidelines. For example, the process for generic approval can be subdivided in to 'new generic' and 'existing generic'. While the process for new generic drugs is up to international standard and bioequivalence data is required for registration, the existing generic which a formulation has been registered before 1991 is exempt. This can create confusion and potentially lead to exposure to unsafe medicine to the public.[8]

2) The fees in the registration processes and other related activities (e.g. registration maintenance) are low, which could lead to manufacturer filing for registration-related activities unnecessarily.[8]

The NLEM selection process has been improved over the years by adopting the evidence-based ISafe and EMCI system to make it more systematic and transparent. In the case of high-cost drugs, economic evaluation and budget impact analysis have been used in both the decision making and price negotiations to increase access. From the study by Sruamsiri R et al., it was found that the introduction of E(2) category helped patients to access more high-cost drugs.[36] However, with the advance in technology and new treatment paradigm in biologic drugs, the issue of balancing the timely access to these innovative drugs and limited availability of budget and resources will be increasing, and hence there is an on-going need to develop this process further. Additionally, the policy to promote traditional medicine may be hindered by the lack of reliable evidence in order to help with the decision making in whether to include a traditional medicine formulation in the NLEM.

There has been no major change in how drug selection is conducted at hospital level. From Umnuaypornlert A and Kitikannakorn N,[26] it was found that the structure of PTCs in 2014 were similar to the guidance provided in the 'Drug and Therapeutic Committees- A Practical Guide 2003' and considerations were based on the NLEM, drug efficacy, drug costs, drug safety, hospital procurement policy, and physician prescribing practices.

On the other hand, the process to select drugs by the manufacturers has been significantly influenced by the targeted medicine list introduced in 2016 and the orphan drug listed which create an additional incentive to the existing criteria based unmet needs and profitability to promote these necessary drugs to market. However, despite these improvements in the chemical-based drugs, the impact is minimal in the area of biologic drugs. This may be due to the fact that there were only five local manufactures with the capacity to handle the complexity of manufacturing biologic products, the lack of technical staff and infrastructure, and the high barrier to obtain this capability due to high investment costs which there were no major incentives for the private sector to pursue.

Policy Recommendations

According to the government initiatives, it is important to evaluate and assess the health impact of these two government measures after the implementation as well as investigate the barriers to access to medicines. The Thai FDA should urgently revise drug registration according to importance based on risk evaluation. High-risk drugs should be reviewed first, and the distinction between biologics and chemical drugs should be made as the level of details required during the review process is different. Additionally, criteria and tools for evaluation and assessment during drug registration processes should be developed in order to standardized both internal and external stakeholders. Furthermore, the drug registration and information should be made publicly available through the publication of a public assessment report in order to promote transparency and allow other relevant government agencies, such as the subcommittee for national essential medicine and hospitals to use the information for their own selection processes. NLEM selection process should revise all of drug listing based

on national public health issues and develop an evaluation and monitoring system. Best practices on the policy and process related to the selection of high-cost innovative drugs and other non-drug medical supplies (e.g. medical food) should be reviewed in order to help determine the best way forward in the provision of these drugs and goods.

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การคัดเลือกยาเป็นหนึ่งในปัจจัยที่เอื้อให้เกิดการเข้าถึงยาของประชาชน จึงจำเป็นต้องให้ความสำคัญในการพิจารณาคัดเลือกยาเข้าสู่ประเทศ สถานบริการ และกระบวนการผลิตและนำเข้าของผู้ประกอบการ โดยมีผู้เกี่ยวข้องในแต่ละระดับที่แตกต่างกัน การศึกษานี้ใช้การทบทวนวรรณกรรมเป็นหลัก โดยมีวัตถุประสงค์เพื่อวิเคราะห์พัฒนาการการคัดเลือกยาที่สำคัญ ปัญหาและอุปสรรค ความสำเร็จ และความท้าทายในอนาคต ผลการทบทวนพบว่าแต่ละระดับมีเกณฑ์หลักที่ใช้ คือ คุณภาพ ความปลอดภัย และประสิทธิผล ซึ่งกระบวนการคัดเลือกยาเข้าสู่ประเทศมีการขึ้นทะเบียนตำรับยาเป็นช่องทางที่สำคัญก่อนจำหน่ายยาในประเทศ และหากไม่สามารถใช้ช่องทางปกติได้จะใช้กลไกยากำพร้าและยาขาดแคลนที่พัฒนาขึ้น การพิจารณายาเข้าสู่บัญชียาหลักแห่งชาติเน้นประเด็นความคุ้มค่า ความเสมอภาค และความสามารถในการจ่ายของรัฐเพื่อครอบคลุมสิทธิหลักประกันสุขภาพ สำหรับการคัดเลือกยาของผู้ประกอบการโดยเฉพาะผู้ผลิตภายในประเทศได้เพิ่มการพิจารณายามุ่งเป้าของประเทศเพื่อให้มี ยาชื่อสามัญใช้ในประเทศ ลดค่าใช้จ่าย มียาใช้สอดคล้องกับผลกระทบด้านสาธารณสุขของประเทศ การคัดเลือกยาของสถานพยาบาลใช้คณะกรรมการเภสัชกรรมบำบัดเป็นผู้ดำเนินการเป็นหลักและคัดเลือกยาตามเกณฑ์ของแต่ละโรงพยาบาลและแนวทางของรัฐที่กำหนด ประเด็นความท้าทายในอนาคต อย.ซึ่งเป็นผู้รับผิดชอบหลักในการคัดเลือกยาเข้าสู่ประเทศจำเป็นต้องดำเนินการอย่างเข้มแข็งในการทบทวนทะเบียนตำรับยา และพัฒนาเกณฑ์การประเมินให้เป็นมาตรฐานเดียวกัน รวมทั้งเผยแพร่ข้อมูลผลการประเมินต่อสาธารณะ เพื่อให้กระบวนการคัดเลือกยาของประเทศมีความโปร่งใส ลดความซ้ำซ้อนและเกิดการบูรณาการเชิงระบบร่วมกัน

คำสำคัญ: **การคัดเลือกยา, การขึ้นทะเบียนตำรับยา, บัญชียาหลักแห่งชาติ, ยามุ่งเป้า, ยากำพร้าและยาขาดแคลน, คณะกรรมการเภสัชกรรมบำบัด**

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Drug Procurement and Distribution

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Abstract Drug procurement and distribution system can be referred as a critical connecting process to effectively assure the affordability and patients' accessibility to essential and quality medicines. There are various existing economic market structures such as monopoly and oligopoly markets. A monopoly implies a single firm that produces or imports the products to the market with no close substitute, while an oligopoly market has a small number of relatively large firms that produce or import similar, but slightly different products. In both cases, there are significant barriers to entry for other enterprises. This situation has resulted in imperfect competition and currently become the challenge to develop the strategic procurement and smart logistic design in order to achieve the affordability and accessibility to essential medicines for the needed patients under the universal healthcare coverage. In Thailand, the emerging or new license medicines may come from the domestic pharmaceutical importers or domestic pharmaceutical manufacturers both in public and private sectors. For domestic manufacturers, most raw materials are imported due to the limited capacity in producing the active pharmaceutical ingredients in the country. After the manufacturing process, the finished products are distributed through distributors and wholesalers to various health facilities in public and private hospitals, clinics, and pharmacies. Besides this, the special management design has come up with the collaboration of the National Health Security Office and the Social Security Office in order to ensure the accessibility to some special access items such as high-cost rare diseases medicines or some orphan drugs like antidotes and antivenom. Moreover, in case of emergencies, the guidelines for managing, procuring and distributing medicines have been established consecutively in order to control the outbreaks that can be prevented by vaccines, toxic leakage, and floods. Currently, the disruptive technology has made a great impact on many businesses especially in the delivery and logistic system, resulting in an emergence of skillful companies providing the services for managing warehouses and delivery system not only for medicines but also other goods. For the government sectors, the Government Pharmaceutical Organization plays an important role in manufacturing and distributing

medicines to the public hospitals. The organization also represented as the supply security partner in Universal Health coverage in Thailand by taking the responsibility in procuring and distributing drugs in the special projects under the National Health Security Office and the Social Security Office via the Vendor Managed Inventory (VMI) system.

Keywords: **drug procurement, drug distribution, drug inventory management**

Introduction

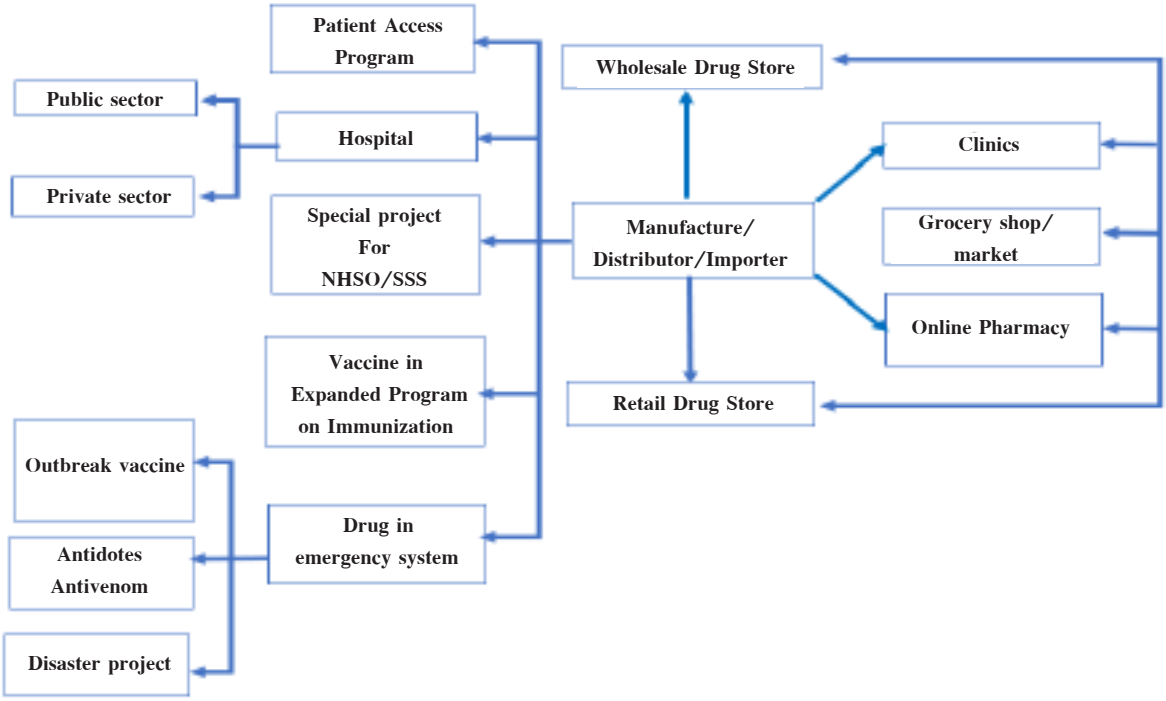
Drug procurement and distribution system can be referred as a critical connecting process to effectively assure the affordability and patients' accessibility to essential and quality medicines. But in the pharmaceutical market, there are various existing economic market structures such as monopoly and oligopoly markets. This situation has created an imperfect competition in the market. If there are more pharmaceutical companies selling similar drugs, it would lead to drug price competition resulting in price reduction; however, it is still not yet at fully competitive level. The evolution of drug procurement and distribution system in Thailand has been developed for decades and currently become the challenge in the strategic procurement and smart logistic design in order to achieve the affordability and accessibility to essential medicines for the needed patients under the universal healthcare coverage.

In Thailand, the emerging or new license medicines may come from the domestic pharmaceutical importers or domestic pharmaceutical manufacturers both in public and private sectors. For domestic manufacturers, most raw materials are imported given that there is limited capacity in producing the active pharmaceutical ingredients in the country. After the manufacturing process, the finished products are distributed through distributors and wholesalers to various health facilities in public and private hospitals, clinics, and pharmacies. Besides this, the special management design has been come up with the collaboration of the National Health Security Office and the Social Security Office in order to ensure the accessibility to some special access items like high cost with rare diseases medicines or some orphan drugs like antidotes and antivenom. Moreover, in case of emergencies, the guidelines for managing, procuring and distributing medicines have been established in order to control the public health situations such as the outbreaks of vaccine preventable diseases, leakage of toxic chemicals, and floods (Figure 1).

In general, the manufacturers and/or importers will deliver medicines to health facilities by themselves. Currently, the logistic system has been drastically changed by the technology, resulting in an emergence of skillful companies managing warehouses and pharmaceutical delivery business. Many pharmaceutical importers presently prefer to dedicate the inventory and logistic system to these logistic companies which represent as the pharmaceutical distributors and being responsible for the inventory under good storage and good delivery practices. As for drug delivery, there is a tracking system which facilitates the drug companies to check delivery status themselves, similar to that of the online counterparts.

In the government sectors, the Government

Figure 1 Drug distribution channels to various health services



Pharmaceutical Organization plays an important role in procuring and distributing medicines to public hospitals, especially distributing drugs to special projects under the National Health Security Office and the Social Security Office via the Vendor Managed Inventory (VMI) system. On the other hand, the wholesalers who act as traders tend to have reducing role because the direct ordering systems from manufacturers are easy and convenient to use with better tracking systems. However, wholesalers still play a crucial role in distributing medicines to service facilities in case of short-term drug shortage. Moreover, they also distribute medicines to those clinics and pharmacies which have fewer demands.

The objectives of this article are (1) to present the process for improveing drug procurement and distribution system in public hospital in Thailand, (2) to describe values of drug sales and distribution through various channels and drug group between 2014 – 2018, and (3) to explain drug procurement and distribution system for special project under Universal Health Coverage Scheme (UCS) and Social Security Scheme (SSS) and emergency crisis. Data were collected through the following activities: (1) the review of documents related to drug procurement and distribution system from 1986 to 2019. The related documents include regulations, orders, announcements, reports and meeting documents including literature on the procurement and procurement of medicines in the country, and (2) interview with representatives from agencies related to drug procurement and distribution systems, including the Permanent Secretary Office, Ministry of Public Health of Thailand

Major Reforms in the Drug Procurement and Distribution System in Thailand

1. Formation of hospital pharmaceutical therapeutic committee

This is a good starting point to reshuffle the drug procurement system in a hospital. During 1986 to 1990, the Ministry of Public Health had improved the efficiency of medical administration by issuing regulations on the purchase of medicines and medical supplies by government agencies under the Ministry of Public Health. Since then, the board named "Pharmaceutical and Therapeutics Committee" has been established in each hospital to be the steering committee responsible for drug selection into hospital formulary, and formulating an annual procurement plan for medicines and medical supplies. The plan must be annually submitted to the Office of the Permanent Secretary, Ministry of Public Health.

2. Digital transformation for drug Inventory system in public hospitals

In 1986, the Office of the Permanent Secretary and the Faculty of Pharmaceutical Sciences, Chulalongkorn University have received funding from the World Health Organization to develop a computer program called "INV" for managing the purchasing orders and inventory transactions for medicines and medical supplies at the hospital warehouses. The nationwide training for pharmacists worked at the hospital pharmaceutical warehouses has been conducted in 1990 and the digital transformation for Drug Inventory system in public hospitals has begun. These result in the reform of the pharmaceutical procurement and warehouse administration in public hospital to become faster and easier when compared to using writing or a typewriter to issue the purchasing orders. This program has been enhanced continuously and still worked in some hospitals until now.

3. Turning the economic crisis into an opportunity to reform the pharmaceutical administration policies.

In 1997, Thailand experienced an economic crisis, also known as "Tom Yum Kung crisis". The government floated the baht, resulting in the baht value falling drastically; the exchange rate skyrocketed from 24 to 56-57 baht per dollar. As a result, the drug prices of the imports rose much higher than the standard medium prices which all the public hospitals have to comply with. Therefore, the government hospitals were unable to purchase drugs according to the procurement regulations issued by the Prime Minister's Office. For this reason, in 1998 the government increased the budgets of drugs and medical supplies for certain ministries. The Ministry of Public Health also received an additional budget of 1,400 million baht; however, it turned out to be a trigger for corruptions during the procurement processes in the 34 provinces.

Consequently, the conclusion of lesson learned from this crisis bought into reforming the pharmaceutical management system under a Good Health at Low Cost master plan. This is to increase efficiency in managing medicines and medical supplies at hospital level under the Ministry of Public Health; starting from selections, procurements, distributions and usage in order to earn good quality yet inexpensive drug prices, with rational utilization.

The reform was done by establishing principles and measures to improve the efficiency of medicines and medical supply management for the pharmaceu-

tical departments under the Ministry of Public Health, in accordance with the procurement regulations issued by the Prime Minister's Office 2535 B.E. (1992) and the procurement regulations for drugs and pharmaceutical supplies (non-drugs) issued by the Ministry of Public Health B.E. 2529 (1986) and the revision 2 in B.E. 2530 (1987). Furthermore, there are additional crucial measures added in the regulations as follows:[1]

1) Determining the proportion of the essential medicine list in the hospital formulary and the proportion of hospital's revenue spending for essential drug procurement.
2) Specifying only one brand for each generic product in the hospital formulary.
3) Emphasizing pooled procurement at provincial and/or department levels for high volume consumption.
4) Encouraging regional and provincial hospitals to manufacture pharmaceutical products to support secondary healthcare facilities.
5) Controlling the hospital drug stocks to no more than 3 months supplies.
6) Evaluating drug utilization in the hospital in order to achieve rational drug use policy.

In 1998, the Office of the Permanent Secretary under Ministry of Public Health proposed the policy of pooled procurement at the provincial level, resulting in budget saving in drug procurement over 171.47 million baht comparing to the market prices and increased to 507.28 million baht in 2001.

In order to ensure the sustainability of transparent administration of pharmaceutical supplies, the Ministry of Public Health incorporation with the National Counter Corruption Commission had established regulations for the procurement of medicines for the Ministry of Public Health on 9 September 2003. The key principle is to increase the economy of scale for drug joint procurement to the regional level using bidding method and conducted the innovative contract called "Fix bidding price for defined items along the committed period with unlimited quantity". In 2007 the cabinet approved the principles proposed by the Ministry of Public Health on 13 March 2007 allowing the Ministry of Public Health to implement key performance measures to improve the efficiency of drug procurement for the whole country (according to the letter issued by the Secretariat of the Cabinet no. 0506/4261 - dated 22 March 2007). Consequently, the Ministry of Public Health has constantly proceeded with the drug pooled procurement at the regional level since 2008.

4. Development of Electronic Medicines and Medical Supply Procurement System

Thailand has developed many laws and regulations involving medicines and medical supplies procurement for decades in order to establish the better procurement practice represented the transparent administration, effective management and the government budget saving at the end. Until the disruptive technology has emerged, most of the businesses have move to the era of digital platform and impacted on the amendment of laws and regulations involving drug procurement. The electronic medicines and medical supplies procurement has evolved since then.

4.1 Electronic Auction (e-auction) System

In the year 2006, the Comptroller General's Department issued the regulations of the Prime Minister's Office on electronic procurement 2006 commonly known as e-auction regulations dated 31

January 2006, effective from 1 February 2006. The e-auction regulations enforce a wider range of government agencies including the government agencies, state enterprises, public organizations and other government agencies which affiliated with or under supervision of the legal management department of which their activities, projects or construction activities costs 2 million baht or more.

This regulation defines that the method of bidding process for bidders to submit price proposals only via electronic channels. However, as for the other steps, they still need to comply with the procurement regulations issued by the Prime Minister's Office B.E. 2535 (1992). Consequently, procurement process took longer when compared to the original bidding method.

When there was an amendment on the Prevention and Suppression of Corruption act B.E. 2542 (1999), the parliament passed an act of Corruption Prevention (No. 2), B.E. 2554 (2011), where in section 103/7 paragraph1, states that government agencies have to conduct the detailed information of the procurement regarding costs, especially standard medium prices, calculations of the standard prices in an electronic system and make it available publicly for the purpose of information validation.

On 8 March 2013, the Ministry of Finance circulated the letter specifying rules, guidelines and procedures for disclosure of the government medium prices. For drug procurement, the medium prices shall be determined as follows:

1) Drugs in the National List of Essential Medicine shall use the prices as announced by the Ministry of Public Health. If there is no listed price, the prices of the most recent purchases within the last 2 fiscal years will be used. If there is no purchase within the last 2 years, a market price will be used as a reference by considering the prices from the markets including from various websites.

2) Drugs not listed in the National List of Essential Medicine use the prices of the most recent purchases within the last 2 years. If there is no purchase within the last 2 years, a market price will be used as a reference, by considering the prices from the markets including the price from various websites.

After using the e-auction for drug procurement, the minimum bidding criteria and criteria for calculating medium drug prices, these cause the procurement process taking longer than before. The re-ordering or any other purchasing methods need approvals from the Comptroller General's Department. Consequently, the procurement procedure is delayed. All these lead to major concerns such as the drug reserves may not be sufficient, unable to purchase due to drug shortage and there might be no vendor selling the drug. For example, in the case of only one bidder entering the bidding process, the process must be canceled and need to be restarted. As a result, a procurement of medicines which has only one registered pharmaceutical company offering in Thailand cannot be performed by e-auction.

4.2 Electronic Market (e-market) and Electronic Bidding (e-bidding) System

In 2015, the Committee on Procurement, Office of the Civil Service Commission (OCSC) released a notification from the Office of the Prime Minister on guidelines for procuring supplies using electronic marketing (e-market) and electronic bidding (e-bidding), dated 3 February 2015, and announced in the Government Gazette on 4 February 2015. These are:

1) Electronic market method (e-Market), including procurement of goods with uncomplicated specifications, general products that require government agencies to purchase are to be listed in the e-catalog system, which can be proposed in 2 ways as follows:

1.1) Proposing via Request for Quotation (RFQ), for which a procurement that costs over 100,000 baht but not more than 5,000,000 baht

1.2) Proposing via an electronic auction (Thai Auction), for which a procurement that costs over 5,000,000 baht

2) Electronic bidding method (e-bidding), which is a procurement for goods that cost over 100,000 baht and have complex features or specific requirements, and/or products that are not listed in the e-market system. The criteria for selecting a winning bidder can be chosen by one of the following criteria:

2.1) By price basis; these are in the cases that the specifications of bidders and quality of goods already meet the requirements. Bidders shall propose only by price.

2.2) By price performance; these are in the cases that even though the specifications of bidders and quality of goods have been specified, but they are still not met with the requirements and needs. This will also encourage bidders who offer quality goods but not the lowest prices to have a chance to win electronic bidding and comply with good government inventory management principles

4.3 Electronic Government Procurement (e-GP) System

In February 2017, the Ministry of Finance issued an act for the Government Procurement and Procurement Administration 2560 B.E. (2017), enforcing all government agencies (i.e. central government sectors, provincial government sectors, local government sectors, state enterprises, public organizations, independent organizations, constitutional organizations, court administrative unit, autonomous university, authorities under the parliament or under the supervision of the parliament, independent state agencies and other agencies as specified in the ministerial regulations). The act became effective on 24 August 2017. Accordingly, seven ministerial regulations were issued by the Ministry of Finance on procurement and government supplies management to support the act.

The amendment of the new system is the attempt to harmonize and consolidate the benefit from the previous procurement acts as well as regulation to more pragmatic and effective system. Nevertheless, the different parts of e-GP obviously distinguished are:

1) To define an annual procurement plan and publish the plan in the information network of the Comptroller General Department and government agencies.

2) Ones who are responsible for the procurement consideration must not be stakeholders in the offerors or contracted parties in the procurement.

3) Companies participating in submitting proposals to government agencies must be registered with the Comptroller General's Department.

4) For the procurement via electronic methods, it must be operated in the Comptroller's Network Information System via e-GP system.

5) Fraudsters, conspirators or supporters shall be penalized with imprisonment for one to ten

years and/or fined from twenty thousand baht to two hundred thousand baht.

Working under the acts or ministerial regulations from early on until present, especially at the beginning, several departments including the departments under the Ministry of Public Health have experienced operational difficulties resulting in operation delays. These government agencies have discussed for guidelines and requested for exemptions from time to time. Additionally, the relevant committees have considered and provided answers to the queries, set new guidelines and provided exemptions in some cases where problems occurred so that the departments can conduct the procurements effectively. However, the Information Network via the Electronic Government Procurement of the Comptroller General's Department: e-GP, still needs more development and improvement for stability and more user's friendly.

Drug Sales and Distribution through Various Channels between 2014-2018

During 2014 - 2018, the annual drug sales distributed through hospitals, pharmacies and private clinics and other channels in Thailand has a total value ranging from 110,928.35 million baht to 125,686.35 million baht (Table 1). The most drug sales are through hospitals (68.39 -67.67%), followed by pharmacies (26.57-27.04%) and other channels such as clinics (5.04-5.09%) respectively. During that time the drug sales across all channels tended to increase i.e. the sales through hospitals, pharmacies and others, such as clinics, the value increased by 12.11 percent, 15.31 percent, and 18.87 percent respectively (Figure 2).

Referring to the drug market survey, the highest selling values of the top 3 drugs in June 2019 are injectable antibiotics (23,183 million baht), drugs in cardiovascular diseases (19,981 million baht) and anti-cancer drugs (18,880 million baht), as shown in Figure 3.

It is noticeable that the injectable antibiotics have decreased by 13% in sales, which could be a result of the government policy on the antibiotic usage control. This is in order to prevent people from drug resistance, in collaboration with many government sectors and hospital health service units.

Drug Procurement and Distribution System for Special Projects in the Universal Health Coverage Scheme and the Social Security Scheme[5,6]

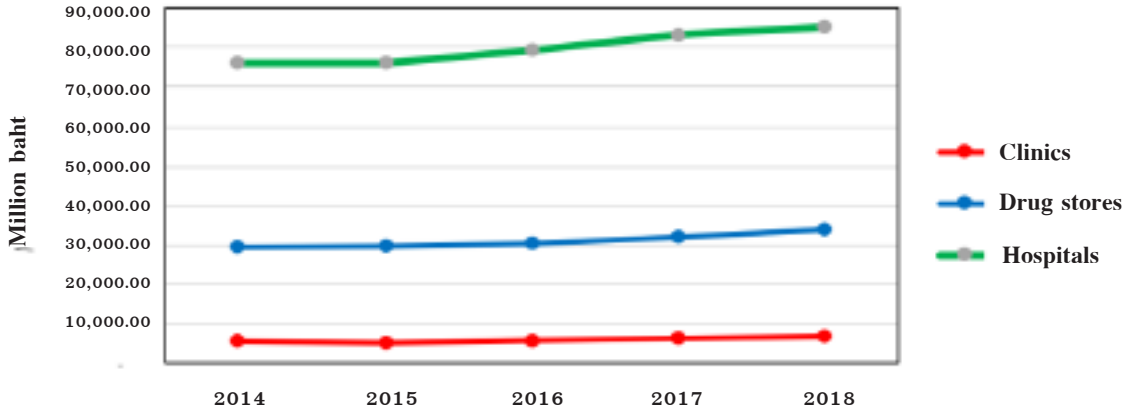
Among three main health insurance schemes in Thailand, namely the Civil Servant Medical Benefits Scheme (CSMBS), Social Security Scheme (SSS)

Table1 Drug sales through various channels between 2014-2018 (million Baht)

	2014	%	2015	%	2016	%	2017	%	2018	%
Hospitals	75,860.88	68.39	75,733.47	68.59	79,143.68	68.66	82,983.94	68.44	85,050.29	67.67
Pharmacies	29,477.66	26.57	29,712.94	26.91	30,475.92	26.44	31,993.03	26.39	33,991.50	27.04
Others	5,589.81	5.04	4,968.44	4.50	5,651.43	4.90	6,270.00	5.17	6,644.56	5.29
Total	110,928.35	100.00	110,414.85	100.00	115,271.02	100.00	121,246.97	100.00	125,686.35	100,00

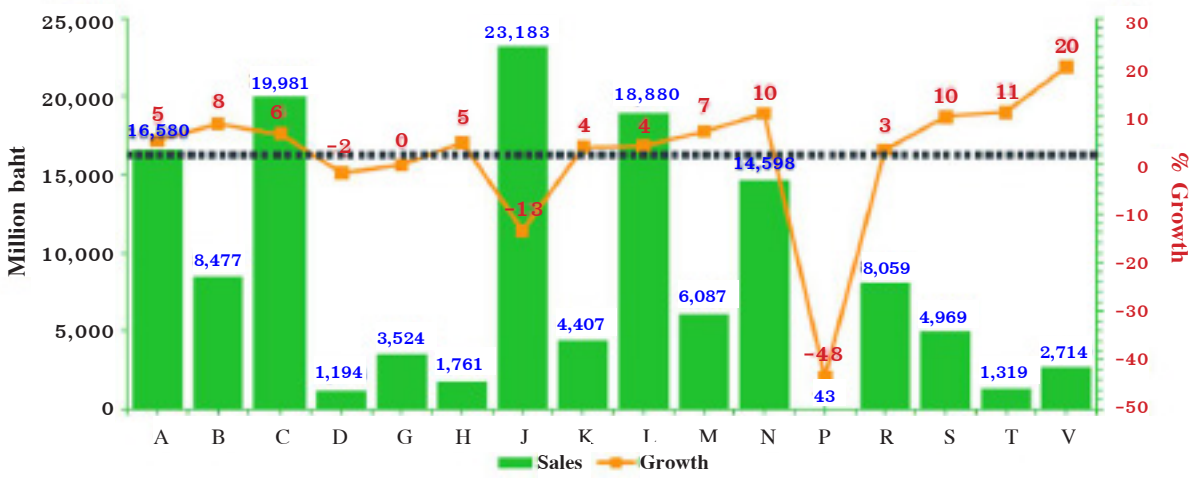
Source: IQVIA Thailand National Sales Audit. Quarterly drug market review in Thailand during 2014-2018[2]

Figure 2 Trends of drug sales through various channels during 2014- 2018



Source: Quarterly drug market review in Thailand during 2014-2018, Quintiles and IMS Health, Inc, Thailand[3]

Figure 3 Drug sales and the percentage of growth of drug sales, classified by drug groups



A: Alimentary tract & metabolism
B: Blood + blood forming organs
C: Cardiovascular system
D: Dermatological system
G: Genito urinary system & sex hormones
H: Systemic hormonal preparation (excluding sex hormones)
J: Anti-infective system
K: Hospital solutions
L: Antineoplastic and immunomodulating agents
M: Musculoskeletal system
N: Central nervous system
P: Parasitology
R: Respiratory system
S: Sensory organs
T: Diagnostic agents
V: Various

Source: IQVIA Thailand National Sales Audit. Quarterly market review 2Q19, June 2019[4]

and Universal Coverage Scheme (UCS), the UCS has the major proportion of population coverage since it covers the rest of the population not covered by the others. Thus, the UCS consuming the highest annual health expenditure and escalating more than 2 times in the past decade.[7] However, the capitation rate per year for universal health coverage (UHC) beneficiaries (no more than 100 USD per capita) is low and not enough for including the innovative medicines from the emerging market. In order to avoid the influx of the new and expensive medicines without supporting evidences, the UCS and SSS will rely on the approved items from National Essential Medicines Sub-committee before including into the benefit package.

Nevertheless, the financing of UHC, operated by the National Health Security Office (NHSO) has grown up continuously and become a major challenge for sustainability. In order to ensure the accessibility to essential medicines for the beneficiaries, the NHSO and SSS have come up with the special projects for selected high cost medicines and assigned the Government Pharmaceutical Organization (GPO) to conduct the central procurement. This leads to higher purchasing power and subsequently higher negotiating power.

All the selected medicines must have quality specifications before central bargaining. These specifications are determined with reference to the pharmacopeia, experts' opinions and stakeholder's opinions. Some life-threatening medicines with frequent reports on quality problems must have pre-marketing surveillance through a third-party laboratory or an international laboratory before the procurement. To gain more quality assurance in the central purchasing, a post-marketing surveillance for monitoring suspected inferior quality products has put into the agenda, as in the case of fixed-dose combinations in tuberculosis (TB) under the collaboration with the Thai Food and Drug Administration (FDA). Moreover, all vaccines used in the National Expanded Program on Immunization (EPI) must obtain approval and get the lot released from the Department of Medical Sciences, Ministry of Public Health.

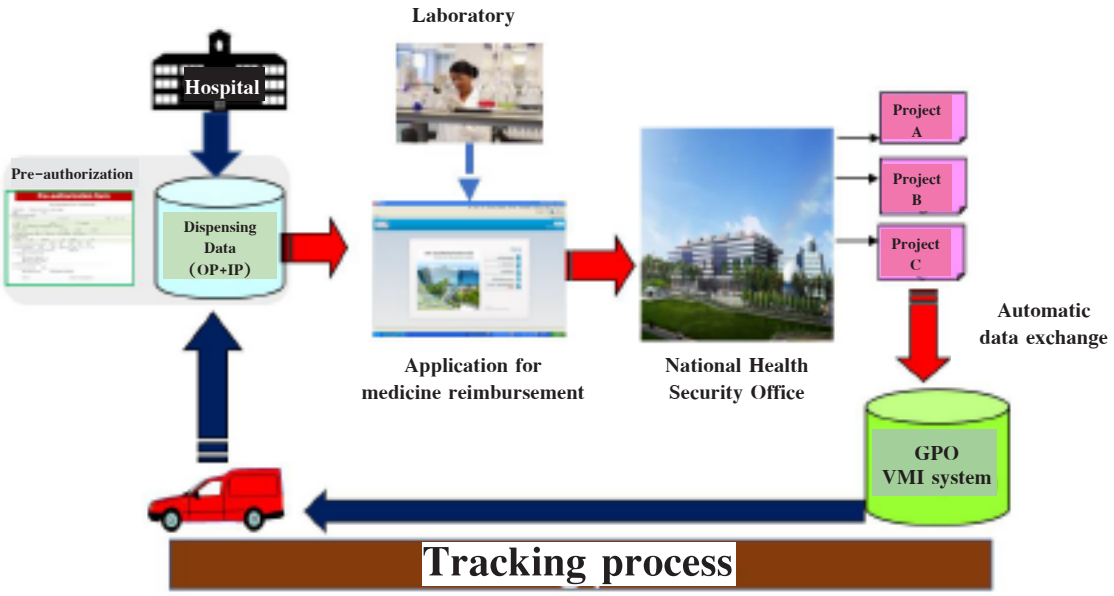
For the delivery system, all the special access items such as high cost medicines and orphan drugs will be centrally procured by the GPO and directly delivered to the health facilities by using the Vendor Managed Inventory (VMI).[8] The registered hospitals for each group of medicines will request the initial stock at the beginning of the provision of a new benefit package. Once there is utilization of any item in the provided list, the hospitals will input or upload the individual prescribing data with pre-authorization to the NHSO for further processing and generating the purchasing order by projects and hospitals. All purchasing orders will be automatically transferred to the GPO's vendor managing inventory program. Finally, all medicines will be shipped and replenished to the hospital warehouse within three to five days (Figure 4).

This system can ensure the accessibility to essential medicines for the patients although some items are of high cost and some are of no interest to import from pharmaceutical companies based on the low and uncertain consumption rate. For the payment design, the medicines reimbursement can compensate the closed-end payment mechanism especially capitation or DRG with global budget. The VMI can also dramatically cut the purchasing budget in pharmaceutical products by reducing the redundant distribution in warehouse at the regional and provincial levels and overstock at the hospital level.

Drug Procurement and Distribution System during Emergencies

For emergency circumstance[9] such as the big flood in 2011 which covered vast areas of the country for a long period of time, the patients were unable to get access to the public health services; the preparation should be enforced so that the patients could have been evacuated from the flooded areas. Also, there should be proactive services to give patients access to essential medicines according to the patients' conditions as well as receiving continuous medication.

Figure 4 Drug procurement and distribution for the special projects in UCS and SSS



The flooding also caused many hospitals to temporarily stop the drug productions due to the flood overflowing into the factories and the cut-offs in major transportations. In addition, it created difficulties in transportation of raw materials and finished drugs, resulting in shortages of drugs in both drug manufacturer and hospital sides.

In order to relieve these types of chaos, the Ministry of Public Health has appointed a committee and a working group to help solve flood problems in terms of medicine and public health, being a center to collect the issues regarding health related to floods. This working group consists of representatives from related departments such as the Food and Drug Administration, Department of Disease Control, Department of Health, Department of Medical Services, Department for Development of Thai Traditional and Alternative Medicine, and Government Pharmaceutical Organization. The group has standardized drug support procedures and guidelines for medicines and medical supplies on the following areas: distributions, communications to the problematic areas, and performance evaluations by appointing the Government Pharmaceutical Organization to a national reserve agency for medicines and medical supplies, known as National Stockpile.

Regional public health agencies have also managed the problems in the area, including management of patients with chronic diseases who are unable to receive services at the hospital. There is a division of geographic area into zones in order to have a large community hospital performing as a center for basic drug support to the other community hospitals in the area. However, there are still obstacles in the operation.

In case of outbreaks where vaccines and/or anti-toxic biomedicine are required; for example, the bird flu (2004), botulism from consumption of processed bamboo shoots packed in aluminum containers (bamboo shoot disease: 1998-2006), influenza pandemic (2009), diphtheria (2011-

2015), and measles (2016-2019), the Department of Disease Control under the Ministry of Public Health and the NHSO has reserved the vaccines and antiviral drugs in order for supports during epidemic occurrences in Thailand as follow:

Vaccines for public health emergencies. It is a duty of the Department of Disease Control to reserve vaccines for prevention and control the diseases which periodically spread in the country including vaccines for measles elimination and polio eradication. These reserved vaccines are diphtheria-tetanus (dT) vaccine, measles-rubella-mumps (MMR) vaccine or measles-rubella (MR) vaccine, and oral polio vaccine (OPV). When a suspect case is identified, the provincial health office or hospital must report and request for vaccination support to the Department of Disease Control.[10-12]

For influenza vaccines to support pandemic of which the most recent outbreak occurred in 2009, Thailand by the Ministry of Public Health has implemented public-private partnership policy by negotiating with pharmaceutical company to provide influenza vaccine to Thailand under a condition that if an epidemic occurs, the pharmaceutical company will deliver the vaccine to the Government Pharmaceutical Organization. Consequently, this collaboration has bought to the establishment of a joint venture between the Government Pharmaceutical Organization and a private company for development the packaging process for the vaccine. For this arrangement, Thailand does not have to provide advance payment. If the Ministry of Public Health had not started the negotiations with the vaccine production company, the vaccination reserves would have gone through the normal procedures. This means that Thailand would have to pre-order vaccines in advance for years and when outbreaks occur, it does not guarantee if Thailand will finally receive the vaccines in time even though the deposit for the vaccines has been paid in advance. In the meantime, the GPO has optained technology transfer on production and preparation for establishing vaccine production facilities for seasonal influenza and pandemic influenza at the upstream level. The scale of production will range from producing initial ingredients to packaging. This has enabled the country to be self-reliant and secured in vaccine reserves. Nonetheless, the production must be generated at least 10 million doses per year in order to breakeven the production costs.

2) Anti-toxic biomedicine to support public health emergencies. It is a responsibility of the NHSO to reserve antitoxic biomedicines for treatments, for example, diphtheria antitoxin and botulinum antitoxin. When investigating for the disease outbreaks and a suspect is found, the Provincial Health Office or the responsible hospital must report to and request for vaccination support from the Department of Disease Control or the Toxicology Center at Ramathibodi Hospital, Mahidol University, a WHO Collaborating Center in Thailand.[13,14]

Further Improvement on Drug Procurement and Distribution

The following issues are the areas need to improve drug procurement and distribution in Thailand:

1) The criteria for determining the items needed list for central procurement and distribution shall be done

2) Defining a direction to harmonize the drug

procurement and distribution system for public health insurance fund at the national level.

3) Monitoring the rational drug procurement and distribution in online pharmacy

4) Implementation research on special procurement of orphan drugs, antitoxic drugs, vaccines for pandemic control to ensure sustainability and supply security.

5) The study of drug management during disaster and emergency should be taken into concern

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บทคัดย่อ: การจัดหาและการกระจายยา

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ระบบการจัดหาและกระจายยาถือเป็นกระบวนการสำคัญในการเชื่อมต่อระบบการเข้าถึงและประกันการเข้าถึงยาของผู้ป่วยเพื่อให้มั่นใจว่าผู้ป่วยสามารถเข้าถึงยาที่มีประสิทธิผลและมีคุณภาพ ซึ่งการจัดหาต้องมีการพิจารณาลักษณะของตลาดยาซึ่งมีหลายประเภท ทั้งตลาดผูกขาดที่มีผู้ขายเพียงรายเดียว หรือตลาดกึ่งผูกขาดที่มีผู้ขายน้อยราย หรือหากมีผู้ผลิตออกจำหน่ายกันมากขึ้นและส่งผลให้ยานั้นมีการแข่งขันกันในตลาดมากขึ้นจนเกิดการแข่งขันกันด้านราคาที่ลดลงแต่ไม่ถึงขั้นแข่งขันสมบูรณ์ ระบบการจัดหาและกระจายยาในประเทศไทยเริ่มต้นจากอุตสาหกรรมยาซึ่งมีทั้งยาที่ผลิตภายในประเทศและนำเข้าจากต่างประเทศ โดยผู้ผลิตและผู้นำเข้าในภาครัฐและเอกชน สำหรับผู้ผลิตภายในประเทศ มีการนำเข้าวัตถุดิบส่วนใหญ่จากต่างประเทศ เนื่องจากข้อจำกัดด้านการผลิตวัตถุดิบตัวยาสำคัญในประเทศ ต่อมามีการกระจายยาสำเร็จรูปผ่านผู้แทนจำหน่าย (distributors) และผู้ค้าส่ง (wholesalers) ไปยังสถานบริการด้านสุขภาพระดับต่าง ๆ ทั้งโรงพยาบาลรัฐและเอกชน คลินิกและร้านยา นอกจากนี้ ยาจากผู้แทนจำหน่ายยังกระจายไปยังช่องทางอื่น ๆ นอกเหนือจากระบบข้างต้น ได้แก่ โครงการพิเศษของสำนักงานหลักประกันสุขภาพแห่งชาติและสำนักงานประกันสังคม การบริหารจัดการยากำพร้า และในกรณีสถานการณ์ฉุกเฉินได้มีแนวทางในการบริหารจัดการการจัดหาและกระจายเพื่อรองรับสถานการณ์ ได้แก่ การระบาดของโรคที่ป้องกันได้ด้วยวัคซีน การเกิดการรั่วไหลของสารพิษ และการเกิดอุทกภัย ในปัจจุบันระบบการจัดการขนส่ง (logistic system) ได้พัฒนาไปอย่างมาก ทำให้เกิดบริษัทที่ทำธุรกิจด้านการบริหารคลังยาและจัดส่งยาให้กับสถานบริการขึ้นมากมาย ในภาครัฐองค์การเภสัชกรรมมีบทบาทในการจัดหาและกระจายยาให้กับลูกค้า โดยเฉพาะการกระจายยาในโครงการพิเศษให้กับหน่วยบริการในระบบหลักประกันสุขภาพแห่งชาติและระบบประกันสังคมผ่านระบบ Vendor Managed Inventory (VMI).

คำสำคัญ: การจัดหายา, การกระจายยา, การบริหารคลังยา

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The Impact of Drug Financing System under Thailand Universal Health Coverage (UHC) on the Performances of Drug System

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Abstract The drug system has a direct impact on the country's health system. A well performing of drug system is crucial for advancing the health system. However, its performance is extremely dependent on how well resources are being deployed. A strong finance system is essential to effectively manage monetary resources in the drug system. This review and analysis of how well the current financing system supports drug system performance provides beneficial feed-back information to inform actions on how to improve the drug system. Six performance indicators for how current financing mechanisms contribute to drug system performance. The review found a continuously increasing trend of drug spending, driven by the use of highly expensive health technology. Good access to essential medicines listed in the national list which is the drug benefit package of all major public health insurance schemes. Higher efficiency was found in the close-ended payment basis scheme than the fee-for-service basis payment scheme. However, there were inequities in accessibility to higher cost drugs among major health insurance schemes. The over- and -under-utilization of drugs relating to payment methods is of concern as an issue rational drug use. The current financing system encourages intensive cost-driven competition in drug markets, which is disadvantageous for Thailand local drug industry. The continuous increasing trend of drug importation value was found. This signifies the country's dependence

on imported drugs which negatively affect to the national drug security. The review identified 4 major recommendations. Those are the need for (1) the effective financing system to facilitate access to high cost drug, (2) financing mechanisms to strengthen local manufacturers capacity on research and development, (3) payment mechanism containing drug expenditure of the Civil Servant Medical Scheme, and (4) the measures to address inequity in access to medicines among beneficiaries covered by different health insurance schemes.

Keywords: **finance system; drug system; drug financing system; drug benefit package**

Introduction

The finance system is an important component for any operational management. The drug system is usually framed using an operation management perspective. The drug operation system is composed of four main components: selection, procurement, distribution, and use. The system performances are extremely depend on how well the resources, which are the system inputs, are being managed. Financial management in the context of domestic and international policy and legislation to be analyzed as it directly affects the performance of the drug system.

Thailand achieved universal health coverage (UHC) since 2002. A total of 99.4% of the entire Thai population has been covered by three major public health insurance schemes. These are the Civil Servant Medical Benefit Scheme (CSMBS) for government officers and dependents, the Social Security Scheme (SSS) for private workers and the Universal Coverage Scheme (UC) which covers all Thai populations not covered by the previously mentioned employment-based health insurance schemes. The financing sources, drug benefit packages and related payment mechanisms among the schemes are summarized in Table 1.[1-3]

This review aims to depict the situation of drug system performance relating to the current drug financing system.

Table 1 Drug benefit packages in Thailand

	Civil Servant Medical Benefit Scheme (CSMBS)	Social Security Scheme (SSS)	Universal Coverage Scheme (UC)
Beneficiary	Government officers and dependents including their parents and children	Employees in private organizations	All Thai population who are not covered by CSMBS or SSS or any other schemes.
Number of beneficiaries (millions)	5.1	12.2	47.8
Responsible agency	Comptroller General's Department (CGD)	Social Security Office (SSO)	National Health Security Office (NHSO)
Source of fund	Government budget from taxation	Contributions from employees, employers and government	Government budget from taxation

Table 1 Drug benefit packages in Thailand (continued)

	Civil Servant Medical Benefit Scheme (CSMBS)	Social Security Scheme (SSS)	Universal Coverage Scheme (UC)
Drug benefit package	- Medicines included in national list of essential medicines (NLEM) - Medicines beyond NLEM listed in the access program or in case the clinical necessities declared	- Medicines included in national list of essential medicines (NLEM)	- Medicines included in national list of essential medicines (NLEM)
Payment method	- Out-patient service: fee-for-service at the price the providers charge - In-patient service: bundled payment according to Diagnosis Related Groups system (DRGs)	- Out-patient service: capitation (per head per year) - In-patient service: bundled payment according to Diagnosis Related Groups system (DRGs) with close-ended budget	- Out-patient service: capitation (per head per year) - In-patient service: bundled payment according to Diagnosis Related Groups system (DRGs)

Analysis of drug system performance relating to the current finance system

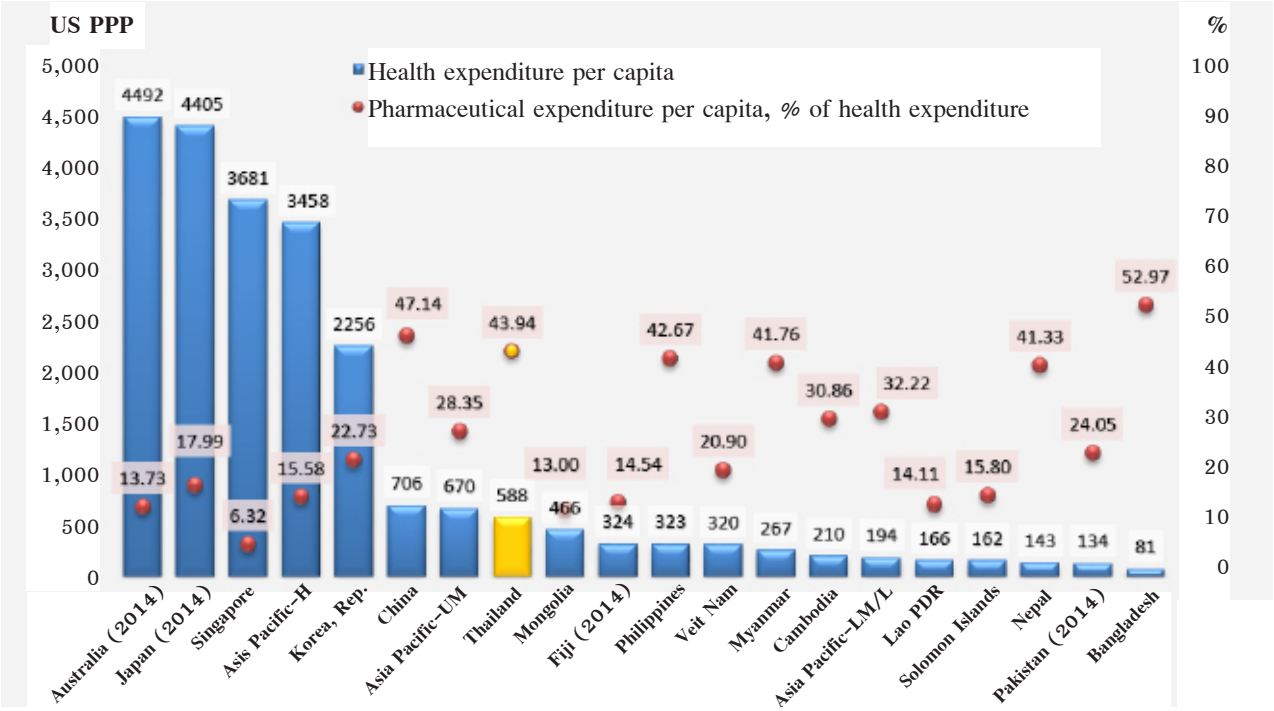
Analysis drug system performance relating to financial management in this review includes drug and health expenditure, access to medicines, rational drug use, efficiency, equity and sustainability.

1. Drug Expenditure

In 2015, Thailand health expenditure per capita was 588 US PPP[4] or approximately 7,268 Thai Baht (12.4 Baht per US PPP, at 2018),[5] which is the highest comparing to CLMV countries (Cambodia, Lao, Vietnam, Myanmar). However, Thailand health expenditure was considerably low to moderate when compared with developed countries (Australia, Japan, Singapore).

For drug expenditure per capita, the Asia-Pacific countries were categorized into three groups according to the proportion of drug expenditure in relation to health expenditure. The first group was developed countries of Australia, Japan, Singapore, South Korea; and drug expenditure per capita accounted for less than 25.0% of health expenditure. The second group was developing countries of Mongolia, Fiji, Vietnam, Lao, Solomon and Pakistan; and drug expenditure per capita accounted for less than 25.0% of health expenditure. The third group was developing countries of China, Philippines, Myanmar, Cambodia, Nepal and Bangladesh; and drug expenditure per capita accounted for more than 25.0% of health expenditure. Thailand fitted into the third group, and its drug expenditure per capita accounted for 43.9% of health expenditure. This is the highest comparing to CLMV countries (Cambodia, Lao, Vietnam, Myanmar) as shown in Figure 1. However, Thailand drug expen-

Fugure 1 Health expenditure and the proportion of drug spending per capita among Asia-Pacific countries in 2015



Sources: https://www.oecd-ilibrary.org/social-issues-migration-health/health-at-a-glance-asia-pacific-2018/health-expenditure-per-capita-2015_health_glance_ap-2018-graph112-en

Thailand data: http://www.fda.moph.go.th/sites/drug/SitePages/Statistic.aspx

diture might be overestimated in this reference report, because the data used drew on the annual value of drug manufacturing and importing.[6]

Trends show that Thailand's health and drug expenditure tends to be increasing continuously. Thailand's health expenditure accounted for 3.7% of the gross domestic product in 2015.[7] It increased from 2.3 hundred billion Baht in 2000 to 3.5 hundred billions in 2015; this is an increase of 1.2 hundred billions Baht in 15 years. The proportion of drug expenditure in relation to health expenditure also followed the same trend. Over a period of 15 years, the proportion of drug spending doubled from 21.2% of health expenditure to 43.9%, shown in Figure 2. This increasing trend due to many factors including the high price of new technology, ageing populations, disease epidemiology, changing approaches to disease management and the impact from health insurance systems.

Thailand drug spending during 1996 to 2015, can be categorized into three periods according to different spending trend. In the first period, before the implementation of UC scheme (1996-2001), drug spending increased on average by 1.8 billion baht per year. A faster increasing trend (averaging 7.6 billion Baht per year) was found during the second period following the implementation of UC scheme and before the CSMBS (2002-2005) with its direct claim processing. In the third period (2006-2010) after the CSMBS implementation of direct claim processing, the average increase of drug spending was 17.5 billion Baht per year as shown in Figure 3. The highest annual drug spending (1.73 hundred billion Baht) was in 2010. After this, the Comptroller General's

Department (CGD) launched reimbursement restriction measures to control drug spending. Spending then slightly decreased and changed in a range of 1.4-1.6 hundred billion Baht, as shown in Figure 3.

Figure 2 Health and Pharmaceutical expenditure and Thailand gross domestic product during 2000-2015

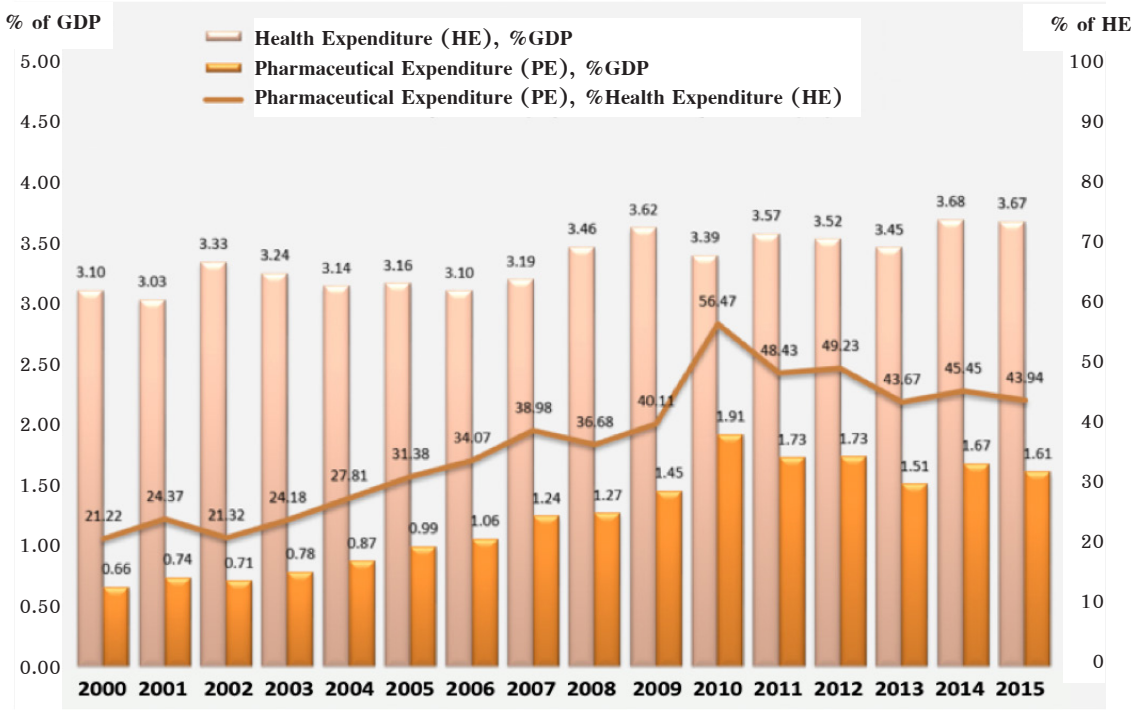
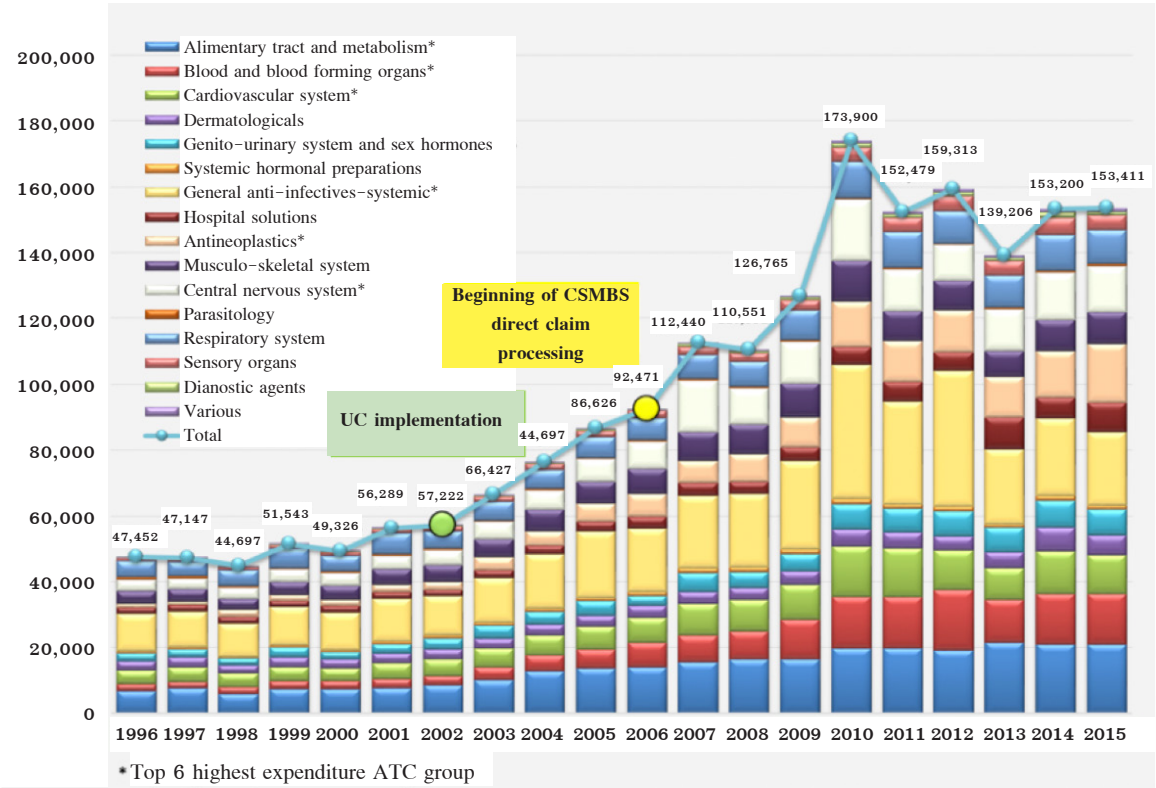


Figure 3 Thailand domestic drug expenditure classified by the Anatomical Therapeutic Chemical (ATC) Classification System during 1996-2015 (real value)



It is clearly that financing mechanisms effect drug spending. Spending increased at slower rate during the early period prior to UHC with an emphasis on out-of-pocket financing. Then, spending increased at a faster rate after the implementation of the UC scheme, due to enhanced access to drugs through health insurance finance. However, once the CSMBS's reimbursement policy was modified to direct claim processing between health care providers and the CGD. This replaced the previous policy where beneficiaries had to pay in advance and then claim reimbursement via their affiliations to CGD. The policy change caused a significant increase in drug spending because the more convenient reimbursement process encouraged the greater service utilization. However, other factors such as higher drug prices from more expensive technology; biologic drugs, bigger proportion of aging population also have played a role to increase in drug spending.[8] As shown in figure 2, the trend of increased spending was found particularly in drug use in treating central nervous system disorders, blood and blood forming organs, cancer and cardiovascular ill-health; these relate to diseases with increasing incidence in ageing populations. There was a significant increase in the use antineoplastic drugs which tend to be more expensive as they are developed through advance technology and are in high demand.

2. Access to medicines

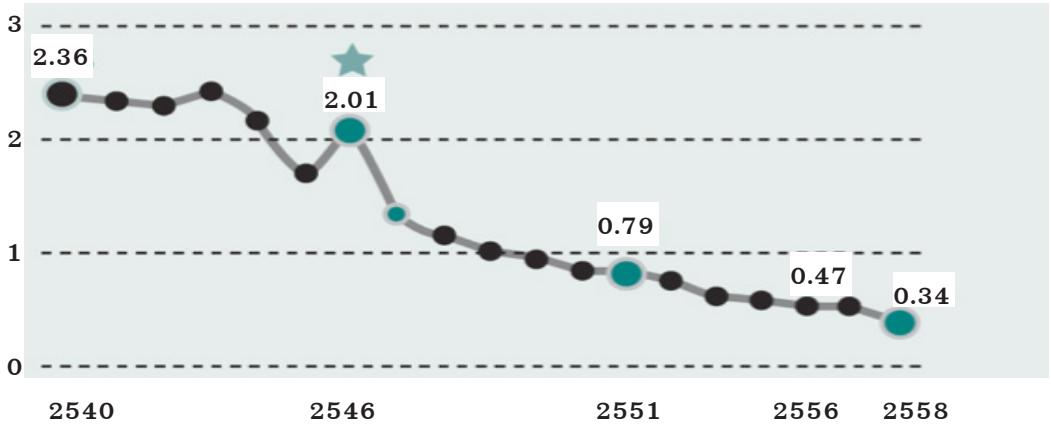
Sixteen years of UHC system in Thailand has resulted in a significant increase of access to health services for Thai people. The percentage of impoverished households due to the of health care expenditure decreased from 2.0% in 2003 to 0.3% in 2015 as shown in Figure 4

In 2010, unmet health needs were 1.4% for outpatient services and 0.4% for inpatient services. In 2015, the percentage of unmet health needs for outpatient services remained stable and in-patient services decreased to 0.1%.[10] The major causes of the unmet health needs are long waiting times for outpatient services and geographic accessibility for inpatient services.[11]

2.1 Access to essential medicines

The major health insurance schemes covering 99.4% of the Thai population, have enforced the

Figure 4 Percentage of impoverished households from the burden of health care expenditure[9]



national essential drug list as the drug benefit package. All beneficiaries are eligible to access listed medicines without additional payment. In general, the Thai people then has good access to national essential medicines [12]

Under the capitation payment system, there is no motivation for providers to dispense the expensive drugs to beneficiaries. The NHSO then launched the special access program which includes financial measures and central procurement to negotiate fair prices for medicines with limited accessibility such as antidotes, clopidogrel and very expensive medicine. Since 2008, the expensive medicines listed in the E2 category are reimbursed separately from capitation and Diagnostic-Related Groups.[13] The E2 category is one of medicine category from 5 categories (A to E) in Thai national list of essential medicine. Medicine listed in this category is very expensive, high technology, but essential for some patients with specific condition. The uses of these medicines have significant impact to affordability of both society and individual.

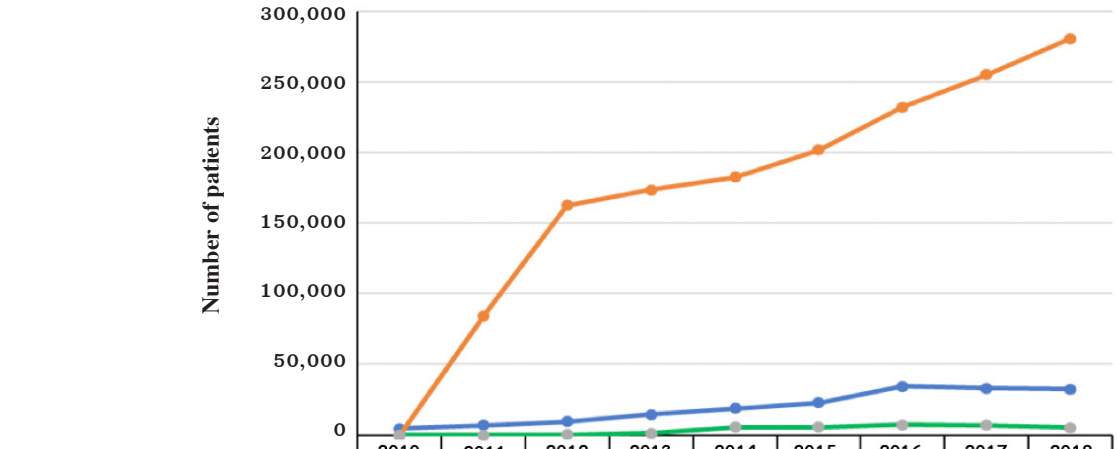
A fixed-fee schedule is used for the anti-cancer drugs prescribed according to the protocol, while other medicines in this special program are reimbursed by the products. Patients under UC scheme then have increasing access to essential medicines in the special access program as shown in Figure 5.

The SSS manages the benefit package of expensive drugs similar to the UC scheme.[12] The CSMBS reimburses essential medicines in category E2 by fee-for-service based with prior authorization.

2.2 Access to non-essential medicines

Access to non-essential medicines is harder for beneficiaries in UC and SSS capitation-based scheme compared with the fee-for-service CSMBS. Under UC and SSS, expensive non-essential anti-cancer drugs might be used and reimbursed but under a very limited payment scheme, while in CSMBS, the

Figure 5 Number of UCS patient who accessed essential medicines in category E2, clopidogrel and antidotes



	2010	2011	2012	2013	2014	2015	2016	2017	2018
Patient access to Category E2	4,446	6,891	9,546	14,635	18,980	22,931	34,487	33,162	32,644
Patient access to Clopidogrel	0	84,455	162,562	173,745	182,432	201,795	232,052	255,257	280,783
Patient access to antidote	0	0	134	1,381	5,505	5,708	7,141	6,917	5,312

Sources: NHSO database of category E2 medicines, clopidogrel and antidotes

non-essential medicines listed in Oncology Prior Authorization program are reimbursed on a fee-for-service basis without ceiling. The OCPA program has been launched in 2006 to reduce financial burden for CSMBS beneficiaries who need to use the high price non-essential medicines. Currently, there are 19 listed medicines for 29 diseases included in OCPA program such as Sorafenib, Osimertinib, Panitumumab. In addition, CGD has also launched other access program of non-essential medicines for other diseases: RDPA (rheumatic disease prior authorization), DDPA (dermatology disease prior authorization). The reimbursement of other non-essential medicines are considered on a case by case basis.[12]

3. Rational Drug Use

Mechanisms to promote rational drug use are applied in the national list of essential medicines (NLEMs). The conditions required when prescribing medicines with risks are defined; for example "Use only for the specified indications" or "Must be prescribed by the medical specialists". These conditions are also enforced under the reimbursement conditions.[14]

In the UC scheme, reimbursement of anticancer medicines is separate from capitation value and is on fixed-fee schedule basis. The reimbursement conditions intend to promote rational use of drugs are required. The fee-for-service payment with a fixed-fee schedule is applied if the medicines are prescribed corresponding to the defined protocol. If not, the reimbursement ceiling at 2,300 Thai Baht per visit (2019 average rate: 1 USD = 31.1 Thai Baht) is additionally applied. In out-patient services, the reimbursement ceiling is 4,000 baht per visit (2019 average rate: 1 USD = 31.1 Thai Baht) applied for those medications prescribed for non-protocol cancer treatment. For in-patient services, if the medicines are not prescribed in correspondence to the treatment protocol, the additional reimbursement for the medicine costs is not eligible. The only reimbursement permitted is in accordance with the DRGs.[12]

However, when reviewing the different reimbursement systems among major health insurance schemes, and considering drug uses for a particular disease, it was found that medication used in the close-ended payment schemes are less expensive but with, limited choices of medicines, compared with the fee-for-service scheme. This might reflect the over-utilization of medicine in the fee-for-service scheme, and under-utilization in the close-ended reimbursement scheme.

4. Efficiency

The NHSO pays for over 90.0% of medication costs using closed-end payment methods (capitation, and DRGs with limited overall budget), and the minority are paid by fixed-fee schedule. This payment strategy promotes operational efficiency because there are no incentives for the health care providers to falsely induce the excessive health care service uses. The inclusion of the cost of medicines in capitation value automatically encourages health care providers to strictly prescribe essential medicines for the patient under UC scheme. In contrast, the fee-for-service at the price the provider charge in CSMBS was found to be high; prescriptions of non-essential medicines accounted for 41.0% of the total prescription drug expenditure and 67.0% of drug expenditure for out-patient services in CSMBS.[15]

A Health Technology Assessment (HTA) is another mechanism to enhance the efficiency and sustainability of the drug finance system. HTA has been employed to ensure that decisions to include new expensive medicines in the benefit package are based on cost-effectiveness and the country's ability to pay.

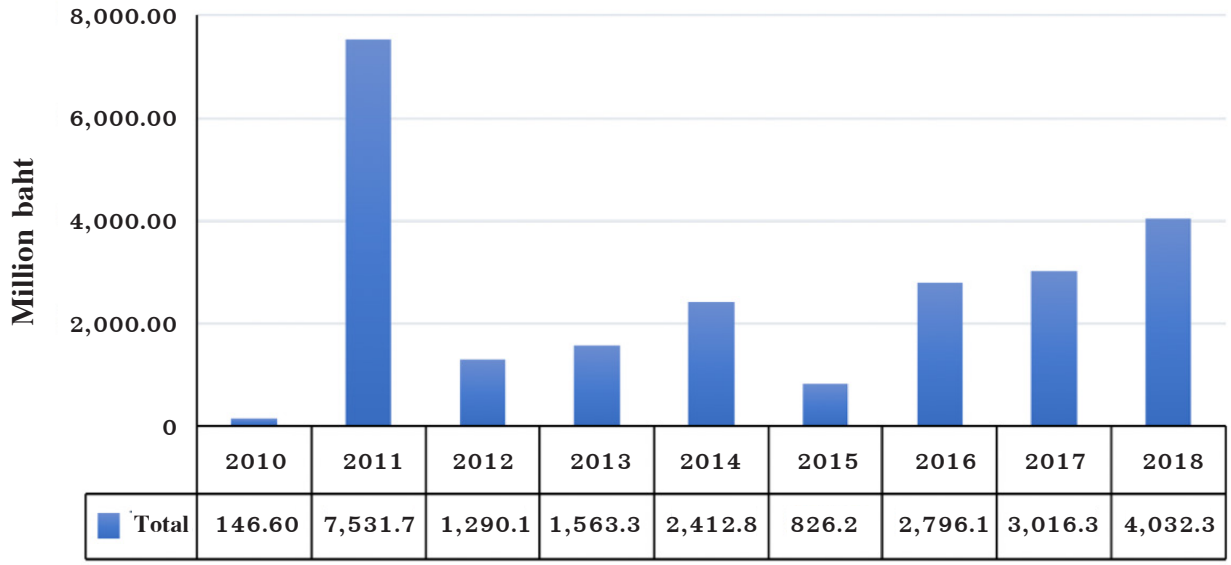
The NHSO is the healthcare services purchaser covering the majority of the Thai population. It holds negotiating power of big volume for central drug purchasing of expensive patented medicines (medications in E2 category of the essential medicines list). Between 2010-2018 the NHSO could save 90 million Baht (2018 average rate: 1 USD = 32.3 Thai Baht) through central and strategic purchasing of expensive drugs.[16] The central purchasing of E2 category of essential medicines, antiplatelet and antiretroviral drugs by the NHSO could cumulatively save 23,615.86 million Thai Baht (2018 average rate: 1 USD = 32.3 Thai Baht) of the government health budget during 2010 to 2018 as shown in Figure 6.

In order to increase the efficiency of drug utilization at the level of healthcare facilities affiliated with ministry of public health, a number of strategies have been implemented to control drug spending. For example, pooled purchasing at provincial level or regional health level, selecting only one product for each medication by generic name, replacing the patent expired drugs with the locally-made products and, regulating the number of drug items for each facility according to their size.

5. Equity

The availability of the comprehensive benefit package and no out-of-pocket payments at the point of service has resulted in the reduction of household health expenditure from 34.0% of total national health expenditure in 2000 (before the implementation of UC scheme) to 12.0% of total national health expenditure in 2014. Ultimately, this can prevent the households from bankruptcy caused by their health care costs.[17] This reflects the improvements of

Figure 6 The saving value from central procurement between the fiscal years 2010-2018



Source: NHSO Purchasing information of E2 category medications, antiplatelet and antiretroviral drugs

equity in access to health care services among people with different socioeconomic statuses.

However, different reimbursement methods among the major public health insurance schemes can cause inequity in access to medicine among beneficiaries, especially access to expensive medicines.[12] In relation to out-patient services, CSMBS (fee-for-service based) provides better access to medicine than the capitation based scheme (UCS, SSS). When considering drug use for a particular disease, it was found that medicine used in close-ended payment scheme were less expensive, limiting the choice of medicines compared with those medicines more widely available in fee-for-service scheme.

For in-patient services, there are no significant differences in medication access because all major health insurance schemes reimburse the medication costs by bundled payment methods, in line with the DRGs system.

5. Sustainability

Tax is the main source of funding for major public health insurances, and this is the most progressive and sustainable financing source because high-income earners will pay higher tax rates than low-income people.[18] Currently, 76% of Thailand's health expenditure is from government spending. Thailand's health expenditure accounts for 4% of Gross Domestic Product (GDP),[19] and this remains lower than many developed countries. However, results from one study forecast the increasing health expenditure in the future influenced by high-cost technologies more than changing population structures.[20]

Another dimension of sustainability is national drug security which relates to how finance is managed in the health system. The UHC led to the majority of drugs being consumed through the public hospitals (75.0% of total consumption value). Due to closed ended payment (such as capitation, DRGs), hospitals have to increase their operational efficiency by minimizing their service delivery cost. Medicines were then purchased at as low as possible price. Public procurement regulations give the market privilege to the Government Pharmaceutical Organization (GPO) the private drug manufacturers by allowing the GPO to be first priority supplier for public hospitals. Moreover, the current market situation and regulation is not favoring the growth of Thai local manufacturers. Competition from low cost Indian and Chinese manufacturers, together with the requirements of Good Manufacturing Practice - Pharmaceutical Inspection Co-Operation Scheme (GMP-PIC/S), effective since 1st August 2016, (which leads to higher manufacturing costs for the private local manufacturers),[21] make it disadvantageous in the cost-driven market.

The 2017 data presents the total income of domestic pharmaceutical manufacturers at 67,919.53 million Baht (2017 average rate: 1 USD = 33.9 Thai Baht), while the income of pharmaceutical and medical product importers and distributors (mostly foreign companies) was 402,881.32 million Baht (2017 average rate: 1 USD = 33.9 Thai Baht). Another source of data from national drug consumption studies[22, 23] found a high average growth rate of drug importation value at 24.3% per year during 2000 to 2010, while local manufacturing value grew by just 9.1% per year in the same period. The proportion of drug importation value for overall consumption increase from 58.1% to 74.1% in ten years. This information signifies that Thailand drug consumption

tends to rely increasingly on importation, which might present a future challenge to the country's self-reliance in access to medicines.

Recommendations for future improvements

There are four important recommendations for Thailand's drug financing system which will promote drug system performances:

1) An effective financing system to facilitate access to high value but expensive drugs because the treatment of diseases tend to increasingly rely on complex and expensive health technologies such as biologic drugs.

2) Financing mechanisms to strengthen local manufacturers and promote investment in research and development capacity. The growth of high capacity local manufacturers would enhance the country's self-reliance on medicine access.

3) Financing mechanism to address inequities in medicine benefit packages and accessibility among the beneficiaries who are covered by different public health insurance schemes.

4) Effective financing mechanism to contain the drug expenditures of the fee-for-service based scheme (CSMBS) such as improving the drug reimbursement method to become a fixed-fee schedule instead of fee-for-service at the price the health care providers charge.

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บทคัดย่อ: ผลกระทบของระบบการเงินการคลังด้านยาภายใต้หลักประกันสุขภาพถ้วนหน้าของประเทศไทยต่อผลการดำเนินการของระบบยา

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ระบบยาเป็นระบบซึ่งส่งกระทบโดยตรงต่อระบบสุขภาพ ระบบยาที่มีผลการดำเนินการที่ดีมีความจำเป็นอย่างยิ่งต่อการพัฒนาระบบสุขภาพ อย่างไรก็ตาม ผลการดำเนินการของระบบยาขึ้นอยู่กับว่าได้มีการจัดการการใช้ทรัพยากรที่เป็นปัจจัยนำเข้าของระบบได้ดีอย่างไร ระบบการเงินการคลังที่เข้มแข็งมีความจำเป็นสำหรับการจัดการทรัพยากรที่เป็นตัวเงินของระบบยา การทบทวน และวิเคราะห์ผลของระบบการเงินการคลังในปัจจุบันว่าได้มีส่วนส่งเสริมสนับสนุนผลการดำเนินการของระบบยาหรือไม่อย่างไร จะเป็นประโยชน์ในฐานะข้อมูลป้อนกลับ ที่จะชี้ให้มีการดำเนินการด้านการเงินการคลังเพื่อส่งเสริมผลดำเนินการของระบบยา งานทบทวนวรรณกรรมชิ้นนี้ วิเคราะห์ผลของระบบการเงินการคลังที่มีต่อผลการดำเนินการของระบบยาผ่านตัวชี้วัดผลการดำเนินการของระบบยาจำนวน 6 ตัวชี้วัด การทบทวนวรรณกรรมพบแนวโน้มการเพิ่มขึ้นของค่าใช้จ่ายด้านยาอย่างต่อเนื่องซึ่งมีสาเหตุสำคัญจากการใช้ยาเทคโนโลยีสูงราคาแพง ประชาชนสามารถเข้าถึงยาในบัญชียาหลักแห่งชาติได้ดี เนื่องจากเป็นสิทธิประโยชน์ด้านยาของระบบหลักประกันสุขภาพภาครัฐหลัก ๆ ทั้ง 3 ระบบ ระบบประกันสุขภาพที่มีกลไกการจ่ายค่ายาแบบปลายปิด มีประสิทธิภาพสูงกว่าในระบบที่มีการจ่ายค่ายาแบบปลายเปิด หรือจ่ายเป็นรายรายการ อย่างไรก็ตาม มีความเหลื่อมล้ำในการเข้าถึงยาโดยเฉพาะยาที่มีราคาแพงระหว่างผู้มีสิทธิ์ในระบบประกันสุขภาพภาครัฐหลัก ๆ การใช้ยาที่มาก หรือน้อยเกินไป เนื่องจากความแตกต่างของวิธีการจ่ายค่ายาระหว่างระบบประกันสุขภาพ สะท้อนปัญหาการใช้ยาอย่างสมเหตุสมผล ระบบการเงินการคลังปัจจุบันส่งเสริมให้เกิดการตลาดยาที่มีการแข่งขันด้วยต้นทุนที่ต่ำอย่างเข้มข้นซึ่งเป็นข้อเสียเปรียบของอุตสาหกรรมยาภายในประเทศของไทย ประกอบกับแนวโน้มที่มีมูลค่าการนำเข้ายาเพิ่มขึ้นอย่างต่อเนื่อง ชี้ว่าประเทศไทยมีบริโภคยาที่พึ่งพาการนำเข้าเพิ่มขึ้น ซึ่งไม่เป็นผลดีต่อความมั่นคงทางยาของประเทศในอนาคต การทบทวนวรรณกรรมชิ้นนี้ได้เสนอ 4 ข้อเสนอแนะสำคัญด้านการเงินการคลัง เพื่อพัฒนาผลการดำเนินการของระบบยา: ระบบการเงินการคลังที่ส่งเสริมให้มีการเข้าถึงยาที่มีประสิทธิผลดี แต่ราคาแพง ระบบการเงินการคลังที่เพิ่มความเข้มแข็งให้กับอุตสาหกรรมยาภายในประเทศให้เพิ่มการลงทุนในการวิจัยพัฒนายาใหม่ การเพิ่มประสิทธิภาพการเงินการคลังเพื่อควบคุมค่าใช้จ่ายด้านยาของระบบสวัสดิการรักษาพยาบาลข้าราชการ และมาตรการเพื่อลดความเหลื่อมล้ำในการเข้าถึงยาของผู้มีสิทธิ์ระหว่างระบบประกันสุขภาพที่มีวิธีการบริหารจัดการสิทธิประโยชน์ด้านยา และวิธีการเบิกจ่ายค่ายาแตกต่างกัน

คำสำคัญ: **ระบบการเงินการคลัง; ระบบยา; การเงินการคลังด้านยา; ชุดสิทธิประโยชน์ด้านยา**

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Irrational Antibiotic Use and Distribution in the Thai Community: a Complex Situation in Need of Integrative Solution

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Abstract: Irrational use of antibiotics is a complex problem. The root of the problem is not only identified in hospitals, but it is also found in many sectors of the community. At the system level, people conveniently have access to medicines through a variety of sources, including hospitals, pharmacies, and grocery stores. At the individual level, people lack of knowledge and misunderstand about antibiotics; and they are unaware of the consequences of irrational antibiotic use. Additionally, antibiotics are used irrationally in livestock and agriculture. Consequently, people and society are at risk of antimicrobial resistance. Formerly, the interventions for rational drug use have been mainly focused on operations in public health facilities. However, due to the complexity mentioned above, solutions cannot be carried out solely in the hospitals. Integrated interventions for all sectors in society are needed – including empowering people to have better health and drug literacy, supporting collaborative work between all sectors in a community, and implementing laws and regulations to control improper access to medicines – together with extensive interventions in hospital settings

Keywords: **medication use in community; antibiotics; antimicrobial resistance; system complexity**

Introduction

Antibiotics have been used extensively due to their efficiency in killing bacteria, helping to save lives and treat illnesses. They have not only been used in humans, but also in livestock, agriculture, and fishery. Overuse of antibiotics resulting from a lack of concern about consequences leads to antimicrobial resistance (AMR). This causes many public health problems, such as

longer treatment duration, higher cost of treatment, and higher death rates.[1]

Irrational use of antibiotics is a complex problem; the root of the problem is not only found in hospitals, but it is also found in many sectors of the community. Despite ongoing interventions, the problem still exists. Thus, different perspectives are needed with the cooperation of many sectors.

The objectives of this article is to describe the situation of antibiotic use and distribution in the community in order to raise an awareness of the complexity of the AMR problem in Thai community. Data used in this article are collected from research articles and reports on the distribution and use of antibiotics in Thailand between 2006 and 2019; and were analyzed to understand the situation of antibiotic use and distribution in the community as well as interventions for the problem. Recommendations to solve irrational antibiotic use in the community are also proposed.

Distribution of Antibiotics in the Thai Community

Approximately 25,000 distributors, retailers, and wholesalers were licensed for pharmaceutical sales in 2017. However, records of Thai Food and Drug Administration (FDA) did not differentiate among those groups. Therefore, the amount of antibiotic sales to individual patients cannot be precisely monitored.[2] Thai people have access to antibiotics through many settings, such as hospitals, health centers, and pharmacies. According to the 1987 Drug Act, most of antibiotics are classified as dangerous drugs that can be purchased only in pharmacies and dispensed by a pharmacist.[3] However, in Thailand, antibiotics can be found in grocery stores. Previous studies showed that 20-70% of grocery stores sold antibiotics.[4-11] Tetracycline and penicillin V were the top antibiotics found in grocery stores.[4-6,9,11]

Between 2017 and 2019, a survey of the project to promote safe drug use in the community, which was launched by Thai Food and Drug Administration (FDA) since 2015, showed that out of 22,830 households, 11% of them had leftover antibiotics, most commonly amoxicillin and tetracycline. People reported that they received the antibiotics from public hospitals, pharmacies, and grocery stores.[12,13] In addition, antibiotics, such as norfloxacin and amoxicillin, were found in school nursing units in many schools.[14-16] These data reflect that, in Thailand, people have access to antibiotics from various sources, through prescriptions by healthcare practitioners, or non-prescriptions and self-medication by non-qualified personnel. As a result, the society is at risk of AMR.

The Use of Antibiotics

Easy access to antibiotics from a variety of sources is an issue of unsafe drug use that poses the risk of AMR for society. The problem is even more complicated and serious with the behavior of Thai people toward antibiotic use, caused by misunderstanding and attitudes about antibiotics as a magical medicine for the treatment of any illnesses caused by "inflammation" (means ak-seb in Thai) of various organs and systems of the body. The misunderstanding of these properties has extended to the treatment of diseases and abnormal symptoms that occur in animals and plants in livestock and agriculture.

1) Behaviors of antibiotic use in humans

Self-medication is a common health behavior in Thailand to treat common health illnesses. Self-medication of Thai people has increased from 20% in 2005[17] to 27% in 2015.[18] Antibiotics are always mentioned as one of the medicines used for self-medication.

A health survey of 19,468 Thai people in 2014 reported that people experienced colds (46.2%), diarrhea (19.7%), and simple wounds (9.1%) in the past 6 months.[19] About half of them reported using antibiotics. A national survey by the National Statistical Office of Thailand (NSO) and the International Health Policy Program (IHPP) in 2017 showed that 8% of Thais used antibiotics in the past month for the treatment of colds, fever, and sore throat.[20]

Aside from antibiotics seeking behavior to treat minor illnesses, people still have other inappropriate antibiotic use behaviors, such as failing to complete the entire course of antibiotics when their condition improves, and consuming lozenges that contain antibacterial drugs.[21]

A lack of knowledge and misunderstanding about antibiotics are an important factor that affects the behavior of antibiotic use among Thai people. Consistent findings from collected data in single site[22-33] and multiple sites[12,13,20,21,34-38] researches were observed. For instance, evaluation of the Antibiotics Smart Use (ASU) Project between 2007 and 2011 in 15 provinces showed that 25-50% of Thai people understood that "antibiotics kill all types of germs, both viruses and bacteria".[34-36] The national survey by the NSO and IHPP in 2017 found that Thai people misunderstood that antiseptic/antibiotics can kill the virus or treat the flu.[20] A test of knowledge about antibiotics among 20,750 elderly people, revealed that the average knowledge was 1.75 points out of 6 points. The lowest score was for the item "when having simple wound or abcess, you must take antibiotics."[12,13]

Most Thai people refer to"antibiotics" as "anti-inflammatory drug" (ya kae ak-seb) – a term that has been used for a long time.[12,13,37,38] Using the name"anti-inflammatory" causes misunderstanding about antibiotic properties, resulting in misuse. Whenever they feel sick, such as having a cold or sore throat, they perceive that there is inflammation in their throat and often request for antibiotics.[39,40] Tetracycline was used for the treatment of any kind of inflammation, especially for endometritis. Amoxicillin was used for sore throats and colds while norfloxacin was used for diarrhea.[41] The findings were consistent with studies among healthcare practitioners which reported that Thai people were unconcerned about antibiotic use and AMR, and always requested for antibiotics. Failing to receive antibiotics from one place, they would seek them out from another place.[40,42]

2) Antibiotic use in livestock and agriculture

In Thailand, antibiotics have been used extensively in agriculture and livestock, making the anti-microbial problem more complicated. Data show that antibiotics such as ampicillin, amoxicillin, and tetracycline are used in orchards, such as citrus and pamello, to control disease in plants caused by bacteria.[6,43,44] At present, no antibiotics have been registered by the Department of Agriculture to be used in plants, indicating that farmers bought antibiotics that were intended to be used in humans for the use in agriculture.

In animal farms for domestic consumption and for

export, antibiotics have been used extensively, especially for chickens and aquatic animals.[45] To obtain large quantities of products in a shorter farming period farmers use antibiotics in animals, such as pigs[45,46], chicken[45-47], cows[46], and aquaculture[45]. Antibiotics are used throughout the life of the animal with the purpose of both treating and preventing diseases, reducing death, extending life, and pro- moting growth.[45,46] Most farmers were aware that a veterinarian must be consulted with respect to the use of drugs. However, while most farmers consulted veterinarians initially, they bought antibiotics on their own for long-term use.[45,46]

The misuse of antibiotics in agriculture due to a need to increase productivity and a lack of awareness of the long-term effects is an important issue. Amoxicillin, colistin, doxycycline, oxytetracycline and tilmicosin were generally used for the prevention and treatment of animal diseases.[46,47] The lack of awareness has a direct impact on the growing problem of drug resistance. In livestock farms, a high proportion of AMR was found, especially on farms with intensive antibiotic use.[48]

Antibiotic residues and environmental contamination are becoming a global problem. Research findings showed contamination of waste water with ciprofloxacin and norfloxacin in hospitals and with ciprofloxacin in pig farms in Thailand. The concentration of ciprofloxacin in pig farm wastewater was 21.98 times higher than wastewater in hospitals. Tetracycline was found in hospital wastewater, community wastewater, and pig farm wastewater. Tetracycline in pig farm wastewater was 45.67 times more concentrated than the wastewater of hospitals.[49]

Interventions for Rational Antibiotic Use at the National and Community Levels

Irrational antibiotic use in hospitals and communities has been a long-term issue in Thailand. Academics and civil society have been aware of and trying to solve the problem since 1988. Promotion of rational drug use began to implement through the National Drug Policy in 2011 and the National Drug System Development Strategy 2012-2016. Rational use of medicines was one of the strategies in these national policies.[50]

An important starting point was the implementation of the ASU Project in 2007 by the Thai FDA. It aimed to reduce unnecessary prescriptions of antibiotics for minor illneseses, including upper respiratory tract infections, acute diarrhoea, and simple wounds. This initiative had resulted in serious awareness of the issue and cooperative work from various sectors, including government, private, citizens and civil society, to promote the rational use of antibiotics.[51]

The concept of rational use of antibiotics, has been integrated or linked to national policy. For example, in 2009, the National Health Security Office (NHSO) stipulated that rational antibiotic use would be key performance indicators (KPI) of hospital settings. The KPI were used for paying compensation to hospitals which achieved the approved standards for appropriate use of antibiotics for the conditions, as part of the Pay for Performance (P4P) policy.[51] In 2015, the 8th National Health Assembly raised the issue of resistant bacteria crisis and integrated problem management as a national agenda. It was noted that the issue is very important to Thai health and a national mechanism is needed for the integration

between relevant departments and parties.[52] In 2017, the rational drug use policy, prevention and control of antimicrobial resistance (AMR) and encouraging rational drug use (RDU), were announced under 12th National Strategic Plan for Public Health by the Ministry of Public Health (MOPH). One of objectives was to reduce morbidity rates due to AMR and inappropriate use of antibiotics.[53] The government announced the Thailand Antimicrobial Resistance Management Strategic Plan 2017-2021, which is the first Thai strategic plan that focuses on resolving the problem of AMR.[54]

Previously, the interventions for rational drug use mainly focused on operations in public health facilities, which has helped to solve the problem to a certain extent. Since the problem of antibiotic overuse/misuse is more complex than controlling medication in hospitals and because it is an issue relevant to problems at many levels, it needs a more integrated perspective and collaboration of various groups of people. The national policy focusing on the community is still unclear. Although there have been ongoing attempts to develop rational use of drugs in the community from various sectors, including government, private, and community, these are sparse. In some areas, although there are cognizant and enthusiastic personnel, continuous support at the national and organizational levels are lacking. Although there are various models of interventions in the community, there is still a lack of integration between related organizations, a lack of community participation, and a lack of standard tools to support work and system evaluation.[55]

In 2018, MOPH appointed a working group to develop rational and safe drug use systems in the community (RDU community).[56] A framework and guidelines for rational and safe drug use system in the community was developed. Furthermore, the resolution of the community-centered system management for becoming a rational drug use country was announced in the 12th National Health Assembly in 2019.[55]

Community-driven Collaboration

Community-level operations can be accomplished through collaborative efforts from people in many sectors. Lessons learned from the local core group that successfully implemented Antibiotics Smart Use Project (ASU) at the community level suggest that the success factors included having a team of change agents as leaders to provide resources, driving the ASU along with other projects in the community, having mutual agreement in the community, and having continuous evaluation. Strategies for scaling up ASU included creating a key driver in the community, persuading groups or individuals of importance or authority within the area to be a team of change agents, defining ASU as an important community policy, and campaigning of ASU by the local change agent team. Various community interventions were used, such as educating and raising concerns through social networks, healthcare providers, and news reporters.[57] The campaigns through mass media and change agents can increase knowledge and awareness about rational use of antibiotics.[25,38]

Laws and Regulation Requirements

In addition to operations at the community level, formulation of a legislation to set up standards at the national level is needed to control the spread and misuse of antibiotics more effectively. From 2017-2019, there was a process to review and reclassify the status of antimicrobials for humans and animals, resulting in withdrawal of oral colistin formulations[58]

and reclassification of antimicrobials from over-the-counter drugs to dangerous drugs (e.g. sulfacetamide eye drop and silver sulfadiazine cream).[59] However, the regulatrory system for monitoring and controlling the distribution of antibiotics is still needed.

Empowering People for Rational Mediciation Use

Drug literacy is an important factor for desirable health behaviors. Therefore, supporting people to gain access, understand, evaluate, and apply drug and health information appropriately through drug literacy is crucial. Health literacy is therefore a national agenda as it appears in various national development plans, such as the 12th National Health Development Plan (2017-2021), and Strategic Health Plan for Health Promotion and Disease Prevention (2017-2021).

Conclusions and Challenges

Thailand needs health system management policies for rational drug use, which should connect all health service units at all levels to the community. Effective participation of government, private, civil society, and citizen is indispensable. Empowering people through better health and drug literacy, supporting community participation as well as strengthening government, private, and local communities to create a mechanism to ensure the rational use of antibiotics are needed.

Drug use behaviors in hospitals, clinics, pharmacies, and communities are related to each other. Currently, there is no connection of practice between hospitals and communities due to a lack of information on drug distribution and use at the community level, resulting in the inability to assess the country's overall medication consumption. Data is available at the hospital level, but lacking in the other areas, such as in community pharmacies, and agriculture. Availability of this relevant information will help to determine appropriate decisions in setting better interventions for rational use of antibiotics. Therefore, developing data and information system at all levels to ensure continued program development and for the purposes of monitoring and evaluation is essential.

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บทคัดย่อ: สถานการณ์การใช้และกระจายยาปฏิชีวนะในชุมชนของไทย: ปัญหาซับซ้อนทีต้องจัดการแบบบูรณาการ

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การใช้ยาปฏิชีวนะอย่างไม่สมเหตุผลเป็นปัญหาที่มีความซับซ้อนซึ่งไม่ได้เกิดในสถานพยาบาลเท่านั้นแต่เกิดขึ้นจากหลายส่วนในชุมชนด้วยประเด็นในเชิงระบบ ประชาชนสามารถเข้าถึงยาโดยสะดวกจากแหล่งที่หลากหลายทั้งจากสถานพยาบาล ร้านยาและร้านค้าปลีก และประเด็นในระดับบุคคลที่ขาดความรู้ ความเข้าใจเกี่ยวกับยาปฏิชีวนะ ขาดความตระหนักในผลกระทบจากการใช้ยาอย่างไม่สมเหตุผล การนำยามาใช้ในการปศุสัตว์ และการเกษตรเชิงพาณิชย์ ผลกระทบของปัญหาเกิดเป็นความเสี่ยงทั้งต่อตัวผู้ใช้ยา และต่อปัญหาการดื้อยาต้านจุลชีพของสังคม มาตรการแก้ไขปัญหาการใช้ยาที่ไม่สมเหตุผลที่ผ่านมา มักมุ่งเน้นที่การดำเนินงานในสถานพยาบาลภาครัฐเป็นหลัก แต่เนื่องจากความซับซ้อนของปัญหา การแก้ปัญหาจึงไม่สามารถดำเนินการได้เพียงทางฝั่งสถานพยาบาลเท่านั้น แต่จำเป็นต้องจัดการแบบบูรณาการจากทุกภาคส่วนในสังคม ได้แก่ การเพิ่มศักยภาพของประชาชนให้มีความรอบรู้ด้านสุขภาพและยา การสนับสนุนการทำงานอย่างบูรณาการของชุมชน การดำเนินการทางกฎหมายและระเบียบข้อบังคับเพื่อควบคุมการเข้าถึงยาอย่างเหมาะสม ร่วมกับการดำเนินการอย่างต่อเนื่องในสถานพยาบาล

คำสำคัญ: **การใช้ยาในชุมชน; ยาปฏิชีวนะ; การดื้อยาต้านจุลชีพ; ความซับซ้อนของระบบ**

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The Current Situation of the Herbal Medicinal Product System in Thailand

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Abstract This report aimed to review and update current situation of herbal medicinal product (HMP) system of Thailand and provide recommendations for sustainable development of HMP system. Research papers and official database and documents of public and private agencies on related subjects were compiled and brain storming of experts in the field was then performed to formulate recommendations. It was found that although government policy to promote the use of HMPs in public health services was issued for more than 40 years, inputs of HMP system, i.e.

industry, research and development, and human resources, are not efficient enough to effectively support advancement of HMP system and directly impact on HMP management. Regarding the selection of HMP, registration of the products has noticeably grown; however, very few scientifically-developed HMP got license. In addition, only 10% of the medicines selected into the National List of Essential Medicines (NLEM) were HMPs. For the procurement of HMP in public health service facilities, similar to western medicine products, the purchase price must not exceed the standard price of each item of HMP, yet only 25 items of HMP have standard prices established. Concerning the distribution of HMP, the information regarding where HMP are distributed to is still lacking, but it becomes clear that an increasing number of HMPs are distributed to consumers via online channel. Regulatory measure is therefore needed to prevent the risk of distribution of HMP via improper channel. In terms of the utilization of HMP, in 2017 the value of HMP reimbursed from three public health security systems was 274.6 million baht. Major challenges on the development of HMP system are the quality of herbal materials and HMPs as well as the availability of the products that meet the requirements of Thai traditional medicine practitioners and medical doctors in the health service system.

Keywords: **herbal medicinal product, Thailand, health system**

Introduction

Herbal medicine (HM) is truly rooted in Thai culture since ancient times and it is presently incorporated into health services. It not only has benefits to health, but is also acknowledged for its economic and cultural value.[1]

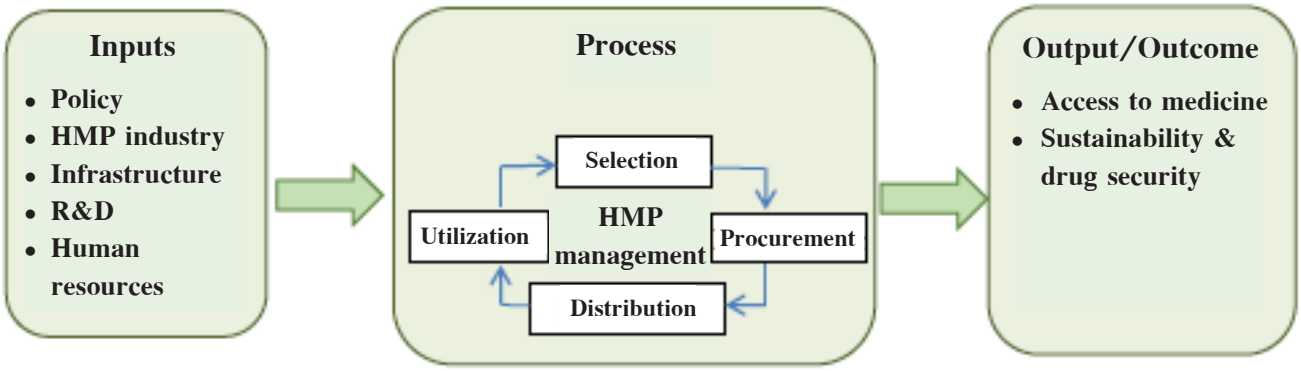
In 2018, sales of herbal medicinal products (HMP) in Thailand were 42.4 billion baht with 11% annual growth rate from 2017. Herbal topical analgesic is the fastest growing market segment with a 14% annual increase (data from Ministry of Commerce). The value of HMP manufacture has gradually risen throughout the period of 2008-2016 according to statistics from the Thai Food Drug and Administration (TFDA). This data infers that HMP has been and will become more accepted among consumers. The integration of Thai traditional medicine (TTM) including HMP into the mainstream health system is a policy of the Thai Ministry of Public Health (MoPH). However, it may not meet the demand of prescribers because 40% of HMP prescription in the government hospitals were outside the list of HMP in the National List of Essential Medicines (NLEM) so far (data from Health Data Center of MoPH).

This article explores current situation of inputs and the HMP management in Thailand. Policy recommendations are then given in order to improve the efficiency and sustainability of HMP.

Method

The last report on the Drug System of Thailand was published 17 years ago in 2002, this research in 2019 therefore aims to provide up-to-date information on the HM system of Thailand. It is a part

Figure 1 Conceptual framework of herbal medicinal product in Thailand



of the Health Systems Research Institute project for the "Situation analysis of medicine system of Thailand" with the scope depicted in the conceptual framework below (Figure 1).

The report presents the inputs including policy, HMP industry, infrastructure supporting the industry, research and development (R&D), and human resources. The 4 main components of HMP management: selection, procurement, distribution and use were gathered from researches and the official database and documents of public and private agencies. Finally, experts in the field of HMP undertook brain-storming and analysis of the data, giving comments and formulating suggestions.

Results

1. Inputs

1.1 Policy

The Alma-Ata Declaration on Primary Health Care initiated by WHO in 1978, calls on Member States to use indigenous medicine and HM as a part of Primary Health Care (PHC), and this was a turning point for Thailand to bring back Thai traditional knowledge into health services.[2] The R&D in HMP especially folk remedies was later extensively conducted by researchers of the MoPH and universities leading to a wider use of single herb remedies in public health settings. In 1999, the List of HMP in the NLEM was announced, later covered by the public health insurance system and TTM practitioner positions as government officers and employees in the MoPH was established. This led to the gradual increased used of selected TTM formulas and single HMP from the NLEM in the health service system.

Over the past five years (2015-2019), the Thai government has paid high attention to support local wisdom and the development of innovative Thai herbal products. This endeavor was sated in the 2017 Constitution of Thailand and emphasized the role of government to promote and support the development of TTM wisdom to maximize its benefit for the good health of all Thai people.[3] Additionally, several measures have been established to promote the use of traditional knowledge including HMP. These include the Master Plan on Thai Herbal Development (2017-2021), the first comprehensive plan to promote the herbal industry with the goal of becoming the Association of Southeast Asian Nations (ASEAN) region leader in exporting herbal raw materials and products.[4] At local regional level, four 'herbal cities'; herbal product development centers are specified in the plan, later expanding fourteen provinces through-

out the nation. A lack of continuous budget support for implementing this plan is the major obstacle to achieve the above-mentioned goals. So far, there is no comprehensive evaluation on how this plan help improve efficiency and effectiveness of herbal industry.

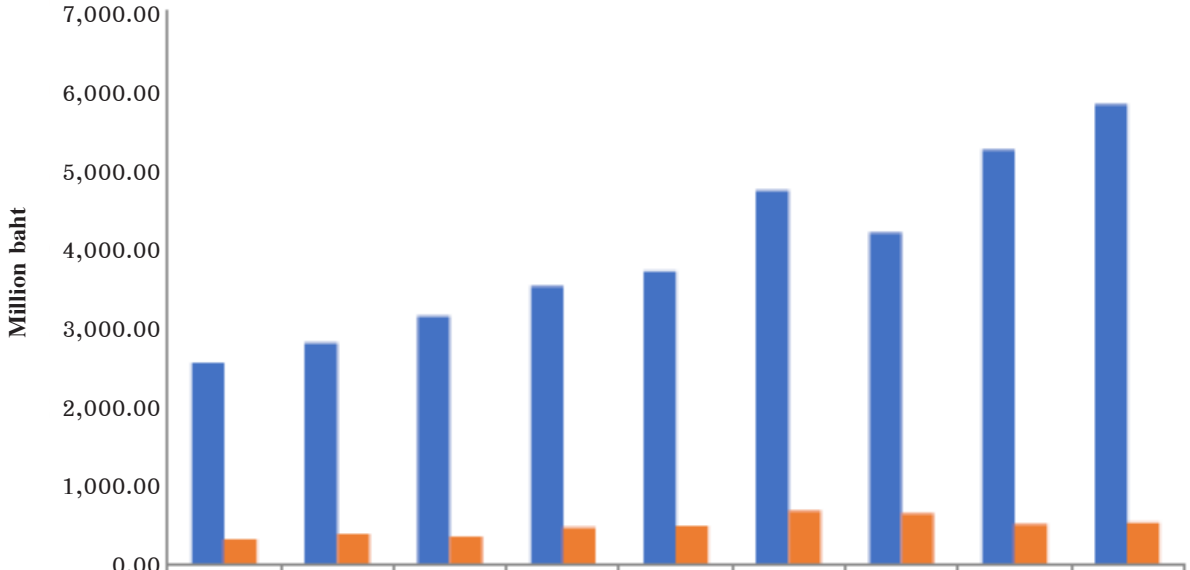
1.2 HMP industry

Based on MoPH Notification on "Specifications of Criteria and Procedures for the Production of Traditional Medicines (TM) According to the Laws on Drugs B.E. 2559" (2016), Manufacture of HMP can be divided into three categories based on sales volume and risk of HMP to health (oral or external use, dosage forms or manufacturing technology). For category A manufacturer who produce 'high risk' oral products or whose production volume of oral HMP products is worth more than 20 million baht per year, Good Manufacturing Practice (GMP)- Pharmaceutical Inspection Co-operation Scheme (PIC/S) production standard is required, those who do not meet the earlier criteria and are in categories B and C producing other oral and topical HMPs, must follow the Fundamental Manufacturing Practice (FMP) to ensure the quality of their products. Currently, the manufacturing standard for HMP is consideration by TFDA due to the change of law regulating HMP according to the Drug Act to Herbal Product Act B.E. 2562 (2019).

To date, there are 71 HMP manufactures which 47 and 24 were certified GMP PIC/S and FMP, respectively (data from TFDA on July 2019). Most of them are small and family-run businesses with insufficient capacity for R&D.[3] While the domestic production value of HMP has increased over a ten-year period, import value has remained stable over the same period of time (data from TFDA) (Figure 2). This implies that the HMP industry has achieved self-reliance at a certain level but still needs to tackle some challenges in order to improve efficiency.

In addition to private manufacturers, the state-run

Figure 2 Production and import value of HMP for human during 2008-2016



	2008	2009	2010	2011	2012	2013	2014	2015	2016
Production	2,556.40	2,799.29	3,135.52	3,516.90	3,703.60	4,722.78	4,194.90	5,237.35	5,815.54
Import	327.78	398.19	359.02	474.13	500.43	690.61	658.91	521.51	541.88

enterprises such as Government Pharmaceutical Organization (GPO) and Defense Pharmaceutical Factory (DPF), and some hospitals under MoPH or universities, also play a role in the production of HMP. A report from the Department of Thai Traditional and Alternative Medicine (DTAM), shows there are about 90 government hospitals producing HMP, with varied production capacity regarding the number and dosage forms of HMP items. Of these, with the support of DTAM, 47 are WHO GMP-certified production facilities (data from a meeting for policy dissemination on June-7, 2017). This is in order to preserve health wisdom that meet the health needs of local people. The development model of the HMP value chain is explicit in Surat Thani province, one of the herbal cities located in the South, making the 'Surat Model' an example to follow for other provinces. In addition to contract farming at the upstream level, a whole range of measures is carried out throughout the value chain to support the production and utilization of HMP and provision of TTM services. Part of the provincial UHC capitation received is allocated for the production and distribution of HMP for all hospitals in Surat Thani and other provinces.[5]

1.3 Infrastructure

1.3.1 Supply of herbal raw materials

Both the quality and quantity of herbal raw materials are one of the main challenges for Thai HMP industry. There are around 13-15 large traders who are wholesalers, importers and/or producers of HMP in Bangkok.[2] Many herbs are scarce or are not native plants of Thailand and hence herbal raw materials derived from such herbs need to be imported.[6,7]

Herb prices are unstable and vary according to production quantities and demand. As mentioned previously, contract farming is one way to solve this problem but it requires both side to honour the contract made. At present, some traders have begun classifying herbal raw materials and set the price based on their qualities; however, the majority of farmers still have no bargaining power.[2]

1.3.2 Quality standards and laboratory service

The quality of HMP available that fail to meet national pharmacopeia standards is another main concern. The 2018 report of the Department of Medical Sciences (DMSc) shows finding of research conducted in 140 items of HMP sampling from the market where only 86.43%, 96.43%, 97.86% met the standard specifications of microbial, heavy metal and pesticide limits, respectively.[8]

For many decades, the DMSc, DTAM and TFDA have continuously put effort into establishing suitable standards to support the HMP industry, such as production standards for different levels of manufacturers[9], Thai Herbal Pharmacopeia (THP)[10], Thai Herbal Preparation Pharmacopoeia (THPP)[11] and selected Monographs of Thai Materia Medica. In addition, DMSc and Regional Medical Sciences Centers can also provide laboratory services for manufacturers to analyze and issue certificate of analysis for HMP manufacturers.

1.4 R&D on Thai Herbs

R&D is crucial to move the HMP industry forward and create innovative products in accordance with Thailand 4.0 strategy. Figure 3 shows research budgets and the number of research projects on Thai medicinal plants (2014-2018). Figures remained stable during 2015-2017 but markedly increased in 2018 as a result of the First National Master Plan on Thai Herbal Development (data from National

Research Council of Thailand, Agricultural Research Development Agency, Thailand National Nanotechnology Center and Department of Thai Traditional and Alternative Medicine).

When breaking down the value chain into downstream, midstream and upstream levels, it was found that midstream is more attractive to researchers as seen in Figure 4. Studies on pharmacological activities and

Figure 3 Number of research projects on Thai medicinal plants and budget during 2014-2018

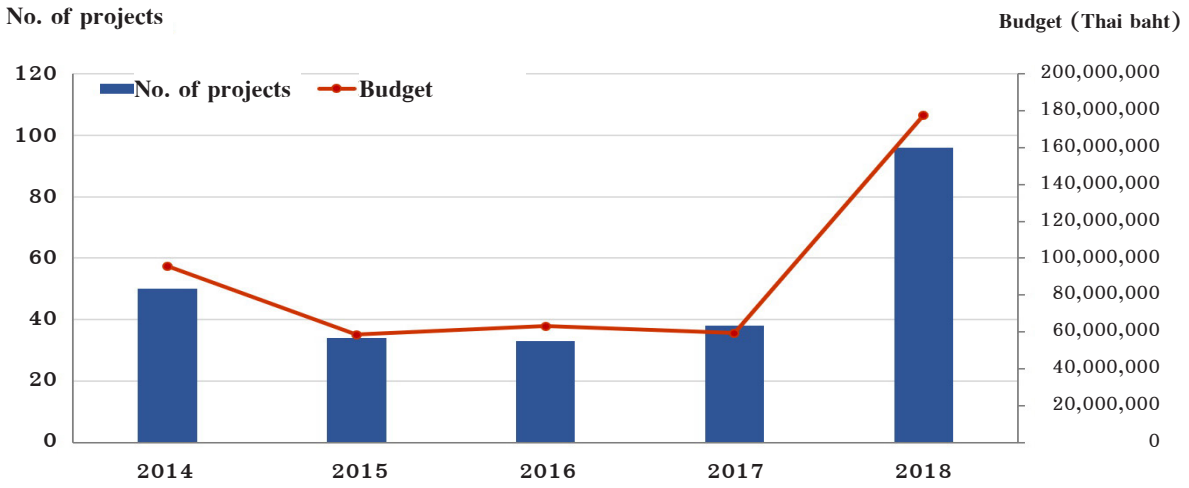
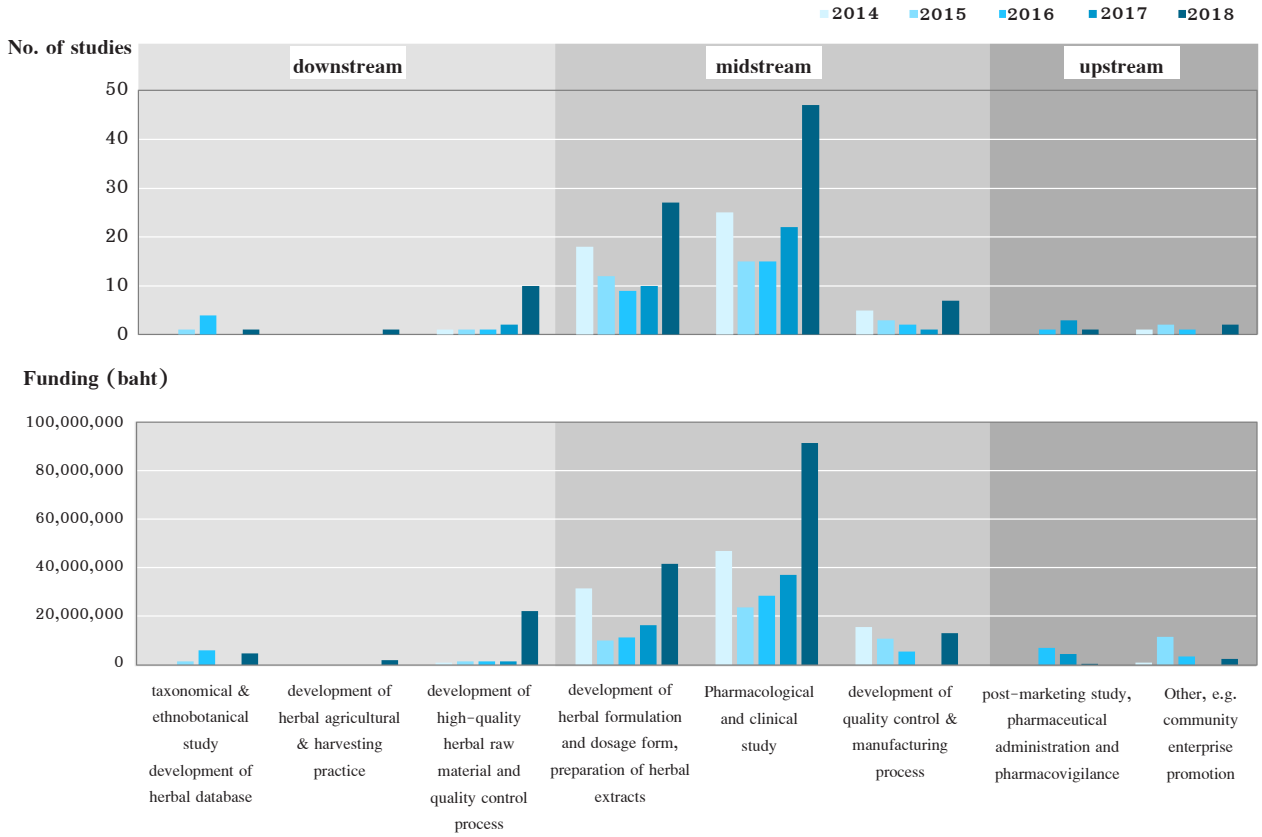


Figure 4: Researches on Thai herbs according to the value chain of herbal products



formulation development of herbal products have been the first and the second priority issues conducted during 2014-2018.

1.5 Human resources

TTM and Traditional Chinese Medicine (TCM), particularly acupuncture, are officially recognized in Thai health system; however, there are much more personnel in TTM than those in TCM in public health settings. Based on the data of MoPH,[12] as of 1 September 2019, there were 2,813 TTM practitioners working in MoPH. Meanwhile, of 59 provincial health offices responding to the 2017 survey conducted by the Institute of Thai-Chinese Medicine DTAM, there were 220 medical doctors trained in acupuncture and 70 of them working in MoPH hospitals.[12]

Medical doctors normally prescribe research-based single HMP whereas TTM and TCM practitioners prefer to prescribe multi-ingredient HMP. At health center level, MoPH also promote prescribing selected items of HMP in NLEM by community health nurses. In pharmacies, patients can receive various HMPs from pharmacists without prescription.

Vadhnapijyakul and Suttipanta (2014)[13] conducted a survey in 139 hospitals and found that 97.4% of prescribers were physicians. Of interest, around 69.9% of TTM practitioners did not perform diagnosis and prescribe HMP because they were not authorized to do so by the hospitals. Around 20% of medical doctors seldom referred patients to TTM practitioners for further treatment. The research also found that hospitals did not have a sufficient sup- porting system for TTM, for example not qualified working area for HMP production and TTM services. TTM practitioners were high variation in positions, number and educational degree in each hospital.[13]

Realizing the significance of HMP as a part of health services, health professionals and relevant agencies have organized trainings to build capacity on integrating TTM into health care services. Topics include basic principles of TTM for medical doctors, clinical research methodology for TTM practitioners provided by the DTAM, and production and rational use of HMP for pharmacists organized by pharmacy council.

2. HMP product management

2.1 Selection

Consultation, review of product dossier, and registration and licensing of HMP is an important process for regulatory and TM authorities (TFDA, DTAM) to screen and select safe, effective and quality HMP into the market. Regarding Drug Act B.E. 2510, drugs are classified into 2 types; modern drugs (MD) and traditional drugs (TD). TD is the remedies recorded in classical textbooks or used by local people.[14] This Act limits development of traditional remedies as it specifies that these remedies do not need to follow science. Data from TFDA showed that the number of TD registered are increasing with slowing growth as seen in Figure 5.

To minimize the limitation of Drug Act on TD, National Drug Committee in 1998 classified TD into four subtypes, i.e., TD, modified TD, herbal drugs with semi-purified compound and modern drugs (pure compound) from herbs. However, in practice there are only two subtypes; traditional drug (TD) and scientifically developed HD (SDHD). Only 13 SDHD could be registered compared to 7,610 TD during 2009-2018 as shown in Table 1.

Figure 5 Cumulative number of registered traditional drugs for human during 2009-2018

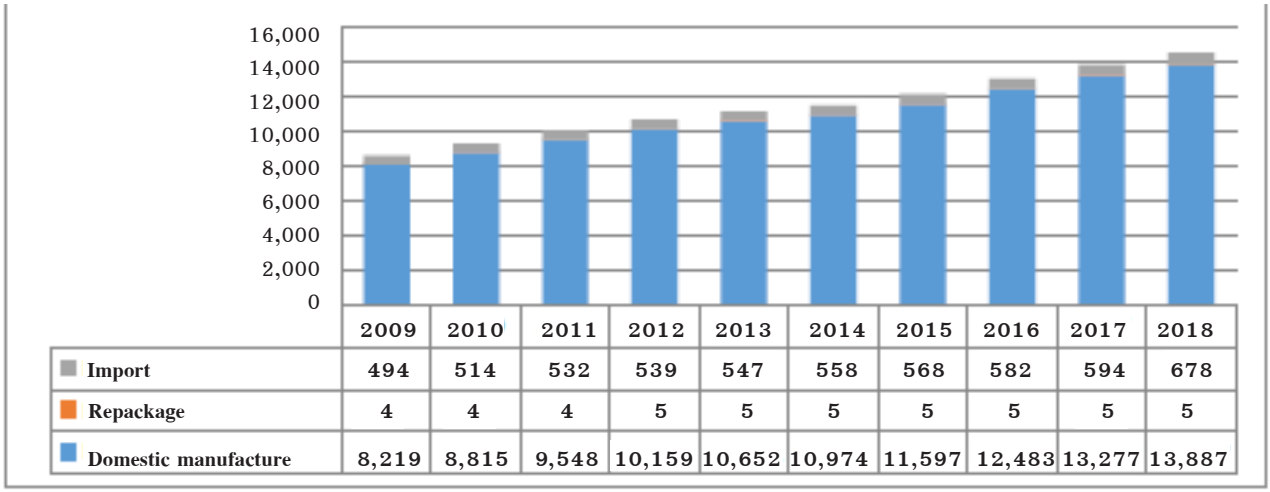


Table 1 Two types of HMP registered with TFDA during a ten-year period (2009-2018)

Types of HD	Year									
	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
SDHDs	3	2	0	0	0	1	0	1	4	2
TDs	488	886	929	834	867	374	694	956	849	733

To ensure more appropriate regulatory measures for HMP, Herbal Product Act B.E. 2562 (2019) was launched in February 2019 to separate HMP from modern drugs. Regarding the new act, herbal products including HMP will be approved to the market via three channels; registration, notification and listing based on risk assessment. Currently, the act is in the process of bye-laws development. In the near future, enforcement of HMP will be changed to this act and there will be more items of HMPs launched to market faster than usual due to the improved process of notification and listing. Based on the risk assessment principle of new law, the distribution channel of HMPs may be changed; this makes preparing TFDA staffs for product approval and post marketing surveillance is vital for the future HMP system.

The NLEM is the effective benefit package list used by three main public health schemes; Civil Servant Medical Benefit Scheme (CSMBS), Social Security Scheme (SSS) and Universal Coverage (UC). Presently, there are 74 items of HMP included in NLEM or just 10% of the list. The number has remained the same since 2014 due to insufficient evidence to support the efficacy and safety of HMP, in comparison with modern drug (MD) which increased almost every year.

In health settings, the Pharmacy and Therapeutic committee (PTC), has a role in approving all drugs including HMPs to be used in the hospitals but they do not have much knowledge on HMP as the majority of PTC members are modern medicine professionals. From the survey of 139 hospitals in 2014, approximately 24% had inadequate items of HMP for treatment.[13] Among these hospitals, about

only 16 items of HMP were available, with the capsule being the most common dosage form found. Hence, the main challenge is insufficient items of HMP to meet the health need.[15]

DTAM has also selected some TTM formulae from various credible sources and included into the 'National Thai Traditional Formulary'. The purposes of this formulary are to promote industrial and hospital production of the selected items, to promote their utilization in health service facilities, and to be used as textbooks for teaching.

2.2 Procurement

The import and export data of herbs from the Ministry of Commerce are available but it was unspecified as to how much was used for medical purpose. Therefore, only statistics of export and production values retrieved from TFDA is presented in Figure 5.

The total value of HMP procurement is not available. Government Procurement and Supplies Management Act B.E. 2560 requires state agencies, including public hospitals, throughout the country to follow procedures with the aim of increasing transparency in the government's procurement processes. Government hospitals have to buy any drug not exceed the standard price, by generic name and at least 60% of procurement budget for the items in NLEM.[16] Majority of HMP purchased is under NLEM and only 25 items of HMP have the standard price compared with 293 items of the modern drugs.

2.3 Distribution

HMPs are available in both public and private health facilities. Only over-the-counter (OTC) remedies or non-prescription medicines which are considered safe and effective enough for commonly found minor conditions are sold without prescription according to the Drug Act B.E. 2510. Although there are limited distribution channels of HMPs as mentioned earlier, they are still found in non-pharmacy stores. A survey by Booddawong B et al.[17] showed that 436 items of HMPs from a total number of 2,991 drugs were available in 613 groceries in 8 provinces. These stores received their supplies from several sources such as wholesale dealers (32.5%), drug stores type 1 (31.5%), drug stores type 2 & 3 (14.7%) food trucks (11.5%), department stores (7.7%) and others (2.6%). Routes of distribution were direct delivery, postal service and medicine trucks. Information about the HMP distribution channel at national level is lacking.[7]

Interestingly, HMP is increasingly available online, although legally it is not permitted. The Euromonitor International 2019 (data from Ministry of Commerce) showed that some items of HMP, such as herbal balm, herbal inhaler and cough pills have gained more popularity among tourists. These online sales and distribution channels for tourists should also be taken into consideration under the Herbal Product Act B.E. 2562.

2.4 Use

Data on the public use of HMP among insurers of three public health schemes are presented in the Table 3. Among the three schemes, service users under UC consumed more HMPS compared to the other two schemes; and UC covers about 75% of Thai population. In 2018, utilization of HMP was reimbursed as 274.60 MB.

Statistics of the Health Data Center in 2016-2018 showed an increase of HMP use in term of items and numbers of prescription. HMPs in NLEM was

prescribed at approximately 60% of all HMP prescription (59.02%, 61.18% and 63.27% in 2016, 2017 and 2018 respectively). People over 60 years old used HMPs the most (32.53%) compared with other age groups.

Although patients are able to access to HMPs from health settings, many of them self-medicate with HMPs without informing health professionals. Tantipidoke R, et al. found three patterns of HMP use; use of HMPs before starting allopathic medicine, concurrent use of HMPs and conventional drugs and use of HMPs as a complementary treatment.[18] Another study shows that only 50% of users had knowledge on HM while 21.6% of them used HMPs with no medical indications.[19]

Adulteration of HMPs with modern medicines, especially with steroids, is commonly found in rural communities. During 2008-2009, DMS investigated 1,584 HMP samples from all over the country. Finding showed 283 samples (17.87%) were adulterated with modern medicines and that tablets were the most frequently adulterated dosage form. Notably, 47% of adulterated samples, more than one modern medicines were detected. The modern medicines identified were steroids, NSAIDs, antihistamines, and psychotropic substances. Samples from the northeastern part of Thailand were found to be the most adulterated.[20]

At the local level, during 2005-2009, 136 of 626 samples or 21.7% of HMPs from the Public Health Regions 4 and 5 were adulterated with steroids, equivalent to the average dexamethasone 0.319 mg/g, ranging between 0.010-1.119 mg/g. Capsule dosage form had the highest amount of steroids (1.081-1.119 mg/g).[21]

Safety monitoring of HMPs

In Thailand, the Health Product Vigilance Center (HPVC) under TFDA is responsible for safety surveillance of health-products and the adverse product reaction (APR) reporting system. From HPVC statistics, only 3,583 records, out of all 761,921 records (0.47%) related to herbal products during 2000-2018.

Thai vigibase, the national APR database collecting report throughout the country, showed that there were 1,216 records with 1,983 incidences that may be associated with herbal products during 2006-2015. About 20.2% of this figure were serious APR. The top five herbs (accounting for more than 10% of APR) were *Andrographis paniculata*, *Curcuma longa*, *Derris scandens*, *Cissus quadrangularis* and *Centella asiatica*, while oral traditional recipes for musculoskeletal conditions were the cause of highest APR records.

Discussion

During the past two decades, the promotion of HMP use has strongly been implemented by the MoPH due to the national policy on the integration of TTM into health service system and because the goal of HMP development is to achieve drug security. Coverage for HMPs in public health schemes and additional on-top capitation from National Health Security Office (NHSO) for the provision of HMP services in health service facilities, have been the main driving force. In the future, various measures such as investment in R&D for both HMPs and raw materials[22], encouragement of qualified traditional practitioners and folk healers,[23] development and implementation of the evidence-based clinical practice

guidelines (CPG),[24] public empowerment on the use of HD for self-care to relief common minor diseases and symptoms[25] should also be strengthened in order to achieve sustainable HMP system.

Access to medicine is the main output of HMP system. According to the medicines access framework from a WHO-Management Sciences for Health (MSH) consultative meeting held in Ferney-Voltaire in 2000[26], access to medicine can be measured in four dimensions of availability, accessibility, affordability and acceptability.[26]

Out of the four aspects of access to medicine, acceptability on HMP is not a problem because HMP is a part of Thai culture. Regarding the availability of and accessibility to HMPs, there are currently about 20,000 items of HMPs available in the market (TFDA statistics), but there are only 74 items included in the NLEM. Collection of solid clinical evidence to support the selection of HMPs into the NLEM should start at the health setting level. With support from the DTAM, clinical trials with collaborating hospitals can then be conducted to determine efficacy and safety of new items of HMPs for future addition into NLEM. The consideration of the PTC is a critical step to make HMPs available for patients, technical support from the DTAM will be helpful to provide backup data for TTM practitioners in each public hospital and propose herbal remedies to PTC.

HMPs available in the health services covered by the health insurance systems in Thailand are currently only those named in the NLEM; however, these HMPs solve only common minor illnesses or symptoms. Only a few hospitals encourage TTM practitioners to prepare herbal remedies based on TTM theory and local health wisdom for their patients. Some hospitals have therefore made an attempt to increase herbal medication availability in their settings to accommodate the practice of TTM practitioners. For example, Kabchoeng hospital in Surin province has 36 herbal preparations and occasional extemporaneous preparations used for ten groups of symptoms, including emergency care for treating venomous snake bites.[27] Prapokklao hospital in Chantaburi province operates psoriasis clinic to serve patients who do not respond well to modern medicine. The treatment results show improvement in slowing the progression of disease.[28]

Lastly, affordability of healthcare services should be taken in to account, if there are more HMPs added to public health insurance, through affordability at individual level is not a problem now. Of note, inequity of accessibility to HM among service users under the three public health insurance systems should be addressed for example, the prescription of personalized HM formulas can be reimbursed from CSMBS only.

Challenges

The main challenges facing the HMP system which urgently need to be addressed are the quality of raw materials, quality of finished products, and promoting practice of health professionals. To improve con- sumer and patient accessibility to quality HM products, the standards of raw materials and finished products should be enforced more strictly during registration and procurement process. The substitution of HMPs to modern medicines should be endorsed as a national policy to upgrade quality of HMP value chain. The farmers and manufactures will have a clear list of HMP target to cultivate and produce whereas the DTAM and TFDA will plan better on researches

of the specific HMPs. At the same time, government investment in basic infrastructure, such as central laboratories to conduct quality tests or even product stability test, routine market surveillance and strengthening the capabilities of HMP businesses are also required. These will create trust among health professionals especially physicians wishing to prescribe HMPs for their patients

The findings of this study show that HMPs in NLEM have not met the demand of prescribers; medical doctors and TTM practitioners yet. Therefore, addition of more new herbal remedies in NLEM and allowing individualized multi-ingredient HM preparations to be covered by all public health insurance schemes are top priority issues.

Conclusion

In conclusion, Thailand's present HM system can serve only basic medical needs or act as a complement to western medicine. To upgrade HMP to be a mainstream service, compiling TTM theory and folk medicine, promoting TTM practice, improving the quality of herbal raw materials and finished products, and well as research and development throughout value chain of HMPs are strongly recommended.

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บทคัดย่อ: สถานการณ์ปัจจุบันของระบบยาจากสมุนไพรในประเทศไทย

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รายงานนี้มีวัตถุประสงค์เพื่อรวบรวมสถานการณ์ปัจจุบันและจัดทำข้อเสนอแนะเพื่อพัฒนาระบบยาจากสมุนไพรที่ยั่งยืน โดยรวบรวมและวิเคราะห์ข้อมูลจากฐานข้อมูล และเอกสารของหน่วยงานที่เกี่ยวข้อง รวมถึงงานวิจัยต่าง ๆ สังเคราะห์และระดมสมองผู้เชี่ยวชาญ ผลการศึกษาพบว่า แม้ประเทศไทยจะมีนโยบายการพัฒนายาจากสมุนไพรเพื่อนำมาใช้ในการดูแลสุขภาพของประชาชนที่ชัดเจนมากกว่า 40 ปี แต่ปัจจัยนำเข้าของระบบยา อันได้แก่ อุตสาหกรรมยาจากสมุนไพร การวิจัยและพัฒนา และทรัพยากรมนุษย์ ยังไม่เอื้อต่อการพัฒนาและส่งผลกระทบโดยตรงต่อการจัดการยา กล่าวคือ การคัดเลือกยา พบว่าที่ผ่านมาการขึ้นทะเบียนยามีการเติบโตเพียงเล็กน้อย แต่ยาพัฒนาจากสมุนไพร กลับขึ้นทะเบียนได้น้อยมาก รายการยาจากสมุนไพรที่อยู่ในบัญชียาหลักแห่งชาติยังมีเพียงร้อยละ 10 ของรายการยาทั้งหมดในบัญชี การจัดหายา ยังมีปัญหาเช่นเดียวกับยาแผนปัจจุบัน คือระเบียบการจัดซื้อกำหนดให้ซื้อได้ไม่เกินราคากลาง ในขณะที่มีเพียง 25 รายการยาที่มีราคากลาง การกระจายยา ยังขาดข้อมูลว่ายาจากสมุนไพรกระจายไปที่ใดในสัดส่วนเท่าใด แต่มีแนวโน้มว่ามียาจากสมุนไพรกระจายสู่ผู้บริโภคผ่านช่องทางออนไลน์มากขึ้น ซึ่งต้องมีการควบคุมกำกับเพื่อป้องกันความเสี่ยงที่จะเกิดขึ้น การใช้ยา ยาจากสมุนไพรที่ถูกเบิกจ่ายผ่านระบบหลักประกันสุขภาพของรัฐทั้งสามกองทุน มีมูลค่าประมาณ 274.6 ล้านบาท ในปี พ.ศ. 2561 ความเร่งด่วนในการพัฒนาระบบยาจากสมุนไพร คือ คุณภาพผลิตภัณฑ์ และการมียาจากสมุนไพรที่สอดคล้องกับความต้องการของผู้ประกอบวิชาชีพในการดูแลรักษาผู้ป่วยตามความจำเป็นทางสุขภาพ

คำสำคัญ: **ยาจากสมุนไพร, ประเทศไทย, ระบบสุขภาพ**

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The Landscape of Biologics Drug System in Thailand

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Abstract Biologics, breakthrough pharmaceutical products that change the treatment paradigm of many diseases, have unique characteristics that could impact country drug system overall. The aim of this study is to analyse the current situation of biological drugs and gaps in Thailand drug system. We have found that regulations of most biological products in Thailand have been developed slowly and is currently up to international standard and Thailand is currently drafting a new cell therapy act to better regulate advanced therapy medicinal products. While regulations of biologics are not a major concern, access to innovative biologics that are high cost is still an issue. Strengthening research and development of biologics in the country is a key activity done by the Royal Thai Government to lower the cost, improve accessibility and boost Thailand economic growth while innovative pricing mechanisms for high-cost drugs is utilized as a short-term strategy to increase access. The infrastructure of the supply chain of the drug is largely well-established through existing vaccine cold chain system. Human resources development for every sector along the value chain of the biologics drug system is, however, an urgent issue and should be addressed to strengthen the biologics drug system in Thailand.

***Keywords*: biologics; vaccine; access; research and development; personalized medicine**

Introduction

Biological products, also known as biologics, are breakthrough pharmaceutical products that change the treatment paradigm of many diseases. The unique characteristics of biologics include its composition, size and structure, complexity of product development and manufacturing process, stability of the product and its immunogenicity.[1] Biologics are produced from

living cells (such as bacteria, plant or animal) and therefore the product itself is dependent on the manufacturing process. Any small changes in this process may change the safety and effectiveness of the product. The best-known biological products, such as vaccines and insulin, have been available for a long time. With progress in recombinant and hybridoma technology, biological products now available in the market have become more advanced and include bloods and derivation of bloods, vaccines, monoclonal antibodies (mAbs) and proteins and advanced therapy medicinal products (ATMP). Globally, and in Thailand, biologics have become increasingly more important, yet the overall landscape of how biologics could have an impact on the Thailand drug system is still not clear.

The objective of this study is to review the landscape of biological drug products in Thailand. The scope of this study includes the analysis of the current situation of biological drugs including the regulation, patient access biologics, distribution and selection of biological drugs as well as the review of what have been done to bridge the gap in Thailand biological drug system.

Methods

We employed a mixed-methods study comprising a literature review and an in-depth interview to describe the current landscape of biologics in Thailand. PubMed and Google Scholar were searched for any articles explaining the biologics situation in Thailand. We also searched government official websites for any grey literatures or official documents relating to biologics drug situation. In-depth interviews with selected key informants including government officials from for example, Ministry of Public health, Department of Disease Control, regulatory agency, experts in biological products, and pharmaceutical companies were conducted to retrieve information not available in the literature, as well as to confirm information retrieved from the literature.

Results

Data from Thai Food and Drug Administration (Thai FDA) has shown that national spending on biologics has increased tremendously from US$547 million (16,513 million Thai baht) in 2009 to US$ 1,664 million (50,182 million Thai baht) in 2018. Biological products used in Thailand are mainly from importation (96.0% biologics spending) making Thailand mainly an importer in the overall global biological market.

Regulation of Biological Products in Thailand

Before 2009, many advanced biological products were classified as “new drug” not “biological product” category. Several biologic products such as vaccine, insulin, recombinant human erythropoietin, bevacizumab, rituximab, trastuzumab and filgrastim were market authorized using criteria for chemical drug products approval. In 2009, the ASEAN harmonization of pharmaceutical registration came into effect.[2] With the mutual recognition of the ASEAN Common Technical Dossier (ACTD), the Thai FDA announced criteria for new biological product approval. At that time, Thailand also experienced a higher incidence of pure red cell aplasia (PRCA), which was suspected to be a severe adverse drug reaction caused by

epoetin. The Thai FDA and other stakeholders including pharmaceutical industry and clinician collaborated to investigate possible causes of PRCA and also reviewed the safety, efficacy and quality of epoetin product registration. Several epoetin products granted both before and after having biological product approval criteria in 2009 were included. After reviewing, it was found that almost 20.0% of the approved dossiers did not have clinical evidence support and 44.0% of them did not use randomized controlled trial study design. The ad hoc committee provided suggestions to improve the regulatory control system which includes the development of biosimilar submission criteria, a request to the pharmaceutical company to submit a risk management plan with the biological drug application, and the re-submission of the epoetin dossier which needs additional documentation.[3] Since then, the Thai FDA have announced several process and criteria relating to biologic product registration as well as criteria to regulate post-approval change such as marketing authorization procedures for vaccines in 2009, updated new drug and new biological product registration criteria in 2015,[4] updated criteria for biosimilar registration in 2018,[5] and updated criteria for new drug and new biological product registration in 2018,[6] and issue criteria specific for regulating post-approval change of vaccine as well as biotherapeutic proteins in 2019. At this point, regulation of the biological products was raised up to international standard.

Regulating biologic products is not only needed at the marketing authorization phase, but also throughout their product life cycle. Since 1999, the Thai FDA employed a safety monitoring programme (SMP) for new drugs including all new chemical, vaccine and biological drugs.[7] Under the SMP, new drugs were conditionally approved and were classified as specially controlled medicines. The safety of these new drugs needed to be monitored. The products were distributed restrictively in healthcare facilities under physicians' close supervision. The Thai FDA required the company to facilitate the reporting of their product's adverse drug reaction (ADR) to the Thai FDA in an appropriate timeframe for at least over a two-year period. After two years, the summary of safety data was reconsidered. If the safety data is satisfied, the products' condition of restrictive distribution can be removed.

Since many biologics are used to treat life-threatening diseases, market approval decisions can therefore sometimes base on the surrogate endpoint rather than the traditional final and long-term outcome or on the use of incomplete phase 3 clinical trial data. These new drugs have different safety issues and a new risk-based approach SMP, which was introduced in October 2017.[7] Under the new risk-based approach SMP, new drugs were divided into four categories and the method of safety monitoring was adjusted according to product's risk level. New drugs approved with an incomplete phase 3 clinical trial will be classified as risk level 1. The active vigilance of all patients for at least two years is required. New chemical entities, new derivatives, new indications, new combinations and new biologics will be classified as risk level 2. Intensified spontaneous reporting for at least two years is required. New delivery systems, administration routes, dosage forms and strengths will be classified as risk level 3. Intensified spontaneous reporting for at least one year is required. Other types of new drugs based on Thai FDA criteria are classified as risk level 4. Mandatory spontaneous reporting

according to Thai FDA recommendations is needed.

The Thai FDA has accepted electronic common technical document (eCTD) applications for new chemical entities, new biological drugs and vaccine since 2006.[8] There were 47, 25 and 37 applications for new biological products and vaccines and 19, 6 and 7 applications for biosimilar products submitted to either the Bureau of Drug Division and Director of Division of Health Product Business Promotion in 2017, 2018 and 2019, respectively. While internal experts (less than 20 staff members) are limited, the trend of biological products is rising. There is a need for more qualified experts to evaluate the biological and biosimilar dossiers, which have a working day time frame of 280 and 230 days, respectively.

More advanced biological products like ATMPs have different regulatory issues. Prior to 2009, stem cell therapy was entirely unregulated in Thailand. As a result, many exaggerated claims and openly advertising stem cell therapies, especially through online channels, were reported. On March 27th, 2009, the Thai FDA announced the control and supervision of drugs and products from stem cells under the Drug Act B.E. 2510. The law required any stem cell use to be first approved by the Thai FDA. However, the law does not include any products created for an individual person and therefore most stem cell treatment used this gap to avoid regulation from the Thai FDA. To control the abuse of fake stem cell treatment, the Thai Medical Council, which governs the practice by licensed physicians, signed the Medical Council's Regulation on Medical Ethics Regarding Stem Cell Research for Human Treatment B.E. 2552 on November 23, 2009. The law became effective on January 11, 2010 requiring all studies on stem cells to be approved and it controls the use of stem cell treatment in all medical schools, private hospitals and clinics.

With an increasing in the number of advanced ATMPs, the Department of Health Service Support, Ministry of Public Health, Thai FDA, Thai Medical Council and leading academic institutions came together in 2019 to draft a new cell therapy act to better regulate research and development, use and authorization of cell therapy in Thailand. The act will include clear categorization of cell therapy as well as quality standards of cell therapy in Thailand.

Access to biologics through Thailand public health insurance

Patient access to biologics under the Thailand public health insurance system varies between the three main health insurance schemes, which are the civil servant medical benefit scheme (CSMBS), the social security scheme (SSS) and the universal coverage scheme (UCS). National List of Essential Medicine is used as a medicine reimbursement list for patients in all three schemes. From our analysis, there are currently 91 biologics listed in 2019 National List of Essential Medicine (NLEM) (10.3% of 882 drugs listed in NLEM). The most common groups of biologics on the 2019 NLEM are immunological products and vaccines (26 products), whole blood and blood products (23 products) and insulin and drugs for the endocrine system (11 products). Monoclonal antibodies for the treatment of malignant diseases listed in 2019 NLEM included rituximab, trastuzumab and basiliximab, which are listed in the E2 access programme under NLEM. Under the E2 access programme, only specific groups of patients with

specific indications listed in NLEM can be reimbursed. It should be noted that no ATMPs are currently reimbursed under the Thailand public health insurance system. As an addition to E2 access programme, CSMBS beneficiaries have other access programme for the reimbursement of biologics that are not listed in NLEM; for example, the use of prior authorization lists including Oncology Prior Authorization (OCPA), Rheumatology Disease Prior Authorization (RDPA) and Dermatology Disease Prior Authorization (DDPA). CSMBS beneficiaries have access to biologics on the NLEM and OCPA. Biologics have been included in all of these lists. For example, rituximab and trastuzumab were included in the NLEM and also in the OCPA list. However, the indications for both drugs on the OCPA list are broader than on the NLEM. Many biologics are included in CSMBS's negative list; for example, adotrastuzumab emtansine, atezolizumab, denosumab and ipilimumab. This indicates that these medicines would not be reimbursed for CSMBS patients.[9]

The reimbursement of biological products is challenging since the evidence available for the reimbursement of these advanced health biological products is often inadequate when compared to evidence available for conventional treatment. Biologics are also known for their high cost, which is because most of these drugs are still under patent owned by the manufacturer. The price of these biologics can be as high as 20,000,000 Thai Baht per year. Thailand has been using Health Technology Assessment (HTA) as a tool to support decision-making for reimbursement since 2004.[10] Results from economic evaluation and budget impact analysis studies are one of the key criteria used by Thai health policy makers for NLEM listing. However, with its high costs, payments for biologics mostly fall under Thailand's willingness-to-pay threshold and are not considered to be a cost-effective intervention; for example, the use of Tocilizumab in systemic juvenile idiopathic arthritis is not cost effective. The use of alternative financial models has been proposed to increase patient access to these medicines; for example, the use of managed entry agreement or valued-based pricing or an alternative channel like orphan drugs and rare diseases reimbursement. These alternative financial models become increasingly important for accelerating access to biologics since these drugs mostly treat rare diseases and have high costs and inadequate data required for regular Health Technology Assessment (HTA) process. With an increasing number of biosimilar products, the assessment of these products also becomes an issue. The question is whether to assess biosimilar products as one specific product different to the reference product or to assess it in the same way as chemical drugs where the efficacy of generics is similar to its originator. Currently, there is no specific HTA guidance on biosimilar products but looking to the future, the upcoming National HTA guidelines will have one chapter dedicated specifically for biosimilar products. Since out-of-pocket payments are the main sources of funding biologics, Patient Assistance Programmes (PAPs) become the main financial support for these self-paid patients. PAPs are pharmaceutical company-sponsored programmes that offer brand name medicines by pharmaceutical manufacturer to patients at a lower cost or sometimes at no cost. PAPs currently available in Thailand varied in design and criteria for eligibility for the program. Most programs utilize fixed scheme which

provides the fixed promotional pattern of "Buy X get Y boxes free" for every patient with the same disease condition.[11]

For vaccines, the access system is slightly different. Access to vaccines in Thailand is provided through Thailand's Expanded Programme of Immunization (EPI) operating since 1977. The programme provides free vaccines for every Thai citizen as well as immigrants and workers from other countries. Thailand EPI is a centralized program in which the National Health Security Office (NHSO) pay for vaccine and immunization services through its capitation payments to primary care facilities. In 2015, government spending on vaccines and immunization services is US$58 million and accounted for 0.7% of the total public health budget.[12] Fifty-seven percent of the spending were on vaccine procurement. In 2019, the Thai EPI programme includes vaccines that cover the following 11 antigens: tuberculosis (BCG vaccine), hepatitis B, diphtheria, tetanus, pertussis, poliomyelitis (OPV and IPV vaccine), measles, mumps, rubella, Japanese encephalitis (JE), influenza vaccine and human Papilloma Virus (HPV vaccine).[13] The coverage rate of vaccine in the EPI program reach 99.0% of the population.[14] The most recent change in the EPI vaccine schedule is the change from tetravalent vaccines to pentavalent vaccines (DTwP-HB-Hib vaccine). This was mainly due to the addition of the Hib vaccine in the standard vaccine list for Thai children.[13]

Even though access to vaccines in Thailand is not a major issue compared with other biologics, the supply security of vaccines became a concern for the Thai government. Several incidences of vaccine shortage were reported in Thailand; for example, the shortage of MMR vaccine due to limited supply and high demand in 2013.[15] This raise the issue of supply security of vaccines during both normal situations and pandemic situations, which is a health security concern in the age of globalization and common air travel.

From Manufacturer to Patients

One unique characteristic of biological products is the need for temperature sensitivity. Product efficacy can drop steeply when kept out of the recommended temperature. Therefore, the cold chain becomes an important factor in the biologics supply chain. Along the product life cycle, many responsible stakeholders such as importers, distributers and hospitals are well aware of the special storage condition of biologics. The cold chain system for vaccines has been implemented since 2009 under the Government Pharmaceutical Organization (GPO)'s vendor management inventory (VMI) programme. In the VMI system, the vaccine supply chain starts at the GPO warehouse and goes directly to district warehouses (at provincial and district hospitals). It then goes from the district warehouses to the Primary Care Units (PCUs) including health centres or hospital immunization clinics. The VMI system has been implemented successfully in Thailand.[16] The transition from the conventional vaccine distribution system to the VMI system was viewed positively by staff and implementers. It saved nearly one-fifth of the total cost of vaccine procurement and distribution in its first year of implementation through more efficient use of resources, lower logistics costs and a smaller number of vaccines procured and distributed.[16] The system, however, should improve the quality of vaccine distribution

services between the GPO and the district warehouses. The system should impose quality control measures such as a systematic quality monitoring system and Good Distribution Practice guidelines. Computerized data loggers were placed inside vaccine boxes on each vaccine shipment between some periods of time.

The quality of the product at the district warehouses and health centres is also of concern. Several studies found an issue in the vaccine supply chain. In one study, almost 80.0% of the refrigerators surveyed could not control the temperature within a two to eight-degree Celsius range, which is the temperature range for biologics.[17] Another study found that hospitals used inappropriate power outlets and had no alternative vaccine storage plans for emergency situations. Currently, temperature sensors have been distributed to hospitals and the overall situation could be improved through training, supervision and monitoring.[18]

Other biologics such as proteins and ATMPs also require a cold chain for distribution to patients. The break in the cold chain of proteins such as monoclonal antibodies could lead to potential pharmacokinetics and pharmacodynamics alterations to these antibodies as well as to the protein structure, which can lead to harmful immune reactions. For ATMPs and autologous cell therapy (ACT), which is considered as a living drug, Chimeric Antigen Receptor T-cell needs an even more complex cold chain. The production of autologous CAR T cell begins with blood cell collection from the patient, laboratory process of CAR T cells at the manufacturing site, and delivery the cells to site of administration. The whole process requires intensive traceability and tracking system to ensure that the product is delivered to the right patient. Cellular products are usually shipped and stored as cryogenic freezing to maintain the stability of product. Strict temperature controls and monitoring are recommended throughout this process to ensure high-quality and safe treatment to patients. However, a focus on the cold chain and traceability of these products is still not much discussed in Thailand.

Many biological products were prescribed to patients to administer at home; for example, recombinant human erythropoietin where the patient needs to inject the drug themselves at home. This might present another problem, not yet investigated, as these patients need to store their biological products in household refrigerators. As biological products are highly expensive and easily lose their efficacy when stored in an inappropriate condition, a new drug management system needs to be considered. Patient registration together with the use of a vendor management inventory and refillable biological products at nearby hospitals might be an innovative management solution. On the other hand, research focusing on the development of new formulations to improve temperature-sensitive products is also needed. A study by Kaplan using a self-standing silk protein matrix showed a six-month stability of vaccines and antibiotics in a 60-degree Celsius condition.

What have been done to bridge the gap in the biological drug system in Thailand?

It is obvious that as biologics become more important, access to biologics is a significant issue. In the area of vaccines, Thailand provides access through its EPI programme. One problem with the vaccine system, however, relates to vaccine security issues; for example, vaccine shortages and vaccine availa-

bility in pandemic situations and vaccines for diseases that are region-specific. We have found several initiatives to bridge the gap in Thailand's biological drug system especially to accelerate the growth in research, development and manufacture biologics.

Research and Development of Biologics

In an effort to lower the cost, improve accessibility and boost Thailand economic growth, providing support to the biologics industry has become a focus for the Royal Thai Government. In 2004, the Royal Thai Government implemented Thailand's National Biotechnology Framework. The biopharmaceuticals industry came under the spotlight again in 2013 when it was included in one of ten industries identified as new economic growth engines in the recent Thailand 4.0 growth model.[19] Thailand 4.0 growth model is an economic model that aims to unlock the country from several economic challenges including "a middle-income trap", "an inequality trap", and "an imbalanced trap". Below is a summary of the ad- vances made in the local biological industry, as well as challenges and obstacles faced.

Queen Saovabha Memorial Institute (QSMI): This is the first biologics manufacturing facility in Thailand, established in 1913. It was also the first vaccine manufacturing facility in South East Asia to produce rabies vaccines and immunoglobulin.[20] The Institute then became part of the Thai Red Cross society in 1917. Current products manufactured by the Institute include: the BCG vaccine in which QSMI is able to produce from the upstream process; Tuberculin PPD and the Rabies vaccine where QSMI imports bulk products from and performs only downstream manufacturing processes. Other products manufactured by QSMI include seven kinds of monovalent snake antivenoms, polyvalent snake antivenoms for both neurotoxic and haematotoxic snakes as well as rabies immunoglobulin from equine and human. Also, part of the Thai Red Cross society hosts a plasma fractionation centre which is the only plasma product manufacturing facility in South East Asia. The plasma fractionation centre has transferred the production of plasma-derived products technology from the Korean Green Cross in 2011.[21] Products from Thai Red Cross's plasma fractionation centre include factor VIII heat-treated freeze-dried cryoprecipitate (HTFDC), human albumin 20.0%, Hepatitis B immunoglobulin for IM, human rabies immunoglobulin for intramuscular injection.

The Government Pharmaceutical Organization (GPO)

Founded in 1964, the GPO is a state enterprise manufacturer of pharmaceutical products under the supervision of the Ministry of Public Health. The GPO started producing vaccines since 1946. It was able to produce mouse-brain-derived inactivated Japanese encephalitis vaccine, diphtheria tetanus and pertussis (DTP) vaccine, snake antivenoms and tetanus antitoxin. These products except Tetanus antitoxin are now all discontinued for several reasons. DTP vaccine was discontinued due to a technical manufacturing issue. Mouse-brain-derived inactivated Japanese encephalitis vaccine was discontinued in 2017 because of the changes to the national immunization policy; there was a switch to the live attenuated Japanese encephalitis vaccines using a cell-based technology platform as it was safer and more effective compared with the mouse-brain-derived vaccine. Snake antivenoms were discontinued since the product line was too similar to

antivenoms produced by QSMI.

Currently, the production of vaccines by GPO includes tetanus antitoxin and live flu (H5N2) vaccine, which are licensed to be used in a pandemic situation. After the bird flu outbreak in 2004, the Flu vaccine plant was initiated by the government in 2007 with 1.41 billion Thai Baht in government funds allocated, matched by the World Health Organization and totalling US$8.72 million (or 290.3 million Thai Baht).[22] The project aimed to manufacture up to 10 million doses of seasonal flu vaccine and was originally due to open in 2013. However, faced with construction and technical problems, factory design and other issues, the project was long-delayed and is expected to be in full operation in 2020. The price of flu vaccines produced by GPO will start at 200 Thai Baht per dose, which is higher than the cost of imported vaccines. The GPO stated that the economies of scale of current production capacity led to the higher price. The GPO also has other vaccines in the research and development stage including inactivated Zika vac in Vero cells, inactivated flu 4 strains in eggs and inactivated pandemic flu in Madin-Darby canine kidney (MDCK) cell.

In 2019, the GPO started to expand their biologics pipeline from vaccines only to proteins drugs. The Chulabhorn Research Institute, PTT Plc. and the GPO signed a cooperation agreement on the research and development of biologics.[23] Prototype of biosimilar Trastuzumab was the first product to be translating from research scale at Chulabhorn Research Institute to an industrial scale. Trastuzumab, under this collaboration, is currently undergo comparability exercise studies as per the guidelines on biosimilar monoclonal antibodies.

GPO Merieux Biological Products Co. Ltd. (GPO-MBP), established in 1996 by the GPO, Sanofi Pasteur and the Crown Property Bureau (Thailand), is the first joint venture between a public and private pharmaceutical company in Thailand. In 2001, GPO-MBP started with Vero rabies vaccine and hepatitis B vaccine as their first two products in Chachoengsao province, Thailand. MMR, influenza and DTP-Hb vaccines were later marketed by GPO-MBP in 2003, 2005 and 2007, respectively.[24] Currently, MMR and DTP-Hb are no longer available on the market due to outdated production technology compared with other MMR vaccines in the market, and the DTP-Hb bulk product supply was discontinued (as bulk product suppliers shifted toward a production of a combined DTP-Hb vaccine). In 2007, GPO-MBP with Acambis, USA and Sanofi Pasture successfully co-developed a recombinant chimeric Japanese encephalitis virus vaccine from research scale to industrial scale. The product was launched in 2010 with Thailand as the product's country of origin. The chimeric JE and MMR vaccine produced by GPO-MBP was WHO prequalified in 2011 and 2014. The product is currently listed in Thailand's EPI programme and is exported to more than 17 countries around the world. Most productions at GPO-MBP are from bulk vaccines where GPO-MBP formulate, sterile filter, fill, freeze dry, label, test and release the finished dosage forms. Since many products are discontinued, GPO-MBP currently produces flu vaccines, JE vaccines and Vero rabies vaccines.

BioNet-Asia

BioNet-Asia is a Thai-French privately held biotech company focusing on the research and development, manufacturing and supply of vaccines. Granted

patents for the construction of *Bordetella pertussis* strains obtained by recombinant DNA technology from Mahidol University, BioNet successfully launched two products of monovalent recombinant acellular pertussis vaccines and combined tetanus, diphtheria and cellular pertussis (Tdap) vaccine in 2016.[25] The first product is more potent and requires a much lower dose of active ingredient of recombinant pertussis in the final vaccine than conventional chemically-inactivated pertussis toxin vaccines. Apart from acellular pertussis, BioNet has also at least ten products in R&D and clinical stages, including vaccines and recombinant proteins such as CRM197 protein carrier which is a carrier protein in conjugate vaccines, dengue and hepatitis B vaccines. The company has also developed and transferred the technology to produce Hib meningitis vaccines to other manufacturers, which commercialize as a pentavalent vaccine in Asia; for example, PentaBio, a pentavalent vaccine produced by Bio Farma in Indonesia.

Siam Biosciences

Established in 2009, Siam Bioscience is 100.0 percent owned by the Crown Property Bureau Equity Company and collaborates with the private sector and Mahidol University.[26] The company started the construction of its production facility in 2011 and had the Pharmaceutical Inspection Co-operation Scheme (PIC/S) certified with products commercialized in 2015. Currently, Siam Biosciences manufactures erythropoietin for anaemia and filgrastim for neutropenia. In 2017, Siam Bioscience expanded its business further by establishing its joint venture company with Cuba-based Centre of Molecular Immunology.[27] This has the purpose of research and development, manufacturing, and commercialization of mammalian cell culture-derived biopharmaceuticals for treatment of various diseases such as cancer, autoimmune diseases and anaemia, with a focus on exportation. Construction of the plant, located in Nonthaburi, Thailand, is expected to be completed with six products launched in 2020.

National Biopharmaceutical Facility (NBF)

The Facility was initiated in 2008 under a collaboration between BIOTEC/ National Science and Technology Development Agency (NSTDA) and King Mongkut's University of Technology Thonburi (KMUTT).[28] The facility consists of two production facilities for microbial fermentation and cell culture. NBF also have downstream processing capabilities and an automatic sterile fill and finish line. These were all designed to comply with international GMP standards and biosafety regulations. The facility has a license from the Thai FDA to manufacture drugs, vaccines and biologics. Currently, NBF provides contract research and manufacturing services (CRAMS) as well as providing scale-up study for biopharmaceutical products. In 2019, NBF signed a memorandum of understanding with private biotech company from South Korea on their joint venture company KinGen BioTech (KGBio) aiming to be the contract manufacturing facility for biologics in the country.[29]

Initiatives on research and development of Advanced Therapy Medicinal Products (ATMPs): The first ATMP product approved in the European Union (EU) and in the United States came in 2009 and 2010, respectively. Globally, ATMPs are still at an early stage and the number of patients treated with ATMPs is very low comparing with traditional biologics. ATMP's efficacy and the fact that it can treat some diseases where conventional approaches are not

effective create interest in industry, universities and research institutes for the research and development of ATMPs globally. In Thailand, several initiatives have started research and development of ATMPs including cancer immunotherapy excellence centre at Chulalongkorn University in which cellular therapy such as CAR T Cell, and allogeneic Natural Killer (NK) cell therapy are under research and development. A pilot clinical study on NK cell therapy has already been done in at least ten patients with promising results. Also undergoing clinical trial phase I studies, two studies of gene therapy in patients with transfusion-dependent β-Thalassemia were done at Ramathibodi hospital, Mahidol University, also show beneficial results.[30]

Establishment of National Vaccine Institute (NVI)

The fragmentation of national work on vaccines, including R&D, led to the establishment of the National Vaccine Institute (NVI). The Thai NVI was officially established in 2012 as a public organization under Royal Decree. The NVI is a Thai public autonomous authority that coordinates vaccine affairs with domestic and international stakeholders. Its mission is to: drive and develop national vaccine policy and strategic plans; promote the nation's capacity through the development of human resources and infrastructure for vaccine research, development and production; build a collaborative network among vaccine experts and professionals domestically and internationally; and generate and manage vaccine information and technology. The NVI's ultimate goal is to lead Thailand towards vaccine security and self-reliance for vaccines in Thailand, including routine vaccines and vaccines for emergency situations. In 2019, the National Vaccine Security Act B.E.2561 was put in place with the aim for Thailand to be self-reliant on vaccines and for Thai citizens to have access to necessary immunization.[31]

Discussion

Our review found several developments in the Thai biologic drug system. The regulatory framework has been developed to make sure that biological products are well regulated, and that patients will receive safe, effective and good quality biologics. With the development of the Cell Therapy Act, Thailand will have the complete regulatory framework for biologics similar to USFDA and European Medicines Agency (EMA). Access to biologics is still however an issue especially for novel protein biologics and ATMPs, since these interventions are still very expensive. Vaccines are of interest to policy makers, particularly the issues of vaccine shortage and vaccine security especially for region-specific infectious diseases such as dengue, and pandemic preparedness such as influenza, zika and Ebola.

In an effort to lower drug expenditure, improve patient access to biologics and boost Thailand's economic growth, the biologics industry becomes a focus for the Ministry of Public Health and other national level policymakers. Progress has already been documented in this review but still there is still much to be done to improve patient access to biologics. To date only rituximab biosimilar is marketed by a local Thai biotech company called Siam bioscience. To accelerate the success of local biotech companies, a range of government policies should be implemented in order to align with the main policy, which promotes the biotech industry. First of all, the national regulatory framework must support local research and develop-

ment for biologics, however this should not compromise the quality, safety and efficacy of the product. National regulatory authority should establish fast-track channel to facilitate approval of local biotech manufacturer including availability of competent regulators to give advice to accelerate a successful marketing authorization of the new biologic or biosimilar. Providing consultation by competent regulator with regard to regulatory science may be necessary for local R&D to move from bench to bed side.

The development of the Cell Therapy Act should also be clear about which ATMPs will be included. Otherwise, overclaimed ATMPs that are not supported with scientific evidence will be more likely to occur, similar to what happened in the USA and Europe. Other policies to support investment in the biologics industry should be revised to match the nature of biologics research and development, which takes on average seven to ten years, such as a tax exemption time frame and the Board of Investment of Thailand (BOI) benefits. Several of these initiatives have already been started by the National Vaccine Institute. Public-private partnerships and joint ventures have been used as key collaborations to transfer advance biotechnology from developed countries and are expected to be the mainstream of technology transfer. More of these are anticipated to take place. Lastly, the development of the biotech industry should not be focused only on the research and development of the product itself but should also include the development of ecosystem of the product development (for example, the availability of an animal study centre that matches with the requirements of animal testing for biologics, , the qualified GMP compliance of laboratory testing with advanced technology for characterization and quality control of biologics, the qualified institute for collection of seed lot or cell bank specific for supporting manufacture of vaccine for local - communicable disease) and the overall health technology management concept (for example where researchers and developers' needs match the needs of the end users, in many cases health care payers).

In parallel, local biotech manufacturers should also apply lessons from other successful biotech cases such as taking Korea as their case study. In the age of digital disruption, the digital transformation of these manufacturing organizations is unavoidable in order to accelerate innovation within the industry. Several biotech start-ups have been initiated in Thailand mostly within universities as small businesses applying deep technology is becoming a global movement.

Even though some biotech companies have successfully commercialized their products, it was found that the government policy does not fully support the commercialization of these products. Some of these products, even though already listed on the NLEM or EPI programme, were not procured due to the higher price compared with products from other countries. It should be noted that the biologics and vaccine industry requires economies of scale to be viable, meaning that higher use of products leads to lower costs of production. Without support from the government, it is difficult for these manufacturers to thrive. One strategy to increase the scale of production is to improve the quality to meet international standard such as getting WHO pre-qualification in order to meet the requirement from international donor like Global Alliance for Vaccines and Immunisation (GAVI) and United Nations International Children's Emergency Fund (UNICEF) for vaccine tender. If

quality standard can meet UN requirement, the local manufacturing can access to big market in order to increase the scale of production with decreased cost of production and further reduction of the vaccine price. Local pharmaceutical price control, currently undertaken by the Thai government, should be balanced against the profit the industry can make to invest in new product research and development. As biosimilar research and development requires clinical trials even though lesser that what is required for the reference product, studies have shown that the price of biosimilar biologics would drop by only 30.0% compared with its reference product. In 2016, Thailand developed an innovation list of novel products and services invented in Thailand which once on the list, are entitled to the benefit of the government procurement programme for the maximum 8 years.[32] The biologics and biosimilar products that were researched and developed in the country could also be on this innovation list.

The manufacturer itself should also consider exporting to other countries to help reach economies of scale. Therefore, a requirement for manufacturers to export is an important factor that should also be supported by the government; for example, introducing regulatory standards as well as health care markets and patient access system that match those in different countries which are the target countries for exporting of biologics locally produced in Thailand, as well as global quality standard such as the WHO prequalification process.

A short-term strategy to improve access to biologics is to use an innovative financing model; for example, the use of Managed Entry Agreements (MEAs). These agreements can be used for high-cost biologics products that are cost-ineffective or doesn't have enough evidences, but patients have unmet medical need. Previously, several MEAs have been implemented for example, the reimbursement of imatinib where Max Foundation provided free imatinib to UCS patients.[33] With these agreements, the risks are shared among payers and the manufacturers. Other tools include patient cost-sharing, revising the reimbursement list to cover first-on drugs that are for patients with life-threatening diseases and who have unmet medical needs.

At last, human resources should be developed for every sector along the value chain of the biologics drug system. Currently, only a few hours of biologics and vaccine topics are included in the Doctor of Pharmacy programme in most pharmacy schools in Thailand. The existing workforce should also be reskilled as these topics were not included in the previous curriculum either. The field should not be limited to the research and development of biologics but also focus on regulatory sciences from both a regulator and manufacturer perspective. The workforce at the hospital level where knowledge about the quality of biologics is needed in order to select and procure the product should also be supported. Lastly, the clinician as well as health care providers should have a better understanding of the differences of these products, compared with chemical small-molecule pharmaceuticals in order to prescribe the drug effectively for the benefit of the patient. Increased understanding of these biological drugs will improve the high confidence to make substitution of biosimilar for reference product to help decrease expenditure of high price reference

product without impaired quality standard and clinical outcome. Furthermore, improved knowledge of biological drugs will help establish effective drug management to reduce the specific risk and abuse related to this type of drugs.

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บทคัดย่อ: สถานการณ์ระบบยาชีววัตถุในประเทศไทย

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ยาชีววัตถุเป็นนวัตกรรมทางสุขภาพซึ่งเปลี่ยนแปลงแนวคิดการรักษาพยาบาลโรคหลาย ๆชนิด อย่างไรก็ตาม ยาชีววัตถุมีคุณลักษณะสำคัญที่เป็นเอกลักษณ์เฉพาะซึ่งส่งผลต่อระบบยาของประเทศโดยรวม การศึกษานี้มีวัตถุประสงค์เพื่อวิเคราะห์สถานการณ์ยาชีววัตถุในระบบยาของประเทศไทย ผลการวิเคราะห์พบว่าประเทศไทยมีการพัฒนาระบบการควบคุมกำกับดูแลยาชีววัตถุของประเทศจนในปัจจุบันมีความทัดเทียมกับมาตรฐานสากลขาดแต่เพียงกฎหมายที่ใช้ในการกำกับดูแลผลิตภัณฑ์เซลล์บำบัดซึ่งกำลังอยู่ระหว่างการดำเนินการ อย่างไรก็ตามพบว่ายาชีววัตถุเหล่านี้ถึงแม้ว่าได้รับอนุมัติทะเบียนแต่การเข้าถึงยังมีจำกัดเนื่องจากส่วนใหญ่มีราคาสูง การเพิ่มขีดความสามารถในการวิจัยและพัฒนายาชีววัตถุเพื่อออกสู่ตลาดโดยผู้ผลิตในประเทศเป็นกลไกหลักที่รัฐบาลไทยใช้เพื่อลดค่าใช้จ่ายด้านสุขภาพ เพิ่มการเข้าถึงและเพิ่มการส่งออกไปยังต่างประเทศเพื่อเพิ่มรายได้ของประเทศ กลไกลทางด้านราคาแบบใหม่ ๆจึงเป็นกลไกที่ใช้ระยะสั้นเพื่อเพิ่มการเข้าถึงยาชีววัตถุเหล่านี้ การกระจายยาชีววัตถุของประเทศไทยพบว่ามีมาตรฐานภายใต้การกระจายวัคซีนของประเทศ อย่างไรก็ตามการพัฒนาบุคลากรที่มีความรู้ด้านชีววัตถุเป็นสิ่งสำคัญที่รัฐควรรีบดำเนินการเพื่อทำให้ระบบยาชีววัตถุโดยรวมมีประสิทธิภาพ

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Situation of Data and Pharmaceutical Information Systems in Thailand

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Abstract Nowadays, advanced information technology (IT) has played a key role in all processes of drug supply chain as well as in the national health insurance system. However, the situation of pharmaceutical information systems in Thailand has not been scrutinized and revised since 2002. This study aimed to review and analyze the current situation of data and pharmaceutical information systems in Thailand as well as to propose recommendations for future development. The study was conducted by reviewing relevant literature and websites in conjunction with organizing semi-structured interviews. The result of the study indicated that in Thailand, the emphasis on an application of IT to efficiently maximize information management and usage had become the national strategic focal point. In general, data and pharmaceutical information systems were sparsely managed by multiple authorized bodies in Ministry of Public Health and could be publicly accessed. Drug information

systems in healthcare facilities and the national health insurance system had been continuously improved and employed for efficiency enhancement in the management and service provision with the goal to achieve desired outcomes of drug and health systems. Regarding future directions for national development, the focus should be on improving the lack of the necessary foundations. The main point was to establish a primary body responsible for the development of the national pharmaceutical information system in all aspects: relevant laws and regulations should be appropriately developed, and personnel should be sufficiently allocated to relevant tasks and undergo IT skill development. Additionally, there should be a formal development of the standard drug codes and standards for data linkages among related organizations. Applications of modern technologies to be able to link and exchange health information efficiently, safely, and seamlessly as well as development of platforms and databases for research purposes should be considered as key focuses.

Keywords: **data, information; information technology; drug system; Thailand**

Introduction

In the past decades, information technology including hardware, software, and information management systems, has been developed rapidly. Telecommunication systems are so robust to seamlessly connect multiple forms of information from several sources, resulting in changes in various areas such as society, education, medicine, and public health. However, the technological revolutions have changed very swiftly in many other industries when compared to the health system which seems to be moving slower due to many reasons.

In Thailand, drug system is also affected by advances in information technology especially in automated pharmaceutical production processes ranging from research, production in industrial plants, drug registration, procurement and distribution from manufacturers or importers to public and private sectors. Throughout the pharmaceutical supply chain from hospitals, clinics, pharmacies to consumers, advanced information technology has been heavily utilized to conduct transactions, starting from purchasing process, delivery management, drug and medical supply management, tracking of drug usage, monitoring drug quality problems before and after sales, managing counterfeit drug issues, observing adverse drug reactions and evaluating drug rationality. This drug information is recorded, created, and continuously developed by certain departments; nonetheless, it is not fully connected.

Drug information and information technology system are very important for health management and development in every country since drug expenditures are relatively high when compared to overall health expenses. During 2012-2013, the proportion of health expenses was higher than 6 percent of gross domestic product (GDP) and tends to increase every year. Moreover, the proportion of drug expenses in 2013 was approximately 24 percent of health expenditures (the cost of drugs, at the manufacturer's prices, is approximately 140,000 million baht).[1] Drug information and information technology system relate to patients or consumers, service providers, manufacturers, importers, regulators, and most importantly, public and private health insurance funds.

Reports on pharmaceutical information situation

are parts of the national pharmaceutical system report which was published in 1994[2] and 2002[3]. The reports have not recently been reviewed even though there were significant changes in advanced technologies and social contexts in all areas.

The objective of this study was to review and analyze the current situation of drug information and information systems in Thailand and synthesize suggestions for future development.

Methods

This article on data information and information system was prepared based on the following steps:

1. Defining the scope of the study to gather important occurrences related to drug information and information technology systems in Thailand between 2002 and 2019.

2. Synthesizing important technological framework of the current drug system and provide examples that would play important roles in enhancing the effectiveness of the drug information system and application to achieve excellent results both in the health system and the drug system. These included availability, affordability, accessibility, rational use, and equity which would lead to national drug security and sustainability based on the conceptual framework developed by the Committee on Drug System Reporting of Thailand B.E. 2562 (A.D. 2019).

3. Gathering information and sources on medicines via drug literature reviews and related websites. Semi-structured interviews were conducted with experts and experienced personnel in pharmaceutical and health information systems. The questions were prepared based on current operations, problems, suggestions for future development, including national development direction as well as suggestions for future research proposals.

The study covered the following areas:

(1) Strategy for the development of health information technology systems of the World Health Organization (WHO), International Telecommunication Union (ITU)[4], twenty-year National Strategy (2018-2037)[5], and strategy for health information technology - issued by Ministry of Public Health for 2017-2026[6]

(2) Existing important information in the pharmaceutical system which included product information, drug registration, product safety, product quality, drug prices, drug usage information, a list of drugs in the national drug list, drug procurement information, and drug distribution information as well as drug code standards

(3) Applications of information technology in various systems, such as the drug procurement and distribution system in the health insurance schemes, orphan drug management system, dialysis fluid delivery system for end-stage renal patients

(4) The laws and important regulations in order to manage a variety of processes in the pharmaceutical supply chain

(5) Provision of recommendations regarding future technologies for improving drug information systems; for example, new technologies in big data and blockchain to link product information and its prescriptions

4. Presenting the results of the study, gather recommendations from reviewers and participants in the workshop on the preparation for pharmaceutical system reports of Thailand (report no. 3) to improve the study.

Results

This article presents only partial reviews from the Thai Drug System Report (report no.3), from the chapter: Pharmaceutical information technology.

1. Related strategies, past situations, and problems in brief.

The national strategies prioritized the use of information technology to efficiently manage the information and drive the system in the same direction based on various relevant standards.[5,6] From the strategy analysis at all levels, the health and drug information system were vital components for all the strategies.

In 2002, the demand for drug information became more important after the launching of the Universal Health Coverage scheme. However, the drug information system still could not be fully developed to be able to quickly and efficiently integrate and share information since well-defined drug codes, detailed information on prescribed medication, tracking on drug manufacturing and import information as well as pharmaceutical management information had not been announced. Moreover, the integration complexity was increased because the difference in multiple health fund compensation schemes resulting in the developments of many disparate information systems. All these complications had become a burden for all service units to efficiently develop their general management plan as well as the medical services. Especially in 2017, a new Public Procurement Act was enacted and the e-Government Procurement (e-GP) system was utilized to organize government procurement. These complicated procedures greatly impacted the management of hospital procurement information systems and significantly increased workloads in the initial stages.

In addition, the improvement of the internet usage had made the online drug sales business grow tremendously; an e-pharmacy was created in the pharmaceutical industry although it was difficult to control. On the other hand, in remote areas not easily accessible to health service providers, there were dangerous drugs being illegally sold without license through local grocery stores to consumers. However, qualified pharmacies had been continuously increasing. There were efforts made to develop information systems to connect prescription information between hospitals and qualified pharmacies to facilitate patient drug receptions and truly increase the quality of drug delivery to the public.

Although laws and policies had both direct and indirect influences on health information technology systems, there was no specific law related to the safety and privacies of the health information usage until 27 May 2019, the Personal Information Protection Act B.E. 2562 was announced[7] in which the information technology and communications section included provisions regarding consumer protection on health products which focus only on advertisement. Therefore, the current law still has not been on a par with the digital technology which is rapidly changing. There were delays in the investigations of crimes as well as limitations on the workforce responsible for thoroughly control and oversee the process.[8] Moreover, regulations for selling drugs and medical supplies via online channels (e-pharmacy or online pharmacy)[9] were still not in place.

There was a shortage in the number of related workforce and there were no clearly defined roles and responsibilities for the personnel. For future workforce

planning, knowledge management and skills in managing health information technology systems needed to be firmly developed.

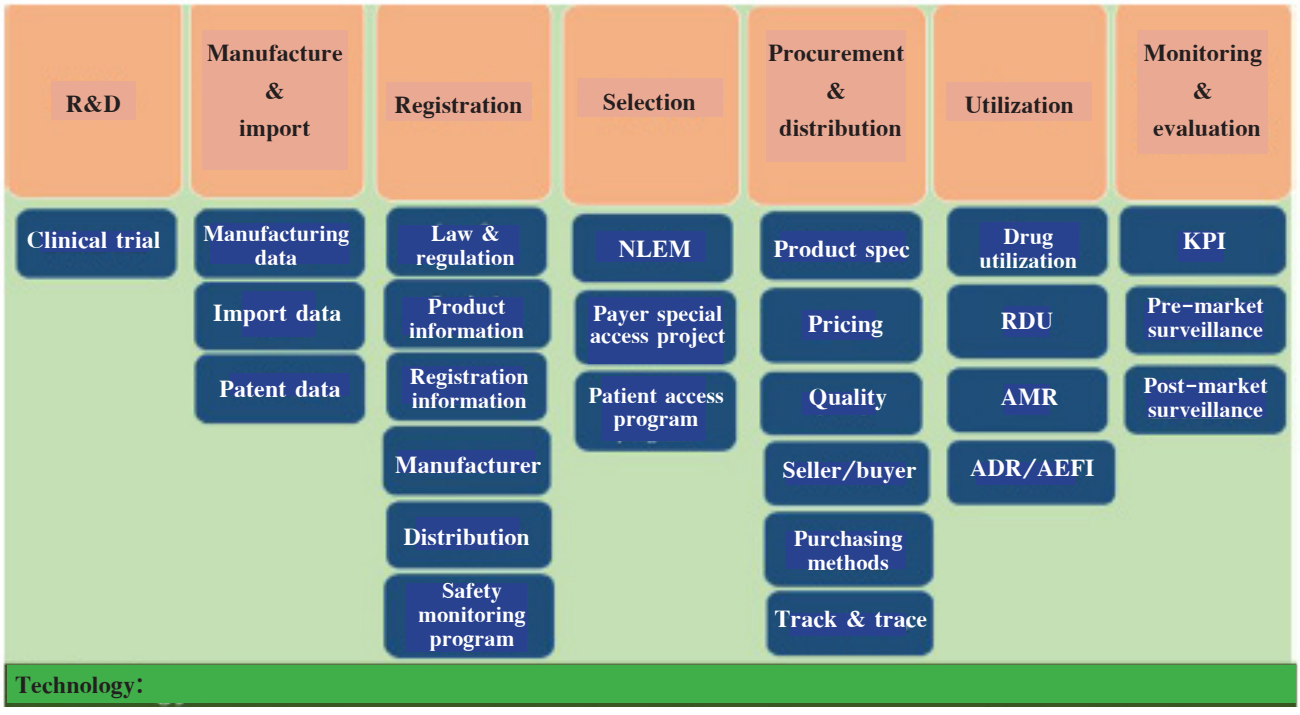
Although consumers could access information more conveniently and quickly with the advanced technology and electronic devices via the internet (the internet-of-things: IoT), they were still unable to fully utilize all new technologies due to the limitations of the users themselves, quality of information and related technologies. Insufficient consumers' health knowledge or health literacy [10, 11] could also prevent consumer from fully realize benefits but instead increase risk exposure.

2. Drug information

2.1 Important information of current drug system

In the drug cycle, there were many types of information being generated which relates to the main activities starting from research and development, production and imports, drug registration, selection, procurement, distribution and usage of drugs - including monitoring and evaluation. There were various technologies which could be utilized to support and make good use of the information, as shown in Figure 1.

Figure 1 Important information of current drug systems and examples of related technology



Note: R & D = research and development; NLEM = National list of essential medicines; spec = specification; RDU = rational drug use; AMR = anti-microbial resistance; ADR/AEFI = adverse drug reactions/adverse events following immunization; KPI = key performance indicator; std. = standard)

2.2 Each type of drug information system of domestic agencies

Thailand had continuously developed important drug information systems based on the drug life cycle since pharmaceutical information is essential in all the processes in the drug supply chain. Additionally, this information was crucial and useful for management for decades, especially in the Ministry of Public Health legally responsible to collect drug information. For example,

1) Pharmaceutical product information which contains information about drug registration, manufacturer and importer, drug registrars and a list of drugs in the National Drug List

2) Drug safety information issued by the Food and Drug Administration (FDA) which contains information on reports of adverse reactions from drugs and surveillance data for adverse reactions from vaccines, issued by the Department of Disease Control

3) Drug quality information which contains information on drug quality assurance, issued by the Department of Medical Sciences, and information on lot release of vaccines

4) Drug price information which contains information on median prices and reference prices, prepared by the Drug and Medical Supply Information Center

5) Drug usage information which contains drug prescribing information from hospitals, rational drug prescribing information, antibiotic prescribing tracking information, and reimbursement information of medical service fees via the Health Insurance Fund

6) Drug code standard information which could specify generic names, trade names, drug strength, and drug types. Since there were many agencies that developed drug code standards causing the service units to have multiple in-use drug code standards. This included the 24-digit drug code which was the first version of the drug codes developed by the Drug and Medical Information Center.[12] Later, Thai Medicines Terminology (TMT) was developed by the Thai Health Information Standards Development Center (THIS) where the health insurance funds as well as the hospitals utilized to disburse medication and purchase drugs via the e-GP system. The Comptroller General's Department also used this terminology for drug monitoring and control.[13] In addition, there were also other types of codes used in pharmaceutical companies such as barcodes and GS1 codes which were applied to use in logistics and warehouses. [14,15] In 2019, The Thai FDA studied and applied the Identification of Medicinal Products (IDMP), a set of five International Standard Organization (ISO) norms being implemented in the Marketing Authorization Application process.[16,17] The IDMP was developed in response to a worldwide demand for internationally harmonized specifications for medicinal products with the basis for the unique identification of medicinal products, in order to respond to the objectives from a variety of regulatory activities (development, registration and life cycle management of medicinal products; pharmacovigilance and risk management).[16]

There were many agencies responsible for constantly producing and maintaining this data system, most of which were in the Ministry of Health. Additionally, these agencies also developed websites to allow people to publicly access the information. Examples of the data sources are shown in Table 1.

Table 1 Examples of important information sources of the current drug system

Process	Information	Example of current data sources
1. Research and development	1.1 Clinical trials	• Thai Clinical Trials Registry (http://www.clinicaltrials.in.th/)
2. Manufacture and import	2.1 Manufacturing data	• Annual reports for the pharmaceutical licensee (http://www.fda.moph.go.th/sites/drug/SitePages/report-form.aspx) • Production value and importing or ordering value (http://www.fda.moph.go.th/sites/drug/SitePages/Statistic.aspx)
	2.2 Import data	• Report Systems of Production and Distribution of Health Products, by Narcotics Control Division (http://www.fda.moph.go.th/sites/Narcotics/SitePages/%E0%B8%A3%E0%B8%B0%E0%B8%9A%E0%B8%9A%20e-sub%20%E0%B8%A2%E0%B8%AA.4.aspx) • Requests for Drug Imports (http://www.fda.moph.go.th/sites/Logistics/SitePages/AllNews.aspx?ListName=DrugNews) • Public guidelines (Requesting permission to import or order drugs) (http://www.fda.moph.go.th/sites/drug/SitePages/Manual-Population.aspx) • Production value and Importing or Ordering Value (http://www.fda.moph.go.th/sites/drug/SitePages/Statistic.aspx)
	2.3 Patent data	• Patented drugs (Sorted by generic name) http://www.fda.moph.go.th/sites/drug/Post/SitePages/Certificate.aspx) • Drug patent information center (https://www.gpo.or.th/Default.aspx?tabid=301&language=th-TH) • DIP :Thailand Patent Search (http://patentsearch.ipthailand.go.th/DIP2013/simplesearch.php) • Drug patent database (http://wwwapp1.fda.moph.go.th/patent/homepage.html)
3. Drug registration	3.1 Laws and regulations	• The Bureau of Drug Control has compiled drug laws (http://www.fda.moph.go.th/sites/drug/SitePages/กฎหมายยา.aspx) • Compiled in the 3rd edition of the Thai Drug System Report in Drug Laws and Drug Selection chapters.
	3.2 Product information	• Folk Doctor Foundation (https://www.doctor.or.th/doctorme/medicine) • Faculty of Pharmacy, Ubon Ratchathani University (https://drugiden.ubu.ac.th/) • Ranelagh Company Limited (https://www.pobpad.com/%E0%B8%A2%E0%B8%B2-a-z) • HonestDocs (https://www.honestdocs.co/drugs) • Medthai (https://medthai.com/drugs/)

Table 1 Examples of important information sources of the current drug system (continued)

Process	Information	Example of current data sources
		• Haamor.com (http://haamor.com./th/วิกิยา) • Pharmaceutical System Research and Development Foundation (http://yaandyou.net/) • List of narcotics (http://www.fda.moph.go.th/sites/Narcotics/List_of_Narcotic/NARCO_list%20_25.04.2019.pdf) • List of active ingredients (http://www.fda.moph.go.th/sites/Narcotics/List_of_Narcotic/PHYCHO_list_25.04.2019.pdf) • List of new generic drugs that are equal in treatment with conventional drugs (orange-book) (http://www.fda.moph.go.th/sites/drug/SitePages/NewDrug-BE.aspx) • Drug information for medical personnel (http://www.fda.moph.go.th/sites/drug/SitePages/ข้อมูลสำหรับบุคลากรทางการแพทย์.aspx) • List of drug information for citizens (http://www.fda.moph.go.th/sites/drug/SitePages/ข้อมูลยาสำหรับประชาชน.aspx) • New drug information (http://www.fda.moph.go.th/sites/drug/SitePages/DrugProducts.aspx) • Search function for common household drugs (http://www.fda.moph.go.th/sites/Drug/SitePages/Queries_Medicine.aspx)
	3.3 Registration information	• Checking product numbers (http://pca.fda.moph.go.th/service.php) • Checking for health product numbers (https://oryor.com/oryor2015/css_check_product.php) • Searching health product numbers (https://oryor.com/%E0%B8%AD%E0%B8%A2/index/check_product) • Searching product information (http://porta.fda.moph.go.th/FDA_SEARCH_ALL/MAIN/SEARCH_CENTER_MAIN.aspx) • Oryor Digital Library (https://oryor.com/%E0%B8%AD%E0%B8%A2/)
	3.4 Manufacturer information	• Company list (http://medicaldevices.oie.go.th/Company List. aspx?tid=1&id=2) • List of committees of Thai Pharmaceutical Manufacturers Association 2018-2019 (http://www.tpma.or.th/V2/home.php?guid=04&page=01) • PReMA member (http://www.prema.or.th/www/en/member.php) • List of GMP Compliance Manufacturers (http://www.fda.moph.go.th/sites/drug/Post/SitePages/Certificate.aspx) • Drugs-Pharmaceutical products-Wholesales and Manufacturers (https://www.yellowpages.co.th/heading/ยา-ผลิตภัณฑ์-ขายส่งและผู้ผลิต)

Table 1 Examples of important information sources of the current drug system (continued)

Process	Information	Example of current data sources
	3.5 Distributors	• Distributors (http://www.prema.or.th/www/en/images/publications/SRAP%20Content%20Handbook%20M123.pdf)
	3.6 Safety Monitoring Program: SMP	• Updated manuals / New drug safety tracking guidelines (Safety Monitoring Program) (http://www.fda.moph.go.th/sites/drug/Shared%20Documents/Law04-Notification-ThFDA/FDA-20120706.pdf)
4. Drug selection	4.1 National List of Essential Medicines: NLEM	• National list of Essential drugs and evidences (http://ndi.fda.moph.go.th/drug_national)
	4.2 payer special access program	• Special projects (https://www.nhso.go.th/frontend/page-contentdetail.aspx?CatID=MTA4Mw==) • NHSO's Annual Reports(https://www.nhso.go.th/frontend/page-about_result.aspx)
	4.3 Patient access program	• GIPAP project (http://www.wongkarnpat.com/viewya.php?id=2277#.XYDwqSgzY2w) • Axios (https://axiosint.com/accessinthailand)
5. Drug procurement and distribution	5.1 Product specifications	• Drug specific characteristics (http://dmsic.moph.go.th/dmsic/index.php?p=1&type=3&s=3&id=4514)
	5.2 Pricing	• Median prices (http://ndi.fda.moph.go.th/drug_value) • Drug and Medical Supply Information Center, Ministry of Public Health (DMSIC) (http://dmsic.moph.go.th/index/index) Median prices (Medicines) (http://dmsic.moph.go.th/index/drugsearch/3) Reference prices for normal purchase (Medicines) (http://dmsic.moph.go.th/index/drugsearch/1) • Searching and comparing system for drug prices in private hospitals (https://hospitals.dit.go.th/app/drug_price_search.php) • Health service fees of service units under the Ministry of Public Health on the website of Health Administration Division (HAD) (https://phdb.moph.go.th/main/index/dep/18)
	5.3 Quality	• Searching information GREEN BOOK (https://bdn.go.th/th/ebook) • Quality inspection reports (http://biology.dmsc.moph.go.th/page-view/77) • List of GMP Compliance Manufacturers (http://www.fda.moph.go.th/sites/drug/Post/SitePages/Certificate.aspx)
	5.4 Seller/ buyer	

Table 1 Examples of important information sources of the current drug system (continued)

Process	Information	Example of current data sources
	5.5 Purchasing method	• Procurement Statistics (Comptroller General's Department) (http://www.gprocurement.go.th/wps/portal/egp/Stat/!ut/p/z1/04_Sj9CPykssy0xPLMnMz0vMAfIjo8zifQ3djQydnQ18DSzdLQwc_Syc3d0szA0tPMz1w8EKDHAARwP9KGL041EQhd_4cP0oVCv8w4zNDBzNA3yd_QM9DAycDaEK8JhRkBsaYZDpqAgADkN7HA!!/dz/d5/L0lDUmlTUSEhL3dHa0FKRnNBLzROV3FpQSEhL3Ro/)
		• Information System on Government spending (https://govspending.data.go.th/dashboard/2)
	5.6 Track and trace	• Rajavithi Hospital (https://www.rajavithi.go.th/rj/?p=10325#)
		• Government Pharmaceutical Organization (https://scm.gpo.or.th/vmi/)
6. Drug utilization	6.1 Drug utilization	• NHSO's Annual Reports (https://www.nhso.go.th/frontend/page-about_result.aspx)
	6.2 Rational drug use: RDU	Examples of knowledge sources
		• Rational Drug Use ; RDU (http://ndi.fda.moph.go.th/drug_use)
		• Instruction manuals for rational drug usage (http://www.fda.moph.go.th/sites/drug/Shared%20Documents/RationalDrugUse/RDU05.pdf)
		• Hospital manuals for rational drug usage (https://www.hsri.or.th/sites/default/files/attachment/RDU%20Book.pdf)
	6.3 Antimicrobial resistance: AMR)	• Drug resistance circumstance (http://narst.dmsc.moph.go.th/)
		• Percentage of antibiotics usage (https://hdcservice.moph.go.th/hdc/main/search.php?search=%E0%B9%83%E0%B8%8A%E0%B9%89%E0%B8%A2%E0%B8%B2%E0%B8%9B%E0%B8%8F%E0%B8%B4%E0%B8%8A%E0%B8%B5%E0%B8%A7%E0%B8%99%E0%B8%B0)
		• Thailand's Antimicrobial Resistance Management Strategy 2017-2021 (http://narst.dmsc.moph.go.th/documentation/AMR%20strategy%202560-2564.pdf)
		• Management System of Antimicrobial Resistance: AMR) (http://www.fda.moph.go.th/sites/drug/SitePages/AMR.aspx)
	6.4 Adverse drug reactions/ adverse events following immunization: ADR/AEFI)	• Health Product Vigilance Center (http://thaihpvc.fda.moph.go.th/thaihvc/index.jsf)
		• Surveillance of symptoms after immunization (http://www.boe.moph.go.th/boedb/prior09/aefi/)
		• Safety Network in Chiang Rai, for Drugs and Health Products (http://crapr.org/crapr/) must log in

Table 1 Examples of important information sources of the current drug system (continued)

Process	Information	Example of current data sources
		• Community of pharmacy practice ADR (https://www.facebook.com/ADCoPT-247094745310607/) There are information on various training courses.
7. Monitoring and evaluation: M&E)	7.1 Key performance indicator: KPI	• Many studies (18-20) shows that Thailand has made efforts to develop drug system indicators at various levels but found that these indicators have not been widely used and continuously monitored, especially at the national level. • Thai Drug Watch & Development Center uses indicators to review the situation of Thailand's drug system in 7 dimensions, such as good governance, self-reliance, safety, equity, drug quality, accessibility and affordability, rational use • The systematic drug analysis results have been reported in these indicators in the 2009 Drug System Situation Report (21) and found no further reports after that.
	7.2 Pre-marketing surveillance	• Pre-marketing surveillance (http://www.fda.moph.go.th/sites/drug/SitePages/SupervisionPrior.aspx)
	7.3 Post-marketing surveillance	• Post-marketing surveillance (http://www.fda.moph.go.th/sites/Drug/Pages/Main.aspx)
8. Others	Drug codes	• TMT drug codes by Thai Health Information Standards Development Center (THIS) (http://tmt.this.or.th/dm9Emxc7e0~oKj7U6OrddW/$/; http://this.or.th/tmtrf_downloads.php) • 24-digit drug codes on THCC website (http://thcc.or.th/homemedicin.php), or, searching through the standard drug code management system (http://drug.nhso.go.th/DrugCode/searchDrug.zul)

3. Information system development

3.1 In service place

For the development of information systems in service places, especially at the hospital level at the initial stages, Information Technology system was implemented to mainly manage pharmaceutical warehouses and subsequently developed programs to provide medical services to patients. However, most system designs lacked of data governance which required data integration and management, information disclosure, and information security.

While drug information systems had been contin-

uously developed in many work processes from various departments; for example, reports on adverse drug reactions or vaccines to the Ministry of Public Health, reports on procurement data to the Medical Information Center for use in the development of median prices and reference prices for government services for the benefit of drug and medical supply procurement, it were still difficult to integrate information across departments or insurance funds due to the limitation in drug information standards. To be able to serves the monitoring of adverse drug reactions, vaccines or herbal medicines, service units should be able to record drug information deep into the production model or serial number to control, regulate safety and, in some cases to manage recalls. With all these reasons, the government had set a twenty-year national strategy plan B.E. 2561-2580 (2018-2037) which harmonize the development of drug information databases, research and innovation databases as well as data links among government agencies. To maximize competitive advantage from data, the development should be modernized, governed and sustainable.[5]

From a review of the information technology systems utilization in Thailand, it indicated that new medical technologies in medicines had been increasingly utilized. This matched the trend of pharmacy practice which had been progressively used to support personnel involved in medical management. For example,

- Doctor prescribing drugs via Computerized Prescriber Order Entry (CPOE) and Electronic Health Record (EHR) where CPOE would prevent medication errors caused by transcribing errors. Moreover, CPOE also increased the possibility to do data mining which assist decision making process with real-time medication control and cost saving; while the EHR supported transferring data in organization efficiently, being able to show basic information and clinical data of patients with real-time processing.
- Drug distribution using an inventory management system by vendors (Vendor-Managed Inventory: VMI), Pharmacy-based Automated Dispensing machine, Unit-based Dispensing Machine, Cytotoxic Preparing Machine, drug delivery through Pneumatic Tube or Dump Waiter
- Medication Administration using Electronic identification, Smart pump, Electronic Medication Administration Record (eMAR)
- Big data collection and analysis using information systems. These also helped to understand the situation and accomplish better decision making
- "RDU – knowing drug issues" is a mobile application developed in associations with many sectors to promote rational drug use (RDU). In addition to providing drug information, the users could save important information about their "personal drug information" as well. This would be very useful in communicating with medical personnel who provide further care.

3.2 Medical information technology development in the health insurance system

National Health Security Office (NHSO) was utilizing information technology in drug procurement and distribution systems with the service units under the national health insurance system. To achieve this,

there was data integration between the personal information from the Bureau of Registration Administration, Ministry of Interior and health insurance rights data from the National Beneficiaries Registration Center, National Health Security Office. The integration eventually benefited individual pharmaceutical service given that records of medication discharges for patients with specific diseases are collected. Patients with specific diseases gain high benefit from the gathered information on the special medicines in the National List E (2) project, antidotes project, the anti-AIDS and tuberculosis project, and the dialysis solution delivery project for end-stage renal patients. Especially in the antidotes project, there was an introduction of geographic information system (GIS). It was utilized in the administration of antidote reserves based on urgent resuscitation and the provision of medical supplies to patients within the time required, even if the patient hospitalized in a remote area. Remarkably, in the first 2 years of the antitoxin project, the record showed that this project could save the lives of near 100 percent of patients. It was considered an outstanding innovation in IT used in medical systems (as shown in Figure 2).

In addition, IT was also utilized in the logistics system of the peritoneal dialysis project by assigning the Thai Post Company to deliver the reagent and check the remaining stock at the patient's home. Health insurance funds and service units could monitor and direct the delivery of dialysis solutions online. Even during the major flood in 2011, patients were still able to receive dialysis fluid at home. Since 2015, the NHSO had started enforcing the service units in the system to submit individual drug usage data, for both outpatients and inpatients, resulting in establishing a database of patients' drug usage in the national health insurance system.

Figure 2 The use of geographic information for establishing an antidote reserve system for the National Health Insurance System

Discussion

Reliable health information and information technology are at the heart of health policy management, development and decision making. It also helps in planning for cost control which tends to increase continuously.[1]

The advancement of information technology in the past played an important role in the production and dissemination of pharmaceutical information which was an important contribution to driving the drug information system. Thai government has a vision to transform the country into the digital economy and society; thus, the usage of information technology systems is incorporated into diverse national strategies. However, these strategies cannot be completely implemented due to the limitation of necessary foundation for policy and strategy development; for instance, an agency who will cooperate in eHealth management at the national level, laws and regulations that support smooth operations and keep up with precipitously change.

In addition, lack of centralized standards for health information systems as well as IT personnel, both in terms of quality and quantity, were considered as reasons that the integration and exchange information still cannot be efficiently performed and respond to end users.

For the sources of medical information, the related government agencies have collected pharmaceutical information related mainly to their duties considering this information has been processed and analyzed for strategic usage within the department. However, third parties may also be allowed to access the information as well. While the information service sections have drastically been improved resulting in quicker and more convenient access, end consumers still need to improve on health literacy and how to use information efficiently. Moreover, there should be continuous development in information systems in the service places and in the health insurance system which help increase the efficiency of management and services.

For the development direction at the national level, it is recommended that a designated national organization should be established to determine strategic directions, formulate policies and master plans for the development of pharmaceutical information systems and health information technology for the country considering medicine is a data set in the health system. In addition, it is necessary to develop a standard supervision mechanism so that various information systems can work together to create seamless data exchange with security and benefits by studying the feasibility of implementing regulations related to the security and privacy of health information to benefit both in personal information protection and society where it is necessary to violate the privacy of individuals. Finally, sufficient and proficient IT personnel both at operation and executive level, responsible for both information systems and health information technology, can be a key success factor.

For future research, to align with the above development direction, it is recommended that there should be a study of data governance including drug code standards and drug data link standards from relevant agencies in all dimensions. These standards include drug prescriptions, prices, diagnostic codes for use in development of Citizen Health Profile. Appropriate standards will help encourage people to be interested in their health information by using big data and blockchain technology to assure that health

promotion information or access to other benefits provided by the government can be done conveniently.

In addition, a research information system should be developed by determining a well-designed platform that consists of necessary information for research purposes allowing researchers to access it by themselves under confidentiality or privacy of data in accordance with the statutory requirements.

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บทคัดย่อ: สถานการณ์ของระบบข้อมูลและสารสนเทศด้านยาในประเทศไทย

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ความก้าวหน้าทางเทคโนโลยีสารสนเทศเข้ามามีบทบาทอย่างมากต่อกระบวนการต่าง ๆ ในห่วงโซ่อุปทานของยา และในระบบประกันสุขภาพ แต่ยังไม่มีการทบทวนสถานการณ์ของระบบข้อมูลข่าวสารด้านยาในระบบยาของประเทศไทยให้เป็นปัจจุบันหลังปี พ.ศ. 2545 การศึกษานี้มีวัตถุประสงค์เพื่อทบทวนและวิเคราะห์สถานการณ์ระบบข้อมูลและสารสนเทศด้านยาในประเทศไทย และเสนอข้อเสนอแนะสำหรับการพัฒนาในอนาคต โดยใช้การทบทวนวรรณกรรมและเว็บไซต์ และการสัมภาษณ์แบบกึ่งโครงสร้าง จากการศึกษาพบว่ามียุทธศาสตร์ระดับชาติซึ่งมีจุดเน้นร่วมกันในการนำเทคโนโลยีสารสนเทศมาช่วยในการบริหารจัดการและใช้ประโยชน์ข้อมูลข่าวสารอย่างมีประสิทธิภาพ ฐานข้อมูลและสารสนเทศด้านยาส่วนใหญ่รับผิดชอบโดยหลายหน่วยงานในกระทรวงสาธารณสุขและมีการเผยแพร่ให้บุคคลภายนอกเข้าถึงได้ ระบบสารสนเทศด้านยาในสถานพยาบาลและระบบประกันสุขภาพได้รับการพัฒนาอย่างต่อเนื่องและนำมาใช้เพิ่มประสิทธิภาพในการบริหารจัดการและให้บริการเพื่อให้บรรลุผลลัพธ์ที่พึงประสงค์ของระบบยาและสุขภาพ สำหรับทิศทางการพัฒนาในระดับประเทศต้องมุ่งเน้นแก้ปัญหาการขาดรากฐานที่จำเป็น ได้แก่ กำหนดหน่วยงานที่รับผิดชอบต่อการพัฒนาระบบสารสนเทศและเทคโนโลยีสารสนเทศสุขภาพของประเทศในทุกด้าน พัฒนากฎหมายและระเบียบอย่างเหมาะสม จัดสรรและพัฒนาบุคลากรที่เกี่ยวข้องให้เพียงพอ ควรมีการศึกษาที่มุ่งเน้นด้านมาตรฐานรหัสยาและมาตรฐานการเชื่อมโยงข้อมูลยาจากหน่วยงานที่เกี่ยวข้องในทุกมิติและมีการนำเทคโนโลยีที่ทันสมัยมาประยุกต์ใช้ โดยมุ่งหมายให้สามารถเชื่อมโยงและแลกเปลี่ยนข้อมูลสุขภาพและยาได้อย่างมีประสิทธิภาพ ปลอดภัย ไร้รอยต่อ นอกจากนี้ควรมีการพัฒนา platform และฐานข้อมูลที่เอื้อต่อการทำงานวิจัย

คำสำคัญ: **ข้อมูล, สารสนเทศ; เทคโนโลยีสารสนเทศ; ระบบยา; ประเทศไทย**

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Current Situation of the Modern Pharmaceutical Manufacturing Industry in Thailand

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Abstract The modern pharmaceutical manufacturing industry in Thailand remains a downstream industry. In 2019, there were 142 GMP certified modern pharmaceutical manufacturing facilities, most of which are manufacturers of finished products containing pharmaceutical chemicals. The manufacturing industry in 2018 was worth 77 billion baht, an increase of 5% from the previous year with a net profit of about 8 %. Although the export of pharmaceutical products has increased, competition is high and the competitive advantages have decreased compared to the potential of import trade. In 2015, the ratio of production value to import value was approximately 35:65. Businesses were more interested in research and development, mostly focusing on the development of generic drugs and new generic drugs in conventional dosage forms. The motivation for production came from the Thai Innovation List policy. Since 2009, documents for drug registration application must comply with the format specified by ASEAN. In addition, drugs approved for registration previously had no expiration date; however, now, the Drug Act, B.E. 2562 (2019) stipulates that registered drugs are valid for 7 years from the date of issue. In 2003, the Ministry of Public Health adopted the World Health Organization guide to Good Manufacturing Practices (GMP), and in 2011, this was superseded by the Pharmaceutical Inspection Co-operation Scheme (PIC/S) GMP. Nevertheless, issues that still need to be addressed include the creation of standardized product code management and traceability systems. It is also recommended that government agencies should have more cooperation with businesses to advance the pharmaceutical industry as well as support the use of locally produced drugs.

Keywords: **modern pharmaceutical manufacturing industry; modern drugs;** good manufacturing practice (**GMP**)

Introduction

The modern pharmaceutical manufacturing industry is one of the most important industries in Thailand since medicine costs are a major expense borne by the public health system. Moreover, the pharmaceutical industry is one of the target industries that must be transformed into an industry of the future, according to the National Strategic Master Plan (2018-

2037).[1-2] Similar to other industries in Thailand, the Thai pharmaceutical industry has focused on production to substitute imported drugs and to export these drugs. The industry focuses on promoting the development of production efficiency and raising production standards with the goal to allow people to access effective and safe pharmaceutical products at reasonable prices. In addition, according to the 20-year national strategy, the National Drug System Development Committee has resolved to accelerate the drug system development strategy to support public health system reform. One important strategy is focusing on increasing the potential of the pharmaceutical manufacturing industry in Thailand. This article is aimed at presenting a review of the current situation of the modern pharmaceutical manufacturing Industry in Thailand and providing recommendations for the direction of the pharmaceutical manufacturing industry in the future for all stakeholders involved in the pharmaceutical industry, public health personnel, or those with an interest to learn more.

Overview: Current Situation of the Modern Pharmaceutical Manufacturing Industry

The current Thai modern pharmaceutical manufacturing industry is still a downstream industry. Most manufacturers import active pharmaceutical ingredients from foreign countries to mix with excipients and produce finished products in the desired dosage forms using pharmaceutical processes and technology. As of October 2018, there were 194 modern pharmaceutical manufacturing facilities in Thailand, 85 from this number located in Bangkok.[3] As of June 2019, there were 142 GMP certified modern pharmaceutical manufacturing facilities in Thailand.[4] In fact, the number of operating facilities was slightly more since some facilities were in the process of improving their manufacturing standards. From 142 the GMP ones, there were 91 pharmaceutical manufacturing facilities producing finished products for humans, 8 for animals, 36 for humans and animals, 4 facilities for manufacturing pharmaceutical chemicals, and 3 facilities for manufacturing both pharmaceutical chemicals and finished products.

Most of the facilities that manufacture finished products specialized in chemical drugs, and there were only 7 biopharmaceutical manufacturing facilities. Classified by ownership, 9 facilities were government-owned or stock-based pharmaceutical manufacturing facilities. The remaining facilities were privately-owned, mostly by Thais, with foreigners owning or holding the major shares of 9 facilities.[5]

In 2018, the modern pharmaceutical manufacturing industry in Thailand was worth approximately 76.9 billion baht (Table 1) with revenue from human pharmaceutical drug sales of approximately 66.4 billion baht (86% of total revenue) and revenue from animal pharmaceutical drug sales of approximately 10.5 billion baht (14% of total revenue). The expansion of revenue in 2016, 2017, and 2018 were 7.1%, 5.6%, and 4.8%, respectively, indicating stagnation of growth. The modest growth is likely a result of illnesses in a growing population as well as an aging population, improved access to treatment channels under the National Health Security System, and a medical tourism industry that is likely to expand.[6] The Government Pharmaceutical Organization in Thailand is the organization with the highest income; in 2018, revenue from its drug sales was 6,784 million baht, accounting for 8.8% of the

Table 1 Business Operations and Income of Modern Pharmaceutical Manufacturing Companies in Thailand

Item	2015	2016	2017	2018
Human drug sales (million baht)	56,200	60,100	63,200	66,400
Veterinary drug sales (million baht)	8,700	9,400	10,200	10,500
Total sales (million baht)	64,900	69,500	73,400	76,900
Sales expansion (%)	N/A	7.1	5.6	4.8
Total net profit (million baht)	5,600	6,300	6,830	N/A
Net return (%)	8.6	9.0	9.3	N/A

Note: Data source: Department of Business Development, Ministry of Commerce[5]

industry's total revenue.[7] If the income distribution of only companies that produce human drugs was considered, 75% of industry-wide revenue came from manufacturers with the top 30 sales.

Although the manufactured drugs were mainly produced for domestic consumption, exports had increased. In 2018, drug exports were valued at 17.9 billion baht, an increase of 3.41% from 2017 and almost double from 2009.[8] The top ten exporting countries in descending order were Myanmar, Vietnam, Cambodia, Japan, Philippines, Hong Kong, Malaysia, Belgium, Laos and Singapore.

Research and Development

While research and development (R&D) is an important step in obtaining new products, over ten years ago, most pharmaceutical manufacturers did not give much importance to R&D.[9] Most of their operations focused on the development of drug formulas to improve drug properties, while the R&D budget comprised less than 1% of total budget. Drugs were manufactured and distributed without using advanced technology or equipment, and in terms of R&D of new drugs (i.e. new chemical entity), Thailand did not have the capacity for investing in technology and personnel. However, the circumstances of pharmaceutical R&D in Thailand has changed dramatically in the last ten years. Many pharmaceutical companies have set up R&D departments with increased budgets. Technology has been used to develop pharmaceutical products in a wider variety of dosage forms. The types of R&D of pharmaceutical products were summarized as follows:

1) Research and development of generic drugs in conventional dosage forms

Almost all product development of modern pharmaceutical manufacturers in Thailand focuses on the development of generic drug formulas. In Thailand, generic drugs are classified according to the definition and information used for registration and fall into 2 types: generic drugs and new generic drugs. Research and development of both types of generic drugs contain the same main steps. The key difference is that new generic drugs are required to undergo a bioequivalence study to prove equivalent drug levels in the body. Such levels directly relate to the effectiveness of drug treatment.[10] These procedures are in accordance with the guidelines and international require-

ments of the Association of Southeast Asian Nations (ASEAN) harmonization of standards[11-13], US Food and Drug Administration, European Medicines Agency (EMA), and International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), which require clear presentation of quality information at every step. The average duration of research is about 2-5 years, and the cost of developing a formula varies depending on the type of product and type of drug. Costs can range from 1 million to 10 million baht or higher if the active ingredients are expensive; in particular, when new drug molecules are applied. For the development of new generic drugs, the cost of the bioequivalence study must also be included. As the average period for a bioequivalence study is between 6-12 months, the cost of a study is generally between 2-5 million baht or higher if the study has specific factors or the drug being studied has a high fluctuation in drug levels in the blood. For this reason, not many companies have the capacity to develop new generic drugs in the market.

2) Research and development of generic drugs using a high technology platform

Certain drugs require high-level technology to formulate or produce, such as modified-release drug products, sterile lyophilized products, inhalers, nasal sprays, etc. Currently, some pharmaceutical manufacturers in Thailand focus on the development of this group of drugs by investing heavily in technology and personnel. The production of drugs using advanced technologies helps reduce the need to import drugs from foreign countries and increases accessibility to those drugs. The advantage for manufacturers using high technology platforms in production is that there are fewer competitors in the market.

3) Research and development of new drugs

Currently, a very small number of new drug formulations have been developed and approved in Thailand. Examples include new fixed dose combination drugs, GPO-VIR (anti-retroviral medication), or drugs developed from herbs such as little ironweed. This may be due to many reasons, for example, unpreparedness of the industrial sector or relevant stakeholders, as well as a lack of clear guidelines for the registration of new drugs produced in Thailand. As a result, even though new research had been conducted by universities, research agencies, and domestic pharmaceutical manufacturers, these studies had not been led to new drug registrations. Nevertheless, at present, circumstances have started to change for the better due to an increase in newly-formed supporting agencies as well as clearer policies, guidelines, and procedures prescribed by government regulators.

In recent years, the government has collaborated with the private sector to carry out activities or projects that support R&D in the pharmaceutical industry as follows:

a) Establishment of agencies providing services to conduct bioequivalence studies: currently, there are 8 agencies that have the capacity to provide these services. These organizations have been certified by the Bureau of Laboratory Quality Standards, Department of Medical Sciences, confirming that these agencies have operational standards that comply with the OECD (Organization for Economic Co-operation and Development) Good Laboratory Practice (GLP) principles or the ISO (International Organization for Standardization) 17025 standards for drug levels in

blood tests.

b) Establishment of organizations to support the development of new drugs that are not new molecules and to improve the quality of generic drugs, e.g. Chulalongkorn Drug Discovery and Drug Development Research Center (Chula4DR) and Chulalongkorn University's Drug and Health Products Innovation and Promotion Center (CU-D-HIP).

c) Implementation of Thailand Center of Excellence for Life Sciences (TCELS), such as formation of an international network to search for new active ingredients and develop new drugs under activities of natural product drug discovery (NPDD); conception of a project for the development of drugs, vaccines, and biologics; and creation of the Excellence Center for Drug Discovery (ECDD).

d) Support from the Technology Management Center (TMC) under the National Science and Technology Development Agency (NSTDA), such as the Innovation Technology Assistance Program (ITAP), Private Sector R&D Promotion Program (RDP).

e) Imposition of new regulations by the Thai Food and Drug Administration (FDA) on the development and registration of generic drugs. The FDA also imposed clear policies, guidelines, and procedures for promoting the development of new drugs in Thailand. Additionally, the FDA announced the criteria for registration of new drugs developed from existing drugs and set up a specialized working group to advise on and be responsible for the registration of drugs in this group.

These agencies and government policies have contributed to the support and promotion of research and development, which has significantly increased over the past decade. Accordingly, the approval of new generic drug registrations during the last 5 years has increased. This reflects the stronger research and development capabilities of organizations in Thailand.

Drug Registration

Pharmaceutical products that are manufactured or imported for the market in Thailand must be registered with the FDA to confirm effectiveness and safety. During the registration process, the registrant must submit supporting documents and academic evidence as required to experts for consideration. In 2009, an agreed upon common format for the preparation of a well-structured Common Technical Dossier, which was determined by ASEAN countries, was required for drug product registration; namely, the ASEAN Common Technical Dossier (ACTD). The ACTD requires more academic evidence, making drug registration more difficult than before.

In 2012, a document on "Guidelines for registration of drug formulas appearing in the Minister's notified pharmacopoeia, using pharmacopoeia standard requirements and methods for analyzing active pharmaceutical ingredients and finished products" was published in order to accelerate and increase efficiency of the consideration process for the registration of drug formulas listed in a pharmacopoeia notified by the Minister or in newer versions. Later, in 2013, there was a notification on "Prescribing documents or evidence of registered modern drug variation" in order to ensure that variations in registered modern drugs are in accordance with academic principles and the ASEAN Variation Guidelines (AVG). In this notification, the terms and conditions for submitting a variation request and required documents are defined. However, the variations listed in the ASEAN Agree-

ment are not comprehensive; therefore, in 2018, the FDA notified an additional list of variations (Non-AVG) absent from the ASEAN Agreement.

A newly launched Drug Act (Issue 6) B.E. 2562 (2019)[14] directly affects drug registration. In this Act, drug registration is valid for only 7 years from the date of issue as specified in the registration certificate. The manufacturers must renew the registration before the registration certificate expires. In addition, when filing for registration, it is required to show documents on the number of patents or petty patent applications that have been published under the Patent Act. In the case that there is a research study to support the drug formula registration, especially in human research, the research must comply with the specified criteria, procedures, and conditions. The provisions of this Act cause manufacturers to be more careful when selecting drug formulas to be registered.

The accumulation of many pending drug formula registrations is currently a significant issue. The issue occurs because of operating procedures and insufficient human resources of the government sector as well as the lack of technical knowledge of industry representatives responsible for the registration. These challenges are recognized by various relevant sectors, which are currently improving the registration process to be more efficient. In addition to improving the operating procedures of the Bureau of Drug Administration, the FDA has also set up a One Stop Service and Consultation Center to facilitate and provide advice to businesses. In addition, both public and private agencies, such as the National Science Technology and Innovation Policy Office, Thai Industrial Pharmacist Association, Regulatory Affairs Pharmacy Association (Thailand), Pharmaceutical Research and Manufacturers Association, Thai Self-Medication Industry Association, Thai Pharmaceutical Manufacturers Association, and the Faculty of Pharmacy of various universities collaborate in trainings or creation of curricula on Good Registration Management (GRM) to increase knowledge for personnel engaged in drug registration.

Pharmaceutical Manufacturing

The incident that has had the highest impact on the domestic pharmaceutical industry in the past ten years was when the Ministry of Public Health passed the Good Manufacturing Practice (GMP) into law for pharmaceutical manufacturers. This was to raise the standards of pharmaceutical manufacturing in the country to international levels. In 2003, the Ministry of Public Health issued a public health regulation, "Prescribing the criteria, procedures, and conditions for modern drug manufacture B.E. 2546 (2003)"[15], and a notification of the Ministry of Public Health, "Prescribing the details regarding the criteria and procedures for the manufacture of modern drugs under the Drug Law B.E. 2546 (2003)"[16], with reference to the GMP regulations of the World Health Organization version 1992. Subsequently, several GMP inspector units worldwide, including Thailand, sought to become members of the Pharmaceutical Inspection Co-operation Scheme (PIC/S) to raise their pharmaceutical manufacturing standards for international trade benefits. Moreover, Thailand had signed the ASEAN Sectoral Mutual Recognition Arrangement for Good Manufacturing Practice Inspection of Medicinal Products (ASEAN MRA on GMP Inspection)[17] on 10 April 2009. This agreement was made to achieve mutual acceptance of the results of the GMP assessment

of ASEAN member states with the condition that member states must use the GMP of PIC/S guidelines or equivalent criteria for inspection. For these reasons, in 2011, the Ministry of Public Health issued a new notification of the Ministry of Public Health, "Prescribing the details regarding the criteria and procedures for the manufacturing of modern drugs under the Drug Law B.E. 2554 (2011)", based on the PIC/S GMP version 2009. This notification also applies to the manufacturing of traditional medicines.

PIC/S GMP regulations that focus on prevention of contamination, cross-contamination, and other process errors, cause many businesses to invest in renovations of their production sites and purchases of new machinery. If it is not possible to improve existing production sites, then it is necessary to construct new ones. As a result, the investment value may reach 200 million – 1 billion baht, depending on the risk or rigor associated with the drug being produced. At the same time, the capacity of personnel working in the pharmaceutical system must be developed and recruiting personnel in various professions, such as pharmacists, engineers, and scientists, are required.

These requirements led to collaboration between public and private sectors, such as the FDA, Thai Pharmaceutical Manufacturers Association (TPMA), Thai Industrial Pharmacist Association (TIPA), International Society for Pharmaceutical Engineering (ISPE) Thailand Affiliate, and the Faculty of Pharmacy of various universities, to organize activities or projects to develop the capacity of personnel in the industry. One of the most important projects was a project requesting support from the FTA fund. Under this project, the TPMA requested for financial support from the Ministry of Commerce, and the Faculty of Pharmacy, Srinakharinwirot University acted as a consultant for project implementation. The activities of this project included creation of working instructions and self-assessment forms, pilot evaluation of the selected pharmaceutical manufacturers by international experts, and organization of training workshops for personnel in the pharmaceutical industry.

In addition, since 2006, the Board of Investment (BOI) has promoted the manufacture of pharmaceutical products and active pharmaceutical substances to facilitate businesses in the Thai pharmaceutical industry to adjust their operations to PIC/S GMP standards, under the condition that pharmaceutical manufacturers applying for tax benefits must receive PIC/S GMP certification within 2 years from operation start date. The benefits received include exemptions for corporate tax, machinery tax, and export duty on raw materials.

The abovementioned activities and projects have greatly contributed to the development of pharmaceutical industry standards in Thailand. Most of the businesses were able to develop their standards to receive PIC/S GMP certification; however, some small businesses were unable to upgrade their manufacturing standards due to insufficient investment and personnel challenges. Moreover, some business owners chose to cease operations rather than invest in meeting industry standards, while others are still in the process of making a decision. For this reason, the number of modern drug manufacturing sites in the country has steadily decreased over the past ten years.

Logistics of the Pharmaceutical Industry

Logistics management refers to the process of planning, delivering effective and efficient flow control, goods storage, services, and related

processes from the starting point of production to the end point of consumers. Logistics management is one part of supply chain management that needs to be efficient and effective[18]. Currently, logistics management in the pharmaceutical industry takes 2 forms: First, the manufacturers or product owners operate their own logistics. Second, the manufacturers or product owners hire a third party logistics company.

In the past, domestic manufacturers and small importers often chose to manage logistics themselves, while large importers, especially multinational pharmaceutical companies, often outsourced to third parties. However, at present, there is a tendency for domestic manufacturers and small importers to use third party services as well in order to reduce administrative costs. The delivery of pharmaceutical products to hospitals must comply with the Good Distribution Practice (GDP), which requires sufficient delivery records for product traceability. In addition, in Thailand, drug deterioration has occurred due to incorrect storage or inappropriate temperature control in storage locations. Therefore, it is necessary to pay attention to the Good Storage Practice (GSP) as well.

A current challenge found in Thailand's drug distribution system is limited traceability. Problems with data traceability often occur, and these problems become more complicated when the drugs are distributed to clinics and drugstores that use wholesale distributors as intermediaries. While online orders have become more popular, and computer systems have made data recording more convenient, limitations in tools, information technology, and product codes persist; as such effective data tracing up to the original point of manufacture remains a challenge. The issue is more pronounced for imported drugs that require many more steps to trace the data back to foreign manufacturers, as well as through the delivery process by either plane, boat, train, or car and include cargo stops at airports, harbors, or railways. In some cases, regional distribution centers are used, which do not directly import drugs from foreign manufacturers. The complexity of the drug distribution chain leads to ineffective data traceability, and often, this shortcoming permits the spread of counterfeit drugs.

Data traceability requires the use of a product code; currently, many organizations designate pharmaceutical product codes for different purposes:

1) Hospitals and service units have their own drug codes for internal use.
2) The FDA uses assigned drug registration numbers when issuing drug formula registration certificates.
3) The Thai Health Coding Center and the Bureau of Health Administration are the main organizations that develop 24-digit drug codes for use in hospitals to link data across the country[19].
4) The Thai Health Information Standards Development Center (THIS) develops Thai Medicines Terminology (TMT) and data maintenance mechanisms.[20]

Developing health data codes is important and should be included in the plan to be implemented at the national level so that the country will have an efficient and integrated health information system. International drug codes are essential for monitoring efficacy, safety and rational use of drugs. At present, many countries have established measures to prevent counterfeit drugs, to track drugs, and to trace data by

using different tools and technologies. A tracking and data tracing system, using globally accepted system such as serialization, which is commonly used in the European Union and the United States, should be considered in Thailand. In addition, supporting systems must be developed throughout the country. Implementation may start between hospitals and government regulators, which are organizations responsible for the country's main drug distribution chain. When strengthened, the system can then be rolled out to clinics and drugstores, which are the last points of distribution before reaching the patient.

Drug Market

The domestic drug market has high competition since the number of importers and distributors, which are the main competitors of domestic manufacturers, have increased significantly. Up until 2018, the FDA issued licenses to import or order modern drugs to a total of 811 companies. Most of the licenses were issued to companies that order generic drugs manufactured in foreign countries to sell domestically. As a result, the number of imported drug formula registrations has increased considerably.[21] In 2015, the proportion of import value to production value was 65:35, whereas, before 2002, production value was higher than import value. For example, in 1995, the ratio of import value to production value was 35:65.[22] The data suggests that the competitiveness of pharmaceutical manufacturers in the country has decreased compared to importers. Import value is higher due to the increased import of biologics, anti-cancer drugs, and other prototypes of patented high-price drugs. In addition, there have been imports of low-price generic drugs from India and China too.

In 2017, Thailand had a total drug market value of approximately 180 billion baht, the second largest market size in Southeast Asia after Indonesia. The market growth rate has been about 5-6% per year, and the value of drugs sold through public hospitals accounts for about 60% of the total drug market value.

As for government procurement, the Government Procurement and Supplies Management Act. B.E. 2560 (2017) was issued to replace the Regulations of the Prime Minister's Office on Procurement B.E. 2535 (1992); but entitlements are still given to the government pharmaceutical manufacturing unit by compelling government agencies to purchase drugs listed on the National List of Essential Medicines by a specific method from the Government Pharmaceutical Organization (GPO) or the Thai Red Cross Society (unless they are unable to produce and sell drugs on time according to the government agency's annual plan)[23]. However, the new Government Procurement and Supplies Management Act provides government agencies with the ability to buy drugs that are in the Thai innovation list by a specific method. The government agencies have to purchase generic drugs in the Thai innovation list to a total value of no less than 30%of the demand plan.This guideline helps motivate private pharmaceutical manufacturers in the country to find opportunities for the development of new generics to compete drugs for which their patents are about to expire.

Recommendations for the Development of the Modern Drug Manufacturing Industry

1) Government agencies must have clear measures to support the domestic pharmaceutical industry by

cooperating with more businesses. For example, the GPO should research and develop drugs and then share the information to private manufacturers. The GPO and private manufacturers should not develop the same new generic drugs. The GPO should establish stability of pharmaceutical raw materials, produce orphan drugs and some essential drugs that the private sector does not produce, create a mechanism for price balance, support the manufacture of target drugs and drugs in the Thai innovation list on a continual basis, and promote the expansion to overseas markets.

2) Upgrade drug logistics by developing Good Distribution Practice (GDP) and Good Storage Practice (GSP) guidelines, and developing drug codes and health information systems in the country to monitor drug quality problems and increase drug safety efficiently.

3) Review the National List of Essential Medicines and the list of non-prescription drugs and update it to be suitable with changes in technology. This will align research and development of domestic drug manufacture with the Ministry of Public Health's policies, namely, the primary medical policy and the policy on development for reducing overcrowding in hospitals.

4) Promote the manufacture of new generic drugs and the use of technology to develop pharmaceutical products in a variety of dosage forms in line with patient needs and public health policies. Set up measures to ensure that the private manufacturers can sell the drugs at appropriate median prices to the public. In addition, there should be a clear policy to support the use of drugs produced in the country, especially drugs that are formulated from pharmaceutical ingredients produced in Thailand, and to enable the public and private sectors to procure raw materials conjointly. Also, there should be a policy on the synthesis or manufacture of various standard substances.

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บทคัดย่อ: สถานการณ์ปัจจุบันของอุตสาหกรรมการผลิตยาแผนปัจจุบันของประเทศไทย

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วารสารวิชาการสาธารณสุข 2563;29(ฉบับพิเศษ):S129-40.

อุตสาหกรรมการผลิตยาแผนปัจจุบันของไทยยังคงเป็นอุตสาหกรรมระดับปลายน้ำ ในปี พ.ศ.2562 มีสถานที่ผลิตยาที่ยังดำเนินกิจการและผ่านการรับรอง GMP จำนวน 142 แห่ง ส่วนใหญ่เป็นการผลิตยาสำเร็จรูปประเภทยาเคมี การผลิตในปี พ.ศ.2561 มีมูลค่าประมาณ 77,000 ล้านบาท โดยขยายตัวเพิ่มขึ้นประมาณร้อยละ 5 จากปีก่อนหน้า กำไรสุทธิประมาณร้อยละ 8 การส่งออกมีแนวโน้มสูงขึ้น การแข่งขันภายในประเทศรุนแรงมากขึ้นโดยศักยภาพในการแข่งขันของผู้ผลิตลดลงเมื่อเทียบกับผู้นำเข้า ในปี พ.ศ.2558 สัดส่วนมูลค่าการผลิตต่อการนำเข้าอยู่ที่ประมาณ 35:65 ผู้ประกอบการให้ความสนใจกับการวิจัยและพัฒนามากขึ้น แต่ส่วนใหญ่เป็นการพัฒนายาสามัญและยาสามัญใหม่รูปแบบทั่วไป โดยแรงจูงใจสำคัญคือนโยบายบัญชีนวัตกรรมไทย การขึ้นทะเบียนยาต้องใช้รูปแบบเอกสารตามที่อาเซียนกำหนดตั้งแต่ปีพ.ศ. 2552 และ พ.ร.บ.ยา (ฉบับที่ 6) พ.ศ. 2562 กำหนดให้ทะเบียนยามีอายุ 7 ปี จากเดิมที่ไม่มีกำหนดวันหมดอายุ กระทรวงสาธารณสุขได้ประกาศใช้หลักเกณฑ์และวิธีการในการผลิตยา (Good Manufacturing Practice; GMP) ตามแนวทางขององค์การอนามัยโลก (WHO GMP) เป็นกฎกระทรวงตั้งแต่ พ.ศ. 2546 และเปลี่ยนเป็นหลักเกณฑ์ GMP ของ PIC/S (Pharmaceutical Inspection Co-operation Scheme) ในปี พ.ศ.2554 ด้านโลจิสติกส์มีประเด็นที่ยังต้องพัฒนาคือการสร้างระบบจัดการรหัสผลิตภัณฑ์ที่ได้มาตรฐานและการตรวจสอบย้อนกลับ ข้อเสนอแนะที่สำคัญของผู้ประกอบการคือ หน่วยงานภาครัฐควรมีความร่วมมือกับผู้ประกอบการมากขึ้นในการพัฒนาอุตสาหกรรมการผลิตยารวมถึงสนับสนุนการใช้ยาที่ผลิตในประเทศ

คำสำคัญ: **อุตสาหกรรมการผลิตยาแผนปัจจุบัน; ยาแผนปัจจุบัน; หลักเกณฑ์วิธีการที่ดีในการผลิตยา**

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Pharmacy Workforce: a Call for Professional Cohesion to Meet the Rising Healthcare Demand

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Abstract Demand for healthcare services in Thailand are in transition, resulting from social changes within the nation and globally. The need for equality, efficiency, quality, and continuity of care requires combined efforts from a variety of stakeholders in the health workforce. Pharmacists responsible for ensuring access to medicines need reformation as well. There has been an increase in the number of pharmacy schools and graduates. Additionally, the pharmacy education curriculum has been gradually adapted to align to the changes. The pharmacy curriculum has transformed from 5-year to 6-year programs, offering three specialty tracks aiming to develop qualified pharmacists to fit with the needs of the job market. However, with the rapid changes in social contexts and the labor market, and limited information regarding pharmacy manpower, professional leaders in the Pharmacy Council of Thailand, pharmacy schools, and professional organizations are urged to work together to set long-term and continuous actions on workforce development in order to develop competent pharmacists for current and upcoming demand.

Keywords: **health workforce; pharmacist; manpower; professional**

Introduction

A competent, motivated, and well-managed health workforce is critical for a well-functioning health system. Therefore, the Sustainable Development Goal (SDG) 3c highlights the need to "substantially increase health financing and the recruitment, development, training and retention of the health workforce".[1] The Ministry of Public Health, Thailand, has set people excellence, a part of the human resource development plan, as one of the four core strategies for its 20-year strategic plan 2017-2021.[2]

The health workforce involves a wide range of people delivering healthcare services. In the pharmaceutical system, which is a part of the health system,

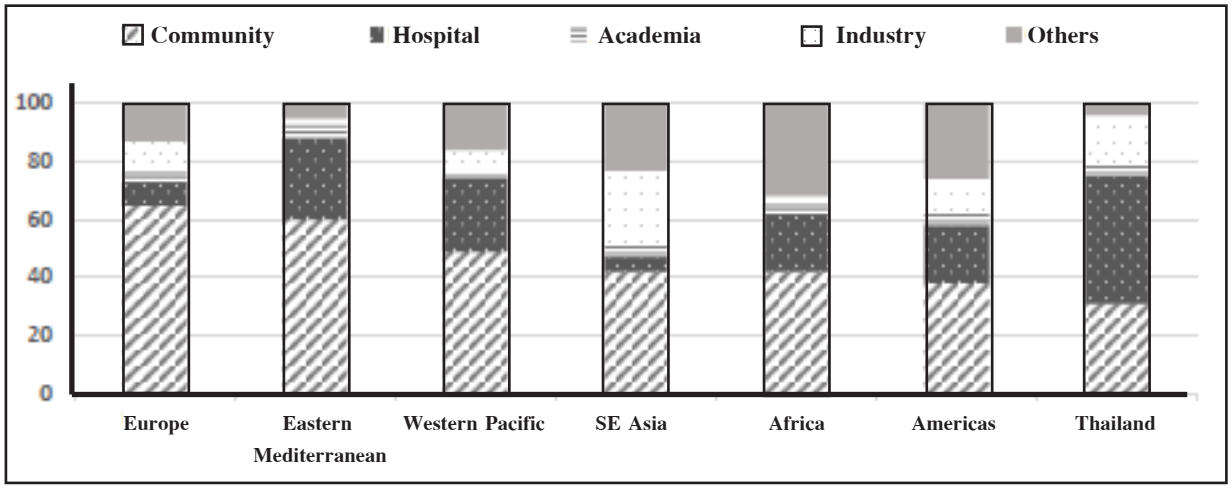
the health workforce comprises not only pharmacists, but also other allied health professionals and supporting personnel, such as pharmacy technicians, public health professionals, engineers, scientists, and administrative staff. Although they do not directly deliver pharmaceutical services, they are essential to the access to effective and safe use of medicines. However, because of limited information regarding the workforce of the Thai pharmaceutical system, this article highlights only the pharmacist workforce.

In Thailand, pharmacists are responsible for all activities regarding the country's access to medicines throughout the drug supply chain: the manufacturers who develop drugs, the pharmacies and hospitals that distribute them, the government agencies that oversee the process, and the primary care units that empower people to use them properly. Therefore, the needs for Thai pharmacist workforce are unique. For example, in Thailand, the majority of pharmacists work in hospitals, community pharmacies, and the pharmaceutical industry[3] (Figure 1), whereas in many developed countries, such as Europe and America, the majority work in community pharmacies, while in Southeast Asian countries, the majority work in community pharmacies and the pharmaceutical industry.[4] The exceptional practice and distribution of Thai pharmacist manpower, therefore, requires the careful integration of the Thai pharmaceutical system context into pharmacist workforce planning and management.[5]

Analysis Framework

In this situation analysis, the Systems Framework of the Commission on Education for Health Professionals for the 21st century[6], the Availability, Accessibility, Acceptability, Quality (AAAQ) dimensions of universal health coverage pertaining to human resources for health,[7] the WHO's working lifespan,[8] and the International Pharmaceutical Federation's (FIP) needs-based educational model[9] were used. The integrated framework suggests health workforce planning as a complex and dynamic interaction between the demand for health services and the supply of education system, which have been driven by population and social needs. As such, healthcare and social contexts of the country are crucial factors to

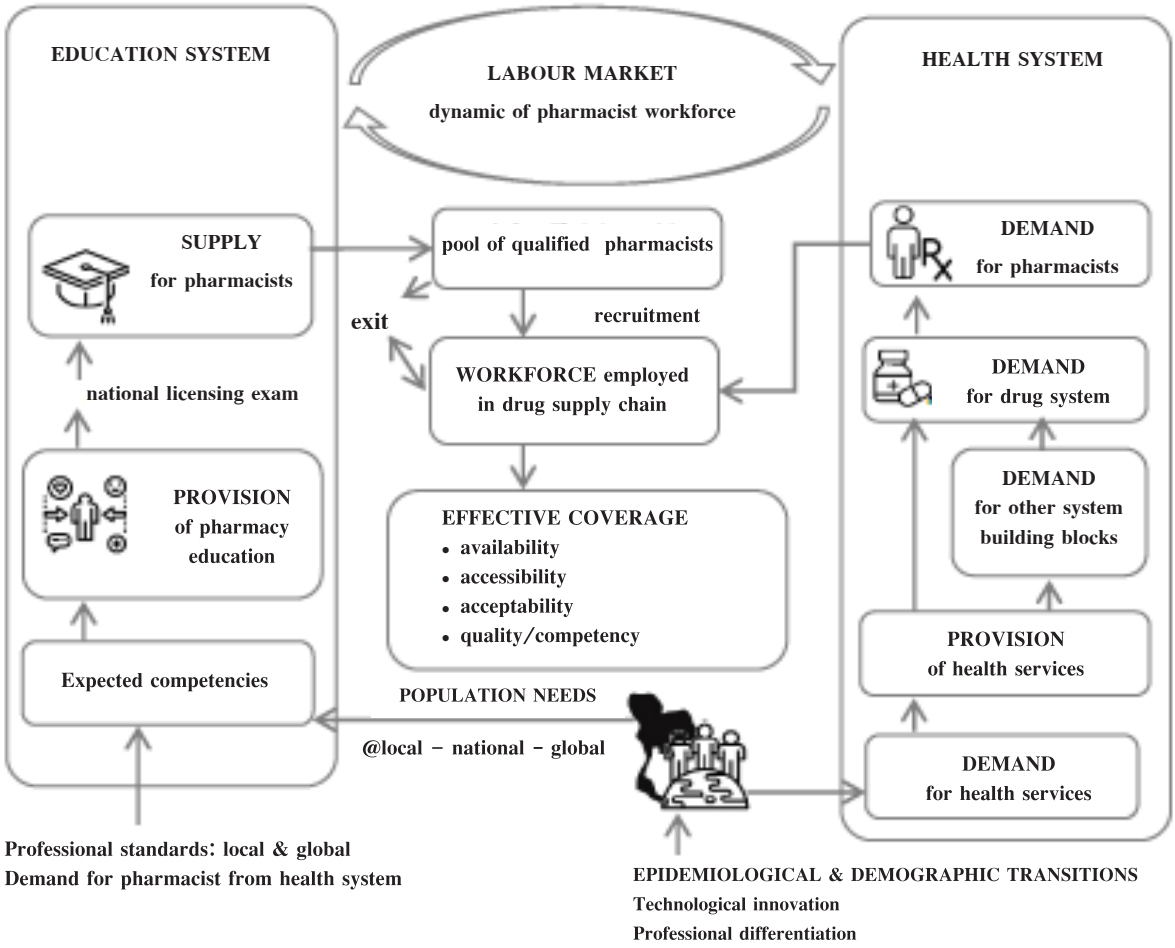
Figure 1 Proportion of pharmacy workforce by sector, displayed by WHO regions compared to Thailand[3,4]



co-create responsive healthcare services and workforce (Figure 2)

Using this framework, we reviewed literature from many sources, including research articles, journal articles, annual reports, and government documents. This article presents the current situation of the pharmacy workforce in Thailand by describing changes in health demand, labor markets, pharmacy education, and workforce situations.

Figure 2 Adapted systems framework for pharmacist workforce[6-11]



Changes in Demand

Demand for the pharmacist workforce is in transition, influenced by its exogenous factors, such as social systems, health systems, pharmaceutical systems, and professional standards. Globalization, global warming, urbanization, economic growth, technology advancement, low birth rate, and high life expectancy are examples of social transitions affecting the health needs of the nation.[12,13]

The rising mortality rates from non-communicable diseases, proportion of aging population, and access to various health products are health challenges where in the traditional medical system focusing on disease treatment may be inefficient. Additionally,

rising costs of healthcare due to achievement of universal health coverage has led to significant challenges in financial management.[14] Therefore, the National Health Development Plan 2017-2021 highlights multi-sectoral participation by the public, private, and academic sectors, and civil society as well as by the people, communities, and local administrations to strengthen the capacity of services at every level and the quality of life of people in all age groups.[15]

There are four national health development stra- tegies that aim to (1) promote health, prevent disease, and protect consumers and the environment through empowering people and communities; (2) reduce inequality and foster fair treatment through developing the primary care system and enhancing service delivery at all levels; (3) create a mechanism to efficiently manage the health workforce; and (4) strengthen health system governance and improve the supporting system for health services.[15]

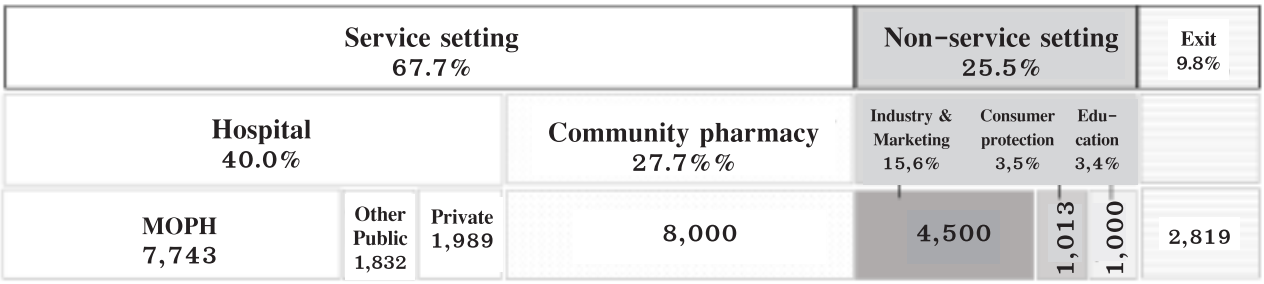
Transitions in social and healthcare systems call for better health workforce management and integration between networks and partners.[7] Four essential standards for the health workforce include availability, accessibility, acceptability, and quality (AAAQ dimension of effective coverage).[10,11]

Labor Market for Pharmacists

Pharmacists are medicine experts who are responsible for ensuring quality and availability of a medicine throughout the supply chain or full life cycle; for example, raw material sourcing, manufacturing, distributing, marketing, regulating, selecting, dispensing, and ensuring patients' safe use.[16] In Thailand, the role of pharmacists has gradually transformed from product orientation (managing medicines and health products) to patient orientation (caring for effective and safe use of medicines in patients) to system orientation (designing and improving the medicines system in hospitals and communities).[5]

In 2016, there were 28,896 active pharmacists. A majority of Thai pharmacists work in the service setting, that is, 40% work in hospitals and 28% in community pharmacies. Outside of the service setting, 16% work in the pharmaceutical industry, 4% in regulation and consumer protection, 3% in academia, and 10% in non-pharmacist areas. The Ministry of Public Health's (MOPH) hospitals hold the largest portion of the pharmacist workforce (26.8%) compared to other public hospitals (6.3%) and private hospitals (6.9%).[3] (Figure 3)

Figure 3. Proportion of the Thai pharmacy workforce in 2016[3]



Pharmacy Education System

Production of pharmacist manpower is an important duty of a school of pharmacy. The Pharmacy Council of Thailand monitors quality assurance by setting professional standards, certifying pharmacy curricula, and licensing pharmacist practitioners to meet the needs of society. The Office of the Higher Education Commission, Ministry of Higher Education, Science, Research and Innovation supervises the management requirements of educational quality assurance.

Currently, there are a total of 19 schools of pharmacy that are accredited by the Pharmacy Council. There are 14 public institutions and 5 private institutions distributed in every region of the country, with most concentrated in Bangkok and the metropolitan area (Table 1). The pharmacy program is a 6-year

Table 1 List of 19 Faculties of Pharmacy in Thailand and number of graduates in 2019[5]

Region	Faculty of Pharmacy (year established)	Type	Track[A]	No. of graduates in 2019
Northern (4)				
Chiang Mai	Chiang Mai University (1964)	Public	C, I	152
Chiang Mai	Payap University (2005)	Private	C	51
Phitsanulok	Naresuan University (1992)	Public	C	85
Phayao	University of Phayao (2008)	Public	C	73
North Eastern (3)				
Khon Kaen	Khon Kaen University (1980)	Public	C, I, SAP	132
Ubon Ratchathani	Ubon Ratchathani University (1993)	Public	C, I	96
Maha Sarakham	Mahasarakham University (1996)	Public	C	92
Sounthern (2)				
Songkhla	Prince of Songkla Unviersity (1978)	Public	C, I	133
Nakhon Si Thammarat	Walailak University (2005)	Public	C, I	53
Central (10)				
Bangkok	Chulalongkorn University (1914)	Public	C, I	156
Bangkok	Mahidol University (1968)	Public	C, I	121
Bangkok	Siam University (2006)	Private	C	56
Nakhon Pathom	Silpakorn University (1985)	Public	C, I, SAP	165
Nakhon Nayok	Srinakharinwirot University (1996)	Public	C, I	83
Chon Buri	Burapha University (2009)	Public	C, I	84
Pathum Thani	Thammasat University (2013)	Public	C, I	20
Pathum Thani	Rangsit University (1987)	Private	C, I	151
Pathum Thani	Eastern Asia University (2008)	Private	C, I	54
Samut Prakan	Huachiew Chalermprakiet University (1993)	Private	C, I	104

[A]Note: C=Pharmaceutical care track, I=Industrial pharmacy track, SAP=Consumer health protection or Social and administrative pharmacy (SAP) track

program (Pharm.D.) with three main specialization tracks: pharmaceutical care (PC), industrial pharmacy (IP), and consumer health protection or social administrative pharmacy (SAP). Each year, the production capacity of approximately 1,900 pharmacists in proportion of the three specialization tracks is around 6:3:1, respectively.

To develop specializations in a post-graduate degree, the Pharmacy Council has established pharmacy colleges to strengthen professional expertise of pharmacist practitioners. The College of Pharmacotherapy of Thailand (C.Ph.T.), the College of Pharmaceutical and Health Consumer Protection of Thailand (CPHCP), and the College of Herbal Pharmacy of Thailand (C.H.P.T.) are three post-graduate colleges currently available. Their main responsibilities are to establish and control academic standards in the pharmacy profession, to provide post-graduate training, and to promote research and academic guidance in each specialization (www.pharmacycouncil.org). Table 2 shows the total number of post-graduate pharmacists from these three colleges.

Situations of the pharmacy workforce

The situations of pharmacist manpower in the pharmaceutical system under the effective coverage framework of AAAQ is presented below.

Availability of pharmacists

As of August 31, 2019, the total number of registered pharmacists was 42,060 people.[17] However, in the pharmaceutical labor market, approximately 29,000 pharmacists are actually working.[3] There are approximately 1,700 -1,900 pharmacist graduates per year and more than 90% pass the licensing exam. Throughout the past 30 years, the number of annual pharmacist graduates has increased 3.8-fold, from 487 graduates per year in 1990 to 1,861 graduates per year in 2019.[17]

The dramatic growth of pharmacist graduates resulted from several factors, such as the increased number of pharmacy schools and graduates produced. Historically, the urgency to increase the pharmacist workforce was due to Thailand's health policies to achieve full coverage of district hospitals where workforce development is essential for well-functioning

Table 2 Total number of specialized post-graduate pharmacists trained from colleges under the Pharmacy Council of Thailand (September 2019)

College (year established)	Short course training certificate	Board certificate
College of Pharmacotherapy of Thailand (C.Ph.T.) (2008)	General residency (1st year), 126 persons Specialized residency (3rd year), 81 persons	81
College of Pharmaceutical and Health Consumer Protection of Thailand (CPHCP) (2011)	309 persons (423 certificates)	106
College of Herbal Pharmacy of Thailand (C.H.P.T.) (2018)	-	18

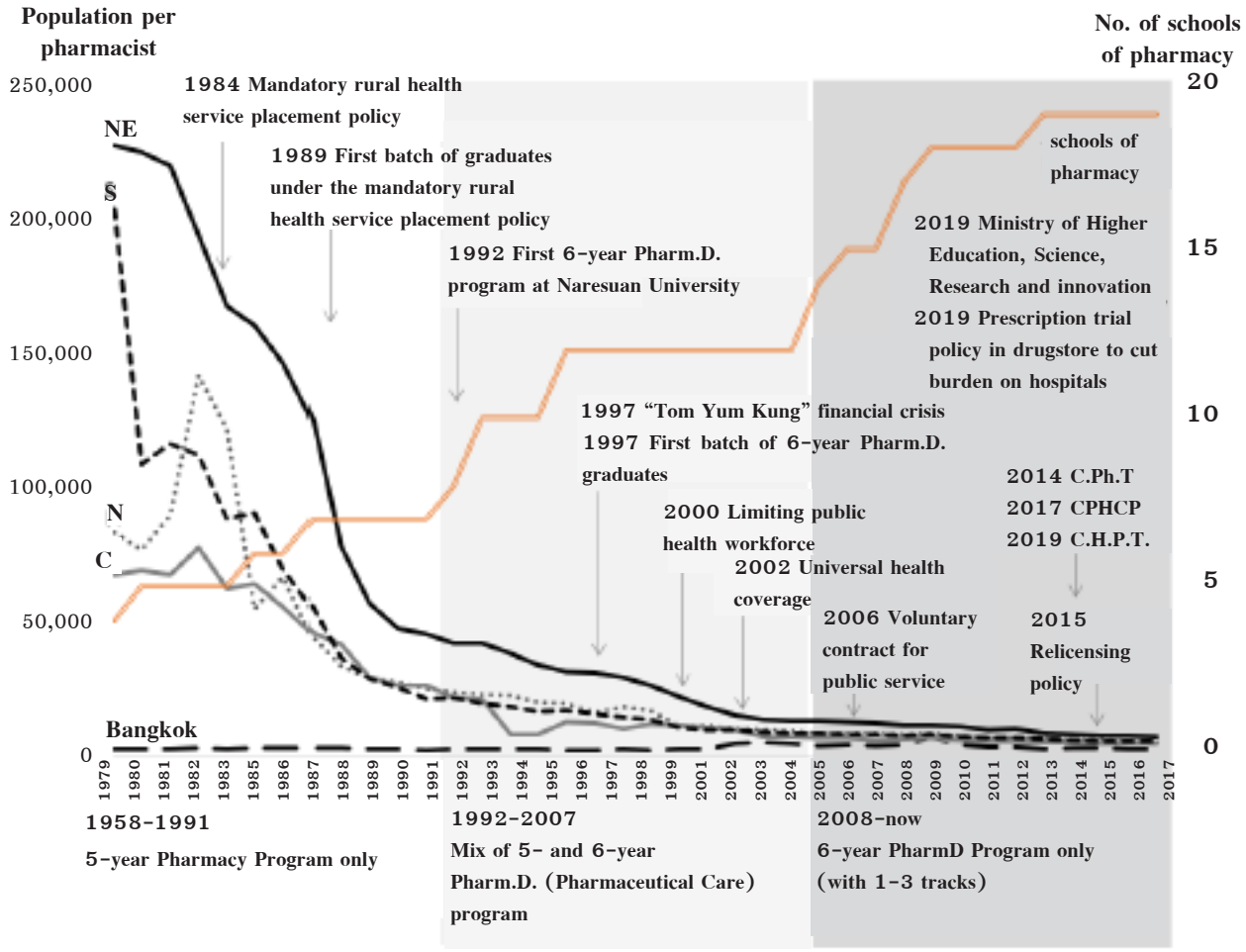
health services under the system.[14] In 1984, the Ministry of Public Health (MOPH) introduced a 2-year mandatory placement in rural health service for all pharmacy students. The mandatory policy and additional financial and non-financial incentives drew a large portion of the pharmacy workforce to public hospitals, which resulted in increased numbers of pharmacists in Thailand. In 2006, the policy was changed from mandatory to voluntary and only those who were willing to work for the MOPH and some other government facilities participated in the service placement.

Accessibility of pharmacists

In 2016, there were 28,896 pharmacists, which is equivalent to 1:2,261 pharmacist per population.3 The ratio was still below the target of 1:2,000 pharmacist per population according to the 20-year national health strategic plan.2 Before the mandatory rural health service placement policy, there was a disparity in pharmacist distribution by region in terms of urban and rural areas. After the policy requiring pharmacist graduates to work in rural district hospitals, the disparity narrowed (Figure 4).[5,18,19]

Although there has been no problem of pharmacist

Figure 4 Population per pharmacist, by region and number of schools of pharmacy (1979-2017)



manpower distribution in government services, there is still a labor shortage of pharmacists in the pharmaceutical industry; about 16% of pharmacists work in industry, such as in manufacturing, distribution, and marketing. The pharmaceutical industry needs more pharmacists to register new products, renew old product licenses, and endorse new products to a variety of target audiences.[20,21]

Restrictions on increasing manpower in the government sector and the MOPH's new health services management plan to offer patients with chronic conditions to fill their prescriptions at nearby community pharmacies would increase employment at community pharmacies. Providing pharmaceutical care services may require more than one pharmacist on duty per pharmacy.[3] To ensure increased accessibility to pharmacist manpower for better access to quality and safe use of medicines, pharmacy workforce planning should focus on ensuring even distribution to both private and public sectors.

Acceptability of pharmacists

To our knowledge, information on the acceptability of pharmacists is limited. There have been studies on customer satisfaction of pharmaceutical services in hospitals or community pharmacies, but not on the pharmacists themselves.[22-28] From limited literature, it is suggested that clients and other healthcare professionals recognize the value of the pharmacist from the quality of services provided to the characteristics of the pharmacists themselves.[29,30] For instance, trust in and reliability on pharmacists are developed from empathy and understanding.[28]

Quality of pharmacists

The Pharmacy Council ensures quality of pharmacists through several processes: certifying pharmacy curricula, developing professional competency standards, conducting pharmacy national licensing exam for new graduates, and requiring practicing pharmacists to earn at least 100 credits of continuing education within 5 years.[31] Continuous adaptation of pharmacy education to match the health needs of Thais is crucial for ensuring quality of pharmacist services. Self-assessments of pharmacy graduates show that transition to a 6-year PharmD program with three specialization tracks (PC, IP, and SAP) helps build confidence in competencies of their specialization.[32] However, information regarding the quality of pharmacist practitioners is also limited since it was not systematically evaluated.

Despite the above post-graduate programs, only 1.6% of pharmacists in the Ministry of Public Health took a leave of absence for further studies while 82% hold a bachelor's degree as their highest degree level. Compared with the medical and dental professions, the proportion of physicians and dentists that took leave for further education is up to 20% and 12%, respectively, while 43% and 24% hold a bachelor's degree, respectively.[33,34]

Challenges in the Thai Pharmacist Workforce

Four key challenges currently exist in the Thai pharmacist workforce. The first challenge is the changes in the pharmaceutical labor market. Due to the policy of limited employment in the public sector, job positions in public hospitals, which have been the main workplaces for pharmacists, will be greatly reduced. With limited practicing pharmacists, there has been an increase in the need for pharmacy services to ensure rational drug use, support service plans, and improve pharmaceutical systems management in hospital ac-

creditation. Pharmacists currently working in public sectors will need to manage their limited time carefully and efficiently.

The second challenge relates to a lack of integrated human resource development plans for pharmacists in all sectors. Currently, pharmacy education focuses on the production of pharmacists for the hospital sector. However, it is more likely that job positions for public hospitals will be limited, while there is a demand for pharmacists in community pharmacies, primary healthcare, and industry. Therefore, professional leaders and educators should work together to plan and balance the professional workforce for the future.

In order to be competent to serve changing health demands, pharmacists need expertise in their area. Current competency standards set by the Pharmacy Council are only the minimum performance required and serve as entry level competencies. For career advancement, continuous human resource development for the profession is needed.

The third challenge relates to supporting systems for manpower development. Pharmacists are a valuable workforce for pharmaceutical systems, but with limited budget, additional pharmacists increase fixed and long-term labor costs. Therefore, in an age of advanced technology, adoption of robots and computer technology to work collaboratively with personnel would improve the efficiency of workforce management.

The final challenge is a lack of a harmonized database and limited research in pharmacist manpower. Accurate, up-to-date, and comprehensive information is essential for planning and decision-making. A database of pharmacist manpower that systematically maintains information on both manpower production and the demand side, and for both public and private sectors is needed.

Opportunities for pharmacist workforce transition

Solutions for the challenges mentioned above require the cooperation of professional leaders and stakeholders of all sectors to analyze the situation and formulate strategies and policies for pharmacist manpower management. The goals for manpower development should be clear with flexible working plans that are adjustable to the rapid change of social and health contexts.

Short-term plan (1 year)

- Invest in a comprehensive database to gather data on all dimensions of the pharmacist workforce and relevant personnel information;
- Plan for long-term pharmacist manpower management by carefully and systematically making joint decisions between professional organizations in all sectors;
- Provide short-course training programs to improve competencies of pharmacists and support personnel to develop professional skills that are currently needed; and
- Revise professional competency standard that allow expertise development.

Intermediate-term plan (2-5 years)

- Develop professional training for new and upcoming roles of pharmacists, such as pharmaceutical care services for patients with chronic conditions at community pharmacies, pharmaceutical systems management in primary care clusters, and data and information management;

- Use computerized technologies and work with supporting personnel to efficiently manage basic pharmaceutical activities of pharmacists in the pharmaceutical system, such as stock control and dispensing, to allow pharmacists to work on advanced professional activities, such as designing and developing pharmaceutical systems; and
- Strengthen pharmacists' roles in pharmaceutical systems in designing and participating in innovative healthcare activities and policy development.

Long-term plan (6-10 years)

- Professional organizations, the Pharmacy Council, educational institutions, and pharmacist practitioners should take this opportunity to reform pharmacist manpower;
- Use comprehensive workforce information to design workforce development systems to support access to medicines in every dimension;
- Design professional activities that support the pharmaceutical system in accordance with the needs of society and the context of the country;
- Design pharmacy education programs and post-graduate programs to support manpower development that meet the needs of the future.

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บทคัดย่อ: กำลังคนเภสัชกร: โอกาสการผนึกกำลังวิชาชีพเพื่อตอบสนองต่อความต้องการทางสุขภาพที่เพิ่มขึ้น

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ความต้องการด้านบริการสุขภาพของประเทศไทยอยู่ในการเปลี่ยนแปลงสืบเนื่องจากการเปลี่ยนแปลงของสังคมทั้งในประเทศ และกระแสการเปลี่ยนแปลงของโลก บริการสุขภาพของประเทศซึ่งมุ่งหวังให้เกิดความเท่าเทียม มีประสิทธิภาพ มีคุณภาพ และ มีความต่อเนื่องจะเกิดขึ้นได้ด้วยความพร้อมและความร่วมมือกันของกำลังคนด้านสุขภาพ เภสัชกรซึ่งเป็นกำลังคนด้านสุขภาพที่รับผิดชอบต่อการเข้าถึงยาของประชาชนก็ต้องมีการปรับตัวเช่นเดียวกัน ในอดีตการศึกษาเภสัชศาสตร์มีการพัฒนามาอย่างต่อเนื่อง มีจำนวนสถาบันที่ผลิตเภสัชกรเพิ่มมากขึ้น บัณฑิตเภสัชศาสตร์ที่ผลิตขึ้นต่อปีก็เพิ่มมากขึ้น หลักสูตรมีการปรับตัวจากการเรียน 5 ปี เป็น 6 ปีที่มีสาขาความเชี่ยวชาญเฉพาะที่จะตอบสนองกับความต้องการของตลาดแรงงาน แต่อย่างไรก็ตามการเปลี่ยนแปลงที่รวดเร็วของสังคม ในขณะที่การขาดข้อมูลด้านกำลังคนเภสัชกรของประเทศไทย เป็นความท้าทายที่ผู้นำของวิชาชีพ สภาเภสัชกรรม สถาบันการศึกษา และสภาวิชาชีพด้านต่าง ๆ ควรผนึกกำลังกันออกแบบการทำงานเพื่อพัฒนากำลังคนเภสัชกรระยะยาวอย่างต่อเนื่อง เพื่อให้มันใจว่าเภสัชกรจะสามารถมีสมรรถนะอย่างเหมาะสมสำหรับการทำงานในปัจจุบันและอนาคต.

คำสำคัญ: กำลังคนด้านสุขภาพ; เภสัชกร; บุคลากร; วิชาชีพ

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International Trade Agreements and Impact on the Medicine System: Causal Relations?

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Abstract This article comprehensively reviews and analyses knowledge and information relating to international trade agreements and their implications during the past 17 years, both within and external to Thailand. To reveal the implications and impact systematically, the conceptual framework for analysis was drafted and the implications were mapped along the medicine value chain. The mapping shows cross-link of the implications and took concerns of health sectors. Focusing on medicines, despite of positive impact, international trade agreements have had significant negative impacts on the Thai medicine system. There is worldwide recognition that expensive prices and higher expenditure of medicines result from the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS); this research identified further implications including: the opening up of market access to government procurement and limitations on policy space for medicine management systems as well as public health. This paper also demonstrates the experiences of Thailand, India and Malaysia regarding TRIPS flexibilities. It was shown that all three countries exercised "other use without authorization of the right holder", which is a TRIPS flexibility, to strike the balance between individual right and obligation in access to affordable essential medicines, although difficulties and consequences were found in the process of exercising this right. Evidence shows that Thailand, as a developing country, may support the voluntary license but must keep all TRIPS flexibilities, including the compulsory license, as tool to overcome barriers to access and ensure the human right to health. Further system research as well as investigation of cross-country impact of FTAs in and among ASEAN members are recommended.

***Keywords*: international trade agreement; implication; impact; medicine; expenditure; compulsory license; government use of license; voluntary license**

Introduction

Economic growth is the backbone of a country's development and income generation is a source of government budget to support all aspects of development including health. One popular strategy many countries favour in driving economics and trade is through international trade agreement. As an international law, parties are bound to FTA commitments, which have measures and punishments. The agreements traditionally aim to support export industry and business by setting concrete trade rules, access to other markets and removal of trade barriers through tariff and non-tariff measures. It was found, however, that the new generation of agreements is beyond trade in goods, and is comprehensive and ambitious. It broaden trade issues to include the protection of investors; setting higher standards for sanitary and phytosanitary measures; setting higher standards of labour; promoting protection of the environment; regulating the legislative process of government policy regarding transparency and participation; increasing access to government procurement and removing the offset of state owned enterprises, according to fair competition and access to other market; extending the rights and market exclusivity of intellectual property, and so on.[1-3] FTAs containing these issues are probably not new for developed or high-income countries, but they are the new generation of FTAs for developing or middle-income countries including Thailand.

Recently, Thailand elected a new government which recommended a policy of pursuing pending and new trade negotiations.[4] This article aims to reveal the following: (1) the implications for and impact on health of the new generation international trade agreements; and (2) how some countries including Thailand exercised the right of TRIPS flexibilities to mitigate the long-term impact of TRIPS in the area of access to medicines as an important issue of a building block of a well-functioning health system.

This article reviewed the following: literature, both published and grey, on trade agreements and impact on medicine; press releases and news of key government organizations and relevant stakeholders and civil society organizations such as Third World Network, Medicins Sans Frontieres; newspapers in Thailand and Malaysia; publicly published international trade agreements; and legal instruments, both international and national.

As mentioned in the study's objectives, this article includes two key topics:

1) The implication and impact of international trade agreements on medicines, including and beyond the TRIPS Agreement (or TRIPS Plus), along the medicine value chain which is a key product and function of a health system. TRIPS allows monopolistic power and it was realized that this had an effect on the price of medicines.[5] In addition, the magnitude of the impact on market exclusivity in Thailand and the overview of the impact of TRIPS mentioned.

2) Experience from three countries on the use of TRIPS flexibilities. TRIPS provide tools or "TRIPS flexibilities" for countries to protect public health and diminish inaccessibility to medicines.

3) The attempt of Thailand, India and Malaysia to make use of such flexibilities (patent use by third parties) to improve access to medicines in accordance with their national laws.

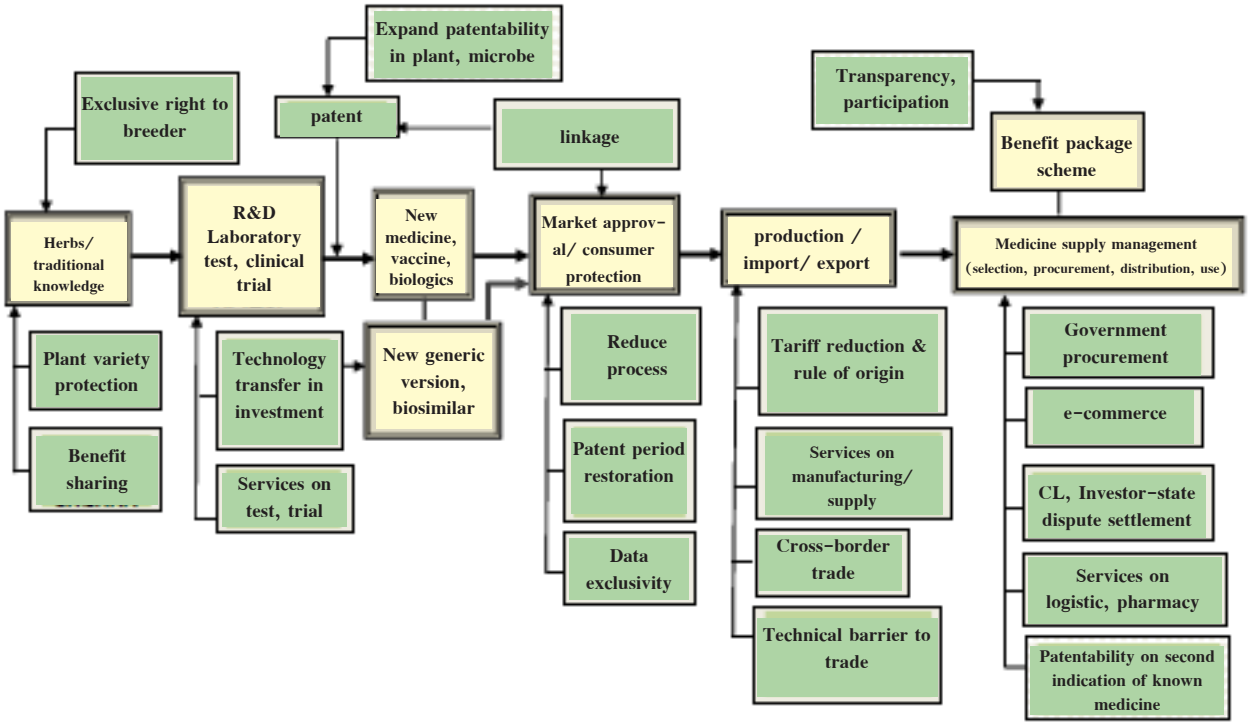
1. Implication and impact of international trade agreements on medicines

This topic illustrates the conceptual framework of and explains on the implication and impact of the new generation of trade agreements along the medicine value chain. The framework was developed from comprehensive and systematic analysis on the content of updated plurilateral agreements; i.e. the International Union for the Protection of New Varieties of Plants (UPOV) 1991 Convention, Government Procurement Agreement (GPA) and FTAs (CPTPP including some international investment agreements) that Thailand has signed or shows interest in signing. The first author drafted and matched the implications found along the medicine value chain.[6] Co-authors reviewed first, followed by experts with various pharmaceutical expertise. The implications were identified from the text of the agreement where either the terms "pharmaceutical", "medicine", "biologic", "vaccine", "health", "Doha Declaration", "TRIPS" were stated; they were interpreted in relation to the implications found in the literature as well as in Thai health policies such as Universal Health Coverage,[7] Medicine System Development and Strategy B.E.2560-2564 and Access to medicines strategy[8] and international reports such as Promoting innovation and access to health technologies,[9] and Access to Medicines from the Health System Perspectives.[10]

Implications were found in all steps along the medicine value chain (Figure 1). Starting with the fundamentals of Research and Development (R&D) for new medicine the following implications were found:

1) Resources (e.g. herbs) are affected by the UPOV 1991, the right of breeder in new plant varieties are protected with a system similar to patent.

Figure 1 Implication of international trade agreements on the value chain of medicine



However, traditional knowledge and genetic resources is subjected to benefit sharing.

2) In R&D, the technology transfer is not able to require as a condition for foreign investment. Services on R&D services are required to be supplied by foreigners without discrimination.

3) The patent system is broadened in the patentability of microbes and plants. The patent filing is linked to the process of marketing approval of generics. An inefficient patent linkage system could delay price competition in generics and delay access to cheaper medicines as a consequence.

4) The trade agreements aim to do the following: limit the policy space and to gain the involvement of stakeholders in policy formulation; shorten and regulate pre-marketing control; extend market exclusivity through patent term restoration and data exclusivity.

5) Once the medicine gets marketing approval, imported medicine as both raw material and finished product enjoys the positive impact of the international trade agreement, i.e. tariff reduction. Unfortunately, it needs to comply with the rule of origin. On trade in services, manufacturing and distribution is open for foreign business and fair competition. A country is required to decrease technical barriers to trade and also facilitate cross-border services.

6) In the medicine supply management cycle (selection, procurement, distribution and use), the trade agreements aim to access government procurement sector with removing the privilege support for Thai business, regulate the data management of e-commerce, limit the use of compulsory license on patent medicines.

Exercising rights is prone to investor-state dispute settlement. Logistics services and pharmacies (drugstores) are open for providers from other parties of the agreement. The patentability and exclusive right on the new use (or indication) of known medicines is available and protected, respectively.

Due to strong patent protection and lower capacity in upstream R&D through innovated medicines in commercial use than developed countries, Thailand relies on imported medicines. This is shown in the major proportion of consumption value, especially of biological products. The impact of international trade agreements on market exclusivity has therefore been assessed. It was also quantified, especially the known issues that result in the extension of market exclusivity, such as patent term extension, patent restoration from the granting delay and the delay of marketing approval, and data exclusivity. On the basis of market exclusivity leading to monopoly power and no price competition by generics, finally it leads to the increase in medicine expenditure, health expenditure and inaccessibility to medicines once the budget for medicines is limited. Three studies quantified the magnitude of this market exclusivity extension for Thailand depending on the one- to ten-year period of extension inclusive of short, medium and long-term impact. In addition, the negative effects of data exclusivity (DE) were quantified. All are stated elsewhere and beyond the remit of this article.[11-13]

2. Use of TRIPS flexibilities: experiences from three countries

However, since the TRIPS provide TRIPS flexibilities, countries must also comply their national law with the flexibilities. The second part of this article reviews the use of TRIPS flexibilities in three countries in which legal systems were differently designed and

exercise the rights according to TRIPS; their legal frameworks and the essence of using such tool is noteworthy. In Thailand, we look at the impact evaluation of issuing the compulsory license by government or government use of license (GUL); in India, the compulsory license (CL) by third party; and in Malaysia, the system design on data exclusivity and compulsory license in parallel with voluntary license.

A. Thailand: comprehensive monitoring and evaluation of compulsory license by government

Thailand issued the GUL on seven medicines, including antivirals for HIV/AIDS, anticancer medicines and anti-platelet aggregation between November 2006 and January 2008[14,15]. Table 1 shows the period of announcement of each medicine. This issuance drew attention from pharmaceutical companies who are the patent owners and their governments' trade representatives and embassies and raised policy questions of whether or not this GUL would have a negative effect on foreign investment and export. Hence, policy and health system research were conducted on various aspects on the impact of GUL policy. Immediate countermeasures from the United States of America government, in line with other intellectual property right protection issues, meant that Thailand was categorized in a Priority Watch List (according to the US 2007 Special 301 Report). As a result, exported commodities of Thailand in the Generalized System of Preferences (GSP) programme (one of the unilateral trade preference programme) had been withdrawn and could not enjoy the benefit of tariff-free trade and quotas from the GSP programme. On trade and economics,[16] the research reveals trends in short-term effect on firstly, the total export value of the products of Thailand by major import countries (Figure 2); and the export value of the commodities that were withdrawn from the GSP programme (polyethylene terephthalate in primary form (plastic), gold jewelry (jewelry) and flat screen colour television sets (colour TV)) shown in Table 2. In comparison with one year before and after issuing GUL, the export value of these selected commodities to the US declined. However, the export value of the same products to the rest of the world increased except colour TV. Secondly, concerning foreign direct investment (FDI) by major investor countries (Figure 3), during the period of the first quarter of 2005 to the third quarter of 2008, the trend in total export value of Thailand markedly increased. The study found a fluctuating trend of annual FDI value between 2005 and

Table 1 Medicine list and date of issuance the government use of licenses in Thailand

Group	Generic name	Issuing date
Anti-retroviral	Efavirenz (EFV)	29 November 2006
	Lopinavir/Ritronavir (LTV/RTV)	24 January 2007
Anti-platelet aggregation	Clopidogrel	25 January 2007
Anti-cancer	Docetaxel	4 January 2008
	Letrozole	4 January 2008
	Erlotinib	4 January 2008
	Imatinib (on condition)	4 January 2008

Source: Summarized from reference No. 14 and 15

Figure 2 Trend in export value of selected commodities

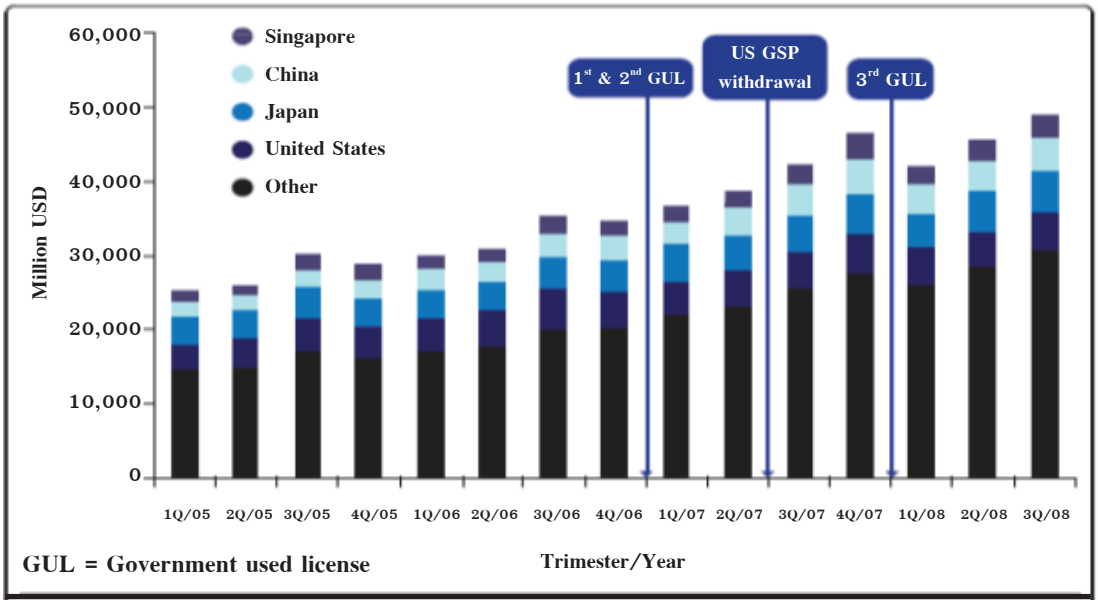


Table 2 Increased costs for US importers and changes in export value for products affected by withdrawal of GSP status (in million USD)

Product	Increased costs for US importer	Change in value of export between one year before and after US GSP withdrawal	
		US	Rest of the world
HS 3907.60.00 (Plastic)	0.4	-128	130
HS 7113.19.50 (Jewellery)	26	-220	723*
HS 8528.72.64 (Colour TV)	4.4	-40	-332**
Total	30.8	-388	+521

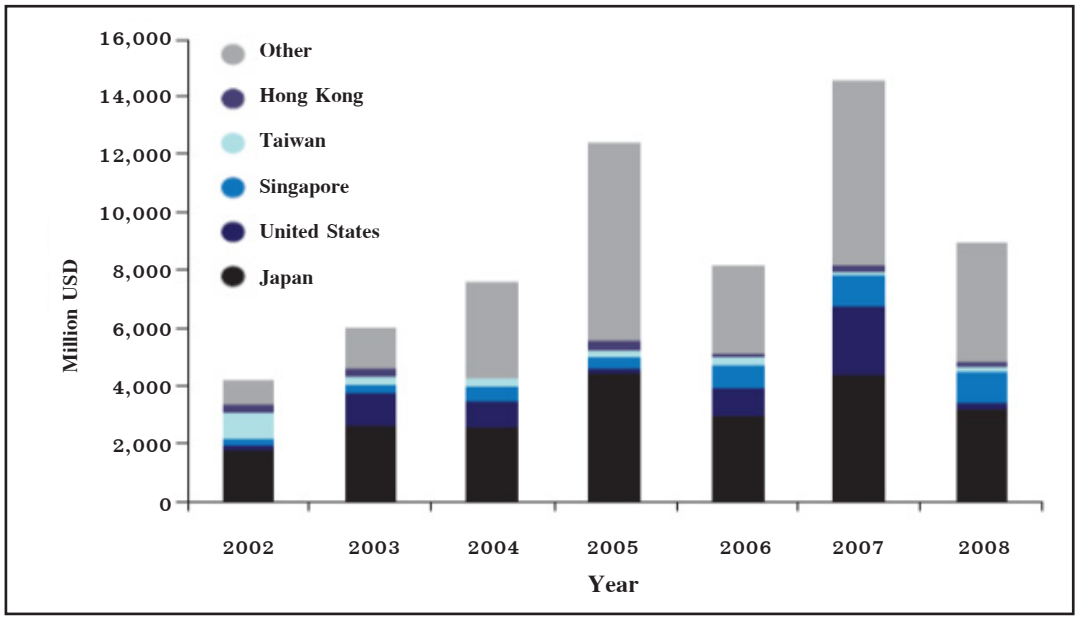
Remarks: * HS 7113.19
** HS 8528

Source: Table 4 of reference no.16

2008. The downward figures in 2006 and 2008 compared with the prior year were due to the political instability in Thailand and the world economic recession, respectively.

For overall health considerations, increase in access to essential and life-saving medicines is the ultimate goal. Saving the government budget is the subsidiary goal. The aforementioned study also estimated the number of patients that could access GUL medicines and their subsequent productivity that contributes to gross national productivity (GDP), deducted by public health expenditure.[16] Regardless of Erlotinib for which data was not completely available, the study found the net benefit of

Figure 3 Foreign direct investment of selected countries in Thailand



Source: Board of Investment of Thailand

the GUL medicines were greater than the alternative medicines. The incremental benefit of such medicines ranges from 2.3 to 67.0%. In addition, the National Health Security Office (NHSO) and Government Pharmaceutical Organization (GPO), which are the main implementors of this GUL policy, systematically collected the actual numbers of patients as well as the estimated budget saving (to get comparison between the price of generic version and the patented medicine) as shown in Table 3 and 4. The data shows that the cumulative saving in five years for all GUL medicines was USD 566.5 million. Later, the saved government budget from GUL was spent on access to non-GUL essential medicines for other diseases and patients.

Concerning policy, another study analysed and summarized the key to Thailand's success. With the synergy between three sides of a triangle - knowledge and evidence generation, mobilization of civil society and public sup-

Table 3 Numbers of patient accessed to selected GUL medicines

Year	Clopidogrel	Letrozole	Docetaxel
2009	5,556	0	321
2010	131,389	1,558	527
2011	76,586*	2,629	879
2012	88,000	1,330	1,439
2013	105,600	1,382	1,447
2014	126,720	2,282	2,893

Note: *indication and use was restricted since then

Source: Bureau of Drug and Medical Supply Management, National Health Security Office

Table 4 Comparing to patented medicines, saved budget (Million USD)

Year	Antiretroviral	Anti-platelet aggregation and anti-cancer
2010	27.3	3.4
2011	56.8	57.0
2012	74.6	37.7
2013	77.3	46.5
2014	88.4	73.3
5-year total saving	338.8	227.7

Source: Bureau of Drug and Medical Supply Management, National Health Security Office

port, and the leadership of politician and policy makers - the GUL eventually succeeded in policy formulation and implementation. The triangle refers to "the triangle that move the mountain" – a well-known conceptualisation of a philosophical and strategic approach to policy advocacy by Dr Prawase Wasi[17]. The first attempt by Thailand to use the GUL was in 1999 for Didanosine (DDI), a medicine for HIV/AIDS. However, at that time policy makers decided on alternative option.[17]

B. India: use of compulsory license by third party

The first use of a compulsory license on Sorafenib tosylate, indicated for patients with late stage hepato-cellular carcinoma (HCC) and renal cellular carcinoma (RCC), sold in India. This innovative medicine had patented in India, held by Bayer Corporation (Bayer), and was launched into the Indian market in 2008. The cost of treatment per patient per month was USD 4,559 (INR 280,000) and Bayer provided the patient assistance programme (PAP) with conditions. In accordance with the Patent Act and regime on the use of CL, a private generic-version manufacturer, Natco Pharma Ltd (Natco), submitted the request for the voluntary license (VL) from the patent owner, Bayer on 6 December 2010. However, the application was refused on 27 December 2010, so the CL process was started by Natco's submission on 29 July 2011 on three grounds of the Patent Act Section 84(1). The Controller General of Patents (Controller) of India filed this prima facie case from the evidence and proposed conditions submitted by Natco.[18-20]

It should be noted that the Section 84(1) of the Patent Act allows any person interested to make an application after 3 years after the date of patent grant and on 3 grounds (a) that the reasonable requirements of the public with respect to the patented invention have not been satisfied, or (b) that the patented invention is not available to the public at a reasonably affordable price, or (c) that the patented invention is not worked in the territory of India. Section 85(5)(iv) also insists that prior to CL application that applicant should make efforts to obtain a license from the patentee on reasonable terms and condition (6 months is provided as a reasonable time period)[18].

After careful consideration, the Controller granted CL to Natco on 9 March 2012 with 13 terms and conditions and including: setting the price of Sorafenib generic version to no more than USD 176 (INR 8,800) per patient per month; reporting the details of

sales to the Controller and licensor on quarterly basis; having the right to manufacture the medicine covered by the patent only at its own manufacturing facility with no outsourcing; paying royalties at the rate of 6% of net sales; ensuring the granting license is solely for making, using, offering to sell and selling the medicine for treatment of HCC and RCC in patients within the Territory of India; supplying medicine for 600 needy and deserving patients per year free of cost; have no right to import medicines covered by the patent; ensuring licensed medicine is visibly distinct from the patented one including the trade name and packaging.[21]

Submissions and argument of the applicant and opponent for CL, and the decision of the Controller can be found elsewhere.[21] The case was not yet finished, with the patent holder appealing the granting; however the Intellectual Property Appellate Board (IPAB), Chennai rejected it in March 2013.[22] Later, Bayer challenged the Controller's decision and IPAB's order through the Bombay High Court where his Writ Petition was dismissed in July 2014.[23]

This first CL of India is important because it set a precedent for future CL in accordance with the three grounds of CL granting. It has a view on the balance between right and obligation includes (a) the reasonable requirement of the public with respect to the patented invention has not been satisfied; (b) the patented invention is not available to the public at a reasonably affordable price; (c) the patented invention is not available in the territory of India. It could also encourage Indian generic manufacturers who have increasingly felt that the legal risk and uncertainty of the patent system prevents the production of generic versions of newer medicines.[19]

C. Malaysia: use of GUL and VL at one time

Introduced in late 2013, countries and the World Health Organization recognised new medicines in the group of direct-acting antivirals (DAA) which is a highly effective treatment (95% cure rate) with less adverse reaction and less treatment duration (8-12 weeks) for chronic Hepatitis C (HCV) than the current treatment medicines which is the combination of Pegylated Interferon injection and oral Ribavirin for 24-48 weeks, with 50% cure rate[24]. However, the first oral form of medicine of the group Sofosbuvir, the backbone of the treatment and needs in combination with another DAA, is excessively high in price at USD 84,000 (RM 0.3 million or THB 2.5 million) per patient per cost of treatment. The prices triggers the problem of access to medicines worldwide because of unaffordability for patients and governments, even in its originated country[25, 26]. Therefore, the global target of eliminating HCV as a major public health threat by 2030 set in the Global Health Sector Strategy on Viral Hepatitis 2016-2021 and adopted in World Health Assembly 2016, would be out of reach.[25,27]

The patent holder, Gilead Science (Gilead) had responded to the worldwide concern on price and availability with strategies on tiered pricing and voluntary generic licensing. Later, it was announced in September 2014 that the company gave voluntary licenses for 91 developing countries and license agreements to 7 generic manufactures based in India in 2014. This campaign of the patent holder allowed the generic manufacturer to supply generic versions which would be expected to sell for significant lower prices in certain countries in the list.[28] This binding, the other way round, limited those generic manufacturers to be unable to supply the generic version to non-listed countries, including China, Brazil, Egypt, Belarus, Thailand, Malaysia, Indonesia and Russia. This announcement

was interpreted as a preemptive move to gain momentum, after a series of patent oppositions in some countries, and prevent effective independent market competition.[29]

Countries that aim to eliminate the disease but were not in Gilead's VL list, such as Thailand and Malaysia, can provide the highly effective DAA, especially Sofosbuvir, at a cheaper medicine price by negotiation with the patent holder. Alternatively, countries can make use of TRIPS flexibilities such as other use without authorization of the patent holder or CL.

With the price of RM 0.3 million per person per treatment course and an estimated 500,000 infected patients, Malaysia, in 2017, issued the CL by government or GUL. Certainly, the preparing phase would be started at least several months beforehand. The Malaysian cabinet approved GUL on 14 September, although Gilead expanded the VL list to include Malaysia, Thailand, Ukraine and Belarus from 24 August 2017[30,31]. GUL would support an expected 400,000 patients in public hospitals and maintain the competition with VL[32]. The GUL Sofosbuvir would be imported from an Egyptian manufacturer in combination form and the VL from India. At the time of the announcement, GUL medicine had been in clinical trials for marketing approval and provided free of charge to HCV patients.[31,33] Malaysia also took this opportunity to fight hepatitis C and issued GUL to improve collaboration among stakeholders and to have South-South collaboration between generic manufacturers of Malaysia and Egypt for medicine combination.[34] It is believed that the GUL supported Gilead's policy on expanding the VL to include Malaysia and three other countries.

Regarding data exclusivity (DE) for the CL, Malaysia issued the Directive on DE under the Control of Drug and Cosmetic Regulation 1984 and it came into force on 1 March 2011. In general, only two types of new medicines could be submitted for DE: new chemical entities and new indication of registered medicines. Within the scope and according to several conditions, the DE could be granted. The Directive indicated two circumstances in which DE cannot be applied for: issuing the CL and a government's necessary action to protect public health and others.[35]

Discussion

This review explores the implication and impact of the new generation of international trade agreements along the medicine value chain, which is complicated and complex. It has advanced the ways in which to define the scope of the impact and cross-cutting issues; for example, the impact of government procurement is not only related to the budget and expense of government but also to the impact on local pharmaceutical manufacturers. Currently, the government procurement law provides privilege to local manufacturers. If the privilege is removed, taking into account different sizes of businesses, it was anticipated that local manufactures could not compete with foreign ones. Finally, without any promotion, the local business would be lost and withdrawn from the market, and Thailand would rely on importation. As a result, evidence on the impact of FTAs and quantifying their magnitude can help to develop negotiated strategies and set compensation for any negatively affected sectors.

With respect to the three country cases, the review gives a sense of the difficulties that countries face when exercising their rights, although they are supported by TRIPS Agreement and countries have full legitimacy. From a health perspective, patients have equity in their right to health, regardless of whether they are the

poorest or better-off. In other words, they have the fundamental right to access essential medicines without any financial barriers. So, with the use of the TRIPS flexibility, CL is one measure to overcome issues of access to essential medicines. Monitoring and evaluation of the impact, as shown by the experience of Thailand, could notionally provide evidence of short-term impact on economics (importation and investment), the ultimate goal of GUL (access for patients), and government expenditure. However, information about the long-term impact is required.

The lesson learned from India concerns the CL by a third party. The private local pharmaceutical producer requested for the provided right to comply with country's patent law. It was mandated that the patented medicines must properly contribute to the publics, e.g. access to affordable medicines in the territory that the patent covered. In addition, both the patentee and the third party have rights to propose and oppose on opposite sides with supported evidence. The fairness and balance of the right of the individual and the obligation to public health, considered by the 'middleman', was markedly observed. The system provides the opportunity to express different views, including authorized organization within the patent system and court. However, the most important consequence was that the process for CL took a long time of several years; three years after the patent was granted, plus the request for VL, plus the process of CL, plus appeal. In this regard, the applicant for CL and the patent office must be firm on the goal and knowledge on patent law, health and pharmaceuticals. Other countries, such as Thailand which has never used the CL by a third party, should explore the legal system on a similar matter.

In the third case, the Malaysian government issued the GUL while the pharmaceutical company provided VL during the same period of considering the GUL. Even though VL was offered the government had not abolished the GUL for a few reasons, particularly as it provided an environment of price competition and relied on more than one source of medicines (Egypt, rather than India alone) which resulted in better security in medicine supply. In addition, nationwide patients in public health facilities can get GUL medicine, while VL medicine is only available in private facilities. The effects on price competition should however be monitored.

Finally, although all three countries used the CL and complied with international and national law, the U.S. unilateral preference system considered that its intellectual property (patent) was not protected efficiently. Countermeasures, therefore, were exercised and Thailand and India were categorized into the Priority Watch List of the Special 301 report while Malaysia had been under consideration, as stated in the 2019 Report.[36]

Recommendations

Focusing on Thailand, the voluntary license can be considered as a useful tool, but all TRIPS flexibilities including compulsory license must be continued as the public has the right to health, and this is a tool to overcome barriers to access. Regarding CL by a third party, Thailand should explore the method and process for using it. Both VL and CL might strengthen the transfer of technology covered by the patent to local R&D and build the capacity of Thai pharmaceutical manufacturing. More system research is needed as well as investigation of cross-country

impact regarding FTAs of and among ASEAN members. This is due to the trend in regional and bilateral FTA and the concept of the global supply value chain; many countries have lots of international trade agreements, resulting in cross-country impact.

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บทคัดย่อ: ความตกลงการค้าระหว่างประเทศ และผลกระทบต่อระบบยา: เหตุและปัจจัย?

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บทความนี้ทบทวนความรู้อย่างรอบด้านและวิเคราะห์ความตกลงการค้าระหว่างประเทศ และผลกระทบหรือประเด็นที่เกี่ยวข้อง ด้วยข้อมูลทั้งในไทยและต่างประเทศย้อนหลัง 17 ปีนับจากปี 2562 เพื่อให้เห็นผลกระทบอย่างเป็นระบบของความตกลงการค้าระหว่างประเทศตลอดห่วงโซ่คุณค่ายา ซึ่งการระบุประเด็นผลกระทบดังกล่าวนำมาซึ่งความห่วงกังวลอย่างมากต่อผลที่จะเกิดขึ้นต่อประเทศไทย แม้ว่าจะมีผลกระทบด้านบวกอยู่บ้าง แต่ผลกระทบด้านลบต่อระบบยามีมากกว่า โดยเฉพาะประเด็นจากความตกลงการค้ายุคใหม่ นอกเหนือจากประเด็นผลกระทบต่อราคายาที่แพง และค่าใช้จ่ายด้ายยาที่สูงขึ้นจากความตกลงทริปส์ซึ่งเป็นที่ทราบกันดีทั่วโลกแล้ว ยังมีผลกระทบจากประเด็นอื่นอีก เช่น การเปิดตลาดด้านการจัดซื้อจัดจ้างภาครัฐ การจำกัดการกำหนดนโยบายด้านการบริหารจัดการระบบยาและนโยบายด้านการสาธารณสุข เป็นต้น บทความนี้ยังได้นำเสนอประสบการณ์ของประเทศไทย อินเดีย และมาเลเซียในการใช้ข้อยืดหยุ่นของความตกลงทริปส์ พบว่าทุกประเทศใช้มาตรการการใช้สิทธิเหนือสิทธิบัตรเพื่อให้เกิดสมดุลระหว่างสิทธิส่วนบุคคลและพันธสัญญาที่มีต่อสาธารณะในการเข้าถึงยาจำเป็นในราคาที่จ่ายได้ แม้จะพบความยากในการใช้และเกิดผลกระทบต่อเนื่องตามมา จากความรู้ต่าง ๆ เหล่านั้นได้แนะนำว่า ไทยอาจสนับสนุนการให้สิทธิโดยสมัครใจ แต่จะต้องคงไว้ซึ่งข้อยืดหยุ่นทั้งหมดของความตกลงทริปส์ซึ่งเป็นสิทธิของประเทศและเป็นเครื่องมือที่จะช่วยแก้ไขปัญหาการเข้าถึงยา โดยที่การใช้จะต้องไม่ยุ่งยาก ไทยควรเพิ่มการศึกษาวิจัยเชิงระบบในด้านผลกระทบข้ามประเทศโดยเฉพาะจากความตกลงการค้าเสรีของสมาชิกและระหว่างสมาชิกอาเซียน

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Political Economy of Thailand Drug System: What Lessons Learned?

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Abstract The political economy, which explains the relationships between individuals and society and between markets and the state, have direct and indirect influences over the health and drug system. This article analyzed the influence of political economy on the drug system in Thailand, by reviews of relevant literature and drew a few lessons. As medicine is one of the four essential needs for human lives; in the era of absolute monarchy, medicines were used as a governing tool to gain loyalty and goodwill among the populace subjects. In the 1932 Siamese Revolution from absolute monarchy to a constitutional monarchy, medicine and public health were not one of the six policy pillars proposed by the Revolutionaries; however every government had given importance to the advancement of the public health system by expansion of public health facilities in every province, district and sub-district nation-wide. In parallel, extension of financial risk protection to the vulnerable population (such as the low income households, the disable, elderly and children under 12 years) and the formal sector public and private employees provided financial access by citizens. Until 2002 Universal Health Coverage was achieved for the whole population. In the Thai drug system; Thailand has followed western allopathic medicine since the time of major reform in the era of King Rama V (1853-1910). Thailand has been under the influence of western countries in terms of academia, business and politics. However various Thailand public health champions had boldly challenged these western influences using wisdom and courage. National List of Essential Medicines was adopted and effectively implemented following the principles recommended by the World Health Organization. Further national drug policies enforced the use of reference drug price for public procurement which contains drug expenditure and improves efficiency. The 1998 drug procurement scandal masterminded by politician was publicized by civil society organizations which led to prosecution and imprisonment. Additionally the pharmaco-vigilance was fully established to monitor adverse drug event and result in immediate withdrawal of certain medicines. Despite pharmaceutical industry filed a law suit to the Administrative Court to retract the withdrawal of Phenylpropanolamine; the court dismissed the case. Furthermore for public health emergency which requires the use of certain expensive patent drugs, with bold leadership, Thailand implemented the compulsory license through legal provisions by the Thai law in the height of political pressure from the US government and pharmaceutical giants. In contrast, the prohibition of excessive and irrational use of Glucosamine was brought to the Administrative Court by Civil Servant Association which, controversially, the Court had ruled its continued use. Drug policies emerged under

different political systems. For example, the National List of Essential Medicine and the reference drug price were established in the partial democracy, the Universal Coverage Scheme was launched in the full democracy, and the use of compulsory licensing was initiated by a coup d'etat government. The key deficiency is the lack of progress in pharmaceutical sciences and related disciplines which support research and development of new medicines or formularies; as more than half were imported finished products and all active pharmaceutical ingredients are imported. The Thai traditional medicine and herbal remedies are confined by a conservative mindset and at early stage of development.

Keywords: **political economy; health economic; drug system in Thailand**

Introduction

Economics is the study which involved the distribution of finite resources so that society gains the greatest benefit. Though at the early stages, Economic was a part of Social Sciences discipline, when making decision on social resource allocation which involved politics, a sub-branch of Political Economy gradually emerged. Economic study had become more of a science by itself, which then called Economics.[1]

Political Economy is a "superstructure" of society and often times it has either direct or indirect, positive or negative consequences on health of the population and health system at large. It is crucial and important to understand the process and outcomes of Political Economy on Thailand health system.

This paper analyzes various dimensions through a number of case studies of Political Economy of the Thai drug system through review of relevant literature as a primary source; and draws a few lessons.

Political Economy in Drug System

1. Historical background of political economy in drug system

Medicine is one of the four essentials (food, shelter, clothes and medicines) for human lives. In the era of absolute monarchy, medicine was used as a means to gain loyalty among the subjects. This was applied in the Ratanakosin era during the reign of King Rama I (1737-1809) where medicine knowledge were collected, distributed and transformed into inscriptions. Later during the reign of King Rama III (1788-1851) there was another monumental effort to assemble and distribute knowledge of medicine. Eventually older inscriptions were modernized under the govern of King Rama V (1853-1910).[2] In the 1932 Revolution (B.E. 2475), although public health was not one of the six policy pillars declared by the Kana Rasadorn (Revolutionaries), it was *de facto* recognized as a major policy and implementation by the Kana Rasadorn; where provincial hospitals were established in all provinces. Subsequently in 1977 policy towards a full geographical coverage of district hospital was initiated and accomplished in 1990, while full geographical coverage of health centre in all sub-districts was launched in 1992 and accomplished by 2001. Parallel reform towards financial risk protection expansion by targeting different population groups was launched since 1975 until Universal Health Coverage was achieved in 2002.

After the Second World War the world entered

into the Cold War era. Since the time of King Rama VI (1880-1925), Thailand chose to ally with the West including medicines, where the 1923 Medical Act (B.E. 2466) which also regulated pharmacists was adopted. The law that regulated medical products throughout its entire process was promulgated in 1967 (B.E. 2510). In 1974, the Consumer Protection Committee was established. This took place during the heroic structural reform of the Ministry of Public Health. The Thai Food and Drug Administration was established followed the United States (US) model of US Food and Drug Administration (FDA) though it was modified to fit the social norms and Thailand context.

The development of the drug system followed the same path of the West; it gave way to transnational corporations that sought to expand their influence and control over the drug system in developing country. However Thailand public health champions were able to face the challenges by using wisdom and courage. Efforts were made to develop a national essential drug list that was in line with the philosophy and principles of essential drug list proposed by the World Health Organization.

The national drug policy advocates the use of reference price for public procurement by all public health facilities throughout the country; it effectively contains medicine expenditure and improves efficiency. Furthermore the strong civil society had uncovered the drug scandal which involved politician and other high rank officials in the Ministry of Public Health, which led to prosecution and imprisonment. Once the public health emergencies which require costly medicine under patent protection; the government, with high leadership of Public Health Minister had successfully applied compulsory licensing in the height of harsh bullying and retaliation by the US government and its proxies pharmaceutical industry. Once information concerning the fatal complications of Phenylpropanolamine (PPA), a decongestant for cough and cold medications and weight loss products was revealed, the Thai FDA had swiftly withdrawn the product from the market and termination of registration. The Administrative Court had reaffirmed the legally correct action by Thai FDA of such withdrawal in the height of strong resistance by the self-interested group in the Medical Council. In contrast to the PPA case, however, the Comptroller Generals Department's prohibition of the excessive and inappropriate use of "ineffective" glucosamine for arthritis, was brought to Administrative Court by Civil Servant Association. The judiciary decided in favor of the plaintiff; ruling the Comptroller Generals Department, as defendant to cancel its administrative order; on the ground of the principle defined in the Constitution. The Department surrendered and did not appeal. All the aforementioned case studies related to political economy are analyzed and discussed at great length below in order to draw a few lessons.

2. Drug consumer health protection system

The US has a system and organization that efficiently protects the drug consumers, namely the Food and Drug Administration or FDA which was founded in 1937; before that time however there were continuous efforts to protect the distribution of drugs but the law was not accepted by the Congress. Corporations cite the spirit of freedom that was inscribed in the declaration of independence, that the US is the land of the freedom, where every man and

woman has the rights to live, freedom and to search for happiness. Manufacturers was interpreted they have freedom in the production and distribution of medicine, and citizens were free to choose whether or not they were willing to buy; the government has no duty in creating a mechanism that may inhibit any citizens' freedom.

This ideology last until the case of the Sulfa drug, which manufacturer used diethylene glycol as a solvent to produce Sulfa suspension, and was used by children. Elixir sulfanilamide was an improperly prepared sulfanilamide medicine that caused mass poisoning in the US in 1937 resulting in over 100 deaths of renal failure. These deaths had a strong association with the use of Sulfa and there were numerous non-fatal cases also suffered from kidney failure. It was discovered that diethylene glycol was highly toxic to kidney; this case convinced the Congress to pass the 1938 Federal Food, Drug, and Cosmetic Act, which established an organization US FDA to regulate medicines safety and quality products. It is clear that medicine is a sophisticated technology, and the general population is not educated, prepared and able to safeguard their own health, hence requires State's interventions. In the first stage the organization's first priority was to primarily focus on safety after which there were regulations to ensure efficacy as well, by requiring manufacturers to provide evidences from credible sources that their product was both safe and efficacious as claimed in their registration filing.

There were efforts to develop standards in both the "research" and "development" of medicine by setting the standards, for pre-clinical research i.e., laboratory and animal research. Clinical research was divided into 3 phases before they were initially registered; there was also a fourth phase for research conducted on a new population, and to closely monitor its safety.

After the outbreak of HIV/AIDS that took the lives of countless people, identified first in the US. The first medicine had been discovered i.e., Zidovudine or AZT and was accepted as safe and effective for the treatment of HIV/AIDS; when the research on human subjects were finished at only Phase II; but there was strong pressure from over one million patients all of whom urged the US FDA to shorten the procedure of registration for AZT, despite having only data from Phase II; which the experts panel who considered the issue agreed to accept, and thus the US FDA agreed to the conditions. All of this was due to HIV/AIDS being a deadly disease without medicines, and that AZT was the first ever possible safe and effective treatment. If research were to be conducted through Phase III it would result in massive losses of lives before a result can be concluded. That is why this case could be considered a major reform of the registration system, by accepting data from phase II clinical research only. This type of registration is limited to medication for illnesses that are fatal and have no other effective existing treatments. Furthermore aside from the reform that occurred to the registration system, drugs that were in this nature were allowed to be used in other countries which has yet to accept the aforementioned drug as an officially registered medication. This system was called "compassionate use," and could be used with general patients or in human research.

All three phases of bio-medical research for the development of new medicines or vaccines which require test in human subjects need to adhere to the ethical principles of human research which has been

continuously developed and improved.

The first instance of a Thai law that regulates medicine was passed in 1909, in the Criminal Act 1908, a regulation which punished those who placed the consumer in danger by distributing adulterated food or medicine, subsequently the 1923 Medical Act which for the first time licensing physicians as well as pharmacist.[3]

The Drug Act 1967 has the most impactful to the quality medical products and the pharmaceutical system as a whole, it has been amended numerous rounds; currently the law is in its sixth version when the last amendment was made in 2019.

Initially the drug protection was left to another organization; this was until 1974 where a major reform in the Ministry of Public Health took place, by establishing the Thailand Food and Drug Administration as a department in the Ministry of Public Health; working to protect consumers of health products, which includes such as medicine, cosmetics, medical device, narcotics and psychotropic substances. The structure and philosophy of the Thai FDA is similar to the US FDA, that it is the sole agency responsible for the consumer protection of all health products, however there are a few key differences as follows:

First, the department responsible for quality of medicines through rigorous laboratory tests is Department of Medical Science, thus the Thai FDA cannot interfere with test results either positive or negative.

Second, the head of US FDA is proposed by the President and approved by the Senate similar to many other Offices. In the case of the Thai FDA however, the secretary general is a government official who holds the position equivalent to the director general, and appointed by Minister of Public Health (MOPH). The Secretary General of the Thai FDA is the secretary of various multi-sectoral committees established by relevant Acts such as Drug Act, Food Act, Cosmetic Act; in many cases each decision has to be approved by the committee first, in contrast to those in the position of Director General in other MOPH Departments, they often hold complete authority within the Department.

Third, the US FDA is much larger than the Thai FDA. In 2000 the US FDA had over nine thousand employees, while the Thai FDA had only one thousand employees. On the other hand the Drug Control Division of the US FDA has more than four thousand employees; while the Thailand has only around one hundred. This is why Thai FDA often relies on and outsource expertises from qualified outside partners.

In the era of the Reagan Administration the socialist world collapsed and the US led the world in advocating the "neo-liberalism"; there were many policies that were implemented, and scholars have come to call this policy package which consisted of ten policies under the "Washington Consensus," which encouraged free trade. One of them was "deregulation" which decreased restrictions and liberated all regulations.[4] Although Thailand did not need to follow these policies, since Thailand relied heavily on the US market, implicitly, Thailand needs to comply with it. Not only policy to limit the size of government workforce, the limited capacities of the Thai FDA is the result from policies in the "Washington Consensus". In line with this policies, the intention of all the existing Acts and related regulations needs reform; the philosophy of "control" has been replaced by "monitor"; such as in the case of the Food Act. However the Drug Act has kept the "control principle" in place.

In summary, it is evident that the Thailand's drug consumer protection system was influenced by many actors such as academia, politics or western countries. Whether it is on the principles of safety and efficacy of drugs, the establishment of organizations and laws, especially after the 2nd World War where the world was plunged into the age of the Cold War, Thailand has been deeply influenced by the United States. The birth of organizations such as the FDA in Thailand for example, was made to follow the format of US FDA; but modified to fit the Thailand health systems context and social environment. When Cold War was over and came along with the neo-liberalisms, Thailand was still under the influences of the United States whether it be ideologies or actions; the trajectories and decisions was more or less influenced by scientific evidence, moral and ethical courage, blessed and by various Thai public health champions. This allows Thailand to face these influences head-on and create systems that fit the context of Thai society with success.

3. National List of Essential Medicines

Currently there are over 155 countries, both developed and developing, that applied the Essential Drug List published by the World Health Organization.

Thailand is vigilant towards the issues that arise from drug usage, including issues such as excessive spending and the lack of essential items; there have been attempts to address these problems through the mindset of the "essential drug list," for over ten years before the model drug list created by the WHO in 1977 was published.

Thailand's essential drug list was later developed into the "National Drug List" which has innovative ideas, and can be used as an example as both a list and a process which possesses a high standard in both academia and governance. The national drug list is the reference benefit packages for all three public health insurance schemes since the 2004 revision. The good governance emerged when all members of the sub-committees and working groups for the revision have to declare "no conflicts of interests" in conducting review of medicines to be included in the National Drug List. It is the first ever in the history in 2004 with strong resistance from various professors who had conflicts of interest with pharmaceutical industries in the previous revisions. The process of improving the National Drug List has been developed until it became good examples to committees, sub-committees and other working groups.[5]

4. Reference drug price for public procurement

While the National Drug List played an important role in ensuring essential drug that promotes health, prevent diseases and treat patients are available; the reference drug price is an important tool that controls the medical spending to be affordable and not causing financial burden to the government who subsidized public health insurance systems and the citizens. Reference price system leads to financial sustainability and system efficiency. It is noteworthy that the Social Security Scheme was the first which adopted the National Drug List as the pharmaceutical benefit package for its members since 1991 when the Social Health Insurance was launched. Later in 2002 the Universal Coverage Scheme which covers the remaining 75% of Thai citizens who are not public or private sector employees also adopted national list of essential medicines as its benefit packages.

The most important factor of the Social Health

Insurance implementing the National Drug List was to ensure that health facilities retain a standard, by ensuring that beneficiaries receive a adequate amount of essential medicine. The Social Health Insurance chose capitation as the payment system for its contractor hospitals (both public and private), however, a flaw with this particular system is that health facilities would often aim to contain its expenditures including medicine, by enforcing a minimum expenditure for medicine according to the National Drug Expenditure, is a minimum guarantee ensuring access to medicines by members.

The Minister of Public Health, Professor Dr Sem Pringpuangkaew, designed a model to contain the costs of medicine, by supporting the National Drug List as a key mechanism in controlling the use of medicine. Starting from 1981 the hospitals in the Ministry of Public Health were required to spend no less than 60% of their drug budget to procure items in the National Drug List; this was enforced through in "the Ministry of Public Health's 1981 regulation on the purchase of medicine by health facilities in the Ministry of Public Health". Following this, there was a Cabinet decision on the 27th August 1985 that the National Drug List's shall be extended to cover all other government health facilities (beyond Ministry of Public Health). This was enforced through the "1986 Regulations of the Office of the Prime Minister on Procurement (issue 7)" that all public hospitals were obliged to procure medicines in National Drug List according to the proportion in the Regulation. Ministry of Public Health must purchase no less than 80% of the drug budget while health facilities owned by other ministries must use no less than 60% of drug budget to procure items in the national drug list.

Besides designating the proportions of the budget there was also a designation for the Ministry of Public Health to be responsible for producing reference price for all essential medicines for procurement purpose. All public health facilities are required to purchase medicine by generic name from the National Drug List, without exceeding the reference price. The reference prices are estimated from the median price of actual purchased items by all public health facilities in the past years; all purchased prices are downloaded on the public website of the MOPH. The reference price was regularly updated by the Ministry of Public Health. However an exception is allowed to procure medicines manufactured by the Government Pharmaceutical Organization (GPO) or the Military Pharmaceutical Factory; but not exceeding 3% of the reference price. With this, the regulations were then developed into the 1992 Procurement Regulations responsible by the Office of the Prime Minister; the Purchasing of Drugs and Medical Supplies was defined in Section 2, Clause 60-64 of the 1992 Procurement Regulations.[6]

The announcement of the reference price was later improved to be within the jurisdiction of the National Drug Development Committee; with the announcement on the 5th April 2019 consisting a total of 49 groups and 1490 listed entries.[7]

5. The 1400 million baht drug scandal in 1998: Role of civil society organizations

5.1 The triggers of scandal

The embezzlement of 1400 million Baht (US$ 46.7 million) was a key history of the political economy related to Thailand drug system.

It began with the 1997 Asian Economic Crisis

triggered by Thailand fall in financial institutions; the Ministry of Public Health was allocated an approved budget of 1400 million Baht, to be used for medicine and pharmaceuticals to mitigate the population as there are major influx of patients from private to public health facilities, hence there is a significant increased in demand for health services in public sector. The Ministry of Public Health distributed the budget into two parts; the regional and general hospitals were given 560 million Baht, and the community (district) hospitals were given 840 million Baht.

Politicians who planned to embezzle and corrupt the budget started by conspiring with high ranking officers in the Ministry of Public Health. The incident began when the Deputy Permanent Secretary of the Ministry of Public Health proposed that the reference price system should be abolished. The Minister of Public Health, using his legal authority, had approved the proposal, and announced that the reference price was to be cancelled by the 15th of December 1997, this paved the way for the purchase of drugs at expensive price; all according to the plan for corruption.

The decision opened up the opportunities for the purchase of medicine with much higher price in 3 possibilities. This included; (1) buying drugs from a designated puppet companies, the companies share the gains from high price to the politician; (2) the health facilities can purchase medicines from any sellers but these sellers must share 10% of the total sales to the politicians; (3) health facilities can purchase medicines from companies designated by the GPO; and share the gains to politicians. In this case the politician is the Minister of Public Health at that time.

The orders were announced by the Ministry of Public Health, through meetings with Executive Directors in the provinces; while the provincial Executive Directors met with "the Minister's team" in a hotel, when the Minister's team convinced them to cooperate using the three corruption tactics. It turns out that many government officials in central and provincial levels were willing to "cooperate" by purchasing large amounts of costly medicine; until the day they were exposed.

The director of Uthai District Hospital in Ayut-thaya province was the first whistle blowers to the public, where high rank Executives in the Ministry deny any allegations. This triggered the high level government officials in the Ministry who had involved in the "rural doctors movement" to come out and expose and publicize the wrongdoings, following this there was a "concerted efforts" by various other civil societies to come out and reveal what has happened.

5.2 The establishment and role of civil society organization

The groups of civil societies mostly active citizens in the Ministry of Public Health began to establish and form a large coalitions across different disciplines such as doctors, pharmacists, dentists and nurses. After the student-led revolution took place on the 14 October 1973; the Rural Doctor Federation was formed, which after the Army cracked down the student fronts on the 6 October 1976; the Federation was renamed as "the Rural Doctor's Society." The pharmacist activists established "Drug Study Group" the 8 March 1975, during the auspice of International Women's Day. In the countryside, the Rural Pharmacists Group was also created.

After the major outbreak of HIV/AIDS in Thailand

in 1990s, various groups of non-government organizations working on HIV/AIDS were established, notably the AIDS Access Foundation. There are many other groups. Dr Sanguan Nittayarumpong, advocated for MOPH budget subsidies to these NGO to support health intervention in particular in the context of HIV/AIDS epidemics. The annual budget subsidies of 49.2 million Baht has been gradually increased.

The civil societies showed up with tremendous support in publicize the corruption, furthermore with the press reported on the scandal for over a month; it pressured the government to respond by referring the case to the Committee on Prevention and Anti-Corruption (which was renamed as the National Anti-Corruption Commission following the 1997 Constitution) and the Audit General to further investigation. In addition the Ministry of Public Health had also nominated an investigation committee. Doctor Banlu Siripanich, a member of Committee on Prevention and Anti-Corruption, who was asked to be a member, requested that he be the Chairman of the investigation committee, to which the Ministry of Public Health obliged to due to pressure from the civil society and press. The investigation results concluded that there was corruption involved. The Prime Minister then had to elect an investigation committee to proceed further with the probe. In conclusion of the probe, there were 2 incidents of punishment which was the Assistant to Permanent Secretary of the Ministry of Health and the Director of Provincial Health Division, both of whom were dismissed from the offices. Furthermore there were removals of Provincial Chief Medical Officers in 5 provinces which included Ayutthaya, Chacheongsao, Nakhonpathom, Pang-nga and Naratiwas.

With high level of societal pressure that the Minister and Deputy Minister of Public Health were forced to resign. The newly appointed Health Minister appointed an investigation team to examine all invoices purchased through the Government Pharmaceutical Organization (GPO). Over the 70,000 purchase orders were by trade name. Huge efforts are required to thoroughly review each of these purchasing orders; with supports from volunteer pharmacists that this monumental task was accomplished.

Investigations found that during the 1998 incident; the total purchased amount was 918,578,694 Baht, with large variation in purchased prices. The mark up ranged from 50% to 300%. If these products were purchased based on the reference price, the estimation of total losses from this scandal was 181,748,170.57 Baht. Investigation results were submitted to the National Anti-Corruption Commission; further new evidence was also received, investigated and submitted. The former Advisor to the Deputy Minister of Public Health, who had been imprisoned, confessed to receiving a cheque of 5 million Baht from drug company which involved in this scandal.

Ultimately the panel of judges of the Criminal Prosecution Department of the Supreme Court had unanimously ruled that the Minister of Public Health was guilty based on the Criminal Law section 149. Considering all the events and circumstances, given that the defendant had pledged his service to the country through seven rounds of being elected as a member of parliament; and served five rounds of Minister positions, and taking into account that the defendant had a Bachelor's degree in law and as a lawyer practitioner; a criminal act such as this corruption deserved a 15-year imprisonment.[8]

The exercise of political power to embezzle the health budget had resulted in 181 million THB (US$ 6 million) loss to the society due to unjustified high price of medicines. The high rank officials who cooperated with corrupted politicians and teams were also punished and dismissed from their positions. The exposure of large scale drug scandal had empowered the active citizens and the civil society organizations. This is not a common case in the history of Thailand health systems. Such fight to clean up the society require utmost courage, endurance, selflessness and persistence by active citizen and civil society organization. One of the leaders in the fight against corruption was later sued, and had to face a lonesome and extensive battle till the charges were finally dropped by the Court, which incurred large expenditure throughout the court processes.

This story reminds us of William Shakespeare's work on "The Merchant of Venice," which was translated by His Majesty King Rama VI and in one of the verse which was composed into Thai, "in the course of justice none of us shall see salvation."

6. The case of PPA: phenylpropanolamine

PPA was used to relieve stuffiness of nose for the treatment of common cold. It is commonly mixed with other anti-allergic and antipyretic. While there were announcements to withdraw PPA as a component of any medication in late 2000 till early 2001. There were more than 450 drugs registered with the Thai FDA which had PPA as a component at the time of announcement. In total there were 447 and 3 pharmacopeia in the private and public sector manufacturers respectively. In addition to PPA, there were Type 3 narcotic drugs in 16 pharmacopeia where PPA was one of the drug components. As such the medicine was announced to be withdrawn by two FDA orders; the first was released on the 14th December 2000, and the second targeted the narcotics combined with PPA formulae on the 12th January 2001.

The withdrawal of PPA has a long story in both the United States and Thailand. In Thailand not only was the incident a major media coverage, it was also a subject of debate that was asked extensively in both the media and the professional organizations, that is the Medical Council. A plastic surgeon went to Administrative Court to sue the FDA so that they may retract both notifications while the Medical Council became a witness of the plaintiff in support for retraction of the FDA order. An interesting observation however is that this plastic surgeon had a rough history with the Medical Council, and was punished several times for unethical conducts on the account of false advertisement. Later, the Medical Council proposed PPA as prescription only medicine, however the proposal conflicted with the studies conducted by Yale University; that the complication on intra-cerebral hemorrhage were from "first time use" which is used to relieve most colds and coughs. Thus the aforementioned risk is unpredictable and even doctors, as prescription medicines only, cannot ensure patients are safeguarded from stroke and intra-cerebral hemorrhage.

The Deputy Secretary General of the Medical Council who vigorously pushed for retaining PPA claimed in a meeting that "politics ordered it" and were "pushing the PPA" against scientific evidence of its fatal side effects. Such movement which was self-interest and against scientific evidence created tensions and badly destroyed the credibility of the

Medical Council.

These petitions by Medical Council against scientific evidence and put patients at risk of using PPA did not have any effects; as the Central Administrative Court decided to dismiss the case which confirmed the legitimacy of FDA orders on the ground of protecting the consumers. The Supreme Administrative Court confirmed to the decision made by the Primary Administrative Court.[9]

The Food and Drug Administration gathered the information, evidence and published in two separate books. These books were the "Truths about PPA (phenyl propanolamine)" which was published in April 2001[10] and the "Controversies on PPA" published in March 2005.[11]

7. The drug patent and the compulsory licensing

7.1 The Drug Patent

Thailand first legislated the drug patent for the first time in 1979[12] which only permitted process patents, later with the strong pressure from the United States and from drug companies resulted in product patents. This has always been boycotted by the civil societies as product patents always results in higher drug prices and inaccessibility by the needy patients. Higher drug prices is a burden to citizens who could not afford to purchase them. Patent results in product monopolies and unjustified high prices.

As the Thai government was pressured by the US to amend the Act, the Deputy Minister of Public Health who at the time was Professor Attasit Vejajiva saw that Thailand would lose many benefits, additionally there would be a major burden placed on the budget of the Ministry of Public Health, which at the time Thailand was facing with major HIV/AIDS epidemic; where antiviral medicines were all patented.

It was the Secretary General of the Food and Drug Administration (Dr Morakot Kornkasem) and the Secretary of the Deputy Minister of Public Health (Dr Jakradham Dhammasak) and Director of theTechnical Division of the Food and Drug Administration (Dr Suwit Wibulpolprasert) all of whom explained to the Prime Minister on how much the price of drugs would increase and add strong pressure on the limited health budget, on medicines for HIV/AIDS epidemics.

However the Prime Minister insisted that it was essential to comply with the US requests as the US had used the Trade Act Section 301, in down grading Thailand from the Priority Watch List (PWL) to the Priority Foreign Country (PFC) list from the year 1991 onwards, which has a penalty measures in place that is the revocation of the Generalized Systems of Preference (GSP), which would have carried heavy repercussions on Thai exports to the US, amounting 40% of total export. The Prime Minister pledged that if the Ministry of Public Health were to receive any repercussion then he would increase the health budget, however it was "flung back" that by then he would have been out of office already.

In conclusion there were additional amendment on the patent act in 1992[13] covering product patents 8 years prior to the schedule dates designated by the World Trade Organization in 2000. As expected, the patented drugs increased in price which led to the utilization of the seven entries of the Compulsory Licenses in the following years.

7.2 The usage of the Compulsory License (CL)

Thailand was the first country in Asia to have been severely affected by the HIV/AIDS epidemics. In 1999, DDI the second line ARV for the treatment of

HIV/AIDS was registered and issued a drug patent, which should not have been possible to register as patent as DDI did not have shown its novelty. This incident sparked a movement within HIV/AIDS patients and the civil society to call for the patent registration with Ministry of Commerce to be revoked, by protesting overnight in front of the Ministry of Public Health. Additionally there were calls for the exercise of Compulsory License in the Thailand Patent Act; however the Ministry of Public Health did not respond to these demands.

The utilization of the Compulsory License that took place for the first time in Thailand occurred in the late months of 2006 and followed into 2007, which was in the era of Dr Mongkol na Songkla who was the Minister of Public Health and General Surayuth Julanont as the Prime Minister. The process included two entries of anti-viral drugs and one cardiovascular medicines. Additionally the government also processed four other cancer drugs at the early of 2008. By concisely stating the reasons and necessity of public health emergencies which where the medicines are not affordable to the patient in the application of Compulsory Licensing while also adhering to the international trade regulations in the TRIPs Agreement as well as following legislative provisions in the Thai Patent Act. It allows the Thai government to use CL; this event caught high attention by the media. The Thai government purchased and supplied high quality drugs that were lower cost than patent products, save lives of the people.

When confronted with the aggressive retaliation by transnational pharmaceutical companies and the bullied United States Government, the Thai government was able to solve the issue which was external peer reviewed by both national and international experts on the legitimacy of Thailand using compulsory licensing. In recognition to their contributions, an award was bestowed to all leaders in the implementation of compulsory licensing granted by the previous Prime Minister who decided to amend the Patent Act due to pressure from the United States.[14-17]

8. The glucosamine incident

Glucosamine was once registered with the Thai FDA as both a drug and food supplements. Later the owner of the drug registration was asked by the FDA to remove the registration from the food supplements while still keeping the registration as a drug; however, this drug was not in the Essential Drug List.

Glucosamine is a medicine that was used to treat knee osteoarthritis and has been evaluated by Thai Royal College of Orthopedic using 5 principles, which was (1) safety (2) efficacy, based on results from research data (3) effectiveness based on medical practice (4) efficiency, by comparing the outcomes with the cost of medicines and (5) benefit, meaning benefit to the population and society as a whole. Based on these five criteria, the Royal College of Orthopedists gave a final summary assessment by using a score of "+/-", which meant that it was unclear whether or not the drug was useful for medical practice in Thailand.

Glucosamine was one of the drugs that the Comptroller Generals Department responsible for Civil Servant Medical Benefit Scheme (CSMBS) decided to suspend its reimbursement; this is in line with the research findings and scientific evidence from 134 research reports. In addition there were also public hearings from all stake holders who agree that the drug

is not cost effective. And governments such as the United Kingdom, Scotland, Sweden and Republic of Ireland and the US Department of Defense did not allow the reimbursement of Glucosamine from the welfare scheme. The US did not categorize Glucosamine as a drug, instead it was categorized as a food supplement, and thus it wasn't possible for hospitals to reimburse from the healthcare system for this product.

This control of the use of Glucosamine in CSMBS came from the abuse of drugs which resulted in extreme high expenditures in CSMBS as shown in 2004 that the total expenditures from this scheme increased from 26,000 million Baht to 61,000 million Baht in 2009, therefore the Ministry of Finance has proposed to the cabinet to abolish the reimbursement of Glucosamine to which the cabinet had approved.

Following this there were retired government officials who filed a law suit to the Central Administrative Court to retract the aforementioned orders by Comptroller Generals Department. The Central Administrative Court has ruled on the 26th of February 2015 on "red court" number Z502/2015 to remove the cabinet's decision. The Comptroller Generals Department did not appeal the case, thus the Administrative Court's decision to remove the order was a final. Finally the Central Administrative Court declared that the order was to be removed on the 19th of May 2015 and was to be published in the Royal Gazette, which was broadcasted on the 20th of May 2015.

Following this there was commentary on the verdict of this case published as a series in the newspapers, which was later reprinted into a single book. A Constitutional Court judge who wrote the prefaces in this book states that this book presents one of the most superb ruling of the court and that it is an invaluable research on administrative law and should be developed to benefit broader areas such as law, administrative justice system and good health administration.

"This book demonstrates the heart that strives for justice and the intention to give benefits to all the people of Thai society. In this book data is presented in a straight-forward manner without any bias towards any party and the discussion chapter was based on clear and truthful information and theories. The suggestions were also creative and gave confidence that there were better solutions for this issue."[18]

Discussion

1. The role of political economy in the health system

Political economy has many roles in the health system such as:

The development of the health sector is challenging and creates much debate within society. To make decisions on results of health is thus related to politics and economics by default.

In every government there must be an evaluation on which problems amongst many are the most pressing, therefore for the government to see the importance of healthcare it is essential for them to understand and increase the desire to work on this sector, furthermore it is important for the government to see that the task is indeed possible.

In revolutionizing the health system, which includes the push for UHC it is vital to manage resources which often times leads to winners and losers that either gain or lose advantages over one another, and therefore

relates to politics and economics evidently.

Political economy is a study that explains and puts heavy emphasis on issues of structural inequality within the health system, furthermore the study is also conscious of the importance of social movement in improving the quality of life for those in poverty.

The weakness of all medical partners is a major obstacle in improving health. Political economy is capable of analyzing the many factors and point out how different organizations can improve in responding to the essential health needs and the needs of the population.[19]

2. Development of health economics in Thailand

The Ministry of Public Health has given much priority to health economics for more than 4 decades, which began by cooperating with the Faculty of Commerce and Accounting of Chulalongkorn University to start training health economics within the Ministry of Public Health; this course was supported by the World Health Organization who sent Anne Mills, a health economist to be a consultant of the course, later Anne Mills had received the Prince Mahidol Award in 2009. By cooperating with the Public Health and London School of Hygiene and Tropical Medicine of University of London, and the Public Health Faculty of Prince Leopold I of Belgium resulted in Thailand increasing its adequate number of health economists, after which led to the creation of numerous research units, for example the International Health Policy Program and the Health Intervention and Technology Assessment Program, which conduct research to develop the national health policy. Their works included capitation payment in the Social Health Insurance and the Universal Health Coverage, which resulted in Thailand health systems is global role model of achieving high level of health status with low cost; so called "good health at low cost".

The development of the public health infrastructure across the country after the revolution in 1932 including the construction of hospitals in all districts and health centers in all sub-districts, the development of the provider payment methods using capitation system, the diagnosis related groups (DRG), and the development of public health personnel by giving scholarships to local students to trained as nurses, midwives and junior sanitarians; so that they return to work in their hometowns. There was also the creation of reformists together with efforts to strengthen the public; this resulted in the major success of the health system.[20]

3. The development of the drug system

3.1 Thai Traditional medicine

Thailand has compiled Thai medical textbooks namely the Praosotpranarai in King Narai the Great Period that mentioned two traditional medicine textbooks. In the era of King Rama I, King Rama II and King Rama III, the traditional medical formularies were compiled and inscribed at Wat Po and Wat Raja-oros. In the era of King Rama V there were compilations and revisions of the medical textbooks; the textbooks were later combined into the Vejasart Royal Textbook of King Rama V which was the root of many other Thai medical textbooks. Later the Ministry of Public Health announced that there were 30,442 Thai medical formularies [21], however the formularies provided little use to the public, even though there were many efforts to revive Thai traditional medicine since the age of Professor Uay Getusingh through the forming of Ayuravej College. The National Economic and Social Development Plans

included many developments of Thai traditional medicine, such as the creation of the Institute of Thai Traditional Medicine and the Department of Thai Traditional and Alternative Medicine. There was also the inclusion of Thai herbal medicine both in the National List of Essential Medicine and in the pharmaceutical benefit package of the Universal Coverage Scheme. However the proportion of traditional Thai medicine usage remained low. Lower than 1% of total health spending was spent on Thai traditional medicine, the reason being poor management of knowledge, in contrast to China which has 20% of all medicine usage as Traditional Chinese medicine. Furthermore China is capable of improving traditional Chinese medicine to the point that it was internationally accepted, such as the use of acupuncture which was recognized by the WHO and used in countries around the world.

China has a long history of writing prescriptions and medical textbooks that used printing technology, unlike Thailand which has not utilized such technologies which resulted in no records being kept on what type of medicine was used in the past, additionally the proportions of drugs and dosages were usually estimates. Additionally medical knowledge was mostly verbally passed on from one person to another, which meant that when it was written down the information may have distorted from the original version. In 1889 the first ever medical school of Thailand was established, where both traditional Thai and Western medicine were taught, however 26 years later the traditional Thai medicine curriculum was later cancelled by Prince Chainatnarentorn who was the Director of the college.[22]

3.2 Modern medicine

Thailand has always accepted foreign knowledge and technology throughout its history; the Praosotpranarai included many foreign medicines from China, India and Western countries.

Since the early days of the Ratanakosin era Thailand has given much significance to the production of medicine, such as: the production of Smallpox vaccine in the era of King Rama III, the creation of the Osotsapa pharmaceutical factory in the era of King Rama V, the production of rabies vaccines in the era of King Rama VI, and finally the training for freeze-dried smallpox vaccine production for countries in Asia. Yet Thailand's pharmaceutical industry did not develop as expected; manufacturers in Thailand were neither able to research nor develop new drugs, moreover fully reliance on imported pharmaceutical active ingredients for local production of generic finished products. On top of that the drugs produced did not comply with the regulations of the international standards of the US, Europe and the WHO.

There were once efforts to produce flu vaccines within the country through the technological transfer from Russia Federation along with more than 100 million Baht in funding from the WHO. Government pharmaceutical organizations took more than 10 years but were still unsuccessful in producing the seasonal influenza vaccines. In contrast to India who also received technology from Russia through Thai scientists but were able to successfully produce and distribute vaccines for the flu within the span of a year or so.

3.3 National List of Essential Medicine, reference price and compulsory licensing

The pharmaceutical industry is a profit maximi-

zation business with much influence on academia, economics and politics according to the book "Selling Sickness: How the World's Biggest Pharmaceutical Companies Are Turning Us All into Patients."[23] The book explains how the treatment guidelines are changed so that patients are prescribed more medicines; changing the way drugs are sold, thus patients who is not really sick are advised to use additional drugs prescribed by doctors.

"The Truth About the Drug Companies : How they deceive us and what to do about it"[24] tells us about how pharmaceutical companies forge information regarding huge investments into the research and development of new drugs, so that they are the only ones who receive the rights to set the highest possible price and creating a long period of monopoly. However in reality, most investments go to drug advertisements and payments to high ranking executives, which results in tremendously high drug expenditures that exceed the economic growth in most countries. Thus it is essential that countries find an effective and efficient way of dealing with these problems.

Thailand was successful in utilizing the National List of Essential Medicine and reference price in controlling drug expenditure and facilitating rational drug use, even though there are still limitations within the Civil Servant Medical Benefit Scheme and private hospitals. Most importantly Thailand was courageous in employing the compulsory license for the 7 patented drugs; an operation which was truly professional despite being the first operation from a government that did not come from an election.

The reference price is effective in controlling the drug expenditure and improves health systems efficiency. Removal of the reference price opens rooms for the 1,400 million Baht drug scandal.

Decision to trigger and implement compulsory licensing is a heroic act as this directly challenged the powers of the foreign drug industries and the US government. It results in an aggressive retaliation from both the foreign drug industries and the governments who were manipulated by or having vested interests with the drug companies. The Director General of the World Health Organization did not have comments on the responses by the pharmaceutical companies. Thailand however acted professionally by addressing every single criticism given in both Thai and English. Interestingly, there were 22 US senators signed a letter in favor of Thailand's argument and decision towards compulsory licensing. Thailand used many methods to gain supporters, such as making an effort to meet with former US president Bill Clinton and directly addressing to the US Speakers of the House of Representatives who was representative of the constituency where the pharmaceutical company were based in, additionally a request was made to clarify details with the Washington Post.

Nevertheless the use of compulsory licensing is difficult to replicate with other drugs nowadays because India, the global producer of generic drugs needs to comply with the Trade Related Aspects of Intellectual Property Rights Agreements of the World Trade Organization, due to this it is hard to produce generic drugs that are reasonably priced. Thus it is essential to study the other flexibilities mode provided by the TRIPS agreement so that more measures can be applied.

3.4 The PPA incident

The PPA incident is an example of FDA's legitimacy to protect health of the people from unsafe

medicines; in this case the fatal complications from intra-cerebral hemorrhage. Difficulties and challenges faced by Thai FDA from pharmaceutical industries, certain academia, and some members of the Medical Council who had self interests and filed the law suit to the Administrative Court. If there were no ethical courage, perseverance, professionalism and determination it would have been impossible to protect the public.

3.5 The glucosamine incident

The glucosamine incident is an example of the influence that the political economy has towards the drug system. A system where the drug industry seeks to gain advantages over the CSMBS; so that certain groups may benefit from it, this view conflicts with the principles of equality of all citizens (no matter they are civil servant or farmers) endorsed by the Thai Constitution. The Thai FDA allowed the registration of glucosamine as drug and food supplement. Additionally the organization responsible for the CSMBS also permitted the disbursement despite the fact that glucosamine is not included in the National Essential Drug List. Furthermore when this benefit was cancelled the court decided by using the "poor integrity" of evidence. The court interpreted the recommendations by the Royal College of Orthopedists with a score of "+/-" which meant evidence was still unclear whether or not the drug was useful for medical practice and should be used on a case by case basis. However, the court interpreted as "Yes" and should be covered. Further the Court cites Article 78(8) of the 2007 Constitution which refers to the role of states in provision of appropriate benefit to civil servants and government officials. However, Article 78(8) creates inequity and contradicts with Article 51 which aims to ensure equal rights to health service by all citizens. However, the 2016 Constitution does not include this in the role of state.

Conclusion

Although Thailand has many difficulties in improving the governance, transparency, crack down corruption in the government, private and political sectors; as after the Revolution of 1932 (from Absolute to Constitutional Monarchy) to 2019 there have been 13 incidents of coup d'etat, termination of Constitution, and new draft a new version of constitution along these political changes, which gave Thailand up to 20 versions of the constitution. Thai politics has been in a chronic vicious cycle of political instability. However the leaders of this country in many eras have given importance to the development of health and the improvement of the drug system, since the time of absolute monarchy to the present day from political leaders who came through democratic election and coup d'etat.

The act of gathering pharmacopeia and distributing the information amongst the population has been around since the birth of Ratanakosin particularly during the era of King Rama III and King Rama V, despite this however Thai traditional medical procedures did not have any form of prescription, moreover passing on knowledge was mostly passed through memory with some even going so far as to withhold information as well. In addition to this, publications were not utilized and the incorporation of science was very little. This almost leads to a stagnation of knowledge and an almost complete lack of use despite the support from government after the WHO called for primary care and encouraged the use of traditional

remedies.

In 2000 the Thai government attempted to revitalize Thai tradition medicine which ranged from passing laws to setting up a department; additionally it was clear that the government supported the use of Thai traditional medicine through integrating them into the National Health Coverage Scheme. Nonetheless the advancement and use of Thai traditional medicine was still extremely scarce and is heading in the wrong direction thus is required to have a major reform.

In the area of modern medicine Thailand has accepted medicine from foreign countries since the age of King Narai the Great; where modern pharmaceutical sciences were taught in universities since 1913, however advancements and research has been developing at an exceedingly sluggish pace as we are still unable to produce our own active pharmaceutical ingredients, on top of this the quality of the medicine does not meet the standards of both the US and Europe unlike India and China. The study of pharmaceutical science especially in the graduate school needs major reforms.

Thailand's biggest achievement is the development of the National List of Essential Medicine and its implementation into the Universal Health Coverage Scheme. Most importantly the enforcement of the use of reference price for all public facility procurements effectively contain drug expenditure. The removal of reference price opens opportunities for drug scandal. When there are problems with the availability of drugs for public health emergencies; use of compulsory licensing had resulted in access to affordable medicines and save lives; though with aggressive retaliation by US government and pharmaceutical industries.

It should be noted that gathering and distributing medical textbooks for the benefit of the population began in the age of absolute monarchy. While the National List of Essential Medicine and the reference drug price were both born in the time of semi-democracy and the Universal Coverage Scheme began in the era of complete democracy, the use of compulsory licensing implemented during a coup d'etat government.

Recommendations

An important accomplishment of Thailand is the development of the drug system which later had established its own National List of Essential Medicine with regular updates and improved governance in the updating process through declare conflicts of interests in the height of dissatisfactions by certain Professors. By learning from the ideologies of the WHO and developing it to fit Thai society, this included the development of the reference price and compulsory licensing. And with the termination of PPA registration and the glucosamine incident, thus it is clear that the lessons learned should be documented to be used as teachings for Pharmacy, Medicine, Economics and Law.

The success factors can be summarized. Aside from following the principles of "the Triangle That Moves the Mountain," which are the three power poles; (a) knowledge and evidence, (b) societal movement, and (c) policy movement. A vital component however is the creation of a reformist group so that it reaches a critical mass and triggers an initial and repercussion movements. An important strategy is to co-work and create a synergy between both government officials and civil society. Working in the public sector creates a deep understanding of the system which paves way

for a reform from within, by working from the civil society perspectives from outside has another power of holding government account and mobilize societal supports and demands.

The health system in Thailand has been extremely successful in refining knowledge and applying of health economics. In the future there must be a development of knowledge and the application of political economy to the analysis of public health system including drug system, so that they may reach the level of effectiveness provided by the application of health economics.

The biggest flaw to the drug system is the limitation of research and development capabilities, including the production of drugs. This is a product of the failure of the education system which gives no value to sciences. Education still could not uproot the insidious mindsets of the superstitious, the education system promotes the act of mindless memorization which discourages the practical and inquisitive mind among the young learners, moreover memorizing the information encourages the use of guesswork. To fix this we must reform the education system of Pharmaceutical Science from the ground up, especially in at the graduate school.

The education and teaching system in Thai traditional medicine and herbal remedies must also be reformed entirely. A change must be made from a system that focuses on memorizing into a system that (a) emphasizes more on understanding (b) promotes the use of science and research and development, so that traditional Thai medicine textbooks could end the stagnation of information and withholding of information, to become more scientifically based so that knowledge can be genuinely developed. Learning from the experiences from China, Japan and Korea should be considered.

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เศรษฐศาสตร์การเมืองเป็นโครงสร้างเบื้องบนของสังคม ย่อมมีอิทธิพลทั้งโดยตรงและโดยอ้อมต่อระบบยา บทความนี้ศึกษาอิทธิพลของเศรษฐศาสตร์การเมืองต่อระบบยาในประเทศไทย โดยวิธีการศึกษาจากเอกสาร ผลการศึกษาพบว่ายาเป็นหนึ่งในปัจจัยสี่ที่จำเป็นต่อการดำรงชีพ ในสมัยราชาธิปไตยผู้ปกครองใช้การเผยแพร่ความรู้เรื่องยาเป็นเครื่องมือในการปกครอง เพื่อสร้างความจงรักภักดีในหมู่ไพร่ฟ้าข้าแผ่นดิน การเปลี่ยนแปลงการปกครองเมื่อ พ.ศ.2475 การสาธารณสุขมิได้กำหนดไว้ในหลักหกประการของคณะราษฎร แต่ทุกรัฐบาลต่างให้ความสำคัญกับการพัฒนาระบบสาธารณสุข โดยการสร้างโรงพยาบาลจนครบทุกจังหวัด อำเภอ และตำบล ในด้านการคลังของระบบสาธารณสุขก็พัฒนาจนเกิดหลักประกันสุขภาพถ้วนหน้าเมื่อ พ.ศ.2545 ในส่วนของระบบยาประเทศไทยเดินตามแนวทางตะวันตกมาตั้งแต่ครั้งปฏิรูปประเทศให้ทันสมัยในรัชสมัยพระบาทสมเด็จพระจุลจอมเกล้าเจ้าอยู่หัว ทำให้ตกอยู่ภายใต้อิทธิพลทั้งทางวิชาการ ธุรกิจ และการเมือง แต่ผู้นำด้านสาธารณสุขของไทยสามารถเผชิญปัญหาอย่างฉลาดและกล้าหาญ มีการพัฒนาระบบบัญชียาหลักแห่งชาติตามปรัชญาและหลักการขององค์การอนามัยโลกอย่างได้ผลโดยมีนโยบายแห่งชาติด้านยาและกลไกราคากลางยา รวมทั้งมีการพัฒนาภาคประชาสังคมจนเข้มแข็ง ทำให้สามารถควบคุมการใช้จ่ายด้านยาได้อย่างมีประสิทธิภาพ เมื่อเกิดการทุจริตยาจากอำนาจทางการเมืองก็สามารถขัดขวาง และนำผู้ทำผิดมาลงโทษได้อย่างมีประสิทธิภาพ เมื่อมีอันตรายร้ายแรงจากยาก็มีกรณีตัวอย่างที่สามารถเพิกถอนได้อย่างรวดเร็ว แม้จะถูกฟ้องร้องให้เพิกถอนคำสั่งก็สามารถต่อสู้จนศาลยกฟ้อง เมื่อมีความจำเป็นต้องใช้ยาราคาแพงจากสิทธิผูกขาด ก็สามารถใช้สิทธิกับสิทธิบัตรได้อย่างมืออาชีพ แต่ยังมีกรณีการใช้ยาที่ไม่สมเหตุผลที่ศาลตัดสินให้ยังคงใช้ได้ต่อไป โดยหน่วยงานที่รับผิดชอบก็ไม่ต่อสู้จนถึงที่สุด น่าสังเกตว่า แม้ระบบการเมืองของประเทศจะไม่พัฒนาเท่าที่ควร แต่ในระบบสาธารณสุขและโดยเฉพาะระบบยาก็สามารถพัฒนาระบบที่ดีขึ้นได้ โดยการรวบรวมและเผยแพร่ตำรายา เกิดขึ้นตั้งแต่ในยุคราชาธิปไตย การพัฒนาบัญชียาหลักแห่งชาติ ราคากลางยา และนโยบายแห่งชาติด้านยา เกิดขึ้นในยุคประชาธิปไตยครึ่งใบ ระบบหลักประกันสุขภาพถ้วนหน้าเกิดขึ้นในยุคประชาธิปไตยเต็มใบ และการใช้สิทธิกับสิทธิบัตรยาเกิดขึ้นในยุครัฐบาลที่มาจากการรัฐประหาร สิ่งท้าทายสำคัญของการพัฒนาระบบยา คือ ระบบการศึกษาเภสัชศาสตร์และระบบที่เกี่ยวข้อง ยังไม่สามารถพัฒนาให้เกิดระบบการผลิตยาอย่างประเทศพัฒนาแล้ว การแพทย์แผนไทยและยาไทยที่ยังมุ่งการอนุรักษ์เป็นหลัก สุดท้ายควรพัฒนาความรู้และการใช้ประโยชน์จากเศรษฐศาสตร์การเมืองกับระบบยาให้ได้เช่นเดียวกับที่ประสบความสำเร็จด้วยดีมาแล้วจากเศรษฐศาสตร์สาธารณสุข

คำสำคัญ: **เศรษฐศาสตร์การเมือง; เศรษฐศาสตร์สาธารณสุข; ระบบยาในประเทศไทย**

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Challenges and Opportunities for Improving the Drug System in Thailand

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Abstract Drug system is a part of the health system where the drug management system plays an important part resulting in people having drugs to use, having equal access to quality medicines, having reasonable usage that matches affordability of their household expenses and those of the country's. The study of various components systematically in all articles of this issue of the Journal provides visibility to many challenges and opportunities to improve the drug system. We synthesized evidence from this supplement issue. The drug system in Thailand still has many challenges and opportunities for improvement in which relevant sectors should promote and implement them, including national mechanisms that monitor trends of those expensive drugs, bargaining for the drug prices, and/or having drug procurement procedures in order to optain reasonable drug prices. Moreover, those drugs shall be used without prejudice and incorrect knowledge and beliefs. There are more issues to be considered such as promoting domestic pharmaceutical production system including generic drug, herbal medicine, and biological materials in order for more self-reliance, producing more experts in the field, having information systems which can efficiently monitor and evaluate performances of various sectors, and improving legal policies which allow implementation of the issues discussed above. Furthermore, all stake-holders involved must be able to adapt to future changes with the main goal of becoming convenience for people to access to essential drugs while unreasonable drug uses are reduced. All the stakeholders must adapt, with an important goal of people being able to easily access to drugs when needed, while unnecessary drug usage be reduced. The system will reduce drug prices; and new drugs will be more effective and specific to the diseases. There will be the use of appropriate technologies to help diagnose and prevent diseases. All of these developments will result in better health of the people.

Keywords: **drug system; opportunities for improvement; future of drug system**

Introduction

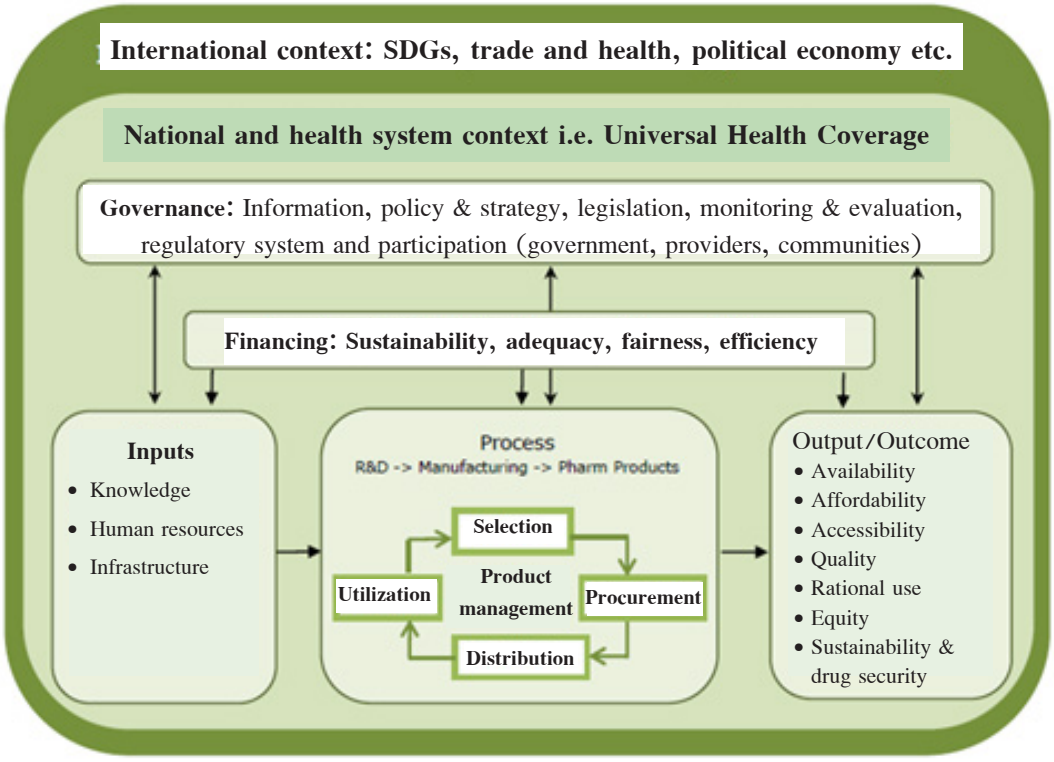
Drug system is a complex system which is directly related to the entire health system and also has an effect on economic and social system in the country. Good drug management system is an important part that will result in people having the necessary medicine to use, having equal access to quality medicines, and having reasonable usage that matches affordability of their household expenses and those of the country's. As a result, the overall system is sustainable.

The connection of each component in the drug system can be explained according to the conceptual framework, developed from the meeting of the Drug System Report Committee of Thailand (Figure 1) where the drug system is a part of the health system with ultimate goal of achieving good health outcomes for Thais. This conceptual framework presents 3 main components of the drug system which are inputs, process and outputs/outcomes, and 2 supporting components which are governance and financing. These are important mechanism for driving the drug system. Each element interacts and connects each other under the contexts from both national and international which are constantly changing. Therefore, pharmaceutical industry and service delivery are involved with various stakeholders at individual, organizational and national levels, such as government sectors and service providers, for example, public and private health centers, and communities, including civil societies.

The 3 main components are:

1) Inputs, such as knowledge, human resources, and infrastructure i.e. places, equipment, technologies, support systems, information system, and budgets.

Figure 1 Conceptual framework of drug system in Thailand, 2018



2) Process, considering from drug supply chain, starts from R&D and manufacturing. From there, the drugs are distributed to service sectors through hospitals and communities, according to the selection process, procurement, distribution and utilization.

3) Outputs/outcomes, about having essential drugs with quality. This means efficacy and safety for Thai people to be able to access to these essential medicines, leading to availability, affordability, accessibility, rational use, equity, drug security and sustainability.

The good governance means that the drug system has fair supervision, monitoring and evaluation and for achieving the goals. The basic components of the drug governance system are policy, strategy, legislation, regulatory system, monitoring and evaluation, information system, and participation from public sectors, service providers and communities. And, the last component is financing. It is used for producing resources and health services with the objectives to achieve efficiency, adequacy, fairness, and sustainability.

All the components of the drug system must be continually improved in order to be well adapted with the situation and changes of those factors in the health system and surrounding factors whether internal or international contexts, including economy, society, law, politics, technology, and the environment. All of these have influenced and affected the drug system. The study of various components systematically in the articles of this special issue of this Journal provides visibility to many challenges and opportunities to improve the drug system. The important key areas are as follow:

1. Challenges

1.1 Drug cost containment

The medication costs in the country continue to rise. The domestic consumption of drugs is estimated at over 180,000 million baht per year, which is about 2.2 percent of the Gross Domestic Product (GDP)[1] – that is almost 50 percent of national total health expenditure. This is considered a high proportion when comparing those of the other countries, even in the group of developed countries which have much higher living costs than that of Thailand. The high drug expenditure is reflected by various factors, such as

1.1.1 Irrational drug use behaviors

These behaviors caused by many factors, starting from drug users (i.e. having little knowledge or having wrong beliefs about the drugs), drug prescribers (i.e. prescribing medication without or not according to recommended dosage and indications), drug manufacturers or drug distributors (having inappropriate distribution sources, i.e. selling) or supplying wrong classes of drugs in pharmacies. In addition, if we assume that the national list of essential medicines has covered all necessary working and cost effective drugs and suitable for the country's affordability, the portion of the drug usage on the list has an average of only 40 percent of overall prescriptions, which is about 66 percent of the total drug costs.[2] This number is far out from the drug usage guidelines stated in the guidance according to the campaign Good Health at Low Cost, where it is recommended that it should be up to 70-90 percent of the total drug costs, depending on the levels of hospitals.[3]

1.1.2 Drug cost control policies and domestic drug pricing

The three public health schemes including Universal Coverage Scheme (UCS), Social Security Scheme (SSS) and Civil Servant Medical Benefit Scheme (CSMBS) are the major drug payers in the country. They establish policies using various methods in order for drug cost control in the systems, such as closed-end payment methods in the UCS and SSS. This causes prescribers to be more careful when prescribing medication that may be considered unnecessary for treatments. The CSMBS has strategies to control the expenditure of non-essential drug lists (pre-authorization method and A-F method), together with requesting cooperation for reasonable drug use. However, using the open-ended payment method, instead, cannot effectively control the cost of medicine as it should be. We find that health expenditure for CSMBS's beneficiaries is much higher than that of the UCS and SSS. This leads to a suspicion of over-spend and unfairness of medical rights.

The drug price policies to determine the selling price at various points, such as factory wholesale and retailed prices, still have no control from the government as they should be. The strategies currently being used, have only price comparisons, price bargaining before being listed in the national essential drug list, and price bargaining before the National Health Security Office will procure these drugs, in case of only for drug list E (2)[4]. In fact, controlling drug prices for new patented drugs and generic drugs still has many ways to do by using effective drug price policies to control drug prices starting from the registration process to the price reviews after knowing the actual outcomes of these drugs on patients. However, various related laws and acts, issued by the Ministry of Public Health and some other ministries, are not conducive to systematic drug pricing.

1.1.3. Policies related to international drug management

The ability of the government to make agreement on trade and investment policies affects the effectiveness of drug procedures throughout the drug supply chain. This causes an impact on the import and export taxes to domestic drug manufacturers. Therefore, negotiations gain benefits to the country will have impacts to the drug price control as well as the country's medical and health expenses. However, in past negotiations Thailand, in most cases, has disadvantages in many ways and does not benefit from the negotiation as much as it should be.

In terms of patents, they provide protections and monopolization to the inventors. In addition, monopolization of modern technologies may hinder the development of Thai generic drugs. Since the Thai pharmaceutical industry is still a downstream, Thailand is still incapable of performing research and development on new drugs that can be produced to the markets commercially. Therefore, the patent system in Thailand gives more benefits to foreign pharmaceutical companies that produce expensive new drugs rather than protecting and granting rights to domestic drug manufacturers.

1.2 Unfairness of pharmaceutical services affecting inaccessibility to essential drugs

Although having a universal health coverage system is one way to reduce gaps and inequality in access to health services, the inequality in services still occurs among people with poor economic status in the society. For example, in some cases, people have to

pay out-of-pocket at private hospitals or pharmacies in order to get services which are not covered by the health insurance system and/or to get drugs, uncovered in the essential drug list at public hospitals. Therefore, the use of the drugs which are not on the national drug list may be an obstacle to the access to these drugs for the UCS and SSS members.

As for those exercising their rights through the CSMBS, although according to the scheme's policies, beneficiaries are eligible for more rights than the other 2 schemes, in some cases there are still issues accessing to certain drugs and health services that the scheme does not make arrangements for its beneficiaries, such as the drug list E (2). And for rare medicine, shortage drugs, and orphan drugs, they are still issues in accessing to these drugs for all the 3 health insurance funds.

1.3 Supporting policies for the inputs for the pharmaceutical system

1.3.1 Domestic pharmaceutical production

Since there is an increasing trend on importing foreign drugs and raw materials, it indicates that the direction of the pharmaceutical production for consumption tends to rely more on imports whereas the domestic drug production tends to steadily decline. Although drug policies on quality and *Good Manufacturing Practice* (GMP) assessment in compliance with the Pharmaceutical Inspection Co-operation Scheme (PIC/S) regulations from the government helps raising the country's pharmaceutical production standards, it also causes those pharmaceutical companies to bear the increased production costs. In general, the drug selling prices in Thailand are determined by the Ministry of Public Health's reference prices, central or regional procurement, and government procurement regulations - including the rights to sell drugs from the Government Pharmaceutical Organization which are restricted. These have caused the market to be rather limited and creating competitions among private sectors.

While, the endorsement and encouragement to use available resources including existing local knowledge is about using traditional medicine or herbal medicine, the production of expensive medicines - biological type, is still limited. For example, research and development of herbal raw materials is still mediocre. Also, quality inspections still require somewhat high technologies, using laboratory operations which are still inadequate and quite expensive. As for the biologicals, it requires high investments in many aspects, such as budgets, registrations, research and development, establishing production units, and other supporting systems. And, the knowhow on production techniques is also very crucial. All these matters have impact on being self-sufficiency of possessing essential medicines for use in the country.

1.3.2 Manpower

Due to the fact that there are changes in population structure, modern technologies, and discovery of more complex diseases, the pharmaceutical system will inevitably require more pharmacists in different grounds. Moreover, aside from having to possess the required skills, pharmacists must also be able to work proactively, work as a team with other professionals in different fields, and adapt to changes effectually. Currently, despite the fact that there is an expansion of educational institutions in order to produce more pharmacists to the market, when considering the national policies and development direction, the number of skilled and specialized pharmacists in the system is

still insufficient for future needs.

1.3.3 Pharmaceutical system information management

There have been issues in the pharmaceutical information system management, ranging from the drug registration, drug production, distribution, and drug consumption in the country. All of these are caused by scattering existing databases developed from users in various parts, divisions, and departments in government sectors. And, the private sectors also have their own databases, using their own drug codes. Therefore, it is very challenging and/or unable to link drug information from these different databases.

This leads to a challenge in pharmaceutical information management being unable to track drug distribution, drug usage in health insurance systems and other health sectors. Likewise, reports on drug production, imports and exports cannot be linked. Moreover, each database has its own problems with standards, data completion and accuracy as well as lacking of continuity, which affect to the data quality and reliability in the pharmaceutical information system.

1.4 Management in value chain: selection, procurement, and distribution

The medicine supply cycle involves selection, procurement, and distribution. The drug procurement and distribution are not only important processes which lead to drug usage and drug accessibility, but they are also important factors determining the effectiveness of the drug system. However, in the drug supply chain, there are still several system limitations, for example:

1.4.1 Drug selection at national level. There is a delay in the drug registration and selection into the national drug list. This may cause harm to business (opportunity loss) and a delay to patients' drug accessibility.

1.4.2 The number of skilled personnel to perform drug and biological registrations is inadequate products, causing a delay in drug registration.

1.4.3 Transparency and work independency of related officers as well as the laws and regulations that support re-evaluations of problematic drug formulas in drug registrations.

1.4.4 Special privileges to the Government Pharmaceutical Organization in drug procurement policies of government hospitals over private companies. This is quite contradicting to a statement in Thailand's constitution where stated that government sectors shall not operate in a way to compete with private sectors.

1.4.5 Even though drug selections to hospitals and drug selection in regional procurement system are having similar criteria in terms of drug registrations, such as factory quality evidence, raw material standards, and drug quality, but these selection processes still require duplicate documents which burdens manufacturers or drug companies in creating and demonstrating these documents. It indicates that the government sectors cannot integrate the necessary information for effectiveness.

1.4.6 Drug registration which focuses on the product-related processes, emphasizing on effectiveness, efficiency and safety as main interests. There is no basis or regulations on drug costs and selling prices in the drug registration process in Thailand.

1.4.7 Thailand's laws do not yet have provisions, allowing patients' accessibility to unregistered drugs but necessitated for treatment, such as orphan drugs, shortage drugs or drugs under research.

1.4.8 The lacks of systematic management to deal

with shortage drugs and orphan drugs, whether in normal or crisis situations.

1.4.9 Issues on drug distribution in the sources that should not be sold, distribution of drugs without licenses, unethical drug distribution including illegal adverts of drugs or improper, over-claimed adverts of health products. The government sectors are unable to comprehensively track and suppress these offenders. In addition, the laws and penalties are weak, causing the offenders who have been prosecuted commit consistent violations over and over.

2. Opportunities for Drug System Development

From all the challenges above, there are opportunities in developments in many areas. This is in order to achieve the main objectives of the drug system. Therefore, the government, as the system administrator, is necessitated to allocate sufficient funds to support all activities, along with to determine a direction of drug system development in the following areas:

2.1 National processes to regulate expensive drug prices to be more reasonable and suitable for household and national affordability

2.1.1 Even though the price negotiation and drug purchasing have been done quite effectively, there are still different kinds of drugs that can be lower.

2.1.2 Promoting import of low-cost generic drugs, supporting domestic drug productions, and endorsing more on domestic productions of vaccines or biotechnology supplies.

2.1.3 Encouraging voluntary licensing to reduce drug prices.

2.1.4 A process to manage orphan drugs, specifically the drugs for rare diseases.

2.1.5 Provision of drug price international monitoring system, through the purchasing and bargaining networks.

2.1.6 Procurement of vaccines or certain drugs must be through long term contracts.

2.1.7 Integration of drug distribution for all health insurance systems in order to increase bargaining power and capability in drug management, especially for expensive drugs

2.2 Vigilance units that monitors movements of the drug system stakeholders, domestically and internationally

There must be reports of drug movements that may affect the pharmaceutical development system on the followings:

2.2.1 Pricing trends of generic drugs including expensive drugs.

2.2.2 Expiring patents can lower the drug prices.

2.2.3 Trends in market entering and drug productions of new manufacturers and existing manufacturers.

2.2.4 Updating on forthcoming new drugs that will replenish the existing ones. These upcoming new drugs could be cheaper but have better treatment efficiency (low cost - high efficiency).

2.2.5 Monitoring of drug distribution, drug promotion and advertisement for inappropriate cases.

2.3 Access to essential quality drugs

Efforts should be made to ensure the system that allows people to access essential quality drugs thoroughly and fairly without having to deal with price barriers to access to necessary drugs, and using the drugs reasonably as needed.

2.4 Standardization of the central drug codes beneficially for internal operations of related departments

This can be linked to activities of other sectors in the pharmaceutical and health systems including medicines, non-medicines, and medical supplies used in hospitals that connect to both the drug and medical systems for:

2.4.1 Using data to monitor and assess quality of work and research and development of drug systems

2.4.2 Managing the supply chain: manufacturing, import, export, registration, distribution, monitoring of drug quality and safety, and drug usage.

2.4.3 Drug administration in hospitals and reimbursements of medical expenses

2.5 Mechanisms to support rational drug use for implemented at the hospitals under the Ministry of Public Health

These mechanisms shall increase importance of setting guidelines and operations according to the policies for both workers and auditors. These also can expand to other related groups. For example:

2.5.1 Other medical institutions outside the Ministry of Public Health, such as other ministries, universities, private hospitals and clinics.

2.5.2 For the public sectors, medication literacy must be established. This is to enable rational use of medication in both medical service centers and communities. In addition, drug stores should be linked to the national health insurance system as well.

2.6 Development of curricula and teaching system in pharmaceutical science to meet future development needs

2.6.1 Systematic planning for the development of pharmaceutical manpower. Design and work closely in pharmaceutical professional organizations, pharmaceutical council, educational institutions and workplaces to position the role of pharmacists, increasing specialized skills in order to work along with other professionals.

2.6.2 Knowledge and skills in managing a pharmacy and taking a role of community pharmacist. This is in order to oversee safety of drug usage, protect consumers, and support the government services.

2.6.3 Knowledge of new drug production, biologicals, herbal medicine and traditional medicine. This is to utilize technologies to develop pharmaceutical products in various formats that respond to internal needs and necessities.

2.7 Enhancement in the quality of pharmacies and pharmacists in order to increase accessibility to essential drugs and elevate the quality of drug usage

Availability of people making more use of private resources and pharmacies can help to alleviate the burden on public health services:

2.7.1 Distribution of drug dispensing to pharmacies. At government hospitals, patients can pick up to their medicine at drugstores. And likewise, in private hospitals, patients can choose to receive their medication with controlled fair pricing.

2.7.2 Management system in pharmacies and community pharmacists plays an important role in overseeing drug usage in the community. This is in order to reduce the loss of drugs caused by unused or misused medication.

2.7.3 Utilizing pharmacies for health promotion and disease prevention, such as risk screening for diseases, providing basic health examination services, offering health advices, consulting on contraception, being a distribution center for contraceptive equipment

i.e. birth control pills, condoms, destroying of unused drugs, and distributing test kits for disease screening.

2.8 Revising and/or legislating laws or policies to support essential drug production domestically

2.8.1 Reducing the monopoly of drug selling by the Government Pharmaceutical Organization in public hospitals. This is in order to create fair competitions.

2.8.2 Promoting the production or import of chemicals, substrates, pharmaceutical raw materials, which are necessary for domestic productions. Having mutual raw material procurements. Having policies to promote synthesis or production of substances in various standards. This is in order to analyze environmental friendly drugs.

2.8.3 Creating incentives for inventing new drugs, i.e. tax measures to reduce production costs and increase quality and factory standards, innovation accounts and patent management.

2.9 Promoting and developing the extensive use of herbal medicine

This is to support the entire process from standardization of medicinal plants, raw material production, collection and development of Thai traditional medicine formulas to have pragmatic evidence. There should be a system to support the production and distribution of these herbal medicines domestically and for exports.

2.10 Mechanisms that help create drug system stability

The appropriate mechanisms include:

2.10.1 Promoting the Government Pharmaceutical Organization to be a research center, developing new drugs, producing orphaned drugs, and rare drugs, and biologicals. Also being a drug pricing unit in order to control price balance, and being able to transfer new technologies to private sectors.

2.10.2 Enhance the logistic systems for medicine and medical supplies to support the growing demands of drugs and drug distribution in the future.

3. Trends and Directions of the Drug System in Thailand – from Past to Present

Thailand has arrived at the point that the drug management system is being organized. The system's various stakeholders, such as pharmacists – an important professions of the drug system in the future, pharmacies – a way for people to access primary health services, hospitals – a service point providing medicines to patients, drug companies and dealers, and people who use health services. Thus, there are the following situations:

Pharmacists: In the past, pharmacists were scarce like other health professionals. But at present there is a trend having more pharmacists. This is an opportunity to expand responsibilities, not just the pharmaceutical services in the hospitals by expanding the coverage of primary care pharmacy and consumer protection in providing drug monitoring services, home visit, promoting health awareness and disease prevention in the community.

Community pharmacies: In the past, most of them were just people who previously worked in pharmacies and sometimes don't have pharmacists stationed in the stores. However currently, there are 20,000 pharmacies registered. There are 14,000 drugstores in type 1 (koryor 1)[5] in which there are pharmacists available in the stores during opening hours.

Hospital: Medicines and other medical supplies are also sources of hospital income, especially the system

that has a fee for service. However, when the health insurance system developed at some point, there were budgets allocated to hospitals in the form of per-capita. This has lowered stress to pay for expensive drugs, topping the differences in drug prices. The practice also helps support the management process of receiving medicines at community pharmacies to reduce congestion at the hospitals.

Pharmaceutical prototype companies: If there are patented drugs, these companies will try to monopolize the market by coming up with a form of evergreen patent, which is partially restructured in order to renew drug patents. But currently, the directions of pharmaceutical companies have changed, that said, the strategies have been adjusted by developing drugs with the participation of other parties. These pharmaceutical companies are establishing balanced points of making profits from the new drug. Originally, they made big profits from expensive drug prices and monopolized patents. Recently, they work more with the system. So, overall drug prices have been decreasing continuously over the years. And, annually the price increase is less than 1 percent. Especially for those running out of patents, the prices drastically decrease.

Domestic drug companies: Due to the fact that there are many commercial contracts resulting in the country's ability to produce drugs not being developed as it should be. However, there are substitutes for the drug productions from China and India. This has contributed to the growing number of inexpensive generic drugs.

Advancement in biotechnology will help making vaccines and diagnostic tests reduce drug usage, but effectively cure diseases. This will cause the amount of medication, used in some cases, tends to decrease.

People: Because of the difficulty of accessing services, especially the lack of faith in the primary care system, receiving secondary and tertiary care are difficult. In most cases, people with minor illness will start curing themselves by buying medicine at drug stores. However, with an advancement of communication and information, people have more knowledge in self-care and medication. In people's perspectives, we can say that there is a disruption of the drug system by (1) people becoming more aware of drug knowledge, (2) there are more channels to purchase drugs, not only at pharmacies. Currently, medicines are purchased via social media. And, (3) Information is easier to find on the internet.

4. Future Pictures

All that is happening in the pharmaceutical system in Thailand is leading to a turning point in the drug system and pharmaceutical management in the future. All stakeholders must adapt, with an important goal of people, when necessary, being able to easily access to drugs while unnecessary drug usage will be reduced. The system will reduce drug prices; new drugs will be more effective and specific to the diseases. There will be the use of other technologies to help diagnose and prevent diseases which create some changes in the drug systems. Future pictures that may occur are as follows:

4.1 People will have more knowledge and understanding about drug usage through various communication channels. And when they have to buy medicine themselves, there will be clearer explanations. Picking up medicines at a drugstore may not be costly because the quality pharmacy system is already in place in the health insurance system. When having to receive medication or medical supplies, patients will know the

prices of medicines and medical supplies, including being able to pick up medicines or medical supplies at quality pharmacies nearby. While having chronic illnesses and continuous medication is needed, a pharmacist will be on hand to provide advice and to take care at home.

4.2 Public services: People themselves will be the main key to prove of identity. And reports of services and drugs received will be through a seamlessly linked information system. People can easily access their own information via appropriate technologies.

4.3 Quality pharmacies will play greater roles in the public health system. They will be the frontline to public consultation, disease screening, and drug reception. And when the qualities pharmacies have increased at one point, they will significantly reduce burden and congestion at hospitals.

4.4 Pharmacists will adjust their roles from bestowing drugs in hospitals to work in providing public health care services. They will give reasonable suggestions for using the drugs, follow up patients who need to take medication at home, provide advices on health issues and disease prevention via a form of pharmacy owners, working with primary care services and hospitals to monitor patients in the community. In the future, more people will be allocated to pharmacists who will take responsibilities in the neighborhood.

4.5 The health service units will adjust their services to accommodate outpatient consultation and transfer more patients to the community, including monitoring drug usage from patients through the linked information system. Secondary hospital and tertiary will add value by focusing on high-level services that need more resources and time, appropriately for the capacity level. And, the burden of community health service center will be reduced.

4.6 The national price negotiation mechanism will be increased in the terms of bargaining, buying and selling. The negotiation to buy expensive drugs will be more concentrated because the key factors of health costs come from drug prices. And in the past, drug prices are quite high because the bargaining power of the buyers is rather weak. In the future, all health insurance schemes will find a way to negotiate the drug prices or negotiate the price of the drugs base on a number of drugs expected to be used, resulting in lowering drug prices.

4.7 Pharmaceutical companies will reduce unnecessary costs through negotiating standard prices.. The companies will tend to develop a patient care system integrated with the central system rather than focusing on selling patented drugs for maximizing profits.

4.8 With the above mechanism and global system integration, drug information, development direction, drug prices, the future direction will be more interchanged. There may be mechanisms at the international level for accessing to information of essential medicines. Since, there will be more drug information exchanged between countries, this could result in normalizing drug prices in different areas.

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บทคัดย่อ: ประเด็นท้าทายและโอกาสพัฒนาระบบยาในอนาคต

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ระบบยาเป็นส่วนหนึ่งของระบบสุขภาพ โดยการจัดการที่ดีในระบบยาเป็นส่วนสำคัญที่จะส่งผลให้ประชาชนมียาจำเป็นใช้ ได้เข้าถึงยาที่มีคุณภาพอย่างเท่าเทียม มีการใช้อย่างสมเหตุผล ตรงกับความสามารถในการจ่ายของครัวเรือนและประเทศ และเกิดเป็นความยั่งยืนของระบบในภาพรวม การสังเคราะห์องค์ประกอบต่าง ๆ อย่างเป็นระบบในบทความอื่นในวารสารฉบับนี้ ทำให้มองเห็นปัจจัยหลายประการที่ยังเป็นประเด็นท้าทายและเป็นโอกาสสำหรับการพัฒนาระบบยา ประเทศไทยยังมีปัจจัยหลายประการที่เป็นประเด็นท้าทายและเป็นโอกาสสำหรับการพัฒนาระบบยา ซึ่งภาคส่วนที่เกี่ยวข้องควรส่งเสริมและดำเนินการ ได้แก่ กลไกระดับชาติที่ติดตามแนวโน้มของยา ราคาแพง ต่อรองราคา จัดซื้อยารวม ให้ยามีราคาที่ถูกลง มีการใช้ที่ปราศจากอคติ ความรู้และความเชื่อที่ไม่ถูกต้อง การสนับสนุนระบบการผลิตยาในประเทศ ทั้งยาสามัญ สมุนไพร ชีววัตถุ เพื่อการพึ่งพาตนเองมากขึ้น การส่งเสริมศักยภาพด้านกำลังคนให้มีความสามารถเฉพาะทาง การมีระบบข้อมูลสารสนเทศที่สามารถเชื่อมโยง ติดตาม และประเมินผลการดำเนินงานในภาคส่วนต่าง ๆได้อย่างมีประสิทธิภาพ ตลอดจนการปรับปรุงนโยบาย กฎหมาย ที่เอื้อต่อการปฏิบัติในประเด็นที่กล่าวในข้างต้น นอกจากนั้นแล้ว ระบบยาโดยผู้มีส่วนเกี่ยวข้องทั้งหมดจะต้องสามารถปรับตัวให้เข้ากับยุคสมัยที่เปลี่ยนแปลง โดยมีเป้าหมายสำคัญคือ การที่ประชาชนได้เข้าถึงยาจำเป็นอย่างสะดวก ในขณะที่มีการใช้ยาที่ไม่จำเป็นไม่สมเหตุผลลดลง ผู้มีส่วนเกี่ยวข้องทั้งหมดต้องมีการปรับตัวโดยมีเป้าหมายสำคัญคือการที่ประชาชนเมื่อมีความจำเป็นต้องใช้ยาจะเข้าถึงยาได้อย่างสะดวกในขณะที่มีการใช้ยาที่ไม่จำเป็นลดลง ระบบจะทำให้ราคายาลดลง มียาใหม่ ๆ ที่ประสิทธิภาพดีและเจาะจงโรคมากขึ้น มีการใช้เทคโนโลยีอื่นเข้ามาช่วยในการวินิจฉัยและการป้องกันโรค ทำให้สุขภาพของประชาชนดีขึ้นจากการเปลี่ยนแปลงของยาและเทคโนโลยีด้านสุขภาพ

คำสำคัญ: ระบบยา; โอกาสในการพัฒนา; ภาพอนาคตของระบบยา

กระทรวงสาธารณสุข

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