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The Nature of Biotechnology Patents: A Tangled Doctrinal Web of Processes and Products That Can Catch All Genes But Save None

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THE NATURE OF BIOTECHNOLOGY PATENTS: A TANGLED DOCTRINAL WEB OF PROCESSES AND PRODUCTS THAT CAN CATCH ALL GENES BUT SAVE NONE

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"The difference between utility and utility plus beauty is the difference between telephone wires and the spider web."
- Edwin Way Teale, *September 18*, CIRCLE OF THE SEASONS (1953)

INTRODUCTION

This year, the modern biotech[1] industry turns 40.[2] Born with the advent of recombinant DNA technology, today's biotech industry has flourished as an important area of clinical practice, research and development. Biotechnology has become especially important in the realm of diagnostics. Through the extraction, isolation, manipulation, comparison and analysis of biological compounds, biotechnology offers medicine a highly reliable way of assessing individual risk factors and treatment options for a vast array of conditions. At the same time, the relationship of biotech patents to naturally occurring human biology has rendered biotech patents vulnerable to validity challenges, leading to significant uncertainty for an industry that relies heavily on large investments in research and development.[3] Last year, the patent eligibility of diagnostic biotechnology was narrowed via the natural phenomenon doctrine in *Mayo Collaborative Servs. v. Prometheus Laboratories, Inc.*;[4] a

1. In this article, "biotechnology" is used when serving as a noun, and "biotech" when serving as an adjective.

2. Biotechnology uses biological building blocks (such as amino acids, proteins, DNA and RNA) to engineer useful biomedical processes and products. *See generally* Lorance L. Greenlee, *Biotechnology Patent Law: Perspective of the First Seventeen Years, Prospective on the Next Seventeen Years,* 68 DENV. U. L. REV. 127 (1991).

3. *See generally* Thomas A. Hemphill, *The Biotechnology Sector and U.S. Gene Patents: Legal Challenges to Intellectual Property Rights and the Impact on Basic Research and Development,* 39 SCI. & PUB. POL'Y 815 (2012).

4. Mayo Collaborative Servs. v. Prometheus Laboratories, Inc., 132 S. Ct. 1289 (2012) [hereinafter *Mayo*].

decision considered confusing by some and dangerously over-reaching by others.[5] For over a century, the Supreme Court has interpreted the natural phenomenon doctrine to be an implied exception to subject-matter eligibility under § 101, which defines the categories of innovations that may be eligible for patent protection.[6] The natural phenomenon doctrine excludes laws of nature, products of nature and abstract ideas from patent-eligible subject matter.[7]

This term, the Supreme Court handed down its decision in *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*—concerning the patent-eligibility of genes associated with breast and ovarian cancer risk[8]—which the Court had previously remanded to the Federal Circuit Court of Appeals for reconsideration in light of *Mayo*.[9] At issue in both *Myriad* and *Mayo* was the validity of certain biotechnology patent claims that closely resembled abstract principles, laws of nature, or natural phenomena. After the Federal Circuit held that *Mayo*, a case about process patents, did not provide the controlling law for the gene patents at issue in *Myriad*, the Supreme Court granted cert on the question of whether genes are patentable subject matter.[10] In a unanimous decision, the Court found that isolated genomic DNA (gDNA) constitutes patent-ineligible natural phenomena, whereas complementary DNA (cDNA)[11] is patent-eligible because it is different from naturally occurring DNA. The Court, however, did not provide any guidance on the implications of the invalidated claims on isolated gDNA for claims on processes involving isolated gDNA. The extent to which §

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5. *See generally* JOHN R. THOMAS, CONG. RESEARCH SERV., R42815, *MAYO V. PROMETHEUS*: IMPLICATIONS FOR PATENTS, BIOTECHNOLOGY, AND PERSONALIZED MEDICINE (2012); *see also* Elizabeth J. Haanes & Jaume M. Cànaves, *Stealing Fire: A Retrospective Survey of Biotech Patent Claims in the Wake of Mayo v. Prometheus*, 30 NATURE BIOTECH. 758 (2012).

6. 35 U.S.C. § 101 (2012).

7. "Natural phenomenon doctrine" is used in this paper to refer to the triad of patentable subject matter exceptions (products of nature, laws of nature and abstract ideas).

8. Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107 (2013) [hereinafter *Myriad*].

9. Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 132 S. Ct. 1794 (2012).

10. Ass'n for Molecular Pathology v USPTO, *rev'd sub nom Myriad*, 689 F. 3d 1303 (Fed. Cir. 2012) *cert. granted in part*, 133 S. Ct. 694 (U.S. Nov. 30, 2012) (No. 11-725), *rev'd in part, granted in part, remanded, Myriad*, 133 S. Ct. 2107 (2013).

11. An essential tool of the biotech industry, cDNA (shorthand for complementary DNA) is a replica of real DNA with none of the introns but all of the exons that are normally found in naturally occurring DNA. The absence of introns, which can be thought of as structural noise, allows scientists to efficiently analyze only the relevant parts of the DNA.

101 jurisprudence regarding biotech patent claims on processes extends to biotech patent claims on compositions of matter —which, as cells and compounds, are themselves "essentially bags of chemical processes"[12]—is usefully informed by an analysis of the unique trajectories that process patent law has followed in the Federal Circuit and Supreme Court. To this end, it is relevant to understand how statutory and judicial patentability categories for processes have developed over time, how flexible their contours have been, as well as when and to what extent they may be subjected to a doctrine of ambiguous scope and relevance.

Part I of this paper will introduce early legal developments concerning biomedical process patents in order to examine the rationales for distinct doctrinal approaches to three different kinds of biomedical processes. This section will explain how, characterized by varying degrees of overlap with compositions of matter, certain kinds of biomedical processes, including biotech processes, were excluded from early attempts to address concerns about monopolies on medical knowledge. After describing the entangled nature of process and product patents in biotechnology, Part II turns to an analysis of the evolution of judicial and statutory standards that reflected this entanglement of biotech patent claims. Part III follows with a review of how the Federal Circuit attempted to address some of these issues by creating and altering analytical frameworks tailored to new kinds of biomedical processes. In contrast, this section then traces the Supreme Court's stronger reliance on patent eligibility limitations to assess the rationale of the natural phenomenon doctrine for addressing the intertwined nature of biotech process and product patents. Part IV then considers the relevance of the natural phenomenon doctrine in assessing the implications of *Mayo* and *Myriad* for biotech process patents, arguing that subject-matter eligibility of claims on genes and other diagnostic biotechnology should properly account for overlapping scopes of preemption between associated process and composition of matter claims in this realm. This paper concludes that due to the natural phenomenon doctrine's implicit purpose—that the preemptive scope of a diagnostic biotech patent be limited to the inventive use of that product—the doctrine is of limited usefulness at the litigation stage; however, the rationale underlying the doctrine, and the importance of the doctrine in limiting monopolies on scientific knowledge, may

12. Dan L. Burk, *The Problem of Process in Biotechnology*, 43 HOUS. L. REV. 561, 568 (2006).

still be pursued through other legal means.

I. BIOMEDICAL PROCESS PATENTS AND THE SPECIAL CASE OF BIOTECHNOLOGY

A. Statutory And Judicial Foundations

For most of the twentieth century, new and useful biomedical process patents were valid under 35 U.S.C. § 101 and enforceable under 35 U.S.C. § 271(a-b). Patent-eligible subject matter is defined by § 101 of the U.S. Patent Act, and includes "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof."[13] Notwithstanding this clear statutory allowance for biomedical process patents, as early as 1862, a patent on using ether as surgical anesthesia was struck down for lack of novelty and obviousness in *Morton v. New York Eye Infirmary*.[14] *Ex parte Brinkerhoff* subsequently expanded on the *Morton* rationale, holding that "methods or modes of treatment of physicians of certain diseases are not patentable" because granting patents for treatment methods would inappropriately lead the public to believe that a particular method would always produce the expected result.[15] As a result, the United States Patent and Trademark Office (USPTO) blocked patents on most "medical methods and modes of treatment" until 1954.[16] This changed when *Brinkerhoff* was overruled by *Ex parte Scherer* on account of medical methods satisfying the subject-matter eligibility criteria of a "useful process" of 35 U.S.C. § 101.[17] However, as Noonan highlights, "[t]he Patent Office still suspiciously scrutinized such patent applications, and required extra data of efficacy in most cases."[18] Following *Scherer*, though, countless patents were issued on biomedical procedures, many of which are closely related to natural laws and phenomena.[19]

Biomedical process patents became increasingly controversial in the late twentieth century as infringement lawsuits threatened physicians' ability to provide quality medical care. For instance, a

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13. 35 U.S.C. § 101 (2012).
14. Morton v. N.Y. Eye Infirmary, 17 F. Cas. 879, 883 (C.C.S.D.N.Y. 1862).
15. *Ex parte* Brinkerhoff, 1883 Dec. Comm'r Pat. 349, *republished in New Decisions*, 27 J. PAT. & TRADEMARK OFF. SOC'Y 797 (1945).
16. Asher Hodes, *Diagnosing Patentable Subject Matter*, 26 BERKELEY TECH. L.J. 225, 229 (2011).
17. *Ex parte* Scherer, 103 U.S.P.Q. 107, 1954 WL 5537 (B.P.A.I. July 23,1954) (concerning a patent on a method of using a pressure jet to inject medicine).
18. William J. Noonan, *Patenting Medical and Surgical Procedures*, 77 J. PAT. & TRADEMARK OFF. SOC'Y 651, 654 (1995).
19. *Id.* at 658-60.

patent on a diagnostic method for Down's syndrome attracted widespread opposition after its owner asserted the patent against medical providers throughout the 1990s.[20] Around the same time, the medical profession's vocal opposition to infringement lawsuits against ophthalmologists who performed medically necessary surgeries brought to light certain undesirable consequences of monopolies on medical processes.[21] In *Pallin v. Singer* (1995), Dr. Pallin, who tried to charge licensing fees for each use of his patented process for cataract surgery, sued Dr. Singer for numerous counts of infringement.[22] In response, the American Academy of Ophthalmology expressed apprehension about "the frightening potential of having to pay a royalty every time a patient's temperature was taken, if such a procedure was patented."[23] In an unpublished consent order, the District of Vermont invalidated some of the claims of Dr. Pallin's patent and enjoined it from being enforced.[24] The American Medical Association (AMA) and the American Society of Cataract and Refractive Surgery subsequently issued statements publicly denouncing the patenting of medical and surgical procedures, bringing the issue to the attention of Congress;[25] their sentiments have generally been echoed by other professional medical societies.[26] Some characterized medical process patents as "an unethical interference with patient care, a disruption of the medical tradition of freely sharing advances with colleagues, and an

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20. Hodes, *supra* note 16, at 230.

21. *See generally* Robert Gunderman & John Hammond, *"Under the Knife" – Patenting Surgical Procedures*, THE ROCHESTER ENG'R 10 (Feb. 2009), http://www.patenteducation.com/images/200902_Limited_Monopoly_-_Patenting_Surgical_Procedures.pdf.

22. Pallin v. Singer, 36 U.S.P.Q.2d 1050 (D. Vt. May 1, 1995).

23. Noonan, *supra* note 18, at 651 (citing *Doctors' Group Opposes Medical Method Patents*, WALL ST. J., Sept. 6, 1994, A14).

24. Pallin v. Singer, 1996 WL 274407, *1.

25. Gunderman & Hammond, *supra* note 21, at 10.

26. The WMA explains that patents are not necessary to incentivize innovation in medical procedures and that they can lead to higher costs of care, reduced availability of physicians licensed to provide certain procedures, and physician uncertainty about whether or not a particular procedure is patented. WMA Statement on Patenting Medical Procedures, Adopted by the 51st World Medical Assembly, Tel Aviv, Israel, Oct. 1999 and amended by the 60th WMA General Assembly, New Delhi, India (Oct. 2009). The AMA ethics code also states that "[t]he use of patents, trade secrets, confidentiality agreements, or other means to limit the availability of medical procedures places significant limitation on the dissemination of medical knowledge, and is therefore unethical." AM. MED. ASS'N, *Opinion 9.095 – The Use of Patents and Other Means to Limit Availability of Medical Procedures*, *in* AMA CODE OF MEDICAL ETHICS (1996, updated 2007), http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion9095.page.

unwelcome expense in a cost conscious modern medical environment."[27]

In response to this public outcry, two new laws were proposed in 1995: H.R. 11272, the Medical Procedures Innovation and Affordability Act, which would limit the use of USPTO funds available to issue process patents; and S.1334, which would amend 35 U.S.C. § 271 to exempt medical practitioners from patent infringement liability.[28] The proponents of these bills pointed out that "many countries exclude therapeutic and diagnostic methods from patent protection and that the United States should follow their lead and 'harmonize' [its] law with theirs."[29] Opponents, however, successfully blocked the bills, citing concerns over adverse effects on research and development in the burgeoning biotech and diagnostic industries.[30]

B. Three Different Kinds of Biomedical Process Patents

In understanding this debate, it is useful to consider the varying degrees of association with patentable objects exhibited by three general categories of patentable biomedical processes: (1) "pure" processes, which include diagnostic, therapeutic and surgical procedures not involving a patented medical product; (2) techniques that are used to isolate or create potentially patentable medical products like DNA; and (3) applications and uses of medical products and compositions of matter, which include "new use" claims.[31] The first of these categories, which does not involve patentable objects, falls primarily within the domain of clinical innovation. With the exception of a handful of non-essential specialties which subsist primarily based on private payment—and, in the absence of demand-generating insurance contracts, have stronger incentives for establishing monopolies over their elective services—the incentive rationale for "pure" process patents in the clinical setting is weak as balanced against ethical considerations. The World Medical Association (WMA) has explained that physicians already have professional obligations and rewards for "attaining and perfecting manual and intellectual skills."[32] Moreover, pure process

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27. Noonan, *supra* note 18, at 651-52.
28. Gunderman & Hammond, *supra* note 21, at 10.
29. U.S. Patent and Trademark Office, Notice of Hearings and Request for Comments on Issues Relating to Patents Protection for Therapeutic and Diagnostic Methods, 61 Fed. Reg. 10320 (Mar. 13, 1996).
30. Gunderman & Hammond, *supra* note 21, at 10.
31. *See* Aaron S. Kesselheim & Michelle M. Mello, *Medical-Process Patents – Monopolizing the Delivery of Health Care,* 355 NEW. ENGL. J. MED. 2036 (2006).
32. World Medical Ass'n, WMA Statement on Patenting Medical Procedures (as

patents present unique enforcement challenges because their infringement—which is transitory (based on discrete acts) as opposed to fixed (in a physical embodiment)—may be difficult to detect.

At the other end of the spectrum lies the third category of biomedical processes, which directly rely on products and compositions of matter. Therefore, these processes primarily implicate commercial innovation requiring substantial non-clinical human and capital investment. Infringement suits in this realm focus on the infringing use of both patented and off-patent products.[33] Notably, because these processes usually involve manufactured goods, their licensing fees can more readily be built into the product prices.[34]

Somewhere along the middle of the spectrum these distinctions become less apparent, particularly when the patentability of associated products and compositions of matter is uncertain. This uncertainty characterizes the second category of processes, which predominantly includes processes directed at the patentable manipulation, extraction, or imitation of biological materials. Product claims directed at biological compounds that are associated with measurement and information-related process claims cannot be seamlessly incorporated into licensing fees, because the biological materials involved are merely extracted from the body. At the same time, while biotech innovations require large investments, they receive substantial public funding[35] and are often developed with significant academic contributions.[36]

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amended in 2009) http://www.wma.net/en/30publications/10policies/m30/.

33. *E.g.*, Synvasive Corp. v. Stryker Corp., 425. F. Supp. 2d 1105, 1109 (E.D. Cal. 2006) (surgical saw blades); Transonic Sys., Inc. v. Non-Invasive Med. Tech. Corp., 75 F. App'x 765, 768 (Fed. Cir. 2003) (blood-flow measurement machine); Medtronic Xomed, Inc. v. Gyrus ENT LLC, 440 F. Supp. 2d 1300, 1306-8 (M.D. Fla. 2006) (apparatus used in the removal of noxious tissue). Many other examples involve technologies used in eye surgeries. *E.g.*, Advanced Med. Optics, Inc. v. Alcon Inc., 361 F. Supp. 2d 370, 374 (D. Del. 2005); Koepnick Med. & Educ. Research Found., L.L.C. v. Alcon Labs., Inc., 162 F. App'x 967 (Fed. Cir. 2005), *reh'g denied* (Jan. 25, 2006).

34. "If a drug or device has been patented, the licensing fee is incorporated into the cost of the drug or device. Accordingly, the physician does not have to worry about inadvertently infringing a drug or device patent, and physicians therefore are not discouraged from using drugs or devices by legal uncertainty about patent infringement." AMA, *Council on Ethical and Judicial Affairs*, *Ethical Issues in the Patenting of Medical Procedures*, 53 FOOD DRUG L.J. 341, 345 (1998).

35. Between 2003 and 2006, "the NIH funded $4.2 – 4.9 billion of genetics research," which makes genetics research "the sixth or seventh most funded research area." Jennifer Reineke Pohlhaus and Robert M. Cook-Deegan, *Genomics Research: World Survey of Public Funding,* 9 BMC GENOMICS 472, 480 (2008).

36. *See generally* Lori Pressman, et al., *The Licensing of DNA Patents by Large U.S. Academic Institutions: An Empirical Survey,* 24 NATURE BIOTECH. 31 (2006).

The differences between the three categories of biomedical process patents reveal limiting factors that might support differentiated degrees of patent protection. The three categories of patentable biomedical processes are in large part defined by their relationship to potentially patentable products. While strong patent protections appear most warranted for the third category of biomedical processes, they appear least warranted for the first category. The second category, covering most biotechnology, might be thought of as falling somewhere in the middle, especially considering the remaining uncertainties about the validity of process claims related to isolated gDNA.

C. The Limited Physician's Immunity Statute

In the aftermath of the *Pallin* case, the differences among biomedical process categories resulted in a brief Congressional stalemate that was broken in 1996 with a narrower third bill. The Physician's Immunity Statute effectively carved out a narrow immunity for physicians' infringement of pure process patents while preserving the subject-matter eligibility and infringement liability of all types of biomedical process patents. To address concerns that patents would obstruct the provision of medical care, 35 U.S.C. § 287—which establishes the conditions for liability for patent infringement—was amended to prevent patent owners from enforcing medical or surgical procedure patents against medical practitioners.[37] The amendment, however, § 287(c) ("Limitation on damages and other remedies; marking and notice"), excludes from its immunity in the infringement of 1) patented products, 2) patented uses of compositions of matter, and 3) biotech patents.[38]

Several limitations of this amendment, which reflect some of the aforementioned differences between process categories, are worth highlighting. To address concerns about protecting research and development investments in the growing biotech industry, "medical activity" was explicitly defined to exclude from immunity biotech processes alongside processes involving patented products, thereby preserving the full scope of intellectual property rights for these processes.[39]

While the Physician's Immunity Statute narrowly addressed some of the unique characteristics of pure process patents that justify

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37. Gerald J. Mossinghoff, *Remedies Under Patents on Medical and Surgical Procedures,* 78 J. PAT. & TRADEMARK OFF. SOC'Y 789, 794-95 (1996).
38. 35 U.S.C. § 287(c) (2012).
39. *Id.* at 797-98.

weaker enforcement rights, it was not calibrated to reflect similar characteristics of the second and third categories of biomedical process patents. First, the product and composition of matter claims associated with certain biotech processes may not be patent eligible, rendering these biotech processes more similar to pure processes. Second, rents for biotech processes are not easily tied to objects that can be sold and therefore defy traditional means of market enforcement.[40] Several attempts to address these policy gaps through legislation have failed to garner the necessary political support.[41] For instance, the unsuccessful Genetic Research and Diagnostic Accessibility Act attempted to carve out physicians' infringement liability for patented biotech processes, because "[e]xempting pure process patents and biotechnology process patents from infringement liability for physicians would cover correlations and diagnostic and treatment methods that form the basis for personalized medical care, an integral component to better and more effective patient care."[42] The following sections will further develop the issues surrounding the doctrinal entanglement of biotech process and composition of matter claims and how their implications for biomedical preemption might otherwise be addressed.

II. PRODUCT AND PROCESS ENTANGLEMENT IN BIOTECHNOLOGY

A. The Dual Nature of Biotech Patents

Although it was repealed by the America Invents Act of 2011, 35 U.S.C. § 103(b) once provided the lone statutory definition of a biotechnology process with respect to patents.[43] As set forth in a 1995 amendment to 35 U.S.C. § 103, a biotechnology process was defined to include genetic alteration of organisms to express exogenous

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40. Moreover, the definition of medical provider is hazier in the realm of biotechnology: because biotech processes involve both clinical and commercial inputs, they are often performed by specialized biotechnology companies that work with and serve medical providers. Therapeutic and surgical procedures, on the other hand, more often necessitate simpler mechanical tools, compounds and implements, and are therefore performed by medical practitioners in the traditional sense.

41. E.g., Animal and Gene Patent Moratorium Bill, S. 387, 103d Cong. (1993); The Genomic Science and Technology Innovation Act of 2002, H.R. 3966, 107th Cong. (2002); The Genomic Research and Diagnostic Accessibility Act of 2002, H.R. 3967, 107th Cong. (2002).

42. J. Befeler, *Seeking a Better Prescription for Physicians: Patent Eligibility for Diagnostic Methods in a Post-Bilski and Prometheus Era*, 35 SETON HALL LEG. J. 484, 514 (2012).

43. § 103 was rendered largely obsolete by *In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995).

nucleotide sequences, manipulate the expression of endogenous nucleotide sequences, and express non-naturally occurring physiological characteristics; cell fusion to produce cell lines expressing specific proteins; and methods of using products created through biotechnology processes.[44] When set forth as part of the Biotechnology Process Patent Act, this definition highlighted a legal recognition that innovation in biotech processes is often driven by discoveries concerning compositions of matter, which may themselves be claimed as processes.[45] The critical consequence of this is the recognition that biotech processes and compositions of matter may overlap in the scope of their preemption of the use of natural laws and natural phenomena.[46] As Burk explains, innovation in the biotech industry relies on "the character of molecules as channels for informational transfer processes," and biotech patents are thus "characterized as much by their processes as by their material make-up."[47] Indeed, as Burk elaborates, this aspect of biotechnology may be of greater consequence than in other realms, because biological materials are "generally valued precisely because of their internal process activity, which in turn typically constitutes the patentable point of novelty."[48] Thus, from an early stage, modern biotechnology has relied heavily on process patents because the products of most biotech processes—proteins—are usually not patentable. Process claims are thus often used to indirectly protect otherwise un-patentable biotech products.[49]

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44. Biotechnology Process Patent Act, Pub. L. No. 104-3 (codified at 35 U.S.C. § 103(b) (2006) (repealed 2011)).

45. For instance, § 103(B), "cell fusion procedures yielding a cell line that expresses a specific protein, such as a monoclonal antibody," allows naturally occurring products to be indirectly protected vis-à-vis the processes that yield them, and § 103(C), "a method of using a product produced by a process defined by subparagraph (A) or (B), or a combination of subparagraphs (A) and (B)," allows naturally occurring products to be indirectly protected vis-à-vis their use. Defining biotechnology in this way ensures that unpatentable biotech products can nevertheless be indirectly protected through their associated processes.

46. As early as 1912, the Second Circuit recognized novelty in the invention of purified biological materials might be tied to the discovery and manipulation of a law of nature. In *Parke-Davis & Co. v. H.K. Mulford & Co.*, the patentability of purified adrenaline was upheld in what is now considered a foundational case in biotechnology patent law. Even at this early stage in the development of the biotech industry, the Second Circuit noted that "[i]t was important, if possible, to ascertain what it was in these glands which possessed these physiological properties, whether it was a 'principle' or a 'condition,' and if it were a 'principle' to isolate it from its environment with other principles." Parke-Davis & Co. v. H K Mulford & Co., 196 F. 496, 497 (2d Cir. 1912).

47. Burk, *supra* note 12, at 563, 568.

48. *Id.* at 568.

49. Kristin Connarn, *Section 103(b): Obviously Unnecessary?* 5 J. HIGH TECH. L.

Diagnostic biotech processes doubly defy traditional doctrinal boundaries: process and composition of matter claims become highly dependent on each other as channels of information, and both process and composition of matter claims become increasingly inseparable from their natural underpinnings. Because the purpose of a diagnostic biotech process is to produce information about the body, diagnostic processes are largely based on natural laws. These processes entail measurement procedures (e.g., calculations, correlations, comparisons) that involve biological materials, which may in turn be valuable primarily for the processes they host. As a result, diagnostic biotech processes and their associated products similarly serve to preempt the use of biological information (e.g., a genetic sequence or correlation) and the compounds that encompass this information (e.g., an isolated gene or expressed protein). As Burk explains, it is not just the embodiment of information but information flow that lies at the core of the web of overlapping claims to diagnostic processes and compositions of matter:

> [S]ince information is encoded as molecular structure, the information is only useful when embodied in such structures, which is to say that, ultimately, no one is really interested in strings of human-readable letters—they are instead interested in what can be done with the structures such letters represent. And that in turn means that by necessity they must be interested in building physical informational structures—the molecules that are the conduit for information transfer . . . The configuration of informational molecules is based upon the interaction with, and so upon the configuration of, precursor molecules. Because such molecular structure is the channel by which information is conveyed, the interaction of macromolecules is the point of interest in biotechnology patenting—and "interactions" should fall formally into the category of processes. But molecular structure defines the parameters for such a process, and structure falls formally into the category of products.[50]

Some commentators have thus raised concerns about the preemptive effects of patent thickets, lack of transparency, and uncertainty in the realm of diagnostic biotech processes.[51] Others

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287, 291 (2005).

50. *Id.* at 587.

51. *See generally* Isabelle Huys et al., *Legal Uncertainty in the Area of Genetic Diagnostic Testing,* 27 NATURE BIOTECH. 903 (2009) (finding, in an analysis of 22

worry about monopolies over vital health information and patent holdouts when diagnostic methods are exclusively licensed.[52]

The interrelated nature of biotech process and composition of matter claims has resulted in the legal entanglement of categorically distinct biotech patent claims despite the (disputed) precedent of *In re Durden*,[53] in which the Federal Circuit held that "each statutory class of claims should be considered independently on its own merits."[54] In practice, a biotech process claim can never truly be separated from the biological materials it implicates, and vice versa. Moreover, the fast pace of technological re-definition of what constitutes a process, due largely to progress in information nanotechnology, has resulted in process patent jurisprudence perennially struggling to keep up with the pace of innovation. At the same time, the relatively abstract nature of processes (as compared to compositions of matter) has prompted more inquiry into the subject-matter eligibility of process patents.

B. Early Jurisprudence Concerning Chemical Processes and Compounds

While patent claims on chemical compounds do not usually raise doctrinal issues related to the preemption of natural phenomena because they do not seek to imitate biology, cases concerning chemical compounds illustrate an early pattern of entangling the analysis of claims to processes and compositions of matter. In *In re Papesch*, the U.S. Court of Customs and Patent Appeals (CCPA) stated "a chemical compound and all of its properties are inseparable.[55] And, as the Federal Circuit explained in *In re Dillon*, it was the long-standing practice of the CCPA to join analyzing chemical structures and properties in determining the patentability

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common genetic tests, that the precise scope of claims is often ambiguous).

52. "[T]he Secretary's Advisory Committee on Genetics, Health and Society expressed concern that 'patenting and exclusive licensing practices might have limited the availability and quality of [patented genetic] tests' . . . [and] that patents for genetic tests may lead to 'hold-outs,' where 'a single entity holding critical technology may refuse to license or may charge what others regard as unfair or disproportional fees even though it holds only one technology of many needed for a clinically useful test.'" Margaret Kubick, *An Uncertain Future: The Impact of Medical Process and Diagnostic Method Patents on Healthcare in the United States,* 9 NW. J. TECH. & INTEL. PROP. 280, 295 (2010); *see also* Robert Cook-Deegan & C. Heaney, *Gene Patents and Licensing: Case Studies Prepared for the Secretary's Advisory Committee on Genetics, Health, and Society,* 12 GENETIC MED. S1 (2010).

53. *See In re* Ochiai, 71 F.3d 1565, 1572 (1995) (citing *In re* Dillon, 919 F.2d 688, 695 (Fed. Cir. 1990)).

54. *In re* Durden, 763 F.2d 1406, 1410 (Fed. Cir. 1985).

55. *In re* Papesch, 315 F.2d 381 (CCPA 1963).

of chemical compounds.[56]

In 1966, the Supreme Court considered the relationship between chemical processes and their output. In *Brenner v. Manson,* the Court was asked to review the rejection of a chemical process patent with an output of undefined utility. The Court upheld the rejection, explaining "a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute."[57] Due to the Court's conclusion that a process lacked utility if its end product lacked the requisite utility, commentators noted that "this reasoning fail[ed] to maintain the conceptual separation of invention between product and process."[58] However, this apparent conflation was not unintentional. On the contrary, the Court recognized a strong rationale for consistency in the patent rules applying equally to process and product patents when they cover essentially the same subject matter, holding that a process could not be patented if what it produced was not patentable.[59] Finding itself in a position where the appropriate rule governing patentability was directed at products rather than processes, the Court nevertheless sought guidance in the spirit of the law.

Similarly, in *Application of Lunsford,* the CCPA stated: "[W]e have frequently found novel chemical processes producing the same product, but in unexpectedly higher yields, to be patentable by reason of that yield, a 'matter of degree.' Should not chemical products, also displaying an unexpectedly higher degree of effectiveness, be treated in like manner?"[60] The Federal Circuit later attempted to address this and analogous questions in a string of cases concerning naturally occurring compounds,[61] noting that often in

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56. *In re* Dillon, 919 F.2d 688, 703 (Fed. Cir. 1990).

57. Brenner v. Manson, 383 U.S. 519, 534 (1966).

58. Burk, *supra* note 12, at 579.

59. "We find absolutely no warrant for the proposition that although Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing, a different set of rules was meant to apply to the process which yielded the unpatentable product. That proposition seems to us little more than an attempt to evade the impact of the rules, which concededly govern patentability of the product itself." *Brenner*, 383 U.S. at 535.

60. *In re* Lunsford, 357 F.2d 380, 384 (C.C.P.A. 1966).

61. In considering the patentability of a chemical process in *In re Durden*, the Federal Circuit stated that "a new process may still be obvious, even when considered 'as a whole,' notwithstanding the specific starting material or resulting product, or both, is not to be found in the prior art." *In re* Durden, 763 F.2d 1406, 1410 (Fed. Cir. 1985). In considering the patentability of a chemical product in *In re*

such cases, "the compounds and their use are but different aspects of, or ways of looking at, the same invention and consequently that invention is capable of being claimed both as new compounds or as a new method or process."[62] Nevertheless, the Federal Circuit was clear that these cases did not produce rigid rules, but rather per se rules that were highly context-dependent.[63]

C. Issues Raised by Statutory Amendments in the Late Twentieth Century

In 1988, the Process Patent Amendment Act (PPAA) further narrowed the divide between process and product patents by assigning process patent holders the right to exclude imported products made by their patented process outside the U.S.[64] The PPAA prompted a string of lawsuits in which biotech process patent holders sued foreign entities for having used their patented processes outside of the U.S. to manufacture and import to the U.S. the products of these processes.[65] At the core of these cases was the question of how biotech products—which, as cells and compounds, were "essentially bags of chemical processes"—should be interpreted under the PPAA.[66] The Federal Circuit ultimately adhered to a broad definition of process, allowing the PPAA to cover those outputs that were twice removed from the original process.[67] On the other hand, when faced with the corresponding question of whether the PPAA protected against the importation of "purely informational 'products" developed outside the U.S. using a patented process, the Federal Circuit adhered to a narrow definition of product as a "manufacture."[68]

Pleuddemann, the Federal Circuit explained that "[w]hen a new and useful compound or group of compounds is invented or discovered having a *particular use* it is often the case that what is really a single invention may be viewed legally as having three or more different aspects permitting it to be claimed in different ways, for example: (1) the compounds themselves; (2) the method or process of making the compounds; and (3) the method or process *of using* the compounds for their intended purpose. 910 F.2d 823, 825-26 (Fed. Cir. 1990).

62. *Pleuddemann*, 910 F.2d at 827.

63. Connarn, *supra* note 49, at 296.

64. Omnibus Trade and Competitiveness Act of 1988, Pub. L. No. 100-418, §§ 9001-07, 102 Stat. 1107, 1563-67 (codified as amended at 35 U.S.C. §§ 154, 271, 287 (1988)).

65. Amgen, Inc. v. U.S. Int'l Trade Comm'n, 902 F.2d 1532, 1533 (Fed. Cir. 1990); Bio-Tech. Gen. Corp. v. Genentech, Inc., 80 F.3d 1553, 1556 (Fed. Cir. 1996).

66. Burk, *supra* note 12, at 573.

67. *See, e.g.*, *Bio-Tech.*, 80 F.3d at 1556 (finding that human growth hormone (hGH) was a product covered by patented process used to make the plasmids necessary for the production of the hGH).

68. Bayer AG v. Housey Pharms., Inc., 340 F.3d 1367 (Fed. Cir. 2003).

In his pioneering assessment of the problem of biotechnologies as channels of information that straddle the boundaries between process and composition of matter patents, Burk traces how the muddled biotech process-product distinction replete in these offshore infringement cases trickled into domestic infringement cases concerning obviousness and utility.[69] Early obviousness cases concerning renovated processes yielded a seemingly straightforward outcome: processes were generally deemed un-patentable if the end product was patentable but the starting material was not, whereas processes were generally deemed patentable if the end product was not patentable but the starting material was.[70] While the outcomes of these cases could be more or less squared with each other, they inconsistently bifurcated the novelty and non-obviousness inquiries when dealing with comparable combinations of process and product claims.[71] In any case, they did not offer much clarity for biotech claims that were characterized by the ambiguous informational correspondence between DNA, amino acid sequences, and the proteins they encode.[72]

In 1995, the Biotechnology Process Patent Act (BPPA) amended 35 U.S.C. § 103 in an attempt to provide some certainty concerning how to navigate the boundary-defying interactions between biotech process and product claims.[73] The amendment established that non-obvious biotech processes, regardless of other precedent concerning subject-matter eligibility, are patentable if they produce a non-obvious product subject to "timely election."[74] Shortly after passage of the BPPA, though, the Federal Circuit issued several opinions that ultimately rendered the amendment obsolete by upholding the primacy of per se rules for biotech patents, which offered far more flexibility for the various degrees of association between processes and compositions of matter.[75] By carving out a narrow solution, the BPPA failed to foresee the various iterations of associated product and process claims which could be exposed to additional grounds for

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69. *See generally* Burk, *supra* note 12.

70. *Id.* at 573.

71. *Id.* at 574.

72. In *In re* Bell, the Federal Circuit reversed the PTO's determination that "amino acid sequence of a protein in conjunction with a reference indicating a general method of cloning renders the gene *prima facie* obvious." *See In re* Bell, 991 F.2d 781, 783 (Fed. Cir. 1993).

73. Act of Nov. 1, 1995, Pub. L. No. 104-41, § 1, 109 Stat. 351, 351 (codified as amended at 35 U.S.C. § 103 (2006, repealed 2011)).

74. *Id.*

75. Connarn, *supra* note 49 at 296 (citing *In re* Ochiai, 71 F.3d 1565 (1995); *In re* Brouwer, 77 F.3d 422 (1996); *In re* Deuel, 51 F.3d 1552, 1559 (1995)).

invalidity challenges if they relied solely on § 103(b).[76] Connarn points out that the "PTO even published a notice stating that the use of § 103(b) should be rare," and that § 103(b) "has never been mentioned in any judicial or administrative decisions."[77] The BPPA was ultimately repealed in 2011 with the America Invents Act,[78] but its legacy, as an attempt to simplify the increasingly confusing realm of biotech process patents, survives as an undercurrent to today's uncertainties regarding the scope of patentable subject matter limitations for the quickly evolving biotech industry.

III. SUBJECT-MATTER ELIGIBILITY AND THE NATURAL PHENOMENON DOCTRINE

A. The Federal Circuit's approach to subject-matter eligibility

The Federal Circuit's chemical compound cases suggested that process patents interlaced with separately patentable products defy doctrinal clarity and therefore require context-specific analysis. In this spirit, when faced with new technologies that did not fit neatly into process patent rules, the CCPA and Federal Circuit developed and refined analytical approaches to evaluate the subject-matter eligibility of process claims. Particularly short-lived tests included the technological arts test (which stated that methods—particularly business methods—were patentable to the extent that they claimed uses of computers or other electronic devices)[79] and the Freeman-Walter-Abele test (which stated that a mathematical algorithm was patentable if limited by physical elements or process steps as long as these elements or steps amounted to more than post-solution activity).[80] However a utility test introduced by the Federal Circuit in 1998 substantially broadened the patentability standards for processes.[81] As Ghosh documents, by 2006, "patents on diagnostic processes and isolated natural products were being routinely granted."[82] This facilitated a proliferation of medical process patents and infringement lawsuits, which gradually helped refine the

76. *Id.* at 299.
77. *Id.* at 301.
78. America Invents Act, Pub. L. 112-29 (2011).
79. *See, e.g., In re* Musgrave, 431 F.2d 882, 893 (C.C.P.A. 1970).
80. *See In re* Freeman, 573 F.2d 1237 (C.C.P.A. 1978); *In re* Walter, 618 F.2d 758 (C.C.P.A. 1980); *In re* Abele, 684 F.2d 902 (C.C.P.A. 1982).
81. State St. Bank & Trust Co. v. Signature Fin. Grp., 149 F.3d 1368, 1377 (Fed. Cir. 1998).
82. Samantak Ghosh, *Prometheus and the Natural Phenomenon Doctrine: Let's Not Lose Sight of the Forest for the Trees*, 94 J. PAT. & TRADEMARK OFF. SOC'Y 330, 336 (2012).

contours of process patentability standards, especially as related to biotechnology.

Faced with validity challenges to new technologies, the Federal Circuit—rather than considering the subject-matter eligibility of biotech process and product claims resembling natural phenomena—adapted its analytical tests to fit the changing contours of the biotech patents,. One of the key precedent-setting challenges to biotech patents arose in 2005 in a case concerning the patentability of expressed sequence tags (ESTs), short cDNA transcripts for identifying nucleic acid sequences in maize genes. In *In re Fisher*, the Federal Circuit held that a "laundry list" of research applications could not impart sufficient § 101 utility on the ESTs in the absence of any indication of "the precise structure or function of either the genes or the proteins encoded for by those [maize] genes."[83] Even though *Fisher* concerned a composition of matter, the Federal Circuit applied *Brenner*, which dealt with a process patent, and concluded that the listed research processes did not fulfill a requirement of specific utility because the utility of their outputs was unclear.[84] In *In re Kubin,* the Federal Circuit—again without addressing § 101 subject-matter eligibility—usefully disentangled some confusion concerning the impact of prior art processes on genetic sequence claims.[85] Without considering whether or not Kubin's application for a patent on an isolated DNA sequence constituted a product of nature, the court invalidated the patent as obvious, explaining that "the claimed invention was reasonably expected in light of the prior art and 'obvious to try.'"[86]

The Federal Circuit alluded to a § 101 eligibility issue in *King Pharmaceuticals v. Eon Lab*s, in which it held that an "otherwise anticipated" diagnostic claim does not become patentable simply "because it includes a step of 'informing' someone about the

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83. "The '643 application generally discloses that the five claimed ESTs may be used in a variety of ways, including: (1) serving as a molecular marker for mapping the entire maize genome, which consists of ten chromosomes that collectively encompass roughly 50,000 genes; (2) measuring the level of mRNA in a tissue sample via microarray technology to provide information about gene expression; (3) providing a source for primers for use in the polymerase chain reaction ("PCR") process to enable rapid and inexpensive duplication of specific genes; (4) identifying the presence or absence of a polymorphism; (5) isolating promoters via chromosome walking; (6) controlling protein expression; and (7) locating genetic molecules of other plants and organisms." *In re* Fisher, 421 F.3d 1365, 1368, 1370 (Fed. Cir. 2005).

84. *Id.* at 1370 (citing Brenner v. Manson, 383 U.S. 519, 529 (1966)).

85. 561 F.3d 1351 (Fed. Cir. 2009).

86. *Id.* at 1361 (citing *In re* O'Farrell, 853 F. 2d 894, 904 (1988)).

existence of an inherent property of that method."[87] While noting that such a claim may constitute an abstract idea, the court stated that "[t]he present case, however, does not present the proper vehicle for determining whether claims covering medical treatment methods are eligible for patenting under § 101 because even if claim 21 recites patent eligible subject matter, that subject matter is anticipated for the reasons discussed below."[88] In one sense, *King*'s reasoning was reminiscent of *Ex parte* Brinkeroff's distaste for patenting modes of informing patients of a possible outcome, although it did not go so far as to prohibit claims including an "informing" step, merely holding that such a step could not itself impart patentability.[89] Again, though, the Federal Circuit's flexibility in tailoring its analysis to the technology in question precluded the need for broader inquiry into the subject-matter eligibility of these overlapping process and product claims.

B. Evolution of the Natural Phenomenon Doctrine in The Supreme Court

Unlike the patent-entrenched Federal Circuit, which has to continuously adapt and respond to the demands of changing technologies, the Supreme Court has a long history of assessing new process patent questions through the theoretical lens of § 101 subject-matter eligibility. When confronted with challenges to patents in emerging fields of technology, the Court has far more often invoked the natural phenomenon doctrine, and it has done so with little regard for doctrinal distinctions between processes and products. Derived from English common law,[90] the natural phenomenon doctrine has been reaffirmed several times by the Court as necessary to avoid unwarranted preemption of research and innovation resulting from the monopolization of basic scientific tools, namely, laws of nature, products of nature, and abstract ideas.[91]

In the earliest of these cases, *O'Reilly v. Morse*, a patent on the telegraph was upheld even though it claimed the natural phenomenon of using electromagnetism as a motive power, because this was "combined with, and passed through, and operate[d] upon, certain complicated and delicate machinery, adjusted and arranged

87. King Pharms. v. Eon Labs, 616 F.3d 1267, 1278 (Fed. Cir. 2010).
88. *Id.*
89. *Id.* at 1278-79.
90. *See, e.g.*, Le Roy v. Tatham, 55 U.S. 156, 175 (1852).
91. *See* Diamond v. Diehr, 450 U.S. 175, 185 (1981); *see also* Bilski v. Kappos, 130 S. Ct. 3218, 3238-39, 3253 (2010).

upon philosophical principles, and prepared by the highest mechanical skill."[92] Similarly, in *Le Roy v. Tatham*, the Court upheld the patentability of the discovery that lead would reunite perfectly after separation under certain conditions, explaining that "[t]he principle may be the new and valuable discovery, but the practical application of it to some useful purpose is the test of its value," and thus, inventiveness.[93] In *Mackay Radio & Telegraph Co. v. Radio Corp. of America*, the Court relied on the natural phenomenon doctrine to narrowly construe a patent claim, limiting its scope to its specific inventive application of a scientific formula for wavelength positioning in antennae.[94] While these cases help illustrate the Court's early precedent concerning the natural phenomenon doctrine, they stopped short of explaining its underlying rationale, because it was not ultimately found to control the questions at bar.

In 1948 the Supreme Court had the occasion to provide a more explicit basis for the natural phenomenon doctrine. In *Funk Bros. Seed v. Kalo Inoculant,* the Court invalidated a patent claim on a mixed culture of bacterial strains chosen for their ability to convert environmental nitrogen into a usable form without adversely affecting the effectiveness of the mixture's other strains of bacteria.[95] While the patent claims in *Funk Bros.* concerned a composition of matter, they effectively preempted the process of using several complementary bacterial strains to promote the useful conversion of nitrogen. In its decision, the Court explained that "[t]he qualities of these bacteria, like . . . the qualities of metals, are part of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men and reserved exclusively to none," and that their combination was nothing more than a basic application in the form of packaging.[96] Even though the new combination of bacterial strains held significant advantages over the individual strains found in nature, the constituent parts of the invention ultimately did little more than "serve the ends nature originally provided and act quite

92. 56 U.S. 62, 117 (1853).
93. 63 U.S. 132, 137 (1859).
94. "While a scientific truth, or the mathematical expression of it, is not patentable invention, a novel and useful structure created with the aid of knowledge of scientific truth may be. But . . . [w]e assume, without deciding the point, that this advance was invention even though it was achieved by the logical application of a known scientific law to a familiar type of antenna. But it is apparent that if this assumption is correct the invention was a narrow one . . . ." Mackay Radio & Tel. Co. v. Radio Corp. of Am., 306 U.S. 86, 94 (1939).
95. 333 U.S. 127 (1948).
96. *Id.* at 130.

independently of any effort of the patentee."[97] To some extent, *Funk Bros.* left courts with some flexibility in defining to what extent a natural phenomenon's use would have to be "dependent" on the handiwork of the inventor in order to be patentable. This inquiry turns out to be critical for diagnostic biotech processes, which also harness natural phenomena to more efficiently undertake reactions that might not be observed as a whole in nature, although each constituent part acts as it would in nature when interacting with other parts of the process.

The next few times the Supreme Court invoked the natural phenomenon doctrine, it did not hesitate to interchangeably apply precedent concerning product claims to process claims, and later on, vice versa. In *Gottschalk v. Benson*, the Court rejected a patent on an algorithm for binary conversion, explaining that "mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work."[98] The Court cited *Funk Bros.* in support of this rule, acknowledging as an aside that although it "dealt there with a 'product' claim, while the present case deals with a 'process' claim . . . the same principle applies."[99] Because the algorithm in question had "no substantial practical application except in connection with a digital computer," the Court found that upholding its patent "would wholly pre-empt the mathematical formula and in practical effect would be a patent on the algorithm itself."[100] The Court likened the claimed process to a law of nature and thus invalidated it, albeit stopping short of finding that the individual claims themselves merely embodied laws of nature.[101]

Similarly, in *Parker v. Flook*, the Court invalidated a patent on a method for updating alarm limits during catalytic conversion by means of a mathematical algorithm.[102] Because all the non-formulaic elements of the patent claims were not novel, the patentability inquiry focused on the application of the independently unpatentable formula. The Court explained that *Mackay Radio* and *Funk Bros.* governed even though those cases concerned product patents, thereby "foreclos[ing] a purely literal reading of § 101,"[103] and emphasizing that "[t]he underlying notion is that a scientific

97. *Id.* at 131.
98. 409 U.S. 63, 67 (1972).
99. *Id.* at 67-68.
100. *Id.* at 71-72.
101. *Id.* at 67.
102. Parker v. Flook, 437 U.S. 584 (1978).
103. *Id.* at 589.

principle . . . reveals a relationship that has always existed."[104] The Court held that "[t]he process itself, not merely the mathematical algorithm, must be new and useful"; as a law of nature, the formula could only be patented via an inventive application of it.[105] Notwithstanding the novelty of applying the formula to the particular process of calculating alarm limit values, the Court found that such an application was not sufficiently novel, as its effect on the alarm limits was limited to the effect of the equation. Considering the preemptive effect of allowing the patent to stand, the Court explained that even though the claims did not "cover every conceivable application of the formula,"[106] these "post-solution" applications could not "transform an unpatentable principle into a patentable process."[107] As in *Benson*, the Court's interpretation of the natural phenomenon doctrine to preclude patentability in this case was not self-evident, and it was accompanied by a harsh dissent. However, the Court explained that it was wary of unprecedentedly expanding the scope of patentable subject matter.[108]

The Supreme Court retreated somewhat from its approach in *Flook* in *Diamond v. Diehr*. Explaining that patentability should be assessed as a whole rather than in parts, the Court upheld the patentability of a rubber curing process involving a thermodynamic equation.[109] Surviving a natural phenomenon analysis, the process patent was deemed valid because it did not simply apply a natural principle to a specific context, wherein "insignificant post-solution activity [would] not transform an unpatentable principle into a patentable process" (as was the case in *Flook*); it was also tied to a rubber-curing machine, and therefore only sought to "pre-empt the use of that equation . . . in conjunction with all of the other steps."[110] The outcome in *Diehr* differed from that in *Flook* only because the anchoring structure itself in *Diehr* passed the test for novelty, thereby limiting the scope of unwarranted preemption. As Hodes explains, "[n]arrowing the scope of the method patent by coupling it to a

104. *Id.* at 593 n.15; *In re* Nuijten, 500 F.3d 1346, 1364 (Fed. Cir. 2007) (Linn, J., concurring in part and dissenting in part) (adding that "[t]his insight . . . is at the core of the judicial doctrine by which laws of nature, natural phenomena, and abstract ideas are excluded from patentable subject matter.").

105. *Flook,* 437 U.S. at 591.

106. *Id.* at 586.

107. *Id.* at 590.

108. *Id.* at 596 ("It is our duty to construe the patent statutes as they now read, in light of our prior precedents, and we must proceed cautiously when we are asked to extend patent rights into areas wholly unforeseen by Congress.").

109. Diamond v. Diehr, 450 U.S. 175, 176 (1981).

110. *Id.* at 187, 191-93.

specific 'structure or process' within the scope of patent-eligible subject matter minimized the danger that patents would cover pure knowledge of the world and hinder harvesting the fruits of such knowledge."[111]

In 2006, the Supreme Court granted cert in *Laboratory Corp. v. Metabolite*,[112] a case about the patentability of a natural correlation, but ultimately dismissed the petition as improvidently granted.[113] It is speculated that the Court dismissed the petition because the issue of patentable subject matter raised on appeal was not properly argued in the lower courts.[114] The dismissal was somewhat remarkable because, by this time, the quickly growing biotech industry was eager for certainty regarding the strength of diagnostic process patents. Upheld by the Federal Circuit, *LabCorp* concerned a patented process of diagnosing vitamin deficiencies by measuring homocysteine levels in the blood through a correlation with B vitamins using any homocysteine-specific testing method.[115] Laboratory Corporation was held liable for inducing infringement by encouraging doctors to order tests for measuring homocysteine, and it was enjoined from using homocysteine-only tests to detect vitamin deficiency.[116] In its appeal to the Supreme Court, Laboratory Corporation argued that the diagnostic correlations, as laws of nature, were not patentable under the natural phenomenon doctrine's exception to § 101.[117] In response, Metabolite argued that overturning the patentability of correlations between disease states and biomarkers could have far-reaching negative effects, including the invalidation of all drug patents, as such patents merely discover certain chemical interactions in the body.[118] These concerns, however, were likely unfounded; chemical processes and products differ significantly from their biochemical counterparts because they generally correlate and interact with biology rather than replicate and imitate biology. Three justices dissented to the Court's dismissal, with Justice Breyer rejecting the *State Street Bank* utility test and calling for a weaker machine-or-transformation test (discussed in the

111. Hodes, *supra* note 16, at 227-28.
112. 548 U.S. 124 (2006) [hereinafter *Labcorp*].
113. *Id*, at 125.
114. Hodes, *supra* note 16, at 230-31.
115. Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings, 370 F.3d 1354 (Fed. Cir. 2004).
116. *Id.*
117. Reply Brief for Petitioner at 1, *LabCorp*, 548 U.S. 124 (No. 04-607).
118. Brief for Respondents at 46, *LabCorp*, 548 U.S. 124 (No. 04-607).

following section).[119] Justice Breyer explained that the mere transformation of a blood sample, which was not the focus of the patent's diagnostic correlation claims, did not render the claims subject-matter eligible.[120] Notably, he expressed concern about the preemptive scope of diagnostic process patents that could serve as barriers to physicians' ability to freely and efficiently exercise their best medical judgment, unencumbered by licensing arrangements and patent searches that would raise the cost of health care.[121] Importantly, Justice Breyer noted that "[p]atent law seeks to avoid the dangers of overprotection just as surely as it seeks to avoid the diminished incentive to invent that underprotection can threaten,"[122] emphasizing the relevance of the scope of preemption of scientific principles.

C. Subject-Matter Eligibility Revisited by The Federal Circuit

Two years later, with *In re Bilski,* the Federal Circuit reconsidered the dominant test for patent-eligible subject matter in a case concerning business methods. In striking down a patent on a business method as an abstract idea, the Federal Circuit held that the machine-or-transformation (M-o-T) test was the ultimate test for process claim subject-matter eligibility under § 101.[123] The M-o-T test, derived from nineteenth century common law, deemed patentable any process that either involves a patented machine (e.g., device, apparatus, or computer) or significantly transforms an article from one state to another, and in doing so attempts to distinguish monopolies on fundamental principles from monopolies on applications of fundamental principles.[124] The Supreme Court considered the M-o-T test in *Bilski v. Kappos*, noting that several amicus briefs shared a concern that continued reliance on the M-o-T test would increase uncertainty, particularly "as to the patentability of software, [and] advanced diagnostic medicine techniques."[125] In *Bilski v. Kappos*, the Supreme Court upheld the outcome of *In re*

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119. *Infra* Part III.C.

120. Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc., 548 U.S. 124, 135-36 (2006) (Breyer, J., dissenting).

121. *Id.* at 138.

122. *Id.* at 127.

123. *In re* Bilski, 545 F.3d 943, 956 (Fed. Cir. 2008) (en banc), *aff'd sub nom.* Bilski v. Kappos, 130 S. Ct. 3218 (2010).

124. *See id.* at 971-72.

125. *Bilski*, 130 S. Ct. at 3227 (citing Brief for Business Software Alliance 24–25; Brief for Biotech. Industry Org. et al. 14–27; Brief for Boston Patent Law Ass'n 8–15; Brief for Houston Intellectual Property Law Ass'n 17–22; Brief for Dolby Labs., Inc., et al. 9–10).

Bilski, but clarified that the M-o-T test was merely one analytical approach to subject-matter eligibility that should be understood as "a useful and important clue, an investigative tool, for determining whether some claimed inventions are processes under § 101."[126] By relegating the M-o-T test to be just one of several considerations, *Kappos* both broadened subject-matter eligibility (by removing the strict requirement for a machine or transformation) and narrowed it (by establishing that the presence of a machine or transformation was no longer sufficient).[127] At the same time, *Kappos* reaffirmed the distinction between the subject-matter eligibility threshold (in determining whether or not something qualifies as a process), and the other statutory requirements of patentability, a distinction that is easily muddled when patentability requirements can be calibrated to have the same limiting effect as subject-matter eligibility standards. Interestingly, Justice Stevens' concurrence in *Kappos* intimated that the natural phenomenon doctrine might apply beyond exact replicas of nature[128]

While tempering the Federal Circuit's reliance on the M-o-T test, the Supreme Court noted that its opinion should not "be read as endorsing the Federal Circuit's past interpretations of § 101,"[129] Indeed, as the Federal Circuit has dealt with the changing pace of technological innovation by creating short-lived tests suitable for determining the questions at hand, the Supreme Court has generally not adopted these tests as controlling law. Rather, on several notable occasions, it has tempered the role of these tests via the "catch-all" natural phenomenon doctrine's ambiguous but flexible contours for fast-changing technology.[130] The Federal Circuit sorted out some of the implications of Kappos for biotechnology with *Classen Immunotherapies, Inc. v. Biogen IDEC*, which the Supreme Court

126. *See, e.g.*, *id.*

127. For an analysis of how the machine-or-transformation test can be usefully supplemented by earlier judicial tests, *see* Jennifer L. Davis, *Patent Law – Patentability Post-Bilski: No Need to Throw the Baby out with the Bath Water when Determining Subject Matter Eligibility Under 35 U.S.C. § 101*, 34 U. ARK. LITTLE ROCK L. REV. 421 (2012).

128. *Bilski*, 130 S.Ct. at 3238-39 (Stevens, Ginsburg, Breyer, and Sotomayor, J.J., concurring) ("The Court also accepts that we have 'foreclose[d] a purely literal reading of § 101,' *Flook, . . .* by holding that claims that are close to 'laws of nature, natural phenomena, and abstract ideas,' *Diamond v. Diehr, . . .* do not count as 'processes' under § 101, even if they can be colloquially described as such.").

129. *Id.* at 3222 (majority opinion).

130. *See* Rebecca S. Eisenberg, *Wisdom of the Ages or Dead-Hand Control? Patentable Subject Matter for Diagnostic Methods After In re* Bilski, 3 CASE W. RES. J.L. TECH. & INTERNET 1, 4-5 (2012), *cited in* Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1304 (2012).

remanded to be reconsidered in light of *Kappos*.[131] *Classen* concerned a patent on a general process for determining ideal immunization schedules, which the Federal Circuit had previously found failed the M-o-T test. The Federal Circuit reversed its position and upheld the subject-matter eligibility of two claims that were "directed to a specific, tangible application"—because they claimed "a method of lowering the risk of chronic immune-mediated disorder, including the physical step of immunization on the determined schedule"—but rejected the patent eligibility of a third claim which, in the absence of a physical immunization step, was merely an "abstract principle that variation in immunization schedules may have consequences for certain diseases."[132]

Not surprisingly, the confines of what is considered to be a natural phenomenon are inherently hazy.[133] Nevertheless, the natural phenomenon doctrine can be an important safeguard to functionally overlapping patent claims that unreasonably preempt the use of natural phenomena, as the jurisprudence surrounding the doctrine has developed interchangeably between product and process claims. Because the Supreme Court is far less involved in the continuous doctrinal recalibration needed to adjust to new technologies, it "has used the doctrine to expand and contract the scope of patentability in response to the changes in technology and socio-economic factors."[134] By reflecting the spirit of the law, patentable subject matter rules can be particularly useful for assessing patents covering relatively new technologies that may not fit neatly into existing analytical frameworks. If they are well-defined, "[p]atentable subject matter boundaries can help to minimize uniformity costs by limiting

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131. Classen Immunotherapies, Inc. v. Biogen IDEC, 659 F. 3d 1057, 1067 (2011).

132. *Id.* at 1066-67. Hodes explains that controversy surrounding the possible presence of a substantively valid transformation in the claims might have been usefully expounded in *LabCorp* with relevance to the natural phenomenon doctrine: "Several commentators have noted that vaccinations transform a patient by conferring immunity. However, the Classen vaccination step is not performed on an actual patient to protect him or her from a specific disease. Instead it is performed on a generic research subject. Indeed, the Classen patent appears to claim merely the performance of a controlled experiment in the field of minimizing vaccine-induced autoimmune reactions. Thus, the Classen transformation might be judged ancillary, insignificant, extra-solution activity. This centrality standard might serve to distinguish processes that produce a direct patient benefit from those that are research tools." Hodes, *supra* note 16 at 232.

133. Ghosh, *supra* note 82, at 333 (quoting Richard Seth Gipstein, *The Isolation and Purification Exception to the General Unpatentability of Products of Nature*, 4 COLUM. SCI. & TECH. L. REV. 2, 3 (2003)) ("Since the precise foundation of the natural phenomenon doctrine 'remains somewhat ambiguous [it] leaves the limits of the doctrine lacking proper delineation' causing much confusion.").

134. Ghosh, *supra* note 82, at 332.

the diversity of innovations that patent law covers, thus making it easier to achieve a more optimal level of protection for a narrower range of innovations."[135] Moreover, to the extent that it can serve the purpose of avoiding unwarranted preemption, the natural phenomenon doctrine substantially reflects the utilitarian theory of intellectual property,[136] which the Court cited in *Kappos* while considering the constitutionally mandated purpose of the patent system.[137]

Because the Supreme Court has applied the rationale for the natural phenomenon doctrine to processes and products alike, it appears highly compatible with some of the issues raised by diagnostic biotech patents. Diagnostic biotechnology is still a relatively new area characterized by special challenges that arise in assessing the extent to which a patentee has manipulated natural processes at the core of diagnostic innovations. In this realm, the undeniable relationship between information and biology makes a compelling case for reliance on the natural phenomenon doctrine. Because biotechnology inevitably defies traditional categories, the catch-all nature of the natural phenomenon doctrine renders it suitable for pressing subject-matter eligibility questions that remain unanswered.

IV. *MAYO*, *MYRIAD* AND THE WAY FORWARD

A. Mayo Collaborative Services v. Prometheus Laboratories, Inc.

Last year, in *Mayo v. Prometheus*, the Supreme Court used the natural phenomenon doctrine to bar the subject-matter eligibility of natural correlations used in a diagnostic process. Responding to the Federal Circuit's continued reliance on the M-o-T test in spite of *Kappos*, the Court clarified that the natural phenomenon doctrine always trumps the M-o-T test.[138] The Court invalidated Prometheus's patent on a diagnostic method that involved administering thiopurines and observing chemical reactions in the body as a basis for dosing advice, stating that the patent improperly claimed a natural law. The claimed natural laws could not rise to the level of patentable subject matter by being limited to a particular

135. Eisenberg, *supra* note 130, at 48.

136. *See, e.g.*, David S. Olson, *Taking the Utilitarian Basis for Patent Law Seriously: The Case for Restricting Patentable Subject Matter*, 82 TEMP. L. REV. 1 (2009).

137. Bilski v. Kappos, 130 S. Ct. 3218, 3254 (2010) (citing *Id.)*.

138. Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1303 (2012).

technological environment or by "simply appending conventional steps, specified at a high level of generality, to laws of nature, natural phenomena, and abstract ideas."[139] Echoing *Flook*,[140] Justice Breyer explained that "a bright-line prohibition against patenting laws of nature, mathematical formulas and the like . . . serves as a somewhat more easily administered proxy for the underlying 'building-block' concern," noting that "the underlying functional concern here is a *relative* one: how much future innovation is foreclosed relative to the contribution of the inventor."[141] Justice Breyer explained that the danger of process patents tying up future innovation becomes acute when a patent "forecloses more future invention than the underlying discovery could reasonably justify."[142]

According to amicus briefs filed in an earlier appeal, Prometheus's overly broad patent—like the Pallin patent that led to the Physician's Immunity Statute—would have increased healthcare costs and decreased treatment effectiveness by interfering with physicians' ability "to make informed treatment decisions based on the latest scientific knowledge."[143] The Court weighed this and other concerns regarding preemption of future personalized medicine research against concerns about disincentivizing biotech and diagnostic research. Building on the arguments laid out in his dissenting opinion in *LabCorp*, Justice Breyer explained that the process claim—especially the "highly general" step instructing physicians to "determine" metabolite levels—would "threaten to inhibit the development of more refined treatment recommendations that combine Prometheus'[s] correlations with later discovered features of the metabolites, human physiology or individual patient characteristics," while leaving unanswered the question of "whether, from a policy perspective, increased protection for discoveries of diagnostic laws of nature is desirable."[144] The AMA welcomed the decision by stating that it prevented harm to patient care by protecting the availability of "critical scientific data" necessary for "sound patient care and innovative medical research."[145] In a way,

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139. *Id.* at 1292.
140. Parker v. Flook, 437 U.S. 584, 593 (1978).
141. *Mayo*, 132 S. Ct. at 1303.
142. *Id.* at 1301.
143. Margaret Kubick, *An Uncertain Future: The Impact of Medical Process and Diagnostic Method Patents on Healthcare in the United States,* 9 NW. J. TECH. & INTELL. PROP. 280, 290 (2010) (quoting Corrected Amici Curiae Brief for the Am. Coll. of Med. Genetics et al. in Support of Defendants-Appellees at 9, Prometheus Labs., Inc. v. Mayo Collaborative Servs., 581 F.3d 1336 (Fed. Cir. 2009)).
144. *Mayo,* 132 S. Ct. at 1302, 1305.
145. Am. Med. Ass'n, Statement, AMA Welcomes Supreme Court Decision to

Mayo categorized Prometheus's biotech process patent as a pure process, thereby addressing one of the policy gaps left by the Physician's Immunity Statute.

B. Association for Molecular Pathology v. U.S. Patent and Trademark Office

After issuing its decision in *Mayo*, the Supreme Court remanded *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, to be reconsidered in light of *Mayo*.[146] Prior to *Mayo*, the Federal Circuit had invalidated Myriad's process claims directed at "comparing" and "analyzing" BRCA sequences as unpatentable abstract ideas.[147] What remained valid amongst the challenged claims were one method claim, "a method for screening potential cancer therapeutics," and composition of matter claims covering the isolated gDNA and cDNA sequences for the BRCA1 and BRCA2 genes (mutations of which are correlated with breast and ovarian cancer risk).[148]

In its decision on remand, the Federal Circuit reinstated its original disposition in its entirety.[149] The majority, written by Judge Lourie, explained that Myriad's "composition claims are mere reflections of a law of nature . . . they are not, any more than any product of man reflects and is consistent with a law of nature,"[150] and therefore, *Mayo*'s process patent analysis did "not control the question of patent-eligibility of . . . claims to compositions of matter."[151] Yet, as detailed at length above, this categorical distinction of precedent is hardly a bright line. When the Supreme Court invoked *Funk Bros.* to apply the natural phenomenon doctrine to *Benson,* it clearly stated that for either a process or product, "the same principle applies."[152] As demonstrated in the previous section, this approach generally runs through Supreme Court precedent concerning the natural phenomenon doctrine. Moreover, regardless of whether or not they precisely claim laws or products of nature, Myriad's patents to isolated gDNA and cDNA effectively serve to

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Invalidate Prometheus Patents (Mar. 20, 2012), http://www.ama-assn.org/ama/pub/news/news/2012-03-20-supreme-court-decision-prometheus-patents.page(*quoted by* THOMAS, *supra* note 5, at 10) (original source no longer accessible).

146. Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office (*AMP v. USPTO*), 132 S. Ct. 1794 (2012).

147. AMP v. USPTO, 653 F.3d 1329, 1354 (2011).

148. AMP v USPTO, 653 F.3d at 1357-58.

149. AMP v. USPTO, 689 F.3d 1303, 1334 (2012).

150. *Id.* at 1331.

151. *Id.* at 1325.

152. Gottschalk v. Benson, 409 U.S. 63, 67-68 (1972).

preempt the use of both naturally occurring compositions of matter (genes) and laws of nature (the information coded for by genetic sequences). In a dissenting opinion to the Federal Circuit's decision, Judge Bryson explained that when a patent "claims a composition of matter that is nearly identical to a product of nature, it is appropriate to ask whether the applicant has done 'enough' to distinguish his alleged invention from the similar product of nature," concluding that Myriad had not made a substantial "inventive contribution" or claimed anything more than a combination of "well-understood, routine, conventional" elements.[153]

The Federal Circuit's holding was again appealed and granted certiorari, this time on the single question of whether or not human genes are patentable.[154] This time, *Mayo*'s suggestion that case law concerning the natural phenomenon doctrine is primarily driven by an avoidance of tying up the basic tools of science, rather than clear categorical exceptions,[155] was found to be relevant to the question of patent-eligibility. In a unanimous ruling (with the exception of some minor concurrences by Justice Scalia on biological explanations), Justice Thomas explained that isolated human gDNA is not patent eligible subject matter under § 101 because it constitutes a law of nature. Specifically, the Court explained that: Myriad did not invent anything by isolating or locating the BRCA1 and BRCA2 genes, but rather identified what already exists in nature; the relevant "patent descriptions simply detail the 'iterative process' of discovery by which Myriad narrowed the possible locations for the gene sequences that it sought;" the claims to isolated gDNA seek to cover the information contained in a genetic sequence rather than chemical compositions themselves; and deference to past USPTO practice was not persuasive in the absence of explicit statutory support for the patentability of isolated gDNA.[156] In contrast, the Court explained that cDNA—with the exception of very short strands free from intervening introns—is patentable because it differs from naturally occurring DNA, which contains both introns and exons.[157]

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153. AMP v. USPTO, 689 F.3d at 1355 (Bryson, J., dissenting).
154. AMP v. USPTO, *rev'd sub nom* Ass'n for Molecular Pathology v. Myriad Genetics, Inc. (Myriad), *cert. granted in part*, 133 S. Ct. 694 (U.S. Nov. 30, 2012) (No. 12-398).
155. Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1292 (2012).
156. Ass'n for Molecular Pathology v. Myriad Genetic, Inc., 133 S. Ct. 2107, 2118.
157. *Id.* at 1119.

C. Re-Envisioning the Natural Phenomenon Doctrine's Preemption Rationale

While Justice Breyer's observation in *Mayo* that "a bright-line prohibition against patenting laws of nature . . . serves as a somewhat more easily administered proxy for the underlying 'building-block' concern"[158] is merely dicta, it suggests that the natural phenomenon doctrine is more concerned with the invention-preemption ratio than categorical limitations. In other words, the doctrine may apply where a physical phenomenon preempts the use of a law of nature, or where an isolated version or a close replica of a physical phenomenon preempts the use of that phenomenon beyond what is warranted by the scope of invention. Along these lines, Yu has argued that perhaps isolated DNA should not be patented simply because it constitutes a source of biological information, even if it is not literally and exactly a physical phenomenon, law of nature or abstract idea. As Yu explains, it is not clear that diagnostic innovations—which essentially look to nature for greater knowledge about the human body and then leverage this knowledge to track and diagnose disease—can be viewed as "inventions" rather than restatements of natural laws.[159] Under this approach, which echoes *Flook* (and, similarly, Justice Stevens' concurrence in *Bilski*), an isolated version or a mirror image of a natural phenomenon—if it embodies naturally occurring information—would not be subject-matter eligible if issuing a patent on it would result in the preemption of all uses of that information.[160]

Such an approach defers to the spirit of the law, which more flexibly reaches those scientific advances that unpredictably redefine how medical technology interacts with nature. As long as the biotech industry is more interested in designing around nature than using nature itself, a literal reading of the natural phenomenon doctrine would render it ineffective in barring monopolies that technically cover imitations of nature but effectively preempt uses of nature itself. Feldman explains how this state of the art, which favors non-naturally occurring phenomena over their naturally occurring counterparts, is embodied in cDNA:

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158. *Mayo*, 132 S. Ct. at 1303.

159. Allen K. Yu, *Within Subject Matter Eligibility – a Disease and a Cure*, 84 S. CAL. L. REV. 387, 401 (2011).

160. The argument against patentability may resound more strongly if a patent claim on an extraction or imitation of a physical phenomenon preempts not only its own use, but also the use of other laws of nature, as plaintiffs claim that Myriad's gene patents do. *See* Reply Brief for Petitioners at 13-17, Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107 (2013) [hereinafter *Myriad*].

> cDNA does not normally exist in the human body, and is naturally created only through the operation of certain retroviruses. Transforming normal DNA into cDNA, however, provides a more efficient tool for researchers and health care professionals who wish to study, diagnose, and treat the disease associated with a gene. In particular, cDNA is tailored to work with bacteria, the organisms commonly used to manipulate human genes and proteins in a laboratory setting. Bacteria do not have the machinery to shorten natural DNA, so we have to create special uninterrupted coding sequences for them. If given an uninterrupted coding sequence, bacteria can translate that sequence into the proper protein. Another advantage of cDNA over natural DNA is that the shorter length makes many laboratory procedures possible that could not be performed effectively with natural, full-length DNA.[161]

While there are a handful of other less efficient applications for naturally occurring gDNA, such as whole genome sequencing, most of these, if used to provide BRCA results, would "inevitably 'isolate' the BRCA1 and BRCA2 genes,"[162] offten creating, at least transitorily, BRCA1 and BRCA2 cDNA in the process.

After *Myriad*, cDNA patents are ideally positioned to nevertheless effectively monopolize the natural phenomena reflected in gDNA sequences. In *Myriad*, the scope of preemption at issue was "the genetic information encoded in the BRCA1 and BRCA2 genes."[163] While this information may be preempted both by patents on isolated gDNA and isolated cDNA, the Supreme Court only found isolated gDNA to fail the subject matter eligibility threshold. Justice Thomas, writing for the Court, explained that the lab technician unquestionably creates something new when cDNA is made."[164] However it is clear that Justice Thomas did not equate "something new" with "something novel," as he qualified the statement by clarifying in a footnote that the Court "express[es] no opinion whether cDNA satisfies the other statutory requirements of patentability."[165] And there are strong arguments that isolated cDNA may fail these requirements. To make isolated cDNA, the isolated

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161. Robin Feldman, *Whose Body Is It Anyway? Human Cells and the Strange Effects of Property and Intellectual Property Law*, 63 STAN. L. REV. 1377, 1388 (2010-2011).
162. Reply Brief for Petitioners, *supra* note 160, at 15.
163. *Myriad*, 133 S. Ct. at, 2109-10.
164. *Id.* at 2110.
165. *Id.* at 2119.

gDNA is merely diluted in a specialized salt water mix, to which primers and a reverse transcriptase are added. A PCR machine then processes the solution after creating amplified cDNA through a process of heating and cooling. This process is well known in the art; here, as with the isolated gDNA, the principle contribution of the inventor is in locating the gene. In *Myriad*, this inventive step, in the absence of any transformation from naturally occurring genes, was found to not be commensurate with the scope of preemption that would result from a patent on the isolated gDNA. While the same conclusion might have been reached with regard to the cDNA, the analysis was not undertaken because, given the transformative step of removing introns, the cDNA did not resemble naturally occurring DNA.

It is important to recognize that claims to cDNA monopolize the same genetic code as isolated gDNA; there is no difference between the *information* monopolized by a patent on isolated gDNA and one on cDNA because they both code for the same thing. To a large extent, the same can be said of process claims involving cDNA and gDNA if they cover the only useful applications of isolated DNA. Reinforcing Justice Thomas's point about monopolizing information rather than molecular structures, Myriad has initiated infringement suits against several companies that have begun producing BRCA1/2 diagnostic tests that purport to use only the isolated gDNA of BRCA 1/2.[166] By maintaining its patent claims on cDNA and processes necessary for using isolated gDNA and cDNA, Myriad can effectively monopolize the same subject matter as it could with the isolated gDNA patents, because both isolated gDNA and cDNA are required for steps in the biotech process of diagnosing genetic susceptibility to breast and ovarian cancer. This feature of biotechnology products—that renders them, primarily and essentially *components* of useful processes—is precisely what justifies a greater focus on the invention-preemption ratio.

Nevertheless, as demonstrated in Part III of this article, patentability requirements can be used to have the same limiting effect as patent eligibility standards.[167] Prior to *Myriad*, it was the long-held practice of the USPTO to grant patents on isolated gDNA.

166. Complaint and Demand for Jury Trial, Univ. of Utah Research Found. v. Ambry Genetics Corp., No. 2:13-cv-00640-RJS (D. Utah July 9, 2013); Complaint and Demand for Jury Trial, Univ. of Utah Research Found. v. Gene by Gene, Ltd., No. 2:13-cv-00643-EJF (D. Utah, July 10, 2013).

167. *See* discussion of *In re Kubin*, *supra* note 87, *King Pharms, Inc. v. Eon Labs, Inc.*, *supra* note 89, and *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, *supra* note 116.

It had been widely believed that because human DNA does not exist in nature in isolated form, isolated gDNA could be patented on the grounds that it is a product of human ingenuity. This view relied on *Parke-Davis & Co. v. H.K. Mulford Co.*, in which Judge Learned Hand found a patent on isolated adrenaline to be valid, noting that the inventor "was the first to make it available for any use by removing it from the other gland-tissue in which it was found, and, while it is of course possible logically to call this a purification of the principle, it became for every practical purpose a new thing commercially and therapeutically."[168] New life was breathed into Judge Learned Hand's conclusion when the Federal Circuit cited it approvingly in finding purified vitamin B-12 to be patent-eligible subject matter.[169] However, as Judge Sweet noted in *Ass'n for Molecular Pathology v. USPTO*, Judge Learned Hand's conclusion about the patentability of purified substances was merely dicta, as the question before him was one of novelty, not subject-matter eligibility.[170] As Harkness points out, the historical reliance on *Parke-Davis* for the assertion that isolated products of nature are patent-eligible subject-matter is fundamentally misguided, because the inventor in that case had already convinced the patent examiner that the isolated compound was physically distinct from the non-isolated one.[171]

Thus, it is still possible that biotech patent standards may be calibrated to appropriately reflect the product-process entanglement of biotech claims. In response to Myriad's infringement suits, allegedly infringing companies can defend themselves by challenging Myriad's patents on cDNA, such as claim 6 of the '282 patent ("An isolated DNA having at least 15 nucleotides of the DNA of claim 2 [which, referencing SEQ ID NO:1, covers cDNA]") on the grounds of novelty or written description. A novelty challenge could take the approach of considering the knowledge about the location and sequence of the BRCA 1/2 genes to be in the prior art. Applying *Diamond v. Diehr*,[172] an alleged infringer of Myriad's cDNA patents could argue that the precise location of the BRCA 1/2, as

168. 189 F. 95, 203 (S.D.N.Y. 1911).
169. Merck & Co. v. Olin Mathieson Chemical Corp., 253 F. 2d 156 (4th Cir. 1958).
170. 702 F. Supp. 2d 181, 224-26 (S.D.N.Y. 2010).
171. Jon M. Harkness, *Dicta on Adrenaline: Myriad Problems with Learned Hand's Product-of-Nature Pronouncements in* Parke-Davis v. Mulford, 93 J. PAT. & TRADEMARK OFF. SOC'Y 363 (2011).
172. 450 U.S. 175, 204 (1981) (citing Parker v. Flook, 437 U.S. 584, 591-95 (1978)) (explaining that "the algorithm is treated for § 101 purposes as though it were a familiar part of the prior art; the claim is then examined to determine whether it discloses "some other inventive concept.'").

unpatentable scientific knowledge, should be considered to be in the prior art, and that claims to cDNA lack "some other inventive step" because the process for isolating DNA and removing its introns is so well known in the prior art. Alternatively, an alleged infringer could argue that claim 6 of Myriad's '282 patent is overly broad and thus anticipated by any previously discovered gene which contains a string of 15 nucleotides (15mer) also found in BRCA 1. Even though the written description describes BRCA 1 as having "no significant homology with known protein or DNA sequences," it does not go so far as to suggest that absolutely no homology exists. In fact, it is likely that several of BRCA 1's 15mers can be found in a previously discovered gene.[173] As an example, claim 1 of U.S. Patent 5,622,829 claims the isolated cDNA of various BRCA 1 alleles, all of which contain far more than 15 nucleotides in common with claim 6 of Myriad's '282 patent.

An alleged infringer could also challenge the validity of claim 6 of the '282 patent as broader than the written description. While the written description only describes the BRCA 1 gene, claim 6—vis-à-vis its reference to SEQ ID NO: 1—covers 15mers known to exist in nearly every human chromosome.[174] This means that claim 6 technically covers the DNA sequences of all other genes that contain a 15mer found in SEQ ID NO: 1. In fact, this problem of overly broad claims is likely to be found in all cDNA patents: As documented by Rosenfeld and Mason, "an analysis of all current US patent claims and the human genome presented here shows that 15mer sequences from all human genes match at least one other gene."[175] If successful in invalidating cDNA claims, these strategies could also be used to challenge process claims which merely apply natural laws by adding mental steps such as analyzing and comparing results, such as claim 2 of Myriad's '857 patent.[176] Linking challenges

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173. A search of the NIH Basic Local Alignment Search Tool (BLAST) for the third line of SEQ ID NO: 1 reveals that nearly every human chromosome contains a 15mer found in that section of the sequence. BLAST (accessed on July 19, 2013), http://blast.ncbi.nlm.nih.gov/Blast.cgi?PAGE_TYPE=BlastSearch&PROG_DEF=blastn&
BLAST_PROG_DEF=megaBlast&SHOW_DEFAULTS=on&SHOW_DEFAULTS=on&BLAST_SPEC=OGP__9606__9558.

174. U.S. Pat. 5,622,829 (filed Apr. 19, 1995).

175. Jeffrey Rosenfeld & Christopher E. Mason, *Pervasive Sequence Patents Cover the Entire Human Genome*, 5 GENOMIC MED. 27 (2013).

176. "A method for diagnosing a predisposition for breast cancer in a human subject which comprises comparing the germline sequence of the BRCA2 gene or the sequence of its mRNA in a tissue sample from said subject with the germline sequence of the wild-type BRCA2 gene or the sequence of its mRNA, wherein an alteration in the germline sequence of the BRCA2 gene or the sequence of its mRNA

of cDNA claims to method claims in this way could serve to calibrate patentability standards in order to minimize overlapping scopes of preemption between related biotech claims.

In the alternative, there are non-litigation means for promoting the spirit of the natural phenomenon doctrine. For example, a recent petition by Senator Patrick Leahy to the NIH calls for march-in rights with respect to Myriad's remaining patents on BRCA 1/2 diagnostic tests.[177] March-in rights, as authorized under 35 U.S.C. § 203, allow federal agencies like the NIH to issue the equivalent of a compulsory license when "action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees."[178] While the NIH has previously rejected march-in petitions concerning life-saving medicines being sold at unaffordable prices,[179] the case of diagnostic biotech patents may be more compelling because cost is not the primary concern. More problematically from a medical standpoint, exclusively licensed DNA patents prevent patient access to confirming (second-opinion) diagnostic tests—a problem which the USPTO was directed to explore with the passage of the America Invents Act.[180] If the primary concern of the natural phenomenon doctrine is unwarranted preemption of scientific tools, a liberal application of it in upholding diagnostic biotechnology patents—whether they be considered processes or products—may be compatible with the exercise of march-in rights. By exercising march-in rights, the government could obtain the ability to sub-license cDNA patents (while reimbursing patentees through reasonable royalties) to avoid wholesale preemption of genetic sequence testing. In doing so, it would promote the spirit of the law in avoiding absolute preemption of natural phenomena, while at the same time leveraging government funds to incentivize useful applications of natural phenomena.

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of the subject indicates a predisposition to said cancer." U.S. Pat. 6,033,857 (filed Mar. 20, 1998).

177. Letter from Senator Patrick Leahy to Dr. Francis S. Collins, Director, Nat'l Inst. of Health (July 12, 2013), *available at* http://www.leahy.senate.gov/download/07-12-13-pjl-to-nih-re_-myriad-march-in.

178. 35 U.S.C. 203(a)(2), Pub. L. 107-273 (2002).

179. Kevin E. Noonan, *Groups Petition for NIH Exercise of March-in Rights Over Abbott Laboratories' Norvir,* PATENT DOCS – BIOTECH & PHARMA PATENT LAW & NEWS BLOG (Oct. 31, 2012), http://www.patentdocs.org/2012/11/groups-petition-for-nih-exercise-of-march-in-rights-over-abbott-laboratories-norvir.html.

180. Leahy-Smith America Invents Act, Pub. L. No. 112-29, § 27, 125 Stat. 338 (2011).

D. The Importance of Safeguarding the Spirit of the Natural Phenomenon Doctrine at the Prosecution Stage

The history of the entanglement of biomedical process patents with biomedical product patents provides some valuable lessons for future assessments of associated product and process claims in biotech patent applications. For instance, when the scope of preemption appears to exceed the scope of invention for biotech claims resembling natural phenomena, "[f]orcing patents with abstract claims into a lower grade of patent might deter many of the current costs associated with abstract patent claims."[181] Yet herein emerges a procedural limitation in applying an arguably antiquated doctrine to a separately conceived litigation process: at the litigation stage, it is not possible for courts to reinterpret or revise the form or scope of gene patents.

If the natural phenomenon doctrine was meant to exclude certain categories of discoveries from patentability before Congress had the opportunity to refine more specific patent validity rules, then perhaps it is more effective at carrying out that function at the outset of patent prosecution. The natural phenomenon doctrine, as many examples in this article have shown, serves the important purpose of ensuring that patents do not contravene their Constitutional objective by too broadly preempting the use of basic scientific knowledge and tools. It does so by balancing the scope of preemption against the scope of invention (defined as the extent to which the claimed product is "markedly different" from what is found in nature), and ensuring that the scope of preemption does not exceed that which is justified by the inventor's handiwork in applying, isolating or manipulating natural phenomena. At the patent prosecution stage, the natural phenomenon doctrine may thus be a useful catch-all analytical tool that allows flexibility in promoting the spirit of patent law as it attempts to keep pace with the progress of science. Yet at the litigation stage, the doctrine perhaps proves too much: In the absence of a procedural mechanism to alter a patent at this stage, the natural phenomenon doctrine cannot be applied with sufficient nuance to limit the scope of preemption to the scope of invention. While the doctrine may be useful—and perhaps even ought to be more liberally construed—at the patent prosecution stage, it was not originally designed to be compatible with today's patent litigation procedures as other statutory patentability requirements were.

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181. JEFFREY M. KUHN, *Patentable Subject Matter Matters: New Uses For An Old Doctrine*, 22 BERKELEY TECH. L.J 89,112 (2007).

As a doctrine of limitation, it must, at the litigation stage, either prove nothing at the expense of unwarranted preemption or prove too much at the expense of patent holders who have been reasonably relying on guidance from the USPTO for many years. At its inception, the natural phenomenon doctrine was simply not designed to fit within the bounds of contemporary patent litigation. So even though it may seem ideally fit for settling some of the more difficult questions raised by diagnostic biotech patents, it may be ill-suited for regular deployment within the narrow space of today's patent litigation process.

Fortunately, in light of *Myriad*, the USPTO is expected to revisit its 2012 Interim Procedure for Subject Matter Eligibility Analysis of Process Claims Involving Laws of Nature[182] to develop more permanent guidelines. At minimum, these should account for the fact that patents on biotech products are likely to preempt the use of naturally occurring biotech processes. For instance, functional claiming could be explicitly limited to those sequences which cannot be found in nature. Guidelines to this effect could be especially useful as biotech patentees consider submitting reissue applications on patents that include claims to isolated gDNA, using narrower claims that explicitly exclude areas of overlap with naturally occurring phenomena.

CONCLUSION

As statutory and judicial standards for biomedical process patents have evolved, they have responded both to changes in technology and public policy concerns. Biomedical process patents have historically been viewed with skepticism because they allow monopolies on applications of medically relevant scientific truths and natural phenomena. When the Physician's Immunity Statute was passed in 1997, it only addressed the patentability implications of a narrow range of biomedical process patents, leaving similar issues related to biotechnology patentability unresolved. At the same time, another set of statutes sought to protect process patents for the

182. Memorandum from Andrew H. Hirshfield, Deputy Comm'r for Patent Examination Policy, USPTO, to Patent Examining Corps, USPTO (July 3, 2012), *available at* http://www.uspto.gov/patents/law/exam/ 2012_interim_guidance.pdf ("While Mayo has provided additional details for the eligibility analysis that the Office developed after Bilski, the technology areas currently being addressed by the Federal Circuit, most notably in Myriad and Ultramercial, will provide insight regarding the full reach of Bilski and Mayo. The Office believes that the prudent course of action is to wait for resolution of these cases before issuing comprehensive updated guidance.").

growing biotech industry, although they did little to address the increasingly complex doctrinal questions for the dual nature of biotech patents. The uncertain legal status of associated process and product claims thus inevitably led to questions about the preemptive scope of these proliferating patents. The Federal Circuit's creation of new analytical tests strove to keep pace with innovation in new kinds of information- and technology-related processes, but the application of these tests to diagnostic biotechnology in particular proved to be short-lived. Uniquely, diagnostic process patents raise fundamental doctrinal questions about what subject matter is eligible for patent protection in light of the tenuous legal relationships between naturally occurring biological processes, their manipulated counterparts and the natural information flows they effectively monopolize. In this milieu, an analytical framework was needed that could properly account for the interconnected nature of compositions of matter and processes in biotechnology. When *Myriad* reached the Supreme Court, the time was in a way ripe for application of the natural phenomenon doctrine, which retains the flexibility necessary to adapt to quickly changing modes of innovation. Indeed, a 2010 World Intellectual Property Organization (WIPO) study found that in many of its member states, it was not until relatively recently that "methods of medical treatment began to be seen more as a patent eligibility criterion stemming from public policy concerns."[183]

As this article has shown, U.S. case law involving the natural phenomenon doctrine regularly interchanged precedent concerning product and process claims Moreover, the natural phenomenon doctrine's focus on the preemption-invention ratio renders it particularly suitable for application to diagnostic biotechnology due to the special problems that arise out of the process-product entanglement with biological information flows. The natural phenomenon doctrine warrants limiting the scope of a diagnostic biotech product claim on the basis of its inventive scope (the extent to which the invention is "markedly different" from nature) being commensurate with its preemptive scope. However, because a nuanced application of the natural phenomenon doctrine yields a result which is only ideally instructive at the patent prosecution stage, at the litigation stage, it can serve only to either substantially protect incentives for innovation in the biotechnology industry or to address

183. SHAMNAD BASHEER ET AL., WIPO STANDING COMM. ON THE LAW OF PATENTS, PATENT EXCLUSIONS THAT PROMOTE PUBLIC HEALTH OBJECTIVES, WIPO SCP/15/3 Annex IV (2010).

the concerns about preemption of laws of nature; but it cannot properly balance the two. Its role at the prosecution stage must therefore be taken very seriously.

As processes become increasingly dependent on biology, "the impact of traditionally patentable subject matter upon the exercise of individual liberties grows,"[184] and the imperative for nuanced scrutiny heightens. After *Myriad*, claims to cDNA can still effectively monopolize the nature embodied in gDNA sequences. *Myriad* 's partial invalidity ruling—which has paved the way for more challenges to Myriad's patents as defenses to infringement suits—forces us to reconsider the relationship between biotech processes and compositions of matter that effectively monopolize the same subject matter. Future developments in patent law concerning subject-matter eligibility for diagnostic biotech patents, such as revisions to patent prosecution guidelines, should explicitly account for the narrowing theoretical distinctions between processes and products in this field. Certainly, biotechnology is not unique in this respect; many commentators have described how similar issues are raised by software and computer technologies.[185] Indeed, the shortsighted solution offered by the Biotechnology Process Patent Act has been compared to the Semiconductor Chip Protection Act, another "statute that was tied specifically to a technology that quickly became outdated."[186] From a birds-eye view, the complexities that arise out of trying to apply traditional patent frameworks to new boundary-defying technologies shed light on the shortcomings of a uniform patent system in adequately calibrating the progress of science within any given field.

184. John R. Thomas, *Liberty and Property in the Patent Law*, 39 HOUS. L. REV. 569, 610 (2002).

185. *See, e.g.*, Andrea Bonacccorsi et al., *From Protecting Texts to Protecting Objects in Biotechnology and Software: A Tale of Changes of Ontological Assumptions in Intellectual Property Protection,* 40 ECON. & SOC'Y 611, 633 (2011).

186. Kristin Connarn, *supra* note 49, at 300.