

STRATEGIC BALANCING OF PATENT AND FDA APPROVAL PROCESSES TO MAXIMIZE MARKET EXCLUSIVITY

DENNIS S. FERNANDEZ
Fernandez & Associates L.L.P.
1047 El Camino Real, Suite 201
Menlo Park, CA 94025
dennis@iploft.com
www.iploft.com

JAMES T. HUIE
Fernandez & Associates L.L.P.
1047 El Camino Real, Suite 201
Menlo Park, CA 94025
jhuie@scu.edu

ABSTRACT

The patentability of products is essential in the biotechnology field, for limited market exclusivity compensates biotech companies' investments in research and development. The biotechnology field also uniquely faces Federal Drug Administration (FDA) approval, which includes considerable additional expense and time issues a biotech company must address. Although balancing the patent and FDA approval processes may be complex, various strategies of patent extension, of accelerating approval processes, and of prolonging generic drug companies' market entry can yield higher profit returns and maximize value company value.

Key Words – United States Patent and Trademark Office (USPTO), Federal Drug Administration (FDA), biopharmaceuticals, FDA clinical studies, New Drug Application (NDA), market exclusivity, generic market entry, Abbreviated New Drug Application (ANDA), patent term extensions, accelerated approval process.

I. INTRODUCTION

Biotechnology startups and their investors are primarily concerned with optimizing the value of the company. A company's value can be measured by the quality and lifetime of its patents. Longer patent terms produce longer market exclusivity, which consequentially leads to increased profits and value. Patents are crucial to protect a company's ideas while FDA approval is necessary to legally market their products. This article addresses and outlines strategies to extend patent terms and maximize market exclusivity while addressing FDA timing considerations.

II. OVERVIEW OF PATENT AND FDA APPROVAL PERIODS

2.1 Patent Approval process

The average prosecution time for a US patent is 3.4 years while the average biotech patent is 4.4 years. Patents require novelty, utility, and unobviousness. If the patent is granted by the United States Patent and Trademark Office (USPTO), then a 20-year monopoly is granted to the inventor in exchange for public disclosure of the invention.

2.2 Preclinical Studies

Preclinical studies offer predictions and provide safety data for initial studies in humans. Researchers use *in vitro* studies and animals with analogous genetic structure, pharmacodynamic responses, metabolic profiles, cellular receptor interactions, and general physiology to humans. Preclinical studies vary on a case by case basis, depending on the complexity and success of initial research.

2.3 Federal Drug Administration Approval Process

Federal Drug Administration (FDA) approval usually requires 10 to 12 years of development and 100 – 500 million dollars in development costs. The FDA approval period is split between the clinical trials and New Drug Application (NDA) approval. During the clinical trials, the FDA uses test populations to study safety, dosage, pharmacologic and metabolic effects, potential side effects, and effectiveness of the product. The NDA process then comprehensively analyzes the

preclinical and clinical reports, applying a risk-benefit analysis to determine if the product will benefit the public at large.

III. PROPER TIMING OF USPTO AND FDA FILINGS TO MAXIMIZE MARKET EXCLUSIVITY

Large expenses accumulate throughout research, development, and FDA approval of a particular biotech product. A longer patent term provides extended market exclusivity, which allows a company to recover its expenses and produce profits. Every day of market exclusivity is a potential profit for a pioneering company because generic drug companies capture 57.6% market share upon entering the market. Therefore expedient and efficient USPTO and FDA approval is necessary to maximize company profits.

See Figure 1

3.1 Beginning with Preclinical Studies

After the initial idea, preclinical studies should be the first step in the USPTO/FDA processes. Biotech patents regularly require experimental evidence to satisfy the utility requirement. Although researchers can concurrently conduct preclinical studies during patent approval process, basic *in vitro* and animal testing effectively support the patent claims. Regarding the FDA, preclinical studies are the rate limiting step for later FDA clinical development because clinical trials cannot begin until there are sufficient extrapolation predictions for human testing. Therefore, preclinical studies should be preformed as soon as possible to expedite the FDA and USPTO processes.

3.2 Filing Patent with USPTO

The largest obstacle for patent applications is the utility requirement. Occasionally an application's utility may not be clear enough without FDA approval. Therefore it is good practice to emphasize practical functionality in the application, along with substantial preclinical evidence.

Nevertheless patent approval strategically should come before FDA trials in view of certain

considerations. If the innovating company begins FDA process before USPTO filing, then it runs the risk of another company patenting the invention before them. Consequently the innovating company would have to license the biopharmaceutical, losing royalties, market exclusivity, and company value; or would have to abandon the FDA process and forfeit millions spent in research and development. Even if the another company does not patent the biopharmaceutical, the innovating company must be careful not to disclose the invention, otherwise it has one year to file the patent before it becomes property of the public domain (internationally, the patent application must be filed before disclosure). Furthermore, issued patents drive FDA approval, speeding up the process. Finally, filing patent applications and receiving approved patents will attract investors that will provide the necessary capital to fund the costly FDA clinical trials.

3.3 Publication of Innovation

In addition to *in vitro* and animal data, safety measures, and predicted dosage, the FDA requires demonstration through review of scientific literature before FDA clinical trials can begin. As mentioned above, the required publication by the FDA should be disclosed *after* the patent has been filed, or the company runs the risk of missing the one-year deadline for patentability.

3.4 Initiating the FDA Approval Process after the Patent Issues and after Preclinical Studies

It is advantageous to immediately begin FDA clinical trials immediately after patent prosecution with the USPTO and preclinical studies have commenced. However a complex issue is to accurately time preclinical studies to end before or concurrently with patent issuance. Each day preclinical studies extend past the issuance date, FDA approval is potentially delayed and the innovating company loses opportunity to exercise market exclusivity.

3.5 Asserting Market Exclusivity after FDA Approval

Once the FDA has approved the biopharmaceutical for US consumers, the

innovating company enjoys market exclusivity for the rest of its patent term. Strategically written patents will effectively and efficiently protect against product infringement by other companies. Including capturing exclusive profits from their product, the innovating company should build reliance on its products to secure its market share once the patent term ends.

IV. EXTENDING THE PATENT TERM AND MARKET EXCLUSIVITY AFTER THE PATENT TERM ENDS

Once the patent term ends, the innovating company loses its market exclusivity privilege as generic manufactures enter the market. There however are processes to extend the life of a patent term through “patent term restoration.” Additionally, the innovating company still enjoys market exclusivity while generic manufactures undergo their required FDA approval process. Finally, there are strategic defenses delay generic market entry. The methods to increase market exclusivity are crucial to maximizing overall profits.

4.1 Patent Term Restoration

The USPTO grants patent extensions to compensate for delays in USPTO examinations and prosecution that extend past three years. Thus the average 1.4 years past the three year mark during prosecution may be tacked onto the 20 year patent term.

Another method of patent extension, due to the FDA approval process, is under the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Watchman Act. The act provides a maximum 5-year extension, and is limited to a 14-year term from the time of FDA approval. The calculation of extension is complex and depends on patent prosecution and approval factors.

4.2 Blocking Generic Manufacturers’ ANDA’s

After the innovating company’s patent term expires, generic companies can begin their FDA approval process on their generic drug equivalent. While the innovating company’s FDA approval

took 10 – 12 years, the Hatch-Waxman Act allows generic companies to use the Abbreviated New Drug Approval (ANDA) process to gain approval within six months.

The requirements for a generic company to file an ANDA application are they must 1) show that the proposed generic drug is the same as, or bioequivalent to, an FDA approved drug; 2) certify that the approved drug was protected by a patent; and 3) the applicant does not use a method of producing the proposed generic drug that is protected by a “method of production” patent.

Because a “production method” patent can be separate from a “drug composition” patent, a tactful patent strategy is to file the production method patent a few years after filing the composition patent. Therefore although the composition would be public domain, the production method’s term would still be running and thus be protected. Put simply, a generic has access to the product itself, but does not have rights to produce the product according to the patented method. This strategy is even more effective with biopharmaceuticals than with traditional chemical pharmaceuticals because of the complexity of macromolecules. While there may be more than one method to synthesize a chemical compound, allowing competitors to design around the method of production patent, it is difficult to engineer around complex microbiological systems. Thus, a delayed production method patent can extend market exclusivity of a biopharmaceutical by protecting its production.*

4.3 Delay Through the “Metabolite Defense”

The “metabolite defense” can be used to stall generic market entry. Metabolites are the metabolized derivatives of the original structure, formed after being introduced into and processed by the body. The strategy is to file patents for the metabolites in years subsequent to the filing date of the main patent. Once the generic version is marketed, the innovating company holding the metabolite patent can bring a patent infringement claim against generic company because the generic company will be making products that inevitably become infringing products once digested by consumers. While the metabolite defense has never actually prevailed in court, the

litigated dispute can delay the generics' market entry for up to six months. This extended market exclusivity leads to increased profits by the innovating company.

4.4 Delay Through Raising "Citizen Petitions"

Similar to raising the metabolite defense in court, an innovating company can file a "citizen petition" with the FDA, which raises safety objections with the particular biopharmaceutical. Although the majority of petitions are rejected by the FDA or withdrawn by companies, the petition delays the FDA review staff from and generic market entry for 6 months or more.

V. AVENUES TO ACCELERATE THE INNOVATING COMPANY'S MARKET ENTRY THROUGH USPTO AND FDA EXCEPTIONS

5.1 USPTO Petition to "Make Special"

One procedure to shorten the USPTO process is to make the application "special," in which the USPTO examiner will process the special patent application before all other categories of applications. The USPTO provides special provisions for biotech inventions that allow a biotech patent to have "special" status. To qualify for a petition to make special, the company must be a "small entity," which is a company with fewer than 501 employees or a nonprofit organization. The petition must also state that the patent applicant's technology will be significantly impaired if a patent examination is delayed. If the situation calls for special status, the FDA approval process can be started earlier and can result in extended market exclusivity.

5.2 FDA's "Well Characterized" Biological/Biotech Products

The FDA can assign a biopharmaceutical as a "well characterized" biotech product if its identity, purity, potency, and quality can be substantially determined and controlled. This status allows a company to alter its manufacturing technologies as long as it can produce the same product. In the past, a company had to establish a fully developed process for the product before clinical trials could

begin, and if it wanted to change its process it would have to repeat clinical trials again. However with a well characterized biotech product, a company can immediately begin FDA clinical trials once it has the product and improve the manufacturing process at a later date.

5.3 FDA's "Expanded Access" Exception

Using Treatment-IND and "compassionate use" single-patient protocols, companies can market unapproved therapies that are undergoing clinical trials when no satisfactory alternatives are available. If the product is appropriate for the healthcare environment, marketing products concurrently with FDA clinical trials can significantly increase profits.

5.4 FDA's "Accelerated Approval" Process

The "accelerated approval" process allows marketing products to patients with serious or life-threatening conditions. A biopharmaceutical's approval may be accelerated if there are adequate and well-controlled clinical trials that ascertain the biopharmaceutical's clinical outcome will provide a considerable therapeutic benefit over existing therapies.

VI. UNIQUE EXAMPLES OF HOW PHARMAGENOMIC INVENTIONS RELATE TO USPTO AND FDA TIMELINES

6.1 Systems Biology

Systems biology currently is in the initial stages of biotechnology converging with information technology software. The systems biology field primarily deals with programmable software for analyzing biological interactions and structures. Because the software processing does not directly affect the human body, system biology inventions would not have to go through the FDA approval process. It would however have to go through the standard patent approval process.

6.2 Biosensors

As a concept, biosensors can be broadly defined as a sensor to detect biological activity at either molecular or macroscopic levels. As technology

advances, biosensors are being used in microarrays to monitor hybridization or can be implanted *in vivo*. FDA examination is only necessary if the biosensor it will directly affect a human system. If a biosensor is used for *in vitro* research, it will not have to undergo FDA approval.

6.3 Future Integration of Bioinformatics into FDA Trials

In the near future, bioinformatics will efficiently speed up FDA clinical trials. Industry reports predict cutting out about 4 years from the FDA approval process. Establishing an FDA bioinformatics infrastructure will potentially lead to many subtle implications, such as how the Hatch-Waxman's 14-year limit will adjust to the shorter FDA process. Nevertheless, the increased period of market exclusivity will be an incentive to develop new therapies.

Along with cutting approval time, discovery and development costs are predicted to decrease by \$137 million dollars per drug. This will likewise provide further incentives for drug companies to attempt to bring new therapies to the marketplace.

VII. CONCLUSION

There are multiple opportunities and strategies to increase market exclusivity for a patent's term. There are also many possible pitfalls in evaluating the USPTO and FDA timelines. Timing is critical for the economic fate of small biotech companies developing novel therapies. A diligent and detailed patent prosecution team is necessary to balance the multiple USPTO and FDA concerns, while maximizing the opportunities to extend patent terms and market exclusivity.

* The passage of Greater Access to Affordable Pharmaceuticals Act (GAAPA) is still pending, which would strike out the third requirement for ANDA filing and eliminate the use of the ANDA blocking strategy mentioned above. Furthermore passage of this act would introduce a 30-day deadline to register patents with the FDA after approval, or be barred from civil actions for patent infringements. It is important that for a company to work with a patent prosecution team that is aware of the most current implications of statutory and judicial implications.

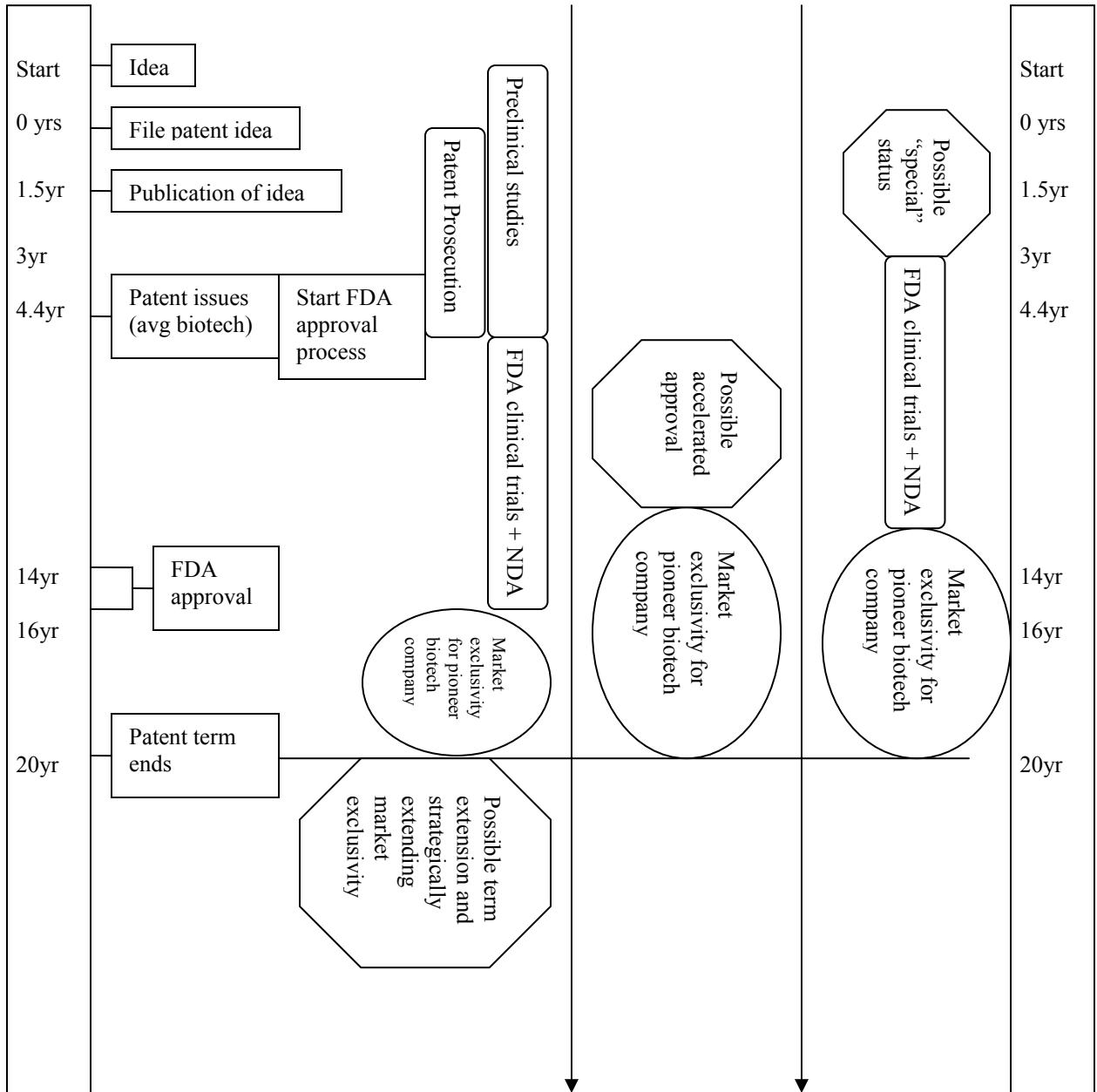


Figure 1