Deciphering the Patent-Eligibility Message in Prometheus, Myriad and Classen

It has been a little more than eighteen months after the Supreme Court issued its opinion on the patent-eligibility of (business) method claims in *Bilski v. Kappos*.[1] In that time, the Federal Circuit has issued opinions in *Prometheus Laboratories, Inc. v. Mayo Collaborative Services*,[2] *Classen Immunotherapies, Inc. v. Biogen Idec*,[3] and *Association for Molecular Pathology v. U.S. Patent and Trademark Office*[4] ("*Myriad*") relating to diagnostic method claims. These decisions came in the wake of the Supreme Court's *Bilski* decision, and two of them (*Prometheus* and *Classen*) were decided on remand from the Court for reconsideration in view of *Bilski*. The Federal Circuit decided the *Prometheus* case on remand, finding (again) that the claims recited patent-eligible subject matter. The Supreme Court has again granted *certiorari* for *Prometheus*; oral arguments were heard late last year and a decision is due by the end of the Court's current term in June. Of the other two diagnostic method claims cases, the Federal Circuit decided that some but not others of the *Classen* claims were patent-eligible, and that none of the method claims at issue in *Myriad* satisfied the Supreme Court test for patent eligibility. Petitions for *certiorari* have been filed in both the *Classen* and *Myriad* cases.

These decisions reflect the struggle in the Supreme Court and the Federal Circuit with the scope of patent eligibility for method claims that produce information rather than a tangible product (something reflected a generation ago in the *Benson v. Gottschalk*,[5] *Parker v. Flook*,[6] *Diamond v. Diehr*[7] cases). Given that the question of patent eligibility is completely dependent on the scope and meaning of properly construed claims, it is curious that in none of the pending cases were the claims construed by the lower courts. Here we provide a comparison of the claims in *Prometheus*, *Myriad*, and *Classen* that might shed some light on the reasoning used by the Federal Circuit in arriving at the answers to the patent-eligibility question posed in each of these cases and a guide (subject to Supreme Court review) for drafting patent-eligible diagnostic method claims.

Perhaps the most clear-cut decision by the Federal Circuit involves the method claims in the patents in the *Myriad* case. These claims all require the steps of "analyzing" or "comparing" a mutated BRCA gene sequence with the wild type, "normal" sequence without any express claim language requiring that either sequence be determined as part of the claim; claim 1 of U.S. Patent No. 5,709,999 and U.S. Patent No. 5,710,001 (fully recited in the footnote) are illustrative.[8]

Significantly, other diagnostic method claims, including ones using antibodies to detect altered BRCA proteins, were not at issue in the case. Also not recited in these claims were "additional, transformative steps," including "the steps of (1) extracting DNA from a human sample, and (2) sequencing the *BRCA* DNA molecule, ... steps [that] necessarily precede the step of comparing nucleotide sequences."[9]

The Federal Circuit panel unanimously agreed that these claims do not satisfy the "machine or transformation" (MOT) test under *Bilski*. These claims "recite[] nothing more than the abstract mental steps necessary to compare two different nucleotide sequences," according to Judge Lourie's majority opinion.[10] Also significant for the Court is that the specification required the term "sequence" to refer "more broadly to the linear sequence of nucleotide bases of a DNA molecule" *per se*.[11] The

panel found that Myriad's method claims can be satisfied (*i.e*., infringed) by "mere inspection" alone, and thus encompass merely an abstract idea.[12]

In contrast, on remand, the Federal Circuit found the claims in *Prometheus* (fully recited in the footnote) to satisfy the MOT test and thus recite patent-eligible subject matter, whether the claim recites an affirmative drug administration step or not.[13] The distinction between the claims in *Myriad* and claim 1 of the *Prometheus* patent can be appreciated in light of the difference in what is being detected in each claim: a naturally occurring nucleic acid in *Myriad* and an administered drug or its metabolite in *Prometheus*. Insofar as patent eligibility for method claims must either satisfy the *Bilski* machine or transformation test or otherwise not be so abstract as to entirely preempt an abstract idea, law of nature, or natural phenomenon, the fact that a drug must be administered would appear to provide the Federal Circuit with its rationale regarding the patent eligibility of the claim 1 of the *Prometheus* patent. Claim 46, on the other hand, does not have an affirmatively recited administration step. However, the "detecting" step recites that 6-thiopurine or one of its metabolites is detected from "a subject administered [one of the recited] drug[s]," again encompassing only those patients who have been transformed by drug administration.

It would seem that the Court refused to exalt form over substance by making a distinction between claims that recite administration of the drug to a subject and claims that are restricted to detecting a drug or its metabolites only in that subset of subjects to whom the drug has been administered; in either case, the Federal Circuit discerned a transformation. Neither of these considerations are likely to be before the Supreme Court, however, since defendant's *certiorari* petition and argument focused on the purported interference these claims create with the practice of medicine as well as the allegation that the portions of the claim that recited the transformation step are not "inventive." In this regard it should be remembered that the case that raised this aspect of medical diagnostic method claims, *Laboratory Corp. v. Metabolite Labs., Inc.*[14] (*LabCorp*), was, like *Myriad*, directed at detecting a naturally occurring metabolite, homocysteine, and not an administered drug as in *Prometheus*.

The most surprising Federal Circuit decision relating to diagnostic method claims is the most recent, the *Classen* case. There, a divided panel found a distinction between the claims of U.S. Patent No. 5,723,283 (fully recited in the footnote), which the majority found *not* to be patent-eligible,[15] and the claims of U.S. Patent Nos. 6,420,139 and 6,638,739 (claim 1 of the '739 patent being representative, and fully recited in the footnote) that *were* patent-eligible according to the majority.[16]

The difference for the panel majority appears to be in whether the determination of an appropriate immunization schedule directs an affirmative (and transformative) step or steps. In the '283 claim, the majority construed the scope of the claim to encompass mere comparison of the results of immunization schedules that produce a conclusion (*i.e*., information) without any further steps in the claimed method. The claims in the '739 patent, in contrast, require that an appropriate immunization schedule be determined, and *then* that a mammal or mammals be immunized according to that schedule to achieve the beneficial result of immunization with the least "incidence, prevalence, frequency or severity' o deleterious side effect.

Another salient difference between the *Myriad* claims and the '283 claim in *Classen* on the one hand, and the *Prometheus* claims and the '739 patent claims in *Classen*, on the other, is that the former claims involve producing intangible information, while the latter use the information to direct the claim practitioner to perform a tangible, transformative step. Claims that only produce information may not be patent-ineligible *per se*; however, as in *Bilski* (and *Benson* and *Flook*) they are more likely to raise patent eligibility concerns. Indeed these considerations arose in the concurring Justices' opinion in *Bilski*.[17]

It remains the case that including active, technology-dependent steps in method claims is prudent, and claims should be drafted that minimize the likelihood that the invention will be characterized as merely an "abstract idea." While this advice is admittedly of a general nature, it does provide a mechanism for assessing claims for patent eligibility: if the claim contains no active, transformative step, or recites mere comparison of information or data, it is likely to be open to a subject matter eligibility attack, either in the Office or in litigation. Insofar as the invention involves a novel (and non-obvious) appreciation of relationships between phenomena (particularly natural phenomena), it is wise to include an "active" step wherein detection of the relationship leads to some activity that is itself transformative. For claims currently in force, it may also be advisable to determine whether reissue in favor of claims reciting an active transformation step is possible to reduce the likelihood of such a challenge. But the simple fact is that any advice is subject to revision the next time the Supreme Court or Federal Circuit opines on patent eligibility of method claims.

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Endnotes

1. 130 S. Ct. 3218 (2010).
2. 628 F.3d 1347 (Fed. Cir. 2010).
3. 659 F.3d 1057 (Fed. Cir. 2011).
4. 653 F.3d 1329 (Fed. Cir. 2011).
5. 409 U.S. 63 (1972).
6. 437 U.S. 584 (1978).
7. 450 U.S. 175 (1981).
8.
    1. A method for detecting a germline alteration in a BRCA1 gene, said alteration selected from the group consisting of the alterations set forth in Tables 12A, 14, 18 or 19 in a human which comprises analyzing a sequence of a BRCA1 gene or BRCA1 RNA from a human sample or analyzing a sequence of BRCA1 cDNA made from mRNA from said human sample with the proviso that said germline alteration

is not a deletion of 4 nucleotides corresponding to base numbers 4184-4187 of SEQ ID NO:1. (the '999 patent)

2. A method for screening a tumor sample from a human subject for a somatic alteration in a BRCA1 gene in said tumor which comprises gene comparing a first sequence selected form the group consisting of a BRCA1 gene from said tumor sample, BRCA1 RNA from said tumor sample and BRCA1 cDNA made from mRNA from said tumor sample with a second sequence selected from the group consisting of BRCA1 gene from a nontumor sample of said subject, BRCA1 RNA from said nontumor sample and BRCA1 cDNA made from mRNA from said nontumor sample, wherein a difference in the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said tumor sample from the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said nontumor sample indicates a somatic alteration in the BRCA1 gene in said tumor sample. (the '001 patent)

9. *Myriad,* 653 F.3d at 1356.
10. *Id.*
11. *Id.*
12. *Id.* at 1357.
13. 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 8x108 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 8x108 red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

    46. A method of optimizing therapeutic efficacy and reducing toxicity associated with treatment of an immune-mediated gastrointestinal disorder, comprising:

    (a) determining the level of m6thioguanine or 6-methylmercaptopurine in a subject administered a drug selected from the group consisting of 6-mercaptopurine, azathiop[urine, 6-thioguanine, and 6-methylmercaptoriboside, said subject having said immune mediated gastrointestinal disorder, wherein the level of 6-thioguanine less than about 230 pmol per 8x108 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 8x108 red blood cells or a level of 6-methylmercaptopurine greater than about 7000 pmol per 8x108 red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject. (U.S. Patent No. 6,355,623)
14. 370 F.3d 1354 (Fed. Cir. 2004).
15. A method of determining whether an immunization schedule affects the incidence or severity of a chronic immune-mediated disorder in a treatment group of mammals, relative to a control group of mammals, which comprises immunizing mammals in the treatment group of mammals with one or more doses of one or more immunogens, according to said immunization schedule, and comparing the incidence, prevalence, frequency or severity of said chronic immune-mediated disorder or the level of a marker of such a disorder, in the treatment group, with that in the control group.
16. 1. A method of immunizing a mammalian subject which comprises:
    (i) screening a plurality of immunization schedules, by
    (a) identifying a first group of mammals and at least a second group of mammals, said mammals being of the same species, the first group of mammals having been immunized with one or more doses of one or more infectious disease-causing organism associated immunogens according to a first screened immunization schedule, and the second group of mammals having been immunized with one or more doses of one or more infectious disease-causing organism associated immunogens according to a second screened immunization schedule, each group of mammals having been immunized according to a different immunization schedule, and

    (b) comparing the effectiveness of said first and second screened immunization schedules in protecting against or inducing a chronic immune-mediated disorder in said first and second groups, as a result of which one of said screened immunization schedules may be identified as a lower risk screened immunization

schedule and the other of said screened schedules as a higher risk screened immunization schedule with regard to the risk of developing said chronic immune mediated disorder(s),

(ii) immunizing said subject according to a subject immunization schedule, according to which at least one of said infectious disease-causing organism-associated immunogens of said lower risk schedule is administered in accordance with said lower risk screened immunization schedule, which administration is associated with a lower risk of development of said chronic immune-mediated disorder(s) than when said immunogen was administered according to said higher risk screened immunization schedule.

17. *Bilski*, 130 S. Ct. at 3256 "For even when patents encourage innovation and disclosure, "too much patent protection can impede rather than 'promote the Progress of . . . useful Arts.'" *Laboratory Corp. of America Holdings v. Metabolite Laboratories, Inc.*, 548 U. S. 124, 126–127 (2006) (BREYER, J., dissenting from dismissal of certiorari). . . . Patents "can discourage research by impeding the free exchange of information," for example, by forcing people to "avoid the use of potentially patented ideas, by leading them to conduct costly and time-consuming searches of existing or pending patents, by requiring complex licensing arrangements, and by raising the costs of using the patented" methods. *Id.*, at 127.").