
DIAGNOSTIC METHOD PATENTS AND HARMS TO FOLLOW-ON INNOVATION

In a series of cases over the past decade, the Federal Circuit and Supreme Court have confronted the patent eligibility of broadly claimed diagnostic methods under § 101 of the Patent Act.¹ These diagnostic method patents claim processes that, generally speaking, first identify a biomarker and then use correlations associated with that biomarker for diagnostic purposes. This Note argues that granting these kinds of broad claims to natural correlations creates unique harms to follow-on innovation, ones that do not occur with other types of patents. Yet these harms have not been specified in the literature or the case law. In light of both these unique harms and the lack of attendant benefits, the Federal Circuit and Supreme Court should revise their approaches to broad diagnostic method patents.

Section 101 of the Patent Act provides that “[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.”² Yet § 101 is subject to several judge-made exceptions: “laws of nature, natural phenomena, and abstract ideas” are not patent eligible.³ Since “sometimes *too much* patent protection can impede rather than ‘promote the Progress of Science and useful Arts,’”⁴ these exceptions are needed to strike a balance between over- and underprotection of innovation. And though natural laws themselves are not patent eligible, *applications* of natural laws are.⁵ The fine line between natural laws and applications thereof is a critical one in the diagnostic method context, given the stakes for patient care.

Proponents of the “prospect theory” of granting broad, early patent rights argue that granting such rights will avoid wasteful and duplicative investment into research and development (R&D). Under this theory, the patentee can more efficiently coordinate the management of

¹ 35 U.S.C. § 101 (2006).

² *Id.*

³ *Diamond v. Diehr*, 450 U.S. 175, 185 (1981). Each articulation of this principle has described the exceptions in a slightly different way. *See, e.g.*, *Ass’n for Molecular Pathology v. U.S. Patent & Trademark Office*, 653 F.3d 1329, 1348–49 (Fed. Cir. 2011).

⁴ *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 126 (2006) (Breyer, J., dissenting from dismissal of certiorari) (quoting U.S. CONST. art. I, § 8, cl. 8). This view has also been expressed throughout the academic literature. *See, e.g.*, Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839, 875 (1990) (“[T]he *scope* of rights is crucial . . . [because] overly broad rights will preempt too many competitive development efforts.”).

⁵ *Diehr*, 450 U.S. at 187.

subsequent R&D without racing.⁶ Proponents argue that failing to grant strong, early patent rights leads to less future innovation, an “invisible” phenomenon because the “loss” of and harms from an invention that is never developed cannot be directly observed. Nonetheless, they argue, existence of these harms can be inferred from the economic arguments for the proposition that patent rights incentivize investment into R&D, and thus it would be a mistake to refuse to grant such patents.⁷

However, the prospect theory has been widely criticized,⁸ and it is equally if not more plausible that granting strong, early patent rights will result in the underdevelopment of technology.⁹ This problem is particularly acute for broad diagnostic method patents, both in terms of the need for follow-on innovation and in terms of the difficulty of such innovation as a doctrinal matter. These harms to future innovation are equally as invisible as those that are assumed to occur without broad, early patents. Yet there is actual evidence to suggest that *these* follow-on innovation harms exist in the diagnostic method context. Further, there is some evidence that the initial invention and at least some subsequent inventions will be developed in the absence of patent protection. Thus, granting these early patents not only creates the feared harms but also may not even achieve the intended benefits.

Part I of this Note briefly sets forth the relevant case law on the patent eligibility of broad diagnostic methods. Part II draws on Food and Drug Administration (FDA) regulations, patent doctrine, and empirical research to detail the specific harms to follow-on innovation that may result from grants of broad patents like those at issue in the described cases. Part III provides reasons why the harms occasioned by the grants of these claims are not likely to be offset by the benefits that are thought to result from the patent system. Part IV concludes by suggesting ways in which this Note might contribute to the scholarly debate on the most preferable means by which to redress the articulated problems with diagnostic method patents.

⁶ See Edmund W. Kitch, *The Nature and Function of the Patent System*, 20 J.L. & ECON. 265, 276–77 (1977) (setting forth the “prospect theory” of innovation).

⁷ See *id.* at 277.

⁸ See, e.g., F.M. SCHERER, *INDUSTRIAL MARKET STRUCTURE AND ECONOMIC PERFORMANCE* 447 n.30 (2d ed. 1980) (noting that the prospect theory is “little influenced by any concern for reality”); Mark A. Lemley, *The Economics of Improvement in Intellectual Property Law*, 75 TEX. L. REV. 989, 1047 (1997); Arti Kaur Rai, *Regulating Scientific Research: Intellectual Property Rights and the Norms of Science*, 94 NW. U. L. REV. 77, 120–21 (1999).

⁹ Merges & Nelson, *supra* note 4, at 873–74 (“The real problem is not controlling overfishing, but preventing *underfishing* after exclusive rights have been granted. . . . [W]e would expect a single rightholder to *underdevelop* — or even ignore totally — many of the potential improvements encompassed by their broad property right.”); see also Suzanne Scotchmer, *Standing on the Shoulders of Giants: Cumulative Research and the Patent Law*, 5 J. ECON. PERSP. 29, 32–33 (1991) (noting that broad protection offers “deficient incentives for second innovators,” *id.* at 33).

I. THE STATE OF THE LAW ON THE PATENT ELIGIBILITY
OF DIAGNOSTIC METHODS

In general, the Federal Circuit has appeared willing to uphold diagnostic method claims that fail to specify the diagnostic method at issue. Moreover, the Federal Circuit's analysis has too often failed to consider the innovation harms caused by the patents it upholds. These conclusions stem from four main cases regarding the patent eligibility of broad diagnostic methods: *Metabolite Laboratories, Inc. v. Laboratory Corp. of America Holdings*¹⁰ (*LabCorp*); *Prometheus Laboratories, Inc. v. Mayo Collaborative Services*¹¹ (*Prometheus*); *Association for Molecular Pathology v. U.S. Patent & Trademark Office*¹² (*AMP*); and *Classen Immunotherapies, Inc. v. Biogen IDEC*¹³ (*Classen*).

The Federal Circuit began down its misguided path to upholding broad diagnostic method patents in *LabCorp*. In that case, Metabolite Laboratories had sued LabCorp for infringing U.S. Patent 4,940,658 (the '658 Patent),¹⁴ which claimed "methods of detecting cobalamin and folic acid deficiency using an assay for total homocysteine levels."¹⁵ Claims one through twelve specified steps for conducting a total homocysteine assay.¹⁶ LabCorp had sublicensed the patent and test from Metabolite, but LabCorp soon switched to an assay developed by Abbott Laboratories and stopped paying royalties to Metabolite.¹⁷ Metabolite then sued for infringement of claim thirteen, "[a] method for detecting a deficiency of cobalamin or folate in warm-blooded animals comprising the steps of: assaying a body fluid for an elevated level of total homocysteine; and correlating an elevated level of total homocysteine . . . with a deficiency of cobalamin or folate."¹⁸ The Federal Circuit held that LabCorp had infringed Metabolite's patent by using Abbott's assay, and then-Judge (now Chief Judge) Rader rejected LabCorp's arguments regarding the invalidity of the '658 Patent.¹⁹ The Federal Circuit's opinion, however, did not discuss the

¹⁰ 370 F.3d 1354 (Fed. Cir. 2004).

¹¹ 628 F.3d 1347 (Fed. Cir. 2010).

¹² 653 F.3d 1329 (Fed. Cir. 2011).

¹³ 659 F.3d 1057 (Fed. Cir. 2011).

¹⁴ *LabCorp*, 370 F.3d at 1358–59.

¹⁵ U.S. Patent No. 4,940,658, at [57] (filed Nov. 20, 1986).

¹⁶ *Id.* col. 41 ll. 1–57.

¹⁷ *LabCorp*, 370 F.3d at 1359. Abbott's assay was "far superior" to Metabolite's. *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 128 (2006) (Breyer, J., dissenting from dismissal of certiorari).

¹⁸ *LabCorp*, 370 F.3d at 1358–59 (quoting '658 Patent col. 41 ll. 58–65). The division between claims one through twelve (which set forth specific steps for conducting one specific diagnostic test) and claim thirteen (which sets forth the general concept of conducting a diagnostic test for this purpose) lies at the heart of this Note.

¹⁹ *See id.* at 1361–68.

scope of claim thirteen, particularly the technological scope of the “assaying” step. Justice Breyer’s dissent from the Supreme Court’s dismissal of certiorari, by contrast, emphasized a fact that the Federal Circuit glossed over: in claim thirteen, “the words ‘assaying a body fluid’ refer to the use of any test at all, whether patented or not patented.”²⁰ Justice Breyer would have concluded that claim thirteen embodies only a natural phenomenon and therefore is invalid.²¹

In *Prometheus*, the Federal Circuit again upheld a broad diagnostic method patent without adequately considering its harms. Prometheus Laboratories had sued Mayo Collaborative Services for infringing two of its licensed patents: 6,355,623 (the ‘623 Patent) and 6,680,302 (the ‘302 Patent),²² which “provide[] a method of optimizing therapeutic efficacy and reducing toxicity associated with 6-mercaptopurine drug treatment of an immune-mediated gastrointestinal disorder.”²³ Prometheus’s patents mainly include two types of claims. The first type, as represented by claim one of the ‘623 Patent, is “[a] method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising: (a) *administering* a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and (b) *determining* the level of 6-thioguanine in said subject”²⁴ The second type “dispenses with the ‘administering’ step and claims only the ‘determining’ step.”²⁵ Based on these patents, Prometheus developed a blood test to measure thiopurine metabolites. Laboratories seeking to use this test would send blood samples to Prometheus, which performed the test and provided the results.²⁶

After purchasing Prometheus’s services for several years, Mayo developed its own test. Before Mayo could market its test, however, Prometheus brought suit.²⁷ The United States District Court for the Southern District of California granted Mayo’s motion for summary judgment of invalidity under § 101,²⁸ but the Federal Circuit reversed, holding that the patents survived the § 101 challenge, as both the “administering” and “determining” steps of the claims constituted

²⁰ *LabCorp*, 548 U.S. at 129 (Breyer, J., dissenting from dismissal of certiorari).

²¹ *Id.* at 138.

²² *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 628 F.3d 1347, 1349, 1351 (Fed. Cir. 2010).

²³ U.S. Patent No. 6,680,302, at [57] (filed Dec. 27, 2001); U.S. Patent No. 6,355,623, at [57] (filed Apr. 8, 1999).

²⁴ *Prometheus*, 628 F.3d at 1350 (quoting ‘623 Patent col. 10 ll. 10–16).

²⁵ *Id.* Claim forty-six of the ‘623 Patent is illustrative. *Id.* at 1350–51.

²⁶ Brief for Petitioners at 7, *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289 (2012) (No. 10-1150), 2011 WL 3919717, at *7 [hereinafter Mayo Brief].

²⁷ See *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, No. 04cv1200 JAH (RBB), 2008 WL 878910, at *1 (S.D. Cal. Mar. 28, 2008).

²⁸ *Id.* at *14.

“transformations” under the machine-or-transformation test.²⁹ Justice Breyer’s opinion for the Supreme Court subsequently invalidated both types.³⁰ However, the Federal Circuit demonstrated its willingness to uphold claims that follow the broad template of the *LabCorp* patents and instruct practitioners to determine a biological fact without restricting the means of determining the fact.³¹

The Federal Circuit’s interpretation and invalidation of the method claims in the next case, *AMP*, provide an instructive contrast to *Prometheus*. In *AMP*, rather than defend an infringement suit from the patent holders, the plaintiffs (among whom were physicians, researchers, and patients) brought an action for declaratory judgment of invalidity on fifteen claims from seven different patents, all relating to the BRCA genes.³² Five of the challenged claims involved methods of “analyzing” or “comparing” BRCA sequences to identify mutations that might predispose their carriers to breast or ovarian cancer.³³ As a representative example, claim one of U.S. Patent 5,709,999 (the ‘999 Patent) claims “[a] method for detecting a germline alteration in a BRCA1 gene . . . which comprises *analyzing* a sequence of a BRCA1 gene or BRCA1 RNA.”³⁴ The Federal Circuit affirmed the lower court’s invalidation of these five claims under § 101.³⁵ Both the district court and Federal Circuit compared the claims-in-suit in *AMP* with those in *Prometheus* and noted that the former did not include determining the BRCA sequence.³⁶

²⁹ *Prometheus*, 628 F.3d at 1357. Under this test, a claimed method “is surely patent-eligible under § 101 if: (1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing.” *Bilski v. Kappos*, 130 S. Ct. 3218, 3224 (2010) (internal quotation mark omitted) (quoting *In re Bilski*, 545 F.3d 943, 954 (Fed. Cir. 2008) (en banc)).

³⁰ See *Prometheus*, 132 S. Ct. at 1294.

³¹ Even though the Supreme Court invalidated the claims in *Prometheus*, the Federal Circuit’s approach remains viable, and thus still worrisome. Opinions from its post-*Prometheus* case law suggest that the Federal Circuit might be creatively interpreting *Prometheus*’s logic. See, e.g., *CLS Bank Int’l v. Alice Corp.*, 685 F.3d 1341, 1357 (Fed. Cir. 2012) (Prost, J., dissenting) (“[T]he majority has resurrected the very approach to § 101 that . . . the Supreme Court laid to rest . . . in *Prometheus*. I cannot agree.”), *reh’g en banc granted*, No. 2011-1301, 2012 WL 4784336 (Fed. Cir. Oct. 9, 2012). But see *PerkinElmer, Inc. v. Intema Ltd.*, No. 2011-1577, 2012 WL 5861658, at *4, *6 (Fed. Cir. Nov. 20, 2012) (invalidating broad diagnostic method claims under *Prometheus*).

³² *Ass’n for Molecular Pathology v. U.S. Patent & Trademark Office*, 702 F. Supp. 2d 181, 184 (S.D.N.Y. 2010) (“Mutations in the *BRCA1/2* genes correlate with an increased risk of breast and ovarian cancer.” *Id.* at 203.).

³³ See *id.* at 213–14.

³⁴ *Id.* at 213 (emphasis added).

³⁵ *Ass’n for Molecular Pathology v. U.S. Patent & Trademark Office*, 653 F.3d 1329, 1358 (Fed. Cir. 2011).

³⁶ See *id.* at 1357; see also *AMP*, 702 F. Supp. 2d at 234–35. The Supreme Court ordered the Federal Circuit to reconsider *AMP* in light of *Prometheus*. *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*, 132 S. Ct. 1794, 1794 (2012). Yet on remand, the Federal Circuit sharply limited *Prometheus*, *Ass’n for Molecular Pathology v. U.S. Patent & Trademark Office*, 689 F.3d 1303, 1325–26 (Fed. Cir. 2012), such that its original analysis in *AMP* survives. *But cf.* *Ass’n for*

The final case in this set, *Classen*, involved methods for lowering the risk of chronic immune-mediated disorders (such as multiple sclerosis) through the use of lower-risk vaccine schedules.³⁷ *Classen* sued Merck for infringement of four patents, but the district court granted summary judgment for Merck on several claims, leaving Merck's counterclaims of invalidity on three patents: numbers 6,420,139 (the '139 Patent), 6,638,739 (the '739 Patent), and 5,723,283 (the '283 Patent).³⁸ As described by *Classen*, the '139 and '739 Patents recite two method steps: "(I) screening two or more immunization schedules; and (II) immunizing according to the lower risk schedule."³⁹ The Federal Circuit construed the '283 Patent as claiming only the first step of the '139 and '739 Patents.⁴⁰ For the majority, this distinction was sufficient to ensure that the '139 and '739 claims constituted patentable subject matter, while the '283 Patent was "barred at the threshold" of § 101.⁴¹ The primary distinction is that the "'139 and '739 patent claims . . . include the subsequent step of immunization," where the immunization step constitutes a specific application of the screening step.⁴² This difference "moves the '139 and '739 claims through the coarse filter of § 101," leaving the '283 claim behind.⁴³

Judge Moore's dissent engaged with the merits of the § 101 issue, concluding that all three patents must be invalid. Invoking Justice Breyer's warning about the "dangers of overprotection" in *LabCorp*,⁴⁴ Judge Moore was appalled by the majority's lack of "analysis of the staggering breadth of the claims and the preemption issues inherent in claims directed to such fundamental principles."⁴⁵ She argued not only that incentives for innovation would remain present even if *Classen* were unable to sustain these particular patents,⁴⁶ but also that the breadth of the patents upheld by the majority means that "nobody else

Molecular Pathology v. Myriad Genetics, Inc., No. 12-398, 2012 WL 4508118, at *1 (U.S. Nov. 30, 2012) (granting certiorari).

³⁷ *Classen Immunotherapies, Inc. v. Biogen IDEC*, 659 F.3d 1057, 1060 (Fed. Cir. 2011).

³⁸ *Classen Immunotherapies, Inc. v. Biogen IDEC*, No. WDQ-04-2607, 2006 WL 6161856, at *1-2 (D. Md. Aug. 16, 2006).

³⁹ Brief for Appellant *Classen Immunotherapies, Inc.* at 6, *Classen*, 659 F.3d 1057 (Fed. Cir. 2011) (Nos. 2006-1634, 2006-1649), 2006 WL 3846638, at *4.

⁴⁰ *Classen*, 659 F.3d at 1061; see also U.S. Patent No. 5,723,283 col. 51 ll. 50-60 (filed May 31, 1985).

⁴¹ *Classen*, 659 F.3d at 1064, 1068.

⁴² *Id.* at 1067.

⁴³ *Id.* at 1068.

⁴⁴ *Id.* at 1079 (Moore, J., dissenting) (quoting *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 127 (2006) (Breyer, J., dissenting from dismissal of certiorari)).

⁴⁵ *Id.* at 1076.

⁴⁶ *Id.* at 1080 ("Mr. *Classen* . . . [is] not without incentives to innovate in this area. He could, of course, claim a method of treating a chronic immune-mediated disorder by using a new and specific immunization schedule. . . . But *Classen* . . . instead . . . claims *the study* of and merely comparing whether the timing of immunization affects chronic immune-mediated disorders.").

can search for new immunogens, for use of new immunizations, to treat either existing or currently unknown chronic immune-mediated disorders without infringing.”⁴⁷ These concerns went unaddressed by the majority.

Viewing these cases together, the “determine-and-infer” template likely controls the patent eligibility of diagnostic methods in the Federal Circuit,⁴⁸ where only diagnostic method claims that adhere to this template are patent eligible.⁴⁹ Claims following this template “initially recite prior-art steps that identify or measure a real-world phenomenon (the ‘determining’ step), and . . . conclude with a newly invented mental step in which the identifier infers useful information about a distinct real-world phenomenon from the measured phenomenon (the ‘inferring’ step).”⁵⁰ The Federal Circuit’s holding in each of the above cases is explainable under the assumption that the Federal Circuit has implicitly adopted “determine-and-infer” claims as categorically eligible under § 101, and that the Federal Circuit has elevated the template from a flexible standard to a bright-line rule.⁵¹

Yet the Federal Circuit’s mechanical analysis too often fails to consider the policy and innovation problems behind the patents it upholds, and there is a clear need for a framework laying out the over-protection problems specifically associated with diagnostic method patents. This Note now moves to provide such a framework.

⁴⁷ *Id.* at 1079.

⁴⁸ While this template does not control in the Supreme Court, the low frequency with which the Court reviews these cases and the Federal Circuit’s propensity to ignore the Court, *see supra* notes 31, 36, suggest that the Federal Circuit’s interpretation may be more consequential.

⁴⁹ *See* Kevin Emerson Collins, *An Initial Comment on Prometheus: The Irrelevance of Intangibility*, PATENTLY-O (Sept. 17, 2009), <http://www.patentlyo.com/collins.intangibility.pdf>. Interestingly, the Federal Circuit’s continued willingness to uphold claims that fail to describe the methods by which they operate dates back to *LabCorp*. In *LabCorp*’s brief before the Federal Circuit, it argued the following in the context of indefiniteness under § 112: “If the Court were to uphold this vague claim, anyone could obtain a patent on any scientific correlation — that there is a link between fact A and fact B — merely by drafting a patent claiming no more than ‘test for fact A and correlate with fact B,’ *without any explanation of the testing or correlation processes.*” Corrected Brief for Appellant Laboratory Corp. of America Holdings at 41, *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354 (Fed. Cir. 2004) (No. 03-1120) (emphasis added). Justice Breyer’s dissent from the dismissal of certiorari cites this passage in full. *LabCorp*, 548 U.S. at 131 (Breyer, J., dissenting from dismissal of certiorari). Further, *LabCorp*’s reply brief before the Supreme Court actually referred to this passage as a “test plus correlate” claim. Reply Brief for Petitioner at 1, *LabCorp*, 548 U.S. 124 (2006) (No. 04-607).

⁵⁰ Collins, *supra* note 49, at 2.

⁵¹ Claims that include a “determining” step (as in *LabCorp* and *Prometheus*) are upheld, while claims that do not (as in *AMP* and *Classen*) are invalidated. *See supra* pp. 1372–75.

II. DIAGNOSTIC METHOD PATENTS AND HARMS TO FOLLOW-ON INNOVATION

In determining where the optimal balance of patent eligibility in the field of diagnostic method patents lies,⁵² several critical questions must be asked: For instance, how broad is the preemptive effect of these patents? What effect will they have on follow-on innovation?⁵³ Are there problems that might arise with these particular patents that do not arise with other types of patents? Justice Breyer's dissent in *LabCorp* recited a litany of harms that might occur if the patent at issue remained in force, including that the patent may "force doctors to spend unnecessary time and energy to enter into license agreements," "divert resources from the medical task of health care to the legal task of searching patent files," and "raise the cost of health care while inhibiting its effective delivery."⁵⁴ Yet these concerns are not specific to the *LabCorp* claims,⁵⁵ and the problems presented by these particular patents are underexplored in the literature.⁵⁶

Essentially, there are at least two particular problems posed by follow-on innovation in diagnostic methods. First, there is a *particularly acute need* for follow-on innovation in this area, primarily due to the existing FDA regulatory scheme and its lack of quality-assurance determinations.⁵⁷ Second, follow-on innovation is *particularly difficult*

⁵² It might be argued that any balance struck on this question will also affect other areas of technology, since patent law is one-size-fits-all. However, such uniformity may not be the case in practice. See Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law*, 89 VA. L. REV. 1575, 1576–77 (2003).

⁵³ When examining follow-on innovation in this context, two main types of improvements might occur. The first type encompasses improvements to the testing itself — such as improvements that speed the testing procedure. The second type encompasses improvements to the correlation — improvements that allow physicians to more sensitively identify states of disease. Justice Breyer's *Prometheus* opinion makes this point in noting that the innovations prevented by Prometheus's claims are innovations *in the refinement of the correlation*. *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1302 (2012). The distinction is not necessarily clean. The improvements in *AMP* — and perhaps in genetic testing more broadly, where improving the range of mutations that the test is able to detect requires improving the test technology itself — straddle this line. The development of platform technologies may be another special case.

⁵⁴ *LabCorp*, 548 U.S. at 138 (Breyer, J., dissenting from dismissal of certiorari).

⁵⁵ The Supreme Court's *Prometheus* opinion similarly lists harms to follow-on innovation more broadly, and notes the harms in that specific case, but it does not discuss harms to innovation from diagnostic method patents. *Prometheus*, 132 S. Ct. at 1301–02.

⁵⁶ Few scholars appear to have acknowledged these points, and none has done so particularly expansively. See, e.g., Declaration of Joseph E. Stiglitz, Ph.D. at 13, *Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office*, 702 F. Supp. 2d 181 (S.D.N.Y. 2010) (No. 09-4515) (briefly noting concerns about "impediment[s] to follow-up research, which might, for instance, result in a lower cost or a more accurate test").

⁵⁷ It might seem odd that this Note appeals to the *lack* of FDA regulations to draw a distinction between diagnostics and other types of patents, as *most* technologies that are granted patent protection are not subject to FDA regulations. However, defenders of diagnostic method patents commonly use arguments that are made in the context of drugs, the development of which *does*

to accomplish in the presence of broad patent claims like those at issue in the relevant case law. Ultimately, various sources of empirical evidence suggest that these problems have been borne out in practice.

A. Need for Follow-On Innovation

There is a particularly acute need for follow-on innovation in this context for two primary reasons. First, these sorts of diagnostic tests are largely unregulated, and therefore external validation of their quality and accuracy is generally lacking. Second, the patterns of innovation in the field of diagnostic testing suggest that initial discoveries must be accompanied by significant subsequent innovation to create the most useful product for consumers.

Two statutes may be used to regulate diagnostic tests. The Federal Food, Drug, and Cosmetic Act⁵⁸ (FDCA) gives the FDA the authority to regulate any medical device, defined as “an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is . . . intended for use in the diagnosis of disease or other conditions.”⁵⁹ Diagnostic tests thus clearly fall within the ambit of the statute.⁶⁰ The FDCA sorts devices into three classes, with Class I⁶¹ devices posing the least risk and Class III⁶² devices the most.⁶³ Class assignment determines the level of FDA regulation involved: the FDA requires manufacturers of all nonexempted medical devices⁶⁴ that are not required to apply for Premarket Approval (PMA)⁶⁵ to submit Pre-

require companies to undergo an extensive, expensive FDA regulatory process. See, e.g., Brief of PhRMA as Amicus Curiae in Support of Neither Party at 19–23, *Bilski v. Kappos*, 130 S. Ct. 3218 (2010) (No. 08-964) (using research into the length and cost of drug development, among other drug-related arguments, to support the proposition that protecting medical processes “serves the primary purpose of patent law,” *id.* at 19). Further, the consequences of a particular need for follow-on innovation in this context are potentially more dire than in cases involving non-health technologies.

⁵⁸ 21 U.S.C. §§ 301–399 (2006).

⁵⁹ *Id.* § 321(h) (emphasis added).

⁶⁰ In regulations interpreting the FDCA, the FDA classifies “in vitro diagnostic products” (IVDs) as devices. 21 C.F.R. § 809.3(a) (2012).

⁶¹ Class I includes simple devices like tongue depressors. See, e.g., *id.* § 880.6230; see also *Medical Device Exemptions 510(k) and GMP Requirements*, FDA, <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpd/315.cfm?GMPPart=880> (last updated Dec. 31, 2012).

⁶² Recently approved Class III devices include transcatheter heart valves and coronary stent systems. *August 2012 PMA Approvals*, FDA, <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/ucm323179.htm> (last updated Oct. 10, 2012).

⁶³ See 21 U.S.C. § 360c.

⁶⁴ Most Class I and some Class II devices are officially exempt from this process. Peter Barton Hutt, *A Brief History of the Regulation of In Vitro Diagnostic Products*, in *IN VITRO DIAGNOSTICS* 1, 5–6 (Scott D. Danzis & Ellen J. Flannery eds., 2010).

⁶⁵ Manufacturers of Class III devices are required to apply for premarket approval. 21 U.S.C. § 360c(a)(1)(C).

market Notification documents under § 510(k) of the statute.⁶⁶ Diagnostic test providers who market tests to other laboratories must proceed through either the § 510(k) or PMA process.⁶⁷ Yet laboratories that “never sell[] the *test kit* to other laboratories, hospitals or doctors” but “only offer[] the testing *service* to them and perform[] this test, when ordered, in-house” can entirely avoid regulation under the FDCA.⁶⁸ Referred to as “laboratory-developed tests” (LDTs), most diagnostic tests fall within this exception and thus escape FDA scrutiny.⁶⁹ The FDA takes the position that it has jurisdiction over LDTs, but it generally exercises its discretion by declining to act.⁷⁰

The Clinical Laboratory Improvement Amendments of 1988⁷¹ (CLIA) give the Centers for Medicare and Medicaid Services (CMS) in the Department of Health and Human Services the authority to regulate and certify laboratories.⁷² Although CLIA “oversight focuses on the quality of the laboratory’s overall operations and does not evaluate directly the safety and effectiveness of the individual tests performed,”⁷³ CLIA also “imposes special requirements on tests that are not subject to FDA clearance or approval, such as LDTs.”⁷⁴ Under these special requirements, laboratories using LDTs must establish “performance specifications” for the tests that include “accuracy, precision, analytical sensitivity, specificity, reportable ranges and others.”⁷⁵ Yet there is a loophole in cases where, as is common, there is no existing proficiency testing system for a given LDT, and in such a case the laboratory sets its own quality-assurance procedures.⁷⁶ Thus in general, CLIA does not require regulators to “assess the clinical validity of the tests offered by clinical laboratories,” and some CMS officials have

⁶⁶ *Premarket Notification (510k): Who is Required to Submit a 510(k)?*, FDA, <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/default.htm#who> (last updated Sept. 3, 2010).

⁶⁷ Peter M. Kazon, *Laboratory Developed Tests*, in *IN VITRO DIAGNOSTICS*, *supra* note 64, at 115, 115.

⁶⁸ *Id.*; see also Gail H. Javitt, *In Search of a Coherent Framework: Options for FDA Oversight of Genetic Tests*, 62 *FOOD & DRUG L.J.* 617, 628 (2007) (noting that “the vast majority of these genetic LDTs are subject to no oversight to ensure that they are safe and effective”).

⁶⁹ Gail H. Javitt et al., *Direct-to-Consumer Genetic Tests, Government Oversight, and the First Amendment: What the Government Can (and Can't) Do to Protect the Public's Health*, 57 *OKLA. L. REV.* 251, 272 (2004).

⁷⁰ Hutt, *supra* note 64, at 7. However, many companies argue that the FDA lacks jurisdiction over LDTs because the tests are not introduced into interstate commerce. Patricia Maloney, *Laboratory Regulation Under the Clinical Laboratory Improvement Amendments of 1988 and State Laws*, in *IN VITRO DIAGNOSTICS*, *supra* note 64, at 69, 91.

⁷¹ Pub. L. No. 100-578, 102 Stat. 2903 (codified as amended at 42 U.S.C. § 263a (2006)).

⁷² Hutt, *supra* note 64, at 6–7.

⁷³ Javitt, *supra* note 68, at 624.

⁷⁴ Kazon, *supra* note 67, at 117.

⁷⁵ *Id.*

⁷⁶ *Id.*

claimed that CLIA does not even permit CMS to monitor the clinical validity of these tests.⁷⁷

These regulations enabled the patent owners in the Federal Circuit's diagnostic method cases to avoid regulation of their diagnostic tests. In *LabCorp*, Metabolite licensed the rights to perform its homocysteine diagnostic test to LabCorp.⁷⁸ However, because it does not appear that Metabolite actually sold LabCorp the test kits, but merely allowed LabCorp to perform the test in-house, LabCorp might plausibly classify its test as an LDT.⁷⁹ *Prometheus* is more clear-cut: because Prometheus was the "sole and exclusive licensee" of the patent,⁸⁰ others wanting to use the test had to purchase Prometheus's services. Unlike Metabolite, Prometheus did not license the ability to conduct the test to others. Prometheus likely could classify its drug metabolite test as an LDT. Myriad's BRCA tests are also considered LDTs.⁸¹

The existing regulatory scheme surrounding diagnostic tests⁸² is therefore vastly different from the regulatory scheme surrounding

⁷⁷ Javitt, *supra* note 68, at 639.

⁷⁸ Second Amended Complaint and Jury Demand at 5, *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, No. 99-Z-870 (D. Colo. Nov. 19, 2001), 2000 WL 34604791, at *5.

⁷⁹ LabCorp has engaged in this practice on other occasions as well, sometimes with negative results. In one instance, LabCorp had licensed a test from Yale University for the diagnosis of ovarian cancer. LabCorp viewed that test as an LDT, but the FDA sent LabCorp a warning letter stating that the test did not qualify as an LDT because it was not developed at LabCorp. Letter from Steven I. Gutman, Dir., Office of In Vitro Diagnostic Device Evaluation and Safety, FDA, to David P. King, President & CEO, LabCorp (Sept. 29, 2008), available at <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2008/ucm1048114.htm>.

⁸⁰ Complaint for Patent Infringement at 2, *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, No. 04-CV-1200-JAH (S.D. Cal. 2004), 2004 WL 2545853, at *2.

⁸¹ Andrew S. Robertson, *The Role of DNA Patents in Genetic Test Innovation and Access*, 9 NW. J. TECH. & INTELL. PROP. 377, 394 (2011). Myriad is also regulated under CLIA. CLINICAL LABORATORY IMPROVEMENT AMENDMENTS CERTIFICATE OF ACCREDITATION (2011), available at <http://www.myriad.com/lib/certifications/Myriad-CLIA-Certification.pdf>.

⁸² One apparent solution to the problem of loose regulation of diagnostic tests is for the FDA or CMS to tighten its regulations. Putting aside the question of whether such a change would be constitutionally permissible, *see supra* note 70, there have been attempts to exercise more stringent oversight. Some have been externally driven. In 2008, Genentech filed a citizen petition requesting that the FDA hold LDTs to the "same scientific and regulatory standards" as other IVDs. Letter from Sean A. Johnston, Senior Vice President and Gen. Counsel, Genentech, to Div. of Dockets Mgmt., FDA (Dec. 5, 2008), available at <http://www.aab.org/images/aab/pdf/Genentech%20FDA%20Petition.pdf>. Others disagreed with Genentech's argument that the FDA should begin regulating all LDTs in this way. *See, e.g.*, Editorial, *A Balancing Act*, 27 NATURE BIOTECHNOLOGY 209 (2009). In 2010, the FDA held a public meeting on the issue. *FDA/CDRH Public Meeting: Oversight of Laboratory Developed Tests (LDTs)*, FDA (Sept. 17, 2010), <http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm212830.htm>. At the time this Note was written, the FDA had not yet issued an official statement on this subject. However, even regulating LDTs to the same degree as Class III devices, to the standard of "reasonable assurance of [their] safety and effectiveness," 21 U.S.C. § 360c(a)(1)(C) (2006), would not eliminate the problems identified in this Note. Not only would such regulation leave untouched the other problems identified here, but also it would be only a partial solution. Merely publicizing the limitations of these tests may not be sufficient to effect change.

drugs, in which drug companies must conduct extensive clinical testing⁸³ and publish the results from their trials in a public database.⁸⁴ The diagnostic test regulatory scheme fails not only to produce such information, but also to disseminate it to the public. Even business methods, which are not governed by any regulatory scheme whatsoever, are likely to produce not only more information, but also more *publicly available* information, than are diagnostic tests.⁸⁵

Because the current regulatory scheme leaves diagnostic tests largely unregulated, the quality and accuracy of these tests remain dubious and unproven. Researchers and patients alike might want to improve a given test in several ways, but if the patentee or exclusive licensee will not license the test for such improvement, the medical community will be left with a body of substandard tests that too often fail to provide patients with accurate information on which to base decisions about medical treatment. Different versions of this undesirable result were borne out in *LabCorp*, *Prometheus*, and *AMP*.

In *LabCorp*, Abbott's test had significant advantages over the test Metabolite licensed to LabCorp. Most importantly, Abbott's test was "faster and less labor-intensive than [Metabolite's] — a crucial advance in light of the increased demand" for the tests.⁸⁶ "Whereas [Metabolite's] method took 'upwards of 18 hours to turn out a result,' the Abbott method reduced that time 'to a matter of minutes.'"⁸⁷ Yet the injunction issued against LabCorp barred it from using *any* tests, including those operating via "the Abbott method."⁸⁸

In *Prometheus*, Mayo had improved on Prometheus's existing diagnostic in three ways. First, it had developed superior assays to measure thiopurine metabolite levels in blood.⁸⁹ Second, Mayo possesses the largest gastroenterology practice in the United States,⁹⁰ and it had used its experience both to provide more detailed information with the test results than did Prometheus⁹¹ and to base toxicity deter-

⁸³ 21 C.F.R. § 312.22-.23 (2012).

⁸⁴ 42 U.S.C. § 282(j)(2)(A)(ii) (2006 & Supp. V 2011).

⁸⁵ See Rochelle Cooper Dreyfuss, *Are Business Method Patents Bad for Business?*, 16 SANTA CLARA COMPUTER & HIGH TECH. L.J. 263, 275 (2000) ("Businesses are largely practiced in public. Accordingly, there is little need to especially encourage disclosure."); Brief of Financial Services Industry Amici Curiae in Support of Reversal at 15, *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124 (2006) (No. 04-607), 2005 WL 3543097, at *15 ("Both the nature of business methods generally, and the transparency of American financial markets in particular, make it unlikely that effective methods will be long concealed . . .").

⁸⁶ Brief for Petitioner at 9, *LabCorp*, 548 U.S. 124 (No. 04-607), 2005 WL 3543099, at *9.

⁸⁷ *Id.*

⁸⁸ *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1371-72 (Fed. Cir. 2004).

⁸⁹ Mayo Brief, *supra* note 26, at 9, 2011 WL 3919717, at *9.

⁹⁰ *Id.* at 8, 2011 WL 3919717, at *8.

⁹¹ *Id.* at 9, 2011 WL 3919717, at *9.

minations on different levels of those metabolites.⁹² Third, Mayo's test would have been twenty-five percent cheaper than Prometheus's.⁹³

AMP most clearly reflects the harms to follow-on innovation that broad diagnostic method patents may cause. The plaintiffs in this declaratory judgment action included two unusual groups: physicians and patients. Individual physicians had received cease-and-desist letters from Myriad for conducting their own BRCA sequencing.⁹⁴ And individual women either had been unable to afford Myriad's test⁹⁵ or had their tests return inconclusive results, leaving them unable to receive further testing due to Myriad's refusal to license.⁹⁶ The size of this second group of women is particularly worrisome, as the complaint alleges not only that "[f]or at least some portions of the life of the patents, Myriad did not perform certain tests that were known to reveal additional mutations that increased the risk of breast and/or ovarian cancer," but also that "Myriad prohibited anyone else from offering those tests to patients."⁹⁷ In 2001, French researchers identified several large-scale rearrangements in the BRCA genes that Myriad's test failed to find. They alleged that Myriad's test failed to catch up to ten to twenty percent of BRCA mutations.⁹⁸ A separate study found that twelve percent of patients with negative results under Myriad's test in fact carried large deletions or duplications.⁹⁹ Yet Myriad waited years before incorporating these rearrangements in its analysis,¹⁰⁰ leaving many women with no way to detect their harmful mutations and perhaps even with false hope from erroneously negative test results.

The FDA's regulatory scheme would fail to provide useful information about quality and accuracy for a given diagnostic test even in the

⁹² Prometheus Labs., Inc. v. Mayo Collaborative Servs., 628 F.3d 1347, 1351 (Fed. Cir. 2010).

⁹³ Mayo Brief, *supra* note 26, at 10, 2011 WL 3919717, at *10.

⁹⁴ See Complaint at 5–6, Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 702 F. Supp. 2d 181 (S.D.N.Y. 2010) (No. 09-CV-04515), 2009 WL 1343027, at *5–6 [hereinafter Myriad Complaint]. In particular, the University of Pennsylvania had been conducting BRCA tests using a technology that was both cheaper and faster than traditional DNA sequencing. Myriad's aggressive enforcement strategies forced the University to shut down its facilities. Declaration of Shobita Parthasarathy at 10–13, *AMP*, 702 F. Supp. 2d 181 (No. 09-CV-04515), 2009 WL 6634220, at *10–13 [hereinafter Parthasarathy Declaration].

⁹⁵ See Myriad Complaint, *supra* note 94, at 27. At least some of these women had health insurance that covered the test, but that Myriad refused to accept. *Id.*

⁹⁶ See *id.* at 25–27.

⁹⁷ *Id.* at 26.

⁹⁸ Steve Benowitz, *French Challenge to BRCA1 Patent Underlies European Discontent*, 94 J. NAT'L CANCER INST. 80, 80 (2002); Karen Norrgard, *Diagnostic Testing and the Ethics of Patenting DNA*, 1 NATURE EDUC. (2008), <http://www.nature.com/scitable/topicpage/diagnostic-testing-and-the-ethics-of-patenting-709>.

⁹⁹ Tom Walsh et al., *Spectrum of Mutations in BRCA1, BRCA2, CHEK2, and TP53 in Families at High Risk of Breast Cancer*, 295 JAMA 1379, 1386 (2006).

¹⁰⁰ Parthasarathy Declaration, *supra* note 94, at 13.

absence of patent protection. But patent protection exacerbates this problem. Companies may use their patents to thwart attempts by academics or other companies to perform independent quality assessment.¹⁰¹ Myriad's aggressive patent enforcement against university researchers is just one example of this practice.¹⁰² While some quality testing was performed and did reveal numerous shortcomings of Myriad's tests, as noted above, these shortcomings would likely have been incorporated into superior tests much earlier in the absence of Myriad's patents.¹⁰³ And while the court in *Classen* ultimately granted summary judgment for the defendant, Classen's initial suit alleged that Merck's participation in a study disputing the validity of the premise underlying Classen's patents constituted infringement of those same patents.¹⁰⁴ Merck had no involvement whatsoever with the study.¹⁰⁵ The thought of using patents to prevent research into validating or invalidating scientific theories is chilling, and Judge Moore's claim in dissent that "Classen claimed a monopoly over the scientific method itself" may not be far from the truth.¹⁰⁶

There is also a second factor driving the particular need for follow-on innovation in this context. The patterns of innovation in diagnostic testing suggest that the first test on the market will not be the most analytically sensitive or practically easy to run, such that significant subsequent innovation will be required to refine the test. Professors Robert Merges and Richard Nelson have articulated a general version of this idea.¹⁰⁷ They have noted that, while some inventions (such as drugs) are "discrete," where the basic invention is an "end" that "does not point the way to wide ranging subsequent technical advances,"¹⁰⁸

¹⁰¹ See generally Brenda M. Simon, *Patent Cover-Up*, 47 HOUS. L. REV. 1299 (2011) (arguing that Congress or the courts should create and recognize a defense to infringement for independent quality assurance testing). Companies tend to use either "the threat of litigation or restrictive licensing practices" to accomplish this goal. *Id.* at 1301.

¹⁰² See *id.* at 1308; see also Myriad Complaint, *supra* note 94, at 5, 18.

¹⁰³ While Myriad would retain its gene patents even if its broad method claims were invalidated, its gene patents are arguably narrower. Some new methods of running diagnostic tests may not require sequencing the gene, and therefore should not infringe the gene sequence patent, although they would infringe the broad method claim.

¹⁰⁴ See Amended Complaint for Patent Infringement at 4, *Classen Immunotherapies, Inc. v. Biogen IDEC*, No. WDQ-04-2607 (D. Md. 2004), 2004 WL 5804510, at *4.

¹⁰⁵ According to the author of that study, Merck "had no involvement with the . . . article or the study reported in the article. Merck did not initiate the article's research; Merck provided no funding for planning, conducting, evaluating results or otherwise underwriting the study; and Merck researchers did not plan or conduct any part of the research or analyze any of the data generated." Brief for Defendant-Cross Appellant Merck & Co., Inc. at 17-18, *Classen Immunotherapies, Inc. v. Biogen IDEC*, 659 F.3d 1057 (Fed. Cir. 2011) (Nos. 2006-1634, 2006-1649), 2007 WL 460138, at *17-18 (internal quotation mark omitted).

¹⁰⁶ *Classen*, 659 F.3d at 1076 (Moore, J., dissenting).

¹⁰⁷ See Merges & Nelson, *supra* note 4, at 880 (proposing four different models of innovation).

¹⁰⁸ *Id.*

other inventions fit a “cumulative technology” model, where advances in the field build on previous developments.¹⁰⁹ The diagnostic tests at issue here fall within this “cumulative technology” category.¹¹⁰

This factor is exacerbated by the § 102 novelty requirement.¹¹¹ To patent the broad claims at issue in these cases, not merely the process-related claims that detail the step-by-step performance of the diagnostic test, the correlation — or at least the idea of using it for medical purposes — must satisfy § 102 and be newly discovered. Therefore, these particular claims can be obtained only very early in the development of these technologies. But if the clinical relevance of the pertinent biomarker is not known prior to the discovery of the correlation,¹¹² there are likely to be few if any diagnostic tests targeted at its measurement.¹¹³ The grant of a patent at this stage, then, effectively “freezes” the invention at an early stage of development, putting the test’s development in the hands of the initial patentee.

B. Difficulty of Follow-on Innovation

Patent protection for these diagnostic methods also makes follow-on innovation particularly difficult to accomplish due to their breadth. In the cases described above, the Federal Circuit has construed the claims quite broadly, to cover the use of *any* diagnostic test: “patented or unpatented,”¹¹⁴ known at the time the patent was granted or not. This is not simply the conventional problem of broad claim scope. As long as a claim follows the template of the above patents such that all new diagnostics will be found infringing, it will be almost impossible to design around the patent, regardless of the new test’s method of action or improvement over the existing technology.¹¹⁵ It is difficult

¹⁰⁹ See *id.* at 881–82; see also *id.* at 898 (“In contrast with product technology, most chemical production processes evolve cumulatively The first versions of new chemical processes tend to be amenable to a wide range of improvements.”).

¹¹⁰ See *id.* at 881–82.

¹¹¹ 35 U.S.C. § 102 (2006), amended by Pub. L. No. 112-211, 126 Stat. 1527 (2012), and Pub. L. No. 112-29, 125 Stat. 285 (2011).

¹¹² This situation is more likely to occur in cases like *LabCorp*, *Prometheus*, *AMP*, and *Classen*, where the patent is to the correlation, not to specific diagnostic steps to be performed.

¹¹³ Of course, this result does not always occur. Before the homocysteine-folate correlation at issue in *LabCorp* had been discovered, physicians might have wanted to test homocysteine levels for other reasons. Yet even in such a case, the correlation would likely create a new market that would expand demand for existing tests, ideally spurring the development of new, superior tests.

¹¹⁴ *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 125 (2006) (Breyer, J., dissenting from dismissal of certiorari).

¹¹⁵ A subsequent inventor would be able to patent her new diagnostic test, but she would be unable to practice it without obtaining a license from the original patentee. In such a “blocking patent” situation, the original patentee similarly cannot practice the new invention without licensing from the subsequent inventor, but the original patentee nevertheless remains able to practice all unpatented methods of the diagnostic as well as those to which they hold patent rights. Blocking patents certainly do not solve this problem. See Lemley, *supra* note 8, at 1009–10.

even to conceive of what “designing around” would mean in this context. Presumably it would require designing around the correlation, which is the essence of the claim.¹¹⁶ A scientist, therefore, would need to identify another predictive biomarker for the same condition — potentially a biological impossibility.

One might expect the § 101 inquiry to screen out these broad claims for violating the “laws of nature” or “natural phenomena” exceptions to § 101, such that when they are upheld, the claims preempt¹¹⁷ all uses of the claimed correlation.¹¹⁸ Yet the Federal Circuit appears to disfavor direct discussion of the preemption issue in favor of the more easily applied machine-or-transformation test, so far pointing to preemption only when invalidating patents. The preemption issue is entirely absent from *LabCorp*, but there is a brief discussion of it in *Prometheus*, in which the court noted that “because the claims meet the machine-or-transformation test, they do not preempt a fundamental principle.”¹¹⁹ This statement stems from the court’s analysis in its en banc opinion in *In re Bilski*, in which it explicitly stated that the machine-or-transformation test substitutes for the preemption inquiry.¹²⁰ Perhaps because of *Bilski* and *Prometheus*, then, the majority in *Classen* referred exclusively to the machine-or-transformation test and lacked any explicit preemption analysis. Judge Moore’s dissent strongly chastised the court as a result.¹²¹ *AMP* brief-

¹¹⁶ See, e.g., *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, No. 04cv1200 JAH (RBB), 2008 WL 878910, at *7 (S.D. Cal. Mar. 28, 2008).

¹¹⁷ Preemption is one example (perhaps the clearest) of Justice Breyer’s “dangers of overprotection” concern as expressed in *LabCorp*. See *LabCorp*, 548 U.S. at 127 (Breyer, J., dissenting from dismissal of certiorari).

¹¹⁸ Scholars have recently begun debating the relative merits of §§ 101 and 112 for this purpose. See, e.g., Dennis Crouch & Robert P. Merges, *Operating Efficiently Post-Bilski by Ordering Patent Doctrine Decision-Making*, 25 BERKELEY TECH. L.J. 1673, 1674 (2010); Michael Risch, *Everything Is Patentable*, 75 TENN. L. REV. 591, 647 (2008). But 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, 59 (2012) (“[E]nablement doctrine hardly offers any clearer or more predictable tools than patentable subject matter for discerning the allowable scope of patent claims.”). Chief Judge Rader is a strong proponent of § 112, see, e.g., *Classen Immunotherapies, Inc. v. Biogen IDEC*, 659 F.3d 1057, 1073–74 (Fed. Cir. 2011) (Rader, C.J., offering additional views), but Justice Breyer recently reaffirmed the continuing vitality of § 101, see *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1303–04 (2012).

¹¹⁹ *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 581 F.3d 1336, 1349 (Fed. Cir. 2009), *granted, vacated, and remanded* by 130 S. Ct. 3543 (2010).

¹²⁰ See *In re Bilski*, 545 F.3d 943, 954 (Fed. Cir. 2008) (“The Supreme Court, however, has enunciated a definitive test to determine whether a process claim is tailored narrowly enough to encompass only a particular application of a fundamental principle rather than to pre-empt the principle itself. A claimed process is surely patent-eligible under § 101 if: (1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing.”), *aff’d but criticized sub nom. Bilski v. Kappos*, 130 S. Ct. 3218 (2010).

¹²¹ *Classen*, 659 F.3d at 1076 (Moore, J., dissenting) (“I am troubled by the majority’s conclusion that the ’139 and ’739 patent claims are directed to patentable subject matter without any

ly referred to the preemption problem in its characterization of the plaintiffs' argument,¹²² and repeated the concern in striking down many of Myriad's claims as "abstract mental processes."¹²³ Regarding Myriad's claims to isolated DNA sequences, Judge Bryson's partial dissent similarly invoked the preemption concern.¹²⁴ Thus, while the sample size is small, the Federal Circuit seems to refer explicitly to the preemption concern only when invalidating patent claims, but refers to the machine-or-transformation test only when upholding them.¹²⁵

The Federal Circuit thus seems dismissive of the preemption issue. Yet examining *LabCorp* and *Prometheus* to discover the exact effects of patents on subsequent innovators reveals fairly broad preemption problems.¹²⁶ In *LabCorp*, the Federal Circuit affirmed the district court's grant of an injunction preventing LabCorp from "performing *any* homocysteine-only test, including without limitation homocysteine-only tests via the Abbott method."¹²⁷ This injunction swept broadly, requiring LabCorp to contract with Metabolite if it wanted to use *any test* for the determination of homocysteine levels. Because the claim formally covered the use of the homocysteine-folate correlation for diagnostic purposes, LabCorp was barred from performing *any* non-Metabolite test — in essence, from performing the "determine" portion of the claim and from using the correlation for diagnostic purposes. To the degree that there was a natural phenomenon at issue, Metabolite was able to use its patents to preclude LabCorp from using any portion of this natural phenomenon.

Prometheus also demonstrates the costs of preemption when broad diagnostic method patents are approved. The patents at issue in that case were explicitly targeted at measuring drug metabolite levels in the

analysis of the staggering breadth of the claims and the preemption issues inherent in claims directed to such fundamental principles.").

¹²² See *Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office*, 653 F.3d 1329, 1349 (Fed. Cir. 2011).

¹²³ *Id.* at 1355.

¹²⁴ *Id.* at 1374 (Bryson, J., concurring in part and dissenting in part) ("[S]ome of Myriad's challenged composition claims effectively preempt any attempt to sequence the BRCA genes.").

¹²⁵ However, the machine-or-transformation test and an in-depth preemption analysis likely do not converge in every case. See Risch, *supra* note 118, at 647 ("[E]ven if barring preemption of 'fundamental principles' were the optimal subject matter rule, the machine or transformation test fails to achieve a systematic resolution of that question.").

¹²⁶ The Federal Circuit invalidated the relevant claims in *AMP*, and the lower court in *Classen* granted summary judgment for the defendant on the infringement charges. Judge Moore's *Classen* dissent, however, did express serious concerns about the preemptive effects of the claims-in-suit. See *Classen*, 659 F.3d at 1078 (Moore, J., dissenting) ("These claims cover any kind of comparison between any two schedules, using any drugs and comparing the incidence of any chronic immune disease.").

¹²⁷ *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1371–72 (Fed. Cir. 2004) (emphasis added).

context of gastrointestinal disorders. The titles of the patents¹²⁸ and their specifications¹²⁹ were clear. Yet Prometheus used its patents not only to prevent Mayo from using or improving upon its test in the gastrointestinal context,¹³⁰ but also to prevent Dr. Rokea el-Azhary, a researcher at Mayo, from disseminating her work on thiopurine metabolites in the dermatology context.¹³¹ It did so despite the fact that Dr. el-Azhary's work suggested a therapeutic range of metabolites in the dermatology context that is quite different from the therapeutic range in the autoimmune gastrointestinal disorder context.¹³² Although the Supreme Court eventually invalidated Prometheus's claims,¹³³ Dr. el-Azhary waited to publish her research for years while the legal battle was ongoing.¹³⁴ Further, the sheer intimidation factor involved in the legal dispute¹³⁵ may be sufficient to discourage her or others from performing research in the future.

C. Practical Implications of These Concerns

Expanding on the problems raised in these individual cases, empirical research bears out this Note's concerns about the impacts of such patents on follow-on innovation more broadly. The problem is not simply that companies are using their patent rights to prevent others from using their diagnostic tests for commercial gain¹³⁶ — it is within the scope of the patentee's right to prevent others from making, using, or selling their invention. More troubling is the use of patents to prevent quality testing or improvements in technology.¹³⁷

¹²⁸ U.S. Patent No. 6,355,623, at [54] (filed Apr. 8, 1999) ("Method of Treating IBD/Crohn's Disease and Related Conditions Wherein Drug Metabolite Levels in Host Blood Cells Determine Subsequent Dosage.").

¹²⁹ *Id.* at [57] (stating that the patent deals with "immune-mediated gastrointestinal disorder[s] such as inflammatory bowel disease").

¹³⁰ See *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 628 F.3d 1347, 1351 (Fed. Cir. 2010).

¹³¹ Mayo Brief, *supra* note 26, at 11, 2011 WL 3919717, at *11.

¹³² See *id.* at 13, 2011 WL 3919717, at *13.

¹³³ *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1297 (2012).

¹³⁴ Mayo Brief, *supra* note 26, at 13, 2011 WL 3919717, at *13.

¹³⁵ *Id.* at 12, 2011 WL 3919717, at *12 ("Prometheus demanded and received discovery of all Dr. el-Azhary's patients' confidential records. Prometheus also required Dr. el-Azhary to answer hours of questions in deposition about these patients and her treatment of them. Prometheus even asserted infringement . . . when she subsequently received reports that did not list the patented 'therapeutic range' — because the ranges were *still in her memory*." (citation omitted)).

¹³⁶ However, such behavior is clearly occurring. See Mildred K. Cho et al., *Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services*, 5 J. MOLECULAR DIAGNOSTICS 3, 5 (2003) (twenty-five percent of respondents said that a patent holder had prevented them from performing a clinical test). In general, Dr. Cho finds that "virtually no respondents, including those from commercial laboratories, thought that the effects of patents and licenses on the cost, access, and development of genetic tests have been positive." *Id.* at 7.

¹³⁷ Most of the research cited in this section is specific to genetic testing and thus may not be perfectly applicable to chemical diagnostics like those in *LabCorp* or *Prometheus*. While further

Regarding the greater need for follow-on innovation in this context, forty-five percent of laboratory heads believe that such patents have decreased the quality of diagnostic tests.¹³⁸ Specifically referencing the shortcomings identified in Myriad's test, the report of the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) stated that "the quality of genetic testing for a condition improves when there are multiple providers."¹³⁹ The Committee went on to explain that "competition among laboratories is a potent mechanism for ensuring quality as it provides clinicians with alternatives and thus harnesses market forces for continued quality improvement."¹⁴⁰ While the existence of patent protection does not necessarily preclude such competition, the aggressive enforcement policies pursued by many of these companies at least place the two in tension. The absence of patent protection would be more conducive to this type of competition.

Regarding the greater obstacles to follow-on innovation presented by such broad patents,¹⁴¹ fifty-three percent of laboratory heads in one survey "decide[d] not to develop a new clinical genetic test because of a patent or license,"¹⁴² and ninety-one percent felt that the existence of diagnostic patents more generally decreased their ability to develop diagnostic tests.¹⁴³ The SACGHS report similarly implied this point, noting that it could find no case in which "a patent-protected test [was] the first to market," but that instead, "tests were quickly developed without patent protection by multiple laboratories and when patent rights were subsequently granted, they were used to narrow or clear the market of already-developed competition, thus limiting access."¹⁴⁴

research is needed to determine whether the results would hold in that context, the differences in innovation patterns between the two are not likely to render these studies entirely irrelevant.

¹³⁸ Cho, *supra* note 136, at 7 tbl.3 (noting also that only four percent of laboratory heads considered the patents to have increased quality).

¹³⁹ SEC'Y'S ADVISORY COMM. ON GENETICS, HEALTH & SOC'Y, U.S. DEP'T OF HEALTH & HUMAN SERVS., GENE PATENTS AND LICENSING PRACTICES AND THEIR IMPACT ON PATIENT ACCESS TO GENETIC TESTS 46 (2010) [hereinafter SACGHS REPORT].

¹⁴⁰ *Id.* at 48.

¹⁴¹ The studies cited here are not specific to the broad claims at the heart of this Note's analysis. That is, narrower claims targeted at the performance of specific diagnostic tests — like claims one through twelve in *LabCorp* — might also be involved. The data may therefore be even more striking when restricted to these broad claims.

¹⁴² Cho, *supra* note 136, at 3.

¹⁴³ *Id.* at 7 tbl.3.

¹⁴⁴ SACGHS REPORT, *supra* note 139, at 2. One example is haemochromatosis, in which not only did the exclusive license clear the market, but also thirty percent of laboratories "reported discontinuing or not developing genetic testing in the light of the exclusive licence granted on the patents covering clinical-testing services." Jon F. Merz et al., *Diagnostic Testing Fails the Test: The Pitfalls of Patents Are Illustrated by the Case of Haemochromatosis*, 415 NATURE 577, 577 (2002).

III. THE POTENTIAL BENEFITS OF BROAD DIAGNOSTIC METHOD CLAIMS

Once it is recognized that broad diagnostic method claims impose social costs on follow-on innovation, it is important to consider the other side of the equation. If there are significant benefits to granting these patents, those benefits might outweigh the attendant costs. Generally, four types of benefits are thought to result from the patent system: increased incentive to invent, increased incentive to develop and commercialize, increased incentive to disclose, and increased coordination and efficiency. However, evidence suggests that there is little need for patents on diagnostic methods.¹⁴⁵

The patent system incentivizes both innovation and the development and commercialization of innovations. These incentives have different valences for different types of inventions. For small-molecule drugs, which must be shepherded through the extensive FDA regulatory process at great cost,¹⁴⁶ the incentives for development and commercialization may be as or more important than the incentives for initial invention. Yet in the cases at issue here, it is important to be clear about what “invention” is at issue. The relevant invention is not a specific diagnostic.¹⁴⁷ Rather, the relevant invention is the natural correlation between biomarker and disease. Thus, the development and commercialization question has comparatively less relevance here.

Further, patents on these claims are probably not needed to incentivize investment into identifying naturally occurring correlations.¹⁴⁸ Most of the correlations described in this Note were discovered with public support. The *LabCorp* correlation was identified by university

¹⁴⁵ Cf. SACGHS REPORT, *supra* note 139, at 31 (“[L]aboratories lacking exclusive rights associated with genetic testing for particular conditions have regularly developed genetic tests for those conditions.”).

¹⁴⁶ See Joseph A. DiMasi et al., *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 151, 165 (2003).

¹⁴⁷ Even if a new diagnostic were the relevant invention, the incentives to invent, develop, and commercialize would still be likely far less important than those for drugs. First, the estimated costs of developing a diagnostic are far lower than the estimated costs of developing a drug. Compare *id.* at 151 (suggesting that the approximate cost of developing a new drug is roughly \$802 million), with SACGHS REPORT, *supra* note 139, at 34 (“[T]he cost of developing a laboratory-developed genetic test . . . is, on average, between \$8,000 and \$10,000.”). And second, the return on investment from diagnostic tests is often relatively low, especially as compared to a new cholesterol drug. Given the unimportance of these incentives, companies are less likely to invest in developing these tests *even when there is strong patent protection*. If the system is broken and there is a dearth of accurate, quality diagnostics, removing patent protection and permitting others to work in these areas cannot meaningfully exacerbate the problem. Even the SACGHS Report could find “no cases in which possession of exclusive rights was necessary for the development of a particular genetic test.” SACGHS REPORT, *supra* note 139, at 2.

¹⁴⁸ The SACGHS report makes this point very clearly in the context of genetic diagnostic tests. SACGHS REPORT, *supra* note 139, at 1 (“[T]he prospect of patent protection of a genetic research discovery does not play a significant role in motivating scientists to conduct genetic research.”).

researchers with NIH grants.¹⁴⁹ The *Prometheus* correlation was identified by Canadian scientists with grants from the FRSQ,¹⁵⁰ an institution analogous to the NIH. In *Myriad*, numerous public-sector scientists were working to locate the BRCA gene, and the inventors listed on the patents received support from multiple NIH grants.¹⁵¹ There is likely some private investment, but funding for the identification of these correlations is almost certainly weighted more heavily toward the public sector than is funding for drug development.

Patents are similarly not necessarily needed to incentivize the disclosure of these correlations. If publicly funded researchers will typically discover these correlations, the researchers will have the usual academic incentive to publish their findings.¹⁵² They may even be required to publish by the terms of their grant or by the norms of particular scientific inquiries.¹⁵³ And even if these correlations have been discovered by corporations, the need to convince insurance companies that any product they market is worth paying for will likely serve as sufficient incentive to force disclosure of the correlation.¹⁵⁴ While there may be situations in which even correlations identified by academic researchers operating under Mertonian norms would not be disclosed, secrecy norms will generally be weaker in the academic or publicly funded context than they would be within a private corporation.

Finally, the argument that patent protection results in more efficient coordination of subsequent innovation both has been rejected as a conceptual matter by many scholars¹⁵⁵ and does not seem to be empirically true in this context. For instance, in *AMP* Myriad was reluctant to incorporate into its BRCA test the advances in technology that managed to occur despite its refusal to license its patents for this purpose.¹⁵⁶ Ultimately, none of the four benefits traditionally associated with the patent system provides a strong case for granting patents on broad diagnostic method claims.

¹⁴⁹ See John Lindenbaum et al., *Neuropsychiatric Disorders Caused by Cobalamin Deficiency in the Absence of Anemia or Macrocytosis*, 318 *NEW ENG. J. MED.* 1720, 1720 (1988).

¹⁵⁰ See C. Cuffari et al., *6-Mercaptopurine Metabolism in Crohn's Disease: Correlation with Efficacy and Toxicity*, 39 *GUT* 401, 406 (1996).

¹⁵¹ See Donna Shattuck-Eidens et al., *A Collaborative Survey of 80 Mutations in the BRCA1 Breast and Ovarian Cancer Susceptibility Gene: Implications for Presymptomatic Testing and Screening*, 273 *JAMA* 535, 541 (1995); Yoshio Miki et al., *A Strong Candidate for the Breast and Ovarian Cancer Susceptibility Gene BRCA1*, 266 *SCIENCE* 66, 71 (1994).

¹⁵² See SACGHS REPORT, *supra* note 139, at 2.

¹⁵³ The Bermuda Rules are an example of this phenomenon. See Eliot Marshall, *Bermuda Rules: Community Spirit, with Teeth*, 291 *SCIENCE* 1192, 1192 (2001).

¹⁵⁴ See SACGHS REPORT, *supra* note 139, at 2 (“[P]atents are not needed to encourage disclosure in industry because a new health care product or service will not be accepted by the clinical community unless there is disclosure . . .”).

¹⁵⁵ See sources cited *supra* note 8.

¹⁵⁶ See Parthasarathy Declaration, *supra* note 94, at 13–14.

IV. CONCLUSION

There are significant societal costs to permitting broad diagnostic method patents, and the societal benefits of permitting such patents seem to be small. This situation may therefore be one in which the “dangers of overprotection”¹⁵⁷ outweigh fears about underprotection, and patent law ought to respond accordingly. Yet the question of how it should respond is difficult. The remedy provided under § 101 might be viewed as “harsh” when compared to other potential remedies,¹⁵⁸ and it would also be critical to ensure that § 101 is responsive to the policy concerns involved.¹⁵⁹ If the goal is not to prevent the grant of these patents entirely but instead to limit their scope to what the patentee described and enabled, § 112 might be more appropriate.¹⁶⁰ The optimal solution would allow inventors to retain the incentives for innovation created by the patent system while also mitigating the harms to follow-on innovation, and the choice between § 101 and § 112 is not obvious. Explicit consideration of the costs and benefits of these potential solutions is a worthwhile endeavor.

Ultimately, this Note describes just one of the particular harms that may result from these broad diagnostic patent claims: the harms to follow-on innovation. The harms to follow-on innovation from these diagnostic method patents are real and potentially significant. The Federal Circuit and Supreme Court ought to take them into consideration as they decide future cases involving these claims.

¹⁵⁷ *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 127 (2006) (Breyer, J., dissenting from dismissal of certiorari).

¹⁵⁸ This remedy is “harsh” in the sense that a claim is either patent eligible or not under § 101 (the inquiry is binary), while under § 112, the question is about what the claim covers (the inquiry takes place along a spectrum). However, this framing may be a false dichotomy because it treats as constant the construction of the claim — *for a given construction*, § 101 is harsher than § 112.

¹⁵⁹ The policy goals behind § 101 may be better suited to redress this issue than are the policy goals behind § 112.

¹⁶⁰ More generally, there are several choice points in the current patenting scheme at which this issue might be addressed, such as at the initial invention stage by choosing not to file a patent or by licensing it nonexclusively, at the infringement suit stage by examining the situation through one or another section of the Patent Act, or later through an adjudication of remedies. There are also a number of points at which the traditional system might be jettisoned for a new paradigm. *See, e.g.*, WILLIAM FISHER, *PROMISES TO KEEP* 199–258 (2004); Steven Shavell & Tanguy van Ypersele, *Rewards Versus Intellectual Property Rights*, 44 J.L. & ECON. 525, 534–41 (2001).