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WORLD PHARMACEUTICAL NEWS

Market Insight - Clarity needed over ASEAN regulators' position on IP

05 August 2009

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The variety and ever-changing nature of regulations governing patent and drug approvals across the Asian region, along with policies which often favour local generics, can pose a daunting challenge for multinational research-based companies. Alan Adcock *and* Clemence Gautier *take a look at some of the major issues and how they can be addressed.*

According to a World Bank report published in July 2008, the 10 members of the Association of Southeast Asian Nations (ASEAN) represent a broad range of economic levels, ranging from high income (Singapore and Brunei) to upper middle income (Malaysia), lower middle income (Thailand, Indonesia and the Philippines) and low income (Laos, Cambodia, Vietnam and Myanmar). But with the increase in foreign investment and the domestic development of specific industries, certain businesses have begun to experience erratic and strained government regulatory hurdles.

ASEAN members have prioritised the improvement of the marketing approval process for pharmaceutical products over the past decade. Recently, the economic grouping has attempted to improve product registration efficiency. The implementation of the ASEAN Common Technical Requirements and Dossier on Quality, Safety and Efficacy, which provide guidelines on analytical and process validation, stability studies and bioavailability/bioequivalence, reflect a desire for harmonisation with the most efficient regulatory practices worldwide.

Despite these strides in the right direction, however, significant issues still remain in many countries, particularly in regard to government initiatives favouring access to cheaper medicines, pro-generic policies, faster drug registration processes for generics and the de-prioritisation of intellectual property (IP) rights owned by the originators/innovators of the drugs.

This is especially true in the pharmaceutical industry, which is generally required to deal with a lack of competent drug regulators in the ASEAN food and drug administrations (FDAs). Such regulators are generally less well versed in IP law than their counterparts in other jurisdictions. Although innovator companies consistently face common obstacles when dealing with such FDAs, it is nevertheless possible to overcome some of these difficulties by informing and co-operating with them.

ASEAN FDAs and patent offices

Pharmaceutical companies believe they face an unbalanced playing field in their competition with generic manufacturers. Innovators encounter significant delays in registering their products and indeed the patents covering those products. Pro-generic policies and regulations in the region have only increased delays for innovators and the shortcuts for generics.

Drug registration in ASEAN countries is generally slow. For a new drug, the process will take at least two years in Thailand, for example. However, the timeframe for obtaining marketing approval for generic drugs is usually shorter: often six months to one year only. This discrepancy can also be observed in other countries. Very often, the reasons for these delays include a lack of staff competent to review the applications and the increasing list of documents required for submission, including clinical studies, which are not usually required for generic drug applications.

Disparities also occur across ASEAN countries regarding patent registration. Countries like Singapore, the Philippines and Indonesia have a reasonable timeframe for the grant of a patent invention: usually up to four years from the application date. At the opposite end of the spectrum, some countries have a non-existent or very slow patent registration system. Examples include Myanmar, which has not yet adopted any patent law (though its World Trade Organization commitments require it to do so by 2013), and Brunei, which will grant patent protection only after the equivalent patent has been granted in the EU, the US, Malaysia or Singapore.

Thailand can be singled out for having one of the slowest patent registration processes in the Asian region. Certain patent applications for pharmaceutical products can take up to 10 years from the application date, and some have taken more than 15, but generally a straightforward application should take between six to eight years.

The delays will affect a pharmaceutical innovator if the patent approval has not been granted by the time

the product is ready for market launch. In such cases, the innovator does not have any enforceable patent rights that would allow it to restrict the activities of third parties. Further delays may be experienced if the additional regulatory approval involves a longer duration than the generally accepted period of two years.

In many countries, a drug innovator may seek an increase in the effective patent life in case of any unreasonable delays for the grant of its patents. However, several ASEAN countries refuse to follow these guidelines, which are deemed to be pro-pharmaceutical industry.

ASEAN governments have justified their pro-generic policies by citing their relatively low GDP figures. For example, 2008 GDP per capita was $3,930 in Thailand and $1,640 in the Philippines.

As evidence of its pro-generic policy, the Thai government has announced the implementation of six compulsory licenses in the past two years. Moreover, the registration process for a generic product is much faster compared with the registration for original drugs due to bioequivalence studies and minimum data protection.

This policy clearly reflects the attitude of the government toward generic companies and pharmaceutical innovators. Further, many generic companies may rely on the Bolar-like provision in the Thai Patent Act, which permits a generic company to rely on the original drug in order to obtain the marketing approval with the Thai FDA after the expiry of the patent.

The Philippines has also demonstrated a pro-generic approach, especially since the adoption of the Universally Accessible Cheaper & Quality Medicines Act in 2008 (also known as the Cheaper Medicines Law). The aim of this Act is to facilitate the distribution of generics and lower the price of the drugs in the market. The changes brought by this new law can be divided into three main categories: (i) strengthening competition, (ii) relaxing patent rules, and (iii) allowing price controls.

To encourage the introduction of generic drugs and medicines into the market immediately after their expiration, the Cheaper Medicines Law has legitimised the "early working" of patents on original drugs.

Compared with other statutes, the Cheaper Medicines Law is more explicit since it expressly authorises a generic company to test drugs for future commercial purposes and to submit data to the regulatory agencies.

patent linkage

Patent linkage is a means of determining whether a drug would infringe a registered patent before the granting of marketing approval. The objective is to prevent the registration of generic drugs before the extinction of the patent for the original drug.

Since 2005, the Philippine Bureau of Food and Drugs (BFAD) has been accepting and processing applications for product registration without the need to verify whether the pharmaceutical being submitted for registration is under patent protection. Moreover, the BFAD is also exempted from respecting such patents, even though they may be aware of their existence, and thus can grant the marketing approval of a generic.

At present, the Thai FDA does not have a firm legal obligation to determine whether a particular drug formula or active ingredient is patented in Thailand when arriving at a decision about whether to grant marketing approval for a generic. Thus, Thailand does not have a formal patent linkage system.

In absence of patent linkage, pharmacists and doctors may believe that patent registration and drug registration are separate rights. In practice, however, these rights are usually linked. Indeed, before applying for marketing approval, pharmaceutical companies dedicate significant resources to patent registration to protect the drugs against counterfeiters.

Countries like the US have been promoting bilateral trade agreements, which usually contain a reference to the implementation of data protection or data exclusivity for a period of five years for pharmaceutical products and three years for new clinical information. This protection is called "TRIPS-plus" since it is not mandatory for the signatories of TRIPS to implement this protection.

Data exclusivity is aimed at safeguarding with the FDAs the registration files for pharmaceutical products that are deemed to contain trade secrets These data, especially clinical studies, are important for generic companies because when filing an approval application, these firms will claim bioequivalence to the original drug, arguing that their pharmaceutical products are clinically interchangeable in terms of efficacy and safety and that they meet the requirements regarding quality standards.

By implementing a data protection system, the FDAs cannot rely on data that are TRIPS-plus protected when registering a generic product. Due to this protection, generics companies would have two options: either conduct clinical trials or wait until the expiration of the data protection.

In Asia, data exclusivity is not always guaranteed because the guidelines across the region are often unclear. However, almost every ASEAN country has set up a data protection or exclusivity system.

Some particularities in these systems are apparent. In Thailand, for example, even though data protection lasts for five years from the date of recordation, the protection available is limited to physical protection. In Malaysia, five-year protection for data exclusivity starts from the date the product obtains the same protection in its country of origin.

Singapore also provides protection for five years, but the protection period begins from the filing date of the originator product. In Vietnam, data protection is not automatic and has to be requested to be applicable. Interestingly, data protection does not apply to new chemical entities in Vietnam.

expediting new drug approvals

Although the foregoing difficulties are significant, strategies are available to overcome them.

The FDAs may sometimes require additional documents or information to grant marketing approval. These requirements, however, can sometimes pose problems for pharmaceutical companies when they come into conflict with IP rights or other interests.

When facing a difficulty regarding the registration of the elements to include on labels, for example, companies could draft a letter or set up a meeting to explain the issues involved. FDA representatives are scientists and may not be knowledgeable on IP matters. Sometimes, a short explanation on the IP rights involved can clarify how the disclosure of certain data, or the content of certain inserts, could contravene patent or trade secret protection.

Writing letters to officials in English is usually not effective since they may not be proficient in the language. All interactions should be conducted in officials' native language to facilitate discussions. Even such a proactive approach may be of limited value because of the common belief that pharmaceutical companies do not try to protect consumers.

It is generally agreed that counterfeits of pharmaceutical products are an unacceptable threat for patients and can lead to dangerous risks such as death or permanent injuries. Drug regulators deem as counterfeit any drugs which contain incorrect ingredients, incorrect amounts of active ingredients, or no active ingredients at all compared with the genuine drug.

According to legal principles, however, counterfeit drugs can cover broader circumstances. Indeed, a drug can be considered counterfeit when the trade name of the drug is identical or similar to the brand name of the innovator drug. In addition, the get-up of a product or trade dress can also be subject to infringement or piracy. Training is usually conducted for FDA representatives about counterfeit drugs or registration processes, but pharmaceutical companies should also try to set up education for them on IP issues.

This could be organised in association with IP offices and/or third parties. Rights granted by two agencies should not be contradictory and thus should be explained carefully during these training sessions.

Pharmaceutical companies, perhaps through industry associations, should try to request and discuss harmonisation between regulatory processes and IP rights, for example by referring to US practice. The point to be made here is that the rights granted within the patent system are undermined and cease to be effective if they can be overcome by other agencies.

Another risk is that companies may reduce the number of products to be launched on the ASEAN markets if they cannot be assured of the protection of their rights. This will lead not only to an increase in generics, but also to a decrease in innovation due to the lack of funds relating to patent protection. The danger of a market dominated by generics, of course, is that the drugs will not be able to respond effectively to new diseases that are certain to arise in the future.

Regulators often officially claim that the reason for the delays in drug approval is that pharmaceutical companies do not disclose enough information in the interest of consumers. However, an increase in confidential documentation could lead to a delay in the launch of a product, or even a withdrawal from the market. Patients will not have access to the drugs available in countries with more reasonable requirements.

Pharmaceutical companies should clearly state that their objective is to provide the widest access to safe and efficient drugs.

conclusions

There are many issues in ASEAN countries when it comes to registering a drug or a patent or protecting inventions. Pharmaceutical originators are faced with slow registration processes for drugs and patents, the absence of linkage between these forms of registration, and various pro-generic policies being increasingly

supported by ASEAN governments including compulsory licensing, expedited marketing approval and failure to recognise data protection.

It is essential that companies begin to work more closely with other agencies, like Asian IP departments, in an attempt to educate FDA representatives about IP rights and the risk of delaying drug approvals.

Changes to the regulatory framework are already underway in the ASEAN countries, especially since these states have begun implementing rules to harmonise their FDA regulations. Such rules are usually based on minimum international requirements.

In Thailand, for example, the Cosmetic Act was amended in 2008 and the Medical Device Act was replaced to comply with the new ASEAN harmonisation rules. Additionally, on January 1st this year the required documents for a new drug application with the Thai FDA became compliant with International Conference on Harmonisation guidelines.

This harmonisation process between regional FDAs should help to facilitate the work of foreign originator companies since they now have similar requirements in all the countries in which they are requesting marketing approval.

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