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 OF THE UNITED STATES PATENT AND TRADEMARK OFFICE,

Respondent.

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

BRIEF OF *AMICUS CURIAE* CARIS DIAGNOSTICS, INC. IN SUPPORT OF PETITIONERS

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INTEREST OF *AMICUS CURIAE*[1]

Amicus curiae Caris Diagnostics, Inc. ("Caris") is a leader in personalized medicine, which is the relatively new science of tailoring therapeutics for individual patients through diagnostic tests for genetic mutations known as biomarkers. By using such molecular profiling techniques, Caris enables patients to receive safe and effective drug therapies for cancer and other serious illnesses.

For example, Caris's laboratories examine tumors to discover biomarkers that are associated with drug resistance or toxicity. A recent study showed that cetuximab (or Erbitux®), a standard treatment for colorectal cancer, shrinks tumors in 40% of patients lacking a particular genetic mutation

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[1] Counsel for *amicus* appear in this matter in their individual capacities and not on behalf of the law firm with which they are affiliated. Counsels' law firm represents many technology companies operating in diverse business sectors, including biotechnology, electronics, software, and internet companies, and such companies may have different opinions on the issues presented by the Federal Circuit's decision below. Nothing in this brief should be attributed or imputed to counsels' law firm or its clients, other than those specific ones on whose behalf this brief is filed.

Counsel for all parties have consented to the filing of this brief, and their consents have been lodged with the Clerk of this Court. No counsel for any party had any role in authoring this brief, and no person other than the named *amicus* and its counsel has made any monetary contribution to the preparation and submission of this brief. *See* Rule 37.

but is *ineffective* in patients possessing the mutation.[2] Before the sequencing of the human genome and the possibility of fast, affordable, and accurate tests for individualized genetic profiles, the treatment would be prescribed generally to colorectal cancer patients, and only time would tell which subpopulation of patients would have treatment-resistant tumors.

Now that biomarkers for resistance to the drug have been discovered, and Caris has developed tests for those biomarkers, an oncologist need not waste valuable time with hit-and-miss treatment. Instead, to obtain early validation of drug choices, the oncologist sends a biopsy to Caris – one of thousands of biopsies that Caris examines daily – which then determines whether the particular patient's tumor has the biomarker associated with drug resistance. Caris's development and provision of such biomarker tests[3] thus enable doctors to devote critical months to effective treatments. Caris's work thereby saves lives

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[2] *See* Astrid Lievre *et al., KRAS Mutations As an Independent Prognostic Factor in Patients With Advanced Colorectal Cancer Treated With Cetuximab*, 26 J. Clinical Oncology 374, 375 (Jan. 20, 2008), *available at* http://jco.ascopubs.org/cgi/content/full/26/3/374; *see also* Christos S. Karapetis, M.D., *et al.*, *K-ras Mutations and Benefit from Cetuximab in Advanced Colorectal Cancer*, 359 New Eng. J. Med. 1757, 1757-65 (Oct. 23, 2008), *available at* http://content.nejm.org/cgi/reprint/359/17/1757.pdf.

[3] Such biomarker tests when used to diagnose a patient's illness or medical condition are known as diagnostics, and when used to diagnose a patient's resistance to a particular drug are known as theragnostics. For simplicity, the term "diagnostics" as used herein refers to both diagnostics and theragnostics.

– as well as the several hundred million dollars that would otherwise be spent on useless, expensive therapy.[4]

In patent terms, each biomarker test is a method for determining the presence of the biomarker in a given patient. A process patent provides the soundest legal protection for the intellectual property underlying each such method, and thus provides the strongest incentive for venture capitalists and large, established companies to invest – and hence fund research, development, regulatory approval, and commercialization – in hopes of obtaining a return in the marketplace. Since roughly half of Americans will get cancer before dying, and about half of these will

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[4] Roxanne Nelson, *GICS 2009: Huge Cost Savings From KRAS Testing in Metastatic Colorectal Cancer*, Medscape Medical News, Jan. 16, 2009, *available at* http://www.medscape.com/viewarticle/586946 (screening for KRAS mutations before initiating treatment with cetuximab or related drugs could result in drug cost savings of $604 million if annual American population with metastatic colorectal cancer undergoes first-line therapy with cetuximab-containing regimen). The savings to the U.S. health care system from genetic profiling to optimize treatment with a single drug are estimated to be more than $1 billion. *See* Paul H. Keckley, PhD et al., Deloitte Center for Health Solutions, *The ROI for Targeted Therapies: A Strategic Perspective Assessing the Barriers and Incentives for Adopting Personalized Medicine*, at 5 (2009) (fig. 2), *available at* http://www.personalizedmedicinecoalition.org/programs/roi_seminar_2009/ROIforTargeted%20Therapies_DCHSstudy_FINAL.pdf (estimated potential annual health care cost savings from individual dosing of Warfarin based on genetic testing are $1.1 billion with a range of $100 million to $2 billion for U.S. health care system).

die of their cancer,[5] continued financing is important not only to Caris and other diagnostics companies but also to public health.

In *In re Bilski,* 545 F.3d 943 (Fed. Cir. 2008), which involved a claim for a business method, the United States Court of Appeals for the Federal Circuit held that the exclusive test for determining whether a process claim recites patentable subject matter under 35 U.S.C. § 101 is whether the claim is (a) tied to a machine or (b) transforms an article into a different state or thing. Only by misapplying this Court's precedents did the Federal Circuit reach its holding. Further, by mandating the machine-or-transformation test for *all* process claims (not just business method claims), the Federal Circuit drastically narrowed the scope of patentable subject matter, undermined the settled expectations of owners of process patents, raised doubt as to the legal protection of new diagnostic and treatment methods, and diminished the ability of biotechnology companies to attract investment capital. Particularly in an economy increasingly based on information and biotechnology, the outmoded "machine tie" and "transformation" analyses are too uncertain of

[5] *See Lifetime Probability of Developing or Dying from Cancer, American Cancer Society*, July 13, 2009, *available at* http://www.cancer.org/docroot/CRI/content/CRI_2_6x_lifetime_probability_of_developing_or_dying_from_cancer.asp (indicating about 1 in 2 males and 1 in 3 females will develop cancer in their lifetime, and 1 in 4 and 1 in 5, respectively, will die from cancer).

application to provide such companies with genuine legal protection. Moreover, the U.S. Patent and Trademark Office ("USPTO") has now adopted new guidelines for review of life sciences patents and is routinely rejecting patents based on the decision below. Without such patent protection, Caris and other biotechnology companies will face a shortage of funding and hence will be unable to make critical discoveries and to translate them into improved patient care. It is not an overstatement to say that biotechnology companies depend for their survival on strong patent protection, as only the limited exclusivity of patents will genuinely compensate such companies and their investors for their significant research and regulatory costs, and for assuming the risk of biological obstacles and fierce marketplace competition.

Accordingly, Caris has a strong interest in ensuring that the decision below is reversed insofar as it held the machine-or-transformation test to be the exclusive test for patentable subject matter in process claims.

SUMMARY OF ARGUMENT

The judgment of the Federal Circuit should be reversed insofar as it held the machine-or-transformation test to be the exclusive test for the patentability of claimed processes under 35 U.S.C. § 101. Subject matter is patentable if it fits into one of

the four statutory categories – process, machine, manufacture, composition of matter – and is useful and man-made. Nothing in the statute or this Court's precedents requires that, to be patentable, a process must either be tied to a machine or transform an article into a different state or thing. Only fundamental principles – laws of nature, natural phenomena, and abstract ideas – are unpatentable subject matter, though an application of a fundamental principle is patentable if useful and inventive. These flexible standards governing patentability should not be replaced with a rigid, Industrial-Age rule requiring the presence of machinery or physical transformation. Such a rule would bar vast areas of innovation from patent protection and would therefore be contrary to Congress's intent that patentable subject matter be broad in scope.

Twice, this Court has ruled expressly that the machine-or-transformation test is not the exclusive test for the patentability of a process under § 101. The Federal Circuit misinterpreted both decisions by baselessly reading into them a directive of exclusivity and by wholly ignoring the decisions' express rejection of exclusivity. The essential holding of the decisions is that a process claim may not preempt a fundamental principle, and not that machine implementation and transformation are the exclusive means by which a process claim can avoid such preemption.

The decision below dramatically weakens patent protection for diagnostics and thus will chill investment and innovation. Although certain steps of some diagnostic methods involve machines or transformations, the focus of diagnostic methods is the generation of information. Thus, it is unclear if machine implementation and transformation are sufficiently central to each method to satisfy the machine-or-transformation test. Such doubt will discourage investment by venture capitalists and larger, mature companies, because of resulting uncertainty as to whether future diagnostic innovations will receive patent protection. Moreover, the decision below applies the machine-or-transformation test to *all* claimed processes – including diagnostic methods – and not just business methods. Consequently, diagnostic method claims are already being rejected under *Bilski*, and many already-issued patents are now subject to invalidity defenses in infringement litigation.

Without the limited exclusivity of patent protection, health care companies and their investors will lose incentive to research, develop, and commercialize new diagnostics. The decision below constitutes the sort of fundamental change in settled patent law that only Congress is equipped to make.

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ARGUMENT

I. THE FEDERAL CIRCUIT MISAPPLIED THIS COURT'S PRECEDENTS, WHICH HAVE NEVER HELD THE MACHINE-OR-TRANSFORMATION TEST TO BE THE EXCLUSIVE TEST FOR THE PATENTABILITY OF CLAIMED PROCESSES

Under this Court's precedents, patentable subject matter under 35 U.S.C. § 101 consists of any man-made and useful process, machine, manufacture, or composition of matter, but must not be laws of nature, natural phenomena, or abstract ideas. Lest lower courts usurp Congress's function, this Court has warned that "courts should not read into the patent laws limitations and conditions which the legislature has not expressed." *Diamond v. Chakrabarty,* 447 U.S. 303, 308 (1980) (citation and internal quotation marks omitted). Moreover, this Court has twice held that subject matter may be patentable even if it does not satisfy the machine-or-transformation test. *See Gottschalk v. Benson,* 409 U.S. 63, 71 (1972); *Parker v. Flook,* 437 U.S. 584, 588 n.9 (1978). Contrary to the statute and these clear holdings, however, the court below held that a process claim cannot recite patentable subject matter under 35 U.S.C. § 101 unless it also satisfies the machine-or-transformation test. That holding is erroneous and should be reversed.

Section 101 is broadly worded:

> 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 therefor, subject to the conditions and requirements of this title.

35 U.S.C. § 101 (emphasis added).[6] According to the plain statutory language, subject matter is patentable as long as it fits into one of the four categories – process, machine, manufacture, composition of matter – and is useful and man-made.[7] As the repeated use of the term "any" indicates, "Congress plainly contemplated that the patent laws would be given wide scope." *Chakrabarty,* 447 U.S. at 308. In *J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc.,* 534 U.S. 124 (2001), this Court stated that § 101 is "extremely broad," *id.* at 130, and is a "dynamic provision designed to encompass new and unforeseen inventions," *id.* at 135. Nothing on the face of the statute

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[6] According to the statutory definitional provision, "[t]he term 'process' means process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material." 35 U.S.C. § 100(b).

[7] Although § 101, which addresses patent eligibility of subject matter, also uses the term "new," it has long been held that novelty and non-obviousness should be addressed under §§ 102 and 103. 35 U.S.C. §§ 102, 103. 35 U.S.C. §§ 102, 103. *See, e.g.*, *Diamond v. Diehr*, 450 U.S. 175, 189-91 (1981). Additional safeguards against undeserved grants of patent protection appear in § 112, which imposes the requirements of enablement, written description, and definiteness. 35 U.S.C. § 112.

requires that, to be patentable, a process (i) be tied to a machine (or, for that matter, to a manufacture or composition of matter) or (ii) transform an article into a different state or thing.[8]

This Court's only limiting gloss on § 101 is that fundamental principles – "laws of nature, natural phenomena, and abstract ideas" – are not patentable subject matter. *Chakrabarty,* 447 U.S. at 309. The reason is that such principles, like mental processes, "are the basic tools of scientific and technological work." *Benson,* 409 U.S. at 67; *Flook,* 437 U.S. at 589, 593 n.15; *Funk Bros. Seed Co. v. Kalo Inoculant Co.,* 333 U.S. 127, 130 (1948) ("[Fundamental principles] are part of the storehouse of knowledge of all men. They are . . . free to all men and reserved exclusively to none."). However, an *application* of a fundamental principle can be patentable under § 101, provided the application is useful and inventive. *See Flook,* 437 U.S. at 594 ("[E]ven though a phenomenon of nature or mathematical formula may be well known, an inventive application of the principle may be

[8] The Federal Circuit itself acknowledged that the machine-or-transformation test does not appear on the face of the statute. *Bilski*, 545 F.3d at 956 n.11 ("the statute itself does not explicitly mention machine implementation or transformation"). As one of the dissents below stated, "The United States Supreme Court has never held that 'process' inventions suffered a second-class status under our statutes, achieving patent eligibility only derivatively through an explicit 'tie' to another statutory category. . . . Yet second-class status is today engrafted on 'process' inventions." *Id*. at 990 (Newman, J., dissenting).

patented."); *Funk Bros.,* 333 U.S. at 130[9] ("He who discovers a hitherto unknown phenomenon of nature has no claim to a monopoly of it which the law recognizes. If there is to be invention from such discovery, it must come from the application of the law of nature to a new and useful end.").[10] If the fundamental principle cannot be applied except in a single, limited fashion, then no patent may be granted on the application; if granted, such a patent would preempt the fundamental principle and hence, in effect, be a patent on the principle itself. *Benson,* 409 U.S. at 71-72. If the claim is drawn so broadly, or is so unrelated to any particular use of a fundamental principle, that it preempts substantially all uses of that principle, it is similarly unpatentable. *Id.* at 68-69.

The question here is whether, in the case of a process claim, the foregoing standards need to be supplemented, or even supplanted, by an exclusive and rigid rule for distinguishing between a

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[9] Although *Funk Bros.* concerned a product claim, its holding applies to a process claim. *Diehr*, 450 U.S. at 188 n.11 (citing *Benson*, 409 U.S. at 68).

[10] *See also Diehr*, 450 U.S. at 187 ("It is now commonplace that an *application* of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection."); *Mackay Radio & Telegraph Co. v. Radio of Am.*, 306 U.S. 86, 94 (1939) ("While a scientific truth, or the mathematical expression of it, is not a patentable invention, a novel and useful structure created with the aid of knowledge of scientific truth may be.").

fundamental principle and a patentable application thereof. In Caris's view, no such supplementation is needed: The rule in question, the machine-or-transformation test, would replace flexible standards – whose merit lies in their ability to accommodate new and unforeseen technologies – with an unduly limited choice, conditioning patentability on the presence of either machinery or physical transformation.[11] The language of the test impermissibly looks backward to the brute physicality of the Industrial Age rather than forward to the subtle realities of the Information Age. As articulated by Thomas Jefferson, author of the nation's first patent legislation, the goal of the Patent Act is that "'ingenuity should receive a liberal encouragement.'" *Chakrabarty,* 447 U.S. at 308 (quoting *5 Writings of Thomas Jefferson* 75-76 (Washington ed. 1871)). Mandating the machine-or-transformation test would bar vast areas of innovation from such encouragement and thus would be contrary to congressional intent.

In assessing the patentability of process claims, this Court has never required the machine-or-transformation test and has twice ruled that it is not the exclusive patentability test for such claims. In *Benson,* the Court, after reviewing its decisions

[11] This Court has recognized that rigid tests are often inadequate for addressing patentability. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 415 (2007) ("We begin by rejecting the rigid approach" used by lower court for determining patentability under 35 U.S.C. § 103).

sustaining patents on the basis of a transformation involving no machine, held:

> 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.*

409 U.S. at 71 (emphasis added).[12] This express holding that the machine-or-transformation test is not the exclusive test for the patentability of claimed processes was reaffirmed in *Flook*:

> 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*.

[12] Inexplicably, the majority below called these statements "equivocal." 545 F.3d at 956. As Judge Newman's dissent observed, there is nothing equivocal about the phrase "We do not hold . . . ." *See id.* at 979 (Newman, J., dissenting).

437 U.S. at 588 n.9 (emphasis added) (citations omitted).[13] Thus, the Court concluded that while claims to processes have been upheld when the process at issue was in fact tied to a machine or transformed an article into a different state or thing, nothing in the Court's holdings has elevated either a machine tie or a transformation into the *sine qua non* of patentability or has turned such facts into legal requirements.

In view of *Flook* and *Benson*, the principal basis for the Federal Circuit's holding may be quickly rejected. The holding was based on the following sentence from *Benson,* which the majority below quoted three times: "Transformation and reduction of an article 'to a different state or thing' is the clue to the patentability of a process claim that does not include particular machines." *Benson,* 409 U.S. at 70; *see Bilski,* 545 F.3d at 954, 955-56, 956. According to the Federal Circuit, the *Benson* Court's use of the definite article "the" – instead of the indefinite article "a" – before the word "clue" proved that the Court meant the machine-or-transformation test to be the *exclusive* test for the patentability of a process. *See Bilski,* 545 F.3d at 955-56 & n.11. Moreover, the Federal Circuit, noting that *Diehr* repeated *Benson*'s "clue" sentence without repeating *Benson*'s and *Flook*'s holding of non-exclusivity, essentially held

[13] The majority below tendentiously omitted the phrase "An argument can be made" from its quotation of this portion of *Flook*. *See* 545 F.3d at 956.

that *Diehr* overruled these non-exclusivity holdings *sub silentio*. For several reasons, the Federal Circuit's conclusions are fatally flawed.

First, if the *Benson* Court had wanted to make transformation the exclusive legal test of patentability for a process untied to a machine, it would have used language far more definite than the hesitant and unemphasized phrase "the clue."

Second, the quite debatable sentence on which the Federal Circuit relied appears in the same *Benson* opinion as the *explicit* holding that a process may be patentable even if it involves no machine implementation or transformation. Because the Court that authored the proposition relied on by the Federal Circuit also held the proposition non-exclusive, any argument for exclusivity is foreclosed.

Third, the Federal Circuit's argument that *Diehr* relied on *Benson*'s "clue" sentence but did not repeat *Benson*'s holding of non-exclusivity, *see Bilski,* 545 F.3d at 956, proves nothing. The process at issue in *Diehr* involved a machine – a rubber molding press – and transformed raw rubber into cured rubber. 450 U.S. at 180, 184. The Court held the process patentable. *Id.* But nothing in the holding remotely stated that a process that involves neither a machine nor a transformation cannot be patentable.[14] That

[14] An additional reason why *Diehr* did not hold that a process involving no machine or transformation is unpatentable under § 101 is that the process at issue there involved *both* a

(Continued on following page)

statement was so firmly rejected in *Benson* and *Flook* that the rejection simply did not need repeating in *Diehr*. Had the *Diehr* Court understood itself to be overruling the explicit non-exclusivity holdings of *Benson* and *Flook,* the majority opinion in *Diehr* would surely have mentioned that understanding. That it did not do so demonstrates that the non-exclusivity holdings of *Benson* and *Flook* remain good law after *Diehr*.

Fourth, the *Diehr* Court itself described *Benson* and *Flook* as holding no more than that a fundamental principle is unpatentable. 450 U.S. at 185. That is, the *raison d'etre* of a machine tie or a transformation was to avoid patenting a fundamental principle – meaning that if a process claim found some other way to avoid claiming a fundamental principle, then that claim would be patentable under § 101. *See Bilski,* 545 F.3d at 1013 ("The Supreme Court stated that all of the transformation and machine linkage explanations simply restated the abstractness rule." (Rader, J., dissenting)). In other words, the *Benson* Court's holding was that the process claim there preempted a mathematical formula (and thus was not drawn to patentable subject matter), and not that the machine-or-transformation test is the only means by which a process claim can avoid such preemption.

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machine and a transformation. *See Bilski*, 545 F.3d at 981 (Newman, J., dissenting). As a result, the issue of whether a process involving no machine or transformation is patentable was not squarely presented.

Finally, *Diehr* shows that the Federal Circuit, by focusing on machinery and transformation, confused instantiation of the governing standards with the standards themselves. *Diehr* held that

> when 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.

450 U.S. at 192 (emphasis added). If transformation had been a critical requirement of the Court's holding, it would not have been mentioned in a parenthetical aside, and it would not have been introduced by "*e.g.*" Indeed, the use of "*e.g.*" implies, contrary to the exclusivity of the Federal Circuit's holding, that any number of means *besides transformation* might be employed to ensure that the claim is drawn to a patentable process rather than an unpatentable fundamental principle.

The Federal Circuit's decision should accordingly be reversed.

II. AN AFFIRMANCE WOULD CALL INTO QUESTION INNUMERABLE PATENTS FOR DIAGNOSTIC METHODS AND WOULD CHILL FUTURE INNOVATION

Venture capital is the lifeblood of biotechnology companies and their life-saving discoveries. But venture capitalists and established companies will make few investments unless the discoveries receive strong patent protection. Any uncertainty in the availability of such protection will chill investment and hence innovation. For several reasons, the decision below, which is not limited to business methods and applies to all processes in every field of endeavor, will dramatically weaken patent protection for diagnostics, and thus will jeopardize funding for the entire industry.

Patents for diagnostics often claim a two-step method that consists of a non-specific assay or other measurement, followed by a correlation between the assay result and a disease, medical condition, or resistance to a particular treatment.[15] The focus of

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[15] In dissent below, Judge Rader, addressing questions raised in the dissent from the dismissal of the writ of certiorari granted in *Laboratory Corporation of America v. Metabolite Laboratories, Inc.*, 548 U.S. 124, 125-39 (2006), cogently explained why such diagnostic method claims recite patentable subject matter under § 101:

> That dissent is premised on a fundamental misapprehension of the distinction between a natural phenomenon and a patentable process. . . .

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each such method is the generation of information useful for diagnosis and treatment. While the first step in such methods is often – though not always – an assay that employs a machine or apparatus (such as a computer, thermocycler, gas chromatograph, gene chip, and/or mass spectrophotometer) and transforms components of tissue or blood samples into detectible chemical complexes (such as antibody-protein or nucleic acid complexes),[16] it is *and will*

> 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. . . . Moreover, testing blood for a dangerous condition is not a natural phenomenon, but a human invention.
>
> The distinction is simple but critical: A patient may suffer from the unpatentable phenomenon of nature, namely high homocysteine levels and low folate. But the 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. Moreover, the sick patient does not practice the patented invention. Instead the patent covers a process for testing blood that produces a useful, concrete, and tangible result: incontrovertible diagnostic evidence to save lives.

Bilski, 545 F.3d at 1013-14 (Rader, J., dissenting).

[16] Not every diagnostic method patent involves an assay, however. When a diagnostic method involves no assay, it may be particularly vulnerable to rejection under the

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remain doubtful whether machine implementation and transformation are sufficiently central to each method to satisfy the machine-or-transformation test. *See Bilski,* 545 F.3d at 961-62 ("The use of a specific machine or transformation or an article must impose *meaningful limits* on the claim's scope . . . . Th[e] transformation must be *central* to the purpose of the claimed process." (emphasis added)); *id.* at 1015 (Rader, J., dissenting) ("[The majority] opinion propagates *unanswerable* questions: What form or amount of transformation suffices? . . . What link to a machine is sufficient to invoke the 'or machine' prong?" (emphasis added)).[17] Such doubt creates a significant disincentive for investment because of the consequent uncertainty as to whether future innovations in molecular diagnostics will be accorded patent protection. *See Bilski,* 545 F.3d at 1014 (Rader, J., dissenting) ("[T]his 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 or Parkinson's . . . .").

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machine-or-transformation test, as the discussion below concerning the '180 Office Action reveals.

[17] Because of the risk inherent in myopic attention to only one step in a process, *Diehr* warns that a court, in assessing the patentability of a claimed process, must consider the claim "as a whole." *Diehr,* 450 U.S. at 188. Yet the majority opinion below runs afoul of this admonition by requiring that, in a process claim, the step involving a transformation – such as might occur during the assay step of a two-part diagnostic method – be "central" to the process. 545 F.3d at 962.

The danger to personalized medicine is clear. Before the year was out, the Federal Circuit had used the decision below to invalidate claims in a patent for an immunization method. *See Classen Immunotherapies, Inc. v. Biogen IDEC,* No. 2006-1634, 2008 WL 5273107 (Fed. Cir. Dec. 19, 2008); *see also King Pharms., Inc. v. Eon Labs, Inc.,* 593 F. Supp. 2d 501, 512-13 (E.D.N.Y. 2009) (invalidating treatment method claim under *Bilski*). On December 3, 2008, in a presentation concerning personalized medicine, the USPTO explicitly applied the holding below to a theragnostic method for selecting a treatment for breast cancer[18] – belying Respondent's assertion in its opposition to certiorari that this matter implicates only business methods and not "frontier technologies," *see* Brief for the Respondent in Opposition, *Bilski v. Doll,* No. 08-964, 2009 WL 1179332, at *14 (Sup. Ct. May 1, 2009). Early in 2009, the USPTO issued guidelines to patent examiners for applying the machine-or-transformation test to process claims in view of the decision below.[19] The guidelines stated that "reciting a specific machine or a particular

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[18] *See* Kathleen Bragdon, Quality Assurance Specialist, Technology Center 1600, USPTO, *A Look at Personalized Medicine*, at slide 16, *available at* http://www.cabic.com/bcp/120308/.

[19] *See* Memorandum dated January 7, 2009, from John J. Love, Deputy Commissioner for Patent Examination Policy to the Technology Center Directors and Patent Examining Corps ("Bilski Guidance Memo"), *available at* http://www.uspto.gov/web/offices/pac/dapp/opla/documents/bilski_guidance_memo.pdf.

transformation of a specific article in an insignificant step, such a[s] data gathering or outputting, is not sufficient to pass the test." Bilski Guidance Memo at 1. Left unclear, however, is whether an assay or other measurement constitutes "data gathering."

USPTO Examiners have begun rejecting diagnostic method claims under *Bilski*. On July 7, 2009, an Examiner rejected U.S. Application Serial No. 10/888,180[20] (the "'180 Office Action"), claim 1 of which was rejected under *Bilski*. Claim 1 described a method for detecting endometrial pathology by detecting a plurality of polypeptides in a test sample to obtain a test profile, comparing the test profile to a reference protein profile, and determining that a patient has an endometrial pathology where a difference is measured with respect to at least one biomarker. Acknowledging the holding below, the Examiner asserted that a claimed process is patentable only if it meets the machine-or-transformation test. '180 Office Action, p. 4 (citing *Bilski*), *available at* http://portal.uspto.gov/external/portal/pair (Application No. 10/888,180; file wrapper). The Examiner then stated that "the claimed subject matter recites steps for obtaining a patient's sample, detecting polypeptides in the test sample to yield a profile, and providing a result to a user in a user

[20] Assigned to Science & Technology Corporation (STC.UNM) at University of New Mexico, on reel/frame no. 021321/0457, recorded 7/31/2008, *available at* http://assignments.uspto.gov/assignments/q?db=pat (Published Application No. 20050100967).

readable format *without requiring any specific machines for performing these steps*." *Id*. (emphasis added). Finally, the Examiner stated that the "claimed subject matter recites steps for obtaining a patient sample and detecting polypeptides . . . [but that] . . . these limitations *do not require any assays for performing these steps and therefore do not explicitly result in a transformation of an article*." *Id*. (emphasis added).[21] Similar rejections are certain to follow.

It is not just pending applications that are now in jeopardy: Hundreds, even thousands, of already-issued patents are now subject to invalidity defenses in infringement litigation. Many such patents recite diagnostic methods involving neither an assay (or other transformative measurement) nor machine implementation. Many others involve an assay in which the transformation of the tissue sample's components may not be considered sufficiently "central to the purpose of the claimed process," *Bilski,* 545 F.3d at 962, because the transformation is incidental to the purpose of generating diagnostic information. Moreover, the jeopardy and uncertainty created by *Bilski* will upset the settled expectations of

[21] Although the Examiner indicated that addition of an assay would overcome the transformation-based rejection, *see* '180 Office Action, p. 4, the addition could well be insufficient in view of the statement in the majority opinion below that "the transformation must be *central* to the purpose of the claimed process." *Bilski,* 545 F.3d at 962.

those who, in obtaining patents for claims that may now run afoul of the machine-or-transformation test, followed the law as it existed at the time of the patent application. *See Festo v. Shoketsu Kinzoku Kogyo Kabushiki Co.,* 535 U.S. 722, 724 (2002) ("'[C]ourts must be cautious before adopting changes that will disrupt the settled expectations of the inventing community.'" (citation omitted));[22] *see also Payne v.*

[22] The *Festo* Court explained:

> The responsibility for changing [settled law] rests with Congress. . . . Fundamental alterations in these rules risk destroying the legitimate expectations of inventors in their property. The petitioner in *Warner-Jenkinson* requested another bright-line rule . . . at the cost of disrupting the expectations of countless existing patent holders. We rejected that approach: "To change so substantially the rules of the game now could very well subvert the various balances the PTO sought to strike when issuing the numerous patents which have not yet expired and which would be affected by our decision." [*Warner-Jenkinson Co. v. Hilton Davis Chemical Co.,* 520 U.S. 17, 32 n.6 (1997)]; see also *id.,* at 41, 117 S.Ct. 1040 (GINSBURG, J., concurring) ("The new presumption, if applied woodenly, might in some instances unfairly discount the expectations of a patentee who had no notice at the time of patent prosecution that such a presumption would apply"). As *Warner-Jenkinson* recognized, patent prosecution occurs in the light of our case law. Inventors who amended their claims under the previous regime had no reason to believe they were conceding all equivalents. If they had known, they might have appealed the rejection instead. There is no justification for applying a new and more robust estoppel to those who relied on prior doctrine.

Festo, 535 U.S. at 739.

Tennessee, 501 U.S. 808, 828 (1991) (adhering to established law, and to consequently settled expectations, is particularly important "in cases involving property and contract rights, where reliance interests are involved"); *Bilski,* 545 F.3d at 977, 993 (Newman, J., dissenting). Some of the more well-known examples of patents now in danger include:

- **Prognosis for Colon Cancer:** Claim 9 of U.S. Patent No. 7,163,801 assigned to National Institutes of Health, U.S. Dept. of Health and Human Services, is directed to a method of determining a prognosis for survival for colon cancer in a patient having stage II colon carcinoma by measuring levels of a biomarker in a colon cancer cell-containing sample: "A method of determining a prognosis for survival for a colon cancer patient having stage II colon carcinoma, comprising: (a) measuring levels of TUCAN polypeptide and one or more biomarker polypeptides selected from the group consisting of cIAP2, Apaf1, Bcl-2 and Smac in a colon cancer cell-containing sample from said colon cancer patient, and (b) comparing the level of TUCAN polypeptide and the one or more selected biomarker polypeptides in said sample to a reference level of TUCAN polypeptide and said one or more selected biomarker polypeptides from normal colon tissue, wherein a lower level of TUCAN polypeptide and a higher level of any of Apaf1, Bcl-2, or

Smac, or a lower level of TUCAN polypeptide and a lower level of cIAP2 in said sample relative to said reference level correlate with increased survival of said patient."

- **Colon Neoplasia Detection:** Claim 13 of U.S. Patent No. 7,485,420, assigned on its face to Case Western Reserve University, identifies a method comprising determining the likelihood that a human subject has colon neoplasia by detecting a vimentin expression level relative to a control: "A method for detecting the likelihood that a human subject has colon neoplasia, comprising detecting vimentin protein or nucleic acid expression level in a sample from the human subject, wherein reduced expression level of vimentin protein or nucleic acid relative to a control sample from a healthy subject is indicative of the likelihood that the human subject has colon neoplasia."

- **Prostate Specific Antigen ("PSA") test for prostate cancer:** Claim 10 of U.S. Patent No. 5,840,501, assigned on its face to Bayer Corp., identifies a method consisting of any immunoassays followed by a correlation: "A method for monitoring the course of disease in a male patient diagnosed with prostate cancer, comprising the performance of a series of immunoassays over time to determine changes in the level of

complexed prostate specific antigen (cPSA) in blood samples obtained from such patient, whereby changes in the cPSA blood level correlate with changes in disease status." PSA is widely used to diagnose prostate cancer.

- **Test for HIV/AIDS:** Claim 1 of U.S. Patent No. RE38352, assigned on its face to Stanford University, identifies a method consisting of any test for a specific nucleic acid mutation, followed by a correlation: "A method of evaluating the effectiveness of antiretroviral therapy of an HIV-infected patient comprising: collecting a plasma sample from an HIV-infected patient; and determining whether the plasma sample comprises nucleic acid encoding HIV reverse transcriptase having a mutation at codon 215, in which the presence of the mutation correlates positively with an accelerated immunologic decline of said patient compared to patients who do not have the mutation." Mutations in the HIV virus within an infected individual are widely used to help people find and take drugs that will make them better, and to avoid drugs that will make them sicker.

- **HER-2/neu test for breast and ovarian cancer:** Claim 1 of U.S. Patent No. 4,968,603, assigned on its face to the University of California, identifies a method consisting of any test for the

amplification level of the HER-2/neu gene, followed by classifying an increased amplification relative to a reference level: "A method for screening patients to determine disease status, said method comprising: measuring the level of amplification or expression of the HER-2/neu gene in a sample from a patient suffering from breast or ovarian adenocarcinoma; and classifying those patients having an increased level of amplification or expression of the HER-2/neu gene relative to a reference level characteristic of normal cells as being more likely to suffer disease relapse or having a decreased chance of survival." HER-2/neu-related tests are widely used to determine which drug should be taken by a breast cancer patient.

- **Test for neoplastic (i.e., cancerous) tissue:** Claim 7 of U.S. Patent No. 5,955,263, assigned on its face to Johns Hopkins University and Genzyme Corp., identifies a method consisting of comparing normal and abnormal proteins, and detecting a mutation-based alteration in the amino acid sequence wherein the alteration indicates neoplasia: "A method to aid in determining neoplasia of a tissue of a human, comprising: comparing (a) p53 proteins in a human tissue suspected of being neoplastic to (b) wild-type p53 proteins in a normal tissue of said human; detecting an alteration in the amino acid sequence

> between the p53 proteins, wherein the alteration is due to a mutation in a p53 gene in the human tissue suspected of being neoplastic, wherein the mutation is selected from the group consisting of: a point, deletion, missense, and frame-shift mutation, wherein an alteration in the amino acid sequence indicates neoplasia." Science Magazine named p53 the "molecule of the year." Mutations in p53 help doctors determine whether a tissue is cancerous.

The repercussions for the future of biotechnology, particularly diagnostics, if the decision below is affirmed would be staggering. The health care industry relies on the economic incentives provided by our patent system, including in large part by the patentability of diagnostic method claims. If such claims were subject to invalidation as unpatentable, health care companies would lose incentive to conduct research into basic diagnostics, to develop personalized medicine tools and diagnostic systems, to validate them, and to have them approved by the FDA – all steps that are tremendously costly and necessary for the public to derive any benefit from new diagnostics. Likewise, venture capitalists, financial firms, and established companies would no longer have incentives to fund or invest in health care companies that pursue the research, development, and regulatory approval of drugs and diagnostic systems. If there is no expectation of a limited right to exclusivity, industry will respond: These areas will

be neglected in favor of other areas for which patent protection is still available.[23]

Weighty policy issues underlie our carefully structured and long-standing patent system. While the decision below would change this framework and impose a further, rigid limitation on patentability,

[23] Harm from declaring diagnostic method claims unpatentable is not limited to the loss of incentives for research and development. Rather, the diagnostics segment of the biotechnology industry – which industry in 2008 generated about $70 billion in revenues, employed 190,000 people, and had a market capitalization of more than $340 billion – could be seriously jeopardized. *See* Glen T. Giovannetti & G. Jaggi, Ernst & Young, *Beyond Borders – Global Biotechnology Report 2009*, p. 34G (2009). As discussed above, an affirmance here could cause numerous two-step diagnostic patents to be rendered void. At a minimum, companies holding those patents – and their investors and financial backers – would face uncertainty as to the value of their patents and the corresponding value of their businesses. It is unquestionable that a biotechnology company's value drops precipitously upon expiration of its patents, demonstrating the economic value afforded by patent protection. For example, in anticipation of the expiration of its patent on the cholesterol drug Zocor in June 2006, Merck announced in December 2005 that it expected sales of Zocor to drop from $4.35 billion in 2005 to $2.45 billion in 2006. *See Merck Plans More Cost-Cutting,* N.Y. TIMES, Dec. 16, 2005, at C5. In 2007, as a result of generic competition, Merck's sales of Zocor were only $877 million. *See* Gina-Louise Monari, *Pressure rises in cardio,* MedAd News, Feb. 2009, *available at* http://www.pharmalive.com/magazines/medad/view.cfm?articleID=7173. Any ruling that would render diagnostic method claims unpatentable would hasten such reduction of value for numerous companies, with devastating effects for the biotechnology industry.

any such revision should be left to the Legislative branch. This Court so stated in *Chakrabarty*:

> The choice we are urged to make is a matter of high policy for resolution within the legislative process after the kind of investigation, examination, and study that legislative bodies can provide and courts cannot. That process involves the balancing of competing values and interests, which in our democratic system is the business of elected representatives. Whatever their validity, the contentions now pressed on us should be addressed to the political branches of the Government, the Congress and the Executive, not to the courts.

447 U.S. at 317; *see Diehr*, 450 U.S. at 182.[24] In sum, any ruling in this case should not upset settled law and expectations concerning the scope of patentability.

[24] Congress can and does amend the patent law when it finds that a change is in the public interest. For example, in 1996, Congress exempted certain medical activity from giving rise to infringement liability. 35 U.S.C. § 287(c) (added by Pub. L. No. 104-208, § 616, 110 Stat. 3009, 3009-67 (Sept. 30, 1996)).

CONCLUSION

The judgment of the Federal Circuit should be reversed insofar as it held the machine-or-transformation test to be the exclusive test for patentable subject matter in process claims.

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