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Strategies for Managing University and Small Business Patent Portfolios in View of Recent Fundamental Changes in the Law

Lisa Tyner

Lisa Tyner is a senior associate at Baker Botts LLP in New York, NY, where she practices all areas of intellectual property law, with an emphasis on patent prosecution, counseling, and litigation. *The author would like to thank Paul Ragusa for his guidance and Christopher Han for his assistance with preparing the article.*

Recent changes in the patent law have narrowed what is considered to be patentable subject matter, especially in the biotechnology and pharmaceutical fields. In particular, a decision by the US Supreme Court, *Mayo Collaborative Services v. Prometheus Labs., Inc.,*[1] threatens loss or significant narrowing of patent protection for certain biotechnological and pharmaceutical innovations. Likewise, the Leahy-Smith America Invents Act (AIA) fundamentally shifts how priority is established and prior art is determined during prosecution. These developments will pose specific challenges to universities and small businesses, but there are steps that can be taken to prepare for and manage these challenges.

Mayo v. Prometheus: A New Standard for Patentable Subject Matter

On March 20, 2012, the US Supreme Court issued a unanimous 9-0 decision in *Mayo Collaborative Services v. Prometheus Labs., Inc.*,[2] holding that Prometheus' methods for optimizing drug dosages in treating immune-mediated gastrointestinal diseases were invalid under statutory patent law, as drawn to patent-ineligible subject matter.

Patent eligibility is governed by 35 U.S.C. § 101, which provides eligibility for any process, machine, manufacture, or composition of matter that is new and useful.[3] However, laws of nature, natural phenomena and abstract ideas are judicially created exclusions to patentable subject matter. In contrast, applications of laws of nature, natural phenomena and abstract ideas may be patent eligible. The issue in *Mayo* was whether the claims fell into an exception to patent eligibility or defined an application thereof.

The claims at issue in *Mayo* were directed to the use of thiopurine drugs in the treatment of certain immune-mediated diseases.[4] The court focused on claim 1 of Prometheus' U.S. Patent No. 6,355, 623:

1. A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:
   (a) administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and
   (b) determining the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder,
   wherein the level of 6-thioguanine less than about 230 pmol per $8x10^8$ red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject, and
   wherein the level of 6-thioguanine greater than about 400 pmol per $8x10^8$ red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.[5]

The first step of the claimed method requires administering a drug that is naturally converted to a metabolite (6-thioguanine), to a subject with an immune-mediated gastrointestinal disorder. It was understood that, because the same dose of a thiopurine drug was metabolized differently in different people, it was important to adjust the dosage of the drug based on the blood concentration of the thiopurine metabolite.[6]

In the Supreme Court opinion, Justice Breyer held that the claims were no more than a description of a natural relation between the thiopurine drug and how it is metabolized by the human body.[7] According to the Court, the "wherein" steps, which recite the indication of a need to adjust the drug dosage if the metabolite level falls outside a specified concentration range, are considered

a recitation of a law of nature[8] and the "administering" step merely identified the audience interested in applying the law of nature.[9]

With respect to the "determining" steps of the claim, which require determining the level of the metabolite in the subject, the court noted that no particular technique for determining metabolite levels was recited in the claim. Consequently, the claim embraced techniques that were "well understood, routine and conventional."[10] Therefore, the court found that the determining steps of the claim did not provide an inventive concept sufficient to ensure that the claim captured an application of a law of nature, rather than the law itself. The determining steps were considered conventional steps, specified at a high level of generality and well-understood by those in the field.[11]

The Court stated that "[t]he question before us is whether the claims do significantly more than simply describe these natural relations. To put the matter more precisely, [d]o the patent claims add *enough* to their statements of the correlations to allow the processes they describe to qualify as patent-eligible processes that *apply* natural laws? We believe that the answer to this question is no."[12]

Therefore, *Mayo* held that the method claims at issue were not eligible for patent protection because they simply added conventional and routine steps to apply an abstract idea. Additionally, the recitation of the machine-or-transformation test used in *Bilski* (to argue the thiopurine was being transformed during the test) could not trump the law of nature exclusion.[13]

The Court further noted that precedent "warn[s] us against upholding patents that claim processes that too broadly preempt the use of a natural law,"[14] and stated that "there is a danger that the grant of patents that tie up their use will inhibit future innovation premised upon them, a danger that becomes acute when a patented process amounts to no more than an instruction to 'apply the natural law,' or otherwise forecloses more future invention than the underlying discovery could reasonably justify."[15] The Court concluded that because Prometheus' claims recited a law of nature and nothing more than the instruction to "apply it," the claims were considered to improperly preempt all uses of the law of nature.[16]

While *Mayo* addressed process claims in particular, product claims covering DNA were reconsidered for patent eligibility under Section 101 by the Federal Circuit in *The Association for Molecular Pathology v. Myriad Genetics Inc.*,[17] (*"Myriad"* case) on remand in view of the *Mayo* decision. On August 16, 2012, the Federal Circuit upheld Myriad's right to patent "isolated DNA." Unsurprisingly, the Federal Circuit maintained their prior holding that Myriad's claims to "comparing" or "analyzing" DNA sequences were not patentable subject matter under Section 101, consistent with *Mayo*. It is likely that *Myriad* will be revisited by an *en banc* panel at the Federal Circuit or by the Supreme Court.

PTO Reaction to *Mayo*

On July 3, 2012, the US Patent & Trademark Office (PTO) issued a memo to provide guidance to examiners for the determination of patentable subject matter in a manner consistent with *Mayo*.[18] According to the PTO, the memo is intended as an interim measure until other relevant cases, including the *Myriad* case, are resolved and comprehensive updated guidance can be issued.

The memo instructs examiners to first determine whether the claimed invention is a process that focuses on a "natural principle." If so, the examiner should consider whether elements are included that ensure that the claim amounts to "significantly more than the natural principle itself."[19] The natural principle must be integrated into the claimed invention such that the natural principle is practically applied (*i.e.*, "is it more than a law of nature plus the general instruction to simply 'apply it"').[20] The memo also indicates that the weighing factors used in the *Bilski* Guidance (including the machine or transformation test), may be applied, but do not ensure that the claim covers patent-eligible subject matter.[21]

The memo uses specific language from the *Mayo* ruling to describe claims that would not be patent-eligible, including those that add "conventional steps, specified at a high level of generality" or "instructions that are well-understood, routine, conventional activity, previously engaged in by those in the field." In addition, the memo indicates that the mere statement of a general concept (natural principle) would effectively monopolize that concept or principal would be insufficient for patent eligibility. "This can be contrasted with a tangible implementation with elements or steps that are recited with specificity such that all substantial applications are not covered," the memo states.

The America Invents Act

On September 16, 2011, President Obama signed the Leahy-Smith America Invents Act (AIA),[22] which made substantial changes to current patent practice.[23] Among those changes is a shift from a "first-to-invent" system to a "first-to-file" system, effective March 16, 2013.[24] Under the new system, in most instances the only issue for determining priority will be the application date.[25] A patent will not be granted to a second inventor to file a patent application if another inventor already has filed a patent application, and such patent application matures into a patent or is published. As such, the first to win the "race to the Patent Office" and file a patent

application can be granted the patent. Clearly, this makes establishing an early filing date for a provisional or non-provisional application critical in ensuring patentability.

The general rule under the AIA is that absolute novelty is required to seek patent protection for an invention.[26] Under the new 35 U.S.C. § 102(a)(1), if the invention is otherwise made available to the public or on sale before the effective filing date of a patent application—anywhere in the world—then no patent protection is available for the invention.[27] Under the prior law, use or sale in a foreign country did not necessarily invalidate a patent.[28] Under the new 35 U.S.C. § 102(a)(2), if the invention was described in a patent or in a patent application that names another inventor and has an earlier effective filing date, no patent can be granted.[29]

There are two potentially important exceptions to the new first-to-file rule that establish a grace period for inventors who publicly disclose their inventions. Under the first exception, disclosures by the inventor, or someone who derived the information from the inventor (*i.e.,* derivation), made less than one year before the filing of the inventor's patent application, will not be considered prior art against the inventor's application.[30]

The second exception, which may be referred to as the "public disclosure exception," circumvents the absolute novelty and first-inventor-to-file rule.[31] Under this exception, an application or patent is not considered prior art to a later filed application if the invention was first publicly disclosed by the inventor of the later filed application, or another who obtained the subject matter from the inventor.[32] These grace period provisions effectively create a "first-to-disclose" system.

Implications for Universities and Small Businesses

For biotechnology-related inventions, the *Mayo* decision impacts certain types of subject matter, such as methods of diagnosis based on the identification of a biomarker; methods of determining whether a patient will respond to a particular therapeutic; methods of optimizing therapeutic efficacy by monitoring clearance of a therapeutic; and methods of optimizing a therapeutic regime by monitoring the development of therapeutic resistance mutations. While *Mayo* will affect all applicants, the decision may have a disproportionate impact on universities and small businesses in this area of technology. While larger companies may opt to retain certain types of method claims (*e.g.,* analytical or diagnostic claims) as trade secrets, trade secrets may not be a viable option for universities or small businesses who do not themselves commercialize such innovations.

In an example specific to the biotechnology industry in the context of the growing field of personalized medicine, a company or university may wish to negotiate a deal where a proprietary diagnostic test is paired with a drug developed by another entity, to be used in tandem in order to tailor treatment to a subset of patients that are particularly well (or poorly) suited for the treatment. In this case, patent coverage of the diagnostic test is essential. In the negotiation process, applications and patents having broad claims are more appealing to investors and licensees, especially early on in the commercialization process, when the final product may be still under development or in the very early stages.

Prior to *Mayo*, the natural laws exception could have been avoided by establishing that either a particular machine is employed, or a tangible transformation occurs, which satisfies the machine-or-transformation test as established in *Bilski*.[33] After *Mayo*, the inclusion of a tangible transformation may not be sufficient, particularly if the transformation occurs via conventional steps specified at a high level of generality. As stated by the PTO's recent guidance, method or process claims that simply add "conventional steps, specified at a high level of generality" or "instructions that are well-understood, routine, conventional activity, previously engaged in by those in the field" are not going to be considered patent eligible. Applicants now must avoid "monopolization" of a natural law and/or inclusion of "conventional steps specified at a high level of generality."

However, it also may be difficult for universities and small businesses to prepare an application that contains unconventional steps or embodiments due simply to lack of funding to carry out more specific research prior to obtaining licensing revenue (*e.g.,* identifying particular techniques, devices, or reagents for "determining" steps of diagnostic claims). Both typically engage in more "basic" research that investigates theory or proof-of-concept, leaving the fine-tuning of products for the end manufacturers who license the patents stemming from the basic research. Furthermore, the race to the patent office under the new first-to-file system will provide added pressure to file quickly and thus further limit the time that can be spent developing unconventional or highly specific embodiments.

The filing of broad claims in the wake of *Mayo* presents an additional risk that should be considered. If a broad method claim is filed in an application, and subsequently rejected as unpatentable under 35 U.S.C. § 101, further amendments can be made to the claim. However, even if the narrower claim eventually issues, concerns may be raised with respect to prosecution history estoppel, wherein a record is created that may be used against the inventor in re-examination, post-grant review, or litigation to interpret claims more narrowly than desired.

Another issue for universities is academic publishing, which is a critical component of the university research model. Under the first-to-invent system, an inventor could develop his invention and publish an article or present it at a conference, and rely on the date of conception to establish priority, although the 35 U.S.C. § 102(b) statutory bar provisions would require that the inventor file a patent application within one year after publication. This first-to-invent system fits in well with the academic research system that is focused on public disclosures.

Under the new first-to-file system, inventors cannot be as sure that a competitor cannot "scoop" them by filing a patent application first by improving on or deriving their invention from a public disclosure. The inventor would then need to argue derivation by showing that the other applicant derived his invention from the inventor's own. However, the law is new and unsettled and derivation may be difficult to prove, as the first inventor bears the burden of proving that the other applicant derived his work from the inventor. Accordingly, filing first is the more desirable option.

Strategies for Universities and Small Businesses

Universities and small business applicants face the challenge of filing applications early to pre-date public disclosures and publications, win the race to the patent office, and entice licensees, while at the same time balancing the need to meet the requirements for patentability under *Mayo,* which often requires additional time, research, and funding to further develop the invention.

Patent Application Drafting

In order to avoid having a patent rejected under the *Mayo* guidelines, applicants should avoid using language that could monopolize the natural law. For example, with respect to a diagnostic claim directed to a correlation between a biomarker and a particular disease, a generic "determining" step should no longer be included. More particular techniques for determining, however, may overcome an assertion that the claim monopolizes the natural law, and should therefore be described in as much detail as possible in the specification and be included, at the very least, in dependent claims.

Applicants should avoid describing conventional steps at a high level of generality. A more specifically described process may overcome a Section 101 rejection, regardless of its conventionality. Alternatively, an unconventional step also could serve to overcome the rejection even if claimed at a high level of generality. In particular, if possible, novel compositions and/or novel or unconventional steps should be included in the claim. Applicants should think creatively to come up with unconventional methods or reagents early on in their research whenever possible. For example, these can include novel biomarkers, primers, or probes that incorporate a new polymorphism, novel antibodies used in immunoassays, or the use of antibodies to new immunodominant epitopes on protein biomarkers.

When drafting new applications, applicants should ensure that the specification includes disclosures that support the subject matter eligibility, enablement, and written description of the specific method claims. The specification should include a broad description of conventional and unconventional techniques that can be used to carry out the method. Where more narrow method claims are introduced, applicants can include a range of claims, each covering an alternative methodology; this can ensure that the application covers multiple methods of applying a natural law but cannot be said to be monopolizing the application of the law.

Another option is to pursue "diagnostic composition" claims, analogous to pharmaceutical composition claims, which cover a composition and/or a kit that is used in the diagnostic method. If the composition and/or kit is novel, the *Mayo* Section 101 restrictions can be avoided.

Addressing First to File

In view of the first-to-file system, in order to establish a filing date, a provisional application should be filed in advance of public disclosure or publication if possible. Even in view of the one-year grace period exceptions following a public disclosure or publication, it is still critical to file an application as early as possible. For example, defeating a third-party early applicant could require proving derivation, as opposed to the inventor's earlier application simply receiving the benefit of the early priority date. Moreover, because many countries do not have similar grace periods, disclosures made prior to filing will continue to be treated as prior art in most jurisdictions outside of the United States. Lastly, until the courts provide guidance on the new provisions, a more cautious approach of filing early is advisable.

The provisional application allows one year for the inventor to expand on the invention and potentially include additional, unconventional embodiments that can help to strengthen the argument for patentable subject matter in view of *Mayo.* In this respect, a"staged filing" or "rolling provisional" approach is beneficial. In this approach, an initial provisional patent application is filed and a priority date obtained as soon as the invention disclosure is completed. As the idea is developed over the next year, new embodiments are added to the original provisional application and filed as a subsequent provisional patent application. When the one year

deadline for filing a US nonprovisional or international PCT application approaches, the provisional applications are combined and filed in a single nonprovisional application.

Prior to implementation of the first-to-file system, it can benefit technology transfer offices and small companies to review their practices for documenting, reviewing, and filing patent applications. Any improvements to the speed and efficiency of that process will help them adapt to the new first to file laws that will go into effect on March 16, 2013. The challenge will be to file earlier, without unduly increasing budgets.

1. *Mayo Collaborative Servs. v. Prometheus Labs., Inc.,* 566 U.S. ___ (2012).
2. *Id.*
3. 35 U.S.C. § 101 states "whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title."
4. *Mayo*, slip op. at 4.
5. *Id.* at 5-6.
6. *Id.* at 5.
7. *Id.* at 9.
8. *Id.* at 9-10.
9. *Id.* at 9.
10. *Id.* at 10.
11. *Id.* "[T]he claims inform a relevant audience about certain laws of nature; any additional steps consist of well-understood, routine, conventional activity already engaged in by the scientific community...." *Id.* at 11.
12. *Id.* at 8.
13. *Id.* at 19.
14. *Id.* at 3.
15. *Id.* at 17.
16. While *Mayo* addressed process claims in particular, product claims covering DNA are currently under review for patent eligibility under Section 101 by the Federal Circuit, in view of the *Mayo* decision, in *The Association for Molecular Pathology v. Myriad Genetics Inc*., Fed. Cir., No. 2012-1406. Oral arguments in *Myriad* were held on July 20, 2012.
17. *The Association for Molecular Pathology v. Myriad Genetics Inc., Fed. Cir., No. 2010-1046.*
18. Memorandum from Andrew H. Hirshfeld, Deputy Comm'r for Patent Examination Policy, on 2012 Interim Procedure for Subject Matter Eligibility Analysis of Process Claims Involving Laws of Nature (July 3, 2012).
19. *Id.* at 3-5.
20. *Id.* at 3.
21. *Id.* at 5-6.
22. H.R. 1249, 112th Cong.
23. On July 23, 2012, the PTO published proposed rule changes implementing the provisions of the AIA that relate to changes to the conditions of patentability. Comments from the public on the rules are due by October 5, 2012. Once finalized, the rules should become effective by March 16, 2013.
24. H.R. 1249 § 3(b).
25. *Id.*
26. *Id.* (the new 35 U.S.C. § 102(a), which provides that a person shall be entitled to a patent unless: (1) the claimed invention was patented, described in a printed publication, in public use, on sale or otherwise available to the public before the effective filing date; or (2) the invention was described in a patent or in a patent application that names another inventor and has an earlier effective filing date).
27. *Id.*
28. *See* 35 U.S.C. § 102(b).
29. H.R. 1249 § 3(b) (the new 35 U.S.C. § 102(a)(2)).
30. H.R. 1249 § 3(b) (the new 35 U.S.C. § 102(b)(1)(A)).
31. *Id.* (the new 35 U.S.C. § 102(b)(2)(B)).
32. *Id.*
33. *Bilski v. Kappos,* 130 S.Ct. 3218, 3226-3227, 561 U.S. ___ slip op. at 6-7 (2010).