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Consider them emerged

Emerging markets are a way of overcoming patent expiries, and much more besides, according to a panel of experts



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How and why are life sciences companies turning their attentions to emerging markets?

Blaine Templeman: Life sciences companies turned their attention there a long time ago. Most large pharma companies implemented international growth strategies that included emerging markets decades ago. The focus has become only more intense. As to why—the US system for commercialisation of products is broken in some respects, and some of the problems result in under-served world markets.

As to how, my clients consider not just one, but a number of factors when working on a product—pricing, logistics, partnering and other concerns—in order to develop a holistic plan for product development and commercialisation. A balanced approach serves both the public good and shareholder interests.

Celine Crowson: Some say that the BRIC countries (Brazil, Russia, India and China) account for roughly half of the global population, and that their economies are generally growing rapidly. Some have predicted that China could become the second largest pharmaceutical market after the US by 2015. Thus, some companies believe that for their continued success and growth, they feel that they must expand their business into emerging markets.

Michael Wise: Life sciences companies have turned to emerging markets for low cost manufacturing, R&D opportunities, and to obtain market share in rapidly growing economies that represent an increasing share of the global pharma market. The rise of a less expensive educated work force and the existence of government incentives for foreign investment combined with fewer environmental, health and safety regulatory burdens make emerging markets an attractive location for manufacturing and R&D facilities.

Emerging markets often have unmet needs for medical products compared to saturated markets in developed markets such as the US and the EU.

With expanding economic development in emerging markets, and governmental healthcare reform in countries such as China, meeting these unmet needs provides potential fast-paced sales growth, especially for relatively inexpensive products that have low IP value.

As emerging markets continue to promote research and development and strengthen IP protection and enforcement, life sciences companies will expand R&D investment and include new product releases in these markets.

Teresa Lavenue: Life sciences companies have expanded into emerging markets with strategies beyond merely entering the market with pre-existing drugs. Some conduct

research locally regarding specific medical needs of local patients and tailor products to those needs. For example, different viral diseases or cancer types may be more prevalent in an emerging region than in the US or in Europe.

Other strategies involve providing access to drugs or developing new combinations that are less expensive to encourage patient compliance. Further, where a large proportion of the population lives in remote areas and as such access to prescription refills can be problematic, companies have explored whether a different dosage form or formulation may be more appropriate.

Additional strategies relate to identifying genetic biomarkers that may be specific to certain patient populations (the presence or absence of certain biomarkers can influence the effectiveness of certain therapies).

Since patient populations in emerging markets may have different biomarkers, companies are researching this aspect too and may include these patient populations in clinical studies.

Michael Roberts: Life sciences companies need to be mindful of not only established markets for their products (and/or services), but also markets that may become commercially valuable in the near or medium-term future. This is particularly important in the life sciences field where product development can take several years. IP protection needs to be put in place, and regulatory hurdles need to be overcome before a product can be put on the market for sale.

Early planning allows life sciences companies to be best placed to be successful in emerging markets.

Paul England: As with so many other product industries, life sciences companies see the emerging markets as an opportunity to reach a vast new body of consumers. But for the big small-molecule pharma companies, in particular, there is an added impetus. This is that the gains to be had from such markets can ease the burden of funding research into new drugs to replace those going off patent.

In addition to this, access to emerging markets with sufficiently strong IP protection affords opportunities to tap into local scientific expertise and other skills for the purpose of research, development and manufacture of new drugs.

Stephen Garner: Maintaining access to affordable healthcare is very important in the emerging markets, where the costs of patented drugs can be prohibitive. In India, for example, it is estimated that patented drugs account for less than 10 percent of total drug sales. Regulatory authorities in some emerging markets may also seek to prevent or delay the patenting of new drugs.

As a result, emerging markets are often viewed as favouring domestic companies and generic drug producers. This discourages foreign investment and can limit the availability of new medicines.

Innovator drug companies rely on the 'reward' of a patent to recover the huge costs associated with bringing a new medicine to market. However, the duration and scope of protection available is severely limited in some emerging markets, with countries setting special requirements for patenting pharmaceuticals, which are more stringent than for any other technology.

It can also be more difficult to obtain the range of patent claims, eg, to new medical uses or specific formulations, needed to provide optimum protection for pharmaceuticals.

Even once a patent is granted, innovators are at a disadvantage when it comes to enforcing their rights in emerging markets. National courts in these countries are often perceived to favour generics over innovators.

Patentees are also more likely to see their technology subject to compulsory licensing, resulting in a loss of control for the patentee over who uses their technology and what royalties they receive.

Despite these challenges, the slowing of sales in developed markets means that companies no longer have an option to ignore the tougher emerging ones.

Garreth Duncan: There are a number of reasons that emerging markets are becoming much more important in the strategies of the research-based pharma industry. One reason is to help counteract the drop in revenue caused by patent expiries on blockbuster drugs.

The big squeeze on government spending that most countries, particularly in Europe, have gone through in the last few years has increased pressure on pricing in these countries, and so is also a big factor as this makes it much more difficult for the industry to make a return on the \$500 million to \$1 billion investment it typically takes to bring a new drug to market based on established markets alone.

Pharma companies assess markets based on factors such as a country's population size, incidence of the disease in that population, and the likely price that can be charged for the drug in that country.

The emerging markets of greatest interest—China, India, Brazil and Russia—all have large populations and rapidly growing middle classes who have access to and are able to pay for much more than they could even a decade ago. These two factors combine to make the market for pharma products in these countries much more worthwhile than before.



How are life sciences companies adapting their IP strategies when entering emerging markets, where laws tend to be different than those in the likes of the US and Europe?

Garner: Life sciences companies are struggling to adapt their IP strategies to obtain commercially meaningful protection in emerging markets.

The scope of patent protection available in emerging markets is typically narrower than elsewhere in the world, especially in the pharma field. There are also more limited options in developing patent portfolios for drugs, which can lead to a shorter duration of protection in emerging markets.

In view of this, drug companies are focusing their IP specifically towards their (pre)clinical candidates, to guard against generic medicines rather than similar products from competitors, and are placing more emphasis on their earlier patent applications, which expire sooner.

The approach taken to patentability is forcing innovators to alter both the timing and also the content of their patent filings to ensure that they maximise the protection available.

Despite improvements, emerging markets are also perceived to offer weaker patent enforcement options. Patentees generally have to accept that their monopoly position is more easily undermined, with national courts often

viewed as acting less favourably towards innovators when considering both the scope of protection provided by a patent and also the extent of any alleged infringement.

Compulsory licences may also be more readily available in the emerging markets and patentees therefore need to price their technology carefully, especially in the pharma sector. Life sciences companies also need to consider carefully the effect that entering an emerging market will have on their global patent strategy.

Duncan: In terms of patenting new active pharma ingredients, I don't think the strategy is that much different for emerging markets or more established markets such as the US, Europe and Japan. The difficulties that pharma companies encounter in emerging markets are more based around secondary pharma IP such as new formulation technology and second medical uses, as well as the lack of patent term extension and the lack of regulatory data protection (or, where it exists, its shorter duration) in many emerging markets.

Breaking into many emerging markets is seemingly as much about marketing strategy than IP strategy. However, to counteract the less favourable IP regime in these countries, it's likely that pharma companies would look to lobby national governments (especially in countries where they have a lot of research jobs) to put more pressure on emerging market countries to conform their patent laws to international standards such as the World Trade Or-

ganization's (WTO) Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS).

However, this is a long, drawn out process that will take much time and patience.

Roberts: It is critical that IP advisors to life sciences companies keep up to date with IP law and practice in emerging markets. This will have an effect not only at the very early stages of enacting IP strategy—for example, drafting a new patent application that is expected to be prosecuted in emerging markets—but also at later stage of prosecution or litigation of different forms of IP such as patents, trademarks or registered designs. IP advisors should have a good relationship with reputable IP attorneys within the emerging markets.

Crowson: Life sciences companies are focusing time and resources to attempt to fully understand both the legal and practical implications of IP law in emerging markets. This often includes engaging local counsel to provide insight into the IP environment and to understand how to work within the local culture to protect the IP most effectively. Life sciences companies are looking at obtaining multiple levels of IP protection beyond just patents. For instance, they may pursue patent protection on a drug compound, but maintain the method of making the compound as a trade secret.

Companies may employ unique methods to assist in tracking or monitoring infringing activities or products. One such example

involves adding tracking compounds into chemicals that can be traced.

England: Because of the importance of maintaining market exclusivity to the business model of research-based life sciences companies, a strategy of strong patent protection is important. The protection and enforcement of the brand against counterfeits is also crucial in order to protect consumers, and avoid reputational damage and millions of dollars worth of lost sales.

As a result, many of the biggest life sciences companies now have sophisticated IP professionals working in teams that cover emerging markets as well as the traditional territories of the US and Europe.

Templeman: Current strategies continue to be similar, in many respects, to those used in the past. Strong maintenance, defence, and enforcement of patent rights are still the first step in protecting a product. But clients are recognising the power of brand, reliable supply, mass production, quality, availability, and pricing.

You may have a product protected by patents, but you must get the rest of the formula right in order to compete in emerging markets.

Lavenue: Many life sciences companies are considering forming collaborations or partnerships

with local business entities, which may lead to a favourable perception that the company, the manufacture, and sale of the drug/product benefits the local economy. For example, the company may have a local partner set up research facilities in the emerging region and hire local talent; or run clinical studies to study local populations; or locally manufacture. By working with local partners, the local culture may be shaped to understand the importance of IP protection.

When a company is considered a 'local' company (by being located in the region and by employing many of the local population), the population and the government may feel that they have a stake (and thus do more) in protecting the company's IP to ensure 'their' company's success.

What are the potential IP challenges for companies entering emerging markets?

Crowson: When considering patenting, each country may have slight variations in what is considered patentable subject matter and what is considered novel and unobvious. A company may be able to obtain a patent for a particular technology in one country but not in another.

Each country may have its own rules regarding what must be written in the patent specification to support patent claims. For example, China

often requires practical verbatim support for any claim amendment and provides limited opportunities for claim amendments.

To assist in navigating the particular country's patent intricacies, companies often solicit local IP counsel input and advice early on in the patent prosecution process, even before the international application is filed, to ensure an application filed in an emerging market is well-positioned.

Duncan: There's no doubt many pharma companies are facing an IP regime in emerging markets that's much less favourable than their established markets.

Although patents for new active substances are essentially allowed everywhere, emerging markets are trying other ways to restrict pharma patenting.

In India, we've recently seen the challenges faced by Novartis in the Gleevec case. Section 3(d) of India's patent law restricts the patenting of new forms of old drugs unless they differ from the original with respect to therapeutic efficacy.

This denies patent protection to other pharma inventions such as those based on improved safety, better pharmacokinetics and metabolism, and improved stability, regardless of whether they are novel and inventive in their own right.



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In addition to India, the majority of emerging markets, including Brazil and China, have no provisions for patent term extension. Also, many South American countries forbid the patenting of second medical uses. Many emerging market countries, such as Brazil, are using the provisions permitted by the WTO Doha Declaration to apply compulsory licensing on HIV/AIDS drugs.

But it's not just legal measures the research-based pharma companies are up against, you only need to look at the hysteria the Gleevec case in India generated to see the general hostility to IP from many in these countries.

Wise: The main IP challenges in emerging markets are the limited scope of protection and the difficulties in enforcing IP rights. The laws and regulations regarding IP protection and enforcement in many emerging markets countries are unpredictable and still evolving. For example, some countries (eg, India and China) were late to provide patent protection for new chemical entities used in pharmaceuticals.

Additionally, the lack of awareness among the general public regarding IP laws and regulations, less experienced and fewer qualified patent examiners, judges and government officials involved in the enforcement of IP rights, and governmental protectionism, especially on the local level, add to the challenges of obtaining and enforcing IP rights in emerging markets.

Lavenue: Further, the lack of reliable redress for patent infringement causes much concern among life science companies entering emerging markets. Companies are forced to consider whether they should continue to conduct business in regions where there is rampant, even government condoned or sanctioned IP misappropriation. Does the loss of income due to grey market sales outweigh any gains made on legitimate sales?

In addition, a company may need to balance the investing of millions to create drugs/products for treating smaller patient populations in emerging markets against diminished IP protection in those markets.

Roberts: My opinion is that key IP challenges are: (i) the scope of protection afforded by registrable IP in emerging markets; and (ii) the enforcement of registered IP.

England: A particular difficulty presented by IP is its territorial nature. Different countries have different laws and standards of protection for IP. Consequently, a patent or trademark that is enforceable in one country may not be enforceable in another, or not as quickly or effectively. Furthermore, some countries abide by very different standards of validity, making some products more difficult to protect than in others. Issues of compulsory licensing may also be faced in some countries, as well as endemic problems of counterfeiting.

These issues are typically highly complex, and getting them right can make an important difference to the success or failure of a product.

Templeman: The greatest challenge is finding practical advice that reflects best practice for the market. Often, the law does not reflect what is actually happening on the ground.

What effect are patent expirations having on companies' decisions to look at emerging markets?

Crowson: With patent expiring in developed nations, life sciences companies realise that the revenue from the patented drug will likely be quickly and drastically reduced by generic sales. Thus, companies may consider emerging markets as promising new sources of revenue for their drugs and products.

However, because relevant patents are expired or may not have ever been obtained in an emerging market, or because there is considerable IP theft in the market, companies may consider selling a branded generic, or working with a local partner to manufacture and distribute drugs/products. Some companies may consider selling a drug as a generic by forming an alliance with an already well-established generic manufacturer in the emerging market to conduct bioequivalence studies and to make and distribute generic drugs.

Roberts: In my view, for many emerging markets it is expected that patents will be enforceable. Patent protection therefore remains a gold standard to underpin commercial success in emerging markets. However, for those



emerging markets where other factors may impact more significantly on success, and for example where there is an environmental bias towards generic rather than innovator companies, the absence of a patent may be perceived as less of an obstacle to success. Such emerging markets may be more attractive to market products are due to go off-patent.

England: In very broad terms, patent expiry on blockbuster drugs results in market competition for originator companies from generic pharmaceuticals and places pressure on profit margins. This is exacerbated by the need for the research-based companies who produced those drugs to find new products. However, the cost of the research to find new drug candidates is very high. Hence one of the ways in which a company can continue to grow revenue and fund this research is to find large new markets.

Templeman: Patent expirations are one of the primary drivers. The other factors include the need to expand profits and the desire to improve public health.

Duncan: Everyone knows the effect patent expiries have had on research-based pharma companies' revenue over the last few years. For example, when Pfizer's patent for Lipitor expired in 2011/2012, its 2012 annual report indicates they lost \$5.6 billion in sales of the drug, which almost accounts for the entire \$6.3 billion decrease in the whole company's revenue that year. Similarly, when AstraZeneca's

patent for Seroquel expired in 2012, it lost \$3 billion in Seroquel sales—more than half of the company's decrease in revenue that year.

Both companies have turned to emerging markets as a way to fill the gap. Pfizer have set up an emerging markets unit, results being available from 2010 onwards. Its 2012 financial report indicates emerging markets revenues increased 7 percent in 2012 compared to 2011, primarily due to volume growth in China, Brazil and Russia, and specifically mentions it's a result of more targeted promotional efforts for key innovative and established products, including Lipitor, Norvasc and Lyrica.

Similarly, AstraZeneca's 2013 full year results, published last month, illustrate this. It has specifically targeted emerging markets as a growth area, and it's been successful: while its revenue in the US and Europe were both down 9 percent in 2013 compared with 2012, its revenue in emerging markets was up 8 percent over the year, mainly driven by China.

The US is worried that the 'Indian IP model' will be copied by other countries—what is your view on this?

Wise: Countries in emerging markets generally have weaker IP protection and enforcement than in developed markets. However, many countries in emerging markets have joined or are trying to join the WTO to take advantage of

the economic benefits of General Agreement on Tariffs and Trade (GATT). Strengthening IP protection through TRIPS is typically a prerequisite to join the WTO. India and China revised their IP laws to join the WTO under TRIPS. As economic growth and education advances in emerging market countries, domestic IP flourishes, which fosters better protection and enforcement of IP rights.

Finally, countries in emerging markets that seek to transition from a labour-intense economy to an innovation-driven economy must strengthen IP protection and enforcement. Consequently, the 'Indian IP model' is unlikely to be a model of choice for countries in emerging markets.

Crowson: India's Intellectual Property Appellate Board (IPAB) has upheld compulsory licences to generic manufacturers on pharma products. Affordability and product access were cited as justifications for such compulsory licences, and the licences have lowered drugs' prices dramatically (although in some cases manufacturers have retained a royalty on sales by Indian generic manufacturers).

The mechanism of compulsory licencing in India is based on Section 84 of India's Patents Act, which provides that an interested person may apply for a compulsory licence to work the patented invention on any of the following grounds: the reasonable requirements of the public with respect to the patented invention have not been satisfied; the invention is not



available to the public at a reasonably affordable price; or the patented invention has not been worked in the territory of India.

Lavenue: Some companies consider whether a compulsory licences can be avoided by forming a partnership with a local company to make and sell drugs locally at a reduced price (with lower costs and increased volume). Some wonder whether reducing product prices in an emerging market will raise the prices in other countries.

Additionally, lost revenues for a product may cause a life sciences company to spend less on R&D and product development. Will less risk be taken on newer technologies?

All of these concerns may make other countries wary of or not eager to embrace a compulsory licence approach with abandon. Rather, the focus may be on encouraging life sciences companies to invest in emerging markets by myriad other means.

Roberts: The TRIPS agreement allows WTO countries to grant a compulsory licence under a patent, subject to various provisions and safeguards. It is of concern that WTO countries might grant compulsory licences too easily, thereby undermining the patent system. Innovator companies have avoided compulsory licences in some emerging markets by reaching agreements on providing drugs at affordable prices.

Whatever model is adopted by emerging markets to ensure important drugs remain accessible, my view is that international trade laws should be respected.

England: India has a well established generics industry that manufactures and supplies the market with off-patent small molecule

pharmaceuticals. This is a significant feature of the Indian economy and one that it is keen to protect. There is no reason to suppose that other countries, with different approaches to the life sciences industry, should therefore necessarily follow the 'Indian IP model'.

In any event, the life sciences business is changing, with biologics and biosimilars becoming ever more important.

This means that companies will adapt to new business models that are not split on the simple generics versus originator basis that is a familiarity of small molecule pharma.

Garner: Each emerging market presents its own challenges but the issues that affect innovators within them rarely occur in isolation. India may be leading the way with its tough stance on pharma patents.

When India issued its first compulsory licence to Bayer's patent for the anti-cancer drug Nexavar, effectively breaking Bayer's monopoly in order to lower the price of the drug, alarm bells started ringing for pharma companies worldwide. The predicted flood of compulsory licences in India has not materialised, possibly because of international pressure.

Nevertheless, compulsory licensing is just one mechanism available to limit the effect of patents driving up drug prices. The demanding approach to patentability taken by the Indian Patent Office is just as effective and is seen as a model for emerging markets, eager to support their generic drugs industries.

The Indian Patents Act places onerous restrictions on the patentability of pharmaceuticals, for example prohibiting patents to new forms, formulations or combinations of known drugs.

The Indian Patent Office has also set a high bar for assessing inventiveness.

These requirements combine to make patenting pharmaceuticals in India a significant challenge, severely restricting the ability of innovators to obtain meaningful protection for authorised drugs.

In view of the increasingly strict requirements for the regulation and authorisation of drugs, and the time taken to bring a new drug to market, emerging markets are in danger of removing the incentives to obtaining patent protection for pharmaceuticals if they adopt the Indian model. Innovators risk the gradual erosion of their patent position in emerging markets if such an approach is taken.

Templeman: As is always the case, there are many good things going on in India. Product innovation and scaling of production are two of those good things. We can learn much from Indian companies, namely, how patent protection must be balanced with the health needs of consumers.

Duncan: The Indian IP model is certainly a matter of concern for the research-based pharmaceutical industry. In my view, Section 3(d) of India's Patent Act is a violation of the TRIPS agreement, which India has signed, as it imposes an additional patentability criterion for pharmaceuticals compared with other inventions.

The TRIPS agreement clearly says you can't do this, as it specifies that patents should be available for all inventions without discrimination as to the field of technology.

However, now India's Supreme Court has affirmed the section in the Novartis Gleevec case, it will undoubtedly give encouragement to other countries that are hostile to pharma IP. Argentina and the Philippines already have a parallel to India's Section 3(d), and other countries are considering it.

The only thing that could reverse this tide would be a challenge to Section 3(d) at the WTO. There's currently a moratorium on WTO members bringing non-violation complaints under the TRIPS agreement at the WTO. At the last WTO ministerial conference in December 2013, it was discussed whether the moratorium should be lifted, or conversely turned into a permanent feature. The moratorium was extended once again, with the understanding a final agreement should be reached by 2015.

Although many countries supported the view that the moratorium should be indefinite, the US and Switzerland disagreed.

If the moratorium is eventually lifted, a challenge could be possible. However, in view of the high awareness of this issue, and the negative publicity that supporters of the law would inevitably generate, does any organisation have the will to see such a challenge through and take the brickbats that will inevitably fly in their direction? **IPPro**