PATENTS

When the Human Genome Project and *State Street* collide

Take a look back to prepare for the next generation of biotechnology patent litigation.

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Biotechnology patent litigation, always complex, is about to become even more challenging. With the ever-growing mountain of genomic data needing to be managed by more and more sophisticated information systems, fields such as bioinformatics are booming, and with the boom has come a new class of patents. Some of these will be challenged in court; when they are, they will form the basis of the next generation of biotechnology patent litigation.

Three events in the past few years have set the groundwork for these bioinformatics patents to issue. First, in 1997, the United States Patent and Trademark Office (PTO) announced that it would allow claims on expressed sequence tags (ESTs) based on their utility as probes[1]. This sparked an increase in the filing of applications for DNA sequences. Second, in 1998, the Court of Appeals for the Federal Circuit handed down *State Street v. Signature Financial Group*[2]. In *State Street*, the court clarified that the tangible application of mathematical algorithms and business methods, as well as data processing and computer programs, were patentable. Finally, this past June saw the completion of the working draft of the human genome. This singular achievement has put a significant amount of new information in the scientific community and will provide countless opportunities for biotechnology entrepreneurs.

In light of these three events, now is the time for the biotechnology industry—especially the bioinformatics sector—to plan actively the crafting of its patents for maximum protection. In order to do this, the industry must understand how the courts have approached biotech patents in the past, and be prepared for how the courts will handle these patents in the future.

Determining patent validity

A patent may be declared invalid on a number of grounds; the four most important ones for biotechnology patent litigants are obviousness, inventorship, enablement, and written description. When bioinformatics patents are in fact litigated, the courts will likely first look to traditional biotechnology case law, which has been focused on patents relating to DNA sequences, for guidance.

A patent is invalid if it is obvious in light of the prior art. From a scientist's point of view, the DNA sequence of a gene may often appear to be obvious—once a protein sequence is known, its DNA sequence might require work to find (including finding the gene), but generally it is knowable. The Federal Circuit, however, has been more generous than one unfamiliar with the patent laws might have predicted, and patents for DNA sequences have been and will continue to be awarded. In *In re Bell*, the Federal Circuit explicitly rejected the proposition that the relationship between a nucleic acid and the protein that it encodes makes a gene *prima facie* obvious even if its correspondent protein is known[3].

Conversely, the Board of Patent Appeals and Interferences has provided an example of when a DNA sequence would be obvious in light of a known protein sequence. In *Ex parte Movva*[4], the board noted two factors that suggested and supported a finding that a prior art rejection based on a probing DNA library was appropriate. First, the gene of interest was part of the family of mammalian genes, and at least three of those mammalian genes showed highly conserved regions. Second, similar genes had been isolated using probes based upon one of the known nucleotide sequences.

As more sequences enter the public sphere, each new sequence has a greater chance of being easier to predict in light of what is known. Thus, potential applicants should continue to file applications for DNA and DNA-related patents, and defendants should always assert that patents for sequences are obvious. Soon, the defendants may prevail.

In addition to being nonobvious, for a patent to be valid the named inventor or inventors must have actually invented something. Thus, there must have been conception, or a definite and permanent idea of the complete and operative invention. This notion is important for two reasons. First, an inventor cannot file an application until he or she has conception of the invention. Second, because under US patent law, priority is given to the first to invent and not the first to file, it is important to establish when an invention is conceived. In *Amgen v. Chugai*, the Federal Circuit held that conception of a nucleotide sequence has not been achieved until after the gene has been isolated[5]. Thus, the invention must also have been reduced to practice before one files an application.

From a practical perspective, the law of inventorship means three things. First, scientists should isolate and characterize a gene or sequence as early as possible. Second, patent applicants should not file applications claiming nucleotide sequences before they have the nucleotide sequences identified and characterized. Third, documentation is important; courts and adversaries will cite lab notebooks as evidence of invention or support to invalidate a patent.

A patent must also enable persons skilled in the art to which it pertains to practice the invention without undue experimentation. With respect to DNA-related patents, the courts have imposed a high bar. Thus, enabling an invention for one species does not necessarily permit one to claim the genus or another species. From a practical perspective, an applicant must show examples of more than a single species in order to claim genetic related inventions across other species.

In *Enzo v. Calgene*[6], Enzo appealed a decision that its claims pertaining to antisense technology generally were not enabled. The Federal Circuit noted that examples other than those of *Escherichia coli* were glaringly missing and deemed invalid the claims to broader classes. Although this holding may appear dubious to some in the scientific community, they should note that the Federal Circuit has also explicitly held that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art[7].

There is no clear standard for determining when enabling an invention for one species provides the basis for enabling an invention for the genus or other species. The absence of a clear line suggests at least

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four strategies. First, applicants should disclose as many species as possible. Second, in a litigation, patent holders should emphasize the similarity between species. Third, alleged infringers should always argue that disclosure of one or a few species does not enable the broad genus or other species. Fourth, alleged infringers should look for evidence of problems in practicing the invention in species other than those disclosed.

In addition to enabling one skilled in the art to practice the invention, a patent specification must also provide a written description of the invention, clearly indicating that the inventor invented the claimed invention. There is an intuitive but unfortunately erroneous and asymmetrical relationship between the written description requirement and the nonobviousness requirement. A description that does not render a claimed invention obvious does not sufficiently describe that invention. But a description that renders obvious a claimed invention does not necessarily satisfy the written description requirement. For biotech patents, the written description requirement is but another statutory scenario under which the genus/species issue surfaces.

In *The Regents of the University of California v. Eli Lilly*[8], the patents at issue related to recombinant DNA technology. The patents disclosed rat insulin–encoding DNA but claimed broader genuses and other species' insulin encoding cDNA (e.g., mammals, vertebrates, and humans). The court held that the applicant was not entitled to those broader claims because of a failure to meet the written description requirement.

The strategies approaching written description issues are similar to those for approaching enablement issues. Applicants and patent owners should describe as much as possible and argue the similarities across species. Their adversaries should emphasize the differences between species and the absence of descriptions of species covered by a genus claim.

What the future holds

The four areas of invalidity described above as applied to biotechnology patents will likely provide the foundation for analyzing future bioinformatics and other related patents. Thus—at least initially—there may be, from the perspective of a bioinformatics patent holder, strict requirements in terms of inventorship, enablement, and written description, but lenient requirements in terms of nonobviousness.

As the courts have been developing a rubric under which to approach biotechnology patent cases, they also have been creating doctrines based on patents that are unrelated to biotechnology but that will likely have a great impact on bioinformatics patent litigation. In *State Street*, the Federal Circuit made clear that business methods were not per se unpatentable. The court also held that any bar to patenting mathematical algorithms was valid only to the extent that the claimed invention represents an abstract idea; once a mathematical algorithm generates a concrete result, it is patentable. Thus, one of the themes of *State Street* was that the 35 USC §101 utility requirement for patentability should not invalidate patents for abstract ideas that, as applied, generate useful, concrete, or tangible results.

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State Street, on its face, has nothing to do with biotechnology patents. The patent at issue involved a method for financial institutions to pool money and to invest it as a partnership. However, *State Street* is not limited to financial or even e-commerce businesses. Its holding extends to a broad class of business-method patents. In the context of biotechnology, this will lead to a significant increase in bioinformatics patent applications. *State Street* will also provide a source for support for litigants who are faced with charges of invalidity under 35 USC §101. As described above, *State Street* implies a policy of viewing the scope of what is patentable as very broad and not barring activity and products of technology as applied to the business world.

The PTO, however, might not be extending the sentiment of the broad holding of *State Street* to all biotech patent applications. On December 21, 1999, the PTO issued the *Revised Utility Examination Guideline: Request for Comments.* Under these guidelines, examiners are instructed to reject claims under 35 USC §101 if the claimed invention does not have a well-established utility and there is no credible assertion of specific and substantial utility by the applicant. "With respect to DNA fragments or ESTs, the USPTO will be looking for a utility particular to the DNA fragment or EST that exists in a real-world context[9]."

Thus, the tension between the new utility guidelines and the tone of *State Street* is clear. There is a sentiment of the Federal Circuit that the patent laws require minimal utility, but there is a policy in the context of biotechnology of the PTO to require more. This uncertainty provides opportunities for litigants and an invitation to the courts to develop new case law. With only a few business-method cases decided in light of *State Street*, there is little precedent under which to develop an instinct as to how the courts will treat this issue.

Regardless of the side on which bioinformatics patent litigants find themselves, they must be prepared for new case law to develop as courts synthesize *State Street*, more traditional biotechnology patent doctrine, and the utility requirements as applied to biotechnology. Bioinformatics patents are a mesh of biology and computer patents, and applicants and litigants need to determine whether to emphasize the biology or computer aspects of their inventions. Their strategies will depend in part on the answers to questions such as these: Will the PTO and the courts continue to be lenient in terms of nonobviousness, and demanding in terms of enablement, inventorship, and written description requirements as they have in the context of biotechnology applications? Will the standards be different for the business method–type patents, which are only now beginning to be litigated, and the bioinformatics patents, which have not yet been litigated? Will *State Street*'s progeny reemphasize that, despite 35 USC §101, anything under the sun is patentable if made by humans, or will there be an increased number of rejections based on a lack of utility in light of *Revised Utility Examination Guidelines*?

These questions and others will all be answered as the effects of the completion of the Human Genome Project are appreciated by society, new patent applications, especially bioinformatics patent applications are filed and litigated, and patent law is applied by the courts. As with most developments in the law, the journey will likely be long and painful, but in biotechnology, entrepreneurs cannot afford not to pay close attention.

1. Auth, D.R. *Nat. Biotechnol.* **15**, 911 (1997).
2. 149 F.3d 1368 (Fed. Cir. 1998), *cert. denied*, 525 U.S. 1093 (1999).
3. 991 F.2d 781, 784 (Fed. Cir. 1993); *see also In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995).
4. 31 U.S.P.Q. 2d 1027 (Bd Pt. App. & Int. 1993).
5. 927 F.2d 1200, 1206 (Fed. Cir.), *cert. denied sub. nom, Genetics Inst. v. Amgen*, 502 U.S. 856 (1991).
6. 188 F.3d 1362, 1375 (Fed. Cir. 1999).
7. *In re Vaeck*, 947 F.2d 488, 496 (Fed. Cir. 1991).
8. 119 F.3d 1559 (Fed. Cir. 1997).
9. Kowalski, T.J. *Nat. Biotechnol.* **18**, 349–350 (2000).