

Patent Strategy for Personalized Medicine in Light of *Bilski*

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Protecting inventions in personalized medicine with patents is essential to making the investment in research and development of those inventions worthwhile.

Absent meaningful patent protection, however, companies will be less likely to pursue such innovation since there is nothing to prevent competitors from free-riding on the back of the many hours and millions of dollars expended by the innovator company.

Personalized medicine diagnostics can produce meaningful improvements in patient outcome and medical economics. Diagnostic innovations developed by University of California Professors Dan Pinkel and Joe Gray allowed for the first time sensitive and accurate measures of gene amplifications in breast cancer patient biopsies. This allows physicians to determine whether Herceptin® (trastuzumab) treatment is likely to improve the patient's outcome because only tumors with the amplification respond to Herceptin®. Pinkel and Gray's remarkable invention was exclusively licensed to a startup (later acquired by Abbott Laboratories), which devoted years of effort and millions of dollars to bring this innovation to market. Considering the cost of a full course of treatment with Herceptin®, approximately \$70,000, the development of the HER2/neu amplification diagnostic test is valuable not only in minimizing use of an expensive treatment for patients for whom it is unlikely to provide benefit, but it also helps patients by not wasting valuable time pursuing a treatment that is unlikely to be beneficial.

Additionally, personalized medicine inventions are useful in predicting who is at increased risk for disease in the future. This knowledge is useful when there are preventive steps that can be taken to mitigate that risk. As research advances, preventive steps to reduce the risk of more conditions will become known. Even if effective measures are not yet known, a patient and her doctor can plan for increased screening and obtain the outcome benefits associated with early detection. Myriad's tests for BRCA-1 and BRCA-2 mutations are a powerful example. By some estimates, a woman with just one copy of certain mutations has a 70 percent chance of developing breast cancer before the age of 60. Here again the basic innovation was made by academic scientists supported by federal funds and then exclusively licensed to a private company that invested heavily to bring it to market. A recent district court decision invalidated Myriad's patent claims for allegedly claiming a law of nature.

Patent protection for an invention like the HER2/neu amplification or BRCA-1/2 diagnostic test is relatively uncomplicated to obtain, as it involves simple detection of a single or small number of biomarkers. For inventions that involve multiple biomarkers, obtaining patent protection can be more complicated. A powerful advanced diagnostic, the *in vitro* diagnostic multianalyte index assay (IVDMIA), requires analysis of multiple biomarkers using an algorithm that combines information from the biomarkers to generate a score. The score is predictive of a particular condition or outcome. For example, using such an approach, CardioDx, a venture-backed startup, developed and marketed a simple blood test that accurately predicts coronary artery disease. In practice, the test identifies patients who are likely to have coronary artery blockages (and who need further diagnostic workup) from those who have chest pain not associated with coronary artery disease.

The personalized medicine industry was able to breathe a collective sigh of relief following the recent unanimous Supreme Court decision in *Bilski, et al. v. Kappos*, 10 C.D.O.S. 7966. *Bilski* considered the limits of what constitutes patentable subject matter under 35 U.S.C. § 101. While the court upheld the Federal Circuit's decision invalidating Bernard Bilski's patent, it struck down as too restrictive the test used by the Federal Circuit to determine which process claims constitute patent-eligible subject matter under 35 U.S.C. § 101.

Section 101 defines the subject matter that may be patented under the Patent Act: "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." Well-established Supreme Court precedent calls out three specific exceptions to § 101's broad patent-eligibility principles: laws of nature, physical phenomena, and abstract ideas.

Bilski filed a patent application directed to methods for hedging against price changes in commodities such as energy. The patent examiner rejected the application under § 101 because it was "not implemented on a specific apparatus and merely manipulates [an] abstract idea and solves a purely mathematical problem without any limitations to a practical application, therefore, the invention is not directed to the technological arts." The Board of Patent Appeals and Interferences (the Patent and Trademark Office's (PTO's) appellate board) affirmed,

adding that the application involved only mental steps that do not transform physical matter, and thus was directed to an abstract idea.

The case next went up to the Federal Circuit. In an *en banc* decision, the court held that “[a] claimed process is surely patent-eligible under § 101 if: (1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing.” *In re Bilski*, 545 F.3d 943, 954 (Fed. Cir. 2008). It also concluded that this “machine-or-transformation” test is the sole test to determine whether a claimed process describes patentable subject matter.

The Supreme Court unanimously affirmed the Federal Circuit’s judgment, but disapproved of the “machine or transformation test” as the exclusive test for determining the patent eligibility of process claims. The court explained that this test does, in many instances, provide “an investigative tool” for determining patentability of certain processes. In sum, the machine or transformation test is a sufficient, but not necessary condition for patentability.

The court’s reliance on the abstract ideas exception to patentable subject matter is likely to not be at issue for patents directed to personalized medicine innovations. Rather, the issue faced by these patents is the law of nature exception considered in *LabCorp v. Metabolite*, 548 U.S. 124 (2006), and more recently in the *Myriad* decision, an issue not squarely addressed in *Bilski*. Nevertheless, the opinion includes language suggesting that many personalized medicine process claims should easily fall within the ambit of § 101. The *Bilski* Court noted that an exclusive “machine or transformation” test would create uncertainty as to the patentability of advanced diagnostic medicine techniques. It also pointed out that “[s]ection 101 is a ‘dynamic provision designed to encompass new and unforeseen inventions.’”

A concurring opinion by Justice Stevens (joined by Justices Ginsburg, Breyer and Sotomayor) also helpfully pointed to the need for the patent law to remain stable and clear and highlighted the balance struck by the patent system between encouraging innovation and avoiding monopolies which stifle competition without any concomitant technological advance. Stevens’ concurrence considered this balance by asking “whether a patent monopoly is necessary to ‘motivate the invention.’” He further wrote, “[S]cholars generally agree that when innovation is expensive, risky, and easily copied, inventors are less likely to undertake the guaranteed costs of innovation in order to obtain the mere possibility of an invention that others can copy.”

A separate concurrence by Justice Breyer (in which Justice Scalia joined) framed the outer bounds of § 101 in terms of pre-emption. According to this analysis, a claim that broadly covers fundamental principles falls outside the scope of § 101 because it would improperly block public access to basic scientific tools: “In particular, the Court has long held that ‘[p]henomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable’ under § 101, since allowing individuals to patent these fundamental principles would ‘wholly pre-empt’ the public’s access to the ‘basic tools of scientific and technological work.’”

Advanced medical diagnostics, such as those that use information derived from multiple genetic variations or biomarker expression levels, certainly fall within the scope of patentable subject matter, according to the guidance provided by the *Bilski* decision. Significant investment is required to develop and market complex personalized medicine diagnostics that prognose risk or outcome based on a number of genetic or biological markers. Such methods do not preempt any basic law of nature because alternative predictive models can be developed using different sets of markers. Consequently, they should not be subject to § 101 rejections under current law.

Of course, whether the assay-and-correlate-style *LabCorp* claims (based on simple relationships between levels of physiologic substances) or those at issue in *Myriad* (that assess cancer risk by determining the presence of certain genetic mutations) can be considered to pre-empt all uses of a law of nature remains unanswered. While pre-emption arguments can easily be articulated, policy consideration as to the public benefit conferred by such tests and significant questions as to whether such tests could successfully be developed and marketed, absent strong patent protection, need to be carefully considered in determining where § 101’s line should be drawn.

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