PRIORITY SETTING OF THE FIRST GENERIC DRUGS REGISTRATION IN THAILAND

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ABSTRACT

The objective of the study was to study the priority setting process of the first generic drugs for registration in Thailand. The study was cross-sectional descriptive policy research. Data was collected from a questionnaire and interviews that asked about the feasibility of generic drug production and the bioequivalence study of the 30 most imported drugs. The ranking list of national drug expenditure from the year 2009-2012, was derived from the Bureau of Drug Control, Thai FDA. The opinion towards the drug registration process was included in the interview questions as well. Descriptive statistics were used to analyze the data.

Six participants from bioequivalence centers and eight from local pharmaceutical manufacturers were interviewed. As a result, the conclusion from the opinion of all participants was that the process of generic drug registration did not correlate with the needs of the country. The timeline of the generic drug registration process was the crucial factor that affected the availability of new generic drugs and needs to be reorganized, including the working process. The sensitivity analysis showed that the amount of drug expenditure that might be saved from generic substitution was up to 49% per year.

Thus, prioritizing the registration process, due to the level of drug expenditure consumed, was the most highlighted recommendation to the Thai FDA. The results of this study may help decrease the overall drug expenditure or, at least, can be used to improve the working process in the drug registration department.

KEY WORDS: PRIORITY SETTING / NEW GENERIC DRUG / DRUG REGISTRATION

74 pages

การวิเคราะห์การจัดลำดับการขึ้นทะเบียนยาสามัญใหม่รายแรกของประเทศไทย
PRIORITY SETTING OF THE FIRST GENERIC DRUGS REGISTRATION IN THAILAND

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บทคัดย่อ

การวิจัยครั้งนี้มีวัตถุประสงค์เพื่อแสดงแนวทางที่สามารถนำไปปรับใช้ในระบบการขึ้นทะเบียนยาสามัญใหม่ของคณะกรรมการอาหารและยา วิธีการวิจัยในการศึกษานี้จะเป็นแบบการวิจัยเชิงนโยบาย โดยเป็นการเก็บข้อมูลและรายงานเชิงบรรยาย มีการตอบแบบสอบถามและสัมภาษณ์ มีการขอข้อมูลตัวเลขมูลค่าการนำเข้ายาจากสำนักยา (สะท้อนถึงปริมาณการใช้ภายในประเทศ) สูงสุด 30 อันดับแรกตั้งแต่ปี พ.ศ.2552-2555 นำมาพิจารณาความเป็นไปได้ในการผลิต และทำการศึกษาชีวสมมูลในประเทศไทย คำถามถึงความคิดเห็นต่อกระบวนการทำงานในการขึ้นทะเบียนยาจะถูกใส่เป็นคำถามในการสัมภาษณ์ และใช้สถิติเชิงพรรณาในการประเมินข้อมูล

ข้อมูลที่ได้ถูกรวบรวมมาจากบริษัททำการศึกษาชีวสมมูล 6 แห่ง และบริษัทผลิตยาสามัญในประเทศ 8 แห่ง พบว่า การขึ้นทะเบียนยาสามัญในปัจจุบันยังไม่ตอบโจทย์ความต้องการของประเทศ และปัญหาความล่าช้าของการขึ้นทะเบียนยังเป็นปัญหาหลักของจำนวนยาสามัญใหม่ ผลจากการวิเคราะห์ความอ่อนไหว พบว่าปริมาณสูงสุดของค่าใช้จ่ายด้านยาต่อปีที่อาจลดลงจากการสนับสนุนการใช้ยาสามัญมีค่า ร้อยละ 49

ดังนั้นการจัดลำดับความสำคัญในการขึ้นทะเบียนยาโดยใช้ปริมาณค่าใช้จ่ายในการนำเข้ายาจึงเป็นสิ่งสำคัญ และเป็นหนึ่งในข้อเสนอแนะต่อคณะกรรมการอาหารและยา โดยผลที่ได้นี้อาจนำไปพิจารณาใช้เพื่อลดงบประมาณด้านยาของประเทศได้ หรืออย่างน้อยที่สุด สามารถนำไปปรับใช้เพื่อเพิ่มประสิทธิภาพในการทำงานด้านการขึ้นทะเบียนยาสามัญ

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LIST OF ABBREVIATIONS

Thai FDA	Thai Food and Drug Administration
BE	Bioequivalence
R&D	Research and Development
GMP	Good Manufacturing Practice
GLP	Good Laboratory Practice
OECD	Economic Co-operation and Development
PIC/S	Pharmaceutical Inspection Co-operation Scheme
ISO	International Organizations for Standardization
GCP	Good Clinical Practice
HSP	Human Subject Protection
ICS	International Conference on Harmonization
IMS	Intercontinental Marketing Service
WHO	World Health Organization
MPH	Ministry of Public Health
GPO	The Government Pharmaceutical Organization
CAGR	Compound Annual Growth Rate

CHAPTER I
INTRODUCTION

Background and rationale

Healthcare expenditure becomes the highlight issue all over the world. Many factors influence i.e. health technology, new drug discovery, aging society etc. (1) Changes in expenditure could be listed into 3 components: the price of drugs, the quantity of drugs consumed and a residual which is a measure of the effect of changes in drug treatment patterns (2). All factors drive the situation get even worse. The study from Kaojarern, S. et al 2011 (3), about outpatient drug utilization at a teaching hospital in Thailand, found that drug oversupply in chronic disease is the major cause of hospital drug budget. This problem mainly derives from civil servants reimbursement system, free of charge. In Thailand, uncontrolled budget leads to many consequences such as the shortage of medicine because of hospital's financial crisis.

The need of new treatment is increasing by the time. Everyone should access to the needed medicine equally. Pharmaceutical companies claim that the high of R&D cost leads to the high selling price, so accessibility to the new drug seems to be inequity. The study from Meyer et al, 2013 surveyed from six countries in Asia Pacific region, including Thailand, between 2009 and 2010 found that poor health and low income are the difficulties in access to the healthcare(4). Even in developed country like the U.S., the financial burden of medical care is faced by one in three persons. This is a result from the National Health Interview Survey (NHIS), January–June 2011(5).

Mixed policies to control healthcare budget have been implemented all over the world. Many countries, such as Germany, Sweden and Netherland, use reference pricing system but this system is applicable only to drug without patents. So the continuing rise in drug expenditure still exists (6). Several studies concerning drug use evaluation were conducted to assess the physician prescribing behavior and manage direct to the point. The successful of this approach depend on the cooperation.

Another policy to control costs by promoting the use of generic drugs is encouraged in most countries. Germany and the U.S. are the samples of a country that implement the physician incentive system for generics substitution (7)(8). In 2008 over 76% of prescriptions in Germany were dispensed as generics, accounting for 36.8% of the market value and saved the German taxpayer Euros 621.5 million (9). In the UK, use of generic drugs has grown significantly, from about 16% of prescriptions in 1977 to 54% in 1994, and this proportion is still rising (5). The data and a retrospective analysis of Generic Drug Savings study in the U.S. by the IMS Institute for Healthcare Informatics to estimate the amount savings contributed by generic pharmaceuticals. According to the report, generic drug use has saved healthcare budget of the U.S. approximately $1.07 trillion over the past decade (2002 through 2011). Data presents $192.8 billion budget savings achieved in single year 2011 (10).

In Southeast Asia, Generics market shares vary from country to country but in general are increasing across the regions. See in Figure1

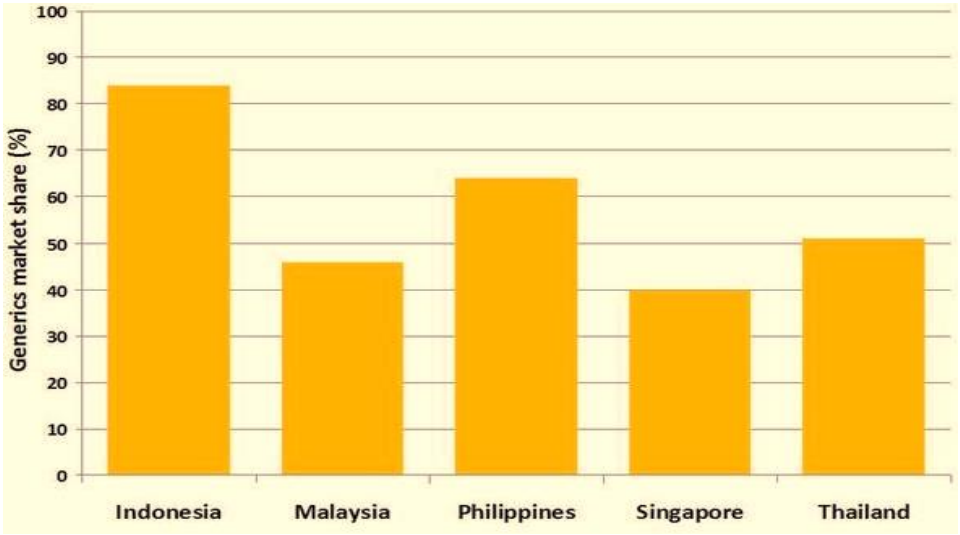


Figure 1.1 2011 Generics market share in selected Southeast Asian countries (IMS, The Jakarta Post, http://gabionline.net/Generics/General/Southeast-Asian-generics-market-to-reach-US-3.9-billion-by-2016. Access date 22 November 2013)

Although the generic drug market in Thailand is quite high as seen in Figure1, (about 50% by volume), the weak support from the government, in the term

of production, pricing and promoting utilization, may affect the number of generic drug in the future.

At present there are several monopoly drugs sold in Thailand, which means that there are no generics. Some still have patent protection but some do not. The ideal concept is the generic version should be available at the first day after patent expiration of the original. But the current situation is not. Thus recently, Thai government shows strong intention to promote production of these off-patent original drugs to be the first new generic drugs in Thailand by releasing the policy.

The policy to encourage the availability of new generic medicines is the acceptance of foreign bioequivalence study in first generic drug registration. Thai FDA hopes to reduce the timeline of generic drug entering the market about 1-2 years which is the period for conducting BE study in general. This policy had been started from June, 2012. Lucky draw of the monopoly chemical entities was conducted a time per month, then per two months later. All the pharmaceutical companies have a right to apply in the program. After they won the lucky draw, they will arrange both foreign bioequivalence study and registration dossier and send to the new generic drug registration department, Thailand's Food and Drug Administration (Thai FDA).

Since the beginning until August 2013, 171 monopoly drugs were included in 11 rounds of lucky draw. The neck of the bottle might be happen in the registration process because of the limitation of the number of registration officer and rapid increasing of workload. So, there should be some guideline to set priority the need for production and registration of these urgent medicines. Factors influencing the priority setting are sales volume, price, capability in research and development (R&D)-production, and bioequivalence study.

The general objective

To study the priority setting process of the first generic drugs for registration in Thailand.

Specific objectives

1. To study the situation of new generic drug in Thailand
2. To find the method to accelerate the availability of essential generic drug

3. To estimate the drug budget that might be saved

Expected outcome and benefit

1. The result of this study will be a data for the decision-maker to support in first generic local production and prevent the new generic drug shortage in the future.

2. Thai FDA registration department can use the data from this study to be a model of working process reorganization.

Definition of terms

New generic drugs

New generics are medicines with the same active ingredients, doses and dosage forms as those of the original products that registered after 1992.

Monopoly drug

A situation in which a single company or group owns all or almost the entire market share for a given type of product or service. By definition, monopoly is characterized by an absence of competition. In this case, it means a single seller of a medicine, one proprietary name.

Bioequivalence

The absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study(11).

Generic Drug

A drug product that is comparable to brand/reference listed drug product in dosage form, strength, route of administration, quality and performance characteristics, and intended use.

First Generic Drug

The first generic version of original/branded drug launched to the market.

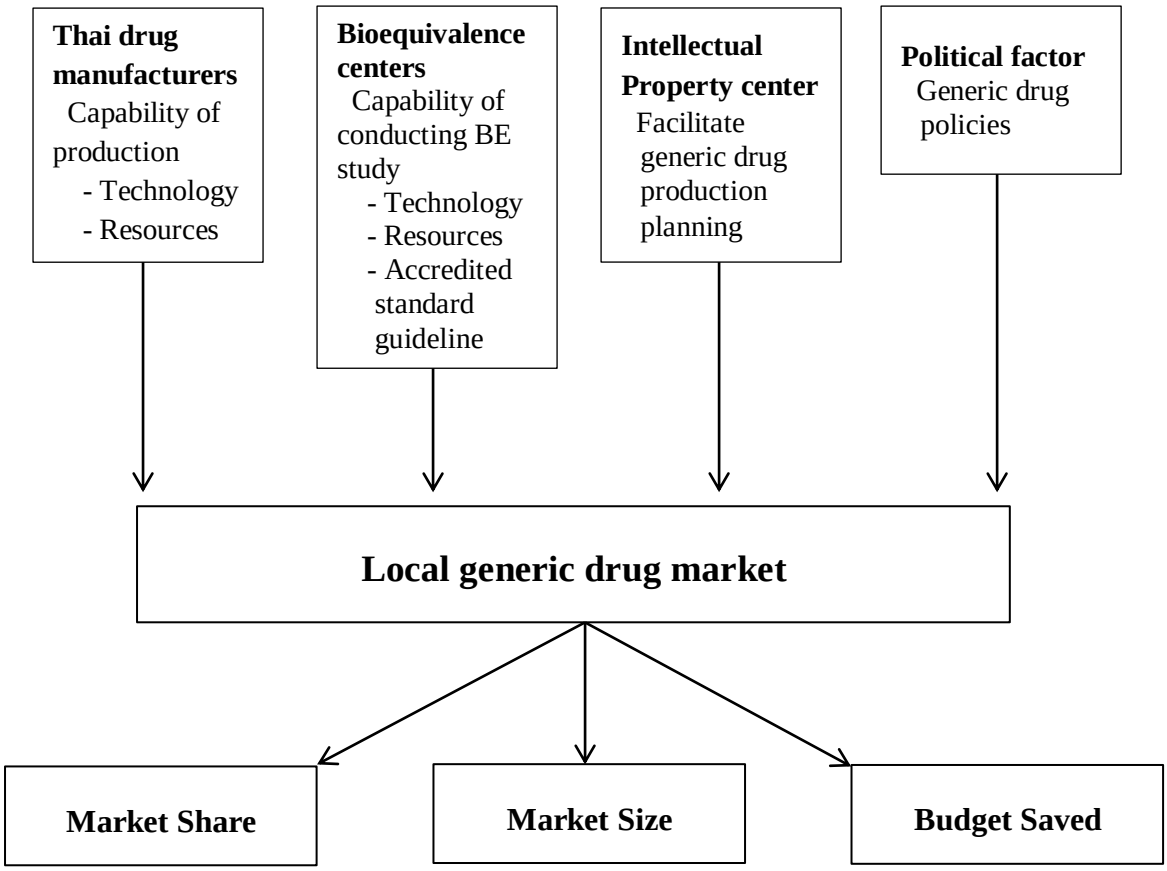


Figure 1.2 Conceptual framework of factors affected generic drug market

Conceptual Framework (Figure 2)

The concept of this study aims to focus on local generic drug market. The factors affected can be identified into 4 main parties.

The first, Thai drug manufacturers play a crucial role because the capability of production and investment are driving the generic drug market. The second factor is bioequivalent centers that responsible for all the BE studies of generic drugs proposed to market in Thailand. The number and quality of generic drugs are mainly controlled by the first two factors. Technology, resources and international standard involved in these factors are needed to be analyzed.

The other two factors are the intellectual property (or patent) and government policy. These factors make the generic drug production easier to planning for production. The researcher adds patent issue and policy in the study as they control the availability of generic drug. In the current situation, it plays a role both as the facilitator and decelerator of local generic drug business.

The researcher uses four indicators, generic marker share, price of generic drugs, market size and budget saved to estimate the impact from four factors.

Marker share is the factor to estimate how much the proportion that the generic drug could own. Price of generic drugs is analyzed in the form of percent of original drugs. These proportions are used to calculate the overall national drug expenditure. Market size makes us see the big picture of drug market. The size of market benefits for planning for drug production, investment and the policy implementation. Budget saved is the final objective of all operation. The more budged saved means the more right direction the generic market is.

CHAPTER II
LITERATURE REVIEW

There are five parts in the literature review as following:

Part 1Laws and regulations concerning pharmaceutical drug production

Part 2Local generic pharmaceutical companies in Thailand

Part 3Bioequivalence centers in Thailand

Part 4Generic drug production in Thailand

Part 5Thai FDA first generic drug policy

Part 6Thailand and overseas generic drug registration process and time-consumed

Part 1 Laws and regulations concerning pharmaceutical drug production

Thailand government has launched many standard guidelines to assure the quality of generic medicines. As follows

1.1 Good Manufacturing practices (GMP) (13)

Good manufacturing practices (GMP) compliance has begun since 1984 as the Thai FDA's campaign. Projects on development of local pharmaceutical industry up to internationally acceptable standards were part of the Sixth National Economic and Social Development Plan (1987–1991) and also of the Seventh Plan (1992–1996). The objective of these projects was to promote and support local drug manufacturers in good manufacturing practices implementation. The first guideline of Thai Good Manufacturing Practices was published in 1987.

Good Manufacturing practices (GMP), applied from Pharmaceutical Inspection Co-operation Scheme (PIC/S) Guide to Manufacturing Practices for Medicinal Products PE 009-9 1 September 2009, is the compulsory in Thailand's Drug Act of B.E.2546 (2003) (12). Manufacturers who are unable to comply with the good

manufacturing practices principles can no longer proceed with the drug business. Drug manufacturers, importers and distributors must apply their quality assurance systems by following the GMP guidelines to guarantee that the drug products have and continue to have the quality as claimed. The Drug Committee will revise and approve the GMP requirements and then declared by the Minister of Public Health.

1.2 Good Laboratory Practices (GLP) (14,15)

New generics registrations require dossiers of both bioequivalence (BE) studies and the required dossiers for generics registration. It is the compulsory that new generic products have to pass BE studies to ensure comparatively therapeutic outcomes. The bioequivalence data must be submitted to the authorities as proofs of the product bioavailability along with product information and quality dossiers. Only BE study conducted in Thailand was allowed in the registration process (13).

About the quality assurance of BE center, Good Laboratory Practices (GLP) are applied. GLP is the international standard run by the organization for Economic Co-operation and Development (OECD). The Good Laboratory Practice (GLP) aims to ensure the high quality and reliable test data related to the safety of industrial chemical substances and preparations.

1.3 International Organizations for Standardization (ISO17025)

Besides GLP, ISO17025 is the alternative standard for BE center in Thailand. This applies only in the ASEAN Guidelines for the Conduct of Bioavailability and Bioequivalence Studies. ISO/IEC 17025 General requirements for the competence of testing and calibration laboratories are the main ISO/CASCO standard used by testing and calibration laboratories. The most updated second release was made in 2005. ISO 17025 is a standard for laboratory competence that accreditation bodies use and is concerned with the technical competence of a laboratory. Accreditations usually serve to demonstrate impartiality and performance capability. Tests conducted to ISO 17025 are usually performed to evaluate a specific property of a sample (16, 17).

1.4 Good Clinical Practices (GCP) (18)

Compliance to the principles of GCPs, including adequate human subject protection (HSP) is the universal agreement as a critical requirement to any clinical test in human subjects. As bioequivalence studies are pharmacokinetic studies conducting in human, they must follow the same GCP guidelines as the clinical trials. GCP is an international quality standard that is provided by International Conference on Harmonization (ICH), an international body that defines standards, which governments can transpose into regulations for clinical trials involving human subjects. The Food and Drug Administration's (FDA's) regulations accept both GCP and HSP for the conduct of clinical trials. These regulations have been in effect since the 1970s. The European Guidelines rule that the report of a bioavailability or bioequivalence study should give the complete data of its protocol, conduct and evaluation complying with GCP-rules.

ICH GCP guidance aims to provide a unified standard for the European Union (EU), Japan, and the United States to facilitate the mutual acceptance of clinical data by the regulatory authorities in these jurisdictions. The guidance was developed with consideration of the current good clinical practices of the European Union, Japan, and the United States, as well as those of Australia, Canada, the Nordic countries, and the World Health Organization (WHO). When conducting any clinical trial data that are proposed to be submitted to the registration department in these areas, GCP guidance should be followed. The principles established in this guidance can also be applied to other clinical test that investigate and may have an impact on the safety and well-being of human subjects (19).

Part 2 Local generic pharmaceutical companies in Thailand

The drug market in Thailand is dominated by foreign manufacturers. Together, the US, France, Germany and Switzerland make up nearly 50 percent of all sales revenue from imported pharmaceutical products. The leading multinational companies in Thailand include Sanofi, Pfizer, Merck, Novartis and GlaxoSmithKline (20).

However, about three quarters of pharmaceutical companies in Thailand are Thai-owned. Leading local manufacturers include Siam Bhaesaj, Greater Pharma, Biolab, Berlin, Siam Pharmaceutical and Thai Meiji (Figure2). There are now 159 Thai Modern Medicinal GMP Conformance Manufacturers (update 13/11/2013, Bureau of Drug Control, Thai FDA). In addition, another major domestic manufacturer is the Government Pharmaceutical Organization (GPO), operate by Thailand's Ministry of Public Health (MPH). The GPO manufactures more than 300 pharmaceutical products, most of which are sold via government hospitals, 80 percent of the market.

TOP 10 PHARMA COMPANIES IN THAILAND
(COMBINED MARKET)

	MAT ~12/2011 LC-BAHT BAHT	MAT ~12/2011 LC-BAHT BAHT%	MAT ~12/2011 LC-BAHT BAHT%
SELECTED TOTAL	110,175,536,105	100.00	1.34
PFIZER INTER.CORP	9,551,192,695	8.67	-1.07
MERCK SHARP&DOHOME	6,115,099,620	5.55	4.34
SANOFI AVENTIS	5,710,316,734	5.18	1.58
NOVARTIS	4,662,778,408	4.23	0.41
GLAXOSMITHKLINE	4,491,160,404	4.08	2.34
ROCHE	4,350,682,435	3.95	1.23
ASTRAZENECA	3,803,096,624	3.45	-9.19
SIAM BHAESAJ CO	3,535,371,440	3.21	1.00
GPO	3,341,445,167	3.03	-2.39
BERLIN PHARM	2,741,798,673	2.49	13.06
OTHERS	61,872,593,905	56.16	0.00

Figure 2.1 Top 10 Pharma Companies in Thailand of year 2011-July 2012 (Source: IMS Thailand, http://issuu.com/focusreports/docs/thailand_pharma_report_june_2012. Access date 14 November 2013)

Part 3 Bioequivalence centers in Thailand

In the past, Thailand has many bioequivalence centers. After the regulation announced at 1st January 2010 obligate the bioanalytical part of bioequivalence trials

should be conducted according to the applicable principles of Good Laboratory Practice (GLP) i.e. EMEA/OECD GLP or WHO GLP STANDARD or ISO/IEC 17025/1999 (21). As the budget for applying center to meet the standard is quite high, the total numbers of bioequivalence centers become lesser. Now there are 9 bioequivalence centers in Thailand that comply with the Thai FDA's accredited standard (Table1).

Nowadays, the bioequivalence business is quite well because the government policy require BE study in Thailand in every generic drug that purposed to market in Thailand. So the profits of the business derive from both local generic drug companies and overseas as well.

Table 2.1 List of Thai FDA's Accredited Bioequivalence centers (Updated Aug, 2013).

Bioequivalent study centers	**Accreditation**	
	GLP	**ISO/IEC17025**
International Bio Service Co., Ltd.	✓	
Medica Innova Co., Ltd.	✓	
Bio-Innova & Synchron Co.,Ltd.	✓	✓
Pharmacy Service Center Faculty of Pharmacy, Chiangmai University	✓	
All Research Co., Ltd.	✓	
Chula-Pharmacokinetic Research Center		✓
Siriraj Clinical Research Center, SiCRC		✓
Pharma Nueva Co.,Ltd.		✓
The Government Pharmaceutical Organization Bioequivalence Study Center	✓	

The data from Part 1, laws and regulations concerning pharmaceutical drug production, imply that the GLP standard is the main standard for BE study in the

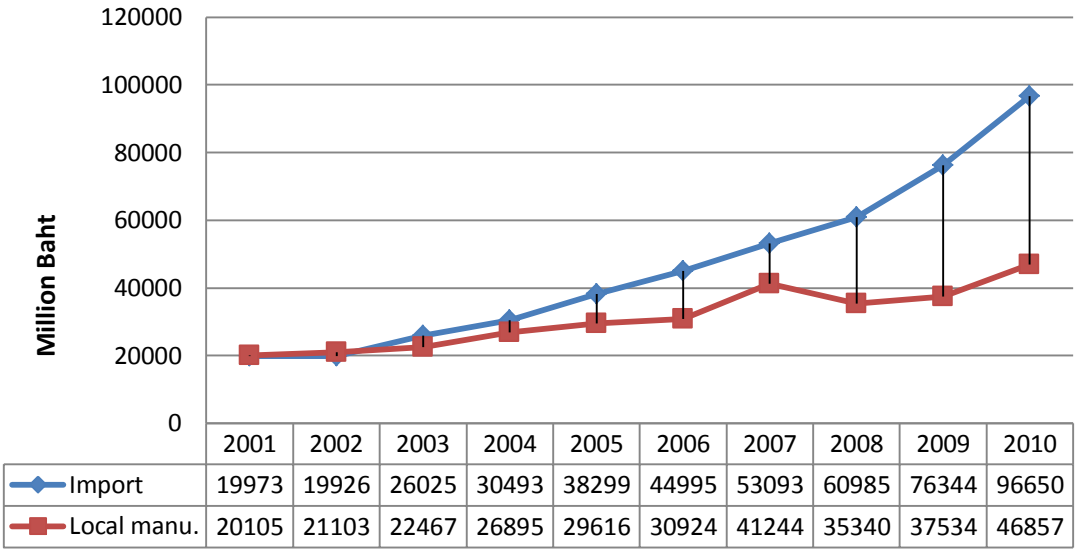
whole group of OECD countries. In order to market the product in Europe or USA, the companies have to select the BE center that accredited by GLP inspectors.

Part 4 Generic drug production in Thailand

From 2010 National drug account report the value of the domestically manufactured drugs (excluded repacking) was 46,895,753,521 Baht the import value was 99,663,791,612 Baht and the export value was accounted for 12,077,467,549 Baht. The overall drug value of domestic consumption (at consumer price) was 144,570,906,916 Baht. The local manufacture drug account approximately 30 percent of total domestic consumption (22).

Generic drug market in Thailand is growing continually because of the policy to control national drug budget. Market share of generic drug accounts about 50 percent of overall Thailand's pharmaceutical market in 2011 and compound Annual Growth Rate (CAGR) from 2006-2011 is 8 percent (Source: IMS Analysis, IMS MIDAS Data, 2011). Even the market share of generic drugs capture more than half of the pharmaceutical market but the value in term of money still great less than imported original products, as seen in figure 4. The drug importation and local production value is significantly higher different by time. So the solution of high drug expenditure by generic substitution is still not successful.

The future trend of local generic market seems to be good. A lot of blockbuster drug patent will be expired in next few years as shown in table1. On the contrary, the trend of local generic production growth is declining indicated by ten years trend of importation and local manufacturing pharmaceutical products in Thailand (Figure4). Data in figure 4 was derived from Bureau of drug control, Thai Food and Drug Administration website. The different of drug importation and local manufacturing value has increasing every year. Until 2010, the different value was more than 50 percent. There are many monopoly drugs in the market that able to do the generic versions. The limitations of production may come from many reasons including Research and Development (R&D) process, registration process, bioequivalence study and patent issue.



	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Import	19973	19926	26025	30493	38299	44995	53093	60985	76344	96650
Local manu.	20105	21103	22467	26895	29616	30924	41244	35340	37534	46857

Figure 2.2 Ten years trend of importation and local manufacturing pharmaceutical products in Thailand. (Bureau of drug control, Thai Food and Drug Administration)

Table 2.2 Samples of the medicine will be expired in the year 2014, 2015 and 2016 (Kathlyn Stone, Which Popular Drugs Are Going Off-Patent in 2013-2016?: About.com/Pharma)

Year	**Medicine name/ Company/ Global sale**
2014	*Nexium (esomeprazole)* is manufactured by AstraZeneca. Global sales in 2010 were $4.9 billion.
	Cymbalta (duloxitine HCI), manufactured by Eli Lilly, Global sales exceeded $4 billion in 2011.
	Celebrex (celecoxib), Pfizer, its manufacturer, reported sales of $2.5 billion in 2011.
	Symbicort (budesonide/formoterol fumarate dihydrate) is manufactured by AstraZeneca. Sales of Symbicort were $3.1 billion in 2011.
	Actonel (risedronate), worldwide sales were $1.6 billion. Actonel is manufactured by Warner Chilcott.

Table 2.2 Samples of the medicine will be expired in the year 2014, 2015 and 2016 (Kathlyn Stone, Which Popular Drugs Are Going Off-Patent in 2013-2016?: About.com/Pharma) (cont.)

Year	Medicine name/ Company/ Global sale
2015	*Abilify (aripiprazole)*, by Bristol-Myers Squibb, global sales reached $4.6 billion in 2010.
	Gleevec (imatinib mesylate) is manufactured by Novartis. Global sales were $4.26 billion in 2010.
	Zyvox (linezolid) ,by Pfizer, reported global sales of $325 million in 2011.
	Avodart (dutasteride), GlaxoSmithKline, reported sales of $973 million worldwide 2010.
2016	*Crestor (rosuvastatin calcium)* by Astra Zeneca, total sales was $6 billion in 2010.

Part 5 Thai FDA first generic drug policy

Before 2002, Thai FDA allowed only local bioequivalence (BE) study in the drug registration process. At 16 December 2002, Thai FDA announced the new regulation that allow foreign BE study in the registration process of the urgent medicines and the medicines that local BE centers unable to conduct. The samples are HIV/AIDs and life threatening medicines (Appendix A).

This announcement was revised in 2012. The new version expands from the criteria of urgent medicine beyond to the chemical entities that do not have the generic version in the same strength, dosage form and active ingredient available in Thailand (Appendix B). The reason for this move is to increase the accessibility of medicine and appeal the market to investors. However, each chemical entity importation right is for one drug company only.

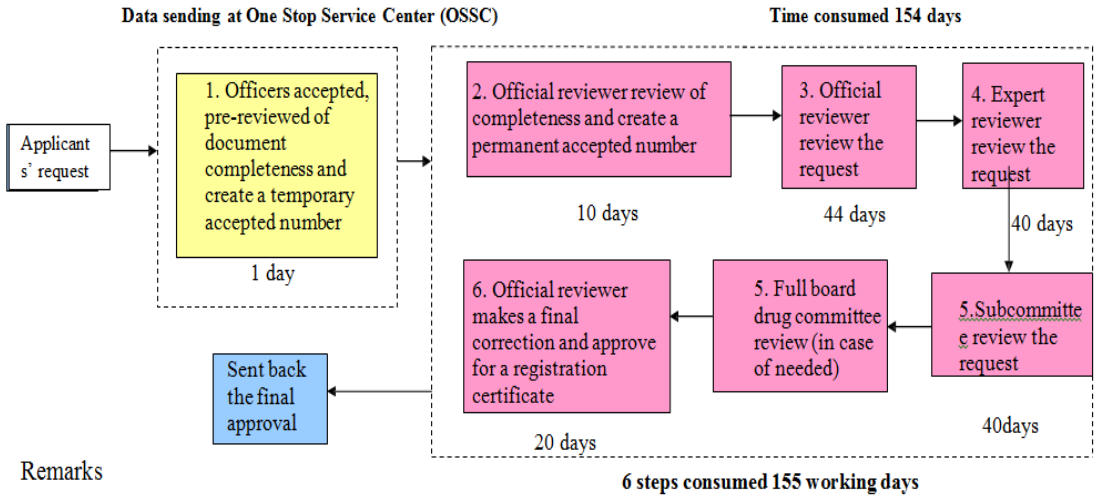
According to the new policy, the lists of new chemical entities have been published on Thai FDA website every month. Every pharmaceutical company has at least 60 days to preparing the foreign BE study and registered dossier of their selected drug. Selection process is by lucky draw. The company which won the lucky draw gets 120 days to make a completed dossier for registration and BE study complied with Thai's standard (Appendix C).

The lucky draw process took place 11 times from June 2012 until August 2013. About 200 items of monopoly drugs was in the policy. That means the work load of registration department will apparently increase in the short period. Finally, it still has no new generic substitution in the market although more than 1 year after lucky draw has passed.

Part 6 Thailand and overseas generic drug registration process and time-consumed

Thai FDA regulate every drug registration request after January 1, 2009 had to comply with ASEAN guideline. The registration dossiers mainly compose of two parts, administrative data and product information part and quality part. The guideline clearly exhibits the arrangement of registration dossier. The same pattern of dossier will make the tangled registration process in each country easier to understand and facilitate the registration among ASEAN countries.

Refer to the announcement from Thai FDA, released at June 24, 2013 on one stop service center website; indicate the time used for government services. Period for any new generic drugs registration is 155 working days. This regulation conforms to ASEAN harmonization product on pharmaceutical registration handbook. The time used in each new generic drug registration process is showed in the figure 5



1. This figure demonstrates only 1 round normal review of each request which excluded the period of
- The time used if the companies got the editing request or further documents
- The period of any change of expert reviewer during the review process
- The period is about 60 working days for full board drug committee review
2. In case of document editing or further documents requested, the managing period is individually identified by case. The reviewer has a right to reject the document if the time is not complied.

Figure 2.3 Process of generic drug registration and time-consumed in Thailand

To review the registration process and time-consumed in other countries, the researcher classified into four groups including USA and Europe, India, Japan and ASEAN countries.

First, regulations in the United States and Europe require technologies for registration of medicinal products in a structured format to facilitate inspections, safety tracking and licensing. Both of these provide a bridge to a 2012 ISO standard called Identification of Medicinal Products, or IDMP, which is expected to go into production use in 2015 or 2016. While there are features common to all three, there will be a significant effort required to provide a system that can migrate the required data to the international standard.

The U.S. Food and Drug Administration (FDA) system is based on a technology called "Structured Product Labeling" and used in Drug Registration and Establishment Listings (DLER). As of June 1, 2009, USFDA no longer accepts paper submissions for drug registration and listing unless a waiver is granted. Moving from a paper-based format to an electronic system will improve the timeline of registration and also the accuracy of the data review. To transmit the submission, firms must use the FDA's Electronic Submission Gateway (ESG) (23, 24)

The review and approval are conducted by the Center for Drug Evaluation and Research (CDER) that has a number of offices organized under the center director. The USFDA registration process of Abbreviated New Drug Application (ANDA) is showed in figure 6. The interesting points in the US ANDA registration are

1. The owners of an ANDA must revel a patent certification prior to take any action.

2. The advisory committee, which is comprised of various medical and scientific experts, is consulted only when there are the issues or controversies arise.

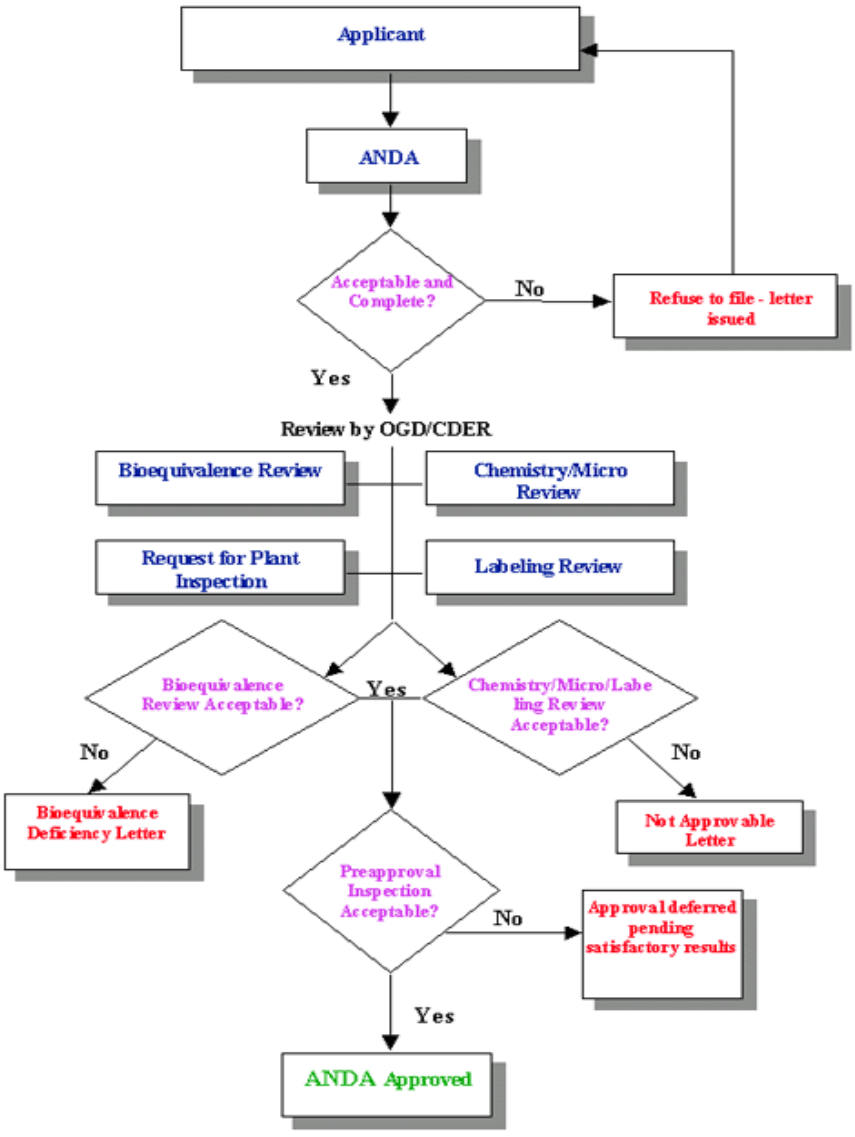


Figure 2.4 The US ANDA registration process (Source: www.medscape.com)

The European Medicines Agency (EMA) has built a system primarily for pharmacovigilance, called Extended EudraVigilance Medicinal Product Dictionary (XEVMPD), which was instituted in 2012. Same as the US requirements, there are two regulatory steps, which are clinical trial application and marketing authorization application, to pass before a drug is approved and marketed in the European countries. There are 28 member states in the European Union (as of July, 2013); Clinical Trial Applications are approved at the member state level, whereas marketing authorization applications are approved at both the member state and centralized levels.

There are many procedures to get the EU market authorization including centralized procedure, mutual recognition procedure, nationalized procedure and decentralized procedure (24). The mutual recognition procedure is used by generic companies as major user. The Mutual Recognition procedure allows applicants to obtain a marketing authorization in the Concerned member states (CMS) other than the Reference member state (RMS), where the drug is previously approved. The Reference Member State grants a Marketing Authorization which is mutually recognized by the Concerned Member States (25).

Applicant submits identical required dossier to all EU member states in which they want marketing authorization. Once one Member State decides to evaluate the medicinal product (at which point it becomes the "RMS"), it notifies this decision to other Member States (which then become the "CMS"), to whom applications have also been submitted. After that, RMS reported its own findings to other states. The time period for this procedure may consume 390 days (25,26,27).

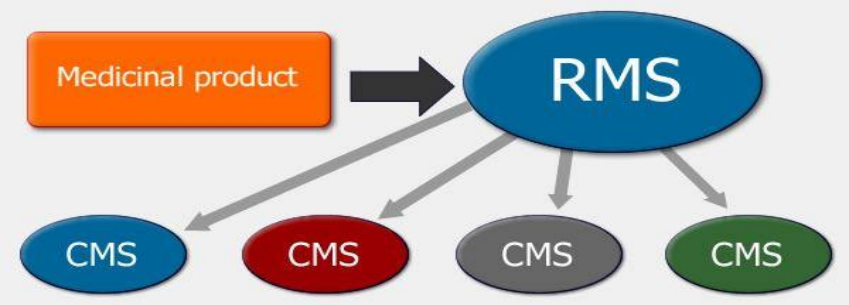


Figure 2.5 The mutual recognition procedure concept of EU drug registration (Source: www.michor-consulting.eu/pharmaceutical-drugs-regulatory-procedures.php)

India still uses paper-based application in the drug regulatory process. The process is still complicated and the researcher cannot find the official generic approval process in any source of data. The approval timeline is 12-18 months (26).

Japan's generic drug approval requires quite the same data as other countries. Since 1 April 2007, all original drug companies must perform post-marketing surveys on new drugs in order to re-examine the efficacy and safety by The Ministry for Health Labor and Welfare (MHLW) for a period of eight years. Applications for generic drugs cannot be approved unless completion of the re-examination and expiration of patents (28).

The Pharmaceuticals and Medical Devices Agency (PMDA)'s Office of OTC/Generic Drugs is responsible for reviewing generic drug applications. Table 2.3 summarizes the number of generic drugs approved each year and the period required for review and other regulatory procedures (not including the time spent by applicants) between fiscal years 2007 to 2011.

Table 2.3 Japan's number of approved generic drugs and review time

Fiscal Year	2007	2008	2009	2010	2011
Approved drugs	3278	1980	3271	2633	3091
Review time (month)	4.5	5.3	7.5	6.9	6.5

To support the registration of generic drugs, PMDA initiated the following two departments for consultation in October 2011: 'consultation on bioequivalence tests for generics', and 'consultation on quality requirements for generic drugs'. Moreover PMDA has increased the number of reviewer by planning to have more than 700 employees in fiscal year 2012. This number is about three times increasing from those employed when PMDA was established in 2004 (29).

CHAPTER III
METHODOLOGY

3.1 Study Design

This will be a descriptive policy research which finding the appropriate approaches to set the priority criteria for first generic registration.

3.2 Data Sources

Data will be collected from:

1. The FDA, Bureau of Drug Control

2. Leading local pharmaceutical manufacturers i.e. The Government Pharmaceutical Organization (GPO), SPS Medical Co., Ltd., Berlin Pharmaceutical Industry Co., Ltd., Biolab Co., Ltd. and Unison Laboratories Co., Ltd. etc.

3. Certified Bioequivalence study institutes in Thailand i.e. International Bio Service Co., Ltd., Medica Innova Co., Ltd., Bio-Innova & Synchron Co.,Ltd., All Research Co., Ltd., Pharma Nueva Co.,Ltd., The Government Pharmaceutical Organization Bioequivalence Study Center etc.

The researcher selected the pharmaceutical companies by the inclusion criteria which are

- The pharmaceutical company is a local Thai company.
- R&D and Product line are available.
- Top 10 on sales revenue
- Willing to be interviewed or sharing the company's information

All local bioequivalence study institutes that willing to participate are included. Participants will be excluded if unable to communicate in Thai or English language. All participants have a right to terminate from this study anytime.

3.3 Study period

The total study period was about 8 months (March-October 2014).

3.4 Study instruments

There were two data collecting forms, one for generic drug companies (No.1) and the other for BE centers (No.2). Data record form No.1 and No.2 was showed in appendix D and E. The confidential codes of participants were used instead of real name and organization. The data collecting forms consisted of two parts:

Part I: Feasibility of generic drug production/ BE study

30 most imported drugs were filled in the form. The respondents answered that they can do the production or BE study on the basis of current capability or not. If the answer was yes, how long of the time needed to conduct? The duration to conduct R&D and BE study was requested in order to forecast the market launching time.

Part II: The opinion toward generic drug market

The interview in depth focused on opinion about the picture of generic drug market in Thailand based on personal experience. The magnitude of market share of the first generic drugs will be interviewed to estimate the volume of budget saving.

3.5 Data Collection

To find the capability of production and BE study, the researcher uses the personal interview and partly questionnaire. The drug importation data are replied by the letter or E-mail.

1. An official letter will be sent to the Bureau of Drug Control to request for data on importation of monopoly drugs for 4 years (2009-2012) in terms of budget

2. Analyzed the data by used Excel program to arrange the data. Select the top 30 in trend of importation, in terms of accumulated budget, mapping and arrange into one list.

3. Invitation form will be sent by hand to the chief of eligible organization to give the study data and make a decision for participation.

4. The Interview will be performed in the 45-60 minutes period. The time, place and interviewees are appointed in advance by phone.

5. If face-to-face interview method was not possible, all the top 30 most imported monopoly drugs are placed in the questionnaire form and mailed to them. The confirmations by phone use for ensure the participant receiving. The researcher will call back the participant if no replied letter within 4 weeks after receiving.

Descriptive statistics were used to analyze data. The proportion and percentage were used to explain the characteristic of respondents.

Table 3.1 Data collection methods summary

Organization	**Collected Data**	**Methods**	**Time and duration of interview/ questionnaire**
The FDA, Bureau of Drug Control	Number of national drug importation in terms of budget	Official letter	1 time
	FDA's registration process	Self-organization review	1-2 times 45-60 minutes/ time
Major local pharmaceutical manufacturers	Generics production possibility and the opinion concerning generic drug market	Interview (If possible) or questionnaire	1-2 times 45-60 minutes/ time
Certified Bioequivalent study institutes in Thailand	Bioequivalence conduction possibility and the opinion concerning generic drug market	Interview (If possible) or questionnaire	1-2 times 45-60 minutes/ time

After sending the participation letter to all accredited bioequivalence centers and 10 leading local generic drug companies, 1 month was the waiting time to reply. All bioequivalence centers and 8 leading local generic drug companies accepted to participate in this study. Only one generic drug company had been interview visit

twice in 3 months later while the rest companies were visited only once. The questionnaires were 100 percent replied in 5 months period.

3.6 Data Analysis

Data analysis will separate in 2 parts

1. Qualitative part

This part focuses on the data from interviews and questionnaires. The verbal or behavioral data was categorized and analyzed for purposes of summarization and tabulation. In this part, a descriptive method will be applied i.e. this is what was said. More interpretive analysis that was concerned with the response such as what may have been inferred or implied, what could be forecasted will be included as well.

The priority of generic drugs that deserve for production and registration in Thailand will be analyzed compare with the government first generic policy the see the successful. The limitation of the policy and the practical recommendations will be proposed. The researcher analyzed descriptive data from interview by using descriptive analysis in term of frequency distribution.

2. Quantitative part

The cost saving will be calculated according to the various scenario. The researcher varied the number of price and market share of generic drugs to see the impact from promoting the use of generic drugs. The price of each drug was referred from referral price in the DMSIC website (http://dmsic.moph.go.th/price/price1_1.php?method=drug).

3.7 Sensitivity Analysis

The financial impact from first generic drug production was analyzed. The sensitivity analysis was done to estimate the national drug expenditure that might be saved in various scenarios. The researcher put three factors in the analysis. According to the expert interview, market share of generic drug in Thailand varied from 20 to 70 percent of overall national drug used. The number of generic drug price came from literature review and summarized to be 30 to 80 percent of original drug price. And the

market size was obtained from Bureau of Drug Control, Thai FDA. The total study period was about 8 months (January-August 2014).

CHAPTER IV
RESULT

The drug importation data was obtained from the Bureau of Drug Control, Thai FDA. The list of top30 most importation drug was created. The list is shown in the table below with the patent expiration year of each drug and generic availability in Thailand. Please noted that name of the drugs will be replaced with A1 to A30 as the confidentiality was requested by data source. The real 30 drug names is alphabetically arranged and shown in the appendix D part.

Table 4.1 Top 30 most imported drugs from the year 2009-2012

Ranking No.	Name code of the drugs	Budget imported (Million Thai Baht)	Patent expiration date[1]	Generic availability in Thailand's market[2]	Generic registration in Thailand[3]
1	A1	4249.10	Jun 17, 2022	No	Yes
2	A2	3506.65	Nov 17, 2019	No	Yes
3	A3	3284.27	Nov 8, 2013	No	Yes
4	A4	2935.45	unidentified [4]	No	No
5	A5	2839.24	2014	No	Yes
6	A6	2581.63	Jan 9, 2014	No	Yes
7	A7	2405.26	Apr 30, 2026	No	No
8	A8	2318.00	unidentified [4]	No	No
9	A9	2281.21	2017 [5]	No	No
10	A10	2004.08	Jun 23, 2022	No	No
11	A11	1878.48	Dec 30, 2018	No	Yes
12	A12	1826.12	May 3, 2020	No	No
13	A13	1797.61	Apr 11, 2026	No	No
14	A14	1528.08	Jan 9, 2014	No	Yes
15	A15	1450.67	Jun 14, 2014	No	Yes
16	A16	1372.59	Feb 22, 2018	No	No

Table 4.1 Top 30 most imported drugs from the year 2009-2012 (cont.)

Ranking No.	Name code of the drugs	Budget imported (Million Thai Baht)	Patent expiration date[1]	Generic availability in Thailand's market[2]	Generic registration in Thailand[3]
17	A17	1322.63	Apr 3, 2018	No	No
18	A18	1313.35	Aug 21, 2015	No	No
19	A19	1268.20	Jun 17, 2022	No	Yes
20	A20	1219.34	Apr 25, 2017	No	No
21	A21	1189.47	Jul 8, 2019	No	No
22	A22	1183.36	Oct 8, 2030	No	No
23	A23	1177.92	Dec 18, 2017	No	No
24	A24	1098.52	Jun 23, 2022	No	Yes
25	A25	1054.54	Aug 23, 2016	No	No
26	A26	1043.04	2017	No	No
27	A27	1020.97	Apr 7, 2029	No	No
28	A28	1012.15	Aug 31, 2020	No	No
29	A29	1001.28	Nov 15, 2017	No	No
30	A30	938.08	2015	No	No

[1] Patent expiration data was referred from Orange book website, USFDA. (http://www.accessdata.fda.gov/scripts/cder/ob/) Updated August 2014

[2] Updated August 2014

3 Data checked from Thai FDA website: http://fdaolap.fda.moph.go.th/logistics/drgdrug/DSerch.asp?id=drug

[4] Cannot found patent expiration date in any data sources. The registration year in Thailand is 1995. (โครงการจัดทำฐานข้อมูลสิทธิบัตรยาแผนปัจจุบัน, 2547, หน่วยปฏิบัติการวิจัยเภสัชศาสตร์สังคม (วจภส.) คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย)

[5] Research and Markets [Internet]. Celebrex Will Remain the Market Leading Brand for Osteoarthritis... [Cited Jun 17, 2008] Available from: http://www.reuters.com/article/2008/06/17/idUS167121+17-Jun-2008+BW20080617

All data was updated in August 2014. Actually, there were 7 items deleted from top 30 most imported list and will not be analyzed in this study. Six items were the biological products which only need to be imported because of limited

manufacturing technology in Thailand. And the other was the antiretroviral drug that had been done the compulsory licensing. The next seven lower ranks were moved up to replace.

According to the data from interview, the time used for developing each generic item was 7-10 years. Table1 shows the expiration date of top 30 most imported drugs in Thailand. So, we can assume that the monopoly drugs expired before year 2025 should be pre-registered to Thai FDA or in the production line. The total drugs that fell in this criterion were 24 items. 14 of 24 items (about 58 percent), which showed in grey area in the table, still were not in the approval process. This issue led to the lack of generic substitution problem even no patent barrier exists. Finally, Thai FDA has released the policy to palliate the problem by allowing foreign bioequivalence study used in the first generic dug registration process but still not fully success.

The researcher put these 30 most consumed drugs in the list to interview to ask for the reasons why they did not interest in these products, ecpecially the 14 items. The aim of interview is to find out the answer from the beginning to the end of the local generic production line. The beginning of the production line consisted of two parts that are possibility (or capability) of generic drug production and BE study. Thai FDA registration capability was identified to be end of the line and added in the interview questions as well.

8 leading local generic drug companies (80% response) and 6 bioequivalence centers (67% response) were the participants of this study. Eight generic drug companies are Thai owned and base in Thailand. 3 of 8 generic drug companies have their own BE center as one of the business sector but under the separate working operation. Every generic drug company has their own research and development (R&D) team and spends a huge budget in formulation of the blockbuster generic versions.

The positions of participants are including R&D team, registration unit, marketing, administrative officer, general manager and chief director. All interviews were done in the private conference room at each company. The circumstance at the time of interview was relaxed and no pressure occurred. The average duration was 45-

60 minutes per time. Second time interview happened in one company since some data had to be collected from the other participant.

The data from interview is classified into 4 parts.

Part 1 Generic drug market in Thailand

Part 2 Possibility of new generic drug production and bioequivalence study in Thailand

Part 3 Thai FDA drug registration analysis

Part 4 The patent barrier of new generic drugs

Part 1 Generic drug market in Thailand

The researcher interviewed to find out the situation of new generic drug in Thailand. The perspective of generic drug companies to new generic market is fair. All eight companies agree that the government policies about generic production and usage are not reflex the real situation. “The policy allowed foreign bioequivalence study in the first generic registration process will erode the local generic companies. Every company wants to be the first in the market. Why does Thai FDA have to create this privilege in spite of high market competition” said by the leading local manufacturer. They revealed that the high profit apparently came from when you are the leader in market.

“The technology of production and bioequivalence study in Thailand is outstanding in ASEAN. But the encouragement from the government to local manufacturer is poor. They should cooperate and guide the entrepreneurs what and how to invest in generic production instead of promoting importation” half of interviewees agreed. The local production was cheaper and can be on-site investigated. “Can we trust the quality of imported medicine just see the document?” all the companies leaved the interesting point about imported generic medicine.

The generic market is gradually growing by the time. The generic substitution seems to be the rule in every hospital. On contrary, the number of local generic companies in the past decade is stable. Many importation companies have been established to serve the increasing need of generic drug instead of local

production. It might be because of the legal requirements of local production account the great investment but the importation is facilitated by many government policies. “In the current situation, it’s very hard to originate the new comer generic company without the low interest loan supported by the government. PIC/S standard consumes much budget since we have to change the infrastructure to meet the criteria of the standard” one of the top-ten local generic drug manufacturers said about the barrier of Thailand’s generic drug market.

Part 2 Possibility of new generic drug production and bioequivalence study in Thailand

To find the methods to accelerate the availability of generic drug, the researcher defined local generic companies and BE centers as the rate limiting step. Six Thailand’s entire accredited bioequivalence centers accepted to be interview, partly answered the questionnaire. All centers confirmed that the current capability of the BE center, including bioequivalence technology, manpower, staff knowledge, the standard, were in the maximum level since all the study lab processes were controlled by the international standard either ISO17025 or GLP. Moreover, ASEAN Guidelines for the Conduct of Bioavailability and Bioequivalence Studies has been completely applied since 2009. “Every drug items in the list can be done the bioequivalence study under the international standard here” was the answer of all BE companies.

The interviewer asked about adequacy of local BE center for serving the need of generic drug companies in Thailand. 5 of 6 companies agreed that the total capability of all BE study centers is enough for the new generic drugs. However, the points to concern are the study duration and cost. From the interview found that the duration from signing BE study contract to final result estimate not more than 7 months. The budget used in each project was about 2 million Baht. One company said “Conduction BE studies in India were more save both time and expense”.

Eight local generic drug companies participated in the study. All Thai drug manufacturing companies gave the answer in the same way which is they have an enough ability to produce almost all the drugs in the given list. “The limitations of local generic drug production are in the same drug groups in every manufacturing

company such as sustained release formulation drug, anti-cancer medicines etc." one of the leading Thai generic drug company gave this information.

Some companies declared the data of generic drugs which now under the registration process. "The drugs in the lucky draw list are not all the monopoly intentionally. Many of them are still in the tardy approval process. And we used to experience the loss of registration dossier during this process" they said.

The researcher tried to find out why they still had not produced these high-imported monopoly medicines. Most of the companies said that "Our production line consisted of only the blockbuster drugs of the world and they did not know which unknown-drugs have consumed a great number of drug budget in Thailand". They also leaved the suggestion to Thai FDA "Thai FDA should discuss among local generic companies before allowing the foreign BE study and imported generic drugs."

The interesting suggestion was the knowledge transfer from academic pharmacy university to the real drug manufacturing of private sector. "The drug manufacturing businesses really need the knowledge helping from academic sectors." They emphasized that the learning project in university should be practical adapted to be in business scale.

In conclusion from the interview data, it could assume that the input factors including local BE centers and generic drug manufacturing companies, are not the main limitation of new generic drug production in Thailand. The ability both conducting BE studies and drug production is in the international accredited standard and have adequate amount of centers. So, what are the real problems that limit the number of new generic drug?

Part 3 Thai FDA drug registration analysis

After analyze the factors concerning production and BE study, the generic drug registration process was also considered. This process had been a crucial role that affecting the overall profit of any drug item. To analyze the registration process, the researcher used the opinion from BE study centers, local generic drug companies with self-data gathering. The interview about this topic took place at the same time as the previous topic.

The opinion from BE centers and local generic drug companies was mainly the suggestions to drug registration department to improve working process. First, every generic drug company emphasized the important of timeline for dossier process. They revealed their experience that "There are no exact timeline for drug registration process at all. The timeline can be extended sometimes because of some appropriate reasons, some maybe not." From the interview information, the time used for generic drug registration was more than 2 years in average. This problem might come from the shortage of manpower while the drug registration dossier has growth continually every year.

"We have to well prepare for the coming Asean Economics Community (AEC) in the next coming year. Infrastructures and investment environment were the priority to consider. If we invested tens of million baht to launch a product but didn't know when we can sell it, why we have to invest. Many investors had changed their generic drug investment to Singapore, Vietnam and Malaysia because of our tardy policies." said by the CEO of the leading generic drug manufacturing company in Thailand.

The other factor that drives the situation of new generic drug become shortage and not the item that consume most of national drug expenditure is the cooperation among private and government sectors. The researcher obtained the information from 3 generic drug companies and 2 BE centers that they wasted the time in communication with the reviewer about the registration or BE dossiers correction. They said "I need two-way communication to explain and clarify how to edit the data. The communications with letter or indirect telephone are not effective and waste the time."

One of the local generic drug companies reveals that in other country gave the privilege to their local generic drug in the registration process to stimulate the number of generic drugs and substitute the original as soon as possible. "The government and private sectors supported each other from the production planning to end up with launching to the market." They concluded in the end of interview.

Part 4 The patent barrier of new generic drugs

The other important issue concluded from interview was the patent barrier. This problem might make the policy not practical as it could be. 70% of interviewed drug companies raised this topic as the priority. Nowadays each company has to face the suit by themselves. The main source of patent information came from the department of intellectual property which only a general information. One company said “I need to ensure that if I market this product, I will not be sued from the patent owner”. “The government section should give local generic manufacturers more confidence. They should not supposed to leave the problem to us since the drug expenditure is the national awareness that need the cooperation from many partied” the company comment.

The problem might come from the language. Some original drug companies register their product by Thai-spelling name and it make patent expire searching extremely difficult. Some companies said that “They may intentionally register by various different and complicated names in order to prohibit us from finding their patent information”. “Sometimes I decide to pause the production plan if the risk from suit is too much uncertainty” the company reveals their solution.

Many companies demand their requests “I think Thailand needs the expertise about multi-national drug legal. Can the registration language or the mean to finding patent will be modified to facilitate the generic companies?” All companies suggested the role model from USFDA website. The orange book website provides all information for all type of drug companies including generic. “The needed patent information can be uncomplicated found just type and click. I know what and how much generic companies registered the product same as mine. It very helps us for production and market planning. Is it possible in Thailand?” the leading generic company leave the question in the end.

Financial impact calculation

Sensitivity analysis was performed to estimate the national drug expenditure that might be saved from generic drug substitution. Three variables included in the model were the market share, market size and price of generic drugs.

Table 6 shows overall drug expenditure (including both from generic and original values) and percent saved per year of one sample in the list. The market share varied from 20 to 70 percent and the price of generic varied from 30 to 80 percent of original drug price. The researcher did this process in Microsoft Excel program in the 14 drugs group that should be planned for production before patent expire. The other 13 drugs were placed the calculation in appendix F. Reference prices came from Thai FDA website and were most updated in March 2014. The result from the calculation showed percent saved was range from 4-49% in every drug. Lower in generic drug price and greater in generic drug market share leads to more save in overall budget. It means that if we have well planning in new generic drug production and promote the generic substitution, we will save drug expenditure up to 49% per year.

Table 4.2 Overall drug expenditure and percent saved per year vary by percentage of market share and price of generic drug (Drug No.A9)

Name code			reference price[1] (Baht)	importation budget 2009-2012 (Baht)	Average use per year (Tablet)	Average budget per year (Baht)
A9			30.2	2,281,214,034.3	18,884,222.14	570,303,508.58
Price of generic (% of brandname)	Generic market share (%)					
	20		30	40	50	60	70
30	490,461,017		450,539,772	410,618,526	370,697,281	330,776,035	290,854,789
	% Decrease	14%	21%	28%	35%	42%	49%
40	% Decrease	501,867,088	467,648,877	433,430,667	399,212,456	364,994,245	330,776,035
		12%	18%	24%	30%	36%	42%
50	% Decrease	513,273,158	484,757,982	456,242,807	427,727,631	399,212,456	370,697,281
		10%	15%	20%	25%	30%	35%
60	% Decrease	524,679,228	501,867,088	479,054,947	456,242,807	433,430,667	410,618,526
		8%	12%	16%	20%	24%	28%
70	% Decrease	536,085,298	518,976,193	501,867,088	484,757,982	467,648,877	450,539,772
		6%	9%	12%	15%	18%	21%
80	% Decrease	547,491,368	536,085,298	524,679,228	513,273,158	501,867,088	490,461,017
		4%	6%	8%	10%	12%	14%

[1] Data from Thai FDA website: http://dmsic.moph.go.th/price/price1_1php?method=drug

CHAPTER V
DISCUSSION

The discussion is divided into 4 parts.

Part 1: The root cause of new generic drug shortage

Part 2: The way to maximize benefit from new generic drugs

Part 3: How to prevent the situation in the future?

Part 4: Limitation of the study

Part 1 The root cause of new generic drug shortage

The availability of new generic drugs needs many supporting factors. The local generic drug manufacturers have to prior planning for production before patent expired. Actually, every company aims to be the first generic item in the market. They apparently have a passion to make a profit from their business. Shorten a timeline of conducting bioequivalence study; follow the updated global standard; setting up a developing class for staffs; make the budget more worth to spend are some of the means that continually occurred for increasing their capability to produce.

But it always has something beyond their vision. The points were seen by the organization which involving in the big picture of generic drug market. As everyone share the same objective to promote the generic drug use for saving cost, the cooperation among each party should happened. The shortage issue should be discussed among Thai FDA, local drug manufacturers and BE centers before the policy was announced. The shortage of new generic drugs may not happened and the acceptance of foreign BE study may not need, or need only in some items, if there is a good connection between government and private sectors.

In 1-2 years ago, Thai FDA may focus on the fastest way to increase the new generic drugs availability. Importations the new generic items by using foreign BE is time-saved but have a chance to not sustainable. The questions about quality and

the way to do quality control may continually rise in the future. The fake lab result issues had got an attention globally. In spite of claimed documents, GMP, PIC/S, GLP and another accredited standard are needed to be field-investigated. Thai FDA should take a few slower steps and realize the importance of local companies that were a root of sustainable generic market.

Part 2 The way to maximize benefit from new generic drugs

The result showed the importance of prioritizing the first generic drug registration in Thailand to the overall drug expenditure. The need for foreign bioequivalence study and importing foreign generic medicine cannot solve the problem sustainably. All expert opinion from interview can be concluded and implied that it should has something change in the drug registration working to solve new generic drug shortage problem. The drug consumption was the factor that most impact to drug budget and should be determined to be the first criterion for drug register prioritization.

The researcher emphasized level of drug consumption as it is easy and quick to apply with the real situation. The manpower was nominated to be one of the most difficult changes in the government sector. So, reforming the working process to be more effective might be the answer. The other reason why the drug consumption was the suitable criteria was the method to analyze after applied. In any transition, there should have some indicators to measure whether it works or not. With this factor, the analysis can be performed via the regular computer program such as Microsoft Excel. The example was shown in the sensitivity analysis part.

Besides the drug consumption, there are some factors that might be included in the criteria for prioritize the drug registration such as

Patent expiration date;

The drugs that nearly patent expire should be considered to have more priority. The manufacturers should indicated the exactly date of patent expiration of the drug in the registration dossier.

Clinical needed;

Clinical need might be considered by the outsource physician or the urgency of the disease situation. The number of patient classified by ICD10 can be used to represent clinical need as well.

Number of generic items in the market;

The chemical entities which have more generic versions in the market should get lower priority than monopoly items.

Reference countries

The generic product that was approved in many developed countries may be nominated to have priority. Because of the high standard and concise registration process, the drugs should be registered faster after were approved in the countries such as USA, European counties.

In conclusion, the researchers try conducting the example of guideline to prioritize the drug registration as follows:

Table 5.1 Sample of criteria checklist for prioritizing generic drug registration

Criteria for prioritize generic drug registration						Points
National consumption last year …….. (Million Baht)	>1000 (... Points)	>800 (... Points)	>500 (... Points)	Less than 500 (... Points)		
Clinical needed	Yes (... Points)		No (... Points)			
No. of substitution in the market	1-2 items (... Points)	3-6 items (... Points)	7-10 items (... Points)	More than 10 items (... Points)		
Reference countries	USA (... Points)	EU (... Points)	Australia (... Points)	Asia (Japan, Korea, Singapore, Malaysia) (... Points)	Other Please specified ……..... …… …… (...Points)	

Table 5.1 Sample of criteria checklist for prioritizing generic drug registration (cont.)

Criteria for prioritize generic drug registration						Points
Patent expiration date	Within 1 year	Within 3 year	Within 5 year	Within 10 year	More than 10 years	
					TOTAL	

The points of any criteria could derive from the discussion among authorized officers. The checklist should be done and recorded under computer-based process. The timeline of registration in every priority should be notified to the owner transparently. Moreover there may be one more factor that should be realized which is manufacturing sources. Because now Thailand has free trade barrier policy, to put the manufacturing sources in the criteria for register prioritization might not possible. But Thai owned manufacturers and BE centers have enough capability and resources in most of generic drug production. The drugs manufactured in country are cheaper as cost cut in the transportation, tax and resource budget. And the important reason why we should prefer local manufacturers is the quality control. Thai FDA can do the on-site investigation in every local company, both generic drug manufacturer and BE centers, to assure the quality than consider only paper dossier. The quality assurance and the tracking back process if the adverse drug reaction happened are the points to concern. And to cost, time and manpower to do the on-site investigation might be considered.

From sensitivity analysis shows that market share and price of generic drug affects the overall drug expenditure. We found that the national drug expenditure is more sensitive to price of generic than market share. In the lower price of generic drugs, the sensitivity of overall drug budget is more sensitive to market share. So, to maximize the benefit from generic drug, the price of generic is the first to realize. The fact that first generic drugs are always sell in the high price (maybe upto 80% of original drug) and get a lot of profit. To decrease the average price of generic in the market might not only come from increasing the number of generic drugs as a single method but also promoting the usage of generic (enlarge the market size). Therefore, accelerate availability of the first generic drugs then facilitate the usage to expand

market size, the number of generic drug in the market will increase and the price will automatically decrease by market mechanism.

At the beginning after implementation, market of each new generic drug is small because of the royalty to original and the price of first generic is still quite high. So, the saved number is predictable to be less than 49% then gradually increase by time. After that, the size of market will be increased together with number of budget saved but by percent of budget saved is still constant.

Part 3 How to prevent the situation in the future?

To prevent the problem in the future, the mindset of the registration department officers will be the first to concern. They should be the decision-maker more than just the facilitator of dossier. Technology can ease the workload in many steps of working. The precious time and the knowledge of staff deserve to use in the critical thinking more than a routine working that might be substituted by technology or assistants. But the legal issues and the same old organization chart might be the top limitations of any changes. ThaiFDA legal should be revised according to the changing of situation. The drug market size, numbers of patients, scientific standards have increasing over time. The same amount of resource might no longer fit properly.

The cooperation between government and private sector should be more intense. Academic sector, government sector and manufacturing sector are playing the crucial role in the development of new generic drug market. The study in the university should mock and reflex the real situation and help solving the problems about manufacturing technology. Be alert that the valuable officers in the future came from the current student in the universities.

So, if every party does the best in their duty, the problems will not cumulative and help preventing the problem in the future

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Part 4 Limitation of the study

The result of this study was scrutinized on the basis of some limitations. As the researchers mention about the difficulties of patent searching in Thailand, so

expiration date of the drugs (see in Table 5) in this study were referred from orange book website. The website contains the detail about all approved medicine in the US including both innovator and generic forms. The 14 most imported-monopoly drugs deserved to be pre-registered regarding the expiration date are came from the US information.

Importation budget were used instead of consumption budget which may reflex the drug expenditure burden better. But the drug consumption data in Thailand is still scattered. Each hospitals or organizations gather their resource consumption individually and some are not even in the computer system. Moreover the computer systems used in Thailand are various. So, to obtain a national drug consumption is still not possible right now. The importation number is electronic-recorded by ThaiFDA and finally chosen to be the best substitution.

CHAPTER VI
CONCLUSIONS AND RECOMMENDATIONS

New generic drug is essential for every country throughout the world. It is not only decrease the national drug budget but also increase the equity of new drug accessibility. The new generic drug production needs the well-prepared and foresees planning from many involving parties. The current government's policy slightly palliates the situation and may not sustainable. Capability of local production and conducting BE study are enough for in-country use so the problem is not directly come from these two factors. Promoting importation of generic drugs does not only raising the questions about quality but also erode the local generic market. The major finding from local pharmaceutical companies and bioequivalence centers found that the registration process is the major factor controlling the generic market and needs to be reorganized. Methods to accelerate the new generic drugs availability mainly involve with Thai FDA, especially the registration department. Manpower is the key limitation and might be hardly to change because of legal problems. Thus, Thai FDA's generic drug registration department should prioritize their working due to the urgency of medicine. The monopoly drugs consumed more national budget should be more alerted from FDA to planning for prior production and also registration.

The other factor that makes the planning of generic production quite difficult is the drug patent. The department of intellectual property, Thai FDA, local manufacturers should have more cooperation to solve this problem. This problem needs the government experienced facilitators in legal issue to support the confidence in generics production. The budget saved estimation from generic drug use is up to 49% of current drug budget per year when the generic market share is 70% and the generic price is 30% of original. This number is altered by market share and price of generic drug.

So, the conclusions of the recommendations to accelerate the availability of new generic drugs are as following:

To Thai FDA's generic drug registration department

1. Prioritization of generic drug registration is the major recommendation that should be urgently implemented.

2. The generic drug registration department should be aware of the trend of generic drug both in the aspect of number and the concerning clinical study.

3. The organization should be revised according to the greater number of drug market size and the need of generic drug use in order to create the stipulated timeline.

4. The legal concerning drug registration should facilitate the working such as registration fee.

5. The registration officers should be more decision-making manner instead of waiting for outside dossier reviewer in almost all cases.

6. The special or accelerated pathway of registration is necessary for these priority drugs.

To local pharmaceutical manufacturers

1. Thai pharmaceutical manufacturers should have more cooperation among each other in term of technology or investment especially in the AEC era.

2. The companies should realize that standards or regulations always improve. So, the foreseen planning is necessary for the rapid change.

3. The quality of registration dossier should get high awareness from the companies.

To Thai FDA

Thai FDA should work more closely with the department of intellectual property for providing the drug patent accessibility to the manufacturers.

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APPENDICES

APPENDIX A

(สำเนา)

ประกาศสำนักงานคณะกรรมการอาหารและยา

เรื่อง การศึกษาชีวสมมูลของยาสามัญใหม่ซึ่งทำการศึกษาโดยสถาบัน

หรือห้องปฏิบัติการของต่างประเทศ

ตามที่สำนักงานคณะกรรมการอาหารและยา ประกาศใช้หลักเกณฑ์และแนวปฏิบัติในการศึกษาชีวสมมูลของยาสามัญ และกำหนดหลักเกณฑ์ให้ผลิตภัณฑ์ยาสามัญใหม่ (New Generic Drugs) ทั้งที่ผลิตในประเทศไทยและนำเข้าจากต่างประเทศ ต้องทำการศึกษาชีวสมมูล (Bioequivalence study) รวมทั้งการศึกษาการละลายหรือปลดปล่อยตัวยาในหลอดทดลอง (*In vitro* dissolution/release study) เปรียบเทียบกับยาต้นแบบ (Original New Drugs) เพื่อเป็นการประกันคุณภาพมาตรฐานและประสิทธิภาพของยาสามัญใหม่ โดยต้องทำการศึกษาโดยสถาบันหรือห้องปฏิบัติการในประเทศไทย ยกเว้นบางกรณีให้ทำการศึกษาโดยสถาบันหรือห้องปฏิบัติการของต่างประเทศได้นั้น

สำนักงานคณะกรรมการอาหารและยาโดยความเห็นชอบของคณะกรรมการยาจึงได้กำหนดหลักเกณฑ์การพิจารณาเกี่ยวกับการศึกษาชีวสมมูลของยาสามัญใหม่ซึ่งอนุญาตให้ทำการศึกษาโดยสถาบันหรือห้องปฏิบัติการของต่างประเทศ ดังต่อไปนี้

1. กรณีที่เป็นยาจำเป็นเร่งด่วน

ได้แก่ ยาที่ใช้ป้องกันและรักษาโรคที่เป็นปัญหาสาธารณสุขที่สำคัญของประเทศ เช่น ยารักษาโรคเอดส์ และยาช่วยชีวิตอื่นๆ ที่ผลิตภายในประเทศและนำเข้าจากต่างประเทศซึ่งคณะอนุกรรมการพิจารณาหลักเกณฑ์การศึกษาชีวสมมูลของยาสามัญเห็นสมควรว่าเป็นยาจำเป็นเร่งด่วน ให้ยอมรับ Bioequivalence study รวมทั้ง *In vitro* dissolution / release study ซึ่งทำการศึกษาโดยสถาบันหรือห้องปฏิบัติการของต่างประเทศได้

2. กรณีที่เป็นยาทั่วไปที่ไม่เร่งด่วน

ได้แก่ ยาทั่วไปที่ไม่เข้าข่ายข้อ 1 ทั้งยาที่ผลิตภายในประเทศ และนำเข้าจากต่างประเทศ ให้ยอมรับผลการศึกษาซึ่งดำเนินการโดยสถาบันหรือห้องปฏิบัติการของต่างประเทศได้ตามความเหมาะสม **เฉพาะ** ในกรณีที่ยานั้นไม่สามารถทำการศึกษา Bioequivalence study และ/หรือ *In vitro* dissolution / release study ในประเทศไทยได้ไม่ว่าจะเป็นการศึกษาทั้งหมดหรือบางส่วนอันเนื่องจากข้อจำกัดบางประการ เช่น สถาบัน / ห้องปฏิบัติการภายในประเทศไม่มีเครื่องมืออุปกรณ์ที่ใช้วิเคราะห์ยานั้น

ข้อจำกัดด้านเทคโนโลยีหรือบุคลากร เป็นต้น ทั้งนี้ผู้ประกอบการต้องแจ้งเหตุผลความจำเป็นให้สำนักงานคณะกรรมการอาหารและยาพิจารณาเป็นแต่ละกรณี

3. กรณีตามข้อ 1 และ 2 ให้อยู่ภายใต้เงื่อนไขดังต่อไปนี้

3.1 การศึกษา Bioequivalence study และ *In vitro* dissolution / release study ที่ดำเนินการในต่างประเทศ ต้องได้เกณฑ์มาตรฐานขั้นต่ำตามหลักเกณฑ์และแนวปฏิบัติในการศึกษาชีวสมมูลของยาสามัญของประเทศไทยตามที่สำนักงานคณะกรรมการอาหารและยากำหนด และให้จัดทำรายงานฉบับสมบูรณ์ตามหลักเกณฑ์ดังกล่าวส่งสำนักงานคณะกรรมการอาหารและยาพิจารณา โดยต้องส่งข้อมูลดิบในกระบวนการศึกษาของ individual subject รวมทั้งวิธีการ validate กระบวนการวิเคราะห์ยาใน plasma และใน dosage form ด้วย

3.2 การพิจารณามาตรฐานสถาบันหรือห้องปฏิบัติการศึกษาชีวสมมูลของต่างประเทศสำหรับกรณียาจำเป็นเร่งด่วนทั้งยาที่ผลิตภายในประเทศ และนำเข้าจากต่างประเทศ ในอยู่ภายใต้ดุลยพินิจของสำนักงานคณะกรรมการอาหารและยา

สำหรับกรณียาทั่วไปที่ไม่เร่งด่วน สถาบันหรือห้องปฏิบัติการศึกษาชีวสมมูลต้องผ่านการรับรองจากสถาบันที่เชื่อถือได้ว่าได้มาตรฐานตามสากล ได้แก่ มาตรฐาน ISO/IEC 17025 หรือ ISO/IEC guide 25 หรือมาตรฐานอื่นใดตามที่สำนักงานคณะกรรมการอาหารและยาเห็นสมควร และต้องผ่านการตรวจมาตรฐานห้องปฏิบัติการและ /หรือสถานที่ผลิตยาโดยคณะผู้เชี่ยวชาญของประเทศไทยตามที่สำนักงานคณะกรรมการอาหารและยาเห็นสมควรด้วย

ประกาศ ณ. วันที่ 16 ธันวาคม 2545
ลงชื่อ นายศุภชัย คุณารัตนพฤกษ์
(นายศุภชัย คุณารัตนพฤกษ์)
เลขาธิการคณะกรรมการอาหารและยา

APPENDIX B

เอกสารหมายเลข ๒

(สำเนา)

ประกาศสำนักงานคณะกรรมการอาหารและยา
เรื่อง การศึกษาชีวสมมูลของยาสามัญใหม่ซึ่งทำการศึกษาโดยสถาบัน
หรือห้องปฏิบัติการของต่างประเทศ (ฉบับแก้ไขเพิ่มเติม) พ.ศ. ๒๕๕๕

โดยที่เป็นการสมควรแก้ไขประกาศสำนักงานคณะกรรมการอาหารและยา เรื่อง การศึกษาชีวสมมูลของยาสามัญใหม่ซึ่งทำการศึกษาโดยสถาบันหรือห้องปฏิบัติการของต่างประเทศ เพื่อเป็นการใช้ประโยชน์จากผลการศึกษาชีวสมมูลของต่างประเทศในการขึ้นทะเบียนผลิตภัณฑ์ยาเพื่อให้ได้ผลิตภัณฑ์ยาสามัญใหม่ที่มีคุณภาพ มีราคาเหมาะสม ช่วยส่งเสริมการเข้าถึงยาของประชาชนให้ทั่วถึง

ในการนี้ สำนักงานคณะกรรมการอาหารและยา จึงออกประกาศไว้ ดังต่อไปนี้

ข้อ ๑. ให้ยกเลิกความในข้อ ๑ และข้อ ๓ แห่งประกาศสำนักงานคณะกรรมการอาหารและยา เรื่อง การศึกษาชีวสมมูลของยาสามัญใหม่ซึ่งทำการศึกษาโดยสถาบันหรือห้องปฏิบัติการของต่างประเทศ ลงวันที่ ๑๖ ธันวาคม ๒๕๔๕ และให้ใช้ข้อความต่อไปนี้แทน

"๑. ผลิตภัณฑ์ยาที่มีความจำเป็นเร่งด่วนทางด้านสาธารณสุข ได้แก่

(๑.๑) ผลิตภัณฑ์ยาที่มีความจำเป็นทางด้านสาธารณสุขต่อการป้องกัน วินิจฉัย บำบัด บรรเทา หรือรักษาโรคของมนุษย์ที่มีความร้ายแรงหรือที่คุกคามต่อชีวิตของผู้ป่วยหรือที่เป็นปัญหาสาธารณสุขที่สำคัญของประเทศ เช่น โรคมะเร็ง โรคติดเชื้อเอชไอวี/เอดส์ เป็นต้น

(๑.๒) ผลิตภัณฑ์ยาจำเป็นทางด้านสาธารณสุขที่ไม่เข้าเงื่อนไขตามข้อ (๑.๑) แต่เป็นยาที่ไม่มีผลิตภัณฑ์ยาสามัญใหม่ในประเทศ โดยมีตัวยาสำคัญ รูปแบบยาและขนาดความแรงเดียวกัน เพื่อให้เป็นทางเลือกทางสาธารณสุขที่ช่วยส่งเสริมการเข้าถึงยาของประชาชน ทั้งนี้ สำนักงานคณะกรรมการอาหารและยาจะพิจารณาเป็นแต่ละกรณีไป

๓. กรณีตามข้อ ๑ และ ๒ ให้อยู่ภายใต้เงื่อนไขต่อไปนี้

(๓.๑) การศึกษาชีวสมมูลและการศึกษาการละลาย/การปลดปล่อยตัวยาในหลอดทดลองที่ดำเนินการในต่างประเทศต้องได้เกณฑ์มาตรฐานขั้นต่ำตามหลักเกณฑ์และแนวปฏิบัติในการศึกษาชีวสมมูลของยาสามัญของประเทศไทยตามที่สำนักงานคณะกรรมการอาหารและยากำหนด และให้จัดทำรายงานฉบับสมบูรณ์ตามหลักเกณฑ์ดังกล่าวส่งสำนักงานคณะกรรมการอาหารและยาพิจารณา

(๓.๒) ผลิตภัณฑ์ยาอ้างอิง/เปรียบเทียบ (reference/comparator) ที่ใช้ในการศึกษาต้องเป็นผลิตภัณฑ์ยาต้นแบบที่ขึ้นทะเบียนในประเทศไทย หรือผลิตภัณฑ์ยาที่แหล่งผลิตนั้นอยู่ในเครือเดียวกับผู้ผลิตยาต้นแบบที่ขึ้นทะเบียนในประเทศไทย หรือผลิตภัณฑ์ยาของผู้วิจัยและพัฒนาเดียวกับผลิตภัณฑ์ยาต้นแบบที่ขึ้นทะเบียนในประเทศไทย ในสองกรณีหลังให้ส่งข้อมูลการศึกษา *In vitro* dissolution เพื่อพิสูจน์ว่าผลิตภัณฑ์ยาอ้างอิง/เปรียบเทียบที่ใช้ในการศึกษาชีวสมมูลนั้น สามารถใช้แทนผลิตภัณฑ์ยาต้นแบบที่ขึ้นทะเบียนในประเทศไทยได้

(๓.๓) ต้องมีเอกสารหลักฐานรับรองมาตรฐานสถาบันหรือห้องปฏิบัติการตามมาตรฐาน ISO/IEC 17025 และ/หรือ GLP หรือมาตรฐานอื่นที่สำนักงานคณะกรรมการอาหารและยาพิจารณาแล้วว่าเทียบเท่ามาตรฐานข้างต้น กรณีที่สงสัย สำนักงานคณะกรรมการอาหารและยาอาจดำเนินการตรวจตรา (inspection) การศึกษาชีวสมมูลในต่างประเทศ ก่อนจะรับผลการศึกษาชีวสมมูลของต่างประเทศ"

ข้อ ๒. ให้เพิ่มข้อความต่อไปนี้ในประกาศสำนักงานคณะกรรมการอาหารและยา เรื่อง การศึกษาชีวสมมูลของยาสามัญใหม่ซึ่งทำการศึกษาโดยสถาบันหรือห้องปฏิบัติการของต่างประเทศ ลงวันที่ ๑๖ ธันวาคม ๒๕๔๕ เป็นข้อ ๔ ข้อ ๕ และข้อ ๖

"๔. จำนวนผู้ประกอบการที่จะได้รับการอนุญาตให้ใช้ผลการศึกษาชีวสมมูลของต่างประเทศเพื่อประกอบการขึ้นทะเบียนผลิตภัณฑ์ยาสามัญใหม่ในกรณีตามข้อ ๑.๒ ให้มีไม่เกินหนึ่งรายต่อตัวยาสำคัญต่อขนาดความแรงต่อรูปแบบยา โดยพิจารณาจากลำดับก่อน-หลังของการยื่นขอของผู้ประกอบการและต้องมีเอกสารข้อมูลตามที่กำหนดครบถ้วน

เมื่อพ้นกำหนด ๑ ปี นับแต่วันที่ผู้ประกอบการรายแรกได้รับการขึ้นทะเบียนผลิตภัณฑ์ยาสามัญใหม่ด้วยผลการศึกษาชีวสมมูลของต่างประเทศ หากไม่มีผู้ประกอบการรายที่สองยื่นขึ้นทะเบียนผลิตภัณฑ์ยาสามัญใหม่ที่มีตัวยาสำคัญ ขนาดความแรงและรูปแบบยาเดียวกันด้วยผลการศึกษาชีวสมมูลที่ดำเนินการภายในประเทศ จะอนุญาตให้ผู้ประกอบการรายที่สองใช้ผลการศึกษาชีวสมมูลของต่างประเทศยื่นขึ้นทะเบียนผลิตภัณฑ์ยาสามัญใหม่นั้นได้

๕. ในการยื่นขอใช้ผลการศึกษาชีวสมมูลของต่างประเทศ กรณีตามข้อ ๑.๒ ให้ปฏิบัติดังนี้

(๕.๑) ให้ยื่นขอได้ครั้งละ ๑ ตัวยาสำคัญต่อขนาดความแรงต่อรูปแบบยา

(๕.๒) เมื่อได้รับอนุญาตให้ใช้ผลการศึกษาชีวสมมูลของต่างประเทศแล้ว ให้ทำการยื่นขอขึ้นทะเบียนผลิตภัณฑ์ยาสามัญใหม่ภายใน ๑๒๐ วัน นับแต่วันที่ได้รับการอนุญาต

หากมิได้ยื่นขึ้นทะเบียนภายในกำหนดระยะเวลาดังกล่าว ให้ระงับการอนุญาตใช้ผลการศึกษาชีวสมมูลของต่างประเทศของผู้ประกอบการรายนั้น และอนุญาตให้ผู้ประกอบการรายอื่นยื่นขึ้นทะเบียนผลิตภัณฑ์ยาสามัญใหม่ด้วยผลการศึกษาชีวสมมูลของต่างประเทศต่อไป

๖. หลักเกณฑ์ วิธีการ และขั้นตอนการดำเนินการยื่นขออนุญาตใช้ผลการศึกษาชีวสมมูลของต่างประเทศเพื่อขึ้นทะเบียนผลิตภัณฑ์ยาสามัญใหม่ให้เป็นไปตามที่สำนักยาประกาศ"

จึงประกาศมาให้ทราบโดยทั่วกัน

ประกาศ ณ วันที่ ๙ มกราคม ๒๕๕๕
ลงชื่อ นายพิพัฒน์ ยิ่งเสรี
(นายพิพัฒน์ ยิ่งเสรี)
เลขาธิการคณะกรรมการอาหารและยา

APPENDIX C

ประกาศสำนักยา
เรื่อง หลักเกณฑ์ วิธีการและขั้นตอนการดำเนินการยื่นขออนุญาตใช้ผลการศึกษาชีวสมมูล
ของต่างประเทศเพื่อขึ้นทะเบียนผลิตภัณฑ์ยาสามัญใหม่

ตามที่สำนักงานคณะกรรมการอาหารและยา ได้ออกประกาศ เรื่อง การศึกษาชีวสมมูลของยาสามัญใหม่ ซึ่งทำการศึกษาโดยสถาบันหรือห้องปฏิบัติการของต่างประเทศ (ฉบับแก้ไขเพิ่มเติม) พ.ศ. ๒๕๕๕ เมื่อวันที่ ๙ มกราคม ๒๕๕๕ ดังนั้น เพื่อให้การยื่นขออนุญาตใช้ผลการศึกษาชีวสมมูลของต่างประเทศเพื่อขึ้นทะเบียนผลิตภัณฑ์ยาสามัญใหม่เกิดความเข้าใจที่ถูกต้องตรงกัน เป็นไปด้วยความเรียบร้อย มีประสิทธิภาพ สำนักยาจึงออกประกาศ ดังนี้

๑. การเลือกรายการยาและจำนวนรายการยาในการยื่นขออนุญาตใช้ผลการศึกษาชีวสมมูลของต่างประเทศ

๑.๑ ผลิตภัณฑ์ยาจำเป็นทางด้านสาธารณสุขต่อการป้องกัน บำบัด บรรเทา รักษาโรคของมนุษย์ที่มีความร้ายแรงหรือที่คุกคามต่อชีวิตหรือเป็นปัญหาสาธารณสุขที่สำคัญของประเทศ สามารถยื่นขอแต่ละครั้งได้โดยไม่จำกัดจำนวนรายการยา โดยให้ผู้ยื่นขอจัดส่งเอกสารหรือหลักฐานทางวิชาการเชิงประจักษ์เพื่อสนับสนุนหรือยืนยันว่าโรคที่ผลิตภัณฑ์ยานั้นจะนำมาใช้มีความร้ายแรง หรือคุกคามต่อชีวิต หรือเป็นปัญหาสาธารณสุขที่สำคัญของประเทศ

ความในวรรคต้นไม่ใช้บังคับแก่ผลิตภัณฑ์ที่ใช้สำหรับรักษาโรคมะเร็ง โรคติดเชื้อเอชไอวี/เอดส์

๑.๒ ผลิตภัณฑ์ยาที่ไม่สามารถทำการศึกษาชีวสมมูล และ/หรือการละลายของผลิตภัณฑ์ยานั้นในประเทศได้ไม่ว่าจะเป็นการศึกษาทั้งหมดหรือบางส่วน เนื่องจากข้อจำกัดบางประการ เช่น ศูนย์ศึกษาชีวสมมูลไม่มีเครื่องมือ อุปกรณ์ที่ใช้ในการวิเคราะห์ ข้อจำกัดด้านบุคลากรและเทคโนโลยี เป็นต้น สามารถยื่นขอแต่ละครั้งได้โดยไม่จำกัดจำนวนรายการยา โดยให้ผู้ยื่นขอจัดส่งหลักฐานเป็นหนังสือจากศูนย์ศึกษาชีวสมมูลที่ได้มาตรฐาน ISO/IEC 17025 และ/หรือ GLP ที่มีในประเทศทั้งหมดเพื่อยืนยันว่าไม่สามารถดำเนินการศึกษาชีวสมมูลของผลิตภัณฑ์ยานั้นได้

๑.๓ ผลิตภัณฑ์ยาที่จะขึ้นทะเบียนเป็นยาสามัญใหม่รายแรกในประเทศ ให้ยื่นขอแต่ละครั้งได้ไม่เกิน ๑ ตัวยาสำคัญต่อขนาดความแรงต่อรูปแบบยา โดยเลือกจากบัญชีรายการยาใหม่ที่ไม่มีผลิตภัณฑ์ยาสามัญที่สำนักงานคณะกรรมการอาหารและยาประกาศ และให้ยื่นขอได้ทุกวันที่ ๑๕ ของเดือน เว้นแต่ตรงกับวันหยุดสุดสัปดาห์ วันหยุดนักขัตฤกษ์ หรือวันหยุดของทางราชการ ให้ยื่นขอได้ในวันถัดไปที่เปิดทำการวันแรก

๒. กรณีตามข้อ ๑.๓ สำนักงานคณะกรรมการอาหารและยาจะประกาศบัญชีรายการยาใหม่ที่ไม่มีผลิตภัณฑ์ยาสามัญ ภายในวันที่ ๑๐ ของเดือน บนเว็บไซต์ของสำนักงานคณะกรรมการอาหารและยา โดยก่อนการเปิดให้ยื่นขอได้ในครั้งแรก จะประกาศให้ทราบล่วงหน้าไม่น้อยกว่า ๖๐ วัน และจะทำการปรับปรุงบัญชีรายการฯ ดังกล่าวให้ทันสมัยเป็นประจำทุกเดือน

หากรายการยาใหม่ที่อยู่ในบัญชีรายการฯ ข้างต้น มีชื่อตัวยาสำคัญ ขนาดความแรงและรูปแบบยาซ้ำกัน แต่มีเลขทะเบียนต่างกัน เนื่องจากมีการนำเข้าจากแหล่งผลิตต่างกัน หรือมีทั้งการนำเข้าและการแบ่งบรรจุ เป็นต้น กรณีดังกล่าวให้ถือว่าเป็นรายการยาใหม่ที่ไม่มีผลิตภัณฑ์ยาสามัญ จำนวน ๑ รายการ

๓. การยื่นขออนุญาตใช้ผลการศึกษาชีวสมมูลของต่างประเทศเพื่อขึ้นทะเบียนผลิตภัณฑ์ยาสามัญใหม่

๓.๑ กรณีตามข้อ ๑.๑ - ๑.๒ ให้ยื่นขอ ณ ห้อง ๓๑๐ (งานรับ – ส่ง) สำนักยา อาคาร ๒ ชั้น ๓ สำนักงานคณะกรรมการอาหารและยา สำนักยาจะแจ้งผลให้ทราบภายใน ๑๔ วันทำการ ยกเว้นกรณีที่ต้องมีการพิจารณาโดยคณะทำงานพิจารณาการใช้รายงานผลการศึกษาชีวสมมูลของยาสามัญใหม่ซึ่งทำการศึกษาโดยสถาบันหรือห้องปฏิบัติการของต่างประเทศ

สำหรับผลิตภัณฑ์ตามข้อ ๑.๑ ที่เป็นผลิตภัณฑ์ยาที่ใช้ในการรักษาโรคมะเร็ง โรคติดเชื้อเอชไอวี/เอดส์ ไม่ต้องยื่นขออนุญาตใช้ผลการศึกษาชีวสมมูลของต่างประเทศ หากประสงค์จะใช้ผลการศึกษาชีวสมมูลของต่างประเทศ สามารถยื่นรายงานการศึกษาชีวสมมูลของต่างประเทศ ณ ห้อง ๓๑๖ (งานยาเคมี) สำนักยา

๓.๒ กรณีตามข้อ ๑.๓ ให้ผู้ยื่นขอมาลงทะเบียนพร้อมกันในวันที่ ๑๕ ของเดือน ตั้งแต่เวลา ๐๘.๐๐ - ๐๙.๓๐ น. ณ ห้องประชุมสำนักงานคณะกรรมการอาหารและยา อาคาร ๔ ชั้น ๖ เพื่อแจ้งความจำนงการยื่นขอ โดยสำนักยาจะจัดให้ผู้ยื่นขอจับสลากลำดับเลขที่ตั้งแต่เวลา ๑๐.๓๐ น. เป็นต้นไป และให้ยื่นขอก่อน-หลังตามลำดับเลขที่ที่ผู้ยื่นขอนั้นจับสลากได้ ณ ห้องประชุมฯ ดังกล่าว

๔. เมื่อได้รับอนุญาตให้ใช้ผลการศึกษาชีวสมมูลของต่างประเทศตามข้อ ๑.๓ แล้ว ให้ทำการยื่นขอขึ้นทะเบียนผลิตภัณฑ์ยาสามัญใหม่ภายใน ๑๒๐ วัน นับแต่วันที่ได้รับการอนุญาต หากมิได้ยื่นขึ้นทะเบียนภายในกำหนดระยะเวลาดังกล่าว ให้ระงับการอนุญาตใช้ผลการศึกษาชีวสมมูลของต่างประเทศของผู้ประกอบการรายนั้น และอนุญาตให้ผู้ประกอบการรายอื่นยื่นขอใช้ผลการศึกษาชีวสมมูลของต่างประเทศเพื่อขึ้นทะเบียนผลิตภัณฑ์ยาสามัญใหม่รายการนั้นต่อไป

จึงประกาศมาให้ทราบโดยทั่วกัน

ประกาศ ณ วันที่ ๑๗ มี.ค. ๒๕๕๕

(นายวินิต อัศวกิจวิริ)
ผู้อำนวยการสำนักยา

Appendix D: Data collection form No.1

Local pharmaceutical manufacturers data collecting form

รหัสผู้เข้าร่วมวิจัย.....

แบบสอบถามประเมินสถานการณ์และศักยภาพของการผลิตยาสามัญใหม่ในประเทศไทย

โปรดให้ความเห็นว่ายาชื่อสามัญต่อไปนี้สามารถพัฒนาสูตรตำรับ (R&D) และนำไปสู่การผลิตเพื่อจำหน่ายจริงที่บริษัทของท่านได้หรือไม่ และใช้เวลานานประมาณกี่เดือน

ชื่อยา	ความแรง	รูปแบบ	สามารถทำ R&D ได้ (√)	ประมาณเวลาที่ใช้ (เดือน)
1. Alfuzosin SR	10 mg	tablet		
2. Budesonide+formoterol*	160/4.5 mcg	dry powders for inhaler (DPI)		
3. Candesartan	16 mg	tablet		
4. Candesartan	8 mg	tablet		
5. Capecitabine	500 mg	tablet		
6. Celecoxib	200 mg	capsule		
7. Donepezil	10 mg	orodispersible tablet		
8. Donepezil	5 mg	orodispersible tablet		
9. Drospirenone+ethinylestradiol*	3/0.03 mg	Film coated tablet		

ชื่อยา	ความแรง	รูปแบบ	สามารถทำ R&D ได้ (√)	ประมาณเวลาที่ใช้ (เดือน)
10. Entecavir	0.5 mg	tablet		
11. Ertapenem	1 gm/1 vial	powders for solutions for injections or infusions		
12. Esomeprazole	20 mg	tablet		
13. Etoricoxib	90 mg	tablet		
14. Ezetimibe	10 mg	tablet		
15. Lansoprazole	30 mg	orodispersible tablet		
16. Manidipine	10 mg	tablet		
17. Manidipine	20 mg	tablet		
18. Mometasone	50 mcg/1 dose	nasal spray		
19. Mycophenolate mofetil	250 mg	capsule		
20. Pregabalin	75 mg	capsule		
21. Rabeprazole	20 mg	enteric-coated tablets		
22. Rosuvastatin	10 mg	tablet		
23. Rosuvastatin	20 mg	tablet		

ชื่อยา	ความแรง	รูปแบบ	สามารถทำ R&D ได้ (√)	ประมาณเวลาที่ใช้ (เดือน)
24. Salmeterol+fluticasone*	25/50 mcg	inhaler		
25. Simvastatin and ezetimibe*	10/10 mg	compressed tablet		
26. Sitagliptin	100 mg	tablet		
27. Tamsulosin	0.4 mg	tablet		
28. Tigecycline	50 mg/1 vial	powders for solutions for injections or infusions		
29. Valsartan and amlodipine*	160/5 mg	Film coated tablet		
30. Valsartan+hydrochlorothiazide*	80/12.5 mg	Film coated tablet		

*ไม่ระบุขนาดยาจากแหล่งข้อมูล ใช้ขนาดยาต่ำสุดในท้องตลาด

แบบสัมภาษณ์ประเมินสถานการณ์และศักยภาพของการผลิตยาสามัญใหม่ในประเทศไทย

บริษัทของท่านเคยผลิตยาสามัญตัวแรกหรือไม่ ☐ เคย ☐ ไม่เคย

หากเคย กรุณาระบุส่วนแบ่งการตลาดที่ท่านได้รับโดยประมาณ..... เปอร์เซนต์

ในมุมมองของท่าน มีปัจจัยใดบ้างที่เป็นอุปสรรคสำคัญต่อการพัฒนาอุตสาหกรรมยาในประเทศ

1. .....

2.....

APPENDIX E: Data collection form No.2

Certified bioequivalent study institutes data collecting form

รหัสผู้เข้าร่วมวิจัย.....

แบบสอบถามประเมินสถานการณ์และศักยภาพในทำการศึกษาชีวสมมูล

โปรดให้ความเห็นว่ายาชื่อสามัญต่อไปนี้สามารถทำการศึกษาชีวสมมูลที่บริษัทของท่านได้หรือไม่ และใช้เวลานานประมาณกี่เดือน

ชื่อยา	ความแรง	รูปแบบ	สามารถทำการศึกษาชีวสมมูลได้ (√)	ประมาณเวลาที่ใช้ (เดือน)
1. Alfuzosin SR	10 mg	tablet		
2. Budesonide+formoterol*	160/4.5 mcg	dry powders for inhaler (DPI)		
3. Candesartan	16 mg	tablet		
4. Candesartan	8 mg	tablet		
5. Capecitabine	500 mg	tablet		
6. Celecoxib	200 mg	capsule		
7. Donepezil	10 mg	orodispersible tablet		
8. Donepezil	5 mg	orodispersible tablet		
9. Drospirenone+ethinylestradiol*	3/0.03 mg	Film coated tablet		
10. Entecavir	0.5 mg	tablet		

ชื่อยา	ความแรง	รูปแบบ	สามารถทำการศึกษาชีวสมมูลได้ (√)	ประมาณเวลาที่ใช้ (เดือน)
11. Ertapenem	1 gm/1 vial	powders for solutions for injections or infusions		
12. Esomeprazole	20 mg	tablet		
13. Etoricoxib	90 mg	tablet		
14. Ezetimibe	10 mg	tablet		
15. Lansoprazole	30 mg	orodispersible tablet		
16. Manidipine	10 mg	tablet		
17. Manidipine	20 mg	tablet		
18. Mometasone	50 mcg/1 dose	nasal spray		
19. Mycophenolate mofetil	250 mg	capsule		
20. Pregabalin	75 mg	capsule		
21. Rabeprazole	20 mg	enteric-coated tablets		
22. Rosuvastatin	10 mg	tablet		
23. Rosuvastatin	20 mg	tablet		
24. Salmeterol+fluticasone*	25/50 mcg	inhaler		

ชื่อยา	ความแรง	รูปแบบ	สามารถทำการศึกษาชีวสมมูลได้ (√)	ประมาณเวลาที่ใช้ (เดือน)
25. Simvastatin and ezetimibe*	10/10 mg	compressed tablet		
26. Sitagliptin	100 mg	tablet		
27. Tamsulosin	0.4 mg	tablet		
28. Tigecycline	50 mg/1 vial	powders for solutions for injections or infusions		
29. Valsartan and amlodipine*	160/5 mg	Film coated tablet		
30. Valsartan+hydrochlorothiazide*	80/12.5 mg	Film coated tablet		

*ไม่ระบุขนาดยาจากแหล่งข้อมูล ใช้ขนาดยาต่ำสุดในท้องตลาด

แบบสัมภาษณ์ประเมินสถานการณ์และศักยภาพในทำการศึกษาชีวสมมูล

บริษัทของท่านสามารถทำการศึกษา BE / วิเคราะห์ผล BE ได้เฉลี่ยปีละ ..... ตัว

ในมุมมองของท่าน มีปัจจัยใดบ้างที่เป็นอุปสรรคสำคัญต่อทำการศึกษาชีวสมมูลในประเทศไทย

1. .....

2.....

APPENDIX F

F-1: Overall drug expenditure and percent saved per year vary by percentage of market share and price of generic drug (Drug No.A10)

Name code			reference price[1] (Baht)	importation budget 2009-2012 (M. Baht)	Average use per year (Tablet)	Average budget per year (M. Baht)
A10			117.33	2,004.08	4,270,178.59	501.02
Price of generic (% of brandname)	Generic market share (%)					
	20		30	40	50	60	70
30	430,877,246.82		395,805,843.01	360,734,439.20	325,663,035.39	290,591,631.58	255,520,227.76
	% Decrease	14%	21%	28%	35%	42%	49%
40		206,377,153.09	410,836,444.64	380,775,241.37	350,714,038.11	320,652,834.84	290,591,631.58
	% Decrease	12%	18%	24%	30%	36%	42%
50		211,067,542.94	425,867,046.27	400,816,043.55	375,765,040.83	350,714,038.11	325,663,035.39
	% Decrease	10%	15%	20%	25%	30%	35%
60		215,757,932.78	440,897,647.91	420,856,845.73	400,816,043.55	380,775,241.37	360,734,439.20
	% Decrease	8%	12%	16%	20%	24%	28%
70		220,448,322.62	455,928,249.54	440,897,647.91	425,867,046.27	410,836,444.64	395,805,843.01
	% Decrease	6%	9%	12%	15%	18%	21%
80		225,138,712.46	470,958,851.17	460,938,450.08	450,918,049.00	440,897,647.91	430,877,246.82
	% Decrease	4%	6%	8%	10%	12%	14%

[1] Data from Thai FDA website: http://dmsic.moph.go.th/price/price1_1php?method=drug

F-2: Overall drug expenditure and percent saved per year vary by percentage of market share and price of generic drug (Drug No.A12)

Name code			reference price[1] (Baht)	importation budget 2009-2012 (M. Baht)	Average use per year (Tablet)	Average budget per year (M. Baht)
A12			36.68	1,826.12	12,446,287.20	456,529,814.46
Price of generic (% of brandname)	Generic market share (%)					
	20		30	40	50	60	70
30	392,615,640.43		360,658,553.42	328,701,466.41	296,744,379.40	264,787,292.38	232,830,205.37
	% Decrease	14%	21%	28%	35%	42%	49%
40		401,746,236.72	374,354,447.85	346,962,658.99	319,570,870.12	292,179,081.25	264,787,292.38
	% Decrease	12%	18%	24%	30%	36%	42%
50		410,876,833.01	388,050,342.29	365,223,851.56	342,397,360.84	319,570,870.12	296,744,379.40
	% Decrease	10%	15%	20%	25%	30%	35%
60		420,007,429.30	401,746,236.72	383,485,044.14	365,223,851.56	346,962,658.99	328,701,466.41
	% Decrease	8%	12%	16%	20%	24%	28%
70		429,138,025.59	415,442,131.15	401,746,236.72	388,050,342.29	374,354,447.85	360,658,553.42
	% Decrease	6%	9%	12%	15%	18%	21%
80		438,268,621.88	429,138,025.59	420,007,429.30	410,876,833.01	401,746,236.72	392,615,640.43
	% Decrease	4%	6%	8%	10%	12%	14%

[1] Data from Thai FDA website: http://dmsic.moph.go.th/price/price1_1php?method=drug

F-3: Overall drug expenditure and percent saved per year vary by percentage of market share and price of generic drug (Drug No.A16)

Name code			reference price[1] (Baht)	importation budget 2009-2012 (M. Baht)	Average use per year (Tablet)	Average budget per year (M. Baht)
A16			25.74	1,372.59	13,331,316.93	343,148,097.90
Price of generic (% of brandname)	Generic market share (%)					
	20		30	40	50	60	70
30	295,107,364.19		271,086,997.34	247,066,630.49	223,046,263.64	199,025,896.78	175,005,529.93
	% Decrease	14%	21%	28%	35%	42%	49%
40		301,970,326.15	281,381,440.28	260,792,554.40	240,203,668.53	219,614,782.66	199,025,896.78
	% Decrease	12%	18%	24%	30%	36%	42%
50		308,833,288.11	291,675,883.22	274,518,478.32	257,361,073.43	240,203,668.53	223,046,263.64
	% Decrease	10%	15%	20%	25%	30%	35%
60		315,696,250.07	301,970,326.15	288,244,402.24	274,518,478.32	260,792,554.40	247,066,630.49
	% Decrease	8%	12%	16%	20%	24%	28%
70		322,559,212.03	312,264,769.09	301,970,326.15	291,675,883.22	281,381,440.28	271,086,997.34
	% Decrease	6%	9%	12%	15%	18%	21%
80		329,422,173.98	322,559,212.03	315,696,250.07	308,833,288.11	301,970,326.15	295,107,364.19
	% Decrease	4%	6%	8%	10%	12%	14%

[1] Data from Thai FDA website: http://dmsic.moph.go.th/price/price1_1php?method=drug

F-4: Overall drug expenditure and percent saved per year vary by percentage of market share and price of generic drug (Drug No.A17)

Name code			reference price[1] (Baht)	importation budget 2009-2012 (M. Baht)	Average use per year (Tablet)	Average budget per year (M. Baht)
A17			762.81	1,322.63	433,472.74	330.66
Price of generic (% of brandname)	Generic market share (%)					
	20	30	40	50	60	70
30	284,365,312.86	261,219,299.02	238,073,285.18	214,927,271.34	191,781,257.51	168,635,243.67
	% Decrease 14%	21%	28%	35%	42%	49%
40	290,978,459.67	271,139,019.23	251,299,578.80	231,460,138.37	211,620,697.94	191,781,257.51
	% Decrease 12%	18%	24%	30%	36%	42%
50	297,591,606.48	281,058,739.45	264,525,872.42	247,993,005.40	231,460,138.37	214,927,271.34
	% Decrease 10%	15%	20%	25%	30%	35%
60	304,204,753.29	290,978,459.67	277,752,166.05	264,525,872.42	251,299,578.80	238,073,285.18
	% Decrease 8%	12%	16%	20%	24%	28%
70	310,817,900.10	300,898,179.88	290,978,459.67	281,058,739.45	271,139,019.23	261,219,299.02
	% Decrease 6%	9%	12%	15%	18%	21%
80	317,431,046.91	310,817,900.10	304,204,753.29	297,591,606.48	290,978,459.67	284,365,312.86
	% Decrease 4%	6%	8%	10%	12%	14%

[1] Data from Thai FDA website: http://dmsic.moph.go.th/price/price1_1php?method=drug

F-5: Overall drug expenditure and percent saved per year vary by percentage of market share and price of generic drug (Drug No.A18)

Name code			reference price[1] (Baht)	importation budget 2009-2012 (M. Baht)	Average use per year (Tablet)	Average budget per year (M. Baht)
A18			223.54	1,313.35	1,468,806.91	328.34
Price of generic (% of brandname)	Generic market share (%)					
	20		30	40	50	60	70
30	282,369,904.02		259,386,307.18	236,402,710.34	213,419,113.51	190,435,516.67	167,451,919.83
	% Decrease	14%	21%	28%	35%	42%	49%
40		288,936,645.98	269,236,420.11	249,536,194.25	229,835,968.39	210,135,742.53	190,435,516.67
	% Decrease	12%	18%	24%	30%	36%	42%
50		295,503,387.93	279,086,533.05	262,669,678.16	246,252,823.28	229,835,968.39	213,419,113.51
	% Decrease	10%	15%	20%	25%	30%	35%
60		302,070,129.88	288,936,645.98	275,803,162.07	262,669,678.16	249,536,194.25	236,402,710.34
	% Decrease	8%	12%	16%	20%	24%	28%
70		308,636,871.84	298,786,758.91	288,936,645.98	279,086,533.05	269,236,420.11	259,386,307.18
	% Decrease	6%	9%	12%	15%	18%	21%
80		315,203,613.79	308,636,871.84	302,070,129.88	295,503,387.93	288,936,645.98	282,369,904.02
	% Decrease	4%	6%	8%	10%	12%	14%

[1] Data from Thai FDA website: http://dmsic.moph.go.th/price/price1_1php?method=drug

F-6: Overall drug expenditure and percent saved per year vary by percentage of market share and price of generic drug (Drug No.A20)

Name code			reference price[1] (Baht)	importation budget 2009-2012 (M. Baht)	Average use per year (Tablet)	Average budget per year (M. Baht)
A20			42.76	1,219.34	7,128,984.40	304.84
Price of generic (% of brandname)	Generic market share (%)					
	20		30	40	50	60	70
30	262,158,420.78		240,819,944.67	219,481,468.56	198,142,992.45	176,804,516.34	155,466,040.23
	% Decrease	14%	21%	28%	35%	42%	49%
40		268,255,128.24	249,965,005.86	231,674,883.48	213,384,761.10	195,094,638.72	176,804,516.34
	% Decrease	12%	18%	24%	30%	36%	42%
50		274,351,835.70	259,110,067.05	243,868,298.40	228,626,529.75	213,384,761.10	198,142,992.45
	% Decrease	10%	15%	20%	25%	30%	35%
60		280,448,543.16	268,255,128.24	256,061,713.32	243,868,298.40	231,674,883.48	219,481,468.56
	% Decrease	8%	12%	16%	20%	24%	28%
70		286,545,250.62	277,400,189.43	268,255,128.24	259,110,067.05	249,965,005.86	240,819,944.67
	% Decrease	6%	9%	12%	15%	18%	21%
80		292,641,958.08	286,545,250.62	280,448,543.16	274,351,835.70	268,255,128.24	262,158,420.78
	% Decrease	4%	6%	8%	10%	12%	14%

[1] Data from Thai FDA website: http://dmsic.moph.go.th/price/price1_1php?method=drug

F-7: Overall drug expenditure and percent saved per year vary by percentage of market share and price of generic drug (Drug No.A21)

Name code			reference price[1] (Baht)	importation budget 2009-2012 (M. Baht)	Average use per year (Tablet)	Average budget per year (M. Baht)
A21			19.2	1,189.47	15,487,909.27	297.37
Price of generic (% of brandname)	Generic market share (%)					
	20	30	40	50	60	70
30	255,736,357.88	234,920,607.82	214,104,857.76	193,289,107.70	172,473,357.64	151,657,607.58
	% Decrease 14%	21%	28%	35%	42%	49%
40	261,683,715.04	243,841,643.56	225,999,572.08	208,157,500.60	190,315,429.12	172,473,357.64
	% Decrease 12%	18%	24%	30%	36%	42%
50	267,631,072.20	252,762,679.30	237,894,286.40	223,025,893.50	208,157,500.60	193,289,107.70
	% Decrease 10%	15%	20%	25%	30%	35%
60	273,578,429.36	261,683,715.04	249,789,000.72	237,894,286.40	225,999,572.08	214,104,857.76
	% Decrease 8%	12%	16%	20%	24%	28%
70	279,525,786.52	270,604,750.78	261,683,715.04	252,762,679.30	243,841,643.56	234,920,607.82
	% Decrease 6%	9%	12%	15%	18%	21%
80	285,473,143.68	279,525,786.52	273,578,429.36	267,631,072.20	261,683,715.04	255,736,357.88
	% Decrease 4%	6%	8%	10%	12%	14%

[1] Data from Thai FDA website: http://dmsic.moph.go.th/price/price1_1php?method=drug

F-8: Overall drug expenditure and percent saved per year vary by percentage of market share and price of generic drug (Drug No.A23)

Name code			reference price[1] (Baht)	importation budget 2009-2012 (M. Baht)	Average use per year (Tablet)	Average budget per year (M. Baht)
A23			14.72	1177.92	20,005,380.43	294.48
Price of generic (% of brandname)	Generic market share (%)					
	20	30	40	50	60	70
30	253,252,112.00	232,638,568.00	212,025,024.00	191,411,480.00	170,797,936.00	150,184,392.00
	% Decrease 14%	21%	28%	35%	42%	49%
40	259,141,696.00	241,472,944.00	223,804,192.00	206,135,440.00	188,466,688.00	170,797,936.00
	% Decrease 12%	18%	24%	30%	36%	42%
50	265,031,280.00	250,307,320.00	235,583,360.00	220,859,400.00	206,135,440.00	191,411,480.00
	% Decrease 10%	15%	20%	25%	30%	35%
60	270,920,864.00	259,141,696.00	247,362,528.00	235,583,360.00	223,804,192.00	212,025,024.00
	% Decrease 8%	12%	16%	20%	24%	28%
70	276,810,448.00	267,976,072.00	259,141,696.00	250,307,320.00	241,472,944.00	232,638,568.00
	% Decrease 6%	9%	12%	15%	18%	21%
80	282,700,032.00	276,810,448.00	270,920,864.00	265,031,280.00	259,141,696.00	253,252,112.00
	% Decrease 4%	6%	8%	10%	12%	14%

[1] Data from Thai FDA website: http://dmsic.moph.go.th/price/price1_1php?method=drug

F-9: Overall drug expenditure and percent saved per year vary by percentage of market share and price of generic drug (Drug No.A25)

Name code			reference price[1] (Baht)	importation budget 2009-2012 (M. Baht)	Average use per year (Tablet)	Average budget per year (M. Baht)
A25			395.86	1,054.54	665,983.00	263.64
Price of generic (% of brandname)	Generic market share (%)					
	20	30	40	50	60	70
30	226,726,986.71	208,272,464.53	189,817,942.36	171,363,420.18	152,908,898.01	134,454,375.84
	% Decrease 14%	21%	28%	35%	42%	49%
40	231,999,707.33	216,181,545.46	200,363,383.60	184,545,221.74	168,727,059.87	152,908,898.01
	% Decrease 12%	18%	24%	30%	36%	42%
50	237,272,427.95	224,090,626.39	210,908,824.84	197,727,023.29	184,545,221.74	171,363,420.18
	% Decrease 10%	15%	20%	25%	30%	35%
60	242,545,148.57	231,999,707.33	221,454,266.08	210,908,824.84	200,363,383.60	189,817,942.36
	% Decrease 8%	12%	16%	20%	24%	28%
70	247,817,869.19	239,908,788.26	231,999,707.33	224,090,626.39	216,181,545.46	208,272,464.53
	% Decrease 6%	9%	12%	15%	18%	21%
80	253,090,589.81	247,817,869.19	242,545,148.57	237,272,427.95	231,999,707.33	226,726,986.71
	% Decrease 4%	6%	8%	10%	12%	14%

[1] Data from Thai FDA website: http://dmsic.moph.go.th/price/price1_1php?method=drug

F-10: Overall drug expenditure and percent saved per year vary by percentage of market share and price of generic drug (Drug No.A26)

Name code				reference price[1] (Baht)	importation budget 2009-2012 (M. Baht)	Average use per year (Tablet)	Average budget per year (M. Baht)
A26				28.03	1,043.04	9,302,887.49	260.76
Price of generic (% of brandname)	Generic market share (%)						
	20		30	40	50	60	70
30	224,253,545.18		206,000,349.64	187,747,154.10	169,493,958.56	151,240,763.03	132,987,567.49
	% Decrease	14%	21%	28%	35%	42%	49%
40		229,468,743.90	213,823,147.73	198,177,551.55	182,531,955.38	166,886,359.20	151,240,763.03
	% Decrease	12%	18%	24%	30%	36%	42%
50		234,683,942.63	221,645,945.81	208,607,949.00	195,569,952.19	182,531,955.38	169,493,958.56
	% Decrease	10%	15%	20%	25%	30%	35%
60		239,899,141.35	229,468,743.90	219,038,346.45	208,607,949.00	198,177,551.55	187,747,154.10
	% Decrease	8%	12%	16%	20%	24%	28%
70		245,114,340.08	237,291,541.99	229,468,743.90	221,645,945.81	213,823,147.73	206,000,349.64
	% Decrease	6%	9%	12%	15%	18%	21%
80		250,329,538.80	245,114,340.08	239,899,141.35	234,683,942.63	229,468,743.90	224,253,545.18
	% Decrease	4%	6%	8%	10%	12%	14%

[1] Data from Thai FDA website: http://dmsic.moph.go.th/price/price1_1php?method=drug

F-11: Overall drug expenditure and percent saved per year vary by percentage of market share and price of generic drug (Drug No.A28)

Name code				reference price[1] (Baht)	importation budget 2009-2012 (M. Baht)	Average use per year (Tablet)	Average budget per year (M. Baht)
A28				235.4	1,012.15	1,074,925.66	253.04
Price of generic (% of brandname)	Generic market share (%)						
	20		30	40	50	60	70
30	217,612,250.00		199,899,625.00	182,187,000.00	164,474,375.00	146,761,750.00	129,049,125.00
	% Decrease	14%	21%	28%	35%	42%	49%
40		222,673,000.00	207,490,750.00	192,308,500.00	177,126,250.00	161,944,000.00	146,761,750.00
	% Decrease	12%	18%	24%	30%	36%	42%
50		227,733,750.00	215,081,875.00	202,430,000.00	189,778,125.00	177,126,250.00	164,474,375.00
	% Decrease	10%	15%	20%	25%	30%	35%
60		232,794,500.00	222,673,000.00	212,551,500.00	202,430,000.00	192,308,500.00	182,187,000.00
	% Decrease	8%	12%	16%	20%	24%	28%
70		237,855,250.00	230,264,125.00	222,673,000.00	215,081,875.00	207,490,750.00	199,899,625.00
	% Decrease	6%	9%	12%	15%	18%	21%
80		242,916,000.00	237,855,250.00	232,794,500.00	227,733,750.00	222,673,000.00	217,612,250.00
	% Decrease	4%	6%	8%	10%	12%	14%

[1] Data from Thai FDA website: http://dmsic.moph.go.th/price/price1_1php?method=drug

F-12: Overall drug expenditure and percent saved per year vary by percentage of market share and price of generic drug (Drug No.A29)

Name code				reference price[1] (Baht)	importation budget 2009-2012 (M. Baht)	Average use per year (Tablet)	Average budget per year (M. Baht)
A29				1,021.72	1,001.28	244,999.28	250.32
Price of generic (% of brandname)	Generic market share (%)						
	20		30	40	50	60	70
30	215,275,775.34		197,753,328.51	180,230,881.68	162,708,434.85	145,185,988.02	127,663,541.19
	% Decrease	14%	21%	28%	35%	42%	49%
40		220,282,188.72	205,262,948.58	190,243,708.44	175,224,468.30	160,205,228.16	145,185,988.02
	% Decrease	12%	18%	24%	30%	36%	42%
50		225,288,602.10	212,772,568.65	200,256,535.20	187,740,501.75	175,224,468.30	162,708,434.85
	% Decrease	10%	15%	20%	25%	30%	35%
60		230,295,015.48	220,282,188.72	210,269,361.96	200,256,535.20	190,243,708.44	180,230,881.68
	% Decrease	8%	12%	16%	20%	24%	28%
70		235,301,428.86	227,791,808.79	220,282,188.72	212,772,568.65	205,262,948.58	197,753,328.51
	% Decrease	6%	9%	12%	15%	18%	21%
80		240,307,842.24	235,301,428.86	230,295,015.48	225,288,602.10	220,282,188.72	215,275,775.34
	% Decrease	4%	6%	8%	10%	12%	14%

[1] Data from Thai FDA website: http://dmsic.moph.go.th/price/price1_1php?method=drug

F-13: Overall drug expenditure and percent saved per year vary by percentage of market share and price of generic drug (Drug No.A30)

Name code			reference price[1] (Baht)	importation budget 2009-2012 (M. Baht)	Average use per year (Tablet)	Average budget per year (M. Baht)
A30			51.04	938.08	4,594,817.64	234.52
Price of generic (% of brandname)	Generic market share (%)					
	20	30	40	50	60	70
30	201,686,763.25	185,270,398.80	168,854,034.35	152,437,669.90	136,021,305.45	119,604,941.00
	% Decrease 14%	21%	28%	35%	42%	49%
40	206,377,153.09	192,305,983.56	178,234,814.03	164,163,644.51	150,092,474.98	136,021,305.45
	% Decrease 12%	18%	24%	30%	36%	42%
50	211,067,542.94	199,341,568.33	187,615,593.72	175,889,619.11	164,163,644.51	152,437,669.90
	% Decrease 10%	15%	20%	25%	30%	35%
60	215,757,932.78	206,377,153.09	196,996,373.41	187,615,593.72	178,234,814.03	168,854,034.35
	% Decrease 8%	12%	16%	20%	24%	28%
70	220,448,322.62	213,412,737.86	206,377,153.09	199,341,568.33	192,305,983.56	185,270,398.80
	% Decrease 6%	9%	12%	15%	18%	21%
80	225,138,712.46	220,448,322.62	215,757,932.78	211,067,542.94	206,377,153.09	201,686,763.25
	% Decrease 4%	6%	8%	10%	12%	14%

[1] Data from Thai FDA website: http://dmsic.moph.go.th/price/price1_1php?method=drug

APPPENDIX G
CERTIFICATION OF APPROVAL

Certificate of Approval

COA.No.MU-DT/PY-IRB 2014/028.0408

Documentary Proof of Faculty of Dentistry/Faculty of Pharmacy, Mahidol University, Institutional Review Board

Title of Project:	Priority Setting of First Generic Drug Registration in Thailand
Project Number:	MU-DT/PY-IRB 2014/PY013
Principle Investigator:	Miss Parnjit Homyen
Coinvestigator:	Associate Professor Dr. Cha-oncin Sooksriwong
Name of Institution:	Faculty of Pharmacy
Approval includes:	1. MU-DT/PY-IRB Submission form version 3, July 31, 2014
	2. Proposal version 2, June 4, 2014
	3. Participant information sheet version 3, July 31, 2014
	4. Consent form version received date February 4, 2014
	5. Questionnaire version received date February 4, 2014
	6. Case record form version received date February 4, 2014
	7. CV version received date February 4, 2014

Faculty of Dentistry/Faculty of Pharmacy, Mahidol University, Institutional Review Board is in full compliance with International Guidelines for Human Research Protection such as Declaration of Helsinki, the Belmont Report, CIOMS Guidelines and the International Conference on Harmonization in Good Clinical Practice (ICH-GCP)

Date of Approval: August 4, 2014
Date of Expiration: August 3, 2015

Signature of Chair:
(Associate Professor Dr. Choltacha Harnirattisai)
Chair

Signature of Dean:
(Associate Professor Chuthamanee Suthisisang)
Dean, Faculty of Pharmacy

Office of Faculty of Dentistry/Faculty of Pharmacy, Mahidol University, Institutional Review, Board
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