Patents provide one of the few protections companies can avail themselves of to help protect their therapeutic monoclonal antibody products. Just as the therapeutic monoclonal antibody field is constantly evolving, so too is the legal environment surrounding these inventions. In a series of articles, the general state of the law surrounding therapeutic antibodies will be explained, and important challenges to this technology area will be discussed. Much is at stake when companies market therapeutic monoclonal antibodies; therefore, a firm understanding of this important form of protection is critically important for anyone developing such products.

Introduction

Therapeutic monoclonal antibodies are big business: eight approved products currently have annual sales of $1B or more. No doubt excellent science, and a bit of good luck, led to the development of these successful products. Wherever big business exists, especially in high margin products such as therapeutic monoclonal antibodies, competition is inevitable. Understanding and planning for this situation are important to the long term protection of any valuable franchise. A sophisticated patent strategy is one of the few tools that companies have to protect their valuable franchises. In part one of a three part series, the basic precepts behind the patenting of therapeutic antibodies in the United States will be outlined. It is important to note that each country has its own set of particular laws and norms about the patenting of antibodies, but it is beyond the scope of this article to address all the differences. Subsequent installments will address more advanced issues, including the increasing difficulty in obtaining meaningful patent protection from the United States Patent and Trademark Office (USPTO), the impact that the eventual approval of biogenerics legislation might have on the therapeutic monoclonal antibody industry; and techniques such as product life cycle management that companies should consider when protecting their franchises.

What is a Patent?

A patent is a legal instrument, similar to a deed of property, that gives the patent owner the right to exclude for a limited period of time. Generally speaking, the patent term is 20 years from the date of original filing, although a number of exceptions and extensions may be available to the patentee. Before it will grant this monopoly right, the USPTO is required to confirm that an inventor is entitled to the patent right. The process by which the USPTO confirms that a claimed invention is patentable is called patent examination.

Through the patent examination process, the USPTO makes a determination that the claimed invention is both novel and non-obvious. The USPTO also confirms, among other things, that the inventor has adequately described and enabled the claimed invention.

Novelty

Novelty can be claimed by the first person to discover a claimed invention. An invention that lacks novelty is “anticipated” by the prior art. In the United States, novelty is governed by Section 102 of the patent statute. The most common “bars” to patentability under this statute are where: (1) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent, or (2) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States....
now generally a rare event, and most therapeutic antibodies are developed against known proteins. This then raises obviousness issues, which is the next patentability standard that the USPTO considers.

**Obviousness**

The standard for obviousness in the United States is governed by Section 103 of the patent statute which provides in relevant part that:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

It is difficult to clearly understand what is obvious from reading this statute alone. The contours of the statute are thus for the US courts to explain. The Supreme Court attempted to give better definition to the meaning of obviousness in *Teleflex v. KSR*, although, as with most decisions by the Supreme Court, the decision raised more questions than it addressed.

On one hand, the *KSR* decision suggests that the Court raised the bar to patentability: “Common sense teaches, however, that familiar items may have obvious uses beyond their primary purposes, and in many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle.” The Court elsewhere stated that “[a] person of ordinary skill is also a person of ordinary creativity, not an automaton.”

But, in other parts of the opinion, the Court recognized that, in most cases, a motivation must exist for one of ordinary skill in the art to combine or extend the prior art to achieve what is claimed. For example, the Court stated that:

“It will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue.”

Similarly, the Court commented that inventions cannot be proven obvious merely by demonstrating that each element was somewhere in the prior art.

Confusing the obviousness question more, the Court revived the “obvious to try” standard for determining obviousness: “[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp.”

The USPTO is presently applying the *KSR* decision with great zeal. For example, only recently the Court of Appeals for the Federal Circuit affirmed the USPTO’s application of *KSR* to reject as obvious a claim to an isolated nucleic acid molecule encoding the CD48-binding region of NAIL proteins. The available prior art disclosed the NAIL protein and monoclonal antibodies that recognized NAIL. Applying the rationale of *KSR*, the Federal Circuit effectively reversed its prior position that “knowledge of a protein does not give one a conception of a particular DNA encoding it.” In short, the Federal Circuit found that all that is required for obviousness under § 103 is “a reasonable expectation of success” from the teachings of the prior art.

Needless to say, these post-*KSR* obviousness rejections can be very difficult to rebut. The *KSR* decision is one of the reasons why the allowance rate at the USPTO has declined in recent years. However, these rejections can be rebutted as subsequent installment of this article will detail. For example, a strong understanding of the prior art and the technical contribution of the invention is part of the solution, as is having a sophisticated claiming strategy. However, solutions that worked yesterday might no longer work; strategies need to evolve with changes in the law.

**Written Description and Enablement**

The next two requirements for patentability are set forth in the first paragraph of Section 112 of the patent statute:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same.

These two requirements—the written description requirement and the enablement requirement—often present challenges to obtaining broad patent protection for therapeutic monoclonal antibodies. It is initially important to understand both how these requirements are the same and how they differ. Indeed, the courts often wrestle with the similarities and differences between these two patentability requirements, and sometimes express confusion as to whether these two requirements are actually a single requirement.

Two cases by the Federal Circuit provide a useful explanation of the written description and enablement requirements. *In re Wands* and *Capon v. Esshar*. The traditional test for written description is whether the specification demonstrates that the inventor had “possession” of the claimed subject matter; thus, the question is how one demonstrates possession. *Capon* addressed whether the specification provided adequate written description for a claim directed towards chimeric genes from segments of known proteins. In resolving written description for this invention, the court provided a multi-part test:

1. the nature of the invention at issue;
2. the predictability of the aspect at issue;
3. the scope of the invention;
4. other considerations appropriate to the subject matter
5. the existing knowledge in the particular field, the extent and content of the prior art; and
6. the maturity of the science or technology.

Thus, even though the applicant had not provided the actual sequence for the claimed invention, the Federal Circuit refused to find that written description had not been shown.
In re Wands is the seminal authority on enablement for biotechnology-related patents. In the context of explaining the enablement of claims to an immunoassay using monoclonal antibodies, the Federal Circuit outlined an eight factor test for evaluating enablement. These eight factors, known as the Wands factors, evaluate enablement in view of:

1. the amount of experimentation provided by the specification;
2. the amount of direction or guidance provided by the specification;
3. whether the specification provides any “working” examples;
4. the nature of the invention;
5. the state of the art;
6. the relative skill of the person of ordinary skill in the art;
7. the predictability of the art; and
8. the breadth of the claims.

Written description and enablement rejections are often applied by the USPTO during examination of therapeutic antibody claims. Generally these rejections are not made against claims directed to the isolated antibodies that are described in the application. Rather, the USPTO applies these rejections with regular frequency against method claims (i.e., method of treating a patient) or against claims to broader classes of antibodies (i.e., antibodies against a broadly defined protein). Again, it is outside the scope of this part of the article to address strategies pertaining to these rejections in detail. Rather, a subsequent installment of this article will look at common such rejections and effective strategies for addressing them. However, the inventor’s ability to secure a patent claim of such scope will depend greatly on how well the inventor is able to marshal the facts and arguments to support the written description or enablement factors, as the case may be. Also, as in the strategies for addressing obviousness rejections, part of the solution is understanding the invention and how best to claim it.

Conclusion

The scope (or breadth) of a patent is measured by the claims. Using the deed of property analogy, broader patent claims cover more territory than narrower patent claims, and importantly, not all properties are equally valuable. The same holds true for patent claims. Obtaining patents of the broadest possible scope therefore is obviously critical to companies developing therapeutic antibodies. Ideally, not only will the company’s own product be protected from the patent, but the company would also have the ability to block a competitor from making, using, or selling their antibody. The challenge then is obtaining the claim of the broadest scope.

Careful drafting of the specification at the outset can greatly assist the applicant in obtaining patents of the broadest scope. However, once the application is written the ability to secure broad claims greatly depends on how well the applicant can marshal the necessary evidence and arguments to address the USPTO’s rejections.

The therapeutic antibody business is constantly evolving, as is the legal framework surrounding it. Understanding that framework is absolutely critical to any company’s ability to adequately protect its investments. The current state of the law and more advanced intellectual property strategies for protecting therapeutic antibody innovation will be explored and explained in the next two installments of this article.

Note: The views expressed herein are the views of the author and should not be attributed to Sterne, Kessler, Goldstein & Fox, P.L.L.C. or any of its current, former or future clients.

4. 35 U.S.C. § 102(a) and (b).
7. 127 S. Ct. at 1742.
8. 127 S. Ct. at 1742.
10. 127 S. Ct. at 1741.
11. 127 S. Ct. at 1742.
18. At least one commentator has noted the similarities between the Wands factors and the Capon factors. Goldstein and Coblentz, Intellectual Property Today at 10–11 (August 2008).
22. Capon, 418 F.3d at 1357–1359.
23. Capon, 418 F.3d at 1361.
24. In re Wands, 858 F.2d at 737.