No. 08-964

In The
Supreme Court of the United States

BERNARD L. BILSKI and RAND A. WARSAW,

Petitioners,

v.

JOHN J. DOLL, ACTING UNDER SECRETARY OF COMMERCE FOR INTELLECTUAL PROPERTY AND ACTING DIRECTOR, PATENT AND TRADEMARK OFFICE,

Respondent.

On Writ Of Certiorari To The United States Court Of Appeals For The Federal Circuit

BRIEF OF MONOGRAM BIOSCIENCES, INC. AND GENOMIC HEALTH, INC. AS *AMICI CURIAE* IN SUPPORT OF NEITHER PARTY

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QUESTIONS PRESENTED

1. Whether the Federal Circuit erred by holding that a "process" must be tied to a particular machine or apparatus, or transform a particular article into a different state or thing ("machine-or-transformation" test), to be eligible for patenting under 35 U.S.C. § 101, despite this Court's precedent declining to limit the broad statutory grant of patent eligibility for "any" new and useful process beyond excluding patents for "laws of nature, physical phenomena, and abstract ideas."

2. Whether the Federal Circuit's "machine-or-transformation" test for patent eligibility, which effectively forecloses meaningful patent protection to many business methods, contradicts the clear Congressional intent that patents protect "method[s] of doing or conducting business." 35 U.S.C. § 273.

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INTEREST OF THE *AMICI CURIAE*[1]

Personalized medicine is universally acknowledged to hold enormous potential for treating diseases, improving the quality of patients' lives and streamlining the drug discovery and development process. Personalized medicine uses molecular diagnostic tests to correlate genetic and molecular biomarkers with clinically useful disease characteristics. The technology has already delivered tremendous results for individual patients, and current research efforts and clinical trials promise significant future improvements in health care.

Personalized medicine companies are typically small and rely on private investment capital to sustain them through the lengthy and expensive research, development and commercialization process. Developing the tests is time consuming and expensive. Personalized medicine companies literally flourish or fail based on their ability to build patent portfolios protecting diagnostic correlations.

The success of personalized medicine in the diagnosis and treatment of breast cancer has been unexpectedly spectacular. Modern sophisticated molecular diagnostic tests allow providers to identify the

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[1] In accordance with Sup. Ct. R. 37, the *Amici* state that this brief was not authored in whole or in part by counsel to a party, and that no monetary contribution to the preparation or submission of this brief was made by any person or entity other than these *Amici Curiae* or their counsel.

30% of patients who have breast cancer tumors that over-express human epidermal growth factor receptor 2 (HER2). These patients can be treated with trastuzumab, an antibody that is more effective and less toxic than traditional chemotherapy or radiation therapy.

Monogram Biosciences, Inc. and Genomic Health, Inc. are publically traded companies recognized as world leaders in the emerging field of personalized medicine. Monogram Biosciences currently offers the HERmark® breast cancer diagnostic assay that accurately quantifies HER2. HERmark® identifies patients likely to respond to trastuzumab with greater precision than currently available tests. In addition, Monogram offers five distinct HIV drug resistance assays used to individualize the selection of antivirals for HIV treatment. Monogram's HIV assays provide a direct measure of the patient's virus' ability to survive in the presence of specific antiviral drugs and are often the primary tests relied on by physicians to determine which HIV drugs will be effective in a specific patient.

Genomic Health currently offers the Onco*type* DX® assay that provides information on the likelihood that a breast cancer patient will experience (1) a recurrence of a tumor; and (2) a clinically beneficial response to chemotherapy. In addition, Genomic Health has completed validation of a colon cancer prognostic assay which it expects to offer commercially in 2010.

Essential to *Amici* is their ability to obtain meaningful proprietary protection for their key discoveries: diagnostic correlations. *Amici* expend tremendous resources in obtaining tumor samples, assaying the samples to discover correlations and searching through and analyzing the results for meaningful statistical significance that could identify those correlations. There are literally hundreds of unsuccessful attempts made for each identified correlation.

Amici have an interest in ensuring that patent claims to the discovered diagnostic correlations remain patentable. *Amici* would have difficulty in continuing with their mission of developing products for patients in the absence of meaningful patent protection. The application of the machine-or-transformation test as adopted by the Federal Circuit to the diagnostic correlations forecloses the ability of *Amici* to obtain commercially meaningful protection for its discovery and products, and threatens the future of the entire field of personalized medicine. Patients can only suffer.

Amici will focus on the first question presented as it relates to correlation claims often sought by personalized medicine companies.

SUMMARY OF ARGUMENT

The patent system creates incentives for research into discovering correlations between biomarkers and

diseases to improve diagnostic tests thereby creating a virtuous cycle progressing science to the benefit of patients and society. The Federal Circuit's requirement that all claims recite a "physical" step, such as a machine or physical transformation step, jeopardizes the future of research in personalized medicine by making many biologically-based inventions unpatentable under 35 U.S.C. § 101. In the end, fewer personalized medicine avenues will be explored and brought to market, and patients will suffer.

The Federal Circuit erred in holding that a process must be tied to a particular machine or apparatus or transform a particular article into a different state or thing to be eligible for patent protection under 35 U.S.C. § 101. The machine-or-transformation test may work in a few cases for determining whether a particular claim is patent-eligible, but it results in "false negatives" for the majority of cases. Specifically, it has been applied to find some claims, such as those on the actual diagnostic correlations, to be patent-ineligible. *Amici* urge the Court to adopt a framework for patent-eligible subject matter that accords with the existing law, a framework that determines that non-physical processes are patent-eligible, a framework that will foster development of personalized medicine technologies.

Consistent with this Court's precedent, *Amici* propose that the Court articulate a framework that considers as a threshold step whether a fundamental principle (i.e., a law of nature, a phenomenon of

nature or an abstract idea) is claimed. For application of the framework, the terms *law of nature*, *natural phenomenon* and *abstract idea* should be construed in the ordinary English sense each as a universal principle having a central role in scientific practice and each as being fundamental. If a law of nature, natural phenomenon or abstract idea is not claimed, the claimed subject matter describes a patent-eligible process. If one of these is claimed, the Court should turn its attention to secondary considerations such as whether the patent claim entirely preempts the law of nature, natural phenomenon or abstract idea. Such a determination can take into account whether the claimed method involves a machine-or-transformation step, but not as the sole determinative test for patentability. *Amici* believe that once the Court sets forth a definitive test, the Court will determine that claim 1 in Bilski's application is patent-eligible because it does not claim a law of nature, natural phenomenon or abstract idea. Similarly, the claims important to personalized medicine companies, claims to the discovered correlations, will be patent-eligible since they also do not involve laws of nature, natural phenomena or abstract ideas.

ARGUMENT

I. PATENTABLE PROCESSES CAN BE EITHER PHYSICAL OR NON-PHYSICAL

35 U.S.C. § 101 provides the basis for patent-eligibility:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

The statute states that there are four separate and distinct categories of patentable subject matter, namely: 1) processes, 2) machines, 3) manufactures or 4) compositions of matter. In addition, 35 U.S.C. § 100(b) provides a broad statutory definition for a process to be used in 35 U.S.C. § 101:

> The term "process" means process, art, or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material.[2]

According to the Oxford English Dictionary, a "process" can be defined as:

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[2] The statutory provision on what constitutes patentable subject matter has essentially been the same since 1793. Until the Patent Act of 1952, the patent statutes used the word "art." The 1952 Act substituted the word "process." To emphasize that no change of meaning was intended, a process was defined as " . . . any process, art or method . . . " 35 U.S.C. § 100(b).

> A continuous and regular action or succession of actions, taking place or carried on in a definite manner, and leading to the accomplishment of some result; a continuous operation or series of operations (The Oxford English Dictionary 6 (2d ed. 1989)).

The term "process" thus does not have a special meaning that would exclude non-physical processes from patent eligibility under 35 U.S.C. § 101.

Nor is there any basis for concluding that the Constitution imposes a requirement that non-physical processes be excluded. According to this Court, Congress has the authority to include non-physical subject matter within the scope of patent-eligible subject matter.[3] In the encompassing language as it used in § 101, Congress chose not to limit patentable subject matter to only physical subject matter; the only limitations are that the subject matter be "new and useful."[4]

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[3] *See e.g.*, *Gottschalk v. Benson,* 409 U.S. 63, 72 (1972), where the Court stated, "It may be that the patent laws should be extended to cover these programs, a policy matter to which we are not competent to speak." *See* also, 35 U.S.C. § 273 and 145 Cong. Rec. H11769, at 11801 (daily ed. Nov. 9, 1999) ("Jt. Conf. Report"), where, in discussing Title 35, Congress expressed the intent that the patent laws may be drawn to physical as well as non-physical limitations.

[4] Other *Amici* extensively treat what it means for a process to be "useful." Accordingly, this brief will not repeat such detailed analysis.

> This Court has consistently and explicitly refused to limit a process to the purely physical. In *Gottschalk v. Benson,* 409 U.S. 63, 71 (1972), even as the Court was denying the patentability of a method of converting binary signals from one form to another, citing *Waxham v. Smith et al.,* 294 U.S. 20 (1935), the Court could not have more clearly stated that a process need not have a machine-or-transformation, a physical step, to be patentable: It is argued that a process patent must either be tied to a particular machine or apparatus or must operate to change articles or materials to a different state or thing. We do not hold that no process patent could ever qualify if it did not meet the requirements of our prior precedents.

Gottschalk, 409 U.S. at 71. In *Parker v. Flook,* 437 U.S. 548, 589 n.9 (1978), the Court repeated and strengthened this rationale:

> 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." *See Cochrane v. Deener*, 94 U.S. 780, 787-788 (1876). 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)

Accordingly, the Court has consistently made it clear that the process category of 35 U.S.C. § 101 should be interpreted broadly to include all subject matter, physical and non-physical.[5] Other than the proscribed categories of laws of nature, phenomena of nature and abstract ideas (*see, e.g., Gottschalk v. Benson,* 409 U.S. 63 (1972); *Parker v. Flook*, 437 U.S. 584 (1978) and *Diamond v. Diehr*, 450 U.S. 175 (1981)) all processes, both physical and non-physical, are patent-eligible.

Amici would urge this Court to hold that processes include all subject matter, physical and non-physical.

[5] Congress has also expressed its intent that a process should include the physical as well as the non-physical. *See, e.g.,* Jt. Conf. Report at 11801, where they indicate that they believe that a process is not limited to the physical but should also include the non-physical.

II. THE FEDERAL CIRCUIT ERRED IN HOLDING THAT A PROCESS MUST BE TIED TO A PARTICULAR MACHINE OR TRANSFORM A PARTICULAR ARTICLE INTO A DIFFERENT STATE OR THING

A. The Federal Circuit Erred In Holding That A "Process" Must Be Tied To A Particular Machine Or Apparatus, Or Transform A Particular Article Into A Different State Or Thing ("Machine-Or-Transformation" Test), To Be Eligible For Patenting Under 35 U.S.C. § 101

Despite admonitions from the Supreme Court, in *Bilski,* the Federal Circuit adopted the physical limitation requirement of the machine-or-transformation test as the *sole test*, effectively denying patentability to much patent-eligible subject matter. Though the Federal Circuit adamantly denied that the machine-or-transformation step required a physical step,[6] the test it ultimately adopted clearly does require a physical step. In articulating the 'transformation' prong of the machine-or-transformation test, the Federal Circuit stated:

> Purported transformations or manipulations simply of public or private legal obligations or relationships, business risks, or other such abstractions cannot meet the test

[6] *In re Bilski,* 545 F.3d 945, 963 (2008), *see id.,* at 964, where the Federal Circuit explicitly stated that it was rejecting any notion of a physical steps test.

> because they are not *physical objects* or substances, and they are not representative of *physical objects* or substances.[7] (emphasis added)

Thus, the Federal Circuit adopts a physical test at the same time that it asserts that it is not adopting a physical test.

Patent-eligible subject matter has been traditionally limited only by whether the subject matter is directed to a law of nature, a phenomenon of nature or an abstract idea. Other than these traditional categories of patent-ineligible subject matter, the courts have been consistent in holding that process steps are patentable despite the fact that they lack a physical limitation, such as a machine-or-transformation step.[8] Indeed, attempting to distinguish between physical and non-physical steps will lead to a futile effort in metaphysics and invite practitioners to 'game' the system.[9] Thus, the Federal

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[7] *In re Bilski,* 545 F.3d at 963.

[8] *See, e.g., Gottschalk v. Benson,* 409 U.S. 63 (1972); *Parker v. Flook*, 437 U.S. 584 (1978) and *Diamond v. Diehr*, 450 U.S. 175 (1981).

[9] *See, e.g.*, *Arrhythmia Research Technology, Inc. v. Corazonix Corp.,* 958 F.2d 1053 (Fed. Cir. 1992), where the Federal Circuit found that the terms "determining" and "comparing" were physical process steps and that electrical signals were inherently physical and *In re Nuijten,* 500 F.3d 1346 (Fed. Cir. 2007), where the Federal Circuit determined that electrical signals, while physical, were too transitory to fall within one of the statutory categories for patentable subject matter. It is unclear why the "transitory" nature of a signal is problematic,

(Continued on following page)

Circuit erred in holding that a process must be tied to a particular machine or apparatus, or transform a particular article into a different state or thing.

B. The Machine-Or-Transformation Test Does Not Properly Distinguish Between Patent-Eligible And Patent-Ineligible Subject Matter

There is quite a bit of patentable ground between a process that is not limited by a physical step, such as a machine-or-transformation step, and a process that is. The machine-or-transformation test, by requiring a physical limitation in the claims, classifies all physical processes as patent-eligible subject matter but misses much non-physical patent-eligible subject matter that is acceptable under this Court's precedent. Namely, the test fails to identify non-physical subject matter which is not a law of nature, natural phenomenon or an abstract idea. As an example, as *Amici* will discuss in section III(B) below, claim 13 of U.S. Patent No. 4,940,658 ("'658")

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since many physical phenomena, such as chemical processes, are equally transitory, but unquestionably patentable. *See also State Street Bank & Trust Co. v. Signature Financial Group, Inc.*, 149 F.3d 1368 (Fed. Cir. 1998), where the transitory nature of the calculated net asset value was not a bar to patent eligibility. As far as "gaming" the system, a clever patent practitioner will be able to say the so-called "magic words" so that a claimed invention is drawn to some sort of a machine or has a physical transformation step. *See* Julie E. Cohen and Mark A. Lemley, *Patent Scope and Innovation in the Software Industry*, 89 Cal. L. Rev. 1 (2001).

patent claims non-physical subject matter which is not a law of nature, natural phenomenon or an abstract idea.

Thus, the machine-or-transformation test does not adequately distinguish between patent-eligible and patent-ineligible subject matter.

C. The Machine-Or-Transformation Test Is Inconsistent With 35 U.S.C. § 101 And This Court's Long-Standing Precedent

The Federal Circuit erred in *In re Bilski* by creating a new and amorphous "machine-or-transformation" test that is inconsistent with 35 U.S.C. § 101 and long-standing Supreme Court precedent. As noted in the dissenting opinions in *Bilski*, the majority's novel test raises more questions than it answers, and indeed creates significant confusion. The Federal Circuit's interpretation of 35 U.S.C. § 101 uprooted years of case law, which should only be done for the most compelling reasons. "Considerations of *stare decisis* have special force in the area of statutory interpretation, for here, unlike in the context of constitutional interpretation, the legislative power is implicated, and Congress remains free to alter what [the courts] have done." *Shepard v. United States*, 544 U.S. 13, 23 (2005). "Where, as here, Congress has not acted to modify the statute in the many years since *Diehr* and the decisions of [the Federal Circuit], the force of *stare decisis* is even stronger." *In re Bilski*, 545 F.3d at 993 (Newman, J., dissenting) (*citing Shepard,* 544 U.S. at 23). The Federal Circuit's

majority decision in *Bilski* is based on a misguided and novel reading of selected Supreme Court quotations; it disrupts both settled precedent and long-standing expectations concerning intellectual property rights, and is bad public policy.

Recent Supreme Court precedent calls for judicial flexibility in carrying out the Constitutional and statutory mandates of the patent system. Indeed, the Supreme Court recently rejected rigid Federal Circuit precedent in *KSR Int'l Co. v. Teleflex, Inc.,* 550 U.S. 398 (2007), when it overruled the "teaching, suggestion, or motivation," or TSM, test for analyzing obviousness under 35 U.S.C. § 103. While recognizing that the TSM test was developed to "resolve the question of obviousness with more uniformity and consistency," the Supreme Court summarily rejected the overly-rigid rule as "contrary to §103 and [its] precedents." *Id.* at 407. Unfortunately, the machine-or-transformation test similarly seeks to achieve consistency and predictability by supplanting the broad and flexible Supreme Court precedent governing patentability under § 101 (*see Diehr*, 450 U.S. at 185; *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980); and *Benson*, 409 U.S. at 93), with a narrow and rigid test. As *KSR* demonstrates, such an effort to achieve predictability, even if well-intended, is not reason enough to disregard controlling precedent.

III. A PROPOSED FRAMEWORK FOR IDENTIFYING PATENT-ELIGIBLE SUBJECT MATTER

A. This Court Should Determine Whether A Law Of Nature, Natural Phenomenon Or Abstract Idea Is Claimed And Construe Those Terms In The Ordinary English Sense

Amici propose a framework that considers as a threshold step whether a fundamental principle (i.e., a law of nature, a phenomenon of nature or an abstract idea) is claimed. If not, the claimed subject matter describes a patent-eligible process. If a fundamental principle is claimed, the patent claim should be analyzed to determine if it entirely preempts the fundamental principle. Such a determination can take into account whether the claimed method involves a machine-or-transformation step, but not as the sole determinative test for patentability. For application of the test, the terms *law of nature*, *natural phenomenon* and *abstract idea* should be construed in the ordinary English sense as universal having a central role in scientific practice and as being fundamental.

As a threshold for the determination of whether patent-eligible subject matter is present, *Amici* propose an investigation of the ordinary English meaning of the words law of nature, natural

phenomenon and abstract idea.[10] *Amici* would propose that the Court adopt a workable definition for each of those terms which could be rationally applied by practitioners.[11] Consistent with the Court's trend towards reading words in an ordinary English way,[12]

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[10] Courts have never determined what exactly is included within the terms "law of nature, natural phenomenon and abstract idea" by construing the boundaries of those terms to determine whether they do, in fact, have one of these fundamental principles before them (*see, e.g.*, *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948) (determining that bacterial qualities of non-inhibition were phenomena of nature); *Flook*, 437 U.S. at 595 (determining that a method of calculating is drawn to non-statutory subject matter); *Gottschalk*, 409 U.S. at 68 (holding that a method of binary conversion was so abstract as to not be patentable); *Diehr*, 450 U.S. at 191 (holding that a claim to a process for curing rubber which employed a mathematical equation did not only entail an abstract mathematical formula and thus was drawn to patentable subject matter). *Amici* believe that such an approach, a sort of " . . . know it when I see it . . . " approach (*see* Justice Potter Stewart's statement in his concurrence in *Jacobellis v. Ohio*, 378 U.S. 184 (1964) for example) has led to much confusion. *Amici* do note that some justices of the Supreme Court have cautioned against trying to define such concepts as a law of nature, natural phenomenon or abstract idea (*see, e.g.*, *Funk Brothers Seed Co.*, 333 U.S. at 133 (Frankfurter, J., concurring). But, we believe that a rational, perhaps flexible, definition would be the best way to make the process and analysis more meaningful.

[11] *Amici* realize that the Courts have also been disposed to consider thinking as patent ineligible. *Amici* believe the Court should also adopt a position that claim language should be construed, when possible, to avoid implicating the process of thinking. The proposal is set forth below.

[12] *See, e.g.*, *Perrin v. United States*, 444 U.S. 37, 42 (1979).

Amici propose that each of the terms "law of nature, natural phenomenon and abstract idea" should incorporate the following elements:

1. That they are universal as defined in terms of ordinary English and thus have a central role in scientific practice; and

2. That they are fundamental, as defined in terms of ordinary English.

For the terms "universal" and "fundamental," *Amici* would propose that the Court adopt the following definitions:

A. Universal:

Something which is an absolute or general concept regarded either as forming or having an absolute, mental or nominal existence; a universal proposition; a general term, notion or idea. (The Oxford English Dictionary (2d ed. 1989))

B. Fundamental:

Something which is a leading or primary principle, rule, law, or article which serves as the groundwork of a system; an essential part. (The Oxford English Dictionary (2d ed. 1989))

For the terms "law of nature", "phenomenon", and "abstract", we would propose the following definitions:

C. Law of Nature:

> In the sciences of observation, a theoretical principle deduced from particular facts, applicable to a defined group or class of phenomena, and expressible by the statement that a particular phenomenon always occurs if certain conditions are present. (The Oxford English Dictionary (2d ed. 1989))

D. Phenomenon:

> In scientific and general use, a thing that appears, or is perceived or observed; an individual fact, occurrence, or change as perceived by any of the senses, or by the mind; applied chiefly to fact or occurrence, the cause or explanation of which is in question. (The Oxford English Dictionary (2d ed. 1989))

E. Abstract:

> Refers to something that is withdrawn or separated from material embodiment, from practice, or from particular examples. Thus, an abstract idea is an idea that is withdrawn or separated from material embodiment, from practice, or from particular examples. (The Oxford English Dictionary (2d ed. 1989))

Accordingly, consistent with this Court's precedent,[13] *Amici* would propose that the terms "law of nature," "natural phenomenon" and "abstract idea" should be defined as follows:

A. Law of Nature

> A law of nature is, in the sciences of observation, a theoretical principle deduced from particular facts, applicable to a defined group or class of phenomena, and expressible by the statement that a particular phenomena always occurs if certain conditions are present. A law of nature has an absolute or general concept regarded either as forming or having an absolute, mental or nominal existence; a universal proposition; a general term, notion or idea. A law of nature is also a leading or primary principle, rule, law or article which serves as the groundwork of a system, an essential part.

B. Phenomenon of Nature

> A phenomenon of nature appears, or is perceived or observed; an individual fact,

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[13] *See, e.g.*, *Gottschalk v. Benson,* 409 U.S. 63 (1972); *Parker v. Flook*, 437 U.S. 584 (1978); and *Diamond v. Diehr*, 450 U.S. 175 (1981), where this Court has consistently justified the exclusion of patent-ineligible categories on the supposition that they were fundamental principles, those containing a fundamental truth, an original cause, a motive, the basic tools of scientific research, part of the storehouse of knowledge available to all. Thus any set of working definitions should include these ideas.

> occurrence, or change as perceived by any of the senses, or by the mind; applied chiefly to fact or occurrence. A phenomenon of nature has an absolute or general concept regarded either as forming or having an absolute or nominal existence; a universal proposition. A phenomenon of nature is also a leading or primary principle which serves as the groundwork of a system, an essential part.
>
> C. Abstract Idea
>
> An abstract idea is an idea that is withdrawn or separated from material embodiment, from practice, or from particular examples. An abstract idea has an absolute or general concept regarded either as forming or having an absolute, mental or nominal existence; a universal proposition; a general term, notion or idea. An abstract idea is also a leading or primary principle which serves as the groundwork of a system, an essential part.

To determine whether claimed subject matter is patent eligible, *Amici* propose this test with definitions in mind:

1. As a threshold step, determine whether a fundamental principle (i.e., a law of nature, a phenomenon of nature or an abstract idea) is claimed. If not, the claimed subject matter describes a patent-eligible process.
2. If a fundamental principle is claimed, determine whether the patent claim

> entirely preempts the fundamental principle. The determination may take into account whether the claimed method involves a machine-or-transformation step. If the claim does not entirely preempt the fundamental principle, then it claims patent-eligible subject matter; if the claim does entirely preempt the fundamental principle, then it does not claim patent-eligible subject matter.

With this test and these definitions in mind, *Amici* now turn to a representative diagnostic claim, claim 13 of U.S. Patent No. 4,940,658.

B. Diagnostic Claims Drawn To Methods Of Predicting Response In A Patient Are Patent-Eligible Because They Do Not Describe A Fundamental Principle

Amici will focus on how the machine-or-transformation test could affect personalized medicine companies, and claim 13 of U.S. Patent No. 4,940,658, the claim that was the subject matter of *Laboratory Corp. of Am. Holdings v. Metabolite Labs. Inc.*, 548 U.S. 124 (2006), provides an excellent vehicle to exemplify application of the proposed framework.[14] The claim is directed to a non-physical

[14] Claim 13 recites: "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

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process, but non-physical processes are patentable, as well.[15]

So, as a first step, the Court should consider whether the process of correlating is drawn to a law of nature, a natural phenomenon or abstract idea, as *Amici* have defined these terms. Under the proposed test, the ordinary English meaning of the words "natural phenomenon" requires that the claimed assay be universal and have a central role in scientific practice. The scientific correlation of homocysteine levels with a deficiency of cobalamin describes a very narrow biological correlation, certainly not something universal and central to scientific practice.[16] In the human body, many biological components, genes, proteins, tissues and even entire organs, work together through very complicated processes. Although the processes are connected, they are very different, and, indeed, a

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homocysteine; and correlating an elevated level of total homocysteine in said body fluid with a deficiency of cobalimin or folate."

[15] One could argue that the "assaying" step, among others, does indeed require some sort of a physical step and requires a machine, as a result. *Amicus* have chosen to focus on the issue at hand, namely the "correlating" aspect of claim 13, and assume that the step does not require an assay step.

[16] Were one to analogize claim 13 to the *Benson* and *Flook* claims, the difference would be that the claims in *Benson* and *Flook* were, according to the Court, to the algorithm, *per se*. Claim 13, on the other hand, is drawn to a very narrow biological correlation. In any case, *Amici* would urge the Court to use extreme caution in completely analogizing biological claims to algorithm claims.

single disease or disorder can often be associated with many different biomarkers in many different biological pathways. With so many different possible markers, even for the same disease, a patent monopoly on any one marker would not preclude scientists from discovering other pathways.

Indeed, the patent monopoly provided by claim 13 (or any claimed biological correlation) would not stifle innovation but would rather motivate others to seek out similar correlations, perhaps even in related biological pathways. Thus, claim 13 would not block the basic tools of research but would foster research. Similarly, in the specification of the '658 patent, the diagnostic process is explained in great detail, including how the claimed correlation would be applied to specific testing subjects, each of these details show that the correlation is not universal and central to the scientific process.

Under the proposed test, the ordinary English meaning of the words "natural phenomenon" require that the claimed assay additionally be fundamental, thus a leading or primary principle, rule, law or article which serves as the groundwork of a system, i.e. an essential part. The correlation exists in some human beings, perhaps as a product of evolution, and as such, it could have been different. And, if it could have been different, as evolution could have taken a different path, it does not describe a leading or primary principle, just an artifact of evolution. This is key: the fact that it could have been different demonstrates that it is not the groundwork for a

system or an essential part. As a result, claim 13, as a correlation is not a fundamental principle and thus does describe patent-eligible subject matter.[17]

In contrast, examples such as $E=mc^2$, Newton's law of gravity, and phenomena of nature such as water freezing or the aurora borealis would certainly constitute laws of nature and natural phenomena in the ordinary English meaning of the word. They each describe an absolute or general concept regarded as forming or having an absolute existence, and they are each universal and central to scientific practice. Each of these phenomena, and the principles behind them, could also be considered as the groundwork of a system, essential and fundamental, in other words. Each of these principles, unlike claim 13 in *Lab. Corp. of Am. Holdings*, very clearly fall into the category of a fundamental principle and would be the sort of patent-ineligible subject matter that would constitute the basic tools of research, the common knowledge of all.

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[17] *Amici* believe this argument can be extended to the subject matter of all diagnostic claims. As examples, please see the claims in U.S. Patent No. 6,680,302 drawn to methods of optimizing therapeutic efficiency, the subject of *Prometheus Labs. v. Mayo Collaborative Servs.*, 2008 U.S. Dist. LEXIS 25062 (S.D. Cal. Mar. 28, 2008), as well as the claims in U.S. Patent No. 5,723,283, claims drawn to a method of determining whether an immunization schedule affects the incidence or severity of a chronic immune-mediated disorder, the subject matter of *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).

As an interesting point of contrast, since almost anything and everything that is a result of nature could be viewed as a natural phenomenon, this would mean that the statutory proscriptions related to patentability would apply to everything. Although Justice Frankfurter was noting that an attempt to define a law of nature would be futile, in *Funk Brothers Seed Co.*, 333 U.S. at 135, his concurring opinion stated:

> Everything that happens may be deemed "the work of nature," and any patentable composite mixture exemplifies in its properties the "laws of nature."

While *Amici* would agree with this statement on its face, *Amici* would note that, since almost every process is impacted by or based upon a law of nature, arguments can be drawn for challenging any patent based upon those grounds. The end result of this reasoning is that nothing, or everything, is patentable, and both results defy logic.

Amici urge the Court to adopt the two part test setting forth the ordinary English definitions set forth above. As applied according to that test and those definitions, claim 13 of the '658 patent are not drawn to fundamental principles and describe patent-eligible subject matter.

IV. THE MACHINE-OR-TRANSFORMATION TEST THREATENS TO STIFLE INNOVATION IN PERSONALIZED MEDICINE

A. Personalized Medicine Is A Growing Field With A Tremendous Potential To Help Patients

Personalized medicine refers to the tailoring of medical treatment to the individualized characteristics of each patient. The technology allows physicians to make treatment decisions based on molecular markers that signal the presence or risk of developing a disease, potential outcome and likelihood that the patient will respond to particular therapies. Diagnostic correlations used to identify the most effective treatment options for an individual patient are critical to personalized medicine.

The use of diagnostic correlations to select the optimal therapy for an individual patient translates to improved and more cost-efficient health care for all. There are two important issues in selecting a treatment: efficacy and risk of side effects. On average, a commercial drug works for only 50% of the target population.[18] Further, every drug and biological therapeutic has undesirable side effects, some of which can be predicted based on a patient's drug metabolism signature. Published estimates show that approximately 5.3% of hospital admissions are

[18] B. Spear, et al., Clinical application of pharmacogenomics, Trends Mol. Med. 7(5):201-204 (2001).

associated with adverse drug reactions (ADRs).[19] Products marketed by personalized medicine companies empower physicians with the ability to treat patients with drugs that target the disease while minimizing undesirable side effects. Personalized medicine products thus spare the patients from suffering through ineffective treatment regimes, increase the probability of positive outcome and decrease the health care costs.

The Oncotype DX® breast cancer assay, product of research conducted by Genomic Health, can predict the *likelihood* that a patient with early-stage, ER+ breast cancer will experience a recurrence of breast cancer within 10 years and whether that patient will benefit from adding chemotherapy to his/her hormonal therapy. The test is based on mRNA levels of 21 genes, and provides a continuous Recurrence Score® (RS) result for each patient that places them in a low, intermediate or high risk category. A patient with a low RS will not significantly benefit from adding chemotherapy, and may be treated with hormonal therapy alone. Considering that about 20% of patients are in this category, this represents a substantial savings (approximately $1930.00 per patient) to the health care system and benefit to those patients who are spared the unnecessary disruption and toxic effects of chemotherapy. On the

[19] C. Kongkaew, et al., Hospital admissions associated with adverse drug reactions, Ann Pharmacother 42(7):1017-1025 (2008).

other hand, a high RS signals that chemotherapy should be added to the patient's regimen. Used in concert with other clinical factors, the Oncotype DX® assay can aid physicians and patients in making personalized and cost-efficient treatment decisions.

The selection and validation of the 21 genes, from potentially thousands of genes, to use in this test and development of RS from the expression levels was the culmination of thousands of hours of research by highly trained scientists at Genomic Health. The selection of 21 genes whose mRNA should be monitored was not the discovery of some mere principle of nature, rather it was the identification that certain arbitrary genes happen to be associated with the risk of cancer. HERmark® is a proprietary diagnostic of Monogram Biosciences that accurately quantifies HER2 total protein expression in patients with breast cancer. Preliminary data from three cohorts of Herceptin-treated patients with metastatic breast cancer who were identified as "HER2 positive" by conventional assays suggesting that HERmark® can identify patients who are likely to respond to trastuzumab with greater precision than currently available tests. To date, thousands of hours of research have been involved in developing HERmark®.

The success of genomics in breast cancer is being repeated in other cancers, as well as in other fields. For example, about 40% of patients with metastatic colon cancer are unlikely to respond to two key therapies: cetuximab and panitumumab, because these patients have certain KRAS gene mutations.

Current practice guidelines recommend that only patients with the normal KRAS gene sequence be treated with chemotherapy, resulting in potential savings of approximately $604 million annually if all patients are first stratified using the KRAS molecular diagnostic.[20]

A patient's genetic profile now allows physicians to determine whether a patient will respond to a particular therapy, and whether the risk of disease for that patient justifies the expense and burden of particular therapy. This information has the potential to increase patient adherence to treatment regimens, decrease costs and failure rates of drug clinical trials by focusing on appropriate sub-classifications of patients. It is no wonder, then, that the FDA has recognized and encouraged the development of personalized medicine pharmacogenic information, and nearly every major pharmaceutical project is incorporating information on genetic variation and effects on the safety and effectiveness of the candidate drug.[21] The importance of supporting further development of this technology has also been recognized by the President's Council on Science and Technology (*2008 Report on Priorities for Personalized*

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[20] National Comprehensive Cancer Network Guidelines in Oncology, Colon Cancer, v.2.2009 (available online at http://www.nccn.org/professionals/physician_gls/PDF/colon.pdf).

[21] *See, e.g.*, Guidance for Industry on Pharmacogenomic Data Submissions (2005); Drug-Diagnostic Co-Development Concept Paper (2005); 21 § C.F.R. 201.57.

Medicine), HHS (*Personalized Health Care Initiative*,), the Legislature (*Genomics and Personalized Medicine Act of 2006* (Obama, S. 3822)) and rules and comments put forth by many other professional, state and federal health care organizations. In her written testimony during Senate confirmation hearings, HHS Secretary Kathleen Sebelius made the following statement:

> As a result of these contributions to improvement in the quality of care, personalized medicine represents a key strategy on healthcare reform. The potential application of this new knowledge, especially when supported through the use of health information technology in the patient care setting, presents the opportunity for transformational change.[22]

In sum, personalized medicine offers a model for efficient and high quality health care.

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[22] Katheen Sebelius, written testimony given during Senate confirmation hearings, April 2, 2009.

B. Because The Machine-Or-Transformation Test Endangers Funding For Personalized Medicine Companies, It Will Undermine Personalized Medicine Companies, Stifle Development And Ultimately Harm Patients

In his dissent in *Lab. Corp. of Am. Holdings*, Judge Rader warns us of the consequences of endangering funding for personalized medicine. He characterized claim 13 of the '658 patent as patent-eligible and lamented that denying patent protection for such a claim will undermine and discourage future research for personalized medicine companies. According to Judge Rader:

> . . . this Court inadvertently advises investors that they should divert their unprotectable investments away from discovery of "scientific relationships" within the body that diagnose breast cancer or Lou Gehrig's disease . . .

Given the long and expensive research, development and commercialization cycles and relatively limited resources of most personalized medicine companies, the patent system is essential to protect and foster innovation that, in turn, attracts financial investors. Denying valuable patent protection for personalized medicine companies will surely advise investors that they should divert their unprotectable investments away from personalized medicine and, as a result, slow the progress of science and harm the interests of human patients.

A strict requirement that a process be tied to a particular machine or transform an article could exclude much of the technology that drives today's information and knowledge-based economy from patent protection, and prospectively hinder innovation in fields of biotechnology, health sciences and personalized medicine. The biotechnology industry touches upon many essential aspects of the U.S. economy, including pharmaceutical therapies, medical diagnostics, agricultures and industrial processes. The biotechnology industry has registered a fast growth since the early 1990s. For instance, their revenues increased from $8 billion in 1992 to $39.2 billion in 2003. The job market forecast of biological technicians is expected to grow by 28.2 percent between 2004 and 2014, and that of biological scientists is projected to grow by 17.0 percent. In the health care sector, the biotechnology industry has more than 370 therapeutic products currently in clinical trials being studied to treat more than 200 diseases. Because diagnostic correlating claims would not be patentable with a strictly machine-or-transformation step, the application of *Bilski's* test threatens to undermine the development of personalized medicine, stem the progress of science and adversely affect the health and quality of life of patients.

Personalized medicine helps patients, and holds tremendous potential for improving their lives by its ability to more precisely identify potential diseases before they arise and select treatment options that are specific to the individual. The key to this

capability is the discovery not of some "scientific truth" or "law of nature" or even "natural phenomena." Rather, it is the discovery, like many medical discoveries before now, of certain relationships – "correlations." The discovery of the correlations should be patentable subject matter in order to encourage and justify investments in the fledgling industry.

Patents are essential to ensure further research and development in personalized medicine and to encourage and protect investment. Patent claims directed to diagnostic correlations are the key to progressing these goals. Patents and the protection provided by them foster innovation as way leads on to way, one discovery leading on to another, and as other personalized medicine companies find other ways to help other patients. Perhaps we will be telling this story ages and ages hence: that we helped small personalized medicine companies improve ourselves. And that has made all the difference.

CONCLUSION

Requiring, as does the Federal Circuit in *Bilski*, that all claims recite a "physical" step, such as a machine or physical transformation step, jeopardizes the future of research in personalized medicine by making many biologically-based inventions unpatentable under § 101. There is no support for the machine-or-transformation test or the idea that only physical processes should be patentable, and *Amici*

urge the Court to hold that all processes are patent-eligible. *Amici* urge the Court to adopt a rational framework for determining patent-eligible subject matter that accords with the existing law, one that involves determining, as a threshold step, whether a fundamental principle (i.e., a law of nature, a phenomenon of nature, or an abstract idea) is claimed. The test should be simple and elegant and the terms *law of nature*, *natural phenomena* and *abstract idea* should be construed in an ordinary English sense as universal and having a central role in scientific practice and also as being fundamental. Once the Court sets forth the test, *Amici* believe the Court will determine that claims to the discovered diagnostic corrections are patent-eligible, such as claim 13 from the '658 patent.

Patents to diagnostic correlations are essential to personalized medicine companies to attract the funding necessary to bring new diagnostics to market. Without adequate patent protection, personalized medicine companies will suffer, new research will dry up and new treatments will not become available to patients.

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