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Is *Mayo v. Prometheus* the End of Diagnostic Patents?




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Introduction

In March 2012, the Supreme Court unanimously ruled in *Mayo Collaborative Services v. Prometheus Laboratories Inc.*[1] that a method for adjusting a drug dosage after observing a patient's reaction to a drug administration was patent-ineligible subject matter under 35 U.S.C. § 101.[2] The Supreme Court overturned the U.S. Court of Appeals for the Federal Circuit and ruled that two patents owned by Prometheus Laboratories are invalid because they covered naturally occurring phenomena.

In its decision, the Supreme Court identified the claimed method to be an unpatentable law of nature. The Supreme Court believed the correlation between 6-thioguanine blood levels and its dosage to be a consequence of the metabolism of thiopurine compounds in the human body, in other words, a natural occurrence. The Supreme Court further opined that any physical and transformative elements of the invention were routine and insufficient to transform an unpatentable law of nature into patent-eligible subject matter.

In this article we provide considerations of the *Prometheus* decision from both a U.S. and a European perspective.

U.S. Considerations

In response to the *Prometheus* decision, the U.S. Patent and Trademark Office (PTO) issued a series of guidelines to examiners to apply the decision to pending patent applications. As a result, a number of Section 101 rejections have been issued applying the *Prometheus* decision and, not surprisingly, claims directed to diagnostic methods were the preferred targets of these rejections.

What ramifications does this decision have for diagnostic patents? Unfortunately, diagnostic gene patents already were under scrutiny in view of *Bilski v. Kappos*[3] and *Association for Molecular Pathology v. U.S. Patent and Trademark Office*,[4] commonly known as the *Myriad* case. The *Prometheus* decision does not neces-

[1] *Mayo Collaborative Services v. Prometheus Laboratories Inc.*, 132 S.Ct. 1289 (2012).

[2] 35 U.S.C. § 101. Inventions patentable. 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.

[3] *Bilski v. Kappos*, 130 S.Ct. 3218 (2010).

[4] *Association for Molecular Pathology v. U.S. Patent and Trademark Office*, 653 F.3d 1329 (Fed. Cir. 2011).

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sarily signal the end of personalized medicine patents; rather, the decision redefines the applicability of the machine-or-transformation test and further clarifies the nature of patent-eligible subject matter.

While many diagnostic patents are under increased scrutiny and some diagnostic methods may be invalidated, it is our opinion that the *Prometheus* decision does not render all diagnostic patents invalid.

First, diagnostic methods that are tied to a transformative step and encompass a robust inventive principle remain patentable subject matter. For example, even though a method for adjusting a drug dosage after observing a patient's reaction to a drug administration was patent-ineligible subject matter under 35 U.S.C. § 101, claims directed to methods of administering a particular drug wherein the dosage is adjusted to specific preferred values of metabolite levels do involve transformative steps and may involve more than routine activity. Hence, these claims may not have been invalidated.

To determine if a claim succeeds or fails to be Section 101 patent-eligible material under *Prometheus*, one may ask the following questions:

(1) Is the claim a method or process claim? If yes, then:

(2) Does the method or process call for applying a law of nature? If yes, then:

(3) Do the steps of the method or process:

(a) Merely call for a particular audience to apply the law of nature or for applying the law of nature in a particular technological environment, or

(b) Call for ''[p]urely 'conventional or obvious' '[pre]-solution activity?' ''

If the answer to either question (3)(a) or (3)(b) is ''yes,'' then the method or process fails to be Section 101 patent-eligible material.

Second, many diagnostic patents contain kit claims. Kit claims are directed to components and instructions for using the components for performing a particular method. It is generally straightforward to determine if a kit claim is infringed, although designing around a kit claim to avoid infringement also may be relatively straightforward. However, the Federal Circuit noted that printed matter accompanying the kit generally falls outside the scope of patent-eligible subject matter circumscribed by 35 U.S.C. § 101, unless there is a '' 'functional relationship' between the printed matter and its substrate.''[5] Because ''the printed matter in no way depends on the kit, and the kit does not depend on the printed matter,'' the ''claimed instructions are not entitled to patentable weight.''[6] Even though kit claims are not necessarily ideal, they do serve a purpose for diagnostic companies and many commercial products are protected by kit claims.

Third, a potentially invalid patent under the *Prometheus* decision may be cured by reissue. 35 U.S.C. § 251 provides for the reissue of defective patents.[7] A patent may be reissued if a patent is deemed wholly or partly inoperative or invalid by reason of the patentee claiming more or less than he had a right to claim in the patent. The *Prometheus* decision may render a patent invalid and the patentee may have claimed more or less than he had a right to claim. If there is sufficient disclosure in the specification for a transformative step and/or kit claims, reissue could be a cure for patents rendered invalid by the *Prometheus* decision.

European Considerations

Prometheus is a decision of the U.S. Supreme Court and, accordingly, is not effective in any of the states of the European Patent Convention (EPC). However, decisions of the U.S. courts are, sometimes, seen as persuasive both by the national courts of the member states and the Boards of Appeal of the European Patent Office (EPO).

The issue of patent-eligible subject matter is not foreign to European courts and to the EPO boards. Article 52(2) EPC provides that certain classes of subject matter are not patentable.[8] Amongst the exclusions are scientific theories, as well as methods for performing mental acts. Therefore, the European statute books certainly have provisions addressing the issues that the Supreme Court considered.

The EPC provides that the exclusions to patentability are to be applied ''as such''[9]. The EPO interprets this as meaning that the exclusion is not to encompass ''inventions'' that incorporate excluded subject matter; in this much, the approach of the EPC is similar to the approach in *Diamond v. Diehr* quoted by the Supreme Court in *Prometheus*. However, the EPO assesses the presence of a non-excluded invention by analyzing the claim for the presence of that uniquely European feature, ''technical'' subject matter. If the claim is ''technical'' the exclusion does not apply.

In the case of the patents considered in *Prometheus*, the EPO most likely would have taken a very different approach than the U.S. courts. The European equivalent was granted by the EPO and has not yet been challenged (EP 1 115 403).[10]

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[5] *AstraZeneca LP v. Apotex Inc.*, 633 F.3d. 1042 (Fed. Cir. 2010).

[6] *In re Ngai*, 367 F.3d 1336 (Fed. Cir. 2004).

[7] 35 U.S.C. 251. Reissue of defective patents. Whenever any patent is, through error without any deceptive intention, deemed wholly or partly inoperative or invalid, by reason of a defective specification or drawing, or by reason of the patentee claiming more or less than he had a right to claim in the patent, the Director shall, on the surrender of such patent and the payment of the fee required by law, reissue the patent for the invention disclosed in the original patent, and in accordance with a new and amended application, for the unexpired part of the term of the original patent. No new matter shall be introduced into the application for reissue.

[8] Article 52(2) EPC: The following in particular shall not be regarded as inventions within the meaning of paragraph 1: (a) discoveries, scientific theories and mathematical methods; (b) aesthetic creations; (c) schemes, rules and methods for performing mental acts, playing games or doing business, and programs for computers; (d) presentations of information.

[9] Article 52(3) EPC: Paragraph 2 shall exclude the patentability of the subject-matter or activities referred to therein only to the extent to which a European patent application or European patent relates to such subject matter or activities as such.

[10] Claim 1 reads as follows: 1. An in vitro method for determining efficacy of treatment of a subject having an immune-mediated gastrointestinal disorder or a non-inflammatory bowel disease (non-IBD) autoimmune disease by administration of a 6-mercaptopurine drug, comprising determining in vitro a level of 6-thioguanine in a sample from said subject having said immune-mediated gastrointestinal disorder or said non-inflammatory bowel disease (non-IBD) autoimmune disease, wherein said treatment is considered efficient if the level

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The claim is clearly in the realms of technical subject matter, as it relates to an *in vitro* assay. None of the exclusions of Article 52(2) EPC would apply to such an invention.

The question would need to be asked if, in the face of relevant prior art, there could be any reason for the holding that part of the subject matter of the claim could not be used for asserting novelty or inventive step. And the answer would be, most probably, no.

An EPO Board of Appeal would be very unlikely to make the same arguments regarding ''laws of nature'' as are made in *Prometheus*. The invention in EP 1 115 403 is in essence about identifying and selecting a population of individuals for treatment. This has long been held to be patentable subject matter in the EPO. In decision T19/86 the technical Board of Appeal, referring to the decision G5/83 of the Enlarged Board of Appeal, held that a new medical use could be patentable based on its applicability to a new group of patients (here, a new group of pigs). In EP 1 115 403, the claim effectively defines a group of patients, and that is patent-eligible subject matter in the EPO. The question could then be asked, whether the definition of that group is novel and inventive.

The national courts of the EPC member states do sometimes differ in approach to the Technical Boards of the EPO, and in the past have issued differing opinions on the subject or exclusions from patentability. However, the current approach of the EPO set forth above is now so firmly established, and the political and judicial pressure on national courts to follow the EPO is so great, that it would be very surprising to see any court deviate from the principles of the EPO jurisprudence outlined above.

In summary, the EPO and the national courts of the EPC member states would be very unlikely to take a view similar to the *Prometheus* decision, or to hold this decision to be persuasive. EPO jurisprudence has considered issues that are very similar in nature, and come to a different point of view. There appears to be no reason why that point of view would be changed as a result of the *Prometheus* decision.

Conclusion

Even though the *Prometheus* decision has ramifications for some method claims of diagnostic patents, it does not spell the end of diagnostic patents. It is unlikely that most diagnostic patents contain only method claims that are directed to natural phenomena. Diagnostic patents with *Prometheus* problems in the United States may be cured by reissue. Furthermore, it is highly unlikely that the EPO and the national courts of the EPC member states would apply the *Prometheus* decision to EP patents.

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of 6-thioguanine is in the range of about 230 pmol per 8x108 red blood cells to about 400 pmol per 8x108 red blood cells.