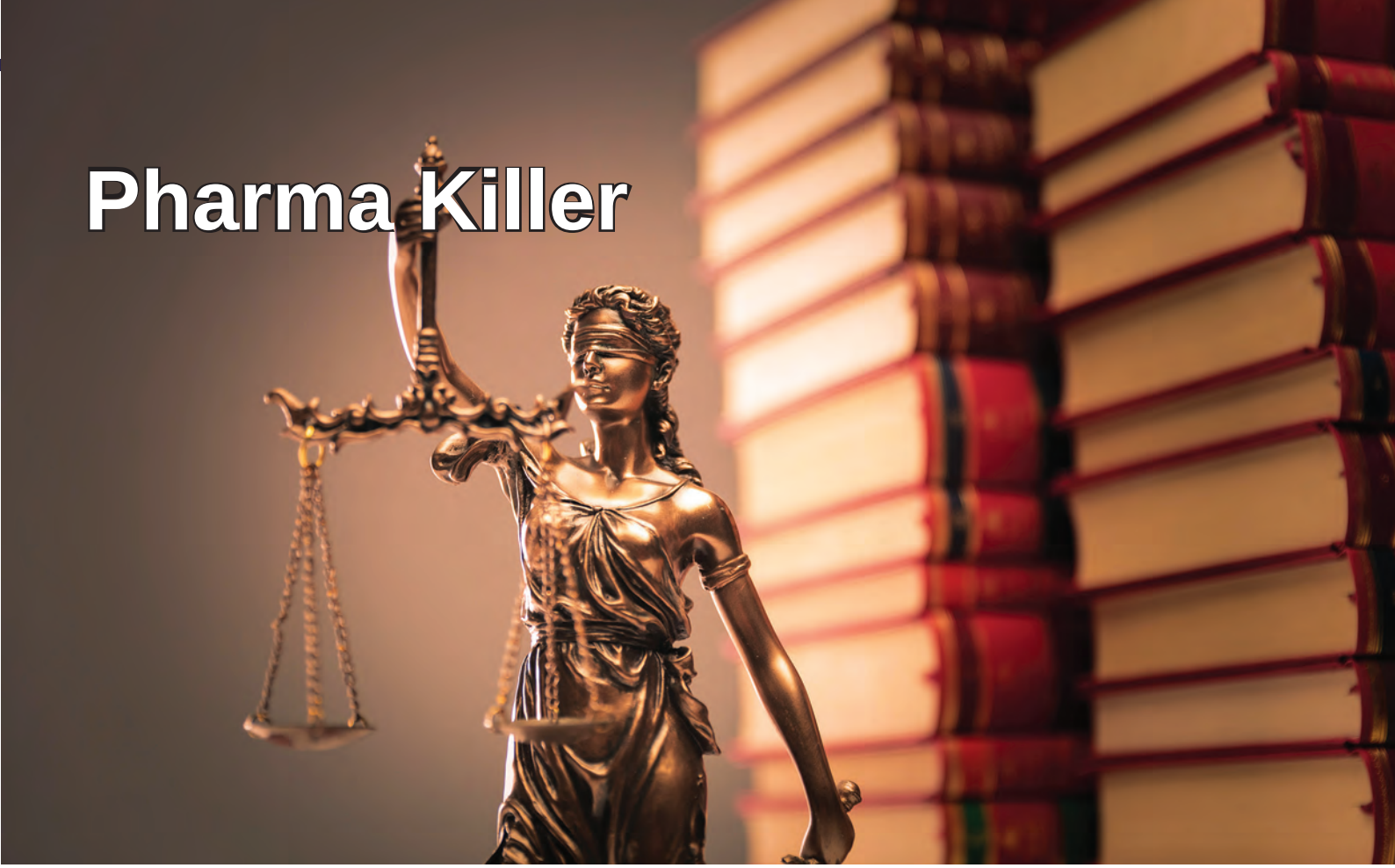
Pharma Killer



Attorneys tell **Johnny Chan** how to prevent litigation in the pharmaceutical industry, from a business and a government perspective.

The pharmaceutical industry is highly IP-intensive, and the drugs developed by innovative pharmaceutical companies are often the company's greatest assets. "For this reason, companies operating in this space must first secure their IP in-house before seeking patent registration and moving to market. This highlights the importance of maintaining robust in-house IP policies and procedures that address the creation and protection of IP developed within the company (whether registrable or not – whether positive or negative know-how)," says Alan Adcock, a partner and deputy director of the Tilleke & Gibbins IP and regulatory affairs groups in Bangkok. "As part of this practice, it is paramount to require all employees and contractors to sign strong employment agreements that include provisions on IP assignment, ownership and confidentiality obligations."

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Similarly, prior to embarking on R&D for new products or processes or commercialization of generic equivalents, a prudent company would conduct a freedom to operate analysis on the drug to confirm the absence of competing drugs in the patent space, or to assess the likelihood that a similar drug will present an obstacle to registration or a risk of future claims for patent infringement, says Adcock.

In the event of collaboration with an outside entity to develop a new drug, the relevant considerations are multiplied.

"In addition to the above, a collaborating company must also consider whether any prior working relationship exists with the collaborating partner (and conduct due diligence to spot any legal, regulatory, technical, or reputational problem areas), the primary aims of the collaboration, and the contributions that each partner will make to the development process. The partnership should be memorialized in a development agreement setting forth the details of the project and the understanding of the parties," he adds. "It is important to conduct this work early in the development process to avoid or mitigate any potential issues from arising later on."

Generics & Authentics

Can branded and unbranded generics be expected to grow faster than patent-protected and non-protected branded drugs? The answer is yes.

More specifically, authorized generics are expected to grow faster than standard generics. "Thus, authorizing a certain drug maker to manufacture the generic before the patents are expired can be one of the possible strategies which the original drug makers can take in order to compensate a decline in sales of the brand-name drug due to launched generics," says Kunimitsu Komatsu, a senior associate at Nakamura & Partners in Tokyo. "The authorized generic can be placed on the market earlier than standard generics. If the brand-name drug has been approved in relation to various indications or applications, the authorized generic can also be used for these indications or applications whereas standard generics cannot be approved for indications

Impact of the Comprehensive and Progressive Trans-Pacific Partnership (CPTPP) in New Zealand

When the United States pulled out of the Trans-Pacific Partnership trade agreement in 2017, it was unclear whether any trade agreement would be possible. However, the remaining parties to the TPP negotiations persevered and signed a revised trade deal, the Comprehensive and Progressive Trans-Pacific Partnership, in March 2018, says Fiona Pringle, a senior associate at Baldwins in Wellington. "The CPTPP includes some provisions that will affect New Zealand's patent law but also removes some of the IP provisions which would have been included with the TPP."

> "If the original drug is covered by a patent in New Zealand, then the **patentee will be notified of anyone** seeking to rely on that drug's clinical trial data prior to granting marketing approval. Currently, New Zealand has no patent linkage system."
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The measures that are included in the CPTPP are:

Grace period for patent applications. The CPTPP retains the requirement from the TPP that all member countries provide a grace period of one year prior to a patent filing date, during which public disclosure by the inventor or their assignee may be disregarded for the purposes of determining whether the invention is new, Pringle says. "Currently, there are only very limited circumstances in New Zealand where a grace period may be available (such as where the disclosures were made in breach of confidence or were for the purposes of reasonable trial)."

Patent linkage. Patent linkage provisions are also included in the CPTPP. "Patent linkage regulates situations where a pharmaceutical supplier wishes to gain marketing approval for a drug on the basis of bioequivalence with a competing drug already in New Zealand (e.g. a generics supplier wishes to introduce a generic version of a name brand drug). If the original drug is covered by a patent in New Zealand, the details of which have been provided to Medsafe (the New Zealand Medicines and Medical Devices Safety Authority which is responsible for the regulation of medicines and medical devices), then the patentee will be notified of anyone seeking to rely on that drug's clinical trial data prior to granting marketing approval," she says. "Currently, New Zealand has no patent linkage system."

Data exclusivity for agricultural and veterinary compounds. The CPTPP retains the requirement for a 10-year data exclusivity period for agricultural chemical products that was part of the original TPP, she says. "However, this has been part of New Zealand law since the term of data exclusivity for agricultural and veterinary compounds was extended to 10 years in late 2016."

Measures that were part of the TPP negotiations but have not been retained in the CPTPP include:

Data exclusivity for pharmaceuticals. Provisions extending the period of data exclusivity for pharmaceutical products and biologics have been discarded, she says. "New Zealand's current period of data exclusivity for new pharmaceutical compounds is five years and this will remain."

Patent term extensions. New Zealand's maximum patent term will remain a non-extendible 20 years, she says. "There are no provisions in the CPTPP providing patent term extensions for unreasonable delays in the patent office or for marketing approval."

- Johnny Chan

or applications covered by any second medicinal use patent still in force."

In addition, doctors and hospitals can effectively receive information on any adverse reaction of the authorized generic because the original drug makers provide such information based on not only the authorized generic but also on their brand-name drugs, Komatsu adds. "Doctors and hospitals in Japan put their trust in the brand-name drugs and are used to preferring them to generics, although the recent rate of generic use in Japan has been increasing."

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Another possible strategy to protect a brand-name drug would be to obtain various patents covering the brand-name drug from various perspectives so as to make the preliminary coordination advantageous, he says. "A further possible strategy would be to enhance the marketability of the brand-name drug, for example, by obtaining approvals of various indications or applications covered by the second medicinal use patents. By using the above strategies in combination, the original drug makers may minimize a decline in their market share."

Generic drugs benefit from reduced overhead costs in that they are not required to conduct full clinical trials or pay marketing costs to develop public awareness of their products, says Alec Wheatley, a consultant in Tilleke & Gibbins' IP group. "This allows them to offer a reduced price point for a product that has already been established and proven in the market. Generics may further take advantage of emerging markets where price of drugs is a primary concern in order to obtain market share."

Nonetheless, there are a number of factors weighing against the growth of generics. "Patented products will continue to benefit from the limited monopoly granted by patent registrations for development of innovative new drugs. This enables patent owners to build up sizable public awareness of their drugs under the brand name, which continues to inure to their benefit long past the expiration of the patent," Wheatley says. "Further, generics may experience high rates of competition and attrition due to the availability of an expired drug patent for use by all."

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For pharmaceutical companies to fully benefit from the time and resources invested in the R&D process, it is imperative to consider filing patent applications for as many aspects of a developed pharmaceutical product as feasible, including an invention patent covering the product itself, and if possible, a process patent covering its formulation, he adds.

A pharmaceutical company can help further ensure protection for its drug by raising the level of public awareness about the product, such as by educating the public of the exclusive rights provided by a patent registration, he says. "A company can draw attention to the fact of patent protection by engaging with participants at all points in its product supply chain, including distributors and procurement officers at private and government hospitals."

Lawsuit Pandemic

As companies have increased their global reach, life science litigation has become more international.

"More IP disputes are happening between emerging Chinese pharma companies and traditional big pharmas, including both patent invalidation proceedings (by SIPO) and patent infringement proceedings," says Ethan Ma, a partner at Orrick,

Herrington & Sutcliffe in Shanghai. “At the current stage, what is especially alarming is the growing number of patent invalidation cases against big pharmas in China. For example, recently there have been cases against AstraZeneca, Daiichi-Sankyo, Novartis, etc., and, in many of them, the patentees lost their patents in China.”

> “Even fewer of these drugs are in fact able to generate enough interest that will enable them to penetrate the global market. It is most often the case with life-saving drugs or blockbuster drugs which can bring about an improvement in the cure or management of long-term, serious diseases.”
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Patent linkage does not work for disputes between the original drug makers. “Since the original drug makers are global companies who sell their products worldwide, their litigation is international,” Komatsu says. “I have handled several cases where disputes arose not only in Japan but also in the US and/or Europe. The companies involved have to consistently address such disputes throughout the world. Sometimes, disputes between the original drug makers seem to result from a patent granted with a broad claim which can cover a medicament under development by another company. In order to ensure a stable drug supply, a patent examiner should pay attention to the influence of granted claims so as to allow a patent having an appropriate scope.”

R&D operations in the pharmaceutical sector, particular development of new chemical entities often involve a large financial outlay. However, not all potential drug candidates result in a final marketable drug, and only some make it past the clinical trials and regulatory approval stage, says Vaishali Mittal, a partner at Anand and Anand in Noida. “Even fewer of these drugs are in fact able to generate enough interest that will enable them to penetrate the global market. It is most often the case with life-saving drugs or blockbuster drugs which can bring about an improvement in the cure or management of long-term, serious diseases.”

Thus, in order to protect their interests globally, most medium-to-large pharmaceutical companies are known to follow a multinational patenting strategy covering several major jurisdictions, Mittal says. “This is important as patents are territorial rights which are enforceable only in the country where the patent has been granted.”

India has in the past decade witnessed some hard-fought patent battles between major international drug companies, such as Roche (Erlotinib, aka Tarceva) and Merck (Sitagliptin, aka Januvia), and local generic drug manufacturers such as Cipla and Glenmark. “While a large number of patent infringement suits are regularly filed by drug patent holders in Indian Courts, specifically the Delhi High Court, for various reasons parties have historically shown a tendency to settle their disputes amicably, usually shortly after grant of injunction, and as a result there have only been a handful of disputes which have progressed to the stage of final determination of infringement,” she says. “Neither of these have however been part of a global, cross-border litigation strategy, as part of which a pharmaceutical multinational would enforce the same patent, possibly against the same infringer, in multiple jurisdictions where said infringer operates.”

Rules

While litigation is inevitable in some occasions, having better regulations in place can definitely help minimize risks.

Insofar as India is concerned, uniformity and persistence in law, legal enforcement and policy-making law can play a key role in streamlining industrial operations and catalyzing growth in its pharmaceutical sector, unhindered by frivolous and frequent litigation and regulatory hurdles, Mittal says. “There is, however, a distinct incoherence in the way litigation, given a particular set of circumstances, is managed and decided from one high court to another, which by itself is terribly out of synchronization with procedure and practice followed by the regulatory bodies and tribunals, such as the Competition Commission of India. Lack of settled jurisprudence, and coherence and clarity in policy has led to a large number of disputes arising within the foreign and local players in the Indian pharmaceutical sphere.”

Law and policy reforms may comprise measures such as placing a larger focus on availability of compulsory licenses for essential and life-saving medicines, ensuring wider access to such medicines as well as appropriate compensation for the right holders, all while avoiding costly litigation or dispute resolution, she says. “While faulty policy-making has handicapped earlier efforts by the government at fixing ceiling prices for particular drug compositions, perhaps a fresh and evenly balanced take on the same may help reduce the inherent friction between licensee and licensor in the pharma industry.”

There could also be an increased emphasis on alternative dispute resolution mechanisms and perhaps even a compulsory direction to disputing parties to initially submit to alternate dispute resolution proceedings before entering full-fledged litigation in an effort to resolve the dispute amicably and through unbiased and assisted negotiation without having to resort to litigation.

“In fact, such a practice is already in place in the Delhi High Court where disputing parties have an option to enter pre-litigation mediation in an effort to avoid having to litigate to resolve the dispute,” she adds. “Moreover, even after a suit is filed, parties are consistently encouraged by the court to enter at least one round of mediation before proceeding to decide the matter by

taking the usual adversarial approach."

Patent linkage is used in Japan as an effective ways to minimize the risk of litigation. "The number of all the patent litigation cases in Japan is not so many – only around 150 per year – but manufacturing and marketing approval of generics often results in disputes between original and generic drug makers," Komatsu says. "In order to ensure a stable drug supply, the drug regulatory authority, the Ministry of Health, Labour and Welfare, asks the original drug makers to submit a list of their patents. Among the listed patents, the MHLW takes into consideration a substance patent and/or a second medicinal use patent, each of which covers an active pharmaceutical ingredient contained in an approved drug. The MHLW does not approve manufacture and sales of generics as long as the above patents are in force."

However, it does not seem that the patent linkage in Japan is fully functioning in order to reduce disputes. "When the substance patent and some of the second medicinal use patents are expired, but the rest of the second medicinal use patents are in force, the MHLW can approve the manufacture and sale of generics except for the indications or applications covered by the patents still in force. This leads to off-label use, which can cause further disputes," he says. "In addition, patent linkage is just a policy of the MHLW, and is not supported by any law. Generics covered by the original drug makers' patents are sometimes approved for unknown reasons. The patent list would not be made public, so the generic drug makers cannot know the listed patents which may cover their products until they apply for marketing approval."

Moreover, the MHLW does not take into consideration original drug makers' patents relating to pharmaceutical formulations and manufacturing methods even if these patents cover approved drugs, and does not evaluate whether these patents actually cover generics, he adds. "Instead, after approving manufacture and sales of generics, the MHLW orders coordination between the original drug maker and the generic drug makers (so-called preliminary coordination) regarding patents which may cover the generics. However, both parties do not always agree with each other."

Besides improved enforcement of patent linkage, another important governmental policy that should be instituted is for regulators to require applicants of generics to disclose any and all related pharmaceutical patents at the FDA drug submission stage before an approval is granted. "Currently, Thailand does not have this requirement for generics – but surprisingly, it does for new drugs. This compulsory disclosure would provide greater clarity to the reviewing officer at the FDA, and could result in a reduction in the number of infringing generics granted approval in non-Bolar exemption jurisdictions," Adcock says. "In turn, this would see a corresponding reduction in the overall potential for litigation by patent owners obliged to monitor both FDA databases for granted generic approvals and the market for infringing commercial activities." AIP