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Legal Affairs

Recent Decisions Curtail Personalized Medicine

Impact of Past and Future Decisions on Industry Development Could Be Onerous

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Personalized medicine is the latest buzzword promising to revolutionize the pharmaceutical industry. Old-fashioned drug development has been based on the law of averages—relying on large clinical trials to identify drugs that prove safe and effective in a majority of patients. Personalized medicine offers the promise of identifying specific individuals, based on their genetic information, who are likely to respond well (or poorly) to a particular therapy.

The promise of personalized medicine is that it will facilitate development of more effective targeted therapies, will invite new (and smaller) players into the pharmaceutical arena, and will offer new commercial opportunities for established pharmaceutical players. For example, the expansion of personalized medicine has generated substantial commercial opportunities for diagnostics companies and for information management (e.g., bioinformatics) companies in the pharmaceutical arena.

Moreover, personalized medicine raises the possibility of smaller, less expensive, and more predictable clinical trials. Simultaneous reductions in risk and expense allow more and smaller companies that otherwise do not have the resources to afford a traditional clinical trial into the pharmaceutical development industry. Additionally, efficacy rates in the targeted populations are likely to be materially higher than they would be in the general population, which will encourage doctors and patients alike to embrace therapies based on personalized medicine products.

Personalized medicine strategies also provide systems for companies with marketed therapeutics to improve efficacy and/or reduce side effects over time, based on, for example, pharmacogenomics studies on patients receiving therapy. Personalized medicine, therefore, simultaneously creates possibilities for improved therapies and new business opportunities. Seems like a good idea, right?

New IP Challenges

Unfortunately, new legal decisions may deflate some of the enthusiasm surrounding the promise of personalized medicine. Recent case law, for example, suggests that developments in personalized medicine may not be protectable under U. S. patent laws.

As has already been extensively discussed in this and other forums (see "Court Ruling May Impact Life Science Patents" published in the February 1 issue of *GEN* and "Enforceable Diagnostic Method Patents" published in the April 1 issue of *GEN*), the United States Federal Circuit, in an en banc decision known as *Bilski* (*In re Bilski (Fed. Cir. 2008)*) has recently defined a test for determining whether method inventions are patentable.

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According to this test, methods are only patentable if they either (1) are tied to a particular machine; or (2) transform an article (or data representing such an article) into a different state or thing.

The inventions that arise in personalized medicine are often methods, and many such methods may not be patentable under the *Bilski* test. For example, one recent case has held that methods of determining whether an immunization schedule affects the incidence or severity of an immune-mediated disorder have been rejected as unpatentable (see discussion of *Classen v. Biogen* in the "Court Ruling May Impact Life Science Patents" published in the February 1 issue of *GEN*).

Similarly, claims to methods of optimizing a therapeutic regimen by administering a drug, determining the level of a particular metabolite, and therefore, establishing the need to adjust the drug dose, were held unpatentable by a lower court (see *Prometheus v. Mayo* (2008 WL 878910)); the Court of Appeals for the Federal Circuit stayed its review until *Bilski* was decided. The current expectation is that the holding of unpatentability will be maintained.

If these claims are not patentable post-*Bilski*, then it is likely that claims that recite, for example, detecting a particular biomarker and modifying a therapeutic regimen in response to the detection are likewise unpatentable. In addition, claims that recite correlating SNPs with particular diseases are likely to be held unpatentable as well.

Indeed, the United States PTO recently posted to its website a slide deck entitled "A Look at Personalized Medicine" that concludes many typical personalized medicine claims are not patentable under the *Bilski* test.

Without the possibility of patent protection to ensure that companies can capture the commercial value of their discoveries, investment in personalized medicine becomes materially less attractive.

Increased Liability Risk

Worse yet, a recent liability decision by the Supreme Court in *Wyeth v. Levine* significantly increases the potential liability risk for companies that develop and/or market pharmaceuticals. According to that case, a pharmaceutical company can be liable for harm to a patient caused when a physician administers a drug product in contravention of the label and of a warning on the label.

In *Levine*, notwithstanding that the FDA had approved the label and its warning, the Supreme Court held that the warning was not sufficiently clear and held Wyeth liable. The holding in *Levine* is, of course, not specific to the personalized medicine industry. The liability that it creates for all pharmaceutical manufacturers, however, may prove particularly daunting to smaller companies who are otherwise attracted to the personalized medicine market.

Impact of New Legal Challenges

Although more important legal decisions are yet to come (Bilski filed a Petition for cert. for the Supreme Court to decide on the patent-eligibility test; and the Federal Circuit has yet to decide on *Prometheus*), it is already clear that *Bilski* has decreased the patent protection available to companies investing in personalized medicine, and *Levine* has increased the liability exposure of all pharmaceutical companies. Does the combination of these two effects spell doom for the personalized medicine industry?

Perhaps not. The stated rationale for the machine or transformation test articulated in *Bilski* is that, by requiring implementation through a specific machine or through transformation of a particular article, the patent laws will ensure that claims will not issue that preempt all applications of a fundamental principle.

If one company cannot preempt all applications, then there is room for other companies to develop competing applications or strategies for exploiting the relevant principle. As is always the case with patents, the magic is in finding a balance between the scope of exclusion that is required in order to ensure sufficient financial reward so that companies are motivated to invest in developing the relevant technology and the scope of exclusion that is so broad it discourages competition.

The expectation is that therapies based on personalized medicine will be less risky, and therefore, less expensive to develop in the first place, such that a reduced patent scope might be more tolerable, or even desirable, in order to stimulate the industry.

The question becomes more subtle, of course, when the analysis is not limited to the scope of patent protection but also embraces the magnitude of downstream risk liability assigned to the development of personalized medicine therapeutics (e.g., under *Levine*). The personalized medicine industry may indeed become an interesting case study on how legal rules can impact business behavior and shape the development of an industry. GEN