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

Anchalee Jitruknatee, B.Pharm.
Kakanang Tosanguan, M.Sc. (Health Economics, Policy and Law)
Yuthtana Doangjai, B.Pharm.
Wannisa Theantawee, B.Pharm.
Juthathip Martro, M.Sc. (International Economics)
Food and Drug Administration, Ministry of Public Health, Thailand

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.

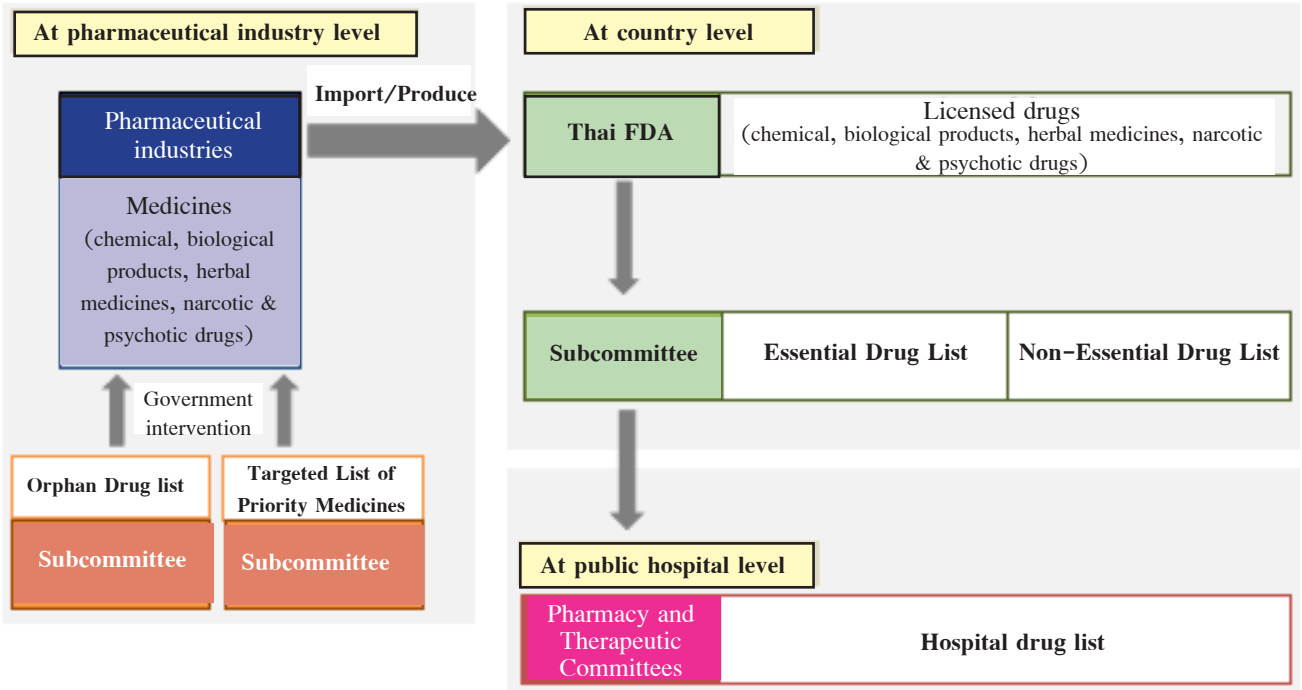
***Keywords*: drug selection, drug registration, national list of essential medicine, orphan drugs, targeted list of priority medicines, Pharmacy and Therapeutic Committee**

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:

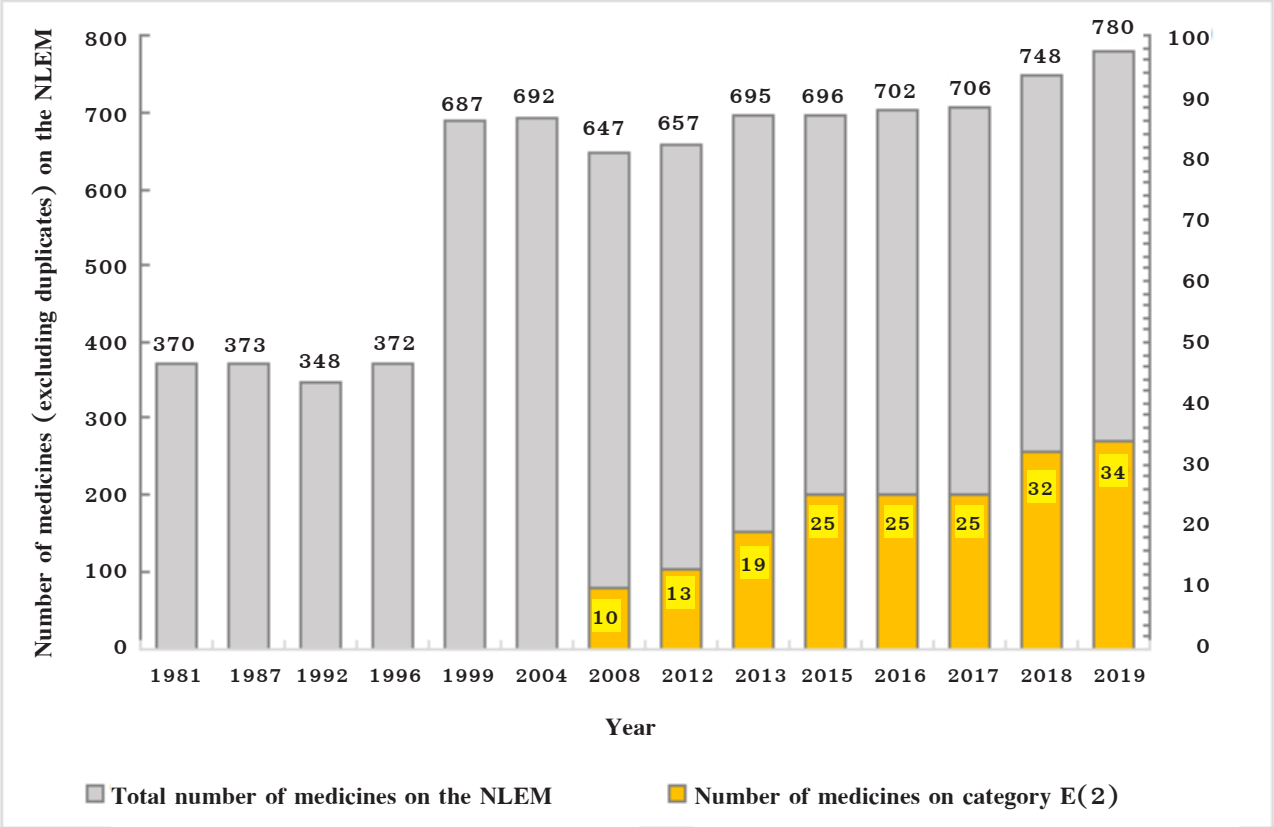
- Category A: Basic medicines for all health facilities, to use as first-line treatment,
- Category B: Alternative, second line medicines of those in Category A,
- Category C: Medicines prescribed only by specialists approved by the hospital director,
- Category D: Medicines used only particular indication 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]

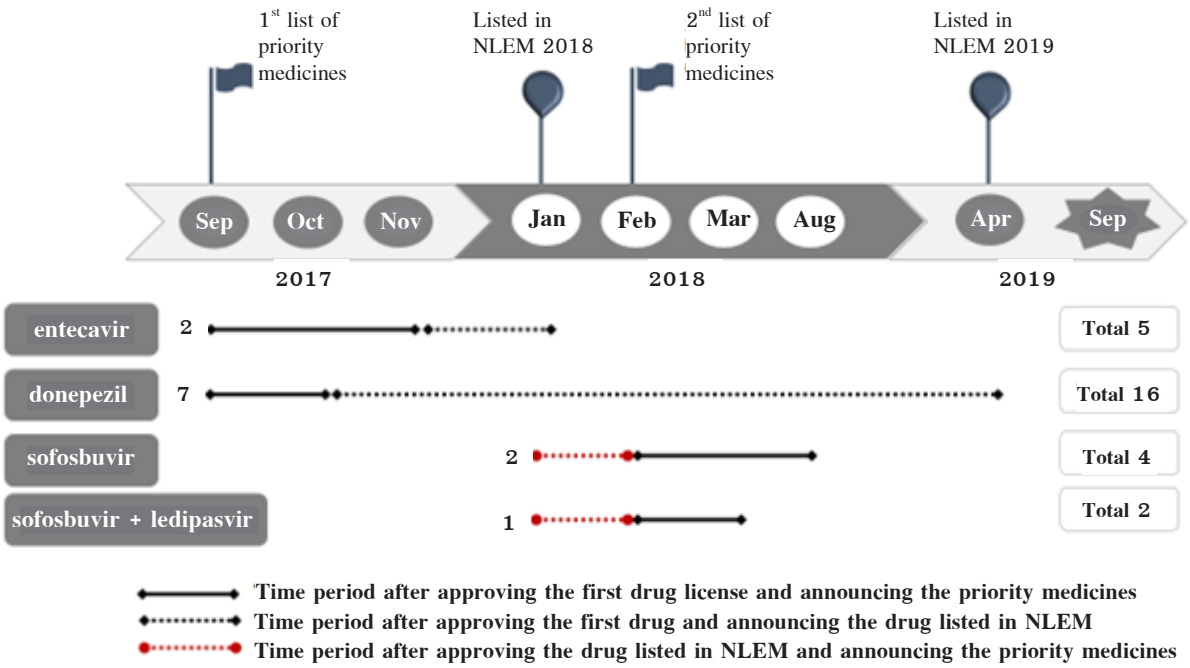
- The reduction of registration fees by 50% as per the Thai FDA announcement on 5th September 2016 and 8 February 2018
- Drug patent information search to provide local manufacturers/importers with the data to develop plans related to the introduction of generic drugs
- Development of reference prices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

References

1. Bigdeli M, Peters DH, Wagner AK, Alliance for Health Policy and Systems Research, World Health Organization Medicines in health systems: advancing access, afford¬ability and appropriate use. Geneva: World Health Organization; 2014.
2. Quick JD, Hogerzeil HV, Rankin JR, Dukes MNG, Laing R, Garnett A, et al. Managing drug supply: the selection, procurement, distribution, and use of pharmaceuticals. Connecticut: Kumarian Press; 1997.
3. WHO Action Programme on Essential Drugs. Public-private roles in the pharmaceutical sector: implications for equitable access and rational drug use. Health Eco¬nomics and Drugs Series, No. 005. Geneva: World Health Organization; 1997.
4. Sakulbumrungsil R, Taychakhoonavudh S, Udomaksorn K, Kessomboon N, Ngorsuraches S, IMS Consulting Group. Pricing and patient access framework to support universal coverage in Thailand, 2016. Bangkok: National Health Security Office; 2016.
5. Holloway KA, Green T. Drug and Therapeutics Committees: a practical guide. Geneva: World Health Organisation; 2003.
6. Working Group to Study and Analyze the Thai Drug System, Health System Research Institute. Thai drug system. Nonthaburi: Health Systems Research Institute; 2002.
7. Holloway KA. Drug policy and use of pharmaceuticals in health care delivery. New Delhi: World Health Organisation; 2012.
8. Usavakidviree V, Yoongthong W, Assawamakin A, Jitraknatee A, Nipatpimjai S. The development of re-evaluation model on marketed drugs and implementations. Thai drug system. Nonthaburi: Health Systems Research Institute; 2012.
9. Usavakidviree V, Yoongthong W, Assawamakin A, Jitraknatee A, Nipatpimjai S. The development of re-evaluation model on marketed drugs and implementations. Food and Drug Administration Journal 2013;20(3): 47-59.
10. Ministry of Public Health. The notification of the Ministry of Public Health on good manufacturing practices for modern drugs. Royal Thai Government Gazette Volume 128. Special issue 75 D (Dated 14 April B.E. 2554).
11. The Drug Act of B.E. 2562 (2019) Royal Thai Government Gazette Volume 136 Issue 50 D (Dated 15 April B.E. 2562).
12. Chongtrakul P, Sumpradit N, Yoongthong W. ISafE and the evidence-based approach for essential medicines selection in Thailand. Essential Drugs Monitor 2005; 34:18-9.
13. Wiwat C, Sriviriyanupap W, Yoongthong W. Doctor Sem Pringpuangkeo - leader of the national list of essential medicines. Bangkok: Faculty of Pharmaceutical Science Chulalongkorn University; 2011.
14. National Drug System Development Committee. National list of essential medicines (No. 2) 2012. Royal Thai Government Gazett Volume 129; Speical Chapter 85 D (Dated 29 March B.E. 2555) [Internet]. [cited 2019 Nov 30]. Available from: http://www.ratchakitcha.soc.go.th/DATA/PDF/2556/E/009/30.PDF
15. National Drug System Development Committee. National list of essential medicines 2015. Royal Thai Government Gazette Volume 132; Section 184 D (Dated 28 May B.E. 2558) [Internet]. [cited 2019 Nov 30]. Available from: http://www.ratchakitcha.soc.go.th/DATA/PDF/2558/E/184/12.PDF
16. National Drug System Development Committee. National list of essential medicines (No. 2) 2016. Royal Thai

Government Gazette Volume 133; Section 255 D (Dated 19 February B.E. 2562) [Internet]. [cited 2019 Nov 30]. Available from: http://www.ratchakitcha.soc.go.th/DATA/PDF/2559/E/255/1.PDF

17. National Drug System Development Committee. National list of essential medicines 2017. Royal Thai Government Gazette Volume 134; Section 119 D (Dated 25 April B.E. 2560) [Internet]. [cited 2019 Nov 30]. Available from: http://www.ratchakitcha.soc.go.th/DATA/PDF/2560/E/119/27.PDF
18. National Drug System Development Committee. National list of essential medicines 2018. Royal Thai Government Gazette Volume 135; Section 230 D (Dated 26 July B.E. 2561) [Internet]. [cited 2019 Nov 30]. Available from: http://www.ratchakitcha.soc.go.th/DATA/PDF/2561/E/230/T11.PDF
19. National Drug System Development Committee. National list of essential medicines 2019. Royal Thai Government Gazette Voulume 136; Section 95 D (Dated 19 March B.E. 2562) [Internet]. [cited 2019 Dec 1]. Available from: http://www.ratchakitcha.soc.go.th/DATA/PDF/2562/E/095/T_0008.PDF
20. National Drug System Development Committee. National list of essential medicines 2013. Royal Thai Government Gazette Volume 130; Section 126 D (Dated 30 September B.E. 2556) [Internet]. [cited 2019 Dec 1]. Available from: http://www.ratchakitcha.soc.go.th/DATA/PDF/2556/E/126/11.PDF
21. Jirawattanapisal T, Kingkaew P, Lee TJ, Yang MC. Evidence-based decision-making in Asia-Pacific with rapidly changing health-care systems: Thailand, South Korea, and Taiwan. Value in Health 2009;12(s3):S4-S11.
22. Teerawattananon Y, Tantivess S, Yothasamut J, Kingkaew P, Chaisiri K. Historical development of health technology assessment in Thailand. Int J Technol Assess Health Care 2009;25 (Suppl 1):241-52.
23. National List Essential of Medicines (no.3) 2008. Royal Thai Government Gazette Volume 125; Section 136 D (Dated 20 June B.E. 2551) [Internet]. [cited 2019 Dec 1]. Available from: http://www.ratchakitcha.soc.go.th/DATA/PDF/2551/E/051/16.PDF
24. Leelahavarong P, Doungthipsirikul S, Kumluang S, Poonchai A, Kittiratchakool N, Chinnacom D, et al. Health technology assessment in Thailand: institutionalization and contribution to healthcare decision making: review of literature. International Journal of Technology Assessment in Health Care 2019:1-7.
25. Sripairoj A, Tangcharoensathien V, Liamputtong P. Pharmacy and therapeutics committee in Thai hospitals under health care reform. Journal of Health Science 2005; 14:119-28.
26. Umnuaypornlert A, Kitikannakorn N. Performance of pharmacy and therapeutics committees of public hospitals in rural Thailand. Mahidol University Journal of Pharmaceutical Sciences 2014;41(1):11-8.
27. Sudchada P, Umnuaypornlert A, Kitikannakorn N. A survey of practical policies to promote rational drug use (RDU) of pharmacy and therapeutics committee (PTC) in Thailand. Srinagarind Med J 2012;27(2):157-66.
28. Pharmacy and Therapeutics Committee (PTC). Criteria for generic drug selcetion by using price performance criteria. Songkla: Songklanagarind Hopitals; 2016.
29. Assawamakin A, Holtorf AP, Maniadakis N. Weighing price and performance for decisions for multisource pharmaceutical bidding in public hospitals in Thailand [Internet]. 2019 [cited 2020 Jan 5]. Available from: DOI: 10.5772/intechopen.83823.
30. Bureau of Drug Control, Food and Drug Administration. Solving the drug shortage issues in Thailand. Nonthaburi: Food and Drug Administration; 2014.
31. Food and Drug Administration. Announcement of the Food and Drug Administration, Re: Orphan drug list 2019. Nonthaburi: Food and Drug Administration; 2019.
32. Subcommittee on drug shortage surveillance and management. Minutes of Subcommittee on drug shortage surveillance and management meeting on 27 August 2019. Nomthaburi: Food and Drug Administration; 2019.

33. Subcommittee on Development of Local Pharmaceutical Industry. Minutes of Subcommittee on Development of Local Pharmaceutical Industry on 1 June 2017. Nomthaburi: Food and Drug Administration; 2017.
34. National Drug System Development Comittee. Minutes of National Drug System Development Comittee in 30 June 2016. Nomthaburi: Food and Drug Administration; 2016.
35. Pattanaphesaj J, Sunthornphanich S, Savetsila S, Hongthong S. Quality of medicines in Thailand: 15 years of data from the quality assurance of medicines program, Department of Medical Sciences, Ministry of Public Health. Journal of Health Systems Research 2018;12(1): 124-36.
36. Sruamsiri R, Wagner AK, Ross-Degnan D, Lu CY, Dhippayom T, Ngorsuraches S, et al. Expanding access to high-cost medicines through the E2 access program in Thailand: effects on utilisation, health outcomes and cost using an interrupted time-series analysis. BMJ Open 2016;17;6(3):e008671.

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อัญชลี จิตรักนที ภ.บ.; คัคนางค์ โตสงวน M.Sc. (Health Economics, Policy and Law); ยุทธนา ดวงใจ ภ.บ.; วรรณนิษา เถียรทวี ภ.บ.; จุฑาทิพย์ มาตรอ M.Sc. (International Economics)
สำนักงานคณะกรรมการอาหารและยา กระทรวงสาธารณสุข
วารสารวิชาการสาธารณสุข 2563;29(ฉบับพิเศษ):S31-44.

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**