

## **Product Lifecycle Management Through Patents**

Strategic planning is not just for big pharma anymore. Specialty pharma, drug delivery, biotech and even generic companies can all greatly benefit from careful and early strategic patent planning concerning products they propose to bring to market. The importance of solid planning with respect to pharmaceutical lifecycle strategy is receiving more and more attention by brand companies.

Big pharma recognizes that new drug development is a high risk venture which takes a great deal of time, has an exceptionally low success rate, and in the case of a successful new drug development, ultimately has a price tag which is typically in excess \$100 million dollars. In the face of stiff, aggressive generic competition, many brand name companies now have lifecycle management teams in place in order to consider strategies to protect their market position long before the expiration of the patents covering their drug. Most brand companies today recognize that lifecycle management cannot start too early, particularly in view of the increasing bold challenges to patent portfolios protecting blockbuster drugs that only a few short years ago in a different patent climate seemed insurmountable.

The usefulness of patent lifecycle management is not limited to big pharma. There are important opportunities for patent protection that should not be (but often are) neglected by specialty pharma, drug delivery and generic companies.

### **Establishing a Patent Lifecycle Management Team**

Effective patent lifecycle management begins with the establishment of an effective team of individuals connected with the development of the new product. An effective patent lifecycle management team should include a person(s) with both “big picture” understanding of the project, and persons who have more specialized understandings of the project. In addition to patent counsel, key personnel from the following departments should be considered for inclusion in the patent lifecycle

management team: drug discovery, drug formulation, drug regulatory affairs, clinical, pharmacokinetics, marketing, licensing, and perhaps someone in upper management. Obviously, not all of these personnel are applicable to all situations.

It is not enough merely to choose a team. Meetings should be established on a regular basis so that everyone on the patent lifecycle team is aware of issues that arise in each person's area of expertise, and to address how those issues may impact the product, potential patent protection, and patent clearance (in appropriate situations).

### **Identifying the Patent Landscape**

For big pharma (and some specialty pharma), the first patents are typically directed to the drug itself. In the case of a new chemical entity ("NCE"), the patent landscape should be researched in order to develop a patent strategy directed to a broad genus, or narrow sub-genus, and perhaps particularly effective compounds, leading ultimately to patent claims covering the lead compound itself. At this early stage, patentability of the process of preparing the NCE, the process of preparing intermediates, and the physical/chemical characteristics of the NCE may be considered (among other things). In-vitro testing for activity may lead to the realization that certain structures provide superior activity as compared to others. Likewise, certain structures may be toxic while others are not. The patent lifecycle management team should assess such situations, as well as the patentability of the drug formulation, changes in formulation methodology (for example, due to scale-up issues), etc. Once the drug enters into Phase I and Phase II clinical trials, the lifecycle team should reassess all of the previous work to ensure that the drug formulation is still beneficially covered by the early patent work. New aspects of the drug formulation which come to light during lifecycle team meetings should be considered with respect to patentability (e.g., new synthetic procedures for the drug itself, new scale-up strategies, new protocols for treatment, changes in dose, mode of administration, time of administration, modifications of the drug formulation, potential use of the NCE with other drug products, and even design protection for package and

dosage forms, etc.) should be considered. Patent protection may be available for aspects of a drug product which are only ascertained during the further clinical testing that continues through phase III and phase IV clinical testing. For example, the new drug product may provide a unique plasma concentration curve. It may present unique effects on the body. New methods may be used to assess the clinical information or to assess the drug itself (analytical). Additional forms of the drug may be discovered (e.g., new polymorphs, active metabolites, stereoisomers, new crystalline structures). Many of these aspects can be developed throughout the life of the product, not just during the regulatory approval stage. Therefore, the lifecycle team should continue to meet regularly so that such potential patent opportunities are not missed.

Subsequent to NDA approval, it is recommended that the lifecycle team continue to meet on a regular basis in order to assess further possibilities for patent protection. Such further possibilities might include line extensions (e.g., new uses/indications for the product), new product combinations or kits, new routes of administration, as well as new drug delivery formulations which are being considered for future commercialization (including but not limited to sustained release), improvements in synthetic procedures, process of manufacture, and the testing of new excipients which may be included in the dosage form in order to improve the characteristics of the dosage form (e.g., improved bioavailability, ease of manufacture, patient acceptability, etc.).

### **Beyond Big Pharma –Specialty Pharma, Branded and Non-Branded Generics**

Patent lifecycle management is not only of import to big pharma, however. In my practice, In my practice, I often see situations when specialty pharma, biotech, drug delivery and generic companies have greatly benefited from careful and early strategic patent planning concerning products they proposed to bring to market. This holds true even when the drug/active has previously been marketed. The concept of patent lifecycle management can also be important for generic companies where, for example, formulation issues need to be addressed. There are many circumstances when patent protection may be available not only for an NDA product, but also for an application filed

with FDA under § 505(b)(2) or an ANDA. Early strategic patent planning often leaves the company in a better position to address patent clearance issues as well. Developing a strong patent portfolio may help these companies defend themselves from predatory competitors, may increase the valuation of the company, and may even be used as a source of revenue via out-licensing, etc. It is rare today that a potential marketing partner or a potential investor does not assess its interest in a deal based in significant part on the potential competitive landscape concerning the product in question. A strong patent portfolio goes can long way in addressing such issues. Although specialty pharma, drug delivery and generic companies are unlikely to engage in the development of NCE's, these concerns still face product development issues during formulation and clinical testing which are similar to the product development issues mentioned previously with respect to big pharma. It is appropriate for specialty pharma, drug delivery and generic companies to also have a patent lifecycle management team in place early in the development stages of a potential product which meets on a regular basis throughout regulatory filing and marketing of the product.

Some specialty pharmaceutical companies in the U.S. have experienced significant growth and have benefited from the acquisition and promotion of ethical drugs and/or late-stage compounds from big pharma. In many circumstances, the specialty pharma does quite a bit more than taking over the marketing of such products. New off-label uses may be investigated, and perhaps new dosages, new combinations with other agents, etc. may be in cards. All of these situations may present patent opportunities.

Other specialty pharma/drug delivery companies have leveraged the company's proprietary drug delivery platform(s) to reformulate and re-brand existing pharmaceutical products. Pharmaceutical formulators will appreciate the fact that even having a well-developed technology platform does not necessarily mean that one active ingredient may simply be substituted for a different active ingredient in that technology platform to thereby arrive at a new formulation which will provide acceptable bioequivalence to a brand-name drug. The technology platform (e.g., a sustained release technology) may have been developed for an active ingredient which is not even within the same drug

class as the target drug, and the desired plasma concentration curve may be entirely different from previous goals. The formulator must then modify the specific formulations made in the past to achieve the desired goals. It is sometimes the case that even a well-developed platform has to be modified, taking into account the desired plasma concentration curve to obtain a bioequivalent product to the brand-name product, accounting also for different physical/chemical properties of the active ingredients themselves (including but not limited to solubility/absorptivity, dosage strength, etc.). It is often the case that the work needed to make such changes leads to new (albeit incremental) inventions which nevertheless may provide an important patent position. Forward-thinking companies have already realized this, and advantageously seek to protect such developments.

Branded generic products, i.e., drug products which are similar to but not considered by FDA to be the “same” as a brand-name drug product (and for which FDA does not require the original proof of safety and efficacy mandatory for approving new brand-name drugs, i.e., a 505(b)(2) filing), are by their very nature different in some significant way from the brand-name drug product. In many such instances, these differences can be parlayed into a useful patent position. For example, the active drug moiety of many brand-name drug products are not particularly soluble, which give rise to formulation difficulties, which in turn give rise to a drug product for which an ANDA filing cannot be made, for example, because of differences in the physical properties of the active itself (e.g., the use of a different salt form, the use of an amorphous form instead of the brand’s crystalline form (or vice-versa), or even a non-equivalent polymorphic form). As another example, other steps may be taken to alter the drug delivery or bioavailability which results in a drug product which cannot be filed as an ANDA. These steps may comprise, for example, a change from the brand-name’s tablet formulation to a multi-particulate formulation, or the manufacture of a formulation which provides an effective but not bioequivalent plasma drug concentration curve. Such changes should be reviewed by the patent lifecycle management team for patentability.

Generic companies, particularly less experienced generics, tend to have small or non-existent patent portfolios. They tend to lack a finely-tuned process for evaluating their own technology, even as they are evaluating the technology of others. Generic companies also tend not to have a procedure in place for preparing or evaluating invention disclosures, just as there is a tendency to regard patent procurement expenses as overhead rather than an opportunity to protect their product and its potential market position, and build value in the company. Depending upon the patent landscape that has been uncovered by virtue of the patent searching which has been undertaken, patent protection may be available for the generic manufacturer's ANDA product. Many of the same considerations that are utilized with respect to designing patent claims for innovator drug products may also be applicable to an ANDA product. Particularly in the case of controlled release products, the generic company undoubtedly is faced with many of the same formulation issues previously mentioned, and in fact has the additional issue of making a bioequivalent product. The ability to protect such developments through patents should not be discounted.

### **Conclusion**

Proactive steps to protect pharmaceutical products through patents should be a concern across the entire playing field in the pharma industry. Early and continuous assessment of a potential product by personnel having expertise across a number of disciplines strengthens a company's ability to properly assess patent opportunities, and may result in the elucidation of new, important ideas. It is imperative that patent counsel be involved at the earliest stages of development. This will enable a smoother, more timely assessment of the potential impact upon existing patent filings, the patent landscape which already exists, and the scope of potential protection for a new invention.

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