Personalized Medicine Patents in Great Legal Turmoil

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INTRODUCTION

The obtaining and enforcement of personalized medicine patent claims have been thrown into great uncertainty due to recent court decisions dealing with eligibility and joint infringement. This article addresses the impact of these decisions (and their pending reviews) on this burgeoning field.

Personalized medicine is a shorthand term for a process of tailoring the administration of therapy to an individual patient, depending on the patient’s predisposition, genetic or otherwise, to respond appropriately to the therapy. For example, proteins in breast, lung and colorectal cancer patients are sometimes measured in cancer therapy before selecting an appropriate treatment. Data from imaging and other laboratory tests can also be used to develop a more effective personalized treatment regime.

Personalized medicine often involves at least two phases: a diagnosis phase, followed by a therapy phase. For example, personalized medicine may involve determining the presence, or absence, of a particular gene mutation, and administering a drug that is more likely to be beneficial based on the result of that determination.

A classic protocol is for a physician to order a diagnostic test from an independent laboratory and then, based on the results, prescribe administration of a drug. The two steps involved in personalized medicine have been the subject of patented process claims, such as those at issue in Prometheus, in which one step may be carried out by the diagnostic lab and the other step by (or induced to be carried out by) the physician. This is known as “split infringement.” The Supreme Court has recently granted cert in the Prometheus case, so its conclusions may not have continued validity. In addition, two-step claims such as those of Prometheus may now also come under attack as being unenforceable.

The unenforceability attack may arise out of a series of recent cases dealing with multi-party infringements, such as Akamai and McKesson, where no one party practiced each step of a method claim. Akamai and McKesson held that if multiple steps in a claim are carried out by different parties, there may not be enforceable infringement unless the parties are in an agency relationship, or unless one party is contractually obligated to the other to perform the steps. Akamai and McKesson each have been granted an en banc rehearing by the Court of Appeals for the Federal Circuit (“CAFC”).

To highlight the legal turmoil in which the field of personalized medicine now finds itself, this article will analyze the impact of the CAFC panel holdings in Akamai and McKesson on multi-step claims, as well as the significance of the Supreme Court’s upcoming review of Prometheus.

PERSONALIZED MEDICINE CLAIMS: ELIGIBILITY AND PATENTABILITY

For several years, patent claims dealing with diagnostic methods used in personalized medicine have been subject to scrutiny under Bilski and its progeny, such as Prometheus. In Bilski, the Supreme Court approved of using the “machine-or-transformation test” as a “useful and important clue” for determining whether a claim includes statutory subject matter. This test determines the eligibility of claimed subject matter based on whether a process is tied to a machine or whether the process involves the transformation of an article. In addition, the CAFC has before it an appeal from the “Myriad Genetics” case, where certain of the method claims related to correlations between genetic mutations and disease were held invalid under Bilski, as being nothing more than ineligible abstract ideas or mental processes.

In Prometheus, where a two-step personalized medicine claim was held eligible by the CAFC – after it had considered the Bilski holding – the claim was directed to administering the drug and determining the level of metabolites of the drug in the patient, the levels of which indicated a need to then increase or decrease the level of drug to be administered. The Court held that either the step of administering the drug, or “determining” the levels of the metabolite were transformative and thus passed muster under 35 U.S.C. § 101. This result suggests that either step standing alone would be enough to confer eligibility to a claim, i.e., a claim to a step of “administering” would not need to contain an additional step for “determining,” or vice versa. The Supreme Court’s decision to review Prometheus, however, creates new uncertainty for the eligibility of personalized medicine method claims. The Court may find that the two steps are necessary to confer eligibility on such a claim, or it may conclude that neither step, alone or in combination, is transformative, or it may uphold the decision (although not the reasoning) of the CAFC. If neither step passes muster then the eligibility of broad personalized medicine claims will be thrown into disarray and only narrow instrument- or method-specific claims will be obtainable.

Regardless of the outcome in Prometheus, however, two steps may be necessary in a personalized medicine claim in any event, in order to overcome patentability issues, such as problems with novelty or obviousness. For example, the drug at issue may already have been used clinically and thus one additional step beyond the “administering” step may be needed to confer patentability on the claimed method. If personalized medicine claims contain two such steps, however, their enforceability may now run afoot of the recent Akamai/McKesson cases, to which we turn next.
SPLIT PERSONALIZED MEDICINE CLAIMS: ENFORCEABILITY

In Akamai, a business method claim was held not to be infringed because the two parties found to jointly practice the method were not in an agency relationship, and neither party was contractually obligated to the other to perform any of the method steps.\sup{10} Akamai’s patents disclosed a system for allowing a website content provider to outsource to the network the storage and delivery of discrete, embedded, portions of its website content. The patents included multi-step method claims, with one step of delivering the base document of a website from a content provider’s computer (while individual embedded objects of the website are stored on a network) and another step of modifying an embedded object’s address to link to an object on the network, a process referred to as “tagging.” It was undisputed that the network provider did not perform every step of the asserted claims. Rather, it provided the information necessary for its customers, the content providers, to modify their web pages, and the content providers performed the tagging step.

The CAFC found that the network provider and the content providers were not in an agency relationship. Rather, the Court found that the content providers acted principally for their own benefit and under their own control and therefore were not the network provider’s agents.\sup{11} The CAFC also found that neither the network nor the content providers were contractually obligated to each other to perform any of the method steps. As a consequence, the CAFC found no joint infringement.

The CAFC held that there could only be joint infringement “when there is an agency relationship between the parties who perform the method steps or when one party is contractually obligated to the other to perform the steps.”\sup{12} The Court further explained that for an agency relationship to exist and thus, for infringement to be found, both parties must consent that the agent is acting on the principal’s behalf and subject to the principal’s control.\sup{13} Within any relationship of agency, the principal initially states what the agent shall and shall not do, in specific or general terms. The CAFC has ordered an en banc rehearing of Akamai’s appeal that focuses on the circumstances that give rise to direct infringement when separate entities each perform separate steps of a method claim and to what extent would each of the parties be liable.\sup{14}

In McKesson, the CAFC found no infringement of claims directed to an electronic method of communication between patients and their doctors (involving doctor-generated personalized web pages).\sup{15} The multi-step claims in McKesson require one step in which patients initiate communication to the doctors (for information) and other steps enabling communication, which are performed by the doctors through their software provider.

The sole issue in McKesson was whether the relationship between the software provider and the patients was such that the step of initiating communications by the patients could be attributed to the software providers. Following the holding in Akamai, the Court found that patients were not performing any of the claimed method steps as agents for the software providers, nor was there a contractual obligation between them and the patients.\sup{16} In fact, McKesson did not argue that an agency relationship existed, but rather argued that the doctor-patient relationship is more than an arms-length relationship and is sufficient to provide attribution at least because of the existence of a doctor-patient privilege. The CAFC disagreed, stating that “the doctor-patient relationship does not by itself give rise to an agency relationship or impose on patients a contractual obligation.”\sup{17} Rather, the Court found that patients acted principally for their own benefit and under their own control. The CAFC has also ordered an en banc rehearing of McKesson.\sup{18}

These two cases, arising in the context of web-based business methods, have direct applicability to the protocols in personalized medicine, and we will now analyze those.

TYPICAL PERSONALIZED MEDICINE SCENARIOS

We will describe two personalized medicine scenarios, to examine the challenges of drafting claims that would be found enforceable and not subject to the problems with split infringement of Akamai and McKesson.

Scenario 1: Doctor/Clinical Laboratory

Following a cancer diagnosis, the patient’s oncologist takes blood in the doctor’s office and sends the blood for analysis to a clinical laboratory. The clinical laboratory analyzes the blood for protein X, and sends the result back to the oncologist’s office. The oncologist then administers (or prescribes the administration of) a specific drug based on the result it receives.

A one-step method claim directed to, for example, “analyzing” the blood for the presence of protein X, would not present a joint infringement issue because only one party, the clinical lab, would perform this step. However, under the reasoning of Prometheus and the Myriad Genetics case, such a claim may run afoul of 35 U.S.C. § 101 if it is not drafted properly or if, as a result of its review, the Supreme Court determines that such a step does not involve a transformation, but is directed merely to an abstract mental process. The CAFC in Prometheus found that claims having only a “determining” step were transformative because some sort of manipulation is necessary to extract the metabolites from a bodily sample and determine their concentration.\sup{19} However, exactly how much “transformation” or physical steps are needed to save a claim from 35 U.S.C. § 101 problems remains to be decided, and it is likely that the Supreme Court will have its own views on the subject.\sup{20}

If a two-step claim is drafted, and the claim recites “analyzing a sample for the presence of protein X,” and then “administering drug Y,” the clinical lab practices the first step and the oncologist practices (or induces) the second step. Under Akamai, joint infringement would be found only if an agency relationship exists between the doctor and the laboratory, or only if the laboratory is contractually obligated to the doctor to perform the analysis step.\sup{21}

It is unlikely that a court would find an agency relationship between the doctor and the clinical laboratory.\sup{22} It is unlikely, in the strict legal sense, that the clinical laboratory acts on the doctor’s behalf. Rather, like the network provider in Akamai and the software provider in McKesson, the laboratory acts for its own benefit and under its own control, especially because a doctor is unlikely to take on the liability associated with being a principal in an agency relationship with the laboratory. Further, if a contract exists between any of the parties involved in this process, it would likely be between the patient and the clinical laboratory, and/or between the patient’s insurance company and the laboratory. Because of the lack of agency between the doctor and

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clinical lab, a two-step claim might not be infringed.

**Scenario 2: Doctor and Clinical Laboratory in One Hospital**

In this scenario, both the patient’s doctor and the clinical laboratory are located in a hospital. As with the above scenario, the clinical laboratory analyzes the blood for protein X, sends the results to the doctor upstairs and the doctor administers (or prescribes) a specific drug based on the laboratory result.

Under this scenario, a patent holder can assert the two-step claim against the doctor, the clinical laboratory and the hospital, arguing that both the doctor and the clinical laboratory are agents of the hospital, or are under contract with the hospital to perform the steps of the claim. However, at least contractually, many lab service providers even within a hospital denote themselves as “independent contractors.” An X-ray service performed in the hospital by the radiology department, for example, is sometimes billed separately from other services provided to a patient within that same hospital. This arrangement may or may not survive close scrutiny from a court evaluating patent infringement, in that the CAFC has repeatedly warned that “[a] party that engages another to perform a step of a claimed method as its agent cannot escape liability simply by designating its agent an independent contractor...”

Neither Akamai nor McKesson addresses the situation where the parties actually performing the claimed steps, while not in an agency relationship or under contract with each other, are both in an agency relationship or under contract with the same third party. In fact, the holding in Akamai that “there can only be joint infringement when there is an agency relationship between the parties who perform the method steps or when one party is contractually obligated to the other to perform the steps,” appears to preclude infringement under this scenario.

**CONCLUSION**

Customizing medicine for individuals appears to be the future of medicine. The turmoil in the law regarding the patentability and the enforceability of personalized medicine claims creates uncertainty in this community. Some single-step claims to such methods have been subject to scrutiny as mere mental steps, and therefore not eligible for patenting. Other such claims must include at least two steps to avoid prior art. When that is the case, additional complicating matters arise because two or more parties may participate in the personalized medicine process, e.g., a doctor and a laboratory, implicating the holdings of Akamai and McKesson. Under these two cases, the patent holder must show that the parties practicing the claimed method steps are in an agency relationship or one party must be under contract to the other to perform the steps. As discussed in this paper, such a showing can be quite difficult.

The CAFC, aware of the long term consequences of its holdings in Akamai and McKesson, has ordered rehearing en banc of both cases. If the CAFC affirms the holdings of Akamai and McKesson, even more emphasis will be placed on keeping the therapy providers legally distinct from the diagnostic providers to avoid any hint of agency. The existing trend of separating diagnostic providers, like radiology providers, within hospitals will therefore continue. It will then be imperative that drafters in the personalized medicine arena obtain claims that would be infringed by either the therapy provider or the diagnostic provider, but not both.

The personalized medicine community, and especially the patent holders among them, should carefully watch the Supreme Court’s review of Prometheus, the CAFC’s imminent decision in the Myriad Genetics case, and its en banc review of both Akamai and McKesson. All of these decisions promise to define how the future will look for patent protection and enforcement in the field.

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**ENDNOTES**

5. Prometheus, 628 F.3d at 1352-53.
8. 628 F.3d at 1350.
9. Id. at 1355.
10. 629 F.3d at 1321.
11. Id.
12. Id. at 1320.
13. Id. at 1319.
16. Id. at 7-8.
17. Id. at 8.
19. 628 F.3d at 1357.
20. See, e.g., In re Grams, 888 F.2d 835 (Fed. Cir. 1989) (finding algorithm-containing claim to a method of diagnosing an abnormal condition in an individual invalid under 35 U.S.C. § 101, despite the fact that the claim contained a step of performing laboratory tests on the individual).
21. See 629 F.3d at 1320.
22. See id. at 1320-21 (“An essential element of agency is the principal’s right to control the agent’s actions.”) (internal citations omitted).
23. Id. at 1320.
24. Id. (emphasis added).