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Of Babies and Bathwater – The Impact of *In Re Bilski* on Life Science Patents

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Abstract

Tension between the broad language of 35 U.S.C. § 101 and limitations of its scope is an emerging issue in recent court decisions attempting to resolve the issue of whether patent claims preempt a natural phenomenon. These decisions significantly impact the patentability of personalized medicine inventions that rely on discovery of correlations between biomarkers and the safety and efficacy of therapeutic treatment in an individual. While a "business methods" case, the Federal Circuit's *In re Bilski* decision may have a profound impact on medical diagnostics and personalized medicine patents by altering the ability of personalized medicine companies to protect the technology behind their products. A patent law that identifies the unique specificities of a particular industry will better serve the advancement of biotechnology and personalized medicine.

Of Babies and Bathwater – The Impact of *In Re Bilski* on Life Science Patents

by MICHAEL J. SHUSTER, PH.D., AND JULEEN KONKEL*

I. Introduction

Patents promote innovation by granting inventors the right to exclude others from practicing their inventions for a limited time. Patents are granted for ideas that are new, useful, and nonobvious.[1] In order to secure patent protection, an inventor must provide a patent specification that describes the invention, enables a person of ordinary skill in the art to make and use the invention, and sets forth the best way the inventor knows or practices the invention.[2]

The quid pro quo contemplated by the Constitution and by Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. This bargain between the government and the inventor grants exclusionary rights in exchange for disclosure and promotes innovation in several ways.[3] First, the inventor's disclosure teaches the public how to make and use the described technology, which becomes freely available once the patent expires. In addition, the patent system promotes innovation by creating incentives for others to design around patented technologies so as to avoid liability for patent infringement. Patents also promote innovation by providing economic incentives for investment in new technologies. These exclusive rights allow investors to recoup a fair rate of return by preventing others from free-riding on their investments.

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1. 35 U.S.C. §§ 101-103 (2006).

2. 35 U.S.C. § 112 (2006).

3. *See* Michael J. Shuster, Pauline Farmer-Koppenol, and H. Thomas Anderton Jr., *Observations on Recent Developments in Patent Law: Is the Generic Claim Turning Into an Endangered Species?*, 3 BURRILL PERSONALIZED MED. RPT. 66 (Nov. 2007).

On the other hand, patents arguably impede innovation. A dense patent landscape can make it difficult to bring new technologies to market because royalty payments reduce profit margins to unattractive levels, or because a required license is unavailable. The patent system promotes innovation when an appropriate balance is struck between the scope of available patent protection and the degree to which that protection advances the art. Accordingly, unless and until an idea is refined and developed to the point where there is a specific practical benefit, there is insufficient justification for permitting an applicant to occupy what may prove to be a broad field.

Recent court cases shed light on what appears to be a renaissance in redefining the scope of patentable subject matter. The tension between the broad language of 35 U.S.C. § 101 and the limitations of its scope by the Supreme Court is often an issue when determining the patent eligibility of a process. This tension arises where the process contains a step involving a mathematical algorithm; however, it is an emerging issue in biotechnology cases where courts must decide whether the claims preempt a law of nature or a natural phenomenon. This article summarizes some of the recent changes in patent law with an emphasis on how the decisions may affect the ability of personalized medicine companies to protect the technology behind the products they create.

II. Patentable Subject Matter Under § 101

Congress has broadly defined the subject matter that can be protected by patent, stating simply, "whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter . . . may obtain a patent . . ."[4] The 1952 Committee Reports that accompanied the Patent Act emphasized the breadth of the statutory subject matter as including "anything under the sun that is made by man."[5] "Process," as defined by statute, is synonymous with "method"[6] and denotes "an act, or a series of acts, performed upon the subject-matter to be transformed and reduced to a different state or thing."[7]

There are several exceptions to this general rule that any process is eligible for patent protection. It is well established that principles,

4. 35 U.S.C. § 101 (2006).

5. *Diamond v. Diehr*, 450 U.S. 175, 182 (1981) (quoting S. REP. No. 82-1979, at 5 (1952)).

6. *See* 35 U.S.C. § 100(b) (2006).

7. *Cochrane v. Deener*, 94 U.S. 780, 788 (1876).

such as "natural phenomena, laws of nature, and abstract ideas," are not patentable under Section 101.[8] However, a process that employs a law of nature or a natural phenomenon in a useful way may be protected by patent law.[9] For example, process claims that contain significant extra-solution activity may transform an unpatentable principle into a patentable process.[10] Recent case law has attempted to define the criteria for determining when a process claim combining unpatentable natural phenomena with significant extra-solution activity may be patentable under Section 101.

To begin, it is helpful to review those cases that underscore the federal district courts' approach to analyzing patentable process claims, starting with the Supreme Court case *LabCorp v. Metabolite,* followed by the recent case of *Ariad v. Lilly* and two cases on appeal before the Federal Circuit—*Classen* and *Prometheus*—and finally the recent Federal Circuit case *In re Bilski*.[11]

A. The Supreme Court's *LabCorp* Decision

With each developing technology, the Supreme Court struggles to define the line separating patentable processes from processes claiming unpatentable principles of nature or abstract ideas. In determining what is patentable, the Court must balance the need to protect and encourage innovation in evolving technologies against identifying claims that preempt all uses or applications of a newly discovered idea or principle.

Justice Breyer's dissent in *LabCorp v. Metabolite* questioned the proper scope of protection for process claims that embody naturally existing biological phenomena.[12] Metabolite licensed a patent based on the discovery of a correlation between high levels of the amino acid homocysteine and deficiencies in two essential vitamins, folate

8. *Diehr*, 450 U.S. at 185.

9. *Parker v. Flook*, 437 U.S. 584, 592 (1978) (distinguishing Morse's invalid claim broadly covering the use of electromagnetism to print at a distance, from Neilson's valid claim for a machine applying the principle that heated air increases the intensity of the heat in a blast furnace).

10. *Diehr*, 450 U.S. at 192 (significant post-solution activity found where mathematical formula used to transform or reduce an article to a different state or thing).

11. *See Lab. Corp. of Am. Holdings v. Metabolite Laboratories, Inc.*, 548 U.S. 124 (2006) [hereinafter "*LabCorp*"]; *In re Bilski*, 545 F.3d 943 (Fed. Cir. 2008); *Ariad Pharms. v. Eli Lilly & Co*., 529 F. Supp. 2d 106 (D. Mass. 2007), *aff'd in part, rev'd in part*, 560 F.3d 1366 (Fed. Cir. 2009); *Classen Immunotherapies, Inc. v. Biogen IDEC*, 381 F. Supp. 2d 452 (D. Md. 2005), *aff'd*, 2008 U.S. App. LEXIS 25661 (Fed. Cir. Dec. 19, 2008); *Prometheus v. Mayo*, No. 04cv1200, 2008 U.S. Dist. LEXIS 25062 at *1 (S.D. Cal. Mar. 28, 2008).

12. *LabCorp,* 548 U.S. at 125.

and vitamin B12.[13] The patent broadly claimed measuring homocysteine (i.e., a "homocysteine assay") and the correlation between the elevated level of homocysteine in the body and a diagnosis of a deficiency in two essential vitamins (i.e., an "assay and correlate" claim).[14] This correlation is an important test in predicting the risk for heart disease. The patent seemed to encompass the use of any methodology for assaying total homocysteine, even assay techniques developed after the licensing university applied for the patent.[15]

Justice Breyer's dissent argued that the Supreme Court should have decided whether Metabolite's "assay and correlate" claim was invalid on the merits because the correlation step claimed a "law of nature,"[16] which, along with natural phenomena and abstract ideas, is excluded from patent protection.[17] This furthers the patent system's constitutional mandate to "promote the Progress of Science and Useful Arts"[18] by assuring that no monopoly is granted that preempts the use of a basic scientific fact. According to Justice Breyer, the correlation claim was little more than a mental step to review the assay results in light of current medical knowledge.[19] The assay step, though not specified in the patent claim, was insufficient to remove the claim as a whole from preempting a natural phenomenon.[20]

Further, Justice Breyer noted that allowing Metabolite's broad "assay and correlate" claim to stand expanded the pool of likely infringers, which may inhibit doctors from using their best medical judgment and could contribute to healthcare costs.[21] Any competent doctor reviewing the test would automatically correlate the results with the presence or absence of a vitamin deficiency and thus be liable as a direct infringer.[22] The mental step articulated in the

13. *Id.* at 128.

14. *Id.* at 129.

15. *Id.* at 136.

16. *Id.* at 132.

17. *Id.* at 126 (quoting *Diehr*, 405 U.S. at 185 (1981)).

18. U.S. CONST. art. I, § 8, cl. 8.

19. *LabCorp*, 548 U.S. at 137.

20. *Id.* at 137-38.

21. *Id.* at 138.

22. *Metabolite Laboratories, Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1364-65 (Fed. Cir. 2004). Note that Metabolite has never enforced its patent directly against physicians.

correlation claim requires a medical practitioner to consider the relationship after looking at the test result. [23]

B. Post *LabCorp* Decisions

Breyer's dissent in *LabCorp* opened the door for challenges to the validity of claims directed to biological phenomena under Section 101. A series of recent patent decisions have addressed the issue of whether patent process claims are unpatentable as wholly preempting natural phenomena or laws of nature.

In the 2007 case *Ariad v. Lilly*, the district court rejected Lilly's argument that Ariad's claims embodied a natural phenomenon.[24] Directed to the inhibition of a regulatory protein (NF-kB), the '516 patent broadly covers a method of altering the activity of NF-kB in a cell.[25] The claims at issue recite a "reducing" NF-kB activity step, but do not articulate a particular agent or substance, or any particular steps, to reduce NF-kB activity in order to practice the invention. [26] Lilly argued that the claims encompassed the NK-kB-IkB autoregulatory loop (the "Autoregulatory Loop"), a natural process in cells.[27] After extensive expert testimony, the district court concluded the Autoregulatory Loop was an incomplete model, and that Lilly had failed to meet its evidentiary burden that the Autoregulatory Loop exists in living cells in the same way it is encompassed in Ariad's claims.[28] Because the Autoregulatory Loop was an incomplete model that may not exist in nature, the process claim could not be considered to preempt a "natural phenomenon" for purposes of Section 101.

Similar to *LabCorp*, the patents at issue in *Classen Immunotherapies, Inc. v. Biogen IDEC* purported to effectively encompass a naturally existing biological correlation between variations in a specific vaccination schedule and the risk of developing

23. *LabCorp*, 548 U.S. at 136.

24. 529 F. Supp. 2d 106 (D. Mass. 2007), *aff'd in part, rev'd in part on other grounds*, 560 F.3d 1366 (Fed. Cir. 2009).

25. U.S. Patent No. 6,410,516 (filed June 5, 1995) (the '516 patent). Claim 1: A method for inhibiting expression, in a eukaryotic cell, of a gene whose transcription in regulated by NF-kB, the method comprising reducing NF-kB activity in the cell such that expression of said gene is inhibited.

26. *Ariad,* 529 F. Supp. 2d at 113.

27. *Id.* at 114-15.

28. *Id.* at 120.

chronic immune-mediated disorders.[29] The patents, not specific to a particular vaccine or vaccine schedule, broadly claimed methods for determining vaccination protocols based on comparing the incidence of immune disorders between treatment groups immunized under different vaccination schedules.[30] The district court concluded that finding a correlation between an immunization schedule and the risk of developing an immune disorder is a natural phenomenon.[31] The claims amounted to an "indirect attempt to patent the idea that there is a relationship between vaccine schedules and chronic immune mediated disorders."[32] Further, the Court noted, the active step of immunizing patients in accordance with a schedule determined to be low risk was insignificant post-solution activity.[33] The court found the patents invalid for encompassing unpatentable natural phenomena.[34]

However, *Classen* did not address the patentability of a field of use claim restriction, such as whether a biological occurrence that exists only as a result of human intervention can be accurately characterized as a natural phenomenon. Such is the issue in *Prometheus v. Mayo*, a district court decision, which held that the correlation between the level of certain metabolites in the blood and effective therapeutic treatment was a "natural phenomenon."[35] The patents at issue claimed three steps: (1) administration of the thiopurine drugs; (2) measurement of the level of certain metabolites in the blood of patients taking thiopurine drugs to determine the metabolite level; and (3) correlation of the metabolite level with an adjustment in drug dosage to avoid toxic side effects.[36] Here, Prometheus unsuccessfully argued that since the drug metabolites only exist in the body as the direct result of medical intervention (i.e., through the administration of the thiopurine drugs), the correlation is manmade, not a natural phenomenon.[37]

29. *Classen Immunotherapies, Inc. v. Biogen IDEC*, 381 F. Supp. 2d 452 (D. Md. 2005).

30. U.S. Patent Nos. 6,420,139 (filed July 6, 2000), Claim 1; 6,638,739 (filed Apr. 18, 2002), Claim 1.

31. Memorandum Order, Classen Immunotherapies v. Biogen IDEC, Civ. No. 04-2607, p. 10 (D. Md. filed Aug. 16, 2006).

32. *Id.*

33. *Id.* at 12.

34. *Id.*

35. *Prometheus v. Mayo*, No. 04cv1200, 2008 U.S. Dist. LEXIS 25062 at *1 (S.D. Cal. Mar. 28, 2008).

36. *Prometheus v. Mayo*, 2008 U.S. Dist. LEXIS 25062 at *3-4.

37. *Id.* at *19.

The *Prometheus* court, citing Justice Breyer's dissent in *LabCorp* in support of its decision, found the claims of the patents in suit to be mere correlations resulting from a natural body process;[38] the court reasoned that it is the human body that naturally converts the thiopurine drug into a therapeutic agent through an enzymatic process.[39] Furthermore, the court found the first two steps of the patent claims, the "administering" and "determining" steps, merely necessary "data-gathering steps" used in the subsequent correlation.[40] The court noted that the "data-gathering" steps are insufficient to make a nonstatutory correlation claim patentable.[41] Even though the patent claims were limited to the level of thiopurine drug in the body, a field of use limitation, because the inventors did not "create" the correlation between thiopurine drug metabolite levels and the therapeutic efficacy and toxicity, the claimed correlation was an unpatentable "work of nature."[42] This rationale is a significant obstacle to companies involved in commercializing medical diagnostics and personalized medicine because these claims necessarily involve an underlying body process.

These decisions greatly impact the patentability of personalized medicine inventions that rely on the discovery of the correlation between biomarkers and the safety and efficacy of therapeutic treatment in an individual. Although it is unclear what effect patenting such correlations will have on the development of personalized medicine, it does appear that in light of these recent decisions broad personalized medicine patents, and specifically process claims, face significant challenges under Section 101.

II. The Machine-or-Transformation Test

The Federal Circuit recently clarified one test for determining patent eligibility of a process under Section 101.[43] The machine-or-transformation test serves as a proxy for assessing whether a process claim seeks to impermissibly preempt the use of a fundamental

38. *Id.*

39. *Id.* at *21.

40. *Id.* at *17.

41. *Prometheus v. Mayo*, 2008 U.S. Dist. LEXIS 25062 at *17-18 (citing *In re* Meyer, 688 F.2d 789, 794 (C.C.P.A. 1982)).

42. *Id.* at *23 (citing Funk Bros. Seed Co. v. Kalo Inoculant., 333 U.S. 127, 130 (1948)).

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

principle.[44] Under the machine-or-transformation test, a claim is patent eligible if (1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing.[45] To that end, certain criteria must be met under either branch. First, use of the specific machine or transformation of an article must convey meaningful limits on the claim's scope to impart patent-eligibility.[46] Second, the involvement of the machine or the transformation must be central to the claim's purpose and not merely insignificant extra-solution activity.[47]

A. The Transformation Test

When not tied to a particular machine or apparatus, the claims must transform an article into a different state or thing to constitute patent-eligible subject matter.[48] By definition, a "process" under 35 U.S.C. § 101 requires some kind of transformation or conversion of subject matter representative of physical activity or objects.[49] Changes to intangible subject matter representative of physical activity or objects are also included in this definition.[50] Prior to *Bilski*, the Federal Circuit in *In re Abele* had defined transformation as it relates to the Section 101.

In *Abele*, the Federal Circuit distinguished between two claims, finding only one to be patentable.[51] The unpatentable claim recited a method of calculating and graphically displaying variances of data from average values without specifying the type or nature of the data, how the data was obtained, or what the data represented.[52] The patentable dependent claim identified the data as "X-ray attenuation

44. *Id.*

45. *Id.* at 961.

46. *Id.* (citing *Gottschalk v. Benson*, 409 U.S. 63, 71-72 (1972)).

47. *Id.* at 962; *see also In re Grams*, 888 F.2d 835, 839-40 (Fed. Cir. 1989) (holding that a data-gathering step combined with an algorithm, without specifying how the data is to be gathered, is a meaningless limit on an algorithm claim because every algorithm inherently requires the gathering of data); *In re Schrader*, 22 F.3d 290, 293-94 (Fed. Cir. 1994) (claims directed to a method of conducting an auction, where claims require selecting winning bids in a manner that maximizes the total price, constitute a mathematical optimization algorithm, and recording the bids on each item, without describing how, is insignificant post solution activity).

48. *Bilski*, 545 F.3d at 961.

49. *Schrader*, 22 F.3d at 294.

50. *Id.* at 296.

51. *In re Abele*, 684 F.2d 902, 909 (C.C.P.A. 1982), *abrogated by In re Bilski*, 545 F.3d 943 (Fed. Cir. 2008).

52. *Abele*, 684 F.2d at 908.

data produced in a two-dimensional field by a computed tomography scanner."[53] The second claim meaningfully limited the scope of the patentable claim by identifying what the data represented and transforming the "raw data into a particular visual depiction of a physical object on a display."[54] In this case, raw data, not the object itself, was transformed into a graphical display. Because transformation of the physical object itself is not a requirement of the transformation test, the claim was patentable.[55]

Furthermore, the Abele patent recited production, detection, and display steps that, absent the algorithm, resulted in a conventional CAT scan process.[56] The court considered the production and detection steps, which were antecedent to the algorithm, to be significant pre-solution "data gathering" activity because the steps were not a requirement of the algorithm but required by other claim limitations.[57] The resultant display step, though non-trival post solution activity because it assists in a doctor's diagnosis, was not the determining factor for patentability.[58]

Unlike the claims in *Abele*, which transform data representative of a physical object, the claims at issue in *Bilski* recited a method practiced by commodity traders for managing "consumption risk" associated with the sale of commodities during a given period.[59] Under the claimed method, a commodity trader initiates a series of swaps with consumers and providers to hedge the price of certain commodities.[60] Bilski had admitted to a United States Patent and Trademark Office Examiner that his claims were not limited to operation on a computer.[61]

The *Bilski* court held that the claims, which were not tied to the use of a computer, did not involve transformation of an article into a different state or thing.[62] The object of the claims, intangible legal obligations and other abstractions, were incapable of transformation

53. *Id.*

54. *Id.*

55. *Bilski,* 545 F.3d at 963.

56. *Abele*, 684 F.2d at 908. Note that the court dissected the claim and evaluated its patentability on the basis of individual limitations, which is in apparent conflict with the Supreme Court requiring analysis of the claim as a whole.

57. *Id.*

58. *Id.*

59. *Bilski*, 545 F.3d at 949.

60. *Bilski*, 545 F.3d at 949.

61. *Id.* at 950.

62. *Id.* at 963-64.

since they did not represent anything tangible.[63] The invention claimed the mental and mathematical process of identifying transactions that hedge risk, and even though this process required physical steps of "initiating" and "identifying," these were considered insignificant post-solution activity, unable to transform an unpatentable principle into a patentable process.[64] The court concluded the claims did not constitute patentable subject matter because they did not involve transformation of an article.[65]

The Federal Circuit left open the possibility that the requirements of the machine-or-transformation test could change upon future developments in technology, and noted that the Supreme Court may ultimately decide to alter or set aside the test in order to accommodate emerging technologies.

III. The Impact of *Bilski* on Biotech Patent Claims

Although *Bilski* is a "business methods" case, the decision has a profound effect on biotechnology, specifically medical diagnostics and personalized medicine patents. The machine-or-transformation test is only one test for determining whether process claims are eligible for patent protection, but it is the standard by which biotechnology claims are currently assessed.

A. *Bilski*'s Impact on Recent and Pending Cases

Take, for example, the claims of the aforementioned *Ariad*, *Classen,* and *Prometheus* cases. Under the machine-or-transformation test, the *Ariad* claim inhibiting gene expression would be considered patentable subject matter because it involves a transformation. There is a transformation of the underlying subject matter, inhibition of gene expression, via the reducing step, which is tied to level of NF-kB regulatory protein. Although the reducing step is vague for failing to recite any particular steps or the use of a particular agent or substance to reduce NF-kB activity, the reducing step represents a change in a tangible intracellular medium and is central to the claimed purpose of the invention. Nevertheless, even though the claims cover a natural body phenomenon and would therefore be permissible under the machine-or-transformation test, they violate the Supreme Court's precedent barring the patenting of natural phenomena.

63. *Id.*

64. *Id.* at 965-66.

65. *Id.*

On the other hand, the *Classen* claims would fail the machine-or-transformation test. The claims in *Classen* recite methods for determining optimal immunization schedules based on comparing incidence of immune-mediated disorders in treatment groups subjected to different schedules.[66] Similar to *Bilski*, whose legal obligations were not limited to any specific transactions, the claims in *Classen* are not tied to any particular vaccine or vaccine schedule or to the use of a computer. The mere correlation between a vaccine and its optimal immunization schedule is not a transformation because the claim is not tied to anything tangible. The patent does not claim any specific technique or technical process of testing vaccine safety and describes only a general inquiry into whether the proposed correlation even exists. As the Federal Circuit recently concluded, the machine-or-transformation test invalidates *Classen's* claims.[67]

Finally, the *Prometheus* claims would constitute patentable subject matter because the claims involve a transformation of the underlying subject matter. The *Prometheus* claims require both "administrating" the drug and "determining" the level of the drug metabolite in the patient.[68] The input is the thiopurine drug; however, what is being "determined" is not the level of thiopurine drug but the level of its metabolite in the body. The underlying physical activity is the injected drug's transformation into quantifiable drug metabolite. The determining step is then carried out by various unspecified assay techniques. The "observation" step required in the *Prometheus* claims, similar to the "correlate" step in *LabCorp*, is most likely not significant post solution activity because it does not alter the underlying substance in any way. Although the *Prometheus* claims technically pass the machine-or-transformation test, the district court found the claims unpatentable because the correlation between thiopurine drug metabolite levels and the therapeutic efficacy and toxicity is considered a natural phenomenon.[69]

However, even if the Federal Circuit were to deem the claims patentable under the machine-or-transformation test, the claims could still be invalidated for other reasons. The goal of the

66. *Classen Immunotherapies, Inc. v. Biogen IDEC*, 2006 U.S. Dist. LEXIS 98106 at *10 (D. Md. Aug. 16, 2006).

67. *Classen Immunotherapies, Inc. v. Biogen IDEC*, 2008 U.S. App. LEXIS 25661 (Fed. Cir. Dec. 19, 2008).

68. *Prometheus v. Mayo*, 2008 U.S. Dist. LEXIS 25062 at *17.

69. *Id.* at *23.

Prometheus claims is to determine the therapeutic dosage in order to avoid toxic side effects. Measuring the level of drug metabolite in the body, where the "determining" step is not limited to specific assay techniques, is obvious and fails for lack of enablement. Further, the district court found the *Prometheus* claims invalid solely on the basis that they claim a natural phenomenon.[70] The courts have yet to reconcile the machine-or-transformation test with the natural phenomenon doctrine. Thus, even though the claims recite patentable subject matter under the machine-or-transformation test, the claims could be invalidated for other reasons.

The impact of *Bilski* on the aforementioned biotechnology claims results in a policing of claim scope, a role more commonly associated with the enablement and written description requirements.

B. *Bilski*'s Impact on Personalized Medicine Claims

The machine-or-transformation test potentially impacts three classes of biotechnology method claims at the heart of personalized medicine: (1) the assay-correlate claim, (2) methods of molecular testing, and (3) methods of treating patients based on specific polymorphisms or haplotypes.

Personalized medicine and medical diagnostics rely on the correlation between the presence of biomarkers or level of specific biomarkers in an individual patient and the safety and efficacy of a certain therapeutic regime. A personalized medicine diagnostic employs at least one variable in an interpretive function to yield a single, patient-specific result (such as "classification," "score," and "index") for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease. These diagnostics can be used to score or classify patient samples based upon quantitative predictive modeling using expression values for single or multiple biomarkers, such as genes, proteins, or protein/protein interactions as inputs. At the heart of personalized medicine is the discovery of the correlation between biomarkers and the efficacy and safety of drugs in an individual.

In terms of biotech and personalized medicine claims, what constitutes significant extra-solution activity has yet to be addressed by the courts. For a process claim to be patentable it must be distinguishable from the underlying idea. It does appear that a claim tied to specific assay techniques and therapeutic results would impart physical steps that meaningfully limit the claim's scope.

70. *Id.*

Similar to the patentable claim in *Abele*, personalized medicine claims require significant quantitative inputs where the data represents tangible molecular objects, such as genes, expressed proteins, and physical factors of age, gender, and weight. This raw data, which is representative of physical matter, is then transformed into a quantitative score by an algorithm. These claims compile data points for specific biomarkers, which are transformed into a map representing the patient's unique phenotypic makeup. The quantitative score is then used to predict, or correlate, the patient's risk of disease or the efficacy of a specific therapy. In other words, personalized medicine assay-correlate claims are not merely the linear correlation between one biomarker and an *in vivo* deficiency.

In addition to assay-correlate claims, the personalized medicine field incorporates methods for molecular testing, such as screening for different polymorphisms or haplotypes in a target gene or protein. Polymorphisms are specific genetic allele variants that result in variations in the functional regions of genes, which include promoter, enhancer and silencer regions that cause differences in drug response through effects on the quality or quantity of the drug's target protein. Haplotypes are combinations of multiple genetically associated polymorphisms that are inherited as a physically linked block associated with a responsive or non-responsive phenotype.

Often, claims reciting methods of molecular testing for a specific polymorphism will also incorporate a method of treatment based on the responsive or non-responsive phenotype, another variation of the assay-correlate claim. These claims cover physical objects, not abstractions, of which representative data is transformed into information concerning the presence of a polymorphism or haplotype that incorporates the known functionality of the polymorphism. The transformation underlying the process is the conversion of intracellular structures and expressed genes/proteins into quantifiable, functional data that is specific to the patient creating a patient specific score. Only once this patient-specific information is known can a therapeutic treatment be recommended. Under the machine-or-transformation test, the method of assaying for genetic polymorphisms or haplotypes the results of which are then correlated with a specific therapeutic treatment is patentable subject matter.

Finally, the renewed emphasis on patentable subject matter raises the question—why? As the legislative history states, Section 101 covers "anything under the sun that is made by man," with a few

limitations.[71] The other sections of the patent statute act to limit and narrow Congress's broad definition of what is patentable subject matter. In an industry such as personalized medicine, which is comprised of correlations representative of the underlying body process, it is difficult to distinguish between claiming a natural body process that preempts all use of a fundamental principle and those inventions tailored to unique and novel inventions.

IV. Practical Implications – Claiming Within the New Rules

Personalized medicine diagnostics are being developed that provide invaluable predictive information for diagnosing or prognosing heart disease, immunological conditions, or for predicting whether a patient will respond to treatment using a particular drug. The information generated by these diagnostics has the potential to generate enormous savings to the cost of medical care by bringing to patients more effective, individualized therapies.

Many challenges lie ahead for companies in the biotechnology field, and the use of Section 101 to challenge a patent's validity is to be expected. It is therefore critical for personalized medicine companies to develop and execute patent strategies that anticipate the possibility of such challenges' eventual success. Should a broad claim be found invalid under Section 101, a comprehensive set of dependent claims reciting assay techniques and correlation methods can provide valuable backup protection. Claims covering theragnostic technologies (i.e., directed at obtaining a specific test result and choosing a specific treatment course according to that result) should be less vulnerable to Section 101 challenges given the inclusion of another step that necessarily limits such claims so that they can not fairly be said to preempt a law of nature. And, if possible, claims should be sought that cover technology used to obtain patient data, such as, claims direct to specific probes, assays, or kits.

V. Conclusion

In light of the recent court cases, it appears the courts are undertaking steps to further define patentable subject matter under Section 101. The tension inherent in balancing the broad language of Section 101 and the limitations on its scope will continue as new technologies push this boundary. What is certain is that the recent

[71] *See supra* note 5.

changes in patent law will affect the ability of personalized medicine companies to protect the technology behind the products they create. The advancement of biotechnology and personalized medicine will be better served by a patent law that identifies the unique specificities of its industry.

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