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The Patent Eligibility of Diagnostic Methods after Prometheus: A Redefined Test for Transformation

Scott Frederick Peachman

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THE PATENT ELIGIBILITY OF DIAGNOSTIC METHODS AFTER *PROMETHEUS*: A REDEFINED TEST FOR TRANSFORMATION

Scott Frederick Peachman[†]

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INTRODUCTION

Diagnostic methods offer a tremendous value to our society, with benefits that usually far exceed their costs. Physicians and laboratory technicians use diagnostic methods to determine the presence of diseases or disorders without having to perform expensive surgery. A series of non-invasive steps, such as obtaining a sample from a patient, running tests on the sample, and interpreting results, is one example of a simple diagnostic method that can yield essential treatment information. A recent study shows that, while diagnostic methods comprise about 5 percent of hospital costs and about 1.6 percent of all Medicare costs, their results may influence up to 60–70 percent of health-care decision-making.¹ There is a noticeably high benefit-to-cost ratio when performing diagnostic methods that warrants our attention to their future development and implementation in health care.

¹ LEWIN GROUP, THE VALUE OF DIAGNOSTICS INNOVATION, ADOPTION AND DIFFUSION INTO HEALTH CARE 147, 148 (July 2005), <http://www.advamed.org/NR/rdonlyres/61EB858F-EC9E-4FAB-9547-09DABF7D2A72/0/thevalueofdiagnostics.pdf>.

Unfortunately, the benefits of diagnostic methods have been diminished by increased competition to develop the most lucrative tests.² Corporations involved in the diagnostic market have placed a “heavy reliance” on obtaining patent protection in order to recoup money spent on research and development.³ Patents enable corporations to block their competitors from making or using any diagnostic method that is similar to a patented method.⁴ While aggressively seeking patent protection may represent a wise business decision on behalf of a diagnostic corporation, it does not take into account the negative implications for society. Some diagnostic method patents are overly broad and include what is arguably an exclusive right to use the human body’s natural pathways or mental faculties.⁵ These sorts of patents hinder the progress of science and medicine by imposing barriers to research and patient treatments that require access to the human body’s natural functions.⁶

While the purpose of the patent system is to enhance social welfare by incentivizing research and development,⁷ the subsequent blocking of critical avenues of research and treatment is contrary to this purpose, and therefore can be seen as an “unintended effect.”⁸ This unintended effect has been acutely recognized by pathology labs, which routinely perform patented diagnostic methods in order to study disease.⁹ The Association for Molecular Pathology (AMP) has stated that while patents “are originally intended to provide incentives” to conduct basic research, they have, in reality, hindered the growth of pathology labs by imposing exorbitant licensing fees.¹⁰ The Supreme

² See John Carol, *Convergence in the Midst of Competition*, BIOTECHNOLOGY HEALTHCARE 31–32, 38–39 (Dec. 2007).

³ See LEWIN GROUP, *supra* note 1, at 62.

⁴ See 35 U.S.C. § 271(a) (2006).

⁵ See *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 135–38 (2006) (Breyer, J., dissenting) (citing *Parker v. Flook*, 437 U.S. 584, 588 (1978)).

⁶ See *id.* at 126–27 (“[S]ometimes *too much* patent protection can impede rather than ‘promote the Progress of Science and useful Arts.’”) (citation omitted).

⁷ STEPHEN A. MERRILL ET AL., *A PATENT SYSTEM FOR THE 21ST CENTURY* 39 (2004).

⁸ See LEWIN GROUP, *supra* note 1, at 62.

⁹ See Barbara A. Zehnbauer, *Clinical Testing of Patient’s Specimens*, in *MOLECULAR GENETIC TESTING IN SURGICAL PATHOLOGY* 171, 184 (John D. Pfeifer ed., 2006) (explaining that these patented diagnostic methods include genetic tests and molecular medicine techniques).

¹⁰ *Id.* at 184. Laboratories that use a patented method without paying a licensing fee may be served with a cease and desist letter. See S. Chandrasekharan et al., *Impact of Gene Patents and Licensing Practices On Access to Genetic Testing for Hereditary Hemochromatosis*, 12 *GENETICS MEDICINE*, S155–S170 (2010). If they create their own internal test similar to the patented method, they may be sued for

Court¹¹ and the American Medical Association (AMA)¹² have also identified this unintended effect on physicians who are forced to conduct extensive patent research before ordering a diagnostic test for a patient.

This Note will attempt to reconcile the traditional role of the patent system, to provide incentives to invent, with its unintended effect of blocking essential avenues of research and treatment. To achieve this end, this Note will focus on what types of diagnostic methods should be eligible for patenting. Clarifying the proper scope of patent eligibility should prohibit patents on overly-broad diagnostic methods while still retaining traditional incentives to invent. In Part I, I will provide background on common diagnostic methods and the factors affecting their development. In Part II, I will provide background on basic patent law principles and the current legal debate over diagnostic method patent eligibility. In Part III, I will discuss two common arguments against granting patents on diagnostic methods. In Part IV, I will discuss the recent *Prometheus* decision and its effect on patent eligibility. In Part V, I will propose a redefined version of the current test for patent-eligible subject matter, the machine-or-transformation test, and apply it to the diagnostic method patents at issue in recent Federal Circuit cases.

I. ATTRIBUTES OF DIAGNOSTIC METHODS

With each passing year, diagnostic methods are becoming more accurate, precise, and comprehensive.¹³ While present diagnostic methods have already been shown to increase patient health and reduce health-care costs,¹⁴ future tests should provide more effective treatments that are better calibrated to treatment risks and perhaps even tailored to individual characteristics.¹⁵ While many diagnostic

infringement. See 35 U.S.C. §271(a); *Lear Siegler Inc. v. Sealy Mattress Co.*, 873 F.2d 1422, 1425 (Fed. Cir. 1989) (discussing the “Doctrine of Equivalents”).

¹¹ *Lab. Corp.*, 548 U.S. at 138 (noting that some diagnostic patents may “divert resources from the medical task of health care to the legal task of searching patent files for similar simple correlations”).

¹² See Aaron S. Kesselheim & Michelle M. Mello, *Medical Process Patents—Monopolizing the Delivery of Health Care*, 355 NEW ENG. J. MED. 2036, 2036 (2006).

¹³ See LEWIN GROUP, *supra* note 1, at 42.

¹⁴ See *id.* at 1; this is generally true when diagnostic tests are accurate. Sometimes diagnostics produce “false negative error[s],” where a disease is present but undetected, and “false positive error[s],” where a disease is not present but detected. *Id.* at 67–68.

¹⁵ *Id.* at 1 (“As such products mature, clinicians and patients will be better able to access the risks and benefits of care options and customized health management strategies to optimize individual health and quality of life.”). This has also been

methods have yet to be implemented for consumers and health-care providers, a few are routinely used today. Common diagnostic methods used by health-care providers include, but are not limited to, medical imaging, blood assays, and genetic tests.

A. Examples of Diagnostic Methods

X-ray methods are a form of medical imaging used to diagnose bone disorders. A high frequency electromagnetic signal is transmitted and becomes attenuated as it passes through the body.¹⁶ The remaining signal is captured on film for subsequent analysis.¹⁷ An alternative to X-ray methods is Medical Resonance Imaging (MRI), which is used to diagnose disease in soft tissues such as the brain, muscles, and heart.¹⁸ MRI methods involve the application of a magnetic field to a patient and the transmission of radio frequency pulses.¹⁹ Resonance energy is emitted by the patient and picked up by a receiver that outputs data onto a screen for viewing.²⁰ To improve image clarity, both X-rays and MRIs involve the oral or intravenous administration of a contrast agent to a patient.²¹

Unlike medical imaging methods, blood assays and genetic tests require a physical sample to be extracted from a patient.²² Blood assays are used to identify immune response deficiencies, drug levels, and other forms of disease.²³ A typical first step is to take a blood sample from a patient using a hypodermic syringe and needle. The blood sample is then subjected to a number of tests involving

referred to as the “promise of personalized medicine.” See Michael O. Leavitt & Raju Kucherlapati, Op-Ed, *The Great Promise of Personalized Medicine*, BOSTON GLOBE, Dec. 26, 2008, at A19.

¹⁶ CHEST X-RAY IN CLINICAL PRACTICE 15 (Rita Joarder & Neil Crundwell eds., 2009).

¹⁷ *Id.*

¹⁸ See GARY LINEY, MRI IN CLINICAL PRACTICE 11 (2006).

¹⁹ See U.S. Patent No. 6,414,488 (filed Mar. 1, 2000).

²⁰ See *id.*

²¹ CONTRAST-ENHANCED CLINICAL MAGNETIC RESONANCE IMAGING 1–2 (Val M. Runge ed., 1997); *Contrast Agents*, AM. SOC’Y RADIOLOGIC TECHNOLOGISTS, <https://www.asrt.org/content/ThePublic/AboutRadiologicProcedures/ContrastAgents.aspx> (last visited Mar. 14, 2011).

²² Blood assays and genetic tests are also a form of in vitro diagnostic as they are performed on samples extracted from the body. Medical imaging methods such as X-ray and MRI that monitor health within the body are referred to as in vivo diagnostics. LEWIN GROUP, *supra* note 1, at 14.

²³ See R. Hussain et al., *Cytokine Profiles Using Whole-Blood Assays Can Discriminate Between Tuberculosis Patients and Healthy Endemic Controls in a BCG-Vaccinated Population*, 264 J. IMMUNOLOGICAL METHODS 95 (2002).

reagents.²⁴ Test results are analyzed individually by a medical technician or in quick succession by a machine.²⁵

Genetic tests are more complex than blood assays and are used to diagnose diseases which can be traced to genetic alterations. Myriad's BRACAnalysis test, for example, is used to diagnose breast cancer.²⁶ The first step is to take a sample from a patient by drawing blood or using a cheek swab or mouthwash.²⁷ The sample is then sent to Myriad for purification of specific gene fragments, amplification, and sequencing.²⁸ The sample sequence is compared against a reference sequence in order to make a diagnosis.²⁹

B. Factors Affecting Diagnostic Method Development

There are three main factors affecting the development of new diagnostic methods: administrative regulation, insurance coverage and reimbursement policies, and industrial competition.³⁰ The FDA regulates diagnostics similarly to medical devices by categorizing them into three risk-based classes.³¹ Class I represents minimal potential for harm, while Class III includes riskier diagnostics such as HIV test kits.³² Class III diagnostics are placed under the most regulatory scrutiny and may be subject to a pre-market approval process.³³

Diagnostics performed in a hospital setting account for 60 percent of the diagnostic industry's revenue,³⁴ therefore their implementation is highly dependent on insurance coverage and reimbursement policies. Medicare reimbursement policies often affect the policies of other medical insurance groups because Medicare is "the largest purchaser of clinical laboratory services in the US."³⁵ The reimburse-

²⁴ *Id.*

²⁵ *Id.* Rapid testing of samples with a machine is known as high-throughput screening.

²⁶ See BRACAnalysis® Questions and Answers, MYRIAD GENETIC LABORATORIES, <https://www.myriadpro.com/node/109/anchor#brfaq1> (last visited Mar. 6, 2012).

²⁷ *Id.*

²⁸ BRACAnalysis® Technical Specifications, MYRIAD GENETIC LABORATORIES I (Feb. 2012), <http://www.myriad.com/lib/technical-specifications/BRACAnalysis-Technical-Specifications.pdf>.

²⁹ *Id.*

³⁰ LEWIN GROUP, *supra* note 1, at 59–63.

³¹ *Id.* at 60.

³² *Id.*

³³ *Id.*

³⁴ *Id.* at 27.

³⁵ *Id.* at 61 (citing INSTITUTE OF MEDICINE, MEDICARE LABORATORY PAYMENT POLICY NOW AND IN THE FUTURE 17 (2000)).

ment rates set by Medicare for diagnostic methods do not always correspond with development costs, and novel diagnostics are often reimbursed at rates similar to outdated tests.³⁶ This reimbursement structure discourages development and may hinder innovation.³⁷

The third factor affecting diagnostic method development is competition to create the most lucrative diagnostic methods. The creation of novel diagnostic methods involves highly technical research that is often risky and expensive.³⁸ To offset this risk and increase the chance of recouping research and development costs, corporations work extremely hard to “protect” their investments through patents. Patent protection ensures that the corporations will benefit exclusively from the success of their inventions for the life of the patent, which is normally twenty years from filing.³⁹ Patents reduce the risk inherent in technology investments, which can aid in the search for third-party funding.⁴⁰

However, recent judicial developments may threaten corporate reliance on patent protection for diagnostic methods. In June 2010, the Supreme Court in *Bilski v. Kappos* revisited what types of inventions should be eligible to receive a patent for the first time in twenty-nine years.⁴¹ The Court expressly invited the Court of Appeals for the Federal Circuit, which has exclusive appellate jurisdiction over patent cases, to impose new limitations on patent eligibility.⁴² Since *Bilski*, the Federal Circuit has decided two cases which have a bearing on the future of diagnostic method patents.⁴³ To understand the recent changes that have come about in patent law, the next section will provide background.

³⁶ *Id.*

³⁷ *Id.*

³⁸ *Id.* at 62.

³⁹ *Id.*

⁴⁰ See George J. Annas, *Surrogate Embryo Transfer: The Perils of Patenting*, HASTINGS CTR. REP., June 1984, at 25, 26 (Dr. Buster, the inventor of surrogate embryo transfer, states that investors would not have funded his research without a “chance to profit from their investment via patenting and licensing the products and processes . . .”).

⁴¹ *Bilski v. Kappos*, 130 S.Ct. 3218, 3223 (2010); see Margaret Kubick, *An Uncertain Future: The Impact of Medical Process and Diagnostic Method Patents on Healthcare in the United States*, 9 NW. J. TECH. & INTELL. PROP. 280–81 (2010).

⁴² *Id.* at 16.

⁴³ See *Ass’n for Molecular Pathology v. USPTO*, 653 F.3d 1329, 1334 (Fed. Cir. 2011); *Classen Immunotherapies v. Biogen Idec (Classen II)*, 659 F.3d 1057, 1059 (Fed. Cir. 2011).

II. BASIC PATENT LAW PRINCIPLES AND THE LEGAL DEBATE OVER DIAGNOSTIC METHOD PATENT ELIGIBILITY

A. Patent System Foundation

The American patent system consists of a legal framework to protect any “new and useful process, machine, manufacture, or composition of matter.”⁴⁴ Congressional authority over patents is granted by Article I, Section 8 of the Constitution, which seeks “[t]o promote the Progress of Science and useful Arts” by granting an exclusive right to an inventor on his invention for a limited time.⁴⁵ Under the utilitarian theory of patent law, this phrase has been interpreted to protect only those inventions that enhance the nation’s social welfare.⁴⁶ In other words, a patent should provide more incentives to create beneficial, new technologies than disincentives to do so.

Four statutory provisions have been enacted to ensure that patents enhance the nation’s social welfare and promote science.⁴⁷ The first provision, 35 U.S.C. § 101 (§ 101) defines patent-eligible subject matter.⁴⁸ Inventions that do not come within the scope of § 101 are deemed non-statutory and ineligible for a patent, regardless of their other characteristics. The second provision defines novelty of invention and how one may lose her patent rights through specific acts.⁴⁹ The third provision defines how inventions must be “non-obvious” to one having ordinary skill in the art.⁵⁰ The fourth provision requires inventions be properly disclosed to the public and described well enough that someone can make and use it.⁵¹

This Note will focus on the first provision, § 101, and more specifically, the first of four enumerated categories within this provision: “new and useful process[es].”⁵² This Note will not analyze the other three categories of § 101,⁵³ nor will it analyze the other three

⁴⁴ 35 U.S.C. § 101 (2011).

⁴⁵ U.S. CONST. art. I, § 8, cl. 8.

⁴⁶ David S. Olson, *Taking the Utilitarian Basis for Patent Law Seriously: The Case for Restricting Patentable Subject Matter*, 82 TEMP. L. REV. 181, 184 (2009).

⁴⁷ §§ 101–103, 122.

⁴⁸ *Id.* § 101.

⁴⁹ *Id.* § 102.

⁵⁰ *Id.* § 103.

⁵¹ *Id.* § 112.

⁵² *Id.* § 101.

⁵³ *Id.* (The other subject matter categories of § 101 are “any new and useful . . . machine, manufacture, or composition of matter, or any new and useful improvement thereof.”).

statutory provisions,⁵⁴ each of which can preclude the issuance of a patent. While diagnostic methods may involve the use of a machine or a patented drug, there is a single category of patent eligibility for the “process” or method itself, which is removed from the physical objects associated with it. For example, in *Prometheus Laboratories, Inc. v. Mayo Collaborative Services (Prometheus II)*,⁵⁵ a laboratory owned a method patent on a multi-step metabolites test that optimizes the delivery of drugs used to treat a specific autoimmune disease.⁵⁶ The laboratory’s method patent covers each step of the metabolite test, but it does not extend to the drugs themselves, which are unpatented and commonly used.⁵⁷

B. The Legal Debate Over Diagnostic Method Patent Eligibility

The history of the *Prometheus II* decision shows that what constitutes a patent eligible diagnostic method is currently up for debate. In this case, a clinical pathology lab associated with the Mayo Clinic in Rochester, NY, purchased and performed Prometheus Laboratories’ patented Thiopurine Metabolites test in order to optimize the treatment of inflammatory bowel disease.⁵⁸ A common problem associated with treating inflammatory bowel disease is that a small percentage of patients poorly metabolize thiopurine drugs, which can produce toxic side effects.⁵⁹ Prometheus’ Thiopurine Metabolites test addresses this problem by minimizing toxic side effects unique to a patient’s metabolic response.⁶⁰ Since this test relies on a patient’s individual ability to metabolize an administered drug, it can be characterized as a personalized method.

After years of paying licensing fees, the Mayo Clinic began using its own version of the Prometheus Thiopurine Metabolites test at its clinics and hospitals.⁶¹ Prometheus Laboratories sued the Mayo Clin-

⁵⁴ *Id.* § 101–103.

⁵⁵ *Prometheus Labs., Inc. v. Mayo Collaborative Servs. (Prometheus II)*, 628 F.3d 1347 (Fed. Cir. 2010).

⁵⁶ *Id.* at 1349–50.

⁵⁷ *See id.* at 1350.

⁵⁸ *See id.* at 1351; see supra Part III.A (for a discussion of Prometheus II in greater detail).

⁵⁹ See A.F.Y. Al Hadithy et al., *Thiopurines in Inflammatory Bowel Disease: Pharmacogenetics, Therapeutic Drug Monitoring and Clinical Recommendations*, 37 DIGESTIVE & LIVER DISEASE 282, 282–83 (2005).

⁶⁰ *See Prometheus II*, 628 F.3d at 1350.

⁶¹ *Id.* at 1351.

ic for patent infringement.⁶² As a defense, the Mayo Clinic argued that the Prometheus patent was invalid because of ineligible subject matter.⁶³ The district court found that the method patent was invalid, but the Federal Circuit reversed (*Prometheus I*).⁶⁴ The Supreme Court granted certiorari in light of its *Bilski* decision,⁶⁵ and the case was vacated and removed to the Federal Circuit.⁶⁶ On December 17, 2010, the Federal Circuit reaffirmed its previous holding that the patent was valid.⁶⁷

The different outcomes reached in *Prometheus* at the district and circuit levels are directly related to two common arguments against granting patents on diagnostic methods. The next section will explain these arguments.

III. TWO COMMON ARGUMENTS AGAINST DIAGNOSTIC METHOD PATENTS

There are two common arguments against granting patents on diagnostic methods. The first is that diagnostic methods may include “laws of nature, natural phenomenon, and abstract ideas” (hereinafter referred to as “general concepts”), which are commonly excluded by patent law.⁶⁸ The second is that granting patents on some diagnostic methods may violate medical ethical standards. The first argument has been of particular importance in recent judicial analysis,⁶⁹ while the latter has been influential but appears to have lost favor in the Federal Circuit.⁷⁰

⁶² *Id.*

⁶³ *Id.* at 1351–52.

⁶⁴ *Prometheus Labs., Inc. v. Mayo Collaborative Servs. (Prometheus I)*, 581 F.3d 1336, 1350 (Fed. Cir. 2009).

⁶⁵ *See Bilski v. Kappos*, 130 S.Ct. 3218 (2010).

⁶⁶ *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 130 S. Ct. 3543 (2010).

⁶⁷ *Prometheus II*, 628 F.3d at 1355.

⁶⁸ *See Diamond v. Diehr*, 450 U.S. 175, 185 (1981) (identifying three categorical exclusions from patent-eligible subject matter).

⁶⁹ *See Bilski*, 130 S.Ct. at 3229 (Reaffirming the importance of applying the traditional three exclusions when evaluating method patents: “In searching for a limiting principle, this Court’s precedents on the unpatentability of abstract ideas provide useful tools.”).

⁷⁰ *See Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 138 (2006) (Breyer, J., dissenting); but *cf. Prometheus I*, 581 F.3d 1336, 1346 & n.3 (2009) (“[*Lab. Corp.*’s] dissent is not controlling law and also involved different claims from the ones at issue here.”).

A. Preemption and the Exclusion of General Concepts

When a diagnostic method requires use of the human body's natural pathways or mental faculties, there are limited ways that this method may be eligible for patenting.⁷¹ The patent laws tend to discourage any method that incorporates a concept or phenomenon within the public domain. Consider, for example, if a patent was granted on a diagnostic method with a step comparing the level of two common metabolites (small, molecular products of metabolism) in order to infer the presence of a disease.⁷² The patent holder (patentee) would have a right to exclude the public from conducting any experiment that includes both steps. This overly broad patent would preempt public use of the human body's natural faculties by giving the patentee the right to exclude in seemingly limitless scenarios that involve comparing these two common metabolites and inferring that there is a disease. Furthermore, future inventors would be deterred from experimenting with these metabolites for fear that they may somehow determine the metabolite levels, subconsciously infer what the relative levels mean, and, as a result, commit patent infringement.

To justify patenting a diagnostic method that uses a general concept, one commentator has said that a necessary calculus should be performed, weighing "the freedom and accessibility of knowledge and ideas necessary to fuel creativity, while at the same time providing enough proprietary control over the products of the knowledge and ideas to provide economic incentives."⁷³ If a diagnostic method involving a general concept was limited to a particular set of drugs or conditions, or limited to diagnosis of specific diseases, the general concept used in the method is necessarily less general and less likely to "preempt" all future public use. Granting a patent on a more specialized application ensures that the general concept remains free to the public, while also offering enough proprietary control to maintain incentives to invent.

The prevailing judicial approach to analyzing whether preemption of a general concept has occurred is a "holistic" utility test.⁷⁴ In *Dia-*

⁷¹ See *Diehr*, 450 U.S. at 185 (identifying three categorical exclusions from patent-eligible subject matter).

⁷² This generalized example is similar to the method patent in *Lab. Corp.* 548 U.S. at 137.

⁷³ See JEFFREY H. MATSUURA, *JEFFERSON VS. THE PATENT TROLLS* 10 (2008).

⁷⁴ See Maureen A. O'Rourke, *The Story of Diamond v. Diehr: Toward Patenting Software*, in *INTELLECTUAL PROPERTY STORIES* 217 (Jane C. Ginsburg & Rochelle Cooper Dreyfuss, eds. 2006) (*Diehr's* holistic approach has since replaced the substantive force of the previous tests for preemption).

mond v. Diehr, the Supreme Court upheld the validity of a patent that applied the Arrhenius Equation to an industrial rubber curing method.⁷⁵ The mathematical equation was limited to a specific patent-eligible process and did not preempt all future public use of the equation. While *Diehr* could have been interpreted narrowly as applying only to industrial methods of transforming matter, such as curing rubber or molding metal, it has since been interpreted broadly,⁷⁶ encouraging a finding of patent eligibility for all methods that *apply* general concepts in a limited and “‘useful’ way.”⁷⁷

The *Diehr* approach is more holistic than past tests for preemption by requiring the patented method to be analyzed as a whole, rather than by each separate step. Under *Diehr*, it is impermissible to evaluate the patent eligibility of a general concept alone once it has been removed from its associated steps.⁷⁸ A critical question to ask when testing for preemption under *Diehr* is “[w]hat did applicants invent?”⁷⁹ In *Diehr*, the court found that the patentee had invented a useful method that applied the Arrhenius equation in a new context to calculate and recalculate cure time associated with rubber production.⁸⁰ Preemption analysis may only consider the invention as a whole, which makes the overall utility and “feel” of the invention more important. A finding of substantial utility decreases the chance that a court will find preemption of a general concept and thus patent ineligibility.

B. An Ethical Dilemma: The Duty to Disseminate Treatment Information and the Duty to Treat

Some diagnostic patents do more than block essential avenues of research—they can also be unethical. One conflict arises from a failure to disseminate treatment information. Physicians have an ethical duty to “advance scientific knowledge” by disclosing all relevant information to “patients, colleagues, and the public,” without considering financial gain.⁸¹ Physician patent owners who demand patent royalty payments from their colleagues violate this ethical duty.

⁷⁵ *Diehr*, 450 U.S. at 177–79.

⁷⁶ See O’Rourke, *supra* note 74, at 216; *In re Alappat*, 33 F.3d 1526, 1583 (Fed. Cir. 1994); *In re Beauregard*, 53 F.3d 1583, 1584 (Fed. Cir. 1995).

⁷⁷ *State St. Bank & Trust Co. v. Signature Fin. Grp., Inc.*, 149 F.3d 1368, 1373 (Fed. Cir. 1998); see O’Rourke, *supra* note 74, at 217.

⁷⁸ *Diehr*, 450 U.S. at 188.

⁷⁹ *In re Grams*, 888 F.2d 835, 839 (Fed. Cir. 1989).

⁸⁰ See O’Rourke, *supra* note 74, at 219.

⁸¹ AM. MED. ASS’N, AMA CODE OF MEDICAL ETHICS, THE PRINCIPLES (June 17, 2001) [hereinafter MEDICAL CODE], available at

1. *Dissemination of Treatment Information: The AMA Response & the Physician's Immunity Statute*

The AMA has recognized the chilling effect that patents can have on a physician's ethical duty to disseminate new treatment methods to his colleagues. In 1992 an ophthalmologist was granted a method patent for performing cataract surgery without stitches.⁸² The ophthalmologist filed a patent infringement suit against another doctor who was performing a similar surgery and asked for a small licensing fee for each use.⁸³ After the case attracted national attention, the AMA released a policy statement condemning such patents as conflicting with a physician's duty to disseminate new medical treatments.⁸⁴ In 1996, Congress responded to the AMA's concern by amending the Patent Act to include the Physician's Immunity Statute.⁸⁵

While a step in the right direction, the physician's immunity statute has not fully addressed the AMA's concern that patents may hinder the dissemination of treatment information. First, the statute only applies to "medical practitioners" who infringe on a patent during "medical activity."⁸⁶ The statute defines medical activity as any "medical or surgical procedure performed *on a body*,"⁸⁷ and specifically excludes "the practice of a process in violation of a biotechnology patent."⁸⁸ Therefore, the immunity statute does not shield medical professionals from liability when performing diagnostic methods. A clinical laboratory physician who performs Myriad's BRACAnalysis test without a license would be liable for patent infringement.⁸⁹

http://www.utcomchatt.org/docs/AMA_Code_of_Medical_Ethics.pdf; see also Cynthia M. Ho, *Patents, Patients, and Public Policy: An Incomplete Intersection at 35 U.S.C. § 287(c)*, 33 U.C. DAVIS L. REV. 601, 624 (2000) (explaining that the AMA's Medical Code of Ethics prohibits withholding knowledge for personal gain).

⁸² See Kesselheim & Mello, *supra* note 12, at 2037.

⁸³ See *Pallin v. Singer*, 36 U.S.P.Q. 2d 1050 (D. Vt. 1995).

⁸⁴ See Kesselheim & Mello, *supra* note 12, at 2037.

⁸⁵ See 35 U.S.C. § 287(c) (2011); see also Gerald J. Mossinghoff, *Remedies Under Patents on Medical and Surgical Procedures*, 78 J. PAT. & TRADEMARK OFF. SOC'Y 789, 789 (1996); Jeff S. Rundle, *The Physician's Immunity Statute: A Botched Operation or a Model Procedure?*, 34 J. OF CORP. L. 944, 945 (2009).

⁸⁶ Mossinghoff, *supra* note 85, at 789; see Kesselheim & Mello, *supra* note 12, at 2037.

⁸⁷ § 287(c)(2)(A) (emphasis added).

⁸⁸ *Id.* § 287(c)(2)(A)(iii).

⁸⁹ See Kesselheim & Mello, *supra* note 12, at 2037; see *Association for Molecular Pathology, v. USPTO*, 702 F.Supp.2d 181 (S.D.N.Y. 2010).; see also Rundle, *supra* note 85, at 949–50 (2009) (“[A] physician is immune from infringement

Commentators⁹⁰ and the U.S. Congress⁹¹ have suggested that the physician's immunity statute should be amended to expand coverage for diagnostic methods.

2. *The Duty to Treat in Lab. Corp.: To Commit Patent Infringement or Medical Malpractice?*

A second conflict arises from the physician's ethical duty to "regard responsibility to the patient as paramount."⁹² In order to comply with this ethical duty, a physician must order all diagnostic tests that are important to a patient's treatment. He may also have a legal duty to the patient to order a test.⁹³ But what if the test is patented? Should the doctor have to choose between violating his duty or committing patent infringement?

A Supreme Court case from 2006 has served as an ethical guidepost for plaintiffs challenging diagnostic method patent eligibility, due to its strongly worded dissent.⁹⁴ In *Lab. Corp. v. Metabolite*, a diagnostic corporation owned a method patent with two steps: (1) conduct a blood assay to determine homocysteine levels, and (2) infer from the homocysteine levels if a patient has a vitamin deficiency.⁹⁵ After analyzing the issues, Justice Breyer and two other justices argued in dissent that the diagnostic method preempted "a natural phenomenon" between homocysteine and vitamin levels within the human body.⁹⁶

when performing a patented surgical procedure to prevent a birth defect in a fetus. That same physician, however, may be subject to infringement liability for using genetic screening to identify a birth defect and then using gene therapy to treat the same condition without raising a scalpel so long as that gene is protected by a patent.") (citation omitted).

⁹⁰ See Kesselheim & Mello, *supra* note 12, at 2040.

⁹¹ See Genomic Research and Diagnostic Accessibility Act of 2002, H.R. 3967, 107th Cong. §3 (2002). Although it failed to pass, Section 3 of this Act would have exempted medical professionals that use genetic diagnostic tests from patent infringement.

⁹² MEDICAL CODE, *supra* note 81.

⁹³ See *Shilkret v. Annapolis Emergency Hosp.*, 349 A.2d 245, 253 (Md. 1975) (holding that a physician owes a duty of care that a reasonable physician would provide in the same class, acting under the same or similar circumstances).

⁹⁴ *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124 (2006) (Breyer, J., dissenting). Although this case was dismissed for an improvident grant of certiorari, Justice Breyer felt compelled to decide it in dissent, explaining that "those who engage in medical research, who practice medicine, and who as patients depend upon proper health care might well benefit from this Court's authoritative answer." *Id.* at 126.

⁹⁵ *Id.* at 129. These are not the actual method claim steps. The actual steps have been paraphrased for the sake of simplicity.

⁹⁶ *Id.* at 135.

The dissenting justices did not find an overall utility in the test, and believed the correlation step to be impermissibly broad.⁹⁷

Ethical considerations consume the rest of the *Lab. Corp.* dissent. To further his argument that the diagnostic method at issue preempted a natural correlation, Justice Breyer stated that the method was “invalid no matter how narrowly one reasonably interprets [the general concepts] doctrine.”⁹⁸ He also cited public policy considerations that weigh against patent eligibility in this case, such as “inhibit[ing] doctors from using their best medical judgment,” and “divert[ing] resources from the medical task of health care to the legal task of searching patent files for similar simple correlations.”⁹⁹

The dilemma presented by *Lab. Corp.* can be summed up by an example. Once a doctor orders a homocysteine assay for his patient from the diagnostic company, he would infringe the company’s patent if the results were used to diagnose a patient for vitamin deficiency.¹⁰⁰ However, in order to comply with his ethical and legal duty, a doctor must treat the patient to the best of his medical knowledge. It would be malpractice for the doctor *not* to consider vitamin deficiency as a cause for elevated levels of homocysteine. This is an example of the “legal catch-22” that currently “ensnares” physicians between one of two options: patent infringement or medical malpractice.¹⁰¹

IV. THE EFFECT OF *PROMETHEUS LABORATORIES V. MAYO CLINIC* ON DIAGNOSTIC METHOD PATENT ELIGIBILITY

A. The Path to *Prometheus I*: Uncertainty for Diagnostic Method Patents

In March 2008 a diagnostic method patent similar to the one upheld in *Lab. Corp.* was invalidated in the U.S. District Court for the Southern District of California. In *Prometheus Labs, Inc. v. Mayo Collaborative Servs.*,¹⁰² the district court analyzed whether the Prometheus[®] Thiopurine Metabolites test preempted a general concept. The test had three steps: (1) administration of a specific drug,¹⁰³ (2) deter-

⁹⁷ See *id.* at 136.

⁹⁸ *Id.* at 135. The Abstract Ideas doctrine has been defined earlier as the exclusion of general concepts. See *supra* Part III.

⁹⁹ *Lab. Corp.*, 548 U.S. at 138.

¹⁰⁰ See Kesselheim & Mello, *supra* note 12, at 2039.

¹⁰¹ *Id.*

¹⁰² *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, No. 04-CV-1200, 2008 WL 878910, at *2 (S.D. Cal. Mar. 28, 2008).

¹⁰³ *Id.* at *5.

mination of a metabolite level through a blood assay,¹⁰⁴ and (3) warning¹⁰⁵ the doctor to change drug dosage if the metabolite level was above or below threshold values defined in the patent.¹⁰⁶ Applying *Diehr*'s holistic approach of preemption analysis, the district court held that the test as a whole encompassed no more than "correlations themselves."¹⁰⁷ The court approvingly cited Justice Breyer's *Lab. Corp.* dissent for this proposition. They also found the broad "infering" step in *Lab. Corp.* and the "warning" step in *Prometheus* to be similar.¹⁰⁸

Those worried about the future of diagnostic method patent eligibility were troubled by the outcome of the district court's *Prometheus* decision.¹⁰⁹ In the face of uncertainty about how the next patent eligibility case will be determined, one place to look for guidance is the U.S. Patent & Trademark Office (USPTO). In 2008 the USPTO held a presentation entitled "A Look at Personalized Medicine."¹¹⁰ The presentation offered an example of one diagnostic method that was clearly patent ineligible,¹¹¹ and another that should be patent eligible.¹¹² The ineligible method determined whether to treat breast cancer, using a two-step process: (1) "considering" data, and (2) "correlating" data.¹¹³ The eligible method was a *treatment* for breast cancer, consisting of three steps: (1) obtaining a sample, (2) amplifying and sequencing DNA isolated from the sample, and (3) treating the patient with a breast cancer drug.¹¹⁴ A permissible inference to make from this presentation is that diagnostic methods with patient treatment steps are more likely to be patent eligible than methods that attempt to

¹⁰⁴ *Id.*

¹⁰⁵ *Id.* at *6.

¹⁰⁶ *Id.* at *5.

¹⁰⁷ *Id.* at *6.

¹⁰⁸ *Id.* at *7-8.

¹⁰⁹ See Ronald I. Eisenstein & David S. Resnick, *Personalized Medicine: IP Under Attack*, PHARMACEUTICAL, MEDICAL DEVICE & LIFE SCIENCES ALERT (Jan. 2009), http://www.nixonpeabody.com/linked_media/publications/Pharma_MedDevice_Alert_01_20_2009.pdf.

¹¹⁰ Kathleen Bragdon, *A Look at Personalized Medicine*, U.S. PAT. & TRADEMARK OFF. 1, available at http://www.cabic.com/bcp/120308/KBragdon_PM.ppt (last visited Mar. 6, 2012).

¹¹¹ See *id.* at 16 (discussing "Example 3: Methods Correlating SNPs and Disease").

¹¹² See *id.* at 17 (discussing "Example 4: Method of Treating Diseases that Correlate with SNPs").

¹¹³ See *id.* at 16.

¹¹⁴ See *id.* at 17.

claim natural thought processes, or steps normally taken to analyze data in the mind.

In September 2009, the Federal Circuit in *Prometheus I*¹¹⁵ reversed the district court's holding of invalidity. The appellants argued that the Prometheus Thiopurine Metabolites test comprised a "method of treatment" despite the lack of this description in their issued patent.¹¹⁶ The Mayo Clinic argued that the Prometheus method did not constitute a method of treatment, and amounted to no more than a natural correlation, citing both the district court opinion and the *Lab. Corp.* dissent.¹¹⁷ The court sided with Prometheus, holding that the administering and determining steps were part of a transformative method of treatment and "the addition of mental steps . . . does not remove the prior two steps from that realm."¹¹⁸ Applying *Diehr's* holistic approach to preemption analysis, just as the district court had done, the Federal Circuit found a useful method of treatment that applied a mental step.¹¹⁹

Prometheus I has been seen as a win for diagnostic methods.¹²⁰ Nevertheless, this decision leaves much for concern. What effect will the ethical considerations of *Lab. Corp.* have in the future? The AMA has denounced *Prometheus I* for allowing a physician to become "an infringer as soon as she makes the mental correlation between the test results and the patient's health."¹²¹ Unfortunately, the AMA's concern has fallen on deaf ears as the Federal Circuit dismissed Justice Breyer's opinion in *Lab. Corp.* as a nonbinding dissent.¹²² Also, why should characterizing the Prometheus[®] Thiopurine Metabolites test as a method of treatment change the result? The patented invention did not change between the district and circuit level. It has always been a method of optimizing a drug dosage to avoid toxic side effects rather than a method of treatment.

¹¹⁵ *Prometheus I*, 581 F.3d 1336, 1350 (Fed. Cir. 2009).

¹¹⁶ The diagnostic method in *Prometheus* is directed to a method of *optimizing* thiopurine treatment and is not an obvious method of treatment on its own. *Id.* at 1340 (The preamble of claim 1 of the '623 patent reads "A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder").

¹¹⁷ See Brief of Appellant at 19 n.2, *Prometheus Labs. Inc. v. Mayo Collaborative Servs.*, 581 F.3d 1342 (Fed. Cir. 2009) (No. 04-CV-1200), 2009 WL 1399726.

¹¹⁸ *Prometheus I*, 581 F.3d at 1348.

¹¹⁹ See *id.*

¹²⁰ See Dov Greenbaum, *New Rules, Different Risk: The Changing Freedom to Operate Analysis for Biotechnology*, 11 N.C. J.L. & TECH. ON. 139, 147 (2010).

¹²¹ Brief of Amici Curiae Am. Med. Ass'n et al. in Support of Respondents at 2, *Bilski v. Kappos*, 130 S. Ct. 3218 (2010) (No. 08-964), 2009 WL 3199621.

¹²² See *Prometheus I*, 581 F.3d at 1346, n.3 ("That dissent is not controlling law and also involved different claims from the ones at issue here.").

B. *Bilski v. Kappos*: A “New” Test for Patent Eligible Subject Matter

In June 2010 the Supreme Court, in *Bilski v. Kappos*,¹²³ revisited the question of patent-eligible subject matter for the first time in twenty-nine years.¹²⁴ While all the potential ramifications of this decision are beyond the scope of this Note,¹²⁵ there are two parts that should bear on medical method patent eligibility: the Court’s distaste for per se exclusions,¹²⁶ and a relaxed test for finding patent eligible subject matter.¹²⁷

In *Bilski*, the Court held that a business method for hedging risk was ineligible for a patent because it preempted, or absolutely barred, the public from using a general economic concept.¹²⁸ In doing so, the Court also reaffirmed the importance of conducting an analysis for preemption of general concepts. The court stated that investigating whether the public is barred from inventing with a general concept is preferred to creating per se exclusions for certain types of inventions.¹²⁹ This effectively keeps the subject matter inquiry broad under § 101.¹³⁰ *Bilski*’s emphasis on not creating per se exclusions beyond “laws of nature, abstract ideas, and natural phenomenon”¹³¹ means that it is unlikely that a diagnostic method with a mental step (such as “warning” or “inferring”) will be categorically barred from patent eligibility in the near future. In fact, a doctrine that embraced this categorical “mental step” exclusion was in effect forty years ago, but has since been abandoned.¹³²

¹²³ *Bilski v. Kappos*, 130 S.Ct. 3218, 3223 (2010).

¹²⁴ The last time the Supreme Court visited 35 U.S.C. § 101 subject matter eligibility was in *Diamond v. Diehr*, 450 U.S. 175, 177 (1981).

¹²⁵ A third part of *Bilski* that bears on medical method patent eligibility is Justice Stevens’s concurrence. See *Bilski*, 130 S.Ct. at 3231 (Stevens, J., concurring). Stevens’s concurrence may signal a shift in the approach to the pre-emption of general concepts analysis. Stevens writes that the majority opinion “never provide[d] a satisfying account of what constitutes an unpatentable abstract idea,” and appeared to use an improper application of novelty and a surprising use of invention type to the exclusion of general concepts. *Id.* at 3236. Stevens’s remarks are directed at the majority’s comment that general concept exclusions should be used as a “tool” to set “a high bar” when considering certain types of invention. *Id.*

¹²⁶ See *id.* at 3228–29.

¹²⁷ See *id.* at 3226–27.

¹²⁸ See *id.* at 3231.

¹²⁹ *Id.* at 3229.

¹³⁰ See *id.* at 3229–30.

¹³¹ See *Diamond v. Diehr*, 450 U.S. 175, 185 (1981) (identifying three categorical exclusions from patent-eligible subject matter).

¹³² Before the CAFC was established, the USPTO Board of Appeals and the CCPA had developed the “mental steps” doctrine, which was used to deny patent

Bilski is also notable for relaxing the test to determine patent eligible subject matter.¹³³ Judicial analysis concerning patent-eligible subject matter is performed in two steps: (1) analyzing whether preemption of a general concept has occurred, and (2) applying the machine-or-transformation test.¹³⁴ While the purpose of the first step is to find patent *ineligible* subject matter, the purpose of the second is to discover patent *eligible* subject matter. The machine-or-transformation test is satisfied when a method “(1) is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing.”¹³⁵ The Federal Circuit held that the machine-or-transformation test was a definitive test for patent-eligible subject matter.¹³⁶ The Supreme Court reversed this holding, bringing the machine-or-transformation test back to its roots as “a useful and important clue” towards finding patent eligibility, but not a dispositive one.¹³⁷

While *Bilski* involved a business method rather than a diagnostic method, the decision should have comparable force as the Federal Circuit formulates new limitations on diagnostic method patents.¹³⁸ The Supreme Court has made it clear that a dispositive machine-or-transformation test is not fit for inventions in the “Information Age.”¹³⁹ New inventions are increasingly sophisticated, and applying the same test can create uncertainty.¹⁴⁰ Without providing specific guidance, the Court went on to say that extra considerations must be present when applying the machine-or-transformation test to emerging fields such as “advanced medical diagnostic tests.”¹⁴¹ The Court has not clearly stated what these considerations are and has entrusted the Federal Circuit with developing them.

protection for process that could be performed in the mind. By 1970, the CCPA adopted a broader view of patentable subject matter and discontinued the doctrine. See O’Rourke, *supra* note 74, at 197–99; *see also* *In re Musgrave*, 431 F.2d 882, 893 (C.C.P.A. 1970) (“We cannot agree . . . that . . . claims . . . are directed to non-statutory process merely because some or all of the claims therein can also be carried out in . . . the human mind All that is necessary . . . is that [a process] be in the technological arts.”).

¹³³ *See Bilski*, 130 S.Ct. at 3231.

¹³⁴ *Id.* at 3224.

¹³⁵ *Id.* (citation omitted).

¹³⁶ *In re Bilski*, 545 F.3d 943, 954 (Fed. Cir. 2008).

¹³⁷ *Bilski*, 130 S.Ct. at 3226–27.

¹³⁸ *Id.* at 3231 (expressly inviting the Federal Circuit to formulate new limitations on patentability).

¹³⁹ *Id.* at 3227.

¹⁴⁰ *Id.*

¹⁴¹ *Id.* The Court states that application of the machine-or-transformation test to emerging technologies will pose questions of “intricacy and refinement.” *Id.*

C. *Prometheus II*: A Second Win for Diagnostic Method Patents

The Supreme Court granted certiorari in the *Prometheus* case in light of *Bilski*'s change in rules for patent eligibility.¹⁴² The *Prometheus I* decision was vacated and the case was remanded to the Federal Circuit.¹⁴³ All eyes were on the Federal Circuit to interpret the *Bilski* decision and impose extra limitations on medical method patents. Many commentators believed that satisfying the machine-or-transformation test would serve as a safe harbor for patent eligibility.¹⁴⁴ Others expected the Federal Circuit to come up with a new test.¹⁴⁵

On December 17, 2010, the Federal Circuit in *Prometheus II* reaffirmed its previous decision and allayed the fears of those concerned about the future of diagnostic method patents.¹⁴⁶ Noticeably swayed by the purported utility of Prometheus Thiopurines Metabolites test,¹⁴⁷ the court held that as a whole “Prometheus has claimed therapeutic methods that determine the optimal dosage level for a course of treatment . . . [in] a series of transformative steps that optimizes efficiency and reduces toxicity of a method of treatment for particular diseases using particular drugs.”¹⁴⁸ Once again, the court found that Prometheus' test constituted a method of treatment, despite a lack of such information in the method steps. The court was unpersuaded by Mayo Clinic's argument that the first two steps—(1) *administration* of a drug, and (2) *determination* of metabolite concentration through a

¹⁴² *Mayo Collaborative Serv. v. Prometheus Labs., Inc.*, 130 S. Ct. 3543 (2010).

¹⁴³ *Id.*

¹⁴⁴ See Eric K. Steffe & Michelle H. Holoubek, *Diagnostic Testing in the Wake of Bilski v. Kappos*, IPWATCHDOG (July 2, 2010, 1:15 PM), <http://ipwatchdog.com/2010/07/02/diagnostic-testing-in-the-wake-of-bilski-v-kappos/id=11474/>; see also Brief of Amici Curiae Biotechnology Industry Organization et al. in Support of Neither Party at 32, *Bilski*, 130 S. Ct. 3218 (2010) (No. 08-964), 2009 WL 2418478.

¹⁴⁵ Courtenay Brinckerhoff, *Catching a Breath After Bilski*, PHARMAPATENTS (June 28, 2010), <http://www.pharmapatentsblog.com/101/catching-a-breath-after-bilski/> (“On remand, the Federal Circuit is likely to decide whether these types of methods cannot be patented because they claim a phenomenon of nature or abstract idea. In doing so, the court may formulate a new test for the patent-eligibility of diagnostic and personalized medicine methods.”).

¹⁴⁶ See *Prometheus II*, 628 F.3d 1347, 1355 (Fed. Cir. 2010).

¹⁴⁷ Kevin E. Noonan, *Prometheus Laboratories, Inc. v. Mayo Collaborative Services* (Fed. Cir. 2010), PATENT DOCS (Dec. 20, 2010), <http://www.patentdocs.org/2010/12/prometheus-laboratories-inc-v-mayo-collaborative-services-fed-cir-2010.html>.

¹⁴⁸ See *Prometheus II*, 628 F.3d at 1359.

blood assay—are not “method of treatment claims no matter how many times Prometheus repeats its Newspeak-like drumbeat that they are.”¹⁴⁹

In holding that the machine-or-transformation test had been satisfied, the court stated that “methods of treatment . . . are *always* transformative when one of a defined group of drugs is administered to the body to ameliorate effects of an undesired condition.”¹⁵⁰ The court seemingly created a per se eligibility for methods of treatment involving drugs, which may be contrary to *Bilski*’s guidance that the rules for patent eligibility should be relaxed and take into account new considerations.¹⁵¹ The court went on to say that the district court erred when characterizing the first two steps as mere “data-gathering steps,” rather than as transformative steps that are “a significant part” of the diagnostic method.¹⁵² What makes the first two steps a significant part of the method and not the last? The court attempted to justify their significance based on the purpose of each step,¹⁵³ however the argument is not entirely convincing.¹⁵⁴

D. The Aftermath of *Prometheus II*: A Limited Application or a Further Broadening of Patent Eligible Subject Matter?

One commentator believes the Federal Circuit made a “dangerously subjective” policy argument in *Prometheus II*.¹⁵⁵ The danger presented by the court’s opinion is that subjectivity may taint the future of diagnostic method patent eligibility by giving undue weight to an invention’s ability to serve as a patient treatment method. Are Prometheus’ claims really drawn towards method of treatment, and should all methods of treatment be transformative? The purpose of the Prometheus Thiopurine Metabolites test is to *optimize* treatment by administering a drug and determining metabolite levels through an assay, which is arguably a diagnostic method that *affects* a method of treatment rather than actually being a method of treatment itself. Can

¹⁴⁹ Supp. Brief of Defendants-Appellees to Address the Effect of *Bilski* at 4, *Prometheus Labs. v. Mayo Collaborative Servs.* 628 F.3d 1347 (Fed. Cir. 2010) (No. 2008-1403).

¹⁵⁰ *Prometheus II*, 628 F.3d at 1356 (emphasis added).

¹⁵¹ See *Bilski v. Kappos*, 130 S.Ct. 3218, 3227–28 (2010).

¹⁵² See *Prometheus II*, 628 F.3d at 1357.

¹⁵³ See *id.*

¹⁵⁴ Joshua D. Sarnoff, *Patent Eligible Medical and Biotechnology Inventions After Bilski, Prometheus and Myriad*, 19 TEX. INTELL. PROP. L. J. 393, 400 (2011) (citation omitted).

¹⁵⁵ See Noonan, *supra* note 147.

any diagnostic method that administers a drug to the human body for treatment satisfy the test for transformation? The Federal Circuit seems to go too far in *Prometheus*.¹⁵⁶ Subjective evaluations of utility and treatment may be given too much weight in overcoming clear arguments against patent eligibility.

Inquiring into the USPTO's guidelines may also help to explain the outcome in *Prometheus*. After *Bilski*, the USPTO issued Interim Guidelines for Determining Subject Matter Eligibility.¹⁵⁷ The guidelines state that § 101 "is merely a coarse filter and . . . only a threshold question for patentability."¹⁵⁸ This would indicate a broad scope for eligible subject matter and a greater reliance on the other patent statutes to negate patentability.¹⁵⁹ The Federal Circuit in *Prometheus II* may not be saying that all methods of treatment using a drug should receive a patent, but rather that diagnostic methods should not be invalidated at the eligibility level. The other statutory provisions offer a better way to filter out inventions that hinder innovation rather than promote it.¹⁶⁰

V. A REDEFINED TEST FOR TRANSFORMATION

Despite *Bilski*'s change to the application of the machine-or-transformation test, the Federal Circuit seemed to apply the test identically in *Prometheus I* and *II*.¹⁶¹ One concern is whether the Federal Circuit has formulated extra considerations for the machine-or-transformation test, which in its previous form was ill-suited for "advanced medical diagnostic tests."¹⁶² Another is whether any method

¹⁵⁶ See Mark A. Lemley et al., *Life After Bilski*, STAN. L. REV. 1315, 1344 (2011) ("The Federal Circuit's analysis . . . would allow too much.").

¹⁵⁷ Interim Guidance for Determining Subject Matter Eligibility for Process Claims in View of *Bilski v. Kappos*, 75 Fed. Reg. 43,922 (July 27, 2010) [hereinafter Interim Guide].

¹⁵⁸ Interim Guide, 75 Fed. Reg. at 43,926.

¹⁵⁹ See 35 U.S.C. §§ 102–103, 112.

¹⁶⁰ For example, if the patent document does not adequately disclose how to make and use the invention, which is required under the enablement requirement of 35 U.S.C. § 112, the public cannot replicate and improve upon the invention, and therefore do not benefit from issuance of a patent. Such a patent does not foster innovation and should not be granted. See also Interim Guide, 75 Fed. Reg. at 43926 ("Sections 102, 103, and 112 are typically the primary tools for evaluating patentability unless the claim is truly abstract . . .").

¹⁶¹ See *Prometheus II*, 628 F.3d 1347, 1355 (Fed. Cir. 2010). ("We similarly reaffirm that the treatment methods claimed in *Prometheus*'s patents in suit satisfy the transformation prong of the machine-or-transformation test . . .").

¹⁶² *Bilski v. Kappos*, 130 S.Ct. 3218, 3227 (2010). The Court in *Bilski* stated that applying the machine-or-transformation test to emerging technologies will pose questions of "intricacy and refinement." *Id.*

that treats a patient through administration of a drug can satisfy the transformation prong.

To provide needed clarity in applying the machine-or-transformation test to medical diagnostic tests, the transformation prong should be redefined. The redefined test for transformation allows for a more nuanced application of the current framework without adding unnecessary limitations or per se exclusions.¹⁶³ Redefining the test for transformation is preferable to using new tests for patent eligibility,¹⁶⁴ as it builds on the current analytical framework and adds just enough additional inquiry to define “the line between a patentable ‘process’ and an unpatentable ‘principle’”¹⁶⁵

Unlike the work of prominent scholars in the field, the redefined test is not a test for creating presumptive subject matter exclusions,¹⁶⁶ or a test that attempts to justify patent eligibility in view of overall utility.¹⁶⁷ This redefined test for transformation challenges our perception of which scientific contributions involving natural pathways are truly inventive, as opposed to those that are mere observations or discoveries of a preexisting natural process. While this is not explicitly a *sui generis* test for transformative diagnostic methods, it is particularly useful for analyzing the patent eligibility of diagnostic methods involving a multi-step physiological process (e.g., administering a drug to a patient so that it may be broken down by the body, or extracting a sample from the patient and analyzing the result).

A. A Proposed Test

The redefined test for transformation test is satisfied by:

¹⁶³ A redefinition of our current framework is preferable to proposing additional limitations. When new limitations are proposed, they must be aggregated with old ones to remain relevant. A redefined test does not suffer from this aggregation effect.

¹⁶⁴ One such test involves a determination of the patent eligibility of differing mental steps. See Andrew W. Torrance, *Neurobiology and Patenting Thought*, 50 IDEA 27, 28 (2009). Dr. Torrance proposes that certain method patents containing unbounded mental steps could impose involuntary liability and should be presumptively ineligible for patenting. *Id.* By contrast, mental steps that can be controlled within the mind are better suited patent eligibility. *Id.* See Lemley et al., *supra* note 154, at 1317, 1346 (proposing a “§ 101 overclaiming test” that renders a claim patent-ineligible when its scope is overly broad relative to its practical application).

¹⁶⁵ *Classen II*, 659 F.3d 1057, 1078 (Fed. Cir. 2011) (quoting *Parker v. Flook*, 437 U.S. 584, 589 (1978)).

¹⁶⁶ See Torrance, *supra* note 164, at 28.

¹⁶⁷ See Lemley et al., *supra* note 156, at 1317, 1329.

A more than predictable transformation of an article into a different state or thing, wherein an article is a particular substance that is smaller than the human body and is sufficiently removed from nature. If the article is extracted from the human body, rather than provided by an outside source, it must be imperceptible and assayable.

The proposed test for transformation tends towards different outcomes depending on whether an article is provided to the body from an outside source, for example, the administration of a drug, or an extraction from the body for subsequent analysis. The Prometheus Thiopurine Metabolites test involves both the administration of a drug to a patient and a subsequent determination step that measures the concentration of a metabolite (product of drug breakdown). Myriad's BRACAnalysis test forgoes the initial drug administration step and begins by extracting genetic samples from human tissue, then comparing and analyzing them.¹⁶⁸ Administration of a drug to the human body presents unique concerns as the natural pathways acting on the administered drug are inherently transformative. Mere observation of an inherent transformation seems too simplistic, and entirely non-inventive, to constitute a patent eligible process on its own.¹⁶⁹ By contrast, determination steps performed on articles that have been extracted from the body often require sophisticated transformative steps in order to take them out of their natural bodily habitat and analyze the result.¹⁷⁰

The following subsections will explain the redefined test for transformation, beginning with the more than predictable requirement. This feature highlights what has already been considered by the Court when evaluating the inventive jump required for a patent eligible process,¹⁷¹ and now makes it an express requirement for transformation.

¹⁶⁸ USPTO v. Myriad Genetics, Inc., 653 F.3d 1329, 1355 (Fed. Cir. 2011).

¹⁶⁹ Dan Hoang, Note, *Prometheus Laboratories v. Mayo Clinic's Gift to the Biotech Industry: A Study of Patent-Eligibility of Medical Treatment and Diagnostic Methods After Bilski*, 9 NW. J. TECH. & INTELL. PROP. 457, 470–71 (2011).

¹⁷⁰ While there are inherently transformative natural pathways for extracting an article, e.g. urination, extraction of a particular genetic sequence or metabolite often requires sophisticated technical tests that cannot be performed without human intervention.

¹⁷¹ The Supreme Court has considered whether natural products continue to function in their normal predictable way during their patent eligibility analysis. See, e.g., *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, in which the Court stated:

"Discovery of the fact that certain strains of each species of these bacteria can be mixed without harmful effect to the properties of either . . . is no more than the

The more than predictable standard arguably provides the greatest “teeth” to the defined test for transformation.

B. Raising the Transformation Barrier: The “More Than Predictable” Standard

The current machine-or-transformation test is silent on the form or amount of transformation required. In the physiology and pathology fields, which routinely use diagnostic methods, the Oxford English Dictionary (OED) defines transformation as “change of form or substance in an organ, tissue, [or] vital fluid.”¹⁷² This definition would suggest that a transformation can occur within a region as large as a bodily organ or as small as an extracted vital fluid sample. While vital fluid in the aggregate is quite large, this definition is not limited to a specific amount of vital fluid. Transformation is also defined in the OED as “a complete change in character [or] condition.”¹⁷³ A “complete” transformation requirement would likely be hard to prove or satisfy.

A compromise between complete transformation, which may be too hard to prove, and no transformation requirement, which could allow for incremental changes in form, would be a more than predictable transformation. A more than predictable requirement should be imposed on diagnostic methods to prevent the patenting of obvious tests that apply common drugs to natural pathways with known chemical reactivities. Natural pathways are inherently transformative and predictably alter the composition of the drugs they encounter. While the addition of a common drug to a well-known pathway may be novel, it would not be inventive, as it would constitute a transformation no greater than those inherent within natural pathways, transformative properties that are “free to all men and reserved exclu-

discovery of some of the handiwork of nature and hence is not patentable. The aggregation of select strains of the several species into one product is an application of that newly-discovered natural principle. But however ingenious the discovery of that natural principle may have been, the application of it is hardly more than an advance in the packaging of the inoculants. Each of the species of root-nodule bacteria contained in the package infects the same group of leguminous plants which it always infected. No species acquires a different use. The combination of species produces no new bacteria, no change in the six species of bacteria, and no enlargement of the range of their utility. Each species has the same effect it always had. The bacteria perform in their natural way. Their use in combination does not improve in any way their natural functioning. They serve the ends nature originally provided and act quite independently of any effort of the patentee.”

Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 131 (1948).

¹⁷² Oxford English Dictionary, Online Edition, available at <http://www.oed.com/view/Entry/204743> (last visited Feb. 27, 2012).

¹⁷³ *Id.*

sively to none.”¹⁷⁴ Patenting the addition of common drugs to natural pathways provides little benefit to society, as it serves mainly to block future inventors from utilizing the inherent transformative properties of natural pathways for practical applications.¹⁷⁵

1. *Scholarly Support for the More Than Predictable Standard*

Commentators have recognized the need to incorporate a measure of creativity¹⁷⁶ or technical sophistication¹⁷⁷ into patent eligibility analysis, particularly for products incorporating natural phenomena or methods involving natural pathways. There are substantial incentives to seek patents on applications of the human body’s natural pathways, such as the NF-KB pathway involved in the expression of numerous genes, and other vital signaling pathways at the crossroads of metabolic function.¹⁷⁸ As a result, we can expect disputes over patent eligibility to continue. To avoid the dangers inherent in subjective assessments of utility or treatment ability to support patent eligibility, as seen in *Prometheus I* and *II*, one commentator has suggested drawing the patent eligibility line between technological innovations and mere discoveries of natural phenomena.¹⁷⁹ She argues that technical innovations are more likely to maintain traditional incentives to invent than simple discoveries of natural processes, which are likely already in the public domain and should remain there.¹⁸⁰

¹⁷⁴ *Funk Bros.*, 333 U.S. at 130.

¹⁷⁵ The district court in *Prometheus* found that alternate uses of the natural phenomenon associated with the Thiopurine Metabolites Test were not practical uses. *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, No. 04-CV-1200, 2008 WL 878910, at *1, *12 (S.D. Cal. Mar. 28, 2008). There was no way to use the natural phenomenon according to the claims without infringing on Prometheus’ patent. *See id.*

¹⁷⁶ *See* Sarnoff, *supra* note 154, at 417; *see also* Shengfeng Chen, Note, *Pathways to Patents: Applying the Written Description Requirement Doctrine to Patents on Biological Pathways*, 30 HASTINGS COMM. & ENT. L.J. 559, 561 (2008) (claiming biological functionality through “reach-through” patents may “cast shadows on future developments”).

¹⁷⁷ Elizabeth I. Winston, *The Technological Edge*, 3 AKRON INTELL. PROP. L.J. 1, 8–9 (2011).

¹⁷⁸ *See* Chen, *supra* note 176, at 564 (“Such biological pathways are perfect candidates for functional claiming”).

¹⁷⁹ Winston, *supra* note 177, at 17.

¹⁸⁰ *Id.* (“The greater the technology required to discover problems in the art, the less likely it is that such problems have already been discovered, and the greater the benefit to the public of disclosing such problems and their solutions through the patent system.”). There is language from the Supreme Court in *Funk Bros* to support the proposition that mere discoveries of natural principles are not inventive and are

These commentators' suggestions to raise the patent eligibility threshold support, at least to some degree, the creation of a more than predictable requirement. However, unlike these commentators, I am suggesting that the more than predictable requirement should define the level of transformation required in the transformation test, rather than serve as an extra consideration during preemption analysis. *Diehr's* "holistic" approach, which is used to analyze patent eligibility in addition to the machine-or-transformation test, already suffers from its own measure of subjectivity, as seen in *Prometheus I* and *II*. Analyzing the predictability of a method during transformation places a requirement where one is noticeably absent and lends itself to better resolutions of unclear patent eligibility cases.¹⁸¹

2. *Judicial Support for the More than Predictable Standard: Judge Moore's Classen Dissent*

On August 31, 2011, the Federal Circuit in *Classen Immunotherapies v. Biogen Idec (Classen II)*¹⁸² reversed its previous holding¹⁸³ that a method for immunizing a patient that lowers the risk of chronic immune-mediated diseases was ineligible for patenting. *Classen's* patent claims called for (1) screening a plurality of immunization schedules, and (2) immunizing a patient according to a subject immunization schedule.¹⁸⁴ The court held that the principles upheld in *Prometheus II*, specifically "claims to methods of treatment . . . are always transformative when one group of a defined group of drugs is administered to the body," supported the patent eligibility of *Classen's* transformative claims.¹⁸⁵ The Court did not engage in any specific analysis as to why immunizing a patient, as called for in step two of *Classen's* claims, was in fact transformative. The Court also cited with approval *Bilski's* guidance that § 101 is only a "threshold test" and that substantive conditions of patentability (i.e., § 102 (novelty)

therefore ineligible for patenting. See *Funk Bros.*, 333 U.S. 127, at 132 ("There is no way in which we could call [this combination inventive] unless we borrowed invention from the discovery of the natural principle itself.").

¹⁸¹ The current machine-or-transformation test does not define the amount of transformation required - it is simply "transformation" of an article into a different state or thing. See *supra* Part V.B.

¹⁸² *Classen II*, 659 F.3d 1057, 1057 (Fed. Cir. 2011).

¹⁸³ *Classen Immunotherapies, Inc. v. Biogen Idec*, 304 Fed.Appx. 866, 867 (Fed. Cir. 2008).

¹⁸⁴ *Classen II*, 659 F.3d at 1060-61.

¹⁸⁵ *Id.* at 1068 (citing *Prometheus II*, 628 F.3d 1347, 1356 (Fed. Cir. 2010)).

and § 103 (non-obviousness)) should remain legally and practically distinct.¹⁸⁶

In a lengthy dissent reminiscent of Justice Breyer in *Lab. Corp.*, Judge Moore criticized the majority for not analyzing why Classen's claims were transformative. She went on to say that Classen's claims "are not directed to any specific treatment steps or drugs or even any specific chronic immune disorder."¹⁸⁷ Judge Moore felt that the intent and effect of Classen's claims were to stop others from using a natural principle and destroy incentives to invent, citing approvingly Justice Breyer's *Lab. Corp.* dissent.¹⁸⁸ She also indicated that any doctor who wished to fulfill his or her duty to a patient by comparing patient immunization schedules would also infringe Classen's claims,¹⁸⁹ leaving a choice between medical malpractice and patent infringement.¹⁹⁰

Judge Moore's dissent can be read to support the more than predictable requirement. Disagreeing with the majority's analysis under § 101, Judge Moore proclaimed that "Classen did not invent the immunological response measured in his claim, and the discovery of this phenomenon alone 'cannot support a patent unless there is some other inventive concept in its application.'"¹⁹¹ Judge Moore's distinction between mere discoveries of natural phenomena and a more inventive contribution supports the concept of a higher patent eligibility threshold, similar to the suggestions of academic commentators.¹⁹² While she does not explicitly endorse a more than predictable transformation requirement, her analysis suggests that the court has applied the holding of *Prometheus* too broadly and has reduced the § 101 threshold to an untenable minimum. A heightened standard for transformation could address both of Judge Moore's concerns.

3. *The Distinction between Predictability and Obviousness*

Critics of the more than predictable requirement would argue that it conflates § 103, the statutory nonobvious requirement, with patent-

¹⁸⁶ *Id.* at 1064.

¹⁸⁷ *Id.* at 1076 (Moore, J., dissenting) (emphasis added).

¹⁸⁸ *Id.* at 1079 (Moore, J., dissenting) (quoting *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 125, 127–28 (2006) (Breyer, J., dissenting from dismissal of petition)).

¹⁸⁹ *Id.* at 1078–79 (Moore, J., dissenting).

¹⁹⁰ This is yet another example of the legal "catch-22" explained *supra* Part III.B.2.

¹⁹¹ *Classen II*, 659 F.3d at 1079 (citing *Parker v. Flook*, 437 U.S. 584, 594 (1978)).

¹⁹² See *supra* Part V.B.1.

able subject matter analysis under § 101. They would also argue that such a combined analysis of patent statutes is contrary to the approach adopted by the Supreme Court in *Bilski* and the Federal Circuit in *Classen*.¹⁹³ However, the courts and the USPTO have clearly differentiated between what is “predictable” and what is “obvious.”¹⁹⁴

Patent Examiners at the USPTO are required to follow the Manual of Patent Examining Procedure (MPEP) when evaluating a patent. MPEP § 2144.08 states that “[o]bviousness does not require absolute predictability; however, at least some degree of predictability is required.”¹⁹⁵ When a court determines if a claimed feature is obvious, it only needs to find evidence of “reasonable expectation of success,”¹⁹⁶ whereas “predictability” suggests something more. Methods that are predictable are undoubtedly obvious, however methods that are obvious are not necessarily predictable.

By setting the transformation requirement at more than predictable, we only inquire as to whether a natural pathway involved in a method claim is so well-known and documented that the end state of an article involved in a transformation is entirely predictable. By defining the requirement this narrowly, natural pathways that are firmly planted in the public domain are withheld from patent eligibility, while those that are less well-known remain free for commercial development and patenting.

C. The Remaining Elements of the Proposed Test

To explain the remaining elements incorporated into the language of the proposed test, I will compare the *Prometheus* decisions, which involved a transformative method of optimizing thiopurine treatment, with *Classen I*,¹⁹⁷ in which the court held that a method for optimizing an immunization schedule was not transformative.¹⁹⁸ These elements reiterate important distinctions that the Federal Circuit has already drawn when analyzing the patent eligibility of diagnostic methods.

¹⁹³ *Classen II*, 659 F.3d at 1064.

¹⁹⁴ MANUEL OF PATENT EXAMINING PROCEDURE § 2144.08(II)(A)(4)(e) (8th ed. 2001).

¹⁹⁵ *In re Rinehart*, 531 F.2d 1048, 1053–54 (CCPA 1976).

¹⁹⁶ *In re O’Farrell*, 853 F.2d 894, 904 (Fed. Cir. 1988).

¹⁹⁷ *Classen Immunotherapies, Inc. v. Biogen Idec (Classen I)*, No. WDQ-04-2607, 2006 WL 6161856 (D. Md. Aug. 16, 2006), *aff’d*, 304 Fed. Appx. 866 (Fed. Cir. 2008), *vacated*, 130 S. Ct. 3541 (2010) (emphasis added).

¹⁹⁸ *See Classen I*, 2006 WL 6161856 at *5-6.

1. *An Article Smaller Than the Human Body*

The redefined test for transformation should be limited to a defined range of articles. *Prometheus I* and *II* show that there is confusion about what constitutes a sufficient article for transformation. In *Prometheus I* and *II*, the Federal Circuit held that the first two steps—(1) administering a particular drug, and (2) determining the optimal level of metabolites—satisfied the transformation test.¹⁹⁹ While the court seemed to identify the drug as the “particular article” and the metabolites as “a different state or thing,” they actually identified another article. The court found a sufficient transformation “of the human body following administration of a drug and the various chemical and physical changes of the drug’s metabolites.”²⁰⁰ The fact that the court found both the human body and metabolites to be transformed is shocking, as the human body is not usually considered an article. The human body is much larger than a drug, organ, or other physical subdivision we might consider observing for a transformation.²⁰¹

Comparison of the *Prometheus* decisions and *Classen I* shows that transformation of the human body is not sufficient for a finding of transformation. The Court in *Classen I* did not find the human body to be a transformed article,²⁰² as did the court in *Prometheus*. However, a transformation of the human body would have occurred after administration of a vaccine. Injection of a vaccine triggers the human immune system response and changes the body to “a different state or thing.”²⁰³ The court in *Classen I* did not see this change in the body as sufficient for overall transformation. While the recent decision in *Classen II* upholding patent eligibility may cast this conclusion into doubt, there is no indication in the majority opinion of what exactly is being transformed, whether the human body or the injected vaccine.²⁰⁴

Regardless of the court’s hidden intent in *Classen II*, transformation of the human body alone should never be sufficient for a finding of transformation.²⁰⁵ This would imply that any process that

¹⁹⁹ *Prometheus I*, 581 F.3d 1336, 1346 (Fed. Cir. 2009).

²⁰⁰ *Id.* (emphasis added).

²⁰¹ See *supra* Part V.B (identifying the OED definition of “transformation”).

²⁰² See generally *Classen I*, 2006 WL 6161856 (The opinion does not mention transformation of the body alone, although the body is arguably being transformed after vaccine injection).

²⁰³ *Id.* at 3225 (citation omitted).

²⁰⁴ See *Classen II*, 659 F.3d 1057, 1076 (Fed. Cir. 2011) (Moore, J., dissenting) (“None of this [transformation] analysis exists in the majority opinion here in *Classen*.”).

²⁰⁵ Transformation should be limited to an article introduced into a process, rather than the surroundings the article is placed into. At a certain level of abstrac-

changes the state of the human body would satisfy the transformation test, an important clue towards finding patent eligibility. Any immunization, blood sample extraction, or mild invasion of the body would theoretically satisfy the transformation test if this was the current state of the law.²⁰⁶

2. *The Article Should Be Particular and Sufficiently Removed from Nature*

The second conclusion reached by comparing the *Prometheus* decisions and *Classen I* is that the administered article must be particular. *Prometheus I* explicitly states that methods of treating the human body are always transformative when administering a *particular* drug.²⁰⁷ *Classen I* points out the lack of a “*particular* vaccine”²⁰⁸ in the vaccination process. The “particular” limitation seen in both cases is reasonable, as diagnostic methods tied to unique articles are less likely to preempt the use of natural pathways. “Particular” means, for example, a patented drug, or a defined class of chemotherapy drugs. A non-particular drug would mean, for example, a pain pill, a cough drop, or a general vaccine. In *Classen II*, the majority opinion’s neglect of this “particular” limitation was pointed out in Judge Moore’s dissent.²⁰⁹

Comparison of the *Prometheus* decisions and *Classen I* also raises new questions. Is there something inherently different between administration of a synthetic drug and a vaccine that would justify patent protection for the former and not the latter? Two differences are worth noting. A drug is typically an *unnatural* substance that chemically breaks down into metabolites that can be viewed through an assay. A vaccine is typically comprised of killed or weakened *natural*

tion, any number of articles could be transformed within a process. See Kevin E. Collins, *An Initial Comment on Prometheus: The Irrelevance of Intangibility*, PATENTLYO (Sept. 17, 2009), <http://www.patentlyo.com/patent/2009/09/an-initial-comment-on-prometheus-the-irrelevance-of-intangibility-1.html>.

²⁰⁶ This could occur during either an “administration” step or a “determination” step.

²⁰⁷ *Prometheus I*, 581 F.3d 1336, 1346 (Fed. Cir. 2009).

²⁰⁸ *Classen I*, No. WDQ-04-2607, 2006 WL 6161856, at *5 (D. Md. Aug. 16, 2006), *aff’d*, 304 Fed. Appx. 866 (Fed. Cir. 2008), *vacated*, 130 S. Ct. 3541 (2010) (emphasis added).

²⁰⁹ *Classen II*, 659 F.3d at 1078 (Moore, J., dissenting) (“No limitations exist on the type of drug to immunize with, the schedules that should be used for the immunization, the type of chronic immune disorder to look for, or any limitation on the control group.”).

microbes²¹⁰ that stimulate white blood cells and cause them to proliferate.²¹¹ Does it matter whether an article is entirely natural or synthetic, or how the article breaks down once inside the body?

Rather than emphasizing the distinction between natural and synthetic, the analysis should focus on whether the drug is sufficiently removed from nature. Vaccines contain a small amount of protein from a virus, however that protein is inactive and isolated through a technological intervention.²¹² If a vaccine is sufficiently isolated to the point that it becomes different “not just in degree, but in kind,” then that would normally be enough to tie it to a patent eligible method.²¹³

Regarding the mechanism of article breakdown, the court found both the synthetic drug in *Prometheus II* and the partially natural vaccine in *Classen II* to be transformative.²¹⁴ The *Classen II* court did not provide any details indicating that article breakdown mechanism is important.

3. *Imperceptible and Assayable*

During a “determination step,” patent eligibility favors articles that were once imperceptible, or could not be seen, and subsequently become perceptible through an assay. In *Prometheus I*, the court stated that “determining the levels of [the metabolites] 6-TG or 6-MMP in a subject necessarily involves a transformation, for those levels cannot be determined by mere inspection.”²¹⁵ The court presumed that “some form of manipulation”²¹⁶ is required to make an object that

²¹⁰ *Vaccines: What is a Vaccine?*, NAT’L INST. ALLERGY & INFECTIOUS DISEASES,

<http://www.niaid.nih.gov/topics/vaccines/understanding/Pages/whatVaccine.aspx> (last updated Aug. 18, 2008); see also Winston, *supra* note 177, at 6.

²¹¹ DONALD VOET, JUDITH VOET, AND CHARLOTTE PRATT, *FUNDAMENTALS OF BIOCHEMISTRY: LIFE AT THE MOLECULAR LEVEL* 209-10 (Wiley & Sons, Inc., 3rd ed. 2008) [hereinafter VOET & VOET].

²¹² See *Vaccines: What is a Vaccine?*, *supra* note 210.

²¹³ See *Parke-Davis & Co. v. H.K. Mulford Co.*, 189 F. 95, 103 (C.C.S.D.N.Y. 1911) (purified adrenaline so superior to previous adrenal gland extracts so as to be distinct not in degree, but in kind). The method of injecting a vaccine however would still need to meet the *more than predictable* standard of transformation. It’s arguably very predictable to immunize the human body with an antigen during vaccination test, as the immunization relies on the inherent response of the human body to the introduction of a foreign agent.

²¹⁴ See *Prometheus II*, 628 F.3d 1347, 1359 (Fed. Cir. 2010); see *Classen II*, 659 F.3d at 1068.

²¹⁵ *Prometheus I*, 581 F.3d 1336, 1347 (Fed. Cir. 2009).

²¹⁶ *Id.*

cannot be seen into one that is visible. This indicates that visualization is a distinguishing feature of transformed articles in a determination claim. If an article was always visible, it is hard to imagine how extraction from the body would change it into a different state or thing.

D. Application of the Proposed Test: Diagnostic Methods in Recent Federal Circuit Cases

To consider what a more than predictable transformation would entail, one could start with three common factors used in establishing the level of ordinary skill in an art.²¹⁷ Such factors include (1) “the types of problems [normally] encountered in the art,” (2) “the sophistication of the technology [involved]”, and (3) the educational background of those working in the field.²¹⁸ These factors will be considered in applying the proposed test to the Federal Circuit’s recent *Prometheus II*,²¹⁹ *Classen II*,²²⁰ and *Myriad*²²¹ opinions.

1. *Prometheus II*

Application of the proposed test to *Prometheus II* leads to the same result as the Federal Circuit, but for different reasons. The initial step, “administration” of the drug to a patient, is properly viewed as a predictable transformation. The human body’s natural pathway for metabolizing mercaptopurines and thiopurine nucleotides was well known to scientists and the medical profession at the time the Prometheus Thiopurine Metabolites test was patented.²²² The drugs were commonly known for treating cancer and gastrointestinal disease. The toxic byproducts of these drugs during patient metabolism were also well known to those skilled in the field.²²³ Any transformation undergone by the drugs would rely on the inherent reactivity of, for example, the gastrointestinal tract in converting them into metabolites. Therefore it is not an inventive application.

²¹⁷ See AM. INTELL. PROP. L. ASS’N, AIPLA’S MODEL PATENT JURY INSTRUCTIONS § 7.3 (2008), available at http://www.aipla.org/learningcenter/library/books/other-pubs/documents/2008_03_27_AIPLA_Model_Jury_Instructions.pdf.

²¹⁸ *Id.*

²¹⁹ *Prometheus II*, 628 F.3d 1347 (Fed. Cir. 2010).

²²⁰ *Classen II*, 659 F.3d 1057 (Fed. Cir. 2011).

²²¹ Ass’n for Molecular Pathology v. USPTO, 653 F.3d 1329 (Fed. Cir. 2011).

²²² See Sarnoff, *supra* note 154, at 401.

²²³ *Id.*

The subsequent “determination” step, however, undergoes a more than predictable transformation. Measuring the level of thiopurine metabolites requires extraction of a human sample, such as red blood cells, and sophisticated techniques to determine the concentration of 6-Mercaptopurine (6-MP) metabolites.²²⁴ The results of the assay are not predictable—and that’s the very reason this assay is being performed. There is no natural pathway for extracting red blood cells containing 6-MP that shows the predictability of this determination method. The 6-MP metabolites are initially unnoticeable and are subsequently visible only after an assay.

The proposed test would therefore favor a finding of patent eligibility through a sufficient transformation at the determination step. However, two other points are worth noting. First, contrary to the Federal Circuit’s findings, transformation of the human body during administration of the drug or during the determination of 6-MP metabolite levels would not be sufficient for transformation. Second, one could argue that an individual’s metabolic response to common chemotherapy drugs is variable, especially in this application, and therefore the administered drug is more than predictably transformed. However, every natural pathway operates at varying levels of efficiency depending on the individual and their health. To justify patent eligibility over established natural pathways due to unforeseen natural variations in activity would elevate formal distinctions over actual effect—which blocks others from exploring the same natural pathway.

2. *Classen II*

Application of the proposed test to *Classen II* would lead to a reversal of the Federal Circuit’s decision. Echoing the concerns of Judge Moore in dissent, *Classen*’s immunization step involves the predictable transformation of a vaccine to a proliferated immune response. *Classen* borrowed the inventive concept inherent within a natural immune response, which is not rightfully theirs to claim. Natural processes such as immune responses reside firmly within the public domain, and any attempt to claim them would hinder researchers and doctors from performing everyday tasks.

Unlike the patent at issue in *Prometheus*, *Classen*’s patent claim involves only an “administration” step and lacks a “determination” step. The inherent change in the human body after immunization is also not sufficient to support a finding of transformation. Therefore, the proposed test would favor a finding of patent ineligibility.

²²⁴ See U.S. Patent No. 6,355,623 at [9] (filed Apr. 8, 1999).

3. *Myriad*

In the case of *Myriad*, application of the proposed test leads to the same result as the Federal Circuit, and for the same reasons. Since *Myriad*'s BRCAAnalysis test does not involve an "administration" step, the proposed test for transformation would normally focus on a "determination" step. However, *Myriad*'s patent claims do not include a determination step.²²⁵ Their patent claims include only "comparing" and "analyzing" nucleotide sequences. Therefore, these claims attempt to control natural mental faculties that are firmly within the public domain.

If *Myriad* had claimed a "determination step," which their kit is designed for, this step would have involved a more than predictable transformation of a human tissue sample into a purified and amplified gene segment. This gene segment would subsequently be used for comparisons between genes located within tumor and non-tumor samples after processing.²²⁶ In order to make this comparison, the gene segments must be purified through sophisticated DNA isolation methods and extended through molecular medicine techniques. These steps transform the genes by taking what is hidden within the body and manipulating it into something markedly different from its natural state.

CONCLUSION

This Note has discussed how to clarify the elusive line between patentable processes and unpatentable principles by redefining the existing machine-or-transformation test. Application of the redefined test for transformation to current diagnostic method patent cases could prevent the Federal Circuit from expanding the broad principles upheld in *Prometheus*—seemingly per se eligibility for diagnostic methods drawn towards treatment of the human body—to future patent eligibility determinations. The redefined test may also be useful to fight the Federal Circuit's recent tendency to lower the § 101 thresh-

²²⁵ *Ass'n for Molecular Pathology*, 653 F.3d at 1357 ("Myriad's claims, in contrast, do not include the step of 'determining' the sequence of *BRCA* genes by, e.g., isolating the genes from a blood sample and sequencing them, or any other necessarily transformative step.").

²²⁶ See Brief for the Appellants at 55, *Assoc. for Molecular Pathology v. USPTO*, 653 F.3d 1329 (Fed. Cir. 2011) (No. 2010-1406), 2010 WL 4600106. Extraction generally refers to gene isolation and amplification techniques. See VOET, VOET & PRATT, *supra* note 209, at 62–65. Processed generally refers to nucleotide sequencing. See *id.* at 53–55.

old to minimal levels. A lowered § 101 threshold has arguably undermined traditional incentives to invent.²²⁷

The Supreme Court delivered its decision in *Prometheus III*²²⁸ sometime after completion of this Note. The Court reversed and held the patent claims to be invalid.²²⁹ Justice Breyer authored the majority opinion and cited with approval many of the issues raised in his dissent from the 2006 *Lab. Corp.* decision.²³⁰ While a full analysis of this decision is beyond the scope of this Note, I would like to briefly mention that the opinion arguably supports the proposed redefined test for transformation.²³¹ While such adoption is not explicit, and other aspects of the opinion may instruct against a more searching transformation test requirement,²³² the Supreme Court recognized that additional analysis under §101 is appropriate to avoid the unintended effect of diagnostic method patents in blocking critical avenues of research and treatment.

²²⁷ While a lower patent threshold makes it easier to obtain an exclusive right and therefore may increase traditional incentives to invent, the lowered threshold may also unduly interfere with the free flow of information by allowing for the creation of too many exclusive rights. *See Mayo Collaborative Serv. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1305 (2012).

²²⁸ *Mayo Collaborative Serv. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289 (2012).

²²⁹ *Id.* at 1305.

²³⁰ *See, e.g., id.* at 1302 (discussing how Prometheus' patent claims "tie up the doctor's subsequent treatment decision" as well as inhibit the development of "later discovered processes that measure metabolite levels in new ways.")

²³¹ The Court's quick dismissal of Prometheus' claims as involving inadequate transformations, acknowledgment that subject matter eligibility analysis under §101 may involve overlapping concepts of novelty or obviousness, and detailed discussion regarding an "inventive concept" may support the proposed redefined test for transformation. *See, e.g., id.* at 1289 ("We recognize that, in evaluating the significance of additional steps, the § 101 patent-eligibility inquiry and, say, the § 102 novelty inquiry might sometimes overlap."); *id.* at 1303 (finding the "administering" step in Prometheus' claims to be an irrelevant transformation, and the second "determining" step to be "satisfied without transforming the blood, should science develop a totally different system for determining metabolite levels that did not involve such a transformation."); *id.* at 1290, 1292, 1294, 1299, 1300 (discussing the importance of an "inventive concept").

²³² *See id.* at 1289 (The Court cautions against mixing inquiries of novelty and obviousness in subject matter eligibility analysis under §101).