FINAL REPORT

The Implications of the Market Exclusivity of New Drugs under Safty Monitoring Program (Project # 152)

Article 1 : The effects of the New Drug Registration Regulations on generic availability in Thailand

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The effects of the New Drug Registration Regulations on generic availability in Thailand

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Executive summary

In early 1990's, Thailand was forced by multinational drug companies to provide market exclusivity to some pharmaceutical products those were not eligibly protected by conventional patenting system. Administrative measures granting short-term monopoly status to these original products had been integrated into the existing regulations on new drug registration. According to the regulations, an original product is firstly approved with conditions that it can be distributed through hospitals or healthcare settings under close supervision of physician and the distributor has to collect the data on drug safety for 2 to 4 years. While the original is under safety monitoring, the Thai Food and Drug Administration (FDA) will not accept the registration file of its generic. In addition, registration of generic product requires bioequivalence data, which is so sophisticate for domestic industry that may delay generic entry and prolong the market exclusivity period of the original. This study aims to assess the effects of the administrative measures on generic availability in the country.

From the year of first enforcement of the regulation in 1991 until the end of 1999, there were 742 new drug products approved with conditions. At 30 June 2000, 54.0% had ended their safety monitoring and got unconditioned registration status. Among these originals, generics of only 11 products (2.9%) had been available.

The original products approved with conditions in 1991 hold the longest period of conditioned registration status that was about 6.5 years. Length of conditional registration among the originals approved each year decreased gradually from 6.5 years for the products approved in 1991 to 1.6 years for those approved in 1998. Most of the conditioned registration period (95.3%) consumed by safety monitoring. Time spent on the evaluation of product's safety data by the FDA was 0.2 year in average.

Eleven products of which the generics had been approved included fluconazole capsules 50, 100, 150, and 200mg; fluconazole injection, ondansetron tablets 4 and 8mg; ondansetron injection; clozapine tablets 25 and 100mg; and ofloxacin injection.

Length of market exclusivity of the eleven original products was 5.7 years in average. Most of market exclusive period consumed by safety monitoring which was about 4.3

years. The time lag between original product unconditional approval and generic application for registration was about one year.

One hundred and eighty-four original products approved unconditionally by the end of 1997 but their generics had not been available were investigated for the import values and pharmaceutical dosage forms. Twenty-five percent of these products were imported at the annual value higher than 10 million baht, among which 76.0% were the products of conventional dosage forms that can be manufactured by local drug industry.

A brainstorming workshop was organized among leading indigenous generic producers, academics and regulatory authorities to identify the obstacles of generic manufacture in the country. Four issues were raised and claimed as major impediments of generic availability, including (1) poor accessibility to the information on patent status of pharmaceuticals products, (2) over-competitiveness among local manufacturers in producing the same generic product, (3) infeasible regulations and standards relating to drug registration and manufacture, and (4) inadequate supports from government sector.

Findings in this study indicate that delayed generic availability in Thailand is not caused by intellectual property right protecting measures that have been integrated into the New Drug Registration Regulations. Poor performance of local pharmaceutical industry due to several factors plays important roles in generic manufacture. Strengthening National Drug Policy process, including policy formulation, implementation, monitoring, and evaluation is recommended in order to achieve the ultimate goal of the country's self-reliance in pharmaceuticals.

บทคัดย่อ

การวิจัยนี้มีวัตถุประสงค์ที่จะศึกษาผลกระทบที่มีต่อการมียาสามัญ (ยาเลียนแบบ) ของตำรับยาที่ถูกจัดว่าเป็นยาใหม่ ซึ่งเป็นผลจากมาตรการด้านการบริหารที่ให้สิทธิผูกขาดทางการตลาดในการจำหน่ายผลิตภัณฑ์ยาต้นแบบบางชนิด ซึ่งไม่อยู่ในข่ายที่จะได้รับความคุ้มครองตามพระราชบัญญัติสิทธิบัตรในประเทศไทย มาตรการดังกล่าวได้ถูกผนวกไว้เป็นส่วนหนึ่งของหลักเกณฑ์การขึ้นทะเบียนตำรับยาใหม่

ตั้งแต่หลักเกณฑ์การขึ้นทะเบียนตำรับยาใหม่มีผลบังคับใช้ในปี 2534 ถึง 2542 มีผลิตภัณฑ์ยาต้นแบบได้รับการอนุมัติให้ขึ้นทะเบียนฯ จำนวนรวม 742 ตำรับ ณ วันที่ 30 มิถุนายน 2543 ตำรับยาต้นแบบร้อยละ 54.0 สิ้นสุดสิทธิผูกขาดทางการตลาดภายใต้หลักเกณฑ์ฯ ฉบับนี้ ระยะเวลาการผูกขาดของตำรับยาต้นแบบที่ขึ้นทะเบียนฯ ในแต่ละปีค่อยๆ ลดลงจาก 6.5 ปี สำหรับตำรับยาต้นแบบที่ขึ้นทะเบียนในปี 2534 เป็น 1.8 ปี สำหรับตำรับยาที่ขึ้นทะเบียนฯ ในปี 2541 ระยะเวลาการผูกขาดส่วนใหญ่ (ร้อยละ 95.3) เป็นเวลาที่ใช้ไปในการติดตามความปลอดภัยของตำรับยาต้นแบบ ในจำนวนตำรับยาต้นแบบที่ขึ้นทะเบียนฯ ไว้ทั้งหมด มีเพียง 11 ตำรับ ที่มียาสามัญได้รับอนุญาตให้ขึ้นทะเบียนฯ แล้ว

ผลการวิจัยนี้แสดงให้เห็นว่า การที่เกิดความล่าช้าในการมีผลิตภัณฑ์ยาสามัญจำหน่ายในประเทศไทยนั้นไม่ได้เป็นผลจากมาตรการด้านการบริหารที่ให้ความคุ้มครองสิทธิในทรัพย์สินทางปัญญา หากแต่เกิดจากการด้อยความสามารถของอุตสาหกรรมยาในประเทศ ซึ่งมีหลายปัจจัยเข้ามาเกี่ยวข้อง ดังนั้น จึงมีข้อเสนอแนะให้ปรับปรุงเสริมสร้างความเข้มแข็งของกระบวนการทางนโยบายของนโยบายแห่งชาติด้านยา อันได้แก่ การกำหนดนโยบาย การนำนโยบายไปปฏิบัติ การกำกับติดตาม และการประเมินผลการปฏิบัติตามนโยบายดังกล่าว ทั้งนี้ เพื่อให้สามารถบรรลุเป้าหมายสูงสุดในการพึ่งพาตนเองทางด้านยาของประเทศ

Abstract

This study aims to assess the effects on generic availability of the administrative measures established in Thailand to provide 2 to 4 year market exclusivity to some pharmaceutical products those were not protected by conventional patenting system. The measures were integrated into the existing regulations on new drug registration.

From the year of first enforcement of the regulations in 1991 until the end of 1999, 742 new original products were approved. At 30 June 2000, 54.0% had ended their exclusive rights. Length of exclusivity period among the originals approved each year decreased gradually from 6.5 years for the products approved in 1991 to 1.6 years for those approved in 1998. Most (95.3%) of the period consumed by safety monitoring. However, among those originals, generics of only 11 products had been available.

Findings in this study indicate that delayed generic availability in Thailand is not caused by intellectual property right protecting measures. Poor performance of local pharmaceutical industry due to several factors plays important roles in generic manufacture. Strengthening National Drug Policy process, including policy formulation, implementation, monitoring, and evaluation is recommended in order to achieve the ultimate goal of the country's self-reliance in pharmaceuticals.

Keywords

Market exclusivity, pharmaceutical product, pharmaceutical industry, original product, generic product, intellectual property right protection, pipeline protection, National Drug Policy, Thailand.

Introduction

Thailand has strengthened intellectual property right (IPR) protection system to comply with international standards set out in the Trade-related Aspects of Intellectual Property Rights Agreement (TRIPS) by revising a number of regulations and more strictly enforcing the laws. The amendment of Patent Act, which became effective in 1992, was one of the attempts. According to the Act, the country has been obliged to expand patent protection to cover both process and product inventions in all fields of technology, including pharmaceuticals, and to increase the protection term to 20 years.

The US pharmaceutical industry, however, filed a petition that the newly amended patent law did not provide protection for existing products patented in other countries between 1 January 1986 and 30 September 1991, the so called "pipeline protection". Under political pressure and the threat of trade sanctions, in 1993, the Thai government established administrative measures to provide a degree of market exclusivity for pharmaceutical products not eligible for protection under 1992 Patent Act *(1)*.

The measures were integrated as part of the regulations on new drug * registration that had firstly been promulgated since 1990, by means of which an original product is primarily registered with conditions *(2)*. The drug could restrictedly be distributed through hospitals or other healthcare settings and used under close supervision of physicians. Concomitantly, under Safety Monitoring Program (SMP), drug distributor has to collect data on adverse drug reactions, from local facilities as well as foreign countries, for at least two years, to report to the Thai Food and Drug Administration (FDA). If there is no evidence indicating serious side effects or it is considered its benefits outweigh the risks, the product will be approved unconditionally and allowed to distribute widely through normal channels. In case of insufficient information, SMP of certain original product may be extended for two times of one-year period *(3)*. Generic product, of which the original is subjected to the safety monitoring could not be applied for registration until unconditional approval of the prototype is granted. Moreover, the measure requires generic producer to conduct bioequivalence study of their products that may cause additional difficulties in the registration of generic product. These measures are expected to provide at least 2 to 4 year market exclusivity to the pipeline products.

Though the delay of generic approval resulting in the exclusive right of the original product generated by the administrative measures is not patent-related, its consequences are predicted to be in the same manners, including high drug price and increased drug expenditures at both national and hospital levels. However, evidence from elsewhere suggests that many factors, other than IPR protecting measures, influence generic availability. It could be seen that there are a large number of pharmaceutical products no longer protected by patents and available to generic producers to manufacture, but many of them are not distributed in developing countries *(4)*.

There are 174 manufacturers and 510 importers of modern drugs in Thailand *(5)*. The Government Pharmaceutical Organization (GPO), a state enterprise under supervision of the Ministry of Public Health (MoPH), is one of the largest manufacturers and distributors of pharmaceuticals in the country. The local pharmaceutical production is mainly secondary production, which is large-scale manufacturing of finished dosage forms, mostly from imported raw materials or intermediate products. Only 25 pharmaceutical ingredients are manufactured, by 10 producers, in the country *(6)*. Over 90% of the raw materials used by local pharmaceutical industry are imported.

Review on the current situation of Thai pharmaceutical technology indicates a lot of weaknesses and non-self-reliance *(7)*. Ninety five percent of the technologies used by local drug producers involve manufacturing of conventional dosage forms, e.g. plain tablet, hard capsule, solution, injection. Almost all of the sustained-release and drug targeting preparations, for example liposome, polymer-drug linkage, are imported and the research and development (R&D) of these products are limited within academic institutes. Using of genetic engineering in the production of biotechnology-derived preparations is at infantile step.

Previous study on the accumulation of generic products in Thailand from 1986 to 1990 reveals that 7 years after the first distribution of innovator products, only 24% were

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* According to the regulations, the term "New drug" covers product of new chemical entity, new indication, new combination, and/or new delivery system, which has never been approved in the country before the date of registration file submission.

imitated by generic producers *(8)*. Multiple factors relating to the delayed production of generics were identified, including development of appropriate formulation, availability of raw materials, and the size of the market.

One of the problems among local pharmaceutical manufacturers is that their capacity on R&D is inadequate, which is resulted in overall weaknesses of the industry. Survey on R&D among private pharmaceutical manufacturers in 1993 demonstrated that most of them (84%) had no R&D division *(9)*. Expenditures on R&D among these firms were approximately 0.5 to 5% of total sale value. Poor R&D competency was claimed to be influenced by various determinants, e.g. inadequate budget, scarcity of qualify personnel, insufficient technology transfer, inefficient management in pharmacy education system, outdated law and regulation *(10,11)*.

As a consequence of 1997 economic crisis, there have been several emerging challenges of local generic industry, the results of which might be the delay of new generic manufacturing. Many companies faced financial difficulties partly due to budgetary constraints among both public and private hospitals and cost containment policy in healthcare. However, such constraints and policy might be considerable opportunities among local producers since they can manufacture very much cheaper products than the innovator *(12)*.

This study aims to assess the effects on generic availability of the New Drug Registration Regulations, in which the IPR protecting measures are integrated. The following specific objectives are also addressed:

(1) To assess the current registration status of the original new drugs registered by means of the regulations.
(2) To appraise the magnitude and pattern of time lag between original product conditional approval and availability of its generic products.
(3) To analyse the characteristics of generic-unavailable products, which might be the determinants of generic availability.
(4) To identify the obstacles of generic availability, other than the exclusivity right of innovator companies.

Methods

(1) Analyse the FDA drug database and/or operation workbooks at Drug Control Division for the current registration status of each of the original new drug products registered in Thailand between 1991 and 1999.
(2) For the innovator product of which the generic is available, document research was conducted on the drug registration files at Drug Control Division for the total time lag between the date of original product conditional approval and the date of its generic approval.
(3) For the innovator product that terminated conditional registration status by the end of 1997 and of which the generic is not available by the end of 2000, document research was conducted on the FDA drug database for its therapeutic category, dosage form, and annual import value.
(4) Organize a brainstorming workshop among leading local pharmaceutical industry, GPO, regulatory authorities, academics, and public R&D institutions to assess the dominant factors affecting the availability of generic product when its original lost its exclusivity.

Results

Current registration status of the original products registered under 1990 New Drug Registration Regulations.

From the first year of enforcement of New Drug Registration Regulations in 1991 until the end of 1999, there were 742 new drug products approved with conditions* (Table 1). Most (54.0%) of them registered during 1998 to 1999. At 30 June 2000, 376 products (50.5%) had ended their safety monitoring and got unconditioned registration status. Among these innovator products, generic versions of 11 products (2.9%) had been approved and 3 (0.4%) were under evaluation.

<<Table 1>>

Length of market exclusivity period of the originals and delay of generic availability

The original products approved with conditions in 1991 hold the longest period of conditioned registration status that was approximately 6.5 years (Figure 1). Length of conditional registration among original products approved each year decreased gradually from 6.5 years for the products approved in 1991 to 1.6 years for those approved in 1998. Most (95.3%) of the conditioned registration period consumed by safety monitoring. Time spent on the evaluation of product's safety was approximately 0.2 year (0.1 to 0.3 year).

<<Figure 1>>

At 30 June 2000, there were 11 new drug products, the generics of which had been approved, including fluconazole capsules 50mg, 100mg, 150mg, and 200mg; fluconazole injection 2mg/ml, ondansetron tablets 4mg and 8mg; ondansetron injection 2mg/ml; clozapine tablets 25mg and 100mg; and ofloxacin injection 200mg/100ml.

Length of market exclusivity of the eleven original products was 5.7 years (3.3 to 7.9 years) as shown in Table 2. Most of market exclusive period consumed by the safety monitoring which was about 4.3 years (76.7%). Average length of original product's safety evaluation was equal to that of generic product evaluation, which was approximately 0.2 year. The time lag between original product unconditional approval and generic application for registration was about one year.

<<Table 2>>

Characteristics of generic-unavailable original products

According to the findings mentioned above, until the end of 1999, 742 original products had been registered conditionally and, at 30 June 2000, 50% of which had completed safety monitoring and passed safety evaluation. With respect to the New Drug Registration Regulations, exclusive right provided to these originals would be terminated and the FDA would accept generic application for approval. However, there were only 11

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* The products that had been voluntarily withdrawn by importer before 30 June 2000 are excluded.

original products imitated by generic producers, whilst the rest remained enjoying their monopolistic profit without any competitor.

To understand the potential impediments of generic availability, other than the exclusivity of innovator companies, the characteristics of the originals that had got unconditional approval by the end of 1997, but their generic registration files had not been submitted to the Drug Control Division at the end of 1999, were investigated*. There were several factors speculated to affect manufacturing feasibility of different generic products, e.g. level of manufacturing technology, cost of and local capacity to conduct bioequivalence study, availability of raw material, competitiveness, and profitability. Two characteristics of un-imitated products were assessed, including pharmaceutical dosage form and average import value per year, in order to select a number of products, on which to be discussed in the brainstorming workshop among local manufacturers and experts.

Regarding the inclusion criteria stated above, there were 184 original products or 94 items** analysed. The total import value of these originals from the year of conditional approval to 1999 was approximately 5.8 billion baht at current year price. Most of the products were anti-infectives, which accounted for 23.4% in term of number of item. Drugs indicated in the treatment of cardiovascular diseases were imported at the highest value, which was 1.5 billion baht or 25.7% of the total.

These products could be classified by pharmaceutical dosage form into 8 major categories (Table 3). Of 94 items, 42.6% were immediate-release oral dosage forms. The import value of these preparations from 1991 to 1999 was 3.4 billion baht or 59.0% of the total.

The products of 3 categories, namely immediate-release oral preparation, plain injection, and topical preparation, those do not require high technology and are able to be manufactured in Thailand accounted for 77.8% and 70.6% in terms of number of item and import value, respectively.

<<Table 3>>

The interested products were classified by average annual import value, from the year of conditional approval to 1999, into 5 strata as shown in Figure 2. Most (54.0%) of the un-imitated original products were imported at the value between 1 and 10 million baht a year. The higher import values were observed in 25% of the original products.

<<Figure 2>>

It was found that among the originals those had been imported at the annual values of more than 10 million baht, 76.1% were the products of conventional dosage form, including immediate-release oral preparation and plain injection. Products of the other categories, including biological product, controlled-release preparation, and lyophilized powder for injection, those require relatively high technology in the manufacturing process and cannot be produced in the country, accounted for 24% of the total items

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* The originals those passed the safety evaluation later than the end of 1997 were not included in order assuring that the unavailability of their generics was not determined by time-constraint.

** An "item" refers to drug with same active ingredient and dosage form, regardless of the difference in strengths and manufacturers/distributors, those are different products according to drug registration rules.

Finally, 18 un-imitated products of which the dosage form could be manufactured by local pharmaceutical industry and the average import values were higher than 11 million baht per year were selected (Table 4).

<<Table 4>>

Obstacles of local generic manufacture

Self-administered questionnaire was developed to assess the determining factors of generic unavailability of the products listed in table 4. The questionnaire was distributed to 8 leading local generic producers those were invited to the brainstorming workshop, including the GPO, to explore the impediments of manufacture and registration of each product.

The workshop was organized on 3 April 2001 participated by 23 key informants from the MoPH, GPO, FDA, Department of Medical Sciences, School of Pharmacy, Thailand Tropical Diseases Research Program, Thailand Pharmaceutical Manufacturers Association, Industry Council of Thailand, eight leading local drug manufacturers, and International Health Policy Program. Research findings mentioned in the previous sections were briefly presented to the forum as background information. Unfortunately, there was no questionnaire returned by the local drug producer.

During the workshop, the participants presented their views and experiences relating to the update situation of the country's pharmaceutical industry, current obstacles of generic manufacture, and also proposed the idea on how to encourage generic availability.

Four issues were raised and claimed as major impediments of local generic manufacture, including the poor accessibility to the information on the patentship of drug products in the country, heavy competitiveness among local pharmaceutical manufacturers those produce the same generic, infeasible regulations and standards relating to drug manufacture and registration, and inadequate supports from public sector.

- *Accessibility to the information on patent status of pharmaceutical products:*

Not only private pharmaceutical producers but also the GPO face the problems that it is difficult, and sometimes impossible, to retrieve accurate information on the status of patent application and patent granting of pharmaceutical products in the country. Though the computerised database has been established by Department of Intellectual Property, Ministry of Commerce (MOC); it is not user-friendly. Since the name of a chemical entity, which is the active ingredient or excipient of pharmaceutical preparation, can usually be expressed in several ways when using different nomenclature systems, e.g. chemical name, International Non-proprietary Name (INN), generic name; at present, due to limitation of database capacity, entering a mismatched search-term might result in incorrect result. Unintentional infringement of drug patent would severely affect the industry in terms of goodwill and high-cost prosecution. As factual information is necessary in planning and decision-making on certain generic manufacture, it is recommended that the administrators and officers of the MoPH and MOC should work with close collaboration to solve the problem.

- *Competitiveness among local generic producers:*

Over-competitiveness among local pharmaceutical producers on the production of identical preparation was one of the impediments. As a marketing strategy, these generic manufacturers have to cut the price to increase sale volume. The situation would be worse if lower price generic products were imported. Moreover, there are disadvantages among private manufacturers to compete with the GPO, since, according to Drug Act [12], the GPO's pharmaceutical products are exempted from approval, thus many time- and budget consuming activities in drug registration, for example conducting a bioequivalence study, could be skipped. In addition, with respect to the regulations on public procurement [13], government healthcare settings and public health agencies must purchase the GPO product, except the product of private company is sold at more than 3% lower price than the state enterprise's. A measure on the quota of certain generic to be manufactured by limited number of local producers, regarding their capabilities and expertise, was proposed. First of all, however, target products to be locally produced for the replacement of the originals should be identified with respect to health needs in the country.

- *Standards and regulations on drug manufacture and registration:*

There have been a lot of recently-promulgated regulations, rules, and standards relating to drug manufacture and registration, some of which, e.g. rules on bioequivalence data, requirements on introducing Good Clinical Practice (GCP) in conducting a clinical study, in the industry's perspectives, are the major obstacles of generic availability. In other words, these regulations and standards are "Technical Barriers-to-Trade" against local industry, meanwhile, providing advantages to the research-based multinational companies (MNCs). Poor capacity on R&D, due to several underlying factors, among local manufactures, not excluding the GPO, has been identified as the antecedent of overall weakness of the county's pharmaceutical industry. Fully-implementation of some regulations and standards without systematic preparing for not only the indigenous manufacturers but also laboratory facilities in public sector can negatively affect the industry.

The difficulties in conducting bioequivalence study include limited number of study institutions, inefficient coordination among agencies responsible for clinical study and serum drug concentration analyses, and high-cost fundamental equipment. In addition, most existing laboratories are university affiliates, thus the human resource and equipment necessary in bioequivalence study are mostly occupied by teaching activities.

Local drug producers accept that introducing GCP in clinical study can assure quality of the study and increase credibility of their products. However, in Thailand, GCP is merely a practice guideline. There is not any explicit indicator of conforming to the statements, moreover, the accreditation system is not established in the country.

- *Supports from government sector*

Political will is key determinant of generic manufacture in the country. Local drug producers experienced lacking of proper supports from public sector, particularly 2 ministries, Industry and Sciences & Technology, which might be due to small size of pharmaceutical industry comparing with the others, lower value of income contribution in term of foreign currency obtained from drug exportation and relatively high proportion of

imported raw materials. MoPH should therefore be the most relevant government agency to play leading roles in facilitating generic production in the country.

It was collectively agreed that, to swiftly encourage local generic manufacture in order to substitute the innovator importation, effective strategies have to be formulated by the public and private collaborations. Missions should be clearly developed for efficient use of national resources by sharing those of public and private sector, and reducing unnecessary competitiveness among local producers, all of which for the benefit of Thai people. In these regards, public agencies have to fully support all activities, recognizing that the returns of pharmaceutical R&D investment are public interests.

Strategies to facilitate manufacture of generic version of priority drug were proposed. It might be feasible that public agencies take responsibility in the R&D investment and risk, and transfer the harvest technologies to the industry. Pharmaceutical producers participating in this program have to comply with the rules on drug pricing, collaboratively set out among representatives of public and private sectors. The procedures should be started from drafting program proposal in details, stating measures and operational plan in all aspects, including objectives, methods, activities, conditions, responsible agencies, supporting agencies, budget, timeframe, and outputs. The proposal would be approved by the National Drug Committee, before passing to the Cabinet for final decision.

Discussion

Beside the objective of safeguarding consumers, provision of the New Drug Registration Regulations aims to provide short-term, i.e. 2 to 4 years, monopoly status to "pipeline products", to which, according to the current law on IPR protection, the patent cannot be granted. This study indicates that the administrative measures forced by multinational pharmaceutical companies and the U.S. government are not key impediment of generic availability in Thailand. Since there is no competitor launched in the market, large proportion of the innovator products remains in exclusive position though safety-monitoring period has been terminated.

Multiple factors play roles in the manufacture of a certain generic product. Possible large market size of a generic, predicting by relatively high annual import value of its original is not the sole determinant. Import values of the un-imitated original products range widely from lower than 1 million to higher than 50 million baht a year, whilst, observations in one of our studies reveal that the corresponding values of some generic-available originals are as low as the lowest one *(13)*. Findings in this study also indicate that though the dosage forms of the original products imitated by local industry are simple and do not require advance manufacturing technology, i.e. capsule, tablet, and plain injection, there are many original products of these dosage forms left with no competition from the imitators. The two factors, market size and dosage form of an original cannot thoroughly explain the availability of its locally produced generic.

As discussed in the workshop, the delay of local-made generic entry seems to be strongly affected by the requirement on indigenous bioequivalence data in generic product registration. However, it should be noted that according to the FDA Criteria on Bioequivalence Study *(14)*, there are exemptions for many kinds of pharmaceutical product, of which the data on comparative bioavailability are not needed, for example intravenous injections, topical preparations for external use (e.g. cream, ointment, eye and

ear preparations), oral preparations used for local activity (e.g. antacid, radiopaque contrast media), oral solutions (e.g. elixir, syrup) those are pharmaceutical equivalent to the original, etc. In addition, bioequivalence data from foreign countries are accepted for the drugs considered high priority in health need aspects, such as antiretrovirals and other drugs used in the treatment of HIV/AIDS.

The information illustrated in figure 1 reveals that the safety-monitoring period of the originals registered conditionally in 1991 and 1992 were longer than five years, in spite the fact that the maximum of 4 years had been permitted with respect to the Regulations. In addition, most (88.9%) of the innovator products, registered with conditions between 1994 and 1997, ended their safety-monitoring in 1997 and 1998, though the monitoring of adverse drug reactions (ADRs) among these preparations might be prolonged to the maximum allowance. These interesting phenomena can be explained by two determining factors, including the FDA policy and criteria on drug selection to the National List of Essential Drugs (NLED). Firstly, according to the FDA Secretary General's policy in 1997 to 1998 to facilitate generic availability, many steps of unconditional approval of the originals were accelerated. Registration status of all innovator products registered since 1991 were intensively reviewed and those had been under safety-monitoring for more than 4 years were asked to submit ADR reports in order to terminate their exclusivity. Secondly, during 1998 to early 1999, the NLED Subcommittee excluded the products under safety-monitoring from the essential drug selection process. The safety-surveillance of a large number of innovator products were terminated and the suppliers eagerly applied for unconditioned registration status since they wanted to have their products listed in the NLED.

Self-reliance in pharmaceuticals, one of the ultimate goals of Thai National Drug Policy (NDP) since firstly established in 1981 is far away to achieve. Large number of original pharmaceutical products is neglected without competition from domestic manufacturers. Previous studies on the weakness of local producers show that the problems have been recognized and multiple factors have been identified for decades. The issues discussed during the workshop indicate that poor competency in R&D, which is resulting in poor performance of the domestic industry, is standstill and cannot be overlooked in the next revision of NDP. To upgrade R&D in pharmaceuticals, relevant infrastructures, e.g. human resource, well-organized agencies, tremendous investment and long-term plan are the pre-requisites. Several measures to strengthen R&D of local drug manufacturers have been stated as part of the current NDP, but there are discrepancies between the policy and implementation. The enormously resource-consume nature of R&D activities might be the reason why the panel proposed more simplistic and short cut strategies, transferring the responsibilities and financial risks in R&D to public sector, to promote indigenous generic manufacture. However, one should keep in mind that though the goal of urgently facilitating generic availability may be achieved, these strategies cannot contribute to sustainable development of local drug industry. Additional approaches including technology transfer and joint venture on R&D among public institutes and private companies should be promoted.

The bigger picture could be seen from the discussions among workshop participants. Visions and missions among stakeholders of the country's drug system are not unique. While the FDA, as drug regulatory authority, emphasizes consumer protection by introducing new rules and standards relating to drug manufacture and registration, the FDA, as the coordinator of NDP implementations, has not properly taken into account the

feasibility and its implications. More holistic views are needed to analyse the impacts of different policy options, as it is one of the vital components of policy formulation process. Vital roles of FDA as the secretariat of the National Drug Committee should be strengthened in order to achieve the major goals of the NDP. Rattanawijitrasin S et al *(15)* suggested establishing the mechanisms to regularly monitor how all aspects of the NDP are being carried out and to evaluate policy outcomes. Moreover, it was recommended that the NDP should be operated in prospective manners, i.e. revision of the policy should be designed not only to solve current problems, but also to address problems that are likely to arise in the future.

Conclusion

Findings in this study indicate that the exclusive rights of innovator companies granted by means of the administrative measures on pipeline protection cause less extent of effects on the delay of local generic manufacture than those resulted from low capability of the country's drug industry itself. To relief negative consequences on health expenditure and accessibility to drugs among Thai people, domestic industry has to be strengthened with close collaborations between public and private sector. The missions cannot be successful without intensive reform in all components of NDP process, including policy formulation, implementation, monitoring, and evaluation.

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Tables:

Table 1: Number of original products by current registration status and the availability of their generic products at 30 June 2000.

Year of original product conditional approval	Registration status of original new drug products				Total
	Number of product with conditional approval	Number of product with unconditional approval			
		Generic product not available		Generic product available	
		Generic product under evaluation	No generic product submission for approval		
1991	1	0	12	2	15
1992	1	2	39	1	43
1993	0	0	28	5	33
1994	0	1	35	0	36
1995	1	0	45	3	49
1996	7	0	72	0	79
1997	22	0	64	0	86
1998	207	0	67	0	274
1999	127	0	0	0	127
Total	366	3	362	11	742

Data source: Drug Control Division, FDA

Table 2: Length of market exclusivity of the original products of which the generic products had been available at 30 June 2000 (years)

Generic name/Dosage form/Strength	Length of Safety Monitoring	Length of original product safety evaluation	Length between original product unconditional approval and generic product application	Length of generic product evaluation	Total length of market exclusivity of original product
Fluconazole Capsules (50mg and 150mg)	6.6	0.2	0.9	0.1	7.9
Fluconazole Injection 2 mg/ml	5.4	0.2	0.9	0.1	6.6
Ondansetron Tablets (4mg and 8mg)	4.3	0.1	1.1	0.1	5.6
Ondansetron Injection 2mg/ml	4.3	0.1	1.1	0.1	5.6
Fluconazole Capsules (100mg and 200mg)	4.3	0.2	0.9	0.1	5.5
Clozapine Tablets (25mg and 100mg)	2.8	0.2	1.0	0.4	4.4
Ofloxacin Injection 200mg/100ml	2.0	0.2	0.8	0.4	3.3
Average	4.3 (76.7%)	0.2 (3.2%)	1.0 (17.1%)	0.2 (3.2%)	5.7 (100%)

Data source: Drug Control Division, FDA

Table 3: Number of item and total import value at current year price from 1991 to 1999 of SMP-ended original products, of which the generics had not been available, by dosage form.

Category of dosage form	Dosage form	Number of item	Import value (million baht)
Immediate-release oral preparation	Hard capsule, plain tablet, film-coated tablet, powder for oral suspension	40 (42.6%)	3,390.9 (59.0%)
Plain injection	Injection, infusion, large volume parenteral, powder for injection	26 (27.7%)	599.3 (10.4%)
Topical preparation	Ophthalmic/Otic solution, cream	7 (7.5%)	70.0 (1.2%)
Controlled-release oral preparation	Enteric-coated capsule, extended-release tablet, sustained-release capsule	4 (4.3%)	481.0 (8.4%)
Controlled-release parenteral dosage form	Implant, depot injection, transdermal therapeutic system	4 (4.3%)	173.8 (3.0%)
Lyophilized powder for injection	-	2 (2.1%)	134.9 (2.4%)
Biological/biotechnology product	Antigen, vaccine, recombinant DNA product	5 (5.3%)	846.7 (14.7%)
Preparation with special device	Meterd-dose inhaler, rotadisk	6 (6.4%)	52.9 (0.9%)
	Total	94 (100%)	5,749.5 (100%)

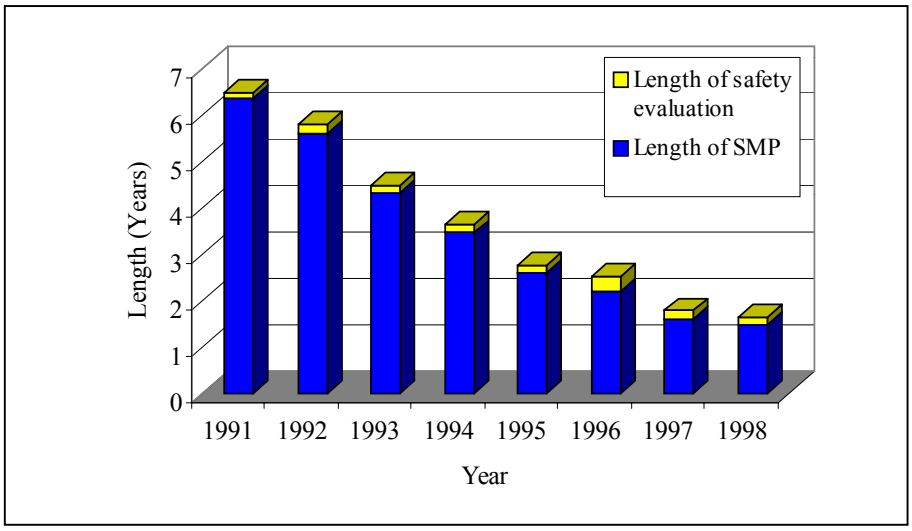
Note: the originals whose exclusivity right had expired by the end of 1997, of which the generics had not been submitted for approval at the end of 1999.
Data source: Drug Control Division, FDA

Table 4: Generic-unavailable SMP-ended original products with basic-technology dosage form and relatively high import values

Import value (million baht)	Number of item	Product
11 to 20	8	Azithromycin powder for oral suspension, Cefodizime powder for injection, Cefprozil injection, Finasteride tablet, Fosinopril tablet, Manidipine tablet, Pravastatin tablet, Sulbactam powder for injection
21 to 30	6	Amlodipine tablet, Cilazapril film-coated tablet, Clarithromycin film-coated tablet, Fluvastatin capsule, Leuprorelin powder for injection, Tibolone tablet
31 to 40	1	Zalcitabine film-coated tablet
41 to 50	1	Desogestrel + ethinyl estradiol sugar-coated tablet
> 51	2	Simvastatin film-coated tablet, Terazosin tablet
Total	18	

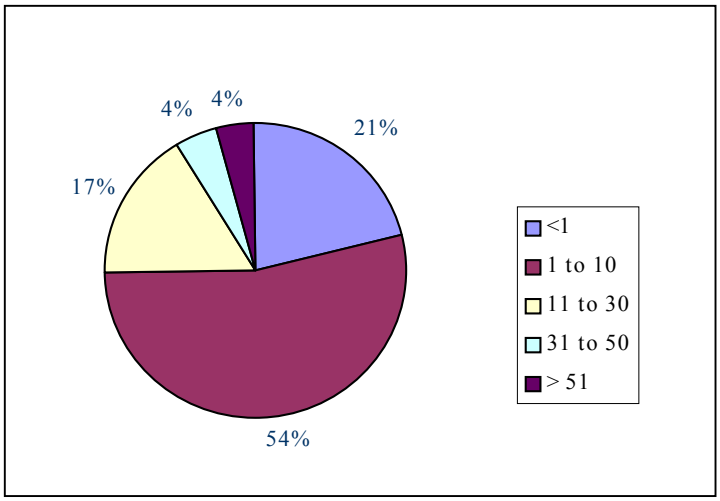
Figures

Figure 1: Average length of conditioned registration of new drug products those had been registered unconditionally at 30 June 2000. (Years)



Data source: Drug Control Division, FDA

Figure 2: Proportion of SMP-ended original products, the generic of which had not been available, by average annual import value, from the year of conditional approval to 1999 (million baht, at current year price)



Note: the originals whose exclusivity right had expired by the end of 1997, of which the generics had not been submitted for approval at the end of 1999.
Data source: Drug Control Division, FDA

Market exclusivity and drug expenditures: the effects of Thailand New Drug Registration Regulations

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Executive summary

In early 1990's, the administrative measures granting short-term exclusive rights to research-based drug companies on the sale of their original new drug products were established and integrated as part of Thailand New Drug Registration Regulations. The regulations comprise 2 provisions, safety-monitoring program and bioequivalence study, resulting in the delay of generic entry. As the appearance of some generic products in the market can decrease the price of their originals, additionally, prices of the generics themselves are lower than those of their innovators are, the delay of generic availability may induce high drug expenditures and increase barriers in the access to drug among patients. This study aims to assess the effects of the original products' exclusivity granted by the regulations on drug expenditures and to estimate the cost-saving among public and private hospitals when generic products entered the market. Eleven generic-approval new drug products containing 4 active chemicals, namely fluconazole, clozapine, ondansetron, and ofloxacin (injection form) are included in the appraisals.

To address the objectives, self-administered questionnaires were distributed by postal mail to 292 public and private hospitals in February 2001. At the end of March 2001, the questionnaires had been completed and returned by 166 settings (56.9%).

Findings from this study indicate that when generic versions of the interested now drugs entered the market, prices of original products remained unchanged while their generics were much cheaper, drug expenditures among sample hospitals decreased significantly, and the accessibility to drugs had been improved.

Unit prices of generic versions of all products were lower than the prototypes'. The gap between prices of the originals and their generics among different products represented by Differential Price Index (DPI) varied from 1.6 to 9.9 in the first year of generic entry in 1999 and increased to 2.1 to 10.9 in 2000. However, during the first two years of generic entry, prices of the innovator products did not change significantly.

Due to lower price of generic products, accompanying with generic substitution in the hospitals, substantial reduction of drug expenditures has been observed. The sample hospitals saved their budget spending on these products for 48.3 and 55.2 million baht in 1999 and 2000, respectively. The total cost-saving of 252.0 million baht during the two consecutive years would be expected if they had replaced all innovator products with the generics.

The accessibility to fluconazole-containing preparations was strongly affected by generic appearance in the market. In 1998, before generic entry, 28 hospitals purchased such products, capsule and injection, at the total volume of 90 thousand DDD. When 6 to 10 times lower-price generic fluconazole capsules available, the number of purchasers increased to 108 and the volume of drug purchased tremendously rose to 693 thousand DDD in 2000. Eight folds increasing in drug consumption does not explain by sudden increase in health needs but significant affordable generic drug price.

Findings from this study not only demonstrate that switching to generic versions of new drug products is an effective measure for cost-containment but also witness the importance of generic availability in the country. To potentiate the magnitude of the positive effects of generic entry on drug cost containment among hospitals and the increased accessibility to drugs, promoting drug price competition and encouraging generic substitution are recommended.

บทคัดย่อ

การวิจัยนี้มีวัตถุประสงค์ที่จะศึกษาผลกระทบที่มีต่อค่าใช้จ่ายด้านยาของโรงพยาบาล ซึ่งเกิดจากการที่หลักเกณฑ์การขึ้นทะเบียนตำรับยาใหม่ของไทยได้ให้สิทธิผูกขาดทางการตลาดแก่ตำรับยาต้นแบบ ในเดือนกุมภาพันธ์ 2544 ผู้วิจัยจัดส่งแบบสอบถามไปยังโรงพยาบาลภาครัฐและเอกชนรวม 292 แห่ง เพื่อเก็บข้อมูลปริมาณและมูลค่าการจัดซื้อยาที่จัดเป็นยาใหม่ซึ่งมียาสามัญ (ยาเลียนแบบ) ในประเทศแล้ว 11 รายการ ซึ่งประกอบด้วยสารออกฤทธิ์ 4 ตัว ได้แก่ fluconazole, clozapine, ondansetron, และ ofloxacin (ชนิดฉีด) โรงพยาบาลที่ตอบแบบสอบถามดังกล่าวมีจำนวน 166 แห่ง (ร้อยละ 56.9)

ผลการวิจัยพบว่า ในช่วงเวลา 2 ปี ที่ยาสามัญออกสู่ท้องตลาด (พ.ศ. 2542 – 2543) ราคาต่อหน่วยของยาสามัญของยาทุกชนิดที่โรงพยาบาลจัดซื้อต่ำกว่าราคาต่อหน่วยของยาต้นแบบของยาชนิดนั้นๆ แต่พบว่า ไม่มีการเปลี่ยนแปลงของราคายาต้นแบบในช่วงระยะเวลาดังกล่าวอย่างชัดเจน เนื่องจากการที่ยาสามัญมีราคาต่ำ และโรงพยาบาลได้นำยาสามัญมาใช้ทดแทนยาต้นแบบ จึงทำให้ค่าใช้จ่ายด้านยาของโรงพยาบาลลดลงถึง 103.5 ล้านบาท การเพิ่มขึ้นอย่างมากของปริมาณการจัดซื้อยาบางชนิด โดยเฉพาะอย่างยิ่ง fluconazole ภายหลังจากมียาสามัญจำหน่าย ในขณะที่ไม่มีความต้องการใช้ยานี้ในประเทศเพิ่มขึ้น แสดงให้เห็นว่า ผู้ป่วยสามารถเข้าถึงยาเหล่านี้ได้มากขึ้น

การที่จะลดค่าใช้จ่ายด้านยาของโรงพยาบาล และเพิ่มการเข้าถึงยาของผู้ป่วยให้มากขึ้น ภายหลังจากการเข้าสู่ตลาดของยาสามัญนั้น จำเป็นต้องส่งเสริมให้มีการแข่งขันด้านราคาระหว่างผลิตภัณฑ์ยาต้นแบบและยาสามัญ รวมทั้งกระตุ้นให้มีการใช้ยาสามัญทดแทนยาต้นแบบให้มากขึ้น

Abstract

The effects on hospital drug expenditures of the market exclusivity granted to innovator products by means of Thailand regulations on new drug registration were assessed. Self-administered questionnaires were distributed by mail to 292 public and private hospitals in February 2001 to collect data on purchase volume and value of 11 generic-approval new drugs containing 4 active chemicals, namely fluconazole, clozapine, ondansetron, and ofloxacin (injection form). The questionnaires were returned by 166 settings (56.9%).

It was found that during the first two years of generic entry, 1999 to 2000, unit prices of generic versions of all products purchased by the hospitals were lower than the prototypes'

but prices of the originals did not change significantly. Due to lower price of generic products and generic substitution in the hospitals, substantial decreasing in drug expenditures of totally 103.5 million baht has been observed. Tremendously increased purchase volume of some drugs, particularly fluconazole, among these healthcare settings when generic entered the market while there was no increasing in health needs, indicates significantly improved accessibility to drug.

To potentiate the magnitude of the positive effects of generic entry on drug cost containment among hospitals and the increased accessibility to drugs, promoting drug price competition and encouraging generic substitution are recommended.

Keywords

Market exclusivity, pharmaceutical product, original product, generic product, intellectual property right protection, pipeline protection, drug expenditures, cost-saving, generic substitution, accessibility, Thailand.

1. Introduction

The New Drug Registration Regulations promulgated in Thailand since 1990 comprise 2 provisions those, more or less, provide short-term exclusive rights to research-based companies on the sale of their original new drug* products. According to the regulations, registration file of the generic, of which the original is under safety monitoring is not accepted by the Thai Food and Drug Administration (FDA), and the imitator has to prove that the generic version is equivalent to its prototype in term of bioavailability *(1,2)*.

Regarding fundamental principle of commodity pricing, increasing competition among suppliers usually decreases prices. The number of different drug products and different generic versions of the same product on the market plays important role, i.e. the presence or absence of generic competition is a key determinant of pricing level *(3)*.

Several studies on the consequences of Trade-related Aspects of Intellectual Property Rights Agreement (TRIPS) revealed the prices of patented drugs would increase because during the period of market exclusivity, research-based companies can charge higher prices for their products, without having to face any competition from low – cost generic producers *(4,5)*. Comparing the average generic prescription price with the average innovator price for the same drug shows price falling as the number of generic manufactures rises *(6)*. Brand-name manufacturers are more likely to give purchasers a discount if those purchasers have the option of switching to a generic competitor.

In some markets, however, the monopoly was driven by promotion of trademarks and other marketing strategies of multinational companies, even in the absence of product patents. Price competition in these markets seemed to be confined only to credible substitute products of similar quality *(7)*. Recent study in Thailand on the implications of the TRIPS Agreement supported such finding *(8)*. Since there were no patented drugs in the Thai market, the original products having a period of monopolistic position and their generics were assessed

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* According to the regulations, the term "New drug" covers product of new chemical entity, new indication, new combination, and/or new delivery system, which has never been approved in the country before the date of registration file submission.

for the price changes. It was found that there was no substantial price reduction after the competitors appeared in the market, which, in the authors' perspectives, might be due to high monopoly power of original producers or low degree of substitution effects of generics according to the segmented pharmaceutical market. The study also revealed that the gaps of equivalent prices between original and generic products were varied and unpredictable.

Study on anti-HIV prices in Thailand demonstrated the dramatic reduction of drug price resulting from the competition among manufacturers *(9)*. It was found that after three companies introduced generic versions of fluconazole in 1998, the original company dropped its price for a 200 mg capsule from $7 to $3.6. One of the generic versions is available for $0.30 per 200mg capsule *(10)*. It has been interpreted that the high drug price is partly linked to the monopoly derived from the exclusive rights held by the original drug manufacturers, either from the patent or during the safety monitoring program *(11)*.

Our previous study demonstrates that from the year of firstly promulgation of the New Drug Registration Regulations in 1991 to 1999, there were 742 original products approved *(12)*. At 30 June 2000, there had been generic versions of 11 new drug products approved by means of the amended regulations. This study aims to assess the effects of the market exclusive right of the original products granted by the regulations on the change of drug prices and expenditures among public and private hospitals.

2. Scope of study

Eleven new drug products, the generic versions of which have been approved by the FDA, including fluconazole capsules 50mg, 100mg, 150mg, and 200mg; fluconazole injection 2mg/ml, ondansetron tablets 4mg and 8mg; ondansetron injection 2mg/ml; clozapine tablets 25mg and 100mg; and ofloxacin injection 200mg/100ml.

3. Methods

3.1 Data collection

(1) Using the FDA drug database and drug distributors' report at the FDA to quantify the annual volume and value of the innovator products and their generics imported or locally manufactured from the year of registration to 2000.

(2) Self-administered questionnaires were sent to the sample hospitals to assess the followings :
- whether they purchased the generic product as a substitute for its original (either generic or original product or both were purchased) when the generic product is available in the market.
- the volume and value of new drug, original and/or generic product, purchased from the year the drug available in the hospital drug list to 2000.

3.2 Calculation

(1) Retail price of each product was estimated by dividing the annual value by volume of drug purchased by each hospital.

(2) Drug cost of each product purchased by sample hospitals in 1999 and 2000 was calculated regarding different proportions of generic substitution, two of which are hypothetical and the rest is actual, as the following:

- Actual drug cost

$$DC_{(actual)} = (V_o \times P_o) + (V_g \times P_g)$$

Where $DC_{(actual)}$ is the actual drug cost, V_o is the volume of original product purchased, P_o is the median retail price of original product, V_g is the volume of generic product purchased, P_g is the median retail price of generic product

- Drug cost if there was no generic substitution introduced by the hospitals

$$DC_{(0\% \text{ generic})} = V_t \times P_o$$

Where $DC_{(0\% generic)}$ is the drug cost if there was no generic substitution, V_t is the total volume of product purchased (either original or generic), P_o is the median retail price of original product

- Drug cost if the hospitals purchased generic product instead of its original

$$DC_{(100\% \text{ generic})} = V_t \times P_g$$

Where $DC_{(100\% generic)}$ is the drug cost if the original product was completely substituted by its generic, V_t is the total volume of product purchased (either original or generic), P_g is the median retail price of generic product

(3) Cost savings for each product in 1999 and 2000 were calculated as the actual cost saving and the cost saving if the original product was absolutely substituted by its generic by the following formula:

- Actual cost saving

$$CS_{(actual)} = DC_{(0\% \text{ generic})} - DC_{(actual)}$$

Where $CS_{(actual)}$ is the actual cost saving, $DC_{(0\% generic)}$ is the drug cost if there was no generic substitution, $DC_{(actual)}$ is the actual drug cost

- Cost saving if the original product was completely substituted by its generic

$$CS_{(100\% \text{ generic})} = DC_{(0\% \text{ generic})} - DC_{(100\% \text{ generic})}$$

Where $CS_{(100\% generic)}$ is the cost saving if the original product was completely substituted by its generic, $DC_{(0\% generic)}$ is the drug cost if there was no generic substitution, $DC_{(100\% generic)}$ is the drug cost if the original product was completely substituted by its generic

4. Sample hospitals

To address objectives 3 and 4, 292 public and private hospitals were selected focusing on large hospitals who might purchase those 11 products to be the study samples by sampling methods as shown in Table 1.

<<Table 1>>

5. Results

5.1 Accepted indications of the pharmaceuticals appraised in this study

Each of the eleven interested products contains active ingredient of different therapeutic categories. All of these products, but ondansetron tablet and ofloxacin injection are essential drugs according to 1999 National List of Essential Drugs (NLED) *(13)*.

Fluconazole is an antifungal indicated in the treatment of invasive candidiasis, including esophageal, oropharyngeal, and vulvovaginal candidiasis. It is also approved for the treatment of systemic candidal infections and cryptococcal meningitis, which are opportunistic infections among HIV/AIDS patients *(14, 15)*.

Clozapine is an atypical antipsychotic indicated only in the management of severely ill schizophrenic patients who have failed to respond to standard neuroleptics or who cannot tolerate the adverse effects produced by those agents *(16)*.

Ondansetron is an anti-emetic indicated for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy; prevention of postoperative nausea and vomiting; and for the prevention of nausea and vomiting associated with radiotherapy *(17)*. With respects to the NLED, ondansetron injection is restricted to be used in patients with acute symptoms on the first day of chemotherapeutic agent administration *(13)*

Ofloxacin is a broad-spectrum anti-infective of fluoroquinolone group. The drug is active against a wide range of aerobic gram positive and gram negative bacteria. It is is indicated in the treatment of bacterial exacerbation of chronic bronchitis, pneumonia, and infections of skin and soft tissues, abdominal cavity, and genito-urinary tract, caused by susceptible organisms *(18)*.

5.2 Volume and value of generic-available new drug products distributed in the country before and after generic approval

Volumes and values of original and generic version of the products containing fluconazole, ondansetron, clozapine, and ofloxacin; imported or manufactured from the year of approval to 2000 are illustrated in Figure 1.

<<Figure 1>>

Fluconazole-containing preparations were imported at the highest total quantity and value, starting from 613 DDD [1 DDD = 200mg *(19)*] or 15.7 million baht, at current year price, in

1991. Peak of importation of the innovator product was reached during 1995 to 1997. The highest import volume observed in 1997 was 691 thousand DDD or 141.7 million baht of its value. Generic fluconazole entered the market in 1998 at a low volume of 66 thousand DDD. Manufacture volume of the generics dramatically increased to 2.44 million DDD in 1999 and dropped to 1.24 million DDD in 2000. Values of generic versions locally manufactured in 1998, 1999, and 2000 were 0.8, 3.5, and 9.64 million baht, respectively.

Oral and injectable ondansetron were approved and firstly distributed in Thailand in 1993. Importation of the drug was rapidly increased to 73 thousand DDD [1 DDD = 16mg *(19)*] or 30 million baht, in 1997. In 1999, when it's generics appeared in the market, the innovator products were not imported into the country. The originals were imported in 2000 at 30 thousand DDD or 19 million baht. Volume of locally produced ondansetron preparations in 1999 and 2000 were 54 and 44 thousand DDD, respectively.

Between 1996 and 1997, annual import volume of original clozapine tablet was 56 thousand DDD [1 DDD = 300mg *(19)*], the value of which was 24 million baht each year. The volume and value of imported drug declined significantly in 1998. The corresponding figures rose to prior levels in the next two years. Generic clozapine products got approval in 1999 and entered the market in the year after. Volume of the generics manufactured in 2000 was 192 thousand DDD, or 0.2 million baht in term of value.

Comparing with the other three drugs, ofloxacin was imported at the smallest volume and value. Original ofloxacin injection was firstly imported in 1996 at 2 thousand DDD [1 DDD = 400mg *(19)*] or 1.5 million baht. The import volume peaked in 1997, which was 4.3 thousand DDD or 4.8 million baht. In 1999, import volume of ofloxacin injection was 1.2 thousand DDD, the value of which was 1.1 million baht. Though generic version of this product was approved in 1998, at the end of 2000 it had not been imported into the country.

During market exclusivity period of eleven products, value of the innovator products imported was 490 million baht at current year price (Table 2). Spending on fluconazole preparation, both oral and parenteral [notably fluconazole capsule 100- and 200mg] accounted for 75% of the total.

<<Table 2>>

5.3 New drugs purchasing among public and private hospitals

Self-administered questionnaires were distributed by mail to 292 sample hospitals in February 2001. By 26 March 2001, the questionnaires had been completed and returned by 166 settings (56.9%). Most of the respondents are MoPH provincial hospitals (31.9%). The respondents in private sector account for 20.1% of the total.

Among 10 new drug products* approved and reported to be manufactured in the country by the end of 2000, there were generic versions of 8 products purchased by sample hospitals, including fluconazole capsules 50mg, 100mg, and 200mg; fluconazole injection (50mg/vial), clozapine tablets 25mg and 100mg; ondansetron tablet 8mg; and ondansetron injection (8mg/4ml). The generics that did not enter respondent hospitals include fluconazole capsule 150mg and ondansetron tablet 4mg.

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* Excluding ofloxacin injection that the generic product had not been imported into the country.

5.3.1 Fluconazole purchasing among public and private hospitals, 1992 to 2000

Original fluconazole had been purchased by sample hospitals since 1992. Volume and value of the drug purchased between 1992 and 2000 are shown in Figure 2. In 1992, which was the year of approval and first distribution of original fluconazole 50 mg capsules, only one private hospital purchased the drug at a small amount of 79 DDD. Other original fluconazole preparations, i.e. 150 mg, 100 mg, and 200 mg capsules, and IV infusion, entered the market in 1994 and 1995. Peak of original fluconazole purchasing was reached in 1997, which was 121 thousand DDD or 28 million baht in term of value. Fluconazole 200 mg capsules accounted for 73% of the total volume of fluconazole products purchased in that year.

When first generic version of fluconazole approved in Thailand in 1998, purchase volume of the original slightly dropped to 90 thousand DDD, or 22 million baht in term of value, however, the generics did not yet appear in the sample hospitals. In 1999, total purchase volume of fluconazole-containing products among these hospitals increased significantly to 401 thousand DDD, 88% of which were those of generics. Market share of the generics rose to 94% of 693 thousand DDD purchased in 2000. The total value of fluconazole products sold to sample hospitals in the two consecutive years, 1999 and 2000, were 25 and 24 million baht, respectively. Among different fluconazole – containing products, fluconazole 200mg capsule was purchased at the highest volume, which accounted for 91% and 95% of the total in 1999 and 2000, respectively.

<<Figure 2>>

Unit price per capsule of fluconazole 200 mg purchased by responding hospitals, at current year price, from 1995 to 2000 is shown in Figure 3. Median prices of original product fluctuated slightly throughout marketing period, starting from 218 baht per capsule during the first three years. The drug was sold to most hospitals at 242 baht per capsule in 1998 to 1999, and 236 baht per capsule in 2000.

Four generic fluconazole 200 mg capsules were sold to hospitals at different prices. Unit prices of each product purchased by different settings varied widely. Median price per capsule of generic 1, the most favorite generic of fluconazole 200mg capsules among sample hospitals, was 42 baht in the first year of distribution, while the other three were cheaper. In 2000, all generic manufacturers cut price of their products to the median price between 22 and 32 baht per capsule.

<<Figure 3>>

In 1998, the year before monopolistic status of original fluconazole capsule ended, the innovator product was used in 28 settings, most of which were the MoPH regional hospitals (Table 3). After generic product entry, in 2000, the number of fluconazole capsule purchasers increased to 108. Among these hospitals, 69% used generic, 9% used original, and the rest used both original and generic.

<<Table 3>>

5.3.2 Clozapine purchasing among public and private hospitals, 1996 to 2000

Two strengths of original clozapine tablets, 25 and 100 mg, were approved in 1995 and firstly appeared in sample hospitals in 1996 at purchase volume of 7.3 thousand DDD or 1.2 million baht at current year price (Figure 4). The volume of drug purchased continually increased to 9.5, 16.2 and 27.7 thousand DDD in 1997, 1998 and 1999, which was 1.6, 3.2 and 5.4 million baht in term of value, respectively. When generic versions of clozapine entered the hospitals in 2000, total purchase volume of clozapine rose significantly to 66.2 thousand DDD, 64.5% of which shared by the generic, while the value of drug purchased slightly increased to 5.5 million baht, 82.5% of which was spent on the innovator product.

<<Figure 4>>

Median prices per 25- and 100-mg tablet, at current year price, of clozapine from 1996 to 2000 are shown in Figure 5. During the first two years of distribution, median prices of original 25- and 100-mg tablets were 14.00 and 53.28 baht per tablet (n = 6 and 7), respectively. The price per 25-mg tablet increased to 16.80 baht (n = 8) in 1998 and slightly dropped to 16.69 baht (n = 4) in 2000, while that of 100-mg tablet was 64.61 baht (n = 13) in 1998 and 65.91 baht (n = 15) in 1999. In 2000, median prices of generic clozapine 25 and 100 mg were 2.40 and 7.40 baht (n = 5 and 6), respectively.

<<Figure 5>>

Table 4 shows the number of clozapine purchasers, before and after generic version available. Before generic products were approved in the country, in 1998, there were 13 hospitals that purchased this drug, most (46%) of which were public psychiatric hospitals. When generic products available, in 2000, number of purchasers of this drug rose to 19, half of which bought original product alone and one-fourth used both original and generic.

<<Table 4>>

5.3.3 Ondansetron purchasing among public and private hospitals, 1993 to 2000

The original Ondansetron-containing products, including 4- and 8-mg tablets and injection of 4-, and 8-mg vial, have been registered in Thailand since 1993 and appeared in responding settings since 1994. Generic versions of these preparations were approved in the country in 1999.

Figure 6 shows volume and value of ondansetron products of all dosage forms and strengths purchased by public and private hospitals between 1994 and 2000. Purchase volume of the drug increased continually from 60 DDD or 50.3 thousand baht in the first year of appearance in the hospitals to 9.9 thousand DDD or 9.4 million baht, in 1997. In 1998, the drug purchased dropped to 5.4 thousand DDD in term of volume or 6.0 million baht in term of value. In 1999 and 2000, which were the first and second year of generics launch, the innovator products were purchased at dramatically increased volume of 11.6 and 13.1 thousand DDD, which were 13.3 and 14.2 million baht in term of value, respectively. Market share in term of volume of generics was 3.5% in 1999 and rose to 25.3% in 2000.

<<Figure 6>>

Unit prices of ondansetron tablet between 1994 and 2000 are shown in Figure 7. During the first three years, median prices per 4- and 8-mg tablet were 187.00 and 374.50 baht (n = 1 and 2), respectively. In 1998, the price inclined to 217.00 and 434.42 baht per 4- and 8-mg tablet (n = 5 and 13), respectively, which were kept steady throughout the next two years. Median price per tablet of generic 8-mg ondansetron tablet, which was the only strength purchased by responding hospitals, was 150.00 baht (n = 4) in 1999 and 185.83 baht (n = 9) in 2000.

<<Figure 7>>

Between 1994 and 2000, ondansetron injections were purchased by hospitals at the unit prices shown in Figure 8. During 1994 to 1996, median price per 8-mg ampoule of original product was 642.00 baht (n = 1, 3 and 6 in 1994, 1995 and 1996, respectively) and gradually increased to 755.16 baht (n = 7) in 1998. During the first two years of generic entry in 1999 and 2000, unit price per ampoule of the original slightly dropped to 744.70 and finally 729.80 baht (n = 14 and 16), while the median prices of the first generic product were 363.8 and 237.20 baht (n = 3 and 8), respectively. The second generic product of 8-mg size entered the market in 2000 at the lower median price of 179.48 baht per ampoule (n = 3).

Unit price of 4-mg ampoule of original ondansetron injection was 322.00 baht (n = 1 and 2) during 1995 to 1996, and slightly increased to 324.26 baht (n = 5) in 1997. In 1998 and 1999, the price rose to 372.00 baht per ampoule (n = 6 and 10) and dropped to 360.00 baht (n = 10) in 2000.

<<Figure 8>>

Number of hospitals that purchased ondansetron tablet, either 4- or 8-mg, before and after generic products were available are shown in Table 5. There were 15 settings, most of which were private hospitals, purchased the original in 1998. After generic products were approved and entered the market, the number of purchasers increased to 23. Among those who purchased ondansetron tablets in 2000, 15 settings (65.2%) purchased only innovator products, 5 (21.7%) purchased only generic versions, and the rest purchased both.

<<Table 5>>

5.3.4 Ofloxacin purchasing among public and private hospitals, 1997 to 2000

Original ofloxacin injection was conditionally registered in Thailand in 1995. Generic version of this drug was approved by the Thai FDA in 1999, however at the end of 2000 it had not been launched in the market. From the year of registration to 2000, injectable ofloxacin preparation has been used in a small number of hospitals, started from 1 regional hospital in 1997 to totally 4 settings, including 1 regional, 1 military, and 2 private hospitals, in 2000 (Table 6).

<<Table 6>>

Purchase volume and value of ofloxacin injection among public and private hospitals, from 1997 to 2000 are shown in Figure 9. In 1997, responding hospital purchased 3 DDD of the drug or 4,380 baht in term of value. Purchase volume and value slightly increased to 7.5 DDD or 12,000 baht in 1998. The corresponding figures significantly rose to 355 DDD in term of volume and 498 thousand baht in term of value in 1999; and 788 DDD or 899 thousand baht in 2000.

<<Figure 9>>

When ofloxacin injection firstly purchased in 1997, its price was 730 baht per vial (Figure 10). In 1998, the drug was sold to the hospital at 800 baht per vial, since then the price dropped to 688 and 535 baht per vial (n = 3 and 4) in 1999 and 2000, respectively.

<<Figure 10>>

5.3.5 Differential Price Index of generic-available new drug products, 1999 and 2000

When generic versions of 8 new drug products were purchased by sample hospitals in 1999 and 2000, various degrees of difference between unit prices of the original and its generic were demonstrated by Differential Price Index (DPI) of each product (Table 7). The DPI, varying from 1.6 to 10.9, reveals the higher price of certain original product than its generic could be observed in all preparations.

Comparing to those of other innovator products, DPI of original fluconazole capsule 200mg, was the highest. During the first two years of generic entry, price of the cheapest generic version of such product was approximately 10 to 11 times lower than the original's. Increased DPI of original products of four fluconazole-containing preparations and ondansetron injection in 2000 indicates more discrepancy between prices of innovator and generic version of these drugs than in the year before, while that of ondansetron tablet was inverted.

<<Table 7>>

5.4 The effects of generic entry on potential cost saving among the hospitals

Findings on new drug products purchasing among public and private hospitals in section 5.2 reveal that unit prices of generic version of the 10 products, excluding ofloxacin injection[*], purchased by sample healthcare settings were lower than those of their originals. Magnitude of difference between price of the original and generic is demonstrated by differential price index, which range from 1.56 for fluconazole injection in 1999 to 10.89 for fluconazole capsule 200 mg in 2000. If the hospitals replaced the innovator products by the generics in the treatment of their patients, decreasing in drug expenditures would be expected.

Estimated cost-savings among sample settings due to generic substitution in 1999 and 2000 are shown in Table 8. The hospitals reduced their expenditures for these new drugs from 120 million baht to 48 million baht or 60% reduction in 1999. The saving increased to 73% in 2000 when larger proportions of generic substitution were introduced. Comparing the actual cost for those 10 products to drug cost if there was no generic substitution at all, total actual cost-saving during 1999 to 2000 was 217 million baht. The hypothetical saving on these products would be 252 million baht if the hospitals had totally substituted all products with their generic versions.
Among the ten generic-available products, fluconazole capsule of all strengths were purchased by sample hospitals at the highest value and the generics shared the highest proportions in term of volume of drug purchased, i.e. 82% and 95% in 1999 and 2000,

[*] Generic version of ofloxacin injection had not been launched in the market.

respectively. During two-year period, the hospitals saved totally 207 million baht or 78% reduction of expenditure for the innovator product by using generic versions and they might save some 18 million baht more if the generics absolutely replaced the originals.

<<Table 8>>

6. Discussion

Dramatically rising in national health expenditures is partly influenced by the use of expensive original products among healthcare settings and the national disease control programs. Findings from this study not only demonstrate that switching to generic versions of new drug products is an effective measure for cost-containment but also witness the importance of generic availability in the country.

Our previous study reveals that between 1991 and 1999, almost 5.8 billion baht was spent on 184 SMP-ended innovator products, of which the generic is not available *(12)*. It is implied that though the New Drug Registration Regulations, which granted exclusive right to the research-based companies, had not been promulgated, Thailand could not save even part of this large amount of budget by using locally produced generic versions. In other words, limited capability in generic manufacture of domestic pharmaceutical industry rather than market exclusivity of the innovator products generated by means of the Regulations was the major determinant of the country's enormous drug expenditures.

Import values of original and manufacture values of generic fluconazole-, clozapine-, and ondansetron-containing preparations illustrated in Figure 1 are not comparable as they are estimated on different basis regarding FDA rules on the annual report submitted by drug suppliers and manufacturers. It should be noted that the values of original products are calculated by using CIF prices, while the corresponding figures of locally produced generic products are calculated by using ex-factory wholesale prices. To appraise the effects of the regulations on drug expenditures, prices of original and generic products purchased by sample hospitals were used in the estimations.

Low price of the generics comparing to their originals and wide range of prices of the same product purchased by different hospitals observed are consistent with the findings of Lertiendumrong J et al *(20)*. Several factors affecting variation of prices of a certain product had been identified, namely purchase volume, payment conditions, supplier's promotion campaign, types of container, and procurement procedures. Lower price of drug could be found in the purchasing of large volume, rapid remuneration to the supplier, and collective bargaining procurement.

Considerable effects of generic entry on pricing of the original products are not definitely demonstrated in this study, i.e. prices of 3 drugs (fluconazole, clozapine, and ondansetron) did not decrease significantly when generics entered. Unit prices of 11 innovator products from the year of approval to 1997 were almost constant. Since all of these products were imported from foreign countries, slightly increasing in their prices found in 1998 could be explained by the devaluation of Thai currency resulted from 1997 economic crisis. However, limitation of this study is that our observations on the consequences of generic entry have been carried out only for two years, it might therefore be too early to anticipate its effects on the price change of the originals.

Cost containment generated by purchasing generic versions of new drug products among the hospitals in 1999 and 2000 indicate increasing trends (Table 8). In addition, our findings demonstrate that reducing in expenditures for these products does not depend entirely on shortening of the monopolistic intervals of the innovator products accompanying with the availability of their generics in the market. Three other factors are shown to involve in and determine the magnitude of potential cost-savings among hospitals, including the difference in drug prices between originals and generics, volume of drug use - that reflexes health needs, and proportion of generic substitution.

Among generic-available new drug products, the entry of generic fluconazole capsules contributed to the largest reduction of drug expenditure, which was due to the highest DPI of the originals, largest purchase volume of generic products, and utmost rate of switching to generics in sample hospitals. For other products, the proportions of generic purchased were found very low in the first year of generic entry, but significantly increased in the second year, which partly resulting in substantial reduction of drug expenditures. To increase cost-saving on these products, two strategies, including promoting price competition among original and generics and enhancing more generic substitution in the hospitals, are recommended.

Positive effects of generic availability on the accessibility to drug are also demonstrated in this study. Slow increasing in the volume of original fluconazole products imported during 1991 to 1997 (Figure 1) did not match the huge health needs in the country due to HIV epidemic and OI incidences, affordability and accessibility to this drug among the people is a problem due to high price of original product. Volume of drug purchased by sample hospitals tremendously increased in 1999 and 2000, when much lower-price generics entered the market. Four to seven fold increasing in drug consumption during 1999 to 2000 does not explain by sudden increase in health needs but significant affordable generic drug price. Increasing in the accessibility to drug after generic versions available is also demonstrated by larger number of the settings that purchased fluconazole capsules in 2000 than those were in 1998 (Table 3).

All six responding hospitals of Department of Mental Health purchased clozapine tablet both before and after generic entry. Meanwhile, the drug was distributed in a very small number of hospitals of other types. Nevertheless the tiny value of cost-saving contributed by generic substitution in sample hospitals, significant improving in the accessibility to clozapine, i.e.2.4 times, could be observed (Figure 4).

Generic ondansetron products, tablets and injection, entered the market in 1999. Generic substitution of this drug in sample settings was the lowest among generic-available SMP-ended products, however remarkably rising in the proportion of generic shares during the two years demonstrates a favorable trend.

Ofloxacin injection is the only product of which the generic has not been distributed in the market. Though the value of drug purchased by sample hospitals increased significantly during 1998 to 2000 (Figure 9), the national import volume and value declined continually (Figure 1). Very small number of purchasers (Table 6), no generic product launched, non-essential drug status, and downward trend of the importation and unit price of ofloxacin injection (figure 10) indicate that there is limited health needs for this drug and it may currently reach the last phase of product lifecycle.

One of the interesting points found in this study is that even though generic products had been launched, a number of hospitals continued using the originals, whilst some of them used both original and generic products. A study on the factors influencing drug purchasing among district and provincial hospitals in Thailand reveals drug quality and prices were the most importance *(21)*. The hospitals more highly trusted in the quality of imported original products than in those of locally produced generics. According to the regulations on generic drug registration, the imitators have to submit the data indicating bioequivalence between their products and the prototypes to the FDA, additionally, bioequivalence testing reports of some locally manufactured generics, including fluconazole and ondansetron, have been published in medical or pharmaceutical sciences journals *(22,23,24)*. However, it seems that these evidences on generic quality could not successfully convince the health professionals to substitute all innovator products with indigenous preparations. Brand loyalty inherited from medical schools and drug promotion strategies are also claimed to be significant determinants of physicians' prescribing behavior *(25)*.

Efficient use of pharmaceuticals in healthcare facilities can be encouraged by introducing relevant interventions, including educational, managerial, and regulatory approach *(26)*. Providing sufficient and updated information to physicians on hospital's drug expenditures, unit prices of the original and its generic products, and cost-effectiveness of certain innovator product and the comparators with similar therapeutic indications play important roles in promoting rational drug use and diminishing inappropriate spending on pharmaceutical products. Policy-makers, public health administrators, academics, and research institutes should put all efforts, in political, financial, and technical aspects, in order to support those cost-containment activities and monitor adverse effects that possibly arise.

7. Conclusion

The market exclusivity of original products generated by the provisions of New Drug Registration Regulations leaded to 4 to 7 year delay of generic approval of the studied products. During the first two years of generic entry, there was no reduction in original price detected, while all generics were purchased at lower prices than their prototypes. The favorable effects of generic entry on the reduction of hospitals' drug expenditures and improved accessibility to some drugs have been demonstrated. To potentiate the magnitude of these implications, strategies on promoting drug price competition and generic substitution should be implemented.

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Tables:

Table 1: Sampling method and sample size of the questionnaire survey, by type of hospital

Hospital type	Sampling method	Sample size
Ministry of Public Health (MoPH) hospital • District hospital • Provincial hospital • Regional hospital • Department of Medical Services • Department of Communicable Diseases Control • Department of Mental Health	All MoPH hospitals were selected, except for district hospitals that only those with more than 90 beds were included in the survey.	183
Non-MoPH hospital • Teaching hospital • Bangkok Metropolitan Administration (BMA) hospital • Hospitals under Ministry of Defense	All teaching hospitals and 4 BMA tertiary hospitals, namely Vajira, Taksin, Klang, and Charoenkrung Pracharak were selected. For the hospitals of Ministry of Defense, those purchased any of the eleven original products, regarding the suppliers' report to the FDA, were included in the survey.	30
Private hospital	All private hospitals those purchased any of the eleven products were included in the sample list. In addition, 25 hospitals among the rest with more than 100 beds were randomly selected.	79
Total		292

Table 2: Import volume and value of 11 original products, from the year of approval to the year of market exclusivity ended.

Product	Market exclusivity period	Volume (x 1,000 DDD)	Value (million baht)
Fluconazole capsules 50- and 150mg	7 yrs. [1991 to 1997]	649	135.3
Fluconazole injection	7 yrs. [1992 to 1998]	18	8.1
Ondansetron tablets 4- and 8mg	6 yrs. [1993 to 1998]	155	34.6
Ondansetron injection	6 yrs. [1993 to 1998]	120	54.2
Fluconazole capsules 100- and 200mg	5 yrs. [1993 to 1997]	1,382	223.7
Clozapine tablets 25- and 100mg	4 yrs. [1995 to 1998]	135	23.2
Ofloxacin injection	6 yrs. [1995 to 2000]*	10	10.4
Total			489.5

Note: * Market exclusivity of original ofloxacin injection is not ended, since its generic has never appeared in the market.

Data source: Drug Control Division, FDA

Table 3: Number of hospitals that purchased fluconazole capsules, of any strength, before and after generic versions available, 1998 and 2000.

Hospital type	Number of purchasers before generic available, 1998	Number of purchasers after generic available, 2000			
		Original alone	Generic alone	Both original and generic	Total
District hospital	1	0	7	0	7
Provincial hospital	7	5	28	3	36
Regional hospital	9	1	13	2	16
DMS hospital	1	0	3	3	6
Teaching hospital	2	0	2	1	3
Military hospital	2	2	3	0	5
BMA hospital	0	0	2	0	2
Private hospital	6	2	17	14	33
Total	28	10	75	23	108

Note: Sample hospitals of the Departments of Communicable Disease Control and Mental Health did not purchase any of the fluconazole capsule products in 1998 and 2000

Table 4: Number of hospitals that purchased clozapine 25- and/or 100-mg tablets, before and after generic versions available, 1998 and 2000.

Hospital type	Number of purchasers before generic available, 1998	Number of purchasers after generic available, 2000			
		Original alone	Generic alone	Both original and generic	Total
Regional hospital	1	0	3	0	3
DMH hospital	6	0	1	5	6
Teaching hospital	2	2	0	0	2
Military hospital	1	2	0	0	2
BMA hospital	1	1	0	0	1
Private hospital	2	5	0	0	5
Total	13	10	4	5	19

Note: Sample district and provincial hospitals and hospitals of the Departments of Medical Services and Communicable Disease Control did not purchase any of the clozapine-containing product in 1998 and 2000.

Table 5: Number of hospitals that purchased ondansetron 4- and/or 8-mg tablets, before and after generic versions available, 1998 and 2000.

Hospital type	Number of purchasers before generic available, 1998	Number of purchasers after generic available, 2000			
		Original alone	Generic alone	Both original and generic	Total
Provincial hospital	1	1	0	1	2
Regional hospital	2	3	1	0	4
DMS hospital	3	1	2	1	4
Teaching hospital	2	2	0	0	2
Military hospital	0	2	0	0	2
Private hospital	7	6	2	1	9
Total	15	15	5	3	23

Note: Sample district hospitals, hospitals of the Departments of Communicable Disease Control and Mental Health, and BMA hospitals did not purchase ondansetron injection product in 1998 and 2000.

Table 6: Number of hospitals that purchased original ofloxacin injection, by hospital type, 1997 to 2000

Hospital type	Number of purchasers in 1997	Number of purchasers in 1998	Number of purchasers in 1999	Number of purchasers in 2000
Regional hospital	1	0	0	1
Military hospital	0	1	2	1
Private hospital	0	0	1	2
Total	1	1	3	4

Note: Sample district and provincial hospitals, hospitals of the Departments of Medical Services, Communicable Disease Control and Mental Health, teaching and BMA hospitals did not purchase ofloxacin injection product during 1997 to 2000.

Table 7: Differential Price Index of new drug products, 1999 and 2000

Drug	1999		2000	
	Median unit price (Baht)	Differential Price Index	Median unit price (Baht)	Differential Price Index
Fluconazole capsule 50mg				
• Generic 1	19.89	1.5	18.26	1.4
• Generic 2	13.53	1.0	13.38	1.0
• Original	78.65	5.8	78.65	5.9
Fluconazole capsule 100mg				
• Generic 1	35.00	1.1	31.60	1.3
• Generic 2	32.10	1.0	23.54	1.0
• Original	135.17	4.2	153.75	6.5
Fluconazole capsule 200mg				
• Generic 4	24.50	1.0	25.00	1.2
• Generic 3	24.61	1.0	21.66	1.0
• Generic 2	31.73	1.3	28.03	1.3
• Generic 1	41.76	1.7	30.00	1.4
• Original	242.44	9.9	235.83	10.9
Fluconazole injection (50 ml/vial)				
• Generic 2	319.70	1.0	239.46	1.0
• Original	498.88	1.6	482.00	2.0
Clozapine tablet 25mg				
• Generic	na	na	2.40	1.0
• Original			16.69	7.0
Clozapine tablet 100mg				
• Generic	na	na	7.40	1.0
• Original			65.49	8.9
Ondansetron tablet 8mg				
• Generic	150.00	1.0	185.83	1.0
• Original	434.42	2.9	434.42	2.3
Ondansetron injection 8mg/4ml				
• Generic 1	363.80	1.0	237.20	1.3
• Generic 2	na	na	179.48	1.0
• Original	744.70	2.1	729.80	4.1

Table 8: Estimated cost-saving due to generic substitution among public and private hospitals, 1999 and 2000 (million baht, at current year price)

Products	1999					2000				
	Drug cost if no generic substitution [1]	% generic substitution	Actual drug cost [2]	Actual cost-saving [3]	Cost-saving if 100% generic substitution [4]	Drug cost if no generic substitution [1]	% generic substitution	Actual drug cost [2]	Actual cost-saving [3]	Cost-saving if 100% generic substitution [4]
Fluconazole capsule	99.63	82.3	28.47	71.16	81.35	165.93	94.5	30.34	135.60	143.62
Fluconazole injection	0.48	26.3	0.43	0.04	0.16	0.47	36.9	0.39	0.09	0.23
Clozapine tablet	5.50	0	5.50	0	na	12.96	59.2	5.58	7.38	11.43
Ondansetron tablet	5.76	2.2	5.66	0.10	2.93	8.48	31.0	7.05	1.43	3.99
Ondansetron injection	7.98	4.3	7.79	0.19	3.51	11.58	16.5	10.97	0.62	4.77
Ofloxacin Injection	0.49	0	0.49	0	na	0.84	0	0.84	0	na
Total	119.83	-	48.34	71.50	87.94	200.27	-	55.17	145.11	164.05

Note:

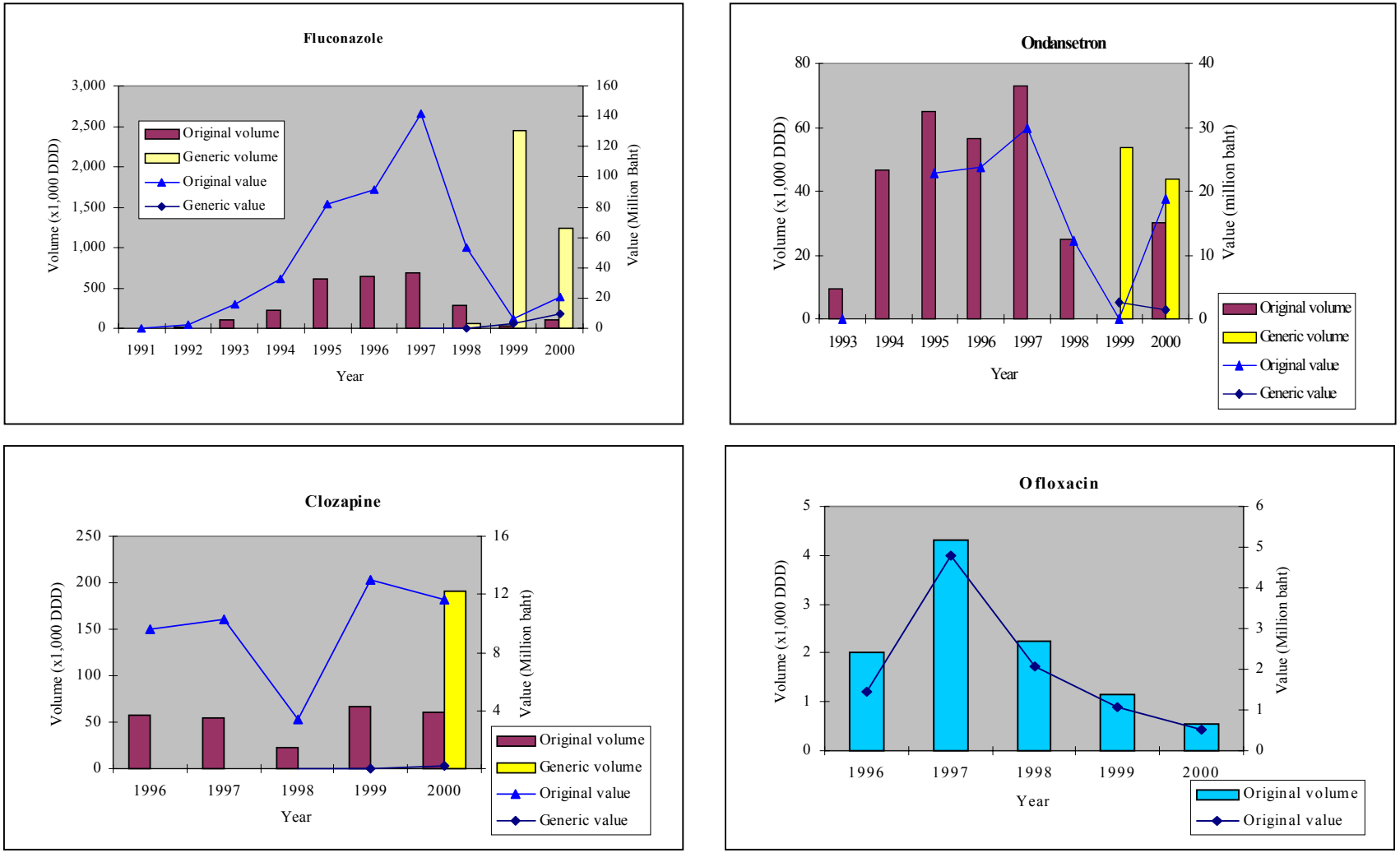
[1] Total purchase volume x median unit price of original product

[2] (purchase volume of original product x median price of original product) + (purchase volume of generic product x median price of generic product)

[3] [1] - [2]

[4] [1] - (total purchase volume x median price of generic product)

Figure 1: Volume and value of original and generic fluconazole, ondansetron, clozapine, and ofloxacin preparations imported/manufactured, from the year of approval to 2000.



Data source: Drug Control Division, FDA

Figure 2: Purchase volume and value of fluconazole – containing products among public and private hospitals, 1992 to 2000

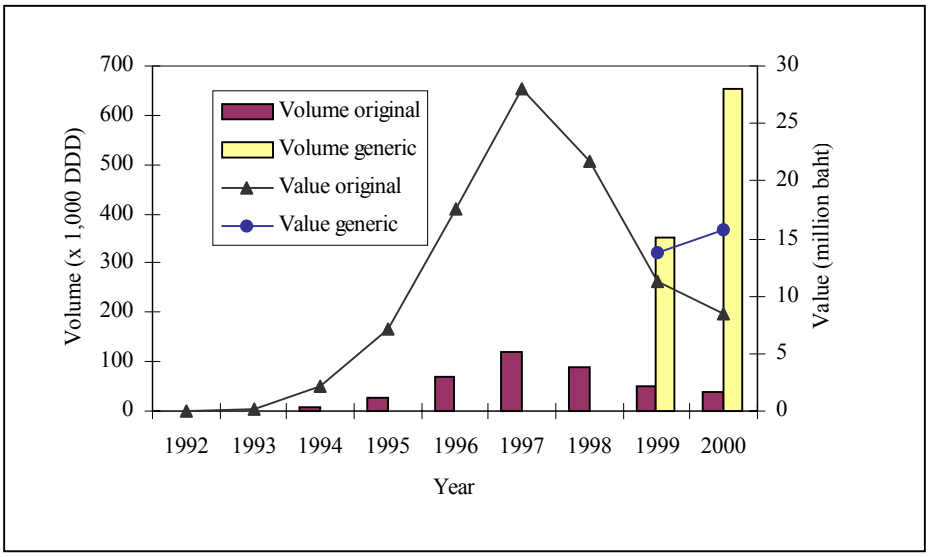


Figure 3: Median price per 200 mg capsule of fluconazole purchased by public and private hospitals, 1995 to 2000 (baht, at current year price)

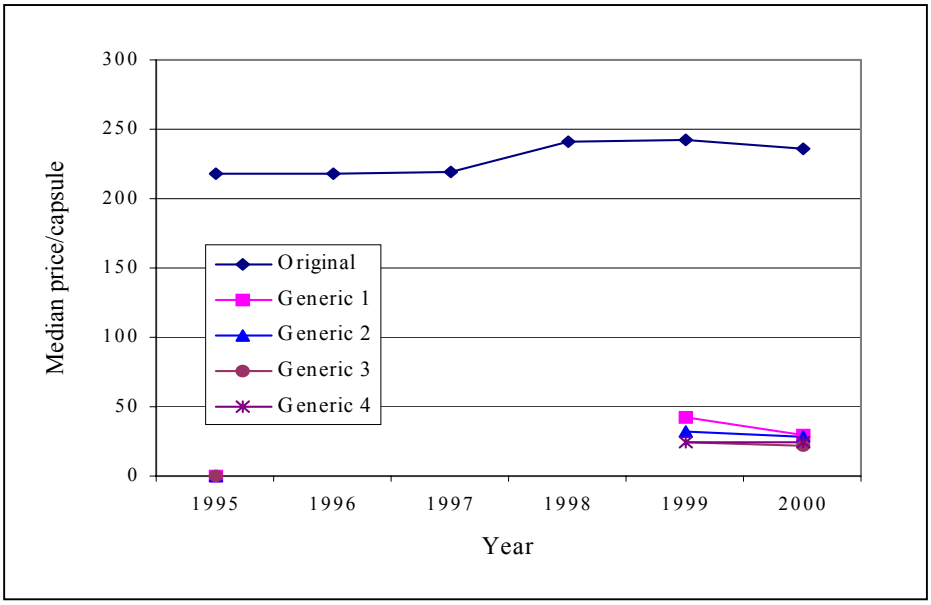


Figure 4: Purchase volume and value of clozapine 25- and 100-mg tablets among public and private hospitals in Thailand, 1996 to 2000

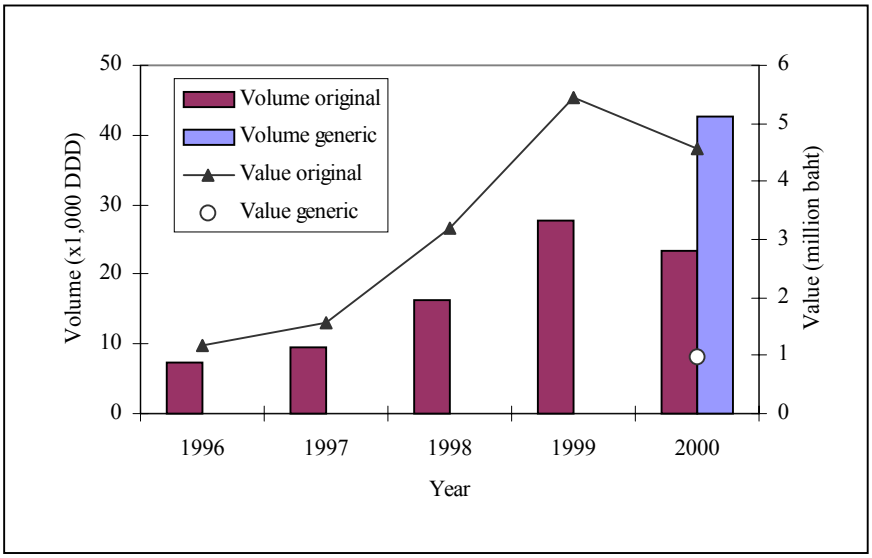


Figure 5: Median price per tablet of clozapine purchased by public and private hospitals, 1996 to 2000 (baht, at current year price)

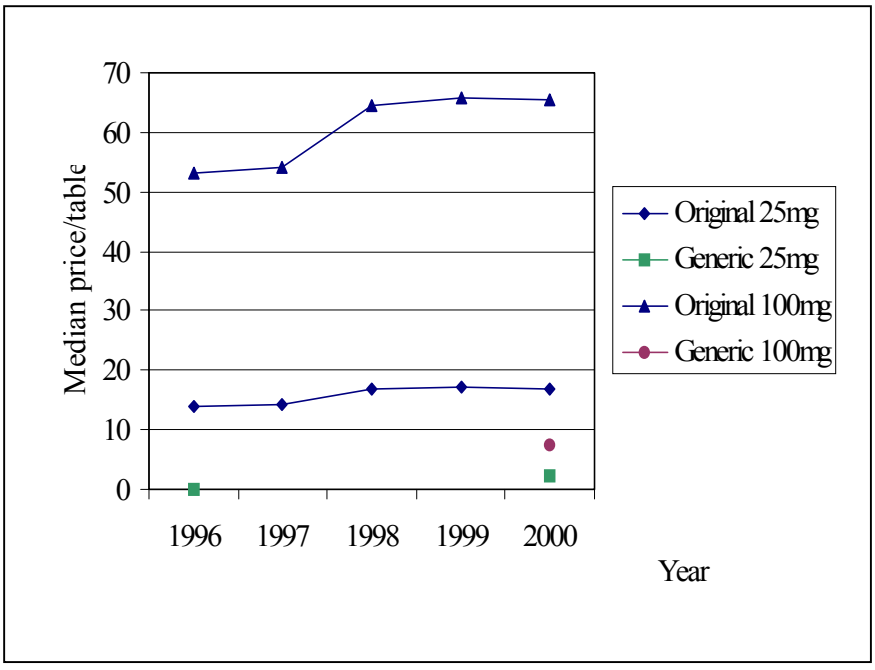


Figure 6: Purchase volume of ondansetron preparations among public and private hospitals, 1994 to 2000 (x 1,000 DDD)

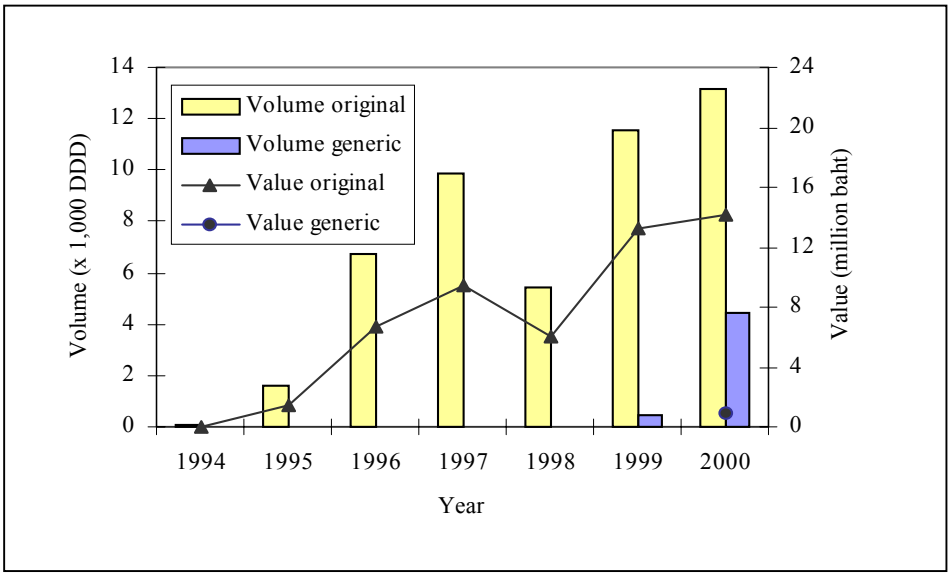


Figure 7: Median price per tablet of ondansetron purchased by public and private hospitals, 1994 to 2000 (baht, at current year price)

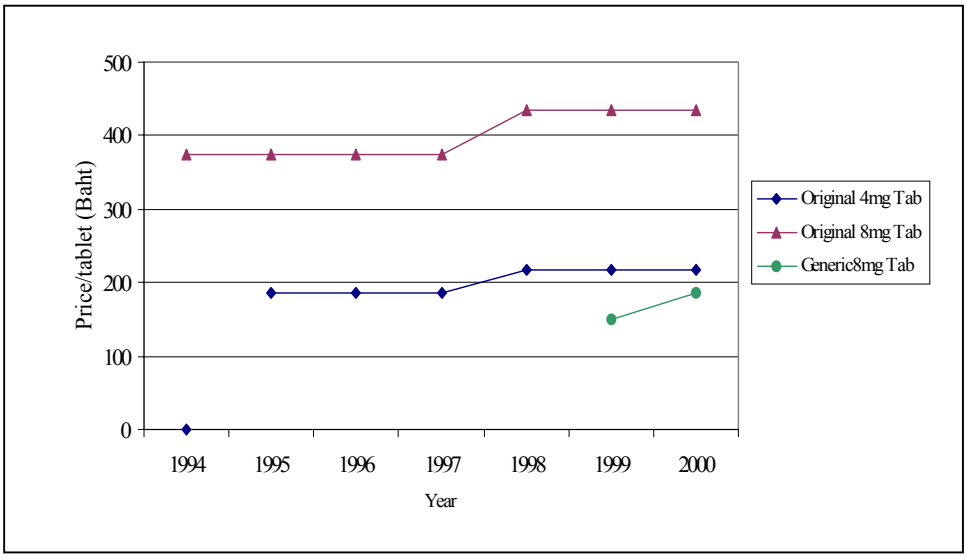


Figure 8: Median price per ampoule of ondansetron injection purchased by public and private hospitals, 1994 to 2000 (baht, at current year price)

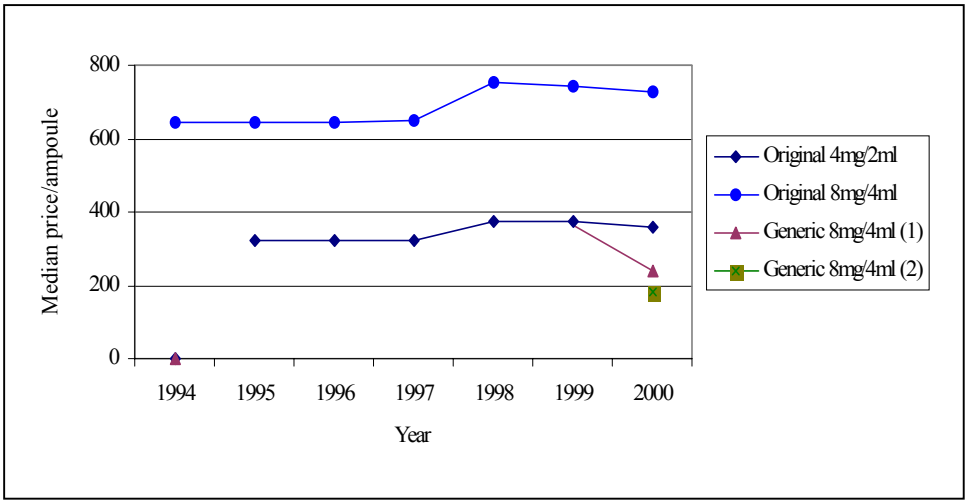


Figure 9: Purchase volume of ofloxacin injection among public and private hospitals, 1997 to 2000.

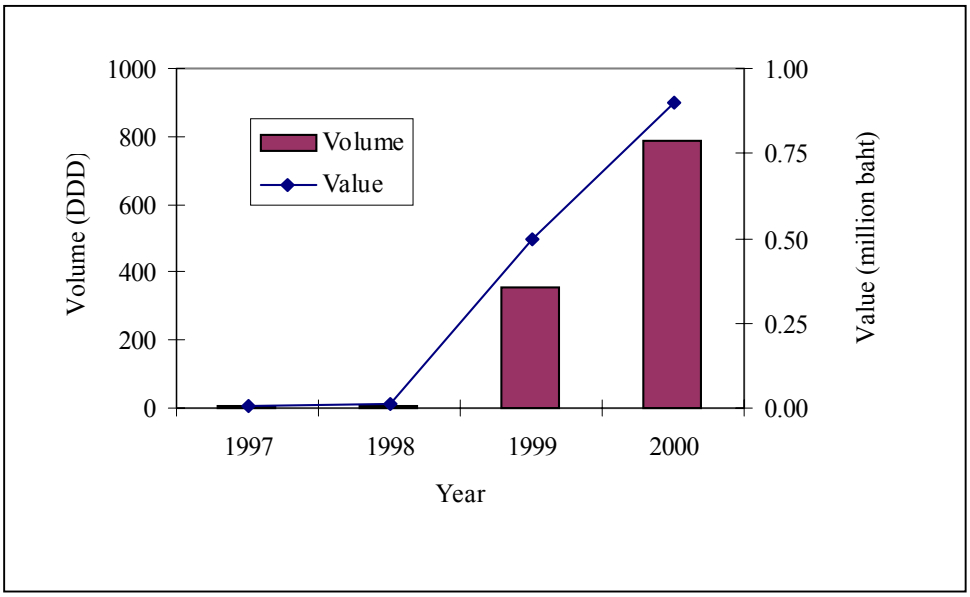


Figure 10: Median price per vial of original ofloxacin injection purchased by public and private hospitals, 1997 to 2000 (baht, at current year price)