Protecting life science patents in Latin America

Regimes for protecting pharmaceutical and biotechnological products via patents are slowly but steadily improving in many Latin American countries. **Managing IP** invited **Alejandro Luna** of **Olivares & Cia**, **Guillermo Carey** of **HarneckerCarey Carey y Cía** and **Regina Kuchle** of **AstraZeneca** to discuss some promising developments and continuing challenges

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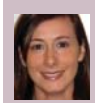

EM: Eileen McDermott
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EM: What regulatory changes have most impacted biotechnology and pharmaceutical patents recently?

AL: There was an amendment to the Mexican General Health Law in June 2009 which defined biotechnological drugs and allowed for the approval of follow-on biologics, or biocomparables.

Then, in September 2010, amendments were made to the Mexican IP Law, including an observation scheme during patent prosecution allowing any third party to raise arguments and provide the examiner with information related to the patentability of an invention. If filed, the information may be considered at the examiner's discretion and it will not suspend the application process. After a patent is granted, any third party can inform the Mexican Patent Office (IMPI) of causes of invalidity and IMPI can consider such information at its discretion as well.

At the same time, the industrial application requirement for patentability was modified to include a need to demonstrate the practical utility of the invention and to fully support such utility in the written description. This amendment of the law was promoted by the generic manufacturers associations, and it has not yet been implemented. We are waiting to observe the first cases to better determine how they will be handled by IMPI's examiners.

During the discussions of these amendments there was an unprecedented opportunity to include an authentic and balanced opposition system for patents, but unfortunately, the interests of some generics companies – which resisted formal opposition proceedings – barred the possibility of improving our patent laws.

EM: Regina, is Mexico's patent system a challenge for pharmaceutical companies?

RK: Mexico's patent linkage regulation enacted in 2003 has aided patent owners in preventing infringing generic entrance prior to patent expiration, although it is sometimes condemned as being unfriendly to healthcare access. Linkage's goal is to have the health regulatory authority (COFEPRIS) dismiss generic health approvals if the applicant has no authorisation to exploit the implied patent.

While this has proven prosperous for the pharmaceutical business model, it has also been characterised by flaws. The chief problem is with the vague language, which (1) fails to include pharmaceutical formulation and medical use patents and (2) is open to wrongful interpretation by both linked regulators, IMPI and COFEPRIS, in a way that these types of patents are overlooked when it comes to health approval for a generic using the patented formulation, for example.

GC: The failure to implement a patent linkage system together with the implementation of a Bolar-type exception have been the most relevant issues to impact bio and pharma patents in Chile.

Although under Chilean legislation a patent registration grants the owner the right to file for civil and criminal actions against any third party who maliciously manufactures, uses, offers or introduces to the market a patented invention or who imports it or is in possession of it for commercial purposes, there is an exception to this right in article 49 of the patent law. The provision states that invention patents do not grant the right to impede third parties from importing, exporting or manufacturing the matter claimed by a patent with the purpose of obtaining the registration or sanitary authorisation of a pharmaceutical product. However, these products may not be commercialised without the patent holder's authorisation.

This constitutes a so-called Bolar type exception, which was included and allowed under the Chile – US Free Trade Agreement, although with different wording and scope. According to the FTA, a party to the Agreement is only allowed to authorise the manufacture and export of the matter protected by the patent, but not the import of that matter, in contrast to article 49.

The FTA also establishes an obligation for patent linkage. However, that obligation has not been implemented or applied in Chile, and there has been no legislative proposal or bill introduced. Therefore, patent linkage is inapplicable in Chile.

From our perspective, the patent linkage provision in the FTA could be considered self executing, which requires no implementation by domestic law. This approach has nevertheless not been shared by the Chilean sanitary authority and government. The situation is worsened by article 49 regarding the Chilean Bolar-type exception to patent rights.

The new pharmaceutical product regulations set to become effective this December further clarify that no patent linkage system is applicable in Chile, since sanitary registration is considered independent from industrial property rights, including patents.

We have informal information that the Ministry of Health and the Ministry of Economy are working on a draft of bill to implement patent linkage provisions (in a form of a judicial patent linkage implementation) but no official bill of law has been published to date. The efforts are being undertaken by the government through inter-ministerial workgroups of discussions to put forth modifications both to our industrial property legislation and regulatory provisions which implement a patent linkage system.

EM: What is the landscape in other Latin American countries?

RK: The damaging impact that a deficient patent procurement system has on pharmaceutical companies should be a chief consideration for all political regimes. This is unfortunately an issue in most Latin America countries; however, some governments are taking measures to at least partially resolve the situation.

We're told Venezuela has not granted a single pharmaceutical patent since 2003

The government of Argentina has dealt with consistent pressure to resolve numerous patent issues for the last several years, including a backlog of up to 12 years for the mere grant of a patent. Local trade association and some law consultants in Argentina have lobbied for what is known as first and second fast track patent procurement by the IP Office (INPI). The first track came into effect in 2003, the second in 2007. Under each, applicants were allowed to meet certain requirements to accelerate their selected high priority patent applications. Many pharmaceuticals benefited from an accelerated rate of granted patents. The third fast track was introduced by INPI on January 11 2011. According to this resolution, patent applicants will request to swap the chronological order of examination of patents to accelerate the procurement of those considered high priority. The advantage is the reduction in procurement time by up to several years, and acceleration of patent issuance for pharmaceutical firms' priority cases.

AL: To our knowledge, the government of Brazil unfortunately has shown no intention of resolving the patent backlog issue. This backlog is not only induced by administrative failures, but also by the application of Article 229-C of the patent law, which provides powers to the health regulatory authority (ANVISA) to review, opine and consent on patent applications for pharmaceutical products, in addition to setting different patentability requirements as those used by Brazil's INPI. Although the Advocate General of Brazil has issued recommendations to limit ANVISA's role in the assessment of patents, this regulatory measure has created legal uncertainty to patent holders' interests and it is believed to undermine the incentive for greater R&D and innovative medicines. We're told that Venezuela has not granted a single pharmaceutical patent since 2003.

An in-house perspective: data package exclusivity

Regina Kuchle, Legal affairs director
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EM: What is the landscape for companies regarding data package exclusivity protection in Latin America?

Most Latin American governments continue to fall short in providing effective recognition and protection for DPE. Governments have been held to international DPE standards under the provisions of either TRIPs or local free trade agreements such as the North America or Central America Free Trade Agreements (NAFTA and CAFTA). In response, government have shown reluctance to meet with such standards by their continued health approvals of generic medicines, for which applicants have wrongfully relied on the safety and efficacy data which exclusivity pertains to the originator.

Pharmaceutical firms sometimes consider the continued lack of governments to properly enforce DPE a deterrent and a barrier when designing a business-investment model for a particular market.

EM: Is a DPE system like the ones in place in developed countries really feasible for developing nations? Is there some other type of model that might represent a compromise?

Data exclusivity is an IP right which affords its owner the exclusive use of test data by which they have proven an original medicine's safety. In countries such as Mexico, Brazil, Argentina, Guatemala and Peru, DPE is often referred to as a barrier to health as it is believed that DPE restrains generics competition and access to affordable quality medicines.

Additionally, DPE is often misconstrued as being one of three measures viewed as extending patent protection. The other two are extension of a patent's expiration date and linkage regulations. In view of these misconceptions, there is a critical need for broader and deeper knowledge of DPE and its exclusive use as an incentive to advance research and development. Policy and lawmakers of referred countries should first understand the DPE's positive impact on human health, especially when high-tech compounds are being reproduced in their generic versions without clinical trials or testing data proving the generic version's safety and efficacy.

Until intensive training is provided for health regulators and involved authorities, governments should decide on the best DPE model consistent with the highest international standards. Further, they should rely on the experience of other markets in adjusting their laws locally and in order to become compliant with FTAs or other international commitments.

EM: What specific efforts have been most effective in obtaining DPE or other bio/pharma-related provisions in the various jurisdictions you deal with?

While actors in the pharmaceutical industry have successfully worked been successful in pressing Congress, health and IP authorities for updating biopharmaceutical laws and other considerations, many officials, lawmakers and politicians' innate misunderstanding of medical science, pharmaceutical innovation and its contribution to human health, makes these efforts quite complicated. The tension between providing access to an efficient healthcare system and the laws that rule the pharmaceutical-related IP aspects comes from a cultural gap found in developing countries.

EM: What would you say is the single most important factor in winning the fight for DPE in developing nations?

Belief in the system. Trust in the legal frameworks and judicial systems despite all identified downsides, and become persistent in asserting the one reward for innovation provided by the Constitution of most states as an individual right. Believing and being persistent in protecting IP assets leads to the generation of creative, pioneering and precedent-setting laws.

Balancing biosimilars

EM: Is there any scheme for protecting so-called biosimilars in your countries?

AL: There is the draft regulation on biologics, which will soon be enacted. The draft includes a definition of comparability tests between an innovator and a biocomparable drug; an indication that biocomparable drugs will use the same name for the active ingredient as the innovator; a proposal to eliminate the three-year limit on the Roche-Bolar type research exemption so that submissions can be made at any time; and a provision indicating that when an innovator or reference drug will be manufactured in Mexico, the pre-clinical and clinical trials must be made locally.

Numerous amicus briefs were filed by the pharmaceutical industry devoted to R&D, domestic and transnational generics, and also by the Mexican authorities, providing the pros and cons of the proposed regulations. After months of discussions, it seems that there is a final draft regulation for biologics, and the pharma industry is anxious and expectant for their publication, as the lack of clear rules has generated a degree of uncertainty concerning approvals of both innovator and biocomparable drugs. Some have indicated that the publication of the new regulation was due for July or August 2011, but as of September there are no signs of publication in the Mexican Official Gazette.

EM: Regina, what impact would regulations on biosimilars in Mexico have on your business?

RK: These regulations should without doubt create legal certainty within the market and allow for the development of biologic and biosimilar products in a timely fashion. It is expected that the regulations should not affect the exclusive exploitation rights of patent holders. One issue still awaiting consensus is the time period prior to a product's patent expiry within which a company may conduct clinical studies to develop biosimilars without implying that the company is infringing patents.

EM: Guillermo, is there any framework for biosimilars in Chile?

GC: Present Chilean law recognises an abbreviated procedure for the registration of pharmaceutical products, similar to an Abbreviated New Drug Application (ANDA) process. However, the application of this system to biological products has generated great controversy.

In July 2006, the Chilean Ministry of Health said that, considering the technical impossibility of exactly reproducing biological products, they had to be excluded from the possibility of abbreviated registration. Therefore, every sanitary application for a biological product must be accompanied with its own clinical studies and be presented as a new pharmaceutical product. A subsequent decree issued by the Chilean Ministry of Health incorporated ambiguous wording that could be interpreted as permitting the registration of biological products under the abbreviated procedure indicating that the applicant for a follow-on biological product will have to demonstrate it has the same active principle, the same quantity of API per pharmaceutical form and the route of administration as the registered innovator biological product. However, we are of the opinion that a follow-on biological, especially biotech products such as interferons or monoclonal antibodies, cannot be submitted under this approach considering that it will never share the same active principle as the innovator biological product.

The new law that will come into effect in December refers expressly to biotech products and states that the Chilean Ministry of Health will set forth a technical norm which will establish the active principles and its presentations for which the authority will be able to accept the abbreviation of clinical studies to accredit the product´s efficacy and safety, based on the existence of another registered biotechnological product which uses the same active principle, unitary dose, pharmaceutical form and course of administration.

Although the traditional simplified procedure will not be applicable for biological products, the new regulations accept the submission of abbreviated clinical studies for a follow on biotechnological. The regulatory authority is evaluating under which international standard it will accept the submission of such abbreviated clinical studies. Nevertheless, all abbreviated clinical studies to be submitted must be comparative in nature to the reference biological product. To date, the technical norm has not been issued, but we expect that agreement will be reached by December 25 2011.

The application of the ANDA system to biological products has generated great controversy

Assessing change

EM: Alejandro, do you think companies have been investing more in R&D in countries like Mexico where the legal framework for pharma and bio patents is getting stronger?

AL: Definitely. Our clients usually ask for advice as to the strength of the patent enforcement system in Mexico, the regulatory proceedings of approvals for new medicines and generics, efficiency of the linkage regulation and data package exclusivity. Their main concerns and questions are focused on time frames and effectiveness of the exclusivity of rights.

Of course, the outlook is not entirely as optimistic as we would like, since we need to highlight to them that the enforcement of patents in Mexico is extremely lengthy and a claim of damages requires a decision beyond shadow of appeal that a patent was infringed. In addition, the damages claim is prosecuted before a civil court in a different venue, so it takes no less than ten years in a patent case to get an award of damages derived from a patent violation.

Fortunately, there is also good news such as the linkage regulation improved by the recent interpretation of the Supreme Court, institutional commitments by IMPI´s higher officers to speed the decisions on patent cases, the institution of the specialised IP court within the Federal Court for Tax and Administrative Matters which has jurisdiction to review all decisions issued by IMPI at first stage in patent infringement cases and a proposal to recognise Data Package Exclusivity in the domestic law under discussion in the Congress.

RK: Pharmaceutical firms in Mexico and other markets are increasingly interacting with health and trade

authorities in their attempt to create understanding of their continued plans for additional investment and businesses, and discuss solutions to the lack of efficient patent enforcement and remedies, as well the lack of data exclusivity protection.

Whether pharmaceutical firms are likely to increase their investments in Mexico despite the current pitfalls of the IP system remains a question. It is unknown whether they are likely to redirect their investments to other markets with stronger IP systems should their requests for solution remain unanswered.

The current Mexican health regulations contradict NAFTA

EM: How have companies responded to uncertainty about patent protection?

RK: Business plans and investments from the R&D-based pharmaceutical industry, including research and development for top scale science medicines, have been negatively impacted by the economic downturn, and firms are making considerable adjustments. Some pharmaceutical firms have been focusing on long term investment schemes and business models in emerging markets, primarily Brazil and Mexico. While this should represent an economic boon to governments, IP protection is often neglected, if not ignored and set aside, instead of being treated as an incentive for greater foreign investment. As a result, pharmaceutical firms have become even more demanding of solutions that will make IP protections more effective and mitigate risks over their assets.

A costly endeavour

EM: What burdens or expenses are imposed as a result of poor protection?

RK: In Mexico, the unfortunate lack of efficient patent enforcement, coupled with the fact that infringement actions must first be heard by IMPI before taking the case before a court of law for remedy, does not help. Pharmaceutical firms need not only to identify potential infringers, design preventive measures that will prevent such actors from entering the marketplace, devise legal and corporate affairs strategies, but also surmount frustration when preliminary injunctions are easily lifted by IMPI itself.

AL: We have faced frustration from some pharma and bio companies which assume that in Mexico there is data package exclusivity (DPE) protection for a minimum of five years, as it is provided in NAFTA. After they have created a business plan relying on DPE, they receive our opinion or the refusal of recognition of this right by the authority, or even worse, a generic product approved based on the innovator´s dossier because the company was not aware that Mexico has not adopted in its domestic law the obligations provided in NAFTA regarding DPE rights. In fact, the current health regulations contradict NAFTA by allowing generics to rely indirectly on the innovator's dossier when proving safety and efficacy through interchangeability tests based on the innovator or product of reference with no exclusivity period.

GC: Publications of sanitary applications, although required by law to be updated bi-weekly, are often delayed approximately two to three months. Therefore, in order to have some timely knowledge of possible third party applications over protected products, companies have been forced to seek other alternatives, such as investigating information on import of the product through Customs databases (or through private services). Initial doubts over implementation of FTA provisions regarding patent linkage also led several pharma companies to request rejection of third party sanitary applications based on their patent rights, which were ultimately unsuccessful and generated considerable costs.

Dispel the myths

EM: How much weight would you say lobbying efforts have? Has there been significant activity by companies or associations?

AL: Lobbying efforts are relevant and crucial in Mexico not only to obtain new and better laws before the Congress but also to eradicate certain myths that have been introduced in the conscious of some Officers of the Mexican Government and the general public about patents and the pharma industry, such as there are patent extensions or that patents ban access to medicines. There is indeed a significant activity by companies and associations conducting lobby efforts before administrative, legislative and judicial authorities in Mexico. Although, there are minor rules, regulating the lobbying activities, personally, I consider that the main companies and associations of Pharma Companies in Mexico devoted to R&D conduct discrete but professional, ethical and lawful lobby efforts.

GC: In Chile, although there is no law regulating lobbying to date, individuals or entities have the right to

approach the authority and make allegations or suggestions. Specifically in the pharma industry the regulatory agency does appreciate information and suggestions given by both innovator and generic companies.

In fact, upon the recent publication of the new sanitary regulations the health authority has received many observations both from innovator and generic companies, whether individually or associated with associations. Both associations have been invited to actively participate in workshops and workgroups regarding specific topics, most importantly, biological products and bioequivalence.

RK: Legitimate lobbying efforts towards an open and continued dialogue between pharmaceutical firms, trade associations and government officials are crucial for a swift change in culture that today relies on harmful industry myths. A culture based on empirical awareness advocating for stronger patent systems to attract investment and encourage research of innovative medicines, balanced with human health and access to affordable innovative medicines, should rule. Because pharma-based IP is often misunderstood as harmful to public health, affecting low income populations who have no access to healthcare, pharmaceutical firms should include transparent and ethical lobby activities about their IP strategies. Lobbying efforts should aim at adding force to the R&D incentive, and should address any wrongful interpretation of the effects of IP laws.

EM: What advice would you give to those seeking to secure rights for bio/ pharma inventions in your country?

GC: The patent department should be thoroughly coordinated with the regulatory department of the company. In fact, many patent litigation process are truncated when the sanitary registration of the product is not coordinated with the patent registration which should cover the same (especially when litigating over sophisticated products such as highly developed pharmaceutical formulations or polymorphism in connection to X-ray diffractograms, for example).

The more coordinated the patent to the registration, the easier the prosecution of the patent regarding the commercialisation of an ANDA infringing product.

A pharmaceutical firm should be open to testing its patents in the courts

AL: First of all, look for advice from a specialist not only in patent law but in the regulatory and pharma legal framework. Secondly, trust and do not be afraid of bringing innovative actions or legal strategies. Mexico is facing a time of change, and there are few precedents, particularly in the field of biologics and some new technologies. My experience shows that some actions initiated as test cases have been resolved in relevant success on the legal issues and from the business perspective.

Finally, I would suggest being patient. The Mexican legal system is full of formal rules and time frames for legal proceedings are lengthy. This combination is often frustrating for clients.

RK: Applying for and successfully obtaining patents or data exclusivity over biopharmaceutical products does not necessarily mean that the originator pharmaceutical firms are free from IP issues that sometimes require strong confrontation. A pharmaceutical firm should take a persistent attitude and be open to testing its patents or other exclusive rights either in courts or in private or public dispute settlements, for which strong negotiating power and will are necessary.