

**From:** betty.ryberg@novartis.com [mailto:betty.ryberg@novartis.com]  
**Sent:** Monday, November 09, 2009 6:10 PM  
**To:** AB98 Comments  
**Subject:** Comments on Interim 35 USC 101 Instructions

November 9, 2009

The Honorable David J. Kappos  
Under Secretary of Commerce for Intellectual Property and  
Director of the U.S. Patent and Trademark Office  
Mail Stop Comments—Patents, Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313–1450

ATTN: Caroline D. Dennison  
*Submitted by email to [AB98.Comments@uspto.gov](mailto:AB98.Comments@uspto.gov)*

**Re: Comments on “Interim Examination Instructions for Evaluating Subject Matter Eligibility Under 35 U.S.C. § 101”**

On September 17, 2009, the United States Patent and Trademark Office (“USPTO”) published a Notice in the Federal Register (Vol. 74, No. 179) requesting comments on the August 27, 2009 Interim Patent Subject Matter Eligibility Examination Instructions (“the Instructions”). As the Instructions are of great importance to Examiners and Applicants alike, we appreciate the opportunity to provide comments on them to the USPTO. The Instructions provide general guidance on examining claims involving “laws of nature” or “natural phenomena,” two categories excepted from patent protection when claimed *per se*. We note, however, that there are no specific examples of how to examine claims that involve testing for a specific marker and the state of health of a subject in whom the marker is detected or measured.

While we agree with the USPTO that the law with respect to patent eligible subject matter under 35 U.S.C. § 101 remains in flux as we await the United States Supreme Court’s decision in the *Bilski* case, we do not believe that decision will necessarily address therapeutic and diagnostic method claims involving correlations. Nevertheless, because such claims are of great importance to many members of the public, including Novartis Corporation, we believe they need to be addressed in the Instructions in view of current Federal Circuit case law.

Since the publication of the Instructions last August, the Federal Circuit rendered its decision in *Prometheus Laboratories, Inc. v Mayo Collaborative Services et al.*, 581 F.3d 1336 (Fed. Cir. 2009). We believe this case provided substantial guidance on the patent eligibility of therapeutic and diagnostic method claims that represent real-world, practical applications of correlations between a detected or measured marker and a subject’s state of health. Consistent with the *Prometheus* decision, we provide herein proposed examples of how to apply the transformation prong of the “machine or transformation

test” of *In re Bilski*, 545 F.3d 943 (Fed. Cir. 2008) to three common formats of claims to therapeutic and diagnostic method claims including these correlations. We recommend that the USPTO incorporate such examples, or ones like them, into the Instructions to provide clear guidance on the patentability of such therapeutic and diagnostic methods.

Significant advancements in medicine now taking place are based on discoveries that specific markers can serve as reliable indicators of human and animal health, including the existence of disease, the likelihood of developing a disease in the future, responsiveness to particular drugs, drug efficacy and drug toxicity. These markers may be genetic sequences, expressed mRNA and proteins, other natural biochemical compounds such as hormones, cytokines, amino acids, types of cells, cellular processes (such as cell division or cell death) or many other natural substances or phenomena. All of the foregoing may be placed in the category of “biomarker.” The markers may also be administered drug substances or their metabolites. Once detected or measured in a patient sample they serve as the basis of a specific diagnosis and/or course of therapy.

There are two common formats to method of treatment claims involving correlations. The first, like some of the claims at issue in *Prometheus*, recites a method of optimally treating a particular disease comprising the administration of a defined group of drugs or a specific drug to a patient followed by a diagnostic test performed on a bodily fluid or tissue of the patient to see if the level of drug (or its active metabolite) is in an acceptable range for efficacy or an unacceptable range of toxicity. In the second common format, the diagnostic step is performed first to test for a biomarker in a patient sample that is indicative or predictive of a specific disease (or drug responsiveness), followed by a step of administering a defined group of drugs or a specific drug to treat or prevent the disease. The reasoning in *Prometheus* applies to both claim formats and compels the conclusion that both represent patent eligible subject matter. The drug administration step in each method is transformative of the patient and easily satisfies the transformation prong of the *Bilski* test. *Prometheus v Mayo*, 581 F.3d at 1345-46.

There is a third common claim format involving correlations that is purely diagnostic, *i.e.*, there is no drug administration step preceding or following the detection or measurement of the marker. Such claims are typically phrased as a method for diagnosing a particular disease by detecting the presence of, or measuring the level of, a particular marker in a patient sample and concluding whether or not the patient has the disease based on the correlation. Such claims are perhaps most famously illustrated by those at issue in *Laboratory Corp. of America Holdings v. Metabolite Laboratories Inc.*, 126 S.Ct. 2921 (2006).

The reasoning in *Prometheus* also applies to such diagnostic claims and, again, compels the conclusion that they are patent eligible. Also at issue in *Prometheus* were claims that did not recite a drug administration step, but only the steps of measuring the marker (in *Prometheus*, a metabolite) and performing the correlation. The Federal Circuit reasoned that the marker measurement step was transformative. The marker was not measurable by mere inspection. A patient sample had to be manipulated to measure the marker and those manipulations satisfied the transformation prong of the *Bilski* test. The

measurement of the metabolite was not insignificant extra-solution activity; it was central to the purpose of the method. *Prometheus*, 581 F.3d at 1347-48.

Thus, where a diagnostic claim that involves a correlation calls for the detection or measurement of a marker in a patient sample, then such claim is patent eligible. Notably, while the claim must recite a measurement, assaying or determining step, the specific analytical equipment or machines used to measure, assay or determine the marker present in the sample need not be recited in the claim. It is important to impress this aspect of the *Prometheus* decision on examiners, or they may incorrectly require that such specific technological implementations of the step be written into such claims to satisfy the subject matter requirement of 35 U.S.C. § 101.

Lastly, we note that the Instructions require a final confirmation step in the determination of whether a process or method claim is patent-eligible or not: "Confirm that the machine-or-transformation test was conducted correctly by considering whether the method is so abstract and sweeping as to have no real world application or pre-empts substantially all practical uses of a mathematical algorithm, a law of nature or a natural phenomena." (August 27, 2009 interim Patent Subject Matter Eligibility Examination Instructions, page 8.) We submit that for the method of treatment and diagnostic claims discussed herein and outlined in the proposed examples submitted herewith, that specify particular diseases and particular markers and call for transformative drug administration and/or marker determination steps, then there is no risk that the method will be so abstract or sweeping as to have no real world application nor will it preempt substantially all practical uses of the correlation.

We appreciate the opportunity to provide these comments in response to the Notice and would be pleased to answer any questions our comments may raise.

Sincerely Yours,

**Betty Ryberg**  
**Vice President, IP Litigation**  
**Novartis Corporation**  
Corporate Intellectual Property  
USNY, 608-1010  
Novartis Corporation  
608 Fifth Avenue  
New York, NY 10020  
USA  
Phone: +1 212 830 2475  
Fax: +1 212 830 2495  
Email : [betty.ryberg@novartis.com](mailto:betty.ryberg@novartis.com)



- **Claim 1. A method of treating disease X comprising:**
  - (a) administering compound Y to a patient having disease X, and**
  - (b) determining the level of compound Y (or an active metabolite of compound Y) in said patient;**

**wherein a level of compound Y (or the active metabolite of compound Y) less than threshold A indicates a need to increase the amount of compound Y subsequently administered to said patient, and**

**wherein a level of compound Y (or the active metabolite of compound Y) greater than threshold B indicates a need to decrease the amount of compound Y subsequently administered to the patient.**
  
- Is there a particular machine? (M2)
  - NO - there is no machine explicitly recited or inherently required.
  
- Is there a transformation of an article? (M5)
  - YES - the patient is transformed by the administration of compound Y and the sample used in the determining step is necessarily transformed by the activity associated with that determining step, if such activity entails more than mere inspection.
  
- Does the transformation impose a meaningful limit and is it more than insignificant extra-solution activity? (M6)
  - YES - both the administration of compound Y and the determining step are central to the method invented by applicant - they are not mere field-of-use limitations or insignificant extra-solution activity.
  
- The Claim is **eligible** (M4)

USPTO Note: Comments submitted by Novartis on Nov. 9, 2009.

- **Claim 2. A method of treating disease X in a patient in need of such treatment comprising:**
  - (a) determining the presence of biomarker Y in a sample from said patient; and**
  - (b) if biomarker Y is present, administering a therapeutically effective amount of compound A.**
  
- Is there a particular machine? (M2)
  - NO - there is no machine explicitly recited or inherently required.
  
- Is there a transformation of an article? (M5)
  - YES - the patient is transformed by the administration of compound Y and the sample used in the determining step is necessarily transformed by the activity associated with that determining step, if such activity entails more than mere inspection.
  
- Does the transformation impose a meaningful limit and is it more than insignificant extra-solution activity? (M6)
  - YES - both the determining step and the administration step are central to the method invented by applicant - they are not mere field-of-use limitations or insignificant extra-solution activity.
  
- The Claim is **eligible** (M4)

USPTO Note: Comments submitted by Novartis on Nov. 9, 2009.

- **Claim 3. A method of diagnosing disease X in a patient comprising: determining the presence of biomarker Y in a sample from said patient, wherein the presence of biomarker Y in said sample is indicative of disease X.**
  - Is there a particular machine? (M2)
    - NO - there is no machine explicitly recited or inherently required.
  - Is there a transformation of an article? (M5)
    - YES - the sample used in the determining step is necessarily transformed by the activity associated with that determining step, if such activity entails more than mere inspection.
  - Does the transformation impose a meaningful limit and is it more than insignificant extra-solution activity? (M6)
    - YES - the detection step is central to the method invented by applicant - it is not a mere field-of-use limitation or insignificant extra-solution activity.
- The Claim is **eligible** (M4)

USPTO Note: Comments submitted by Novartis on Nov. 9, 2009.