Problem Patents

Lee Caffin and Vandana Mamidanna at Think IP Strategy highlight the importance of assessing current patents before embarking on new drug development and clinical trials

The patent regime has always played a crucial role in the research-driven pharmaceutical and biotechnology industries. Notwithstanding variations in the drug type and therapeutic area, an innovator company spends about $1 billion (£700 million) on each new drug developed to market. Hence, it is important for any innovator drug company to ensure that there are no blocking patents at each developmental stage; this is essential before commencing expensive, advanced clinical trials (1).

The drug industry has, in recent years, moved its research emphasis away from primary care studies significantly and is much more focused on therapeutic areas like oncology, CNS and anti-inflammatory conditions. The potential for overlapping research and consequently patent claims is inevitably higher as research converges. The genomic revolution and the development of routine biotech assays, product synthesis and development techniques have made targets – and the drug molecules with affinity for such targets – readily accessible. The risk of encroaching on third-party patents is therefore further elevated as molecules are made and tested with increasing efficiency.

FREEDOM TO OPERATE 101

A freedom to operate (FTO) search and analysis is primarily intended to identify potential barriers to product launch in a specific market. A good assessment enables the company to assess clearly the patent infringement risk and aid in the design of a country-by-country strategy for the commercialisation of the drug product. It should, however, be noted that there is an inherent uncertainty in any FTO assessment as the analysis can never be up-to-date in the true sense due to the time lag between patent filing and publication (18 months). It is therefore recommended that the FTO review is updated periodically to identify any relevant newly published patent applications. The expeditious filing and publication of one's own patent applications to the potential drug product and its use, synthesis, formulation and dosage regimen will provide some degree of comfort in 'first to file' countries. The inherent uncertainties in the present US 'first to invent' system, however, tempers the advice that one can provide with certainty regarding FTO. Defensive publications have also been used historically to limit the risk of a third-party patent issuing covering an aspect of the drug product being filed later. However, as a prior art measure to anticipate any later filed patent applications, a defensive publication may also inadvertently anticipate or make obvious later related innovator inventions, and therefore one needs to carefully assess the relative benefits of publishing versus filing a provisional (priority) patent application.

WHEN TO SEARCH?

It is always prudent to conduct an FTO search and analysis in the early stages of product development rather than to wait until the launch stage. Depending on one's view of the scope of the 'safe harbour' provisions under a country's patent law, you should consider identifying at the outset of a new project any broadly relevant research tool patents, for example, covering assays, targets, antibody types, processing techniques and so on. If such patents are identified, it may be cost-effective to negotiate a licence to use the patent, rather than rely on 'safe harbour' or wait until a project has advanced through proof-of-concept before approaching the patentee or seeking an invalidity position.

Searches are conducted routinely to identify areas of high intensity patents before any synthetic work is performed. A broad landscape search may help scientists develop in areas of lower patent intensity if, as is often the situation, there are various chemotype paths one can follow. Also, as previously mentioned, as projects progress through the various stages of development, it is important to keep the searches up-to-date and in line with any modifications, for example to the product form (such as salt or polymorph), the process used, the formulation developed, the target indication or the route of administration.

WHAT TO SEARCH FOR?

An FTO search seeks to identify granted patents and pending applications which a company may risk infringing by commercialising a drug product. A good search looks at all reasonably available sources, including computerised databases and search engines that provide access to patents worldwide. Biological sequence databases including both nucleic acid and protein sequences are also available, as are patent assignment databases, patent maintenance-fee records and so on. The key here is to be able to define the subject matter of the search in the most precise manner and then to build a good search strategy. It becomes highly critical to capture the entire product in a search and often requires a close interaction between the searcher, the patent attorney and inventors to design a comprehensive search strategy. Although chemical structure searches are fairly straightforward, searching for relevant patents in the biotechnology area presents a unique problem since a biotech product may be covered by multiple technology platforms and research tools. It is also problematic to devise a comprehensive search strategy to cover formulation developments, since excipients are often named differently and there are many patents which claim the function of the excipient or formulation, for example by its time to maximum plasma levels or its dissolution profile.

IDENTIFYING PROBLEMATIC PATENTS

Following the FTO search and initial analysis to weed out clearly irrelevant search 'hits', the searcher, or more usually the patent attorney, will look to further narrow the set of patents requiring a full analysis. At this stage of the FTO analysis one asks oneself: do any of the third-party patent claims literally cover, or could they, under the Doctrine of Equivalents, cover the technology used or contemplated? If the answer is yes, then further detailed analysis is required to confirm where the patents with problematic claims are still in force, and consider if a workaround would be possible or if an invalidity analysis should be conducted. Such a tiered approach is often the most effective way of conducting the FTO review. For a product which may be launched worldwide, it is clearly important to understand the global FTO position and to recognise the complexity of the analysis that arises from individual country jurisdictional differences, the dynamic nature of the country patent laws and so on.

There are additional challenges when patent applications are identified with broad claims, as is often the situation. One cannot simply ignore the reality that patents may issue from any such application, and at a minimum the applications need to be tracked in their prosecution. Managing risks from third-party pending applications is discussed in a later section.

As emerging markets become even more of a focus for drug companies, there is an increasing need to consider the FTO landscape in countries such as China, India, Russia and Brazil. Large companies can use their local internal network to identify any particular local patent issues, for example Chinese-only patents. Alternatively, companies may hire a preferred local counsel to keep a watch on areas of interest or specific patents that may be a potential issue.

DEALING WITH PROBLEMATIC PATENTS

To design a good FTO strategy requires careful business and legal considerations to balance potential risks with anticipated benefits. The FTO strategy considers all options and then decides on the approach that best fits the goals of the company and its tolerance for risks. The factors that determine this include, among others, the nature of technology, organisational goals, available licensing opportunities, validity position of the patent and jurisdiction. Again it's best to have a step-wise approach to arrive at an optimum solution to deal with a given patent situation. This may simply include waiting until the patent expires or, alternatively, steering research, or making changes to the product or process in order to avoid infringement risks. If re-designing to clearly avoid infringement is not a viable option, other alternatives such as licensing the blocking patent, obtaining an invalidity opinion or seeking to invalidate the patent through a Patent Office opposition or re-examination, or litigating in the courts may be considered.

Licensing implies obtaining an authorisation from the patent holder to use the patented technology on stipulated terms for an agreed period of time. In some cases, it may be the optimal path to clear the commercialisation of a new technology or product. However, in the biotechnology field for example, licensing may become an unprofitable option if the product is covered by multiple patents owned by multiple parties, thus leading to a royalty stacking scenario. A strategy used by device and IT companies is to patent in the third-party 'space' and look to develop intellectual property (IP) bargaining chips if a problematic patent arises. This is a strategy that may become more prevalent in the biotech and small molecule area.

If a licensing or a workaround strategy is unavailable or not cost-effective, senior management will need clear

Licensing implies obtaining an authorisation from the patent holder to use the patented technology on stipulated terms for an agreed period of time. In some cases, it may be the optimal path to clear the commercialisation of a new technology or product. However, in the biotechnology field for example, licensing may become an unprofitable option if the product is covered by multiple patents owned by multiple parties, thus leading to a royalty stacking scenario.

guidance on the risks and implications of continuing to develop a product towards the marketplace if covered by a third-party patent. The risk of being successfully sued and either blocked from the market by an injunction or paying a significant royalty to the patent holder can only be assessed following a thorough review of the relevant patent claims for validity. This will in turn require a detailed analysis of the patent prosecution and the art cited. Inevitably, further searches will need to be performed to seek out additional prior art that may impinge on the validity of the relevant patent claims. The prosecution history may also identify other issues that may limit the ability to assert claims, such as written description, enablement and best mode (35U.S.C 112) issues or inequitable conduct in the US. It is worth noting that in *Ariad Pharmaceuticals, Inc v Eli Lilly & Co*, the CACF in an *en banc* decision confirmed the Written Description requirement as separate from Enablement, also stating that when an applicant simply claims a desired result, he must demonstrate that he has invented species sufficient to support a claim to the functionally-defined genus (2). It is reasonable to assume that this decision will be referenced extensively in subsequent biotech and small molecule patent cases to attempt to limit claims to what the patentee 'possessed' as his invention at the time of filing.

If good invalidity arguments are available, depending on the particular jurisdiction, the type of arguments available, the stage of product development, the patent status and other legal and economic consideration, one can contemplate a pre-emptive strike on the patent using invalidity procedures at the Patent Office level, namely re-examination and opposition. An alternative but much more expensive option is to seek to revoke the patent in a court setting where such pre-emptive action is available before an infringement suit is filed by the patentee. It is, however, pertinent to note that invalidity is a complex question of law and fact, and predicting the outcome of a potential invalidity suit is difficult in all but the most clear-cut of situations, such as where the claims are anticipated by a fully enabled prior art reference.

About the authors

Lee Caffin is an expert in intellectual property strategy, particularly in the life sciences arena. His particular expertise lies in licensing and lifecycle management, including generic defence strategies. Lee has worked for major global companies, including Abbott, where he held the positions of Division Vice President of Global IP Strategy and Global Head of Pharmaceutical Patents. He was responsible for developing the in-house IP departments at Aventis and Takeda from the ground up and has mentored many US and European Patent Attorneys. As European Patents Head at Takeda Pharmaceuticals, Lee managed all aspects of building a new European Patent Department in London. Email: lee@thinkipstrategy.com

Vandana Mamidanna is an experienced IP lawyer and patent attorney based in Mumbai and Hyderabad, India. Vandana has extensive experience in pharmaceutical and intellectual property law, and holds a Bachelors degree in Pharmaceutical Technology, a law degree from Mumbai University and a Masters of Law from George Washington University. She has managed various portfolios in the Intellectual Property, Regulatory Affairs, Project Management and Business Development sector within several large Indian and multinational pharmaceutical companies. Vandana maintains a keen interest in the latest developments in IP and has lectured in cyber law, legal information systems and intellectual property, and holds several academic positions. Email: vandana@thinkipstrategy.com

Although the Federal Circuit in *In re Seagate Technology, LLC* rejected the affirmative obligation to obtain opinion of counsel to avoid a charge of wilful infringement, as was required under previous precedent law, a positive freedom to operate opinion may help in limiting damages generally if the courts ultimately find for the patentee, especially in situations where a claim has been laid of inducing infringement (3).

Pending patent applications pose a particular problem when one is seeking to communicate the level of risk to FTO to senior management. They are often filed with broad claims with no realistic prospect of issuing with such scope. The patentee may limit claims during prosecution, thereby removing the immediate FTO issue, but may, and often will, file a continuation or divisional application seeking to recapture aspects of the invention 'carved out' from the parent application. One may simply place a watch on the prosecution development, including a watch on the filing of any continuation or divisional application. However, some jurisdictions allow for the filing of third-party observations during patent prosecution (for example the European Patent Office), which may help to confine the scope of the resulting patent(s) if good art can be cited. There is an added benefit in that such art referenced overseas will need to be brought by the patentee to the attention of the US Examiner investigating the corresponding US case, unless the art is merely cumulative to that already available to him/her. Another tactic is to publish as a smokescreen. Clearly if a patentee with pending claims is aware that such claims will potentially implicate a third-party development activity, the patentee will do everything in their power to obtain issued claims which cover the activity. A smokescreen publication strategy, for example on active compounds from an alternative series to those of real interest, may lead the patentee to assume that broad claims are not worth fighting for and only seek issuance of claims of real interest to the patentee.

References

1. Adams CP, Brantner VV, Spending on New Drug Development, *Health Econ* 19: pp130-141, February 2010
2. *Ariad Pharmaceuticals, Inc v Eli Lilly & Co* (Federal Circuit 2010)
3. *In re Seagate Technology, LLC*, 497 F.3d 1360 (Federal Circuit 2007)