

# *Bilski's* "Machine-or-Transformation" Test: Uncertain Prognosis for Diagnostic Methods and Personalized Medicine Patents

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## INTRODUCTION

United States patent law and policy embrace an expansive scope for patent eligible subject matter in order to effectuate the Constitutional mandate “to promote the Progress of Science and useful Arts by securing for limited Times to . . . Inventors the exclusive Right to their . . . Discoveries.”<sup>1</sup> Supreme Court precedent clearly articulates the minimal restraints on patent eligible subject matter: only inventors who seek to claim a natural law, natural phenomenon, abstract idea, or mental process should be barred at the threshold of the United States patent examination system.<sup>2</sup> These minimal restraints, collectively referred to herein as the “Fundamental Principles Exception,” reflect the balance between policies of liberally encouraging innovation while preserving fundamental concepts, principles, and ideas for free and unfettered use by all.<sup>3</sup>

Even a patent claim that recites a fundamental principle may be patent eligible so long as the claim as a whole is not drawn solely to the principle.<sup>4</sup> The operative question under the Fundamental Principles Exception is whether the claim defines an application of the principle with sufficient particularity so as not to preempt all uses and implementations of the principle.<sup>5</sup> If so, then the claim recites patent eligible subject matter and is not excludable under

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<sup>1</sup> U.S. CONST. art. I, § 8, cl. 8.

<sup>2</sup> See, e.g., *Diamond v. Diehr*, 450 U.S. 175 (1981); *Diamond v. Chakrabarty*, 447 U.S. 303 (1980); *Parker v. Flook*, 437 U.S. 584 (1978); *Gottschalk v. Benson*, 409 U.S. 63 (1972).

<sup>3</sup> When addressing the question of *patent eligible* subject matter, it is crucial to understand and remember that a determination of *patent eligibility* is made at the very beginning of the patent examination procedure and is analytically distinct from the rigorous statutory requirements of *patentability*. While a patent may easily satisfy the eligibility test—it is meant to be a low bar for access to the system—it must still satisfy the requirements of novelty, nonobviousness, enablement, etc., before a *patent eligible* claim is determined to be a patentable claim. Patent eligibility must not be confused with patentability.

<sup>4</sup> See *In re Bilski*, 545 F.3d 943, 953 (Fed. Cir. 2008) (en banc), *cert. granted sub nom. Bilski v. Doll*, 129 S. Ct. 2735 (2009), *argued sub nom. Bilski v. Kappos*, No. 08-964, 2009 WL 3750776 (Nov. 9, 2009).

<sup>5</sup> See *Diehr*, 450 U.S. at 203; see also *Parker*, 437 U.S. at 599; *Gottschalk*, 409 U.S. at 71; *Bilski*, 545 F.3d at 1011 (Rader, J., dissenting).

the Fundamental Principles Exception. In *In re Bilski*,<sup>6</sup> the Federal Circuit disparaged this inquiry as “hardly straightforward” and articulated the proxy “machine-or-transformation” test as the sole and definitive test to determine patent eligibility of process claims.<sup>7</sup> Under that test, the operative questions are whether the claimed process is tied to a particular machine or apparatus or whether it transforms a particular article into a different state or thing.<sup>8</sup> In either case, the particular machine or transformation also must “impose meaningful limits on the claim’s scope” and must not involve “insignificant extra-solution activity” or “mere data-gathering” to “impart patent eligibility.”<sup>9</sup>

While the Federal Circuit’s *Bilski* decision restricts business method patents, there is apprehension in the intellectual property community that the machine-or-transformation test will unfairly limit patents in the life sciences, particularly claims directed to diagnostic and screening methods.<sup>10</sup> Having taken up *Bilski* on certiorari, the Supreme Court is poised to settle the question whether the machine-or-transformation test is the exclusive, mandatory test for patent eligibility of processes under 35 U.S.C. § 101. In our view, the Court should answer the question in the negative and reemphasize the Fundamental Principles Exception as the governing test because it is, contrary to the Federal Circuit’s characterization, straightforward and more likely to lead to a sound result than the highly subjective and complicated machine-or-

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<sup>6</sup> 545 F.3d 943 (Fed. Cir. 2008) (en banc), *cert. granted sub nom.* *Bilski v. Doll*, 129 S. Ct. 2735 (2009), *argued sub nom.* *Bilski v. Kappos*, No. 08-964, 2009 WL 3750776 (Nov. 9, 2009).

<sup>7</sup> *Id.* at 954.

<sup>8</sup> *Id.*

<sup>9</sup> *Id.* at 961–62.

<sup>10</sup> See Christopher Holman, *Bilski: Assessing the Impact of a Newly Invigorated Patent Eligibility Doctrine on the Pharmaceutical Industry and the Future of Personalized Medicine*, CURRENT TOPICS MED. CHEMISTRY (forthcoming) (manuscript at 18), available at <http://ssrn.com/abstract=1424493>; Matthew Ward & Jack Redfern, *US Patent Law: No Longer Concrete, Tangible and Useful*, MONDAQ, Mar. 30, 2009, <http://www.mondaq.com/unitedstates/article.asp?articleid=77112>. See generally Michael R. Samardzija, *Recent Patent Rulings Can Impede the Progress of Personalized Medicine: The Bilski and Classen Decisions Can Render Numerous in Vitro Diagnostic Claims Unpatentable*, BIOPHARM INT’L, Aug. 2009, at 2, 2, available at <http://biopharminternational.findpharma.com/biopharm/Business+Articles/Recent-Patent-Rulings-Can-Impede-the-Progress-of-P/ArticleStandard/Article/detail/615147>.

transformation test. The Fundamental Principles Exception is a broader, more flexible test to determine the threshold question of patent eligibility, which is consistent with well-settled law and public policy. In Part I of this article, we briefly survey the law and policy that supports a broad, flexible test to determine patent eligibility. In Part II, starting with the important *Laboratory Corp. of America Holdings v. Metabolite Laboratories, Inc.* (“*LabCorp*”)<sup>11</sup> case, we analyze patent eligibility of personalized medicine patent claims at issue in recent cases and contrast the limitations of the machine-or-transformation test against the simpler, more flexible approach of the Fundamental Principles Exception. We conclude that while the machine-or-transformation test may be a useful way to assess certain types of inventions, it should not be the mandatory, exclusive test for determining patent eligibility of process patents.

#### I. THE LAW AND POLICY SUPPORTING A BROAD, FLEXIBLE TEST FOR PATENT ELIGIBILITY

As Judge Rader so aptly noted in his dissent in *Bilski*, one of our founding fathers, Thomas Jefferson, articulated the policy underpinning the Patent Copyright Clause<sup>12</sup> of the Constitution: “Nobody wishes more than I do ingenuity should receive a liberal encouragement.”<sup>13</sup> Mr. Jefferson recognized the importance of commercial incentives attendant patent exclusivity as a sharp spur to innovation and progress in the sciences and useful arts. The liberal encouragement of ingenuity and innovation intended to be fostered by the grant of exclusive patent rights was reflected in the

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<sup>11</sup> 548 U.S. 124 (2006).

<sup>12</sup> U.S. CONST. art. I, § 8, cl. 8.

<sup>13</sup> 5 WRITINGS OF THOMAS JEFFERSON 75–76 (Washington ed. 1871); see also *Bilski*, 545 F.3d at 1011 (Rader, J., dissenting) (“The Patent Law of the United States has always embodied the philosophy that ‘ingenuity should receive a liberal encouragement.’” (quoting WRITINGS OF THOMAS JEFFERSON, *supra*, at 75–76)). Mr. Jefferson also recognized the danger of overprotection of patent rights, noting the difficulty of “drawing a line between the things which are worth to the public the embarrassment of an exclusive patent, and those which are not.” *Graham v. John Deere Co.*, 383 U.S. 1, 9 (1966) (citing Letter from Thomas Jefferson to Isaac McPherson (Aug. 13, 1813), reprinted in 13 THE WRITINGS OF THOMAS JEFFERSON 326, 334 (Andrew A. Lipscomb & Albert Ellery Bergh eds., 1905)).

almost boundless language of the Constitution that provides for the time-limited, exclusive right of inventors to their "Discoveries."<sup>14</sup> In the case of patent eligibility for process or method claims, the language of 35 U.S.C. § 101 is broad and clear: "any new and useful process" or "any new and useful improvement thereof" is patent eligible.<sup>15</sup> Therefore, *any* new process that has practical utility and is not excludable under the Fundamental Principles Exception is patent eligible and entitled to examination for compliance with patentability requirements.

In *Diamond v. Diehr*,<sup>16</sup> the Supreme Court articulated that a process claim which includes a fundamental principle is patent eligible as long as the process as a whole represents "an *application* of a law of nature or mathematical formula."<sup>17</sup> In *Diehr*, the invention under consideration was a physical and chemical process for molding precision synthetic rubber products, where the claimed process steps included the use of a mathematical formula.<sup>18</sup> The Court cautioned against reading limitations into the patent laws not expressed by the legislature<sup>19</sup> and went on to clarify that in a case where an inventor discovered a previously unknown natural law or phenomenon (more recently exemplified in the diagnostic method claimed in the *LabCorp*<sup>20</sup> case): "[i]f there is to be invention from such a discovery, it must come from the application of the law of nature to a new and useful end."<sup>21</sup>

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<sup>14</sup> U.S. CONST. art. I, § 8, cl. 8. While discoveries arguably include natural laws and phenomena, it always has been understood that *patent eligible* discoveries include "anything under the sun that is *made by man*." *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980) (emphasis added) (quoting S. REP. NO. 82-1979, at 5 (1952), *reprinted in* 1952 U.S.C.C.A.N. 2394, 2399; H.R. REP. NO. 82-1923, at 6 (1952)). Citing a long line of precedent, the Court noted that "laws of nature, physical phenomena, and abstract ideas have been held not patentable." *Id.* Even though the dividing line between *patent eligible* inventions and ineligible fundamental principles is, of course, sometimes quite difficult to draw, the Supreme Court consistently has adhered to that broad flexible standard and refused to restrict patent eligibility by imposing a more limited, rigid test.

<sup>15</sup> 35 U.S.C. § 101 (2006).

<sup>16</sup> 450 U.S. 175 (1981).

<sup>17</sup> *Id.* at 187.

<sup>18</sup> *Id.* at 177.

<sup>19</sup> *Id.* at 182.

<sup>20</sup> *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 125 (2006).

<sup>21</sup> *Diehr*, 450 U.S. at 188 n.11 (quoting *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948)).

The Court distinguished a claim that, as a whole, would preempt all uses of a mathematical formula—a patent ineligible abstract idea—from the claim at issue in *Diehr*, which applied a mathematical formula for a particular use:

[W]hen a claim containing a mathematical formula implements or applies that formula in a structure or process which, when considered as a whole, is performing a function which the patent laws were designed to protect (e.g., transforming or reducing an article to a different state or thing), then the claim satisfies the requirements of § 101.<sup>22</sup>

The takeaway, in short, is that a process or method claim is patent eligible if, when considered as a whole, it defines an application of a fundamental principle with sufficient particularity so as not to preempt all uses and implementations of the principle.

The policies of promoting the progress of science and useful technologies, liberally encouraging innovation and ingenuity, maintaining a strong patent system, and helping to sustain emerging industries and long-term job growth all support well-settled Supreme Court precedent articulating process patent eligibility requirements. A broad, flexible test, as embodied in the Fundamental Principles Exception, encourages inventors and investors alike to commit significant human and financial capital to research and development efforts in many different fields. This is particularly true in the emerging fields of medical and genetic diagnostics. Although estimates vary widely, it can cost hundreds of millions of dollars and take more than ten years to develop a

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<sup>22</sup> *Id.* at 192. As noted in Judge Newman’s dissent in *Bilski*, the use of the exemplary “e.g.” in the parenthetical contradicts the majority’s determination that “machine-or-transformation” is the definitive, mandatory test for assessing patent eligibility. *In re Bilski*, 545 F.3d 943, 982 (Fed. Cir. 2008) (en banc) (Newman, J., dissenting), *cert. granted sub nom. Bilski v. Doll*, 129 S. Ct. 2735 (2009), *argued sub nom. Bilski v. Kappos*, No. 08-964, 2009 WL 3750776 (Nov. 9, 2009); *see also* *Parker v. Flook*, 437 U.S. 584, 589 n.9 (1978) (“The statutory definition of ‘process’ is broad. An argument can be made, however, that this Court has only recognized a process as within the statutory definition when it either was tied to a particular apparatus or operated to change materials to a ‘different state or thing.’ As in *Benson*, we assume that a valid process patent may issue even if it does not meet one of these qualifications of our earlier precedents.” (internal citations omitted)).

successful biologic drug or genetic screening test.<sup>23</sup> Broad access to the patent system, to the fullest extent permitted under the Constitution and without limitations that have not been expressed by Congress, is crucial to the support of these emerging technologies.

## II. PATENT ELIGIBILITY OF DIAGNOSTIC METHODS AND OTHER PERSONALIZED MEDICINE INVENTIONS

### A. *The LabCorp Case*

Accurate and early diagnosis of cobalamin (Vitamin B<sub>12</sub>) and folate deficiencies in humans is important because these vitamin deficiencies can lead to serious, potentially life-threatening, blood and neuropsychiatric disorders.<sup>24</sup> The university researchers who obtained and enforced the diagnostic method claims at issue in *LabCorp*, were conducting research to develop an improved assay (test) for cobalamin and folate deficiencies.<sup>25</sup> The inventors discovered that there were abnormally high homocysteine<sup>26</sup> levels in the blood of patients who suffered from cobalamin and/or folate deficiencies, a specific biochemical correlation that was previously unknown.<sup>27</sup> The inventors used this discovery to develop a new and better test for diagnosing cobalamin and folate deficiencies.<sup>28</sup>

The inventors' patent contains several different method claims that cover new methods for conducting the homocysteine assay itself, for example by using a labeled reference standard and mass spectrometer in a process to determine homocysteine levels (claims

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<sup>23</sup> See, e.g., Nathan Koppel, *Genetic Research Spurs Fight over Patents Tied to the Body*, WALL ST. J., Dec. 10, 2009, at A21.

<sup>24</sup> U.S. Patent No. 4,940,658 col. 1 ll. 32–40 (filed Nov. 20, 1986) (issued July 10, 1990).

<sup>25</sup> See *Lab. Corp.*, 548 U.S. at 125–28.

<sup>26</sup> Homocysteine is a particular species of amino acid known as a "sulfhydryl amino acid." Pål I. Holm et al., *Modulation of the Homocysteine-Betaine Relationship by Methylenetetrahydrofolate Reductase 677 C->T Genotypes and B-Vitamin Status in a Large-Scale Epidemiological Study*, 92 J. CLINICAL ENDOCRINOLOGY & METABOLISM 1535, 1535 (2007).

<sup>27</sup> See *Lab. Corp.*, 548 U.S. at 128.

<sup>28</sup> *Id.*

1 and 7).<sup>29</sup> The patent eligibility of these method claims for determining homocysteine levels was not challenged because they represent a classic, practical application—improving the process of measuring homocysteine—derived from the newly discovered naturally occurring correlation between elevated homocysteine levels and cobalamin or folate deficiencies.<sup>30</sup> The patent also includes a series of diagnostic claims for a method of detecting a cobalamin or folate deficiency.<sup>31</sup> Independent claim 13<sup>32</sup> reads as follows: “[a] method for detecting a deficiency of cobalamin or folate in warm-blooded animals comprising the steps of: *assaying* a body fluid for an elevated level of total homocysteine; and *correlating* an elevated level of total homocysteine in said body fluid with a deficiency of cobalamin or folate.”<sup>33</sup>

A medical diagnostic process claim of this type is characterized by a data determination step, which identifies or measures a biological or chemical marker, followed by a mental step of a physician or medical practitioner who utilizes the information obtained in the first step to infer or recognize the newly discovered phenomenon and diagnose the patient.<sup>34</sup> Though admittedly broad, claim 13 may well define a patent eligible process when assessed under the Fundamental Principles Exception, notwithstanding Justice Breyer’s conclusion to the contrary.<sup>35</sup> A close examination,

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<sup>29</sup> *Id.*; ’658 Patent col. 41 ll. 2–19, 34–35.

<sup>30</sup> *Id.*; see also John A. O’Brien, *Bilski v. Doll—Is the Federal Circuit’s “Machine or Transformation” Test the Only Test for § 101 Subject Matter?*, 977 PLI/Pat 437, 447 (2009).

<sup>31</sup> *Lab. Corp.*, 548 U.S. at 129.

<sup>32</sup> We note that the petition for certiorari in *LabCorp* was dismissed as improvidently granted because LabCorp had failed to raise the § 101 challenge to claim 13 below. *See id.* at 125–26.

<sup>33</sup> ’658 Patent col. 41 ll. 58–65 (emphasis added).

<sup>34</sup> This type of diagnostic method has been coined a “determine-and-infer” claim. *See* Kevin E. Collins, *An Initial Comment on Prometheus: The Irrelevance of Intangibility*, PATENTLY-O, Sept. 17, 2009, at 2, <http://www.patentlyo.com/collins.intangibility.pdf>. Determine-and-infer claims provide powerful commercial incentives for innovation because they broadly convey exclusive rights to new, useful, and nonobvious processes involving recognition of previously unknown biochemical or genetic correlations, metabolic pathways or similar natural phenomena that are highly useful for diagnosing, treating and preventing disease. *See id.* at 5–8. These are precisely the kind of incentives that drive capital-intensive innovation in emerging technologies. *See id.*

<sup>35</sup> *See Lab. Corp.*, 548 U.S. at 134–38 (Breyer, J., dissenting).

however, does reveal the potential for confusion and inconsistent results that may arise depending on the analytical test used to assess patent eligibility.

### 1. Well-Settled Fundamental Principles Analysis

Applying the Fundamental Principles Exception to *LabCorp* claim 13, the pertinent question is: does the claim as a whole define an application of the correlation between elevated homocysteine and deficient cobalamin/folate with sufficient particularity so as not to preempt substantially all uses and implementations of the correlation?

Using this analytical test, the patent eligibility of claim 13 becomes clearer. As so aptly noted by Judge Rader in his *Bilski* dissent:

The fundamental error in that *Lab. Corp.* dissent is its failure to recognize the difference between a patent ineligible relationship—i.e., that between high homocysteine levels and folate and cobalamin deficiencies—and a patent eligible process for applying that relationship to achieve a useful, tangible, and concrete result—i.e., diagnosis of potentially fatal conditions in patients.

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... [T]he invention does not attempt to claim that natural phenomenon. Instead the patent claims a process for assaying a patient's blood and then analyzing the results with a new process that detects the life-threatening condition.<sup>36</sup>

Claim 13 recites a practical application of the identified correlation in the claim preamble—"detecting a deficiency of cobalamin or folate"<sup>37</sup>—and thereby does not preempt all implementations and uses of the newly discovered correlation. While it would be better claim drafting practice to recite the

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<sup>36</sup> *In re Bilski*, 545 F.3d 943, 1014 (Fed. Cir. 2008) (en banc) (Rader, J., dissenting), cert. granted sub nom. *Bilski v. Doll*, 129 S. Ct. 2735 (2009), argued sub nom. *Bilski v. Kappos*, No. 08-964, 2009 WL 3750776 (Nov. 9, 2009).

<sup>37</sup> See *supra* note 33 and accompanying text.

diagnostic level or range for the “elevated” homocysteine level in a wherein clause in the body of the claim, as in *Prometheus Laboratory, Inc. v. Mayo Collaborative Services*,<sup>38</sup> this should not detract from the patent eligibility of the subject matter. Taken as a whole, claim 13 defines a specific application of the discovered correlation—it requires measuring total homocysteine levels to make a specific diagnostic correlation between elevated homocysteine levels and deficient cobalamin or folate levels.<sup>39</sup> The claimed method does not foreclose *all* uses and implementations of the correlation such as, for example, using it to discover and develop improved treatment methods for cobalamin and folate deficiencies or improved methods for measuring other biological or chemical markers that correspond to cobalamin or folate deficiencies. In our view, claim 13 properly capitalizes on the newly discovered correlation by specific, practical application of the correlation to achieve a useful diagnostic process.

Accurate diagnosis is the touchstone for deciding on any treatment regimen in the medical profession, where the guiding principle is: “First, do no harm.”<sup>40</sup> The availability of incentives to encourage inventors to innovate and make diagnostic advances in the medical arts would be severely undercut if the entire class of these method claims were deemed patent ineligible. If there is concern that physicians and other medical practitioners would be liable for infringement of such claims, there is already precedent for Congress to step in and protect them.<sup>41</sup> Title 35 U.S.C. § 287(c) exempts medical practitioners from patent infringement under § 271(a) and (b) (direct and inducement, but not contributory, infringement) for the performance of a certain defined “medical activity” that would otherwise constitute an

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<sup>38</sup> 581 F.3d 1336, 1339 (Fed. Cir. 2009); see U.S. Patent No. 6,355,623 col. 20 ll. 38–39 (filed Apr. 8, 1999) (issued Mar. 12, 2002).

<sup>39</sup> U.S. Patent No. 4,940,658 col. 41 ll. 58–65 (filed Nov. 20, 1986) (issued July 10, 1990).

<sup>40</sup> This mantra is often ascribed to Hippocrates as part of the Hippocratic Oath, however, it is actually derived from a Latin phrase, “Primum non nocere.” Hippocrates came closest to stating these words in his treatise *Epidemics*. See Howard Markel, “I Swear by Apollo”—on Taking the Hippocratic Oath, 350 NEW ENG. J. MED. 2026, 2026–29 (2004).

<sup>41</sup> See 35 U.S.C. § 287(c) (2006).

infringement.<sup>42</sup> This statute was passed after a patent owner tried to enforce a patent covering a process for making a certain type of surgical incision in the eye during cataract surgery.<sup>43</sup> The process patent governing a physician's activity during surgery was unquestionably patent eligible,<sup>44</sup> and the policy response, after heavy lobbying by the American Medical Association, came from Congress in the form of the above-referenced exemption. Congress chose *not* to alter the process patent eligibility rules, even when it was presented with a perfect opportunity to do so, and we submit that the courts should not effect such a result with respect to diagnostic method claims, particularly in the absence of a clear expression from Congress.

Claim 13 provides an excellent example to underscore the important difference between the low threshold requirements for patent eligibility under the Fundamental Principles Exception and the much more rigorous requirements for patentability. Claim 13 defines patent eligible subject matter, but the patentability of the subject matter may still be challenged for other reasons, for example: obviousness, non-enablement, or claim overbreadth. The two concepts must be separated and not confused, but confusion is exactly what occurred when the court in *Parker v. Flook*<sup>45</sup> articulated the "post-solution activity" corollary.<sup>46</sup> In *Flook*, the

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<sup>42</sup> 35 U.S.C. § 287(c)(2)(A) defines "medical activity" as the performance of a medical or surgical procedure on a body, but shall not include (i) the use of a patented machine, manufacture, or composition of matter in violation of such patent, (ii) the practice of a patented use of a composition of matter in violation of such patent, or (iii) the practice of a process in violation of a biotechnology patent.

<sup>43</sup> *Pallin v. Singer*, No. 5:93-202, 1995 WL 608365, at \*1 (D. Vt. May 1, 1995).

<sup>44</sup> *In re Bilski*, 545 F.3d 943, 988 (Fed. Cir. 2008) (en banc) (Newman, J., dissenting) ("We are directed to no authority for the proposition that a new and inventive process involving 'human activity' has historically been treated differently from other processes; indeed most inventions involve human activity."), *cert. granted sub nom. Bilski v. Doll*, 129 S. Ct. 2735 (2009), *argued sub nom. Bilski v. Kappos*, No. 08-964, 2009 WL 3750776 (Nov. 9, 2009).

<sup>45</sup> 437 U.S. 584 (1978).

<sup>46</sup> *Id.* at 590. In *Flook*, the patentee, Dale Flook, applied for a patent on a "Method for Updating Alarm Limits." *Id.* at 585. The "alarm limits" were particular numbers between which a catalytic converter was determined to be operating normally. *Id.* When any of the catalytic conversion process variables exceeded a predetermined alarm limit, the alarm sounded. *Id.* Flook's patent application described and claimed a method of

Supreme Court held that the respondent's process of applying a mathematical algorithm was unpatentable:

[N]ot because it contains a mathematical algorithm as one component, but because once that algorithm is *assumed to be within the prior art*, the application, considered as a whole, contains no patentable invention. Even though a phenomenon of nature or mathematical formula may be well known, an inventive application of the principle may be patented. Conversely, the discovery of such a phenomenon cannot support a patent unless there is some other inventive concept in its application.<sup>47</sup>

While the above-quoted statements are correct, the Court improperly conflated the threshold patent eligibility determination with the substantive determination of patentability or “inventive concept.” Whether the algorithm or natural phenomenon in question is known in the prior art is irrelevant to patent eligibility, but quite relevant to the question of patentability. This type of claim dissection into new and old parts was forcefully condemned by the Court in *Diehr*,<sup>48</sup> precisely because it confused the threshold

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updating alarm limits by utilizing a mathematical algorithm. *Id.* Flook's method was identical to previous systems for updating alarm limits except for the use of the mathematical algorithm. *Id.* at 586. The Patent & Trademark Office Board of Appeals sustained the rejection of Flook's method claims for failing to satisfy the statutory subject matter test under *Gottschalk v. Benson*. *Id.* at 587; *Gottschalk v. Benson*, 509 U.S. 63, 67 (1972). Flook appealed and the Court of Customs and Patent Appeals (“CCPA”) reversed. *Flook*, 437 U.S. at 587; *see also In re Flook*, 559 F.2d 21, 23 (C.C.P.A. 1977). The CCPA read *Benson* as applying only to claims that entirely preempt a mathematical formula or algorithm, and it held the claims to be *patent eligible* for examination because they recited post-solution activity and did not entirely preempt the formula or algorithm used. *Flook*, 437 U.S. at 587. The patent claimed only the right to use the algorithm in the limited context of the catalytic chemical conversion of hydrocarbons. The CCPA reasoned that since “the mere solution of the algorithm would not constitute infringement of the claims, a patent on the method would not preempt the formula.” *Id.* The Supreme Court granted a writ of certiorari. *Id.* at 588.

<sup>47</sup> *Flook*, 437 U.S. at 594 (emphasis added).

<sup>48</sup> *Diamond v. Diehr*, 450 U.S. 175, 188 (1981) (“It is inappropriate to dissect the claims into old and new elements and then to ignore the presence of the old elements in the analysis. This is particularly true in a process claim because a new combination of steps in a process may be patentable even though all the constituents of the combination were well known and in common use before the combination was made.”).

question of patent eligibility with the substantive question of patentability, obviousness in particular, which can only be answered after examination of the patent application and any subsequent administrative or litigation challenges. This confusion, also reflected in Justice Breyer's *LabCorp* dissent,<sup>49</sup> is understandable but dangerous because it threatens to restrict the statutory category of process patents, contrary to black letter law that a new combination of previously well-known process steps may be patentable.<sup>50</sup> Identification of "prior art" process steps and questions of inventive concept or conventional versus nonobvious subject matter are part of a patentability analysis;<sup>51</sup> they play no role in the threshold determination of patent eligible statutory subject matter. Patent eligibility should turn solely on a determination of whether the claim as a whole defines a fundamental principle and whether it preempts all uses and implementations of that principle.

## 2. Machine-or-Transformation Analysis

Viewing *LabCorp* claim 13 through the prism of *Bilski*'s machine-or-transformation test, rather than the Fundamental Principles Exception, adds confusion and complexity. The inquiry focuses on transformation because it is clear that the claimed diagnostic process is not tied to any particular machine or apparatus.

The "assaying" step in claim 13 is a necessary data-gathering step that allows a physician or other medical practitioners to recognize elevated homocysteine levels, which can be correlated to a cobalamin or folate deficiency in a sick patient.<sup>52</sup> Whether that necessary step transforms a blood or urine sample in the process of obtaining the data is not necessarily relevant to the question of

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<sup>49</sup> See *Lab. Corp. of Am. Holdings v. Metabolite Labs. Inc.*, 548 U.S. 124, 137–38 (2006) (Breyer, J., dissenting).

<sup>50</sup> See *id.* at 136–37. The emphasis on the assay step as an "unpatented" procedure or test in Justice Breyer's *LabCorp* dissent is misplaced. The *LabCorp* dissent effectively ignores and sets aside the "unpatented" assay step, rather than assessing the claimed process as a whole as mandated by *Diehr. Id.* at 129.

<sup>51</sup> See *Flook*, 437 U.S. at 594.

<sup>52</sup> U.S. Patent No. 4,940,658 col. 9 ll. 30–57 (filed Nov. 20, 1986) (issued July 10, 1990).

process patent eligibility.<sup>53</sup> Concentrating the analysis on whether a transformation occurs and, if so, whether that transformation imposes “meaningful limits on the claim’s scope,” is “central to the purpose of the claimed process,” or amounts to “insignificant extra-solution activity” or mere data-gathering,<sup>54</sup> misses the big picture and detours the analysis away from the straightforward question of whether the claim defines a practical application of the correlation. The use of words like “meaningful,” “central,” “insignificant,” and “mere” also add unnecessary complexity, subjectivity, and uncertainty to the analysis. Focusing on transformations and the significance or centrality of extra-solution activity in determine-and-infer claims, such as claim 13, is another way of dissecting and separating claim elements, rather than viewing the combination of process steps as a whole to determine what, if any, is the practical application of the process.

These considerations aside, the assay step in claim 13 is transformational, and that transformation is necessary and central to the claimed diagnostic process. Dependent claims 15 and 16, for example, recite transformational chromatographic techniques to be used to measure the homocysteine level in a bodily fluid sample, which in turn provides the necessary data for a physician to make the diagnostic correlation.<sup>55</sup> Yet, one can see how different judges could reach very different conclusions about whether an assay step is central to a diagnostic method or nothing more than mere data-gathering or insignificant extra-solution

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<sup>53</sup> See Collins, *supra* note 34, at 2 (“There is no rational reason to use the tangibility of the transformation affected by the determining steps in a determine-and-infer claim as a peg on which to hang patent eligibility.”).

<sup>54</sup> *In re Bilski*, 545 F.3d 943, 961–63 (Fed. Cir. 2008) (en banc), cert. granted sub nom. *Bilski v. Doll*, 129 S. Ct. 2735 (2009), argued sub nom. *Bilski v. Kappos*, No. 08-964, 2009 WL 3750776 (Nov. 9, 2009). “Each patent examination center, each trial court, each panel of this court, will have a blank slate on which to uphold or invalidate claims based on whether there are sufficient ‘meaningful limits,’ or whether a transformation is adequately ‘central,’ or the ‘significance’ of process steps.” *Id.* at 994 (Newman, J., dissenting).

<sup>55</sup> ‘658 Patent col. 42 ll. 7–18. The chromatographic techniques themselves could even be considered special purpose machines that independently satisfy *Bilski*’s machine-or-transformation test. See *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 581 F.3d 1336, 1347 (Fed. Cir. 2009).

activity that renders a claim patent ineligible.<sup>56</sup> The multi-step analysis required by *Bilski*'s transformation test engenders more confusion and permits more opportunities for inconsistent, subjective judgments on the question of patent eligibility as compared to the well-settled Fundamental Principles Exception, particularly as articulated by the Court in *Diehr*.<sup>57</sup> Adhering to the simpler and more flexible analysis of the Fundamental Principles Exception will provide a firmer foundation for more consistent judgments of patent eligible subject matter.

*B. Classen Immunotherapies v. Biogen: When Transformation Is Not Enough*

Shortly after deciding *Bilski* and prior to *Prometheus*, a Federal Circuit panel applied the machine-or-transformation test to a different type of determine-and-infer claim that did not involve diagnostic methods.<sup>58</sup> In *Classen Immunotherapies, Inc. v. Biogen IDEC*,<sup>59</sup> the district court reviewed claims directed to a method for determining a vaccine schedule used to lower the risk of chronic immune-mediated diseases in mammals<sup>60</sup> and granted summary judgment for the defendant on the grounds that Classen's patents were invalid under 35 U.S.C. § 101.<sup>61</sup> The Federal Circuit then held that the claims failed the machine-or-transformation test without providing any analysis.<sup>62</sup>

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<sup>56</sup> This scenario is illustrated by the inconsistent decisions of the trial and appellate courts in the *Prometheus* case, discussed *infra* Part II.C.

<sup>57</sup> See *Diamond v. Diehr*, 450 U.S. 175, 185 (1981).

<sup>58</sup> *Classen Immunotherapies, Inc. v. Biogen IDEC*, 304 F. App'x 866, 867 (Fed. Cir. 2008).

<sup>59</sup> No. WDQ-04-2607, 2006 WL 6161856 (D. Md. Aug. 16, 2006), *aff'd*, 304 F. App'x 866 (Fed. Cir. 2008).

<sup>60</sup> *Id.* at \*5.

<sup>61</sup> *Id.* at \*6.

<sup>62</sup> *Classen*, 304 F. App'x at 866 ("In light of our decision in *In re Bilski*, we affirm the district court's grant of summary judgment that these claims are invalid under 35 U.S.C. § 101. Dr. Classen's claims are neither 'tied to a particular machine or apparatus' nor do they 'transform[ ] a particular article into a different state or thing.' Therefore we *affirm*." (alteration in original) (internal citations omitted) (quoting *In re Bilski*, 545 U.S. 943, 954 (Fed. Cir. 2008) (en banc), *cert. granted sub nom. Bilski v. Doll*, 129 S. Ct. 2735 (2009), *argued sub nom. Bilski v. Kappos*, No. 08-964, 2009 WL 3750776 (Nov. 9, 2009))).

*Classen* may have been correctly decided, but we do not believe that application of the machine-or-transformation test led the court to the correct result. Claim 1 of U.S. Patent No. 5,723,283 (the “’283 patent”), the principal claim at issue in *Classen*, reads:

A method of determining whether an immunization schedule affects the incidence or severity of a chronic immune-mediated disorder in a treatment group of mammals, relative to a control group of mammals, which comprises immunizing mammals in the treatment group of mammals with one or more doses of one or more immunogens, according to said immunization schedule, and comparing the incidence, prevalence, frequency or severity of said chronic immune-mediated disorder or the level of a marker of such a disorder, in the treatment group, with that in the control group.<sup>63</sup>

The first step in the claimed process recites “immunizing” subjects in a treatment group of mammals; the second step recites “comparing” therapeutic affect data from treatment and control groups.<sup>64</sup> In line with claim 13 in *LabCorp*, claim 1 of the ’283 patent plainly follows a type of determine-and-infer template but without the specificity or particularity of *LabCorp* claim 13.<sup>65</sup> The “comparing” step here,<sup>66</sup> as in *LabCorp* claim 13, is directed to a mental activity that, under *Bilski*, does not qualify as transformational.<sup>67</sup> The “immunizing” step, however, is directed to altering subject mammals from an initial state (i.e., susceptible to a pathogen) into a different state (i.e., immune to a pathogen).<sup>68</sup>

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<sup>63</sup> U.S. Patent No. 5,723,283 col. 51 ll. 50–60 (filed May 31, 1995) (issued Mar. 2, 1998).

<sup>64</sup> *Id.*

<sup>65</sup> Compare *id.* at col. 51 ll. 50–60, with U.S. Patent No. 4,940,658 col. 41 ll. 58–65 (filed Nov. 20, 1986) (issued July 10, 1990).

<sup>66</sup> ’283 Patent col. 51 ll. 57–60; see also *Classen*, 2006 WL 6161856, at \*5.

<sup>67</sup> See *Bilski*, 545 F.3d at 965.

<sup>68</sup> See ’283 Patent col. 51 ll. 54–56; Warren Woessner & Tania Shapiro-Barr, *Federal Circuit Applies Bilski Standard in Classen*, PAT. STRATEGY & MGMT., Mar. 2009, at 1, 4 (“The step of ‘immunizing mammals,’ as recited in the *Classen* claim, entails the transformation of mammals from a nonimmune state to an immune state.”).

As several commentators note, this sort of activity plainly qualifies as transformational under *Bilski*.<sup>69</sup> Of course, it must still be determined whether that transformation is “central” to the claimed process and not “insignificant extra-solution activity” or “mere data-gathering.”<sup>70</sup> The court in *Classen* apparently concluded that the immunizing step was not central to the claimed process or constituted mere data-gathering; otherwise it is difficult to fathom the basis for the court’s decision. While the basis for the court’s conclusion is not expressed, it is quite plausible that a different court might conclude otherwise, reasoning that the preamble language defines a particular patent eligible use and the immunization of the treatment group is central to a method for determining an optimal immunization schedule to prevent immune-mediated disorders.

It is worth recalling that the *Bilski* majority proffered the machine-or-transformation test as a proxy for the Fundamental Principles Exception because the latter inquiry was “hardly straightforward.”<sup>71</sup> But it begs the question: What is straightforward about determining whether a particular transformation is central to a claimed diagnostic or treatment optimization process; or whether it constitutes mere data-gathering; or whether it constitutes insignificant extra-solution activity? In our view, the difficulty of answering these questions is illustrated in *Classen*. In contrast, the Fundamental Principles Exception requires determining whether the claim particularizes an application of a fundamental principle (natural law, natural phenomenon, and/or abstract idea) so as not to preempt all uses of that principle.<sup>72</sup>

Analyzed under the Fundamental Principles Exception, the hallmark of claim 1 in *Classen* appears to be its abstractness and lack of particularity. The claim recites the process steps of performing a medical procedure (immunization according to an

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<sup>69</sup> See Holman, *supra* note 10, at 18; Woessner & Shapiro-Barr, *supra* note 68, at 4.

<sup>70</sup> *Bilski*, 545 F.3d at 962.

<sup>71</sup> *Id.* at 954.

<sup>72</sup> See *Diamond v. Diehr*, 450 U.S. 175, 203 (1981); *Parker v. Flook*, 437 U.S. 584, 599 (1978); *Gottschalk v. Benson*, 409 U.S. 63, 71 (1972); see also *Bilski*, 545 F.3d at 1011 (Rader, J., dissenting).

undefined schedule) on individuals in an experimental treatment group and comparing the incidence (or severity) of a class of disorders in the treatment group to the incidence (or severity) in a control group.<sup>73</sup> The claimed process embodies a general application of the scientific method to a class of chronic immune-mediated disorders.<sup>74</sup> The process is an abstract technique or algorithm for conducting research that mandates varying the conditions in an experimental treatment group with respect to a control group and observing the comparative effects.<sup>75</sup> Although the claim is drawn to the field of vaccine scheduling studies for chronic immune-mediated disorders, there is no particular application claimed. Because of that lack of particularity, claim 1 constitutes an impermissible attempt to preempt the use of the scientific method in the field of vaccine scheduling studies for chronic immune-mediated disorders. The claim does not apply the scientific method to prescribe or optimize a particular vaccine schedule that entails less risk of a particular chronic immune-mediated disorder in a particular subject group.<sup>76</sup> If it did so, that would reduce the claim's preemptive footprint to a specific application in the field of use. As it is, however, the claim is drawn to a general application of the scientific method in research involving all possible vaccination schedules vis-à-vis all possible immune-mediated disorders in all kinds of mammals. We note that the district court applied the Fundamental Principles Exception in its opinion granting summary judgment of invalidity: "Although articulated as a process, the ['283 patent does not claim a specific technique or technical process of testing vaccine safety. Instead,

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<sup>73</sup> '283 Patent col. 51 ll. 50–60.

<sup>74</sup> *See id.* at cols. 51–54.

<sup>75</sup> *See id.*

<sup>76</sup> Indeed, Dr. Classen purportedly discovered that when one or more immunogens, in a pharmaceutically acceptable composition, is first administered at an early age (typically prior to 42 days of age), it can substantially decrease the incidence, frequency, prevalence or severity of, or prevent, at least one chronic immune mediated disorder, and/or a surrogate marker thereof.

*Id.* at col. 7 ll. 35–41. However, Claim 1 fails to recite a vaccination schedule prior to 42 days of age, instead attempting to claim the general investigative method upon which the purported discovery was based to foreclose all other inquiries into optimal vaccination schedules in all mammals.

the [']283 patent describes only a general inquiry of whether the proposed correlation between an immunization schedule and the incidence of chronic disorders exists."<sup>77</sup> In *Classen*, we submit, application of the Fundamental Principles Exception is a more straightforward test and yields the correct result with greater clarity and certainty than application of the machine-or-transformation test.

### C. Patent Eligibility of the *Prometheus* Claims

The *Prometheus* case, which we also believe was correctly decided, illustrates the difficulties inherent in the machine-or-transformation test as applied to method claims in the emerging field of personalized medicine. *Prometheus* is the sole and exclusive licensee of patents claiming methods for determining the proper dosage of thiopurine drugs, which are used for treating both gastrointestinal and non-gastrointestinal autoimmune diseases.<sup>78</sup> These drugs include 6-mercaptopurine ("6-MP") and azathiopurine ("AZA"), a pro-drug that converts to 6-MP, which are used to treat inflammatory bowel diseases ("IBD") such as Crohn's disease and ulcerative colitis.<sup>79</sup> 6-MP is broken down by the body into various 6-MP metabolites, including 6-methyl-mercaptopurine ("6-MMP") and 6-thioguanine ("6-TG").<sup>80</sup> The patents involve determining the concentration of these two metabolites in sick patients.

6-MP and AZA have been used for years to treat autoimmune diseases, but non-responsiveness and drug toxicity may complicate treatment in some patients.<sup>81</sup> The patents, therefore, claim methods that seek to optimize therapeutic efficacy while minimizing toxic side effects. Claim 1 of the '623 patent is representative:

A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising: (a) *administering* a drug

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<sup>77</sup> *Classen Immunotherapies, Inc. v. Biogen IDEC*, No. WDQ-04-2607, 2006 WL 6161856, at \*5 (D. Md. Aug. 16, 2006), *aff'd*, 304 F. App'x 866 (Fed. Cir. 2008).

<sup>78</sup> U.S. Patent No. 6,355,623 (filed Apr. 8, 1999) (issued Mar. 12, 2002).

<sup>79</sup> *Id.* at col. 1 ll. 41–44.

<sup>80</sup> *Id.* at col. 1 ll. 45–48.

<sup>81</sup> *Id.*

providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and (b) *determining* the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder, *wherein* the level of 6-thioguanine less than about 230 pmol per  $8 \times 10^8$  red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and *wherein* the level of 6-thioguanine greater than about 400 pmol per  $8 \times 10^8$  red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.<sup>82</sup>

Emphasizing that the *Prometheus* patent contains “method of treatment” claims, with particular emphasis on the preamble language of “optimizing therapeutic efficacy” and “reducing toxicity,” the Federal Circuit reversed the district court and found the claims patent eligible.<sup>83</sup> There was no serious dispute between the parties that both the administration of a drug providing 6-TG and the determination of the 6-TG level in a patient resulted in transformations, either in the human body or in a blood sample.<sup>84</sup> Instead, the critical issue was whether those steps constituted insignificant extra-solution activity, mere data-gathering or something more.<sup>85</sup> The court, however, strained to explain its rationale for distinguishing the administration and determining steps from mere data-gathering steps, declaring that these steps are “central” to the purpose of the claims because “the administering and determining steps are part of a *treatment protocol*, and they are transformative.”<sup>86</sup> In our view, the mandatory machine-or-transformation test caused the court to strain unnecessarily to try to fit a square peg into a round hole by arguing that the claims are methods of treatment.<sup>87</sup> The claims do not use traditional language

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<sup>82</sup> *Id.* at col. 20 ll. 10–25 (emphasis added).

<sup>83</sup> *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 581 F.3d 1336, 1341 (Fed. Cir. 2009). The district court found that the administration and determining steps amounted to mere data-gathering steps and held the claims to be patent ineligible. *Id.*

<sup>84</sup> *Id.* at 1347.

<sup>85</sup> *Id.*

<sup>86</sup> *Id.* (emphasis added).

<sup>87</sup> *Id.* at 1346.

such as “administering a therapeutically effective amount of 6-TG,” which one would expect to see in a method of treatment claim. Moreover, as the district court pointed out below, the “wherein” clauses do not require any actual change in dosage to optimize the therapeutic efficacy or to reduce toxicity of the treatment.<sup>88</sup> It would have been simpler and more effective had the court applied the analysis required by the Fundamental Principles Exception.

The court articulated its most compelling argument for patent eligibility in an insightful application of the Fundamental Principles Exception:

[T]he claims do not preempt natural processes; they utilize them in a series of specific steps. . . . The inventive nature of the claimed methods stems not from preemption of all use of these natural processes, but from the application of a natural phenomenon in a series of transformative steps comprising particular methods of treatment.<sup>89</sup>

The natural phenomenon at issue is the ability of the human body to metabolize a drug to 6-TG.<sup>90</sup> It is not the claimed correlation between a metabolite level generated from administration of a synthetic drug and an optimal therapeutic or non-toxic dose. The claimed process utilizes the naturally occurring metabolic function to generate measurable metabolite levels that can be compared to optimal levels for optimizing therapeutic efficacy or reducing toxicity. The patent does not claim the naturally occurring metabolic function itself. The correlation defined in the wherein clauses, with specific concentrations of 6-TG recited, is the practical application of a treatment optimization process for a sick patient as recited in the claim preamble.<sup>91</sup> Like the determine-and-infer claims of *LabCorp*,<sup>92</sup> this is all that should be required for patent eligibility,

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<sup>88</sup> *Id.* at 1341.

<sup>89</sup> *Id.* at 1349.

<sup>90</sup> See U.S. Patent No. 6,355,623 col. 4 ll. 60–64 (filed Apr. 8, 1999) (issued Mar. 12, 2002) (stating that both 6-MP and AZA can be metabolized to 6-TG).

<sup>91</sup> *Id.* at col. 2 ll. 16–18.

<sup>92</sup> See *supra* note 34 and accompanying text.

freed from the additional restraints of *Bilski*'s machine-or-transformation test.

*D. Association for Molecular Pathology v. United States Patent & Trademark Office: Omitting the Determination Step*

Inspired by the rulings in *Bilski* and *Classen*, the plaintiffs in *Association for Molecular Pathology v. United States Patent & Trademark Office*<sup>93</sup> invoked § 101, inter alia, to challenge a group of patents owned by Myriad Genetics.<sup>94</sup> The patents cover breast and ovarian cancer-susceptibility genes BRCA1/BRCA2, as well as diagnostic and therapeutic screening methods utilizing those genes.<sup>95</sup> According to plaintiffs, certain claims in the patents violate § 101 under the Fundamental Principles Exception because the claims cover “products of nature, laws of nature and/or natural phenomena, and abstract ideas or basic human knowledge or thought.”<sup>96</sup> The court recently granted summary judgment of invalidity and an appeal is pending.<sup>97</sup>

Claim 1 of U.S. Patent No. 5,709,999 (the “’999 patent”) is representative of the diagnostic method claims at issue in the case:

A method for detecting a germline alteration in a BRCA1 gene, said alteration selected from the group consisting of the alterations set forth in Tables 12A, 14, 18 or 19 in a human which comprises *analyzing* a sequence of a BRCA1 gene or BRCA1 RNA from a human sample or analyzing a sequence of BRCA1 cDNA made from mRNA from said human sample with the proviso that said germ line alteration is not a deletion of 4

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<sup>93</sup> No. 09 Civ. 4515, 2010 WL 1233416 (S.D.N.Y. Apr. 5, 2010).

<sup>94</sup> *Id.* at \*1.

<sup>95</sup> *Id.*

<sup>96</sup> *Id.*

<sup>97</sup> *Id.* Applying *Bilski*'s machine-or-transformation test, the court struck down all of the method claims at issue in the suit. *See id.* at \*46–50. More suprisingly, the court also invalidated the composition claims covering isolated DNA corresponding to the BRCA1/BRCA 2 genes as “not markedly different” than products of nature. *See id.* at \*41–46.

nucleotides corresponding to base numbers 4184-4187 of SEQ ID NO: 1.<sup>98</sup>

Strikingly, and unlike the claims in *LabCorp*, *Classen* or *Prometheus*, this claim recites only an “analyzing” step without further limitation. Although there is no doubt that extensive handling and manipulation of genetic material needs to be performed prior to the claimed “analyzing” step, and that such activity would likely satisfy *Bilski*'s transformation test, those implicit manipulations are not recited as part of the claimed process. In other words, the claim departs from the determine-and-infer template by omitting altogether the “determine” step. The court characterizes claim 1 of the '999 patent as follows: “[w]hile the *purpose* of the claimed method is, for example, to ‘detect a germline alteration in a BRCA1 gene,’ the method actually claimed is ‘analyzing a sequence of a BRCA1 gene.’”<sup>99</sup>

Because claim 1 of the '999 patent, as a whole, is directed to a purely mental process, the claimed process should not withstand scrutiny under the Fundamental Principles Exception.<sup>100</sup> The claim also fails the machine-or-transformation test. The “analyzing” step is not tied to a particular machine nor does it transform a particular article into a different state or thing. There is no claimed assay or “determining” step to determine the sequence of a BRCA1 gene in a human sample, although such a step is implicit in the claim. The claim does not require the physical transformation of a tissue sample or any other physical transformation. Therefore,

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<sup>98</sup> U.S. Patent No. 5,709,999 col. 161 ll. 17–25 (filed June 7, 1995) (issued Jan. 20, 1998) (emphasis added).

<sup>99</sup> See *Ass'n for Molecular Pathology*, 2010 WL 1233416, at \*48 (internal citations omitted) (emphasis in original) (citing '999 Patent col. 161 ll. 17–18, 20–21).

<sup>100</sup> In *Bilski*, the majority characterized the “hedging” claim at issue as directed to a “purely mental process of performing requisite mathematical calculations without the aid of a computer or any other device” followed by an insignificant post-solution step. *In re Bilski*, 545 F.3d 943, 965 (Fed. Cir. 2008) (en banc), *cert. granted sub nom. Bilski v. Doll*, 129 S. Ct. 2735 (2009), *argued sub nom. Bilski v. Kappos*, No. 08-964, 2009 WL 3750776 (Nov. 9, 2009). Quoting *In re Comiskey*, 499 F.3d 1365 (Fed. Cir. 2007), which struck down claims directed to a process for arbitrating a particular kind of commercial dispute, the majority observed that “claims to such an ‘application of [only] human intelligence to the solution of practical problems’ is no more than a claim to a fundamental principle.” *Bilski*, 545 F.3d at 965 (alteration in original) (quoting *Comiskey*, 499 F.3d at 1379).

application of the machine-or-transformation test should not save this claim under § 101.

In contrast, claim 20 of U.S. Patent No. 5,747,282 (the “’282 patent”) does not omit the “determine” step in the determine-and-infer template and therefore requires a closer analysis under § 101. Claim 20 recites:

A method for screening potential cancer therapeutics which comprises: *growing* a transformed eukaryotic host cell containing an altered BRCA1 gene causing cancer in the presence of a compound suspected of being a cancer therapeutic, *growing* said transformed eukaryotic host cell in the absence of said compound, *determining* the rate of growth of said host cell in the presence of said compound and the rate of growth of said host cell in the absence of said compound and *comparing* the growth rate of said host cells, wherein a slower rate of growth of said host cell in the presence of said compound is indicative of a cancer therapeutic.<sup>101</sup>

Unlike claim 1 of the ’999 patent, this claim is not directed solely to a mental process or a naturally occurring phenomenon. The first two steps require “growing” a particular type of cell in the presence or absence of a suspected cancer therapeutic; the last two steps require the mental steps of “determining” and “comparing” growth rates.<sup>102</sup> This claim’s structure leads to the question of whether it is closer to the claim in *Classen* or the claim in *Prometheus*.<sup>103</sup>

In our view, claim 20 in the ’282 patent is a practical application of screening potential therapies for the types of breast

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<sup>101</sup> U.S. Patent No. 5,747,282 col. 156 ll. 15–27 (filed June 7, 1995) (issued May 5, 1998) (emphasis added).

<sup>102</sup> *Id.*

<sup>103</sup> The district court has concluded the former, disparaging the recited transformative steps as “nothing more than preparatory, data-gathering steps to obtain growth rate information” and stating that the transformative steps “do not render the claimed mental process patentable under § 101.” *Ass’n for Molecular Pathology*, 2010 WL 1233416, at \*50.

and ovarian cancers attributable to the altered BRCA1 gene.<sup>104</sup> The growth rates of transformed eukaryotic host cells are not natural phenomena, they are process steps required for trying to identify potential compounds that can treat particular diseases.<sup>105</sup> The process may be obvious or imperfectly enabled, but it should not be deemed patent ineligible.

Like *Classen*, the claim limits application of the principle to a field of use, which is cancer therapeutics.<sup>106</sup> Unlike *Classen*, however, the claim does not attempt to preempt all uses of the principle in that field of use, but is instead limited to a specific application involving particular gene sequences responsible for causing particular types of cancer.<sup>107</sup> As the majority in *Bilski* acknowledged, the Fundamental Principles Exception is essentially an inquiry into the scope of the exclusion effected by the claim.<sup>108</sup> Here claim 20 of the '282 patent is drawn to a specific application of the scientific method to screen potential cancer therapeutics with respect to a particular gene sequence. The claim does not preempt all uses of the principle in all fields or even in the single field of cancer therapeutics.

Application of the machine-or-transformation test would be less straightforward and could possibly lead to a different conclusion, unfairly restricting patent eligibility for claim 20 of the '282 patent and other claims of its ilk (as illustrated by the district court decision). The claimed screening process is not tied to a particular machine or apparatus.<sup>109</sup> Thus, the issue is whether the

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<sup>104</sup> See '282 Patent col. 156 ll. 15–27.

<sup>105</sup> *Id.*

<sup>106</sup> See *id.* at col. 1 ll. 19–23.

<sup>107</sup> *Id.* at col. 1 ll. 24–40.

<sup>108</sup> *In re Bilski*, 545 F.3d 943, 953 (Fed. Cir. 2008) (en banc), cert. granted sub nom. *Bilski v. Doll*, 129 S. Ct. 2735 (2009), argued sub nom. *Bilski v. Kappos*, No. 08-964, 2009 WL 3750776 (Nov. 9, 2009).

<sup>109</sup> The *Bilski* test requires the claimed process to be tied to a particular machine or apparatus. While it has been argued that this “tying” requirement should not be limited only to machines but include other categories of statutory subject matter such as compositions of matter, see *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 581 F.3d 1336, 1343 (Fed. Cir. 2009) (“In addition, Prometheus contends that *Bilski*’s use of ‘machine’ in its machine-or-transformation test must be read as shorthand for all patentable subject matter, including compositions of matter.”), the Court has not expressly ruled on that issue. If the tying requirement allows for tying the claimed

“growing” steps are transformational and, if so, whether the transformation is central to the claimed process or insignificant extra-solution activity.<sup>110</sup> The “growing” steps essentially require an *in vitro* experiment whereby eukaryotic cells containing the BRCA1 gene are cultured in the presence and absence of a suspected cancer therapeutic agent.<sup>111</sup> This kind of activity qualifies as a transformation under *Bilski*, particularly in view of *Prometheus*, because it involves altering a particular article (a eukaryotic cell containing a BRCA1 gene) from an initial state (a single or few cells) to a different state (a larger population of cells).<sup>112</sup> However, some could argue that cells naturally divide (“grow”) without any human intervention and the essentially passive act of providing a proper artificial medium and conditions to allow them to do so *in vitro* is akin to watering a plant in the presence of adequate sunlight. If it is at all doubtful that the latter activity is transformational, then it is doubtful the former activity is too. In any event, the outcome of a machine-or-transformation analysis of claim 20 of the ’282 patent appears to be more uncertain than under the Fundamental Principles Exception and could unfairly exclude this important screening method advance from the category of patent eligible subject matter under § 101.

#### CONCLUSION

The foregoing claims analysis demonstrates that the machine-or-transformation test of *Bilski* is not particularly well-suited to assessing the types of diagnostic and genetic screening methods that are increasingly utilized in the area of personalized medicine. Under that test, it is plausible that a claim such as *LabCorp*’s claim 13 could be excluded as patent ineligible even though application

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process to a particular composition of matter, then claim 1 of the ’282 patent more easily meets the test. *Bilski*, 545 F.3d at 954.

<sup>110</sup> At first blush, the use of the word “transformed” in the claim may lead some immediately to assume that some kind of transformation is involved in the “growing” steps of the claimed process, but that would be a mistake. In the context of the claim, the process of transforming a eukaryotic cell with an altered BRCA1 gene is not recited as a step in the claim. The question whether a transformation occurs as part of a claimed process must be determined only with respect to the recited steps.

<sup>111</sup> ’282 Patent col. 1 l. 61–col. 26 l. 5.

<sup>112</sup> *Id.* at col. 156 ll. 15–23.

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of the Fundamental Principles Exception should lead to the opposite conclusion. The claims at issue in *Prometheus* and claim 20 of the '282 patent in the Myriad Genetics case reflect similar uncertainties. Conversely, applying the machine-or-transformation test to a claim such as *Classen's*, it is plausible that a court could find patent eligibility, even though we believe application of the Fundamental Principles Exception should dictate otherwise. The uncertainty principally lies in assessing whether a particular transformation satisfies the "insignificant extra-solution activity" corollary of the machine-or-transformation test. In our view, *Bilski's* transformation analysis focuses on the wrong question for diagnostic and screening methods and unnecessarily complicates what should be a straightforward assessment of whether patent eligible subject matter is entitled to be examined for compliance with the requirements for patentability. To avoid this kind of uncertainty, especially in the increasingly important areas of medical diagnostics and personalized medicine, the Supreme Court should reemphasize the primacy of the well-settled Fundamental Principles Exception standard for determining patent eligibility of process claims and reject the mandatory, exclusive applicability of the machine-or-transformation test.