

Facilitating the Entry of New Generic Drugs: A Proposal for Thailand

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Thai people are suffering from the high prices charged for brand-name drugs at a time when per capita drug consumption is unprecedentedly high. Per capita drug consumption in 2004 was slightly over 958 baht, an increase of 66 percent over that of 2000.¹ Generic drugs, which cost less than brand-name drugs and are therefore more competitive, play a significant role in increasing access to drugs and reducing the expenditure on them. However, Thai generic drug producers face several important barriers to enter the market: for example, ambiguity concerning the patent status of brand-name drugs, and inadequate research skills and funds to conduct a bioequivalence study. In this article, we offer a proposal to clarify the doubtful status of patents and to provide incentives for generic drug producers to seek market approval for their new drugs. Considering the level of development of the Thai economy and Thai generic producers, we propose an amendment of the Patent Act 1999, the Thailand New Drug Application (TNDA) and the Thailand Abbreviated New Drug Application (TANDA) to facilitate timely entry of generic drugs on the market.

The absence or delay in the entry of certain generic drugs, such as AIDS drugs, could jeopardize the health of Thai people. In addition, Jiraporn (2005) estimates that, on average, a one-year delay in the entry of one generic drug causes an increase in drug expenditure ranging from 4.29 million to 43.95 million baht. The increase in drug expenditure is due to a lack of access to cheaper drugs. There are two important barriers to entry for a generic drug. The first comprises non-patent-related barriers, such as, the ability of generic producers, the cost of a bioequivalence study, the sufficiency of bioequivalence facilities, and the monopolies existing in the generic drug market.²

The second barrier is related to patents. A generic drug may be marketed only after relevant patents of a

brand-name drug have expired. Drug development research is dynamic. New discoveries are possible from the basic stages of drug development to a clinical trial and even a post-clinical trial. Thus, relevant patents could be granted at different points in time both before and after the drug is approved to market, resulting in a risk of patent infringement at any time. Practically, it is not so easy to identify all the relevant patents. The generic producer needs to know all aspects of the brand-name drug so that it can find all the patents associated with all aspects of the brand-name drug. Moreover, to understand the information in the patent and to be able to match patents to an associated brand-name drug, it is necessary to have expertise in pharmacology and chemistry. Last but not least, the generic producers may not acquire the techniques, skills, and experiences necessary to effectively search relevant patents and monitor such new patents. However, even if they are equipped with sophisticated searching techniques, the generic producers still have a hard time in using the current patent database provided publicly by the Department of Intellectual Property (DIP), Ministry of Commerce.

Pharmaceutical multinational enterprises (MNEs) increasingly use multiple patents covering multiple attributes of a single drug, for example, active substance, derivatives of the active substance (such as polymorphs, isomers, and metabolites), formulations, use and process, in order to extend the terms of patent protection. The key method that MNEs producing brand-name drugs have for delaying generic entries—using patenting strategies—is to threaten a generic producer. They do this in order to stop any attempt by such a producer to market a generic drug; otherwise, the MNEs threaten, such a producer could face allegations of patent infringement. The expected reward from pursuing litigation is often less than the expected loss from such a

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course of action. Considering the high legal costs, the time-consuming litigation procedure, uncertainty about the court's decision, and the risk of paying a heavy fine if it loses the case, the generic drug producer is more likely to give up its attempt to market its generic drug. In the presence of ambiguity about the patent status of the brand-name drug, the MNE's patenting strategies become even more effective in delaying the entry of generic drugs.

This article focuses on the barriers related to ambiguity about patent status only. In general, we could facilitate the entry of new generic drugs by reducing the number of relevant patents, revealing all relevant patents, and giving an incentive for the generic companies to challenge unsuitable patents. We propose adding a separate clause about the patentability of pharmaceutical products to section 9 of the Thai Patent Act 1999 (the section covers what is not protected by the Patent Law) in a way similar to that done for the Indian Patents (Amendment) Act 2005, which explicitly states the unpatentable attributes of drugs. If the patent law were amended and then enacted in Thailand, there would not be many trivial secondary patents, which potentially cause delays in the entry of generic drugs. Moreover, we propose new processes for drug and generic drug application, similar to that of the United States New Drug Application (NDA) and Abbreviated New Drug Application (ANDA) respectively. The proposed application processes would require a brand-name company to provide ANDA applicants with relevant patents of a brand-name drug, and award six months of exclusive marketing rights to the first generic company that markets a drug after winning a patent lawsuit against a brand-name drug.

The article is organized as follows: section I provides a brief overview of the structure of the Thai

pharmaceutical market. Section II reviews the effect of competition from generic drugs. Section III analyzes patent-related barriers to entry. Section IV discusses practices of extending exclusive monopoly rights in Thailand. Section V provides a proposal to facilitate generic drug entry. Finally, section VI is the conclusion.

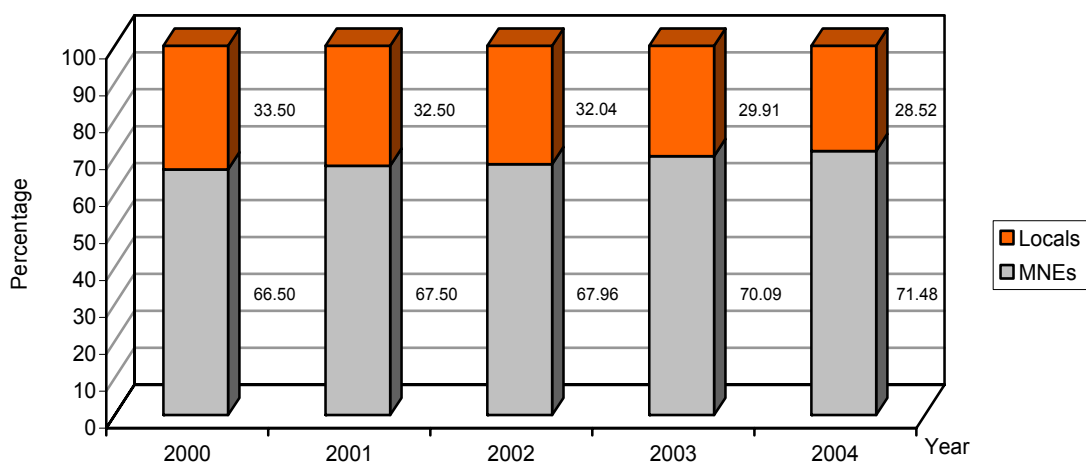
I. THE STRUCTURE OF THAI PHARMACEUTICAL MARKET

The Thai pharmaceutical market has grown considerably. As shown in Figure 1, in 2004, the market had a value of 53,102 million baht, an increase of 64 percent from that of 2000. MNEs play an increasingly significant role in the market. The market share of MNEs has grown at the expense of local producers. In 2004, more than 70 percent of the market share belonged to MNEs, while less than 30 percent of market share belonged to local producers. Most of MNEs' products are brand-name drugs; the majority of sales of brand-name drugs come from off-patent brand-name drugs. In contrast to MNEs, local producers produce mostly generic drugs, which are significantly cheaper than brand-name drugs.

II. PRICE EFFECT OF COMPETITION FROM GENERIC DRUGS

Unlike brand-name drug producers, generic drug producers do not go through a long and costly process of drug development, so they can set the price of a generic drug much lower than the price of a brand-name drug. To give an idea how expensive brand-name drugs are compared with generic drugs, using the data on the

Figure 1 Market Share of MNEs and Local Producers



Note: The sales estimates represent direct and indirect purchases by retail pharmacies from pharmaceutical wholesalers and manufacturers.

Source: Intercontinental Marketing Services (IMS).

expenditure of various AIDS drug formulations in Jiraporn et al. (2004), we find that the average price of generic drugs sold in Thailand in 2004 is only 31 percent that of the average price of brand-name drugs. Lower-priced generic drugs clearly increase access to medicines for low-income and middle-income consumers. While a literature search showed no systematic study of the price effect from generic drug competition in Thailand, such a review on the effects of competition from generic drugs in other countries could provide a better understanding of the issue and serve as a good reference for the Thai pharmaceutical market.

Empirically, the effects of competition from generic drugs are mixed. Caves et al. (1991) studied the price effect of competition between generic drugs and brand-name drugs that became off-patent drugs in the United States from 1976 to 1987. They found that the average price of brand-name drugs drops 2 percent after the first generic drug enters the market. Moreover, the average price of brand-name drugs decreases by 22 percent if there are 20 generic drug competitors. Frank and Salkever (1997) studied 32 brand-name drugs that lost patent protection in the United States during the period 1984-1987. They found that competition from generic drugs increase the price of brand-name drugs. The result is driven by lower elasticity of demand among brand-name drug consumers. Although competition from a generic drug may not always lead to a decrease in the price of a brand-name drug, the generic drug is a cheaper alternative that can substitute for a brand-name drug. Therefore, generic drugs increase people's access to medicine.

III. PATENT-RELATED BARRIERS TO ENTRY

A patent is an exclusive rights granted by the government to a patent holder to sell, distribute, produce, and/or import the product, subject to the patent for a period of 20 years. According to Article 5 of the Thai Patent Act 1999, an invention is patentable if it meets three requirements: novelty, non-obviousness, and industrial usefulness. The clock of protection starts ticking on the date of filing an application for a patent. However, pharmaceutical products can enter the market when granted marketing approval by the Food and Drug Administration (FDA). Thus, the effective period of protection starts from the marketing date and extends to the end of the patent life. After the expiration of relevant brand-name drug patents, a generic drug may enter the market.

As repeatedly claimed by pharmaceutical MNEs, the rationale of patent protection is to compensate pharmaceutical producers for their substantial research and development (R&D) costs and to provide an incentive for the production of innovate new and more effective drugs in the future.³ It is noteworthy to discuss the validity of this claim. As argued by Angell (2005),

there are convincing reasons to believe that the brand-name drug industry is overly protected by patents. Further, the claim about how innovative the industry is remains doubtful. First, most of the new brand-name drugs are not really innovative drugs.⁴ In fact, many new drugs are "me-too" drugs that are versions of already marketed drugs and are no better than already marketed drugs in the same therapeutic class.⁵ Second, quite often, the early stage of R&D of many important drugs, arguably the most important stage, is carried out by government agencies, universities, and biotechnology companies.⁶ Moreover, some of the research is funded by taxes. Therefore, pharmaceutical companies get monopoly rights on drugs that are not truly innovative and have been partly funded by the public. Consequently, it should be clear that practices aiming to extend monopoly rights beyond the patent life are immoral and unfair.

Because the pharmaceutical market is lucrative, a brand-name producer would put a serious effort into extending its monopoly rights beyond the period of patent protection, using complex life-cycle management strategies. Life-cycle management includes strategies such as patenting strategies, a development over an existing drug (line extension), such as changing the dosage of a drug, changing the form of delivery, changing the formulation to add safety, or producing extended-release drugs, switching to over-the-counter (OTC) drugs, entering into manufacturing and distribution agreements, and pursuing marketing strategies to persuade consumers to switch to the new drug, a variant of the already marketed drug.⁷ One strategy alone or a combination of the above-mentioned strategies could be used to successfully extend the monopoly period.

An "evergreening" patent is a widely used patenting strategy that prolongs the period of patent protection.⁸ An evergreening patent is a strategy by which MNEs use multiple patents covering multiple characteristics of a single drug to extend the term of patent protection.⁹ The patents could cover both primary patents and secondary patents that frequently have the potential to delay the entry of generic drugs.¹⁰ While primary patents normally cover an active substance, a formulation, or a use, secondary patents normally cover a new form of a known substance, a new use of a known substance, or a new property of a known substance.¹¹ In practice, generic drug producers have to choose between waiting for the expiration of all relevant patents, or marketing the generic version of the drug and facing the risk of patent infringement litigation and its associated costs. Under certain conditions, an evergreening patent effectively blocks the entry of generic drugs, because it is impossible for generic producers to avoid patent infringement. There are many case studies of evergreening patents and other life-cycle management strategies. Two of the best known cases in the United States are perhaps the Nexium and the Claritin cases.

First, produced by AstraZeneca, Nexium, a brand-name drug used to cure heartburn, is a good study case of how drug companies use life-cycle management to successfully extend the monopoly period of a previous version of the drug, in this case, Prilosec.¹² According to Angell (2005), Prilosec is a mixture of an active and a possibly inactive form (isomers) of the Omeprazole molecule. When Prilosec's patent protection was going to expire in 2001, AstraZeneca was granted a patent on the active form of the Prilosec molecule.¹³ Under the protection of the new patent, AstraZeneca marketed the presumably new product under the name Nexium (in fact, the only new feature is its color, purple). In other words, despite the color, Nexium is equivalent to Prilosec. After receiving marketing approval, AstraZeneca put on one of the most massive marketing campaigns ever conducted to persuade consumers to switch to Nexium. In addition, AstraZeneca made Prilosec an OTC drug and got three years of exclusivity, resulting in larger aggregate sales (including Prilosec and Nexium) in 2002 compared with 2000 when sales of Prilosec reached their peak. Unfortunately, the success of AstraZeneca's strategies comes at the expense of consumers and generic drug producers.

Second, Schering-Plough used a brand-name drug for treating allergies, Clarinex, to extend the monopoly period of its previous version of the drug, Claritin.¹⁴ Just before the patents on Clarinex expired in 2002, Schering-Plough patented the active metabolite of Claritin and marketed it as Claritin. A metabolite is the chemical compound into which a patient's body metabolizes or converts the active ingredient of a drug. In other words, the active ingredient in Clarinex is the molecule into which the body converts Claritin. Therefore, Claritin is equivalent to its previous version, Clarinex. In theory, only patients can directly infringe a metabolite patent by swallowing the drug and then metabolizing it into the claimed molecule. Nevertheless, the metabolite is troublesome to generic producers because the patentee normally sues the generic producers for inducing the infringement by selling the drug. Schering-Plough also made Claritin an OTC drug and undertook a massive marketing and advertising campaign. Unlike Prilosec, Schering-Plough did not get three years of exclusivity for its OTC Claritin, and it has been less successful with Clarinex compared with AstraZeneca's product Nexium.

IV. PRACTICE OF EXTENDING EXCLUSIVE MONOPOLY RIGHTS IN THAILAND

The problems with the practice of extending patent protection are widely acknowledged by governments and anti-trust agencies in many countries, for example, the United States, Canada, India, and Thailand. In Thailand, there is evidence that the practice

of extending a patent's term is widely used. Jiraporn et al. (2004) detected a number of suspicious patents claiming new uses for off-patent drugs, combinations of off-patent drugs and soon to be off-patent drugs, or a combination of off-patent drugs, and a new dose (for instance, from three times a day to two times a day). To further explore the issue, we examine the relevant patents of Prilosec, Nexium, Clarinex, and Claritin in Thailand to see whether there is evidence of suspicious patenting practices, which could delay the entry of generic drugs.

We looked up the relevant patents of Nexium and Losec, as mentioned previously a commercial name for Prilosec in Thailand, in the Thai FDA drug patent database, arguably the most complete database available in Thailand. We could not find any patents on Nexium (its generic name is Esomeprazole). Ranked 18th in sales in Thailand in 1999, Losec (its generic name is Omeprazole) has four relevant patents with expiration dates ranging from December 2017 to November 2018.¹⁵ However, owing to the incompleteness of the data used to construct the database, it is possible that there might be other relevant patents that remain unrecognized or unidentified by the creator of the database. Nonetheless, we suspect that the latest granted patent claiming a new crystalline form of Omeprazole (a polymorph of Omeprazole) could delay the entry of generics.¹⁶ In theory, under certain conditions, a polymorph is therapeutically equivalent to an active substance and thus is not truly novel. In many cases, it is obvious to other people in the field of interest. In practical terms, the presence of the polymorph patent forces generic producers to choose between entering the market, regardless of the patent, and accepting the risk of time-consuming legal processes and uncertain court decisions, or waiting until the polymorph patent expires. Therefore, the patent possibly adds one more year of patent protection to Losec.

Using the Thai FDA drug patent database, we found one patent for each drug, Clarinex (its generic name is Desloratadine) and Claritin (its generic name is Descarboethoxy Loratadine). Clarinex's patent will expire in February 2018, and Claritin's patent will expire in December 2020. Although it is beyond our ability to verify how the two patents differ from each other, it appears that the Clarinex patent is not for a metabolite of the active molecule in Claritin.¹⁷ In fact, the Claritin patent claims extended release of the oral dosage composition.

Other than the above-mentioned drugs, we also found three more drugs with multiple patents, as follows: Zolofit (its generic name is Sertraline), produced by Pfizer, has five patent applications with different expiration dates, ranging from June 2018 to October 2019.¹⁸ All of Zolofit's patents are pending. Taxol (its generic name is Paclitaxel), produced by Bristol-Myers Squibb, has four patent applications with various expiration dates, ranging from March 2016 to March

2002.¹⁹ All of Taxol's patents are pending. In addition, we found two patents associated with Augmentine (its generic name is Amoxicillin and Clavulanic acid).²⁰ One patent is in the process of examination and will expire in July 2012, if it is actually granted. Another one has been granted and is scheduled to expire in April 2015. As mentioned above, the database is incomplete and should be used with caution. It is possible that there might be other relevant patents but unrecognized or unidentified by the creators of the database. These multiple patenting practices are suspicious and possibly delay generic drug entries. DIP must scrutinize those applications and further relevant applications in order to avoid the possibility of delaying the entry of generic drugs. Considering resources of that Department, the ability of the government to screen suspicious patents effectively remains in doubt.

The brand-name drug company's key to success in using patenting strategies is to threaten the generic drug producer so that it would stop any attempt to market the generic drug; otherwise, the generic drug producer could face allegations of patent infringement. The expected reward of becoming involved in litigation is often less than the expected loss. Considering the high legal costs, the time-consuming litigation procedures, uncertainty about the court's decision, and the risk of having to pay a heavy fine if the generic drug producer loses, that producer is more likely to give up its attempt to market its generic drug. In Thailand, the patenting strategies are likely to effectively extend the exclusivity period of the brand-name drug due to two factors.

First, the enforcement of Article 5 of the Thai Patent Law is weak, particularly with regard to the aspects of novelty and non-obviousness. Proving the novelty and the non-obviousness of the drug patent requires extensive knowledge of pharmacology and chemistry. Obviously, DIP does not have sufficient resources and ability to scrutinize or even understand complicated drug patent applications, let alone the ability to recognize secondary patents. Instead of cooperating with experts from FDA or universities, the Department has chosen to keep the task to itself. Sometimes, it makes a decision based on the decisions made by the intellectual property rights (IPR) agencies in developed countries, particularly in the United States and European countries, where the enforcement of IPR appears to be as lenient as anywhere else in the world, except in India. Therefore, it is no surprise that many secondary patents have been granted that are not truly novel and non-obvious. Under certain conditions, these secondary patents could effectively block the entry of generic drugs. Unfortunately, this experience will persist as long as there is no serious attempt to strictly enforce the Patent Law and increase the quality and quantity of human resources in the aforementioned Department.

Second, in reality, it is very difficult to detect all the relevant patents of a brand-name drug, particularly secondary patents, which often are not obvious, or even

trivial improvements or characteristics of a known drug. The generic producers' ability to detect all relevant patents is tremendously lessened due to the ambiguity about the status of a brand-name drug's patent, which is partly caused by the drawbacks in Thai drug patent databases. Using the current databases, it is extremely difficult for generic producers to plan the development of new generic drugs. They would not know when the targeted brand-name drugs could be imitated legally, when to start conducting research on new generic drug development, or when to market the generic drugs.

There are three sources of drug patent information in Thailand. Each of them has advantages and disadvantages. Unfortunately, none of them is truly beneficial to the generic producers. First, the official database provided by DIP is the most comprehensive patent database in Thailand.²¹ There are various useful keyword options, for example, International Patent Classification code (IPC), claims, application number, patent number, inventor's name, applicant's name, and title of invention. Despite being an official and the most important patent database in the country, the database website is difficult to access owing to server problems. It is not user-friendly, at least with regard to searching for drug patents. Almost all keywords must be Thai letters, which frequently causes confusion and inconvenience because there are multiple ways of spelling the Thai version of English-language words.²² More importantly, it is not useful for searching a drug patent simply because one cannot directly search by using convenient keywords such as a generic name or a brand name (trade name).

The second database is the drug patent database available on the FDA website.²³ Constructed by knowledgeable pharmacists and patent law experts, it apparently is the most sound drug patent database in Thailand, and can be easily searched through convenient keywords such as generic name and brand name (trade name), and therapeutic group. Nonetheless, the database has some important drawbacks.

First, the database entries cover the period from 1992 to 2004 only. Therefore, it leaves out patents that expired before 2006. Second, the database was constructed by using all available drug information from the Internet, a secondary source rather than information acquired directly from the brand-name drug producers. As a result, the database might be incomplete and inaccurate; it cannot be used as a legal reference concerning the patent status of a drug. The database must therefore be used with caution.

The third database is the drug patent database provided by the Drug Control Division of the Thai FDA.²⁴ The FDA simply asks new drug applicants to provide patent information on their drugs such as the first country where each patent was granted, application date, date when patent was granted and expiration date. In addition to the information provided, the applicants have to submit an official document relating to the

patent approval and certify the validity of the information provided. However, the penalty for providing invalid patent information is not well elucidated and is likely to be very light or perhaps not exist at all. In spite of the certification of the patent, FDA has no interest in using its resources to recheck the validity of the information provided. New drug applicants would not have any incentive whatsoever to provide all the relevant patents. Completing the list of questions indeed is not without cost such as time. Given the negative net benefit of completing the list, applicants would likely expend minimum efforts in filling out the list. In addition, knowing that it is unlikely that the validity of patent information will be rechecked due to the Department's lack of resources, new drug applicants might provide false information in order to prolong the expiration of a patent. Therefore, it is not rational to believe that the patent information provided is complete and reliable.

While reliable and credible patent information, such as contained in DIP's database, is not in a user-friendly form, and the two user-friendly databases provided by the FDA are likely to be incomplete and unreliable. Updating and maintaining the database constructed by experts might be difficult and costly in the long run. In addition, the fundamental problem of obtaining all the available data is difficult to solve. Thus, a feasible solution seems to be to improve the database provided by the Department of Drug Control, FDA. A possible way to attack the problem of incompleteness and unreliability is to provide enough incentives to new drug applicants to reveal all relevant patent information. The interaction between NDA and ANDA, under the Hatch-Waxman Act, is a good example of how to make a brand-name drug producer reveal all relevant patent information.

The United States NDA and ANDA

The Hatch-Waxman Act is claimed to create a balance between the innovation of, and access to, drugs. On one hand, it lengthens the brand-name producers' exclusive monopoly rights by giving exclusive rights to compensate the period of difficult and costly clinical trials. On the other, it allows the generic drug producers to submit only a bioequivalence study instead of having to replicate costly clinical trial studies. It provides a shortcut for bringing generic drugs to the market through the process called ANDA, which allows the generic drug to start the approval process before the expiration of patents. In addition, NDA links a patent to drug marketing approval and thus clarifies the ambiguity about the status of the patent. Before we proceed to the Thai proposal, it is important to understand how NDA and ANDA work, as briefly explained below.

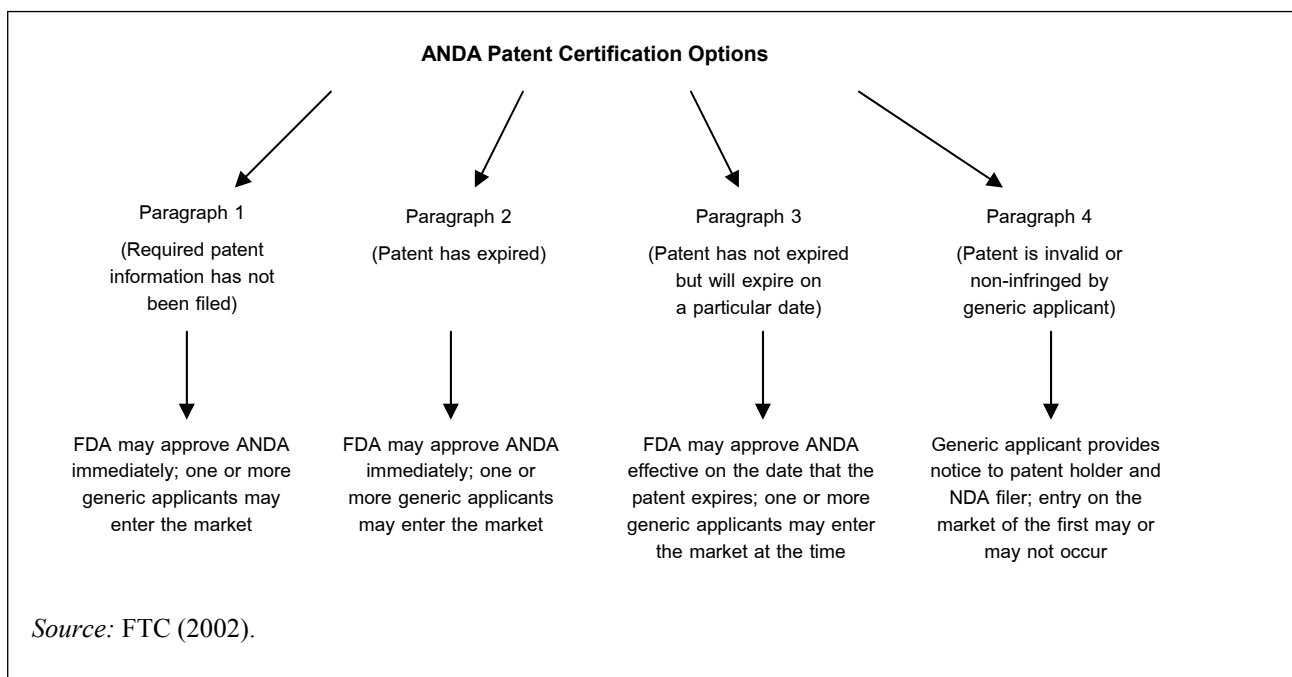
First, a company producing brand-name drugs seeking marketing approval for a new drug has to file a

new NDA. In filing the NDA, the applicant must provide the FDA with information regarding relevant patents of the drug subject to NDA. Once the NDA is approved, the patents are listed in a publication, commonly known as the "Orange Book." The main purpose of the Orange Book is to provide information on patents upon which the ANDA application might infringe.²⁵ It should be noted that more patents can be added later on.²⁶ Second, a generic drug producer seeking marketing approval on its generic drug has to file an ANDA. In filing the ANDA application, the generic drug company may certify that (a) the required patent information has not been previously filed (referred to as Paragraph 1); (b) the patent has expired (referred to as Paragraph 2); (c) the patent has not yet expired and the applicant will seek approval after patent expiration (referred to as Paragraph 3); or (d) the patent is invalid, or the drug for which approval is being sought will not infringe on the patent (referred to as Paragraph 3). If the brand-name drug adds another patent to the list after the certification, the ANDA applicant must re-certify the newly listed patent.

The marketing approval process depends on the types of certification, as shown in Figure 2. Only the applicant making Paragraph 1 or 2 certification may get FDA approval if its drug meets the other requirements. The applicant making Paragraph 3 certification may get effective FDA approval after the patent expiration date. The applicant making Paragraph 4 certification must give notice to both the patent holder and the NDA applicant. According to the Hatch-Waxman Act 1984, once the patent holder and the NDA applicant get notice, they can choose to file a patent infringement lawsuit within 45 days in order to get an automatic 30-month stay of FDA approval, starting from the date of receiving the notice. The stay will expire at the earliest of (a) the date of the patent expiration, (b) a final court's decision, or (c) the expiration of the stay. If they choose not to file the lawsuit, the FDA approval process may proceed. In addition, the Hatch-Waxman Act also grants an exclusive 180-day marketing approval to the first Paragraph 4 ANDA filer. Figure 3 shows how the 30-month stay and the exclusive 180-day marketing approval affect the marketing approval of new generic drugs.

In contrast to Thailand's current system, the brand-name producers have an incentive to list all relevant patents (or even irrelevant patents) because those patents could trigger an automatic 30-month stay. Since the ambiguity of the patent status is a crucial barrier to the entry of a new generic drug, processes similar to NDA and ANDA would be beneficial to Thai generic producers.

Although NDA and ANDA provide an advantage over the current system used in Thailand, they reportedly have two important loopholes.²⁷ First, the brand-name producers often list as many patents as possible, both

Figure 2 FDA Approval Process for ANDA

relevant and irrelevant to the product, in order to abuse the 30-month stay. Moreover, there is a possibility of multiple 30-month stays caused by newly listed patents. Second, the 180-day exclusivity granted to the first Paragraph 4 ANDA filer opens an opportunity for an anti-competitive agreement between the first filer and the brand-name drug company to delay the entry of the generic drug. This is simply because no other generic producers could enter the market until the 180-day exclusivity period has expired. The exploitation of the loopholes is closely watched by the U.S. Federal Trade Commission (FTC) as a possible anti-competitive practice, which generates numerous losses for consumers and the U.S. government.²⁸ Learning from the United States experience, Thailand's new drug approval process must close the loopholes in order to truly facilitate the entry of new generic drugs.

V. PROPOSAL FOR FACILITATING THE ENTRY OF NEW GENERIC DRUGS IN THAILAND

To facilitate the entry of new generic drugs, we propose changes in the Thai Patent Act 1999 and the Thai FDA's current marketing approval processes for new drugs and new generic drugs, as follows:

1) The Proposed Amendment of the Thai Patent Act 1999

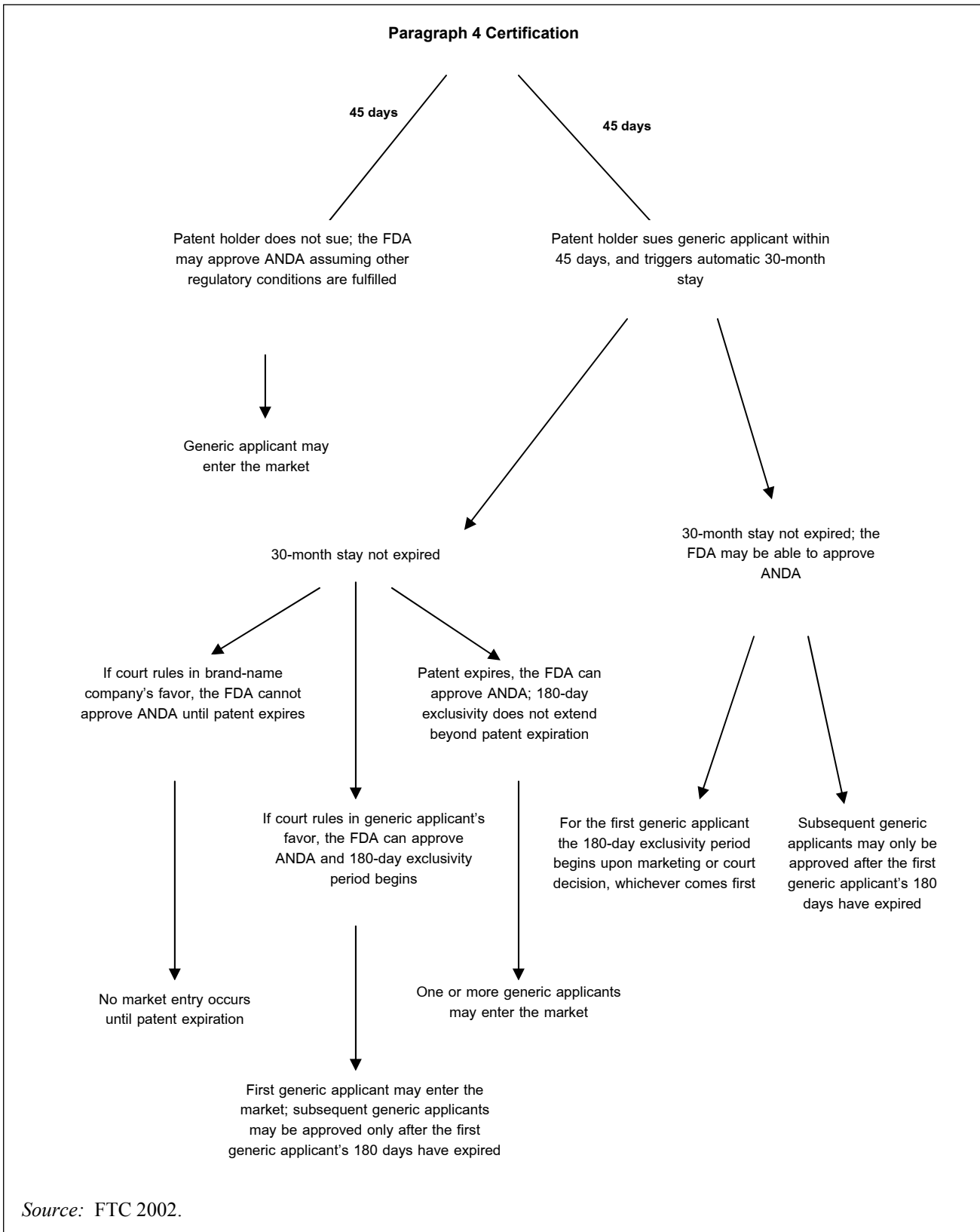
With regard to amending of the Thai Patent Act 1999, we propose adding a separate clause about the

patentability of pharmaceutical products to section 9 of the Thai Patent Act 1999 (the section covers what is not protected by the Patent Law) in a way similar to the Indian Patents (Amendment) Act 2005. The Amended Indian Patents Act, section 3, clause d, explicitly states the conditions under which a pharmaceutical product is not patentable, as follows: "The mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant." As explained by the Ministry of Law and Justice of India, clause d means the following: "For the purpose of this clause, salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy." With a more stringent patent act for Thailand, it would not be very difficult to search for relevant patents, because there are not many trivial and unobvious secondary patents left. In addition, the risk of patent infringement would be reduced.

2) The Proposed Method for New Drug Marketing Approval in Thailand

Although there would be less relevant patents of the brand-name drug, the risk of patent infringement could still exist, particularly for generic producers lacking expertise in searching patents. As mentioned previously, the current linkage between patents and the

Figure 3 Impacts of the 30-Month Stay and the Exclusive 180-Day Marketing Approval



drug marketing approval process does not really solve the problem of ambiguity of patent status because the brand-name drug companies do not really have an

incentive to provide the list of all relevant patents to the Thai FDA. In addition, patents granted after marketing approval would not be listed. After the drug is approved,

the list is no longer exclusive because there might be a newly granted patent that has been left out of the list. Consequently, the ambiguity of the patent status would be temporarily solved. Therefore, we propose TNDA and TANDA, similar to those of the United States NDA and ANDA respectively. The proposed processes would provide an incentive to challenge the validity of the patent and to market the generic drug as quickly as possible. Together with the proposed amendment of the Thai Patent Act, the proposed processes would clear up ambiguity about the patents' status.

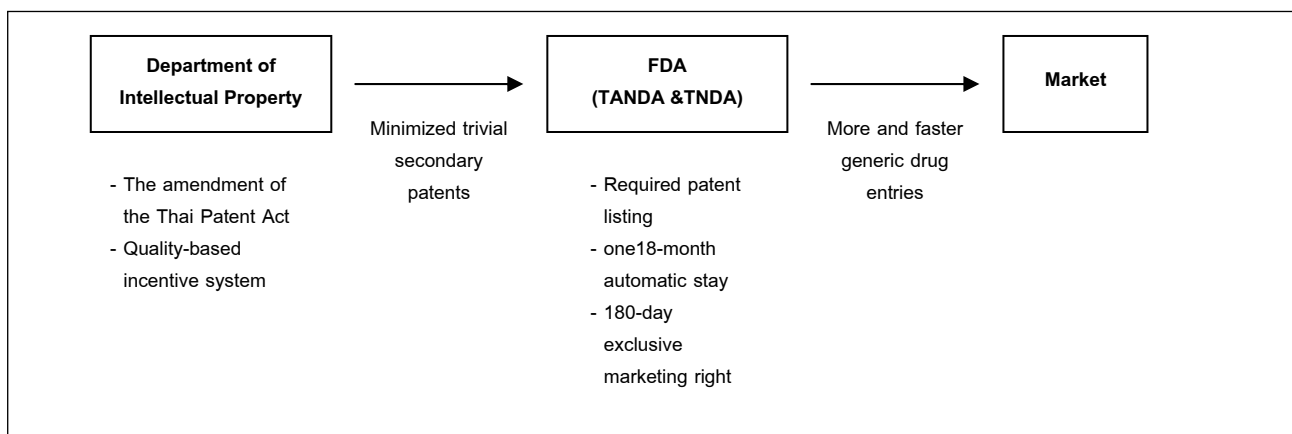
In general, details of TNDA and TANDA are similar to those of the United States NDA and ANDA, except for three factors. First, there would be an 18-month automatic stay instead of a 30-month automatic stay. The rationale for the stay is to give both parties and the court enough time to settle infringement litigation. In Thailand, as far as we are concerned, there have only been two cases of patent litigation related to modern pharmaceutical products, the cases of the Government Pharmaceutical Company versus Bristol-Myers Squibb. The first litigation, mainly involving invalidity of claims, lasted about 17 months. The second litigation, involving validity of a patent, lasted about 15 months. Thus, an 18-month stay would be appropriate and give enough incentive for the brand-name drug companies to list all relevant patents. In fact, the incentive is overwhelming, since an 18-month stay is roughly twice as long as the average time used in the current NDA process for imported drugs, i.e., 9.3 months.²⁹ Second, only one 30-month automatic stay should be granted. With the enactment of an amended Thai Patent Act, the listing of trivial secondary patents is unlikely and thus multiple 30-month stays would perhaps be rare anyway. Third, to prevent anti-competitive agreements between the brand-name drug and the first ANDA filer, 180-day exclusive marketing rights shall be granted to the first generic company that markets a drug under Paragraph 4 certification. In addition, the 180-day exclusive marketing rights would increase competition among generic producers to bring new generic drugs to the market as quickly as possible.

The proposed new drug marketing approval processes would work congruently with the proposed amendment of the Thai Patent Act to help facilitate the entry of new generic drugs in Thailand, as shown in Figure 4. Every proposed feature is designed to complement one another and work as a system, as one feature alone would never succeed. More importantly, they are necessary but not sufficient conditions to facilitate the entry of new generic drugs. Without strict enforcement of the law and a sufficient amount of good-quality patent examiners, the problem would not be easily solved. Therefore, it is important for the government to provide adequate funds and resources to improve the quality of patent examiners. Moreover, an appropriate reward and punishment scheme could be used to give an incentive for patent examiners to enforce the Patent Law strictly. One possible scheme is that the patent examiners could be paid monthly bonuses that would depend on the quality of examined patents. The patent examiner would get one point for each granted patent, but would get minus 10 points for each patent that generic drug companies sue and eventually resulting in the withdrawal of the patent.³⁰ The amount of the bonus would be 200 baht times the net number of points per month.³¹

VI. CONCLUSION

The ambiguity of patent status is certainly one of the important barriers to entry for producers of Thai generics. In this article, focusing on the problem of ambiguity of patent status, we propose an amendment to the Thai Patent Act 1999: a quality-based incentive system for patent examiners and TNDA and TANDA to facilitate the timely entry of generic drugs. All proposed features would work as a system as one feature alone would not be fully effective. The proposed system would lead to more and faster new generic entries. The amendment of the Thai Patent Act together with the quality-based incentive system would reduce the number of trivial secondary patents granted by DIP. As a result,

Figure 4 Proposed Process for Facilitating Entry of New Generic Drugs in Thailand



the risk of patent infringement would be reduced. TNDA and TANDA would solve the ambiguity about patent status and further reduce the risk of patent infringement. In addition, the 180-day exclusive marketing rights would not only provide an incentive for the generic producer to challenge the validity of patents that block entry, but also increase competition between the generic producers to bring new generic drugs to the market as soon as possible. However, the proposed system is a necessary but not sufficient condition to bring new generic drugs to market successfully. There are other important barriers to entry, such as the ability of the generic producers, the sufficiency of bioequivalence facilities, and monopolies in generic markets.

ENDNOTES

- ¹ Drug consumption is calculated from the following formula: consumption value = production value – (export value – import value). All data have been acquired from the Thai Drug Control Division, Food and Drug Administration, Ministry of Public Health.
- ² Instead of going through extremely expensive clinical trials, generic drug producers may demonstrate that a generic drug is the bioequivalent of a brand-name drug and receive marketing approval from the Food and Drug Administration (FDA). Bioequivalence means that the rate and extent of absorption of the generic drug is not significantly different from the rate and extent of absorption of the brand-name drug. The cost of conducting a bioequivalence study trial could be as high as 1-2 million baht which is considered high for the Thai producers, particularly for a study targeting a new off-patent drug. As a result, it is less likely for some generic producers, particularly small and medium-sized producers, to enter the market.
- ³ DiMasi, Hansen, and Garbowski (2002) estimate drug development costs to be US\$ 802 million.
- ⁴ Angell (2005) found that only 14 percent of 415 newly approved drugs in the period 1998-2002 could be called innovative drugs, that is, they contained new molecules and were characterized by significant improvements compared with marketed drugs.
- ⁵ For instance, Crestor, Lipitor, Zocor, Pravachol, Lescol are drugs used to lower cholesterol, and they are variations of Mevacor.
- ⁶ These important drugs include Taxol, Epogen, and Gleevec.
- ⁷ OTC drugs are drugs that are available to consumers without a prescription. In the United States, according to the Hatch-Waxman Act, a drug company can get three years of exclusivity by switching its drug from prescription to OTC if it can show that consumers can understand how to use the drug properly.
- ⁸ Although the scope of life-cycle management strategies is broader than the scope of the evergreening patent, in the literature the evergreening patent and life-cycle management approaches are sometimes used interchangeably.
- ⁹ An evergreening patent also includes a practice called double patenting. Double patenting is a practice in which a patent claims the same uniqueness as an earlier issued patent.
- ¹⁰ For example, a brand-name drug producer might allege that a generic drug company is infringing on a new use patent. Only doctors who prescribe a generic drug for patients—if it has a new use—can directly infringe on the new use patent. Being aware of the risk of patent infringement, doctors might avoid the risk of patent infringement by sticking with a brand-name drug. However, in fact, a patentee usually sues generic producers for inducing patent infringement because they sold the drugs to the doctors.
- ¹¹ For example, salts, polymorphs, metabolites, pure form, isomers and mixture of isomers.
- ¹² More details are available in Angell (2005) and FTC (2002).
- ¹³ Prilosec is marketed in Thailand under the name of Losec. Losec is scheduled to go off patents in November 2018.
- ¹⁴ More details are available in Angell (2005) and FTC (2002).
- ¹⁵ Intercontinental Marketing Services (IMS).
- ¹⁶ A polymorph is a specific crystalline form of a compound that can crystallize in different forms.
- ¹⁷ Application number 062645.
- ¹⁸ Zoloft is used to treat depression and anxiety.
- ¹⁹ Taxol is used to treat some types of cancer.
- ²⁰ Augmentin is used to treat many different bacterial infections, such as sinusitis, pneumonia, ear infections, bronchitis, urinary tract infection, and infections of the skin.
- ²¹ The database is accessible from the following URL: <<http://www.ipic.moc.go.th/>>.
- ²² Rare exceptions include the titles of inventions that sometimes were given in English when the applicants submitted their applications.
- ²³ The database is accessible from the following URL: <<http://www.fda.moph.go.th/>>.

²⁴ The database is accessible from the following URL: <http://wwwapp1.fda.moph.go.th/drug/zone_service/ser019.asp>.

²⁵ Given advanced technology in patent-searching techniques and in monitoring relevant new patents, some brand-name companies actually rely on information in the Orange Book.

²⁶ There are certain rules that govern listing in the Orange Book. However, those rules are not strictly enforced due to the lack of FDA resources. For practical purposes, the brand-name drug can list as many patents (both relevant and irrelevant to the products) as they like at any time, even if the drug is already on the market.

²⁷ FTC (2002) and Angell (2005) provide an excellent review of the issue.

²⁸ In fact, FTC (2002) suggested recommendations regarding the loopholes; however, the U.S. House of Representatives did not approve those recommendations.

²⁹ Chutima et al. (2005).

³⁰ This is a proposed number. It could be substituted by any appropriate number.

³¹ This is a proposed amount. It could be substituted by any appropriate figure.

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