
Innovation Law and Policy: Preserving the Future of Personalized Medicine

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Personalized medicine is the future of healthcare. As such, incentives for innovation in personalized technologies have rightly received attention from judges, policymakers, and legal scholars. Yet their attention too often focuses on patent law, to the exclusion of FDA regulation and health law, areas that may have an equal or greater effect on real-world conditions. And because patent law, FDA regulation, and health law all interact to affect incentives for innovation, they must be considered jointly. This Article will examine these systems together in the area of diagnostic tests, an aspect of personalized medicine which has seen recent developments in all three systems. Over the last five years, the FDA, Congress, the Federal Circuit, and the Supreme Court have dealt three separate blows to incentives for innovation in diagnostic tests: respectively, they have made it more expensive to develop diagnostics, reduced the amount innovators can expect to recoup in the market, and made it more difficult to obtain and enforce patents on them. Each of these changes may have had a marginal effect on its own, but when considered together, the system has likely gone too far in disincentivizing desperately needed innovation in diagnostic technologies. Fortunately, just as each legal system has contributed to the problem, each system can also be used to solve it. This Article suggests specific legal interventions that can be used to restore an appropriate balance in incentives to innovate in diagnostic technologies.

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INTRODUCTION

Every year, nearly ten billion diagnostic tests are performed in the United States.¹ These tests include everything from a standard blood test that measures cholesterol levels to a complex multigene panel that assesses patients for hereditary predispositions to developing various cancers.² Although the tests themselves make up just one or two percent of overall healthcare spending,³ the results of these tests influence more than two-thirds of all treatment decisions.⁴ Yet the already great importance of diagnostic tests to broader treatment decisions is likely only to increase over the next several years, as the idea of personalized medicine — the need to get the right treatment to the right patient at the right time⁵ — plays an increasingly central role in our health policy discourse. In January 2015, President Obama emphasized the importance of personalized medicine by announcing a landmark, \$215 million Precision Medicine Initiative,⁶ which he took care to introduce in his State of the Union address.⁷ Physicians can already prescribe chemotherapy drugs that are targeted to be most effective where tumors have particular mutations, precisely calibrate

¹ STATE HEALTH INFO. EXCH. PROGRAM, STATE HIE BRIGHT SPOTS 1 (2013), available at http://www.healthit.gov/sites/default/files/lab_exchange_bright_spots_exec_summ_final_09302013.pdf.

² See, e.g., Holly LaDuca et al., *Utilization of Multigene Panels in Hereditary Cancer Predisposition Testing: Analysis of More than 2,000 Patients*, 16 GENETICS MED. 830, 836 (2014).

³ See Mark R. Trusheim et al., *Uncertain Prognosis for High-Quality Diagnostics: Clinical Challenges, Economic Barriers and Needed Reforms*, 14 PHARMACOGENOMICS 325, 325 (2013); THE LEWIN GROUP, LABORATORY MEDICINE: A NATIONAL STATUS REPORT 19 (2008), available at <http://www.amcp.org/WorkArea/DownloadAsset.aspx?id=11578>.

⁴ Trusheim et al., *supra* note 3, at 325; see THE LEWIN GROUP, *supra* note 3, at 19 (“The contributions of laboratory tests and services as an essential component and partner in health systems remains under-recognized.”).

⁵ W. Nicholson Price II, *Unblocked Future: Why Gene Patents Won’t Hinder Whole Genome Sequencing and Personalized Medicine*, 33 CARDOZO L. REV. 1601, 1603 (2012) [hereinafter *Unblocked Future*]; *Precision (Personalized) Medicine*, U.S. FOOD & DRUG ADMIN. (Nov. 18, 2015), <http://www.fda.gov/scienceresearch/specialtopics/personalizedmedicine/default.htm>; see Barbara J. Evans, *Seven Pillars of a New Evidentiary Paradigm: The Food, Drug, and Cosmetic Act Enters the Genomic Era*, 85 NOTRE DAME L. REV. 419, 488 (2010) (describing pharmacogenomics).

⁶ Press Release, Office of the Press Sec’y, Fact Sheet: President Obama’s Precision Medicine Initiative (Jan. 30, 2015), available at <http://www.whitehouse.gov/the-press-office/2015/01/30/fact-sheet-president-obama-s-precision-medicine-initiative>.

⁷ President Barack Obama, Remarks by the President in State of the Union Address (Jan. 20, 2015), available at <http://www.whitehouse.gov/the-press-office/2015/01/20/remarks-president-state-union-address-january-20-2015>.

the dose patients receive of particular blood thinners (where either too much or too little may prove fatal), and predict with greater accuracy whether patients are likely to develop certain conditions later in life. Although science is beginning to demonstrate the promise of personalized medicine, as President Obama recognized, there is still much work to be done.

But fully realizing the goals of personalized medicine will not be possible unless physicians have a broad array of innovative diagnostic tests at their fingertips. To achieve their full potential, these innovative tests must not only include “true” diagnostics — those that allow a physician to identify the disease afflicting a symptomatic patient — but they must also allow physicians to assess their patients’ risk for future illness, screen their asymptomatic patients for disease, select and monitor their patients’ treatments, and assess their outcomes.⁸ Achieving each of these individual goals while simultaneously assuring the accuracy and quality of the tests is no easy task, and physicians will need many more high-quality diagnostic tests than currently exist to help them along this path. As such, ensuring that academic researchers and diagnostic testing companies have sufficient resources and incentives to develop those tests is critically important.

Preserving such incentives requires maintaining a precarious balance between the cost of developing an innovation, the ability to protect that innovation,⁹ and the ability to recoup the investment into that innovation.¹⁰ Most scholarly attention to this balance has focused on the role of patent law, considering whether and how patent law enables innovators to protect their investment into a given technology.¹¹ And in many important areas of technology, patents may

⁸ See Trusheim et al., *supra* note 3, at 326-27.

⁹ Investors’ ability to protect their investments is not necessarily a separate variable in this equation. Rather, it is a means to achieving the end goal of recouping the initial investment. But in cases like these, the good to be produced is an information good, and is therefore easily copied. See SUZANNE SCOTCHMER, *INNOVATION AND INCENTIVES* 58 (2004). As such, patents are often critical to the achievement of the end goal, and they are sufficiently important to be treated distinctly here.

¹⁰ See WILLIAM M. LANDES & RICHARD A. POSNER, *THE ECONOMIC STRUCTURE OF INTELLECTUAL PROPERTY LAW* 13-15 (2003); see also *Bilski v. Kappos*, 561 U.S. 593, 650 (2010) (Stevens, J., concurring) (“[W]hen innovation is expensive, risky, and easily copied, inventors are less likely to undertake the guaranteed costs of innovation in order to obtain the mere possibility of an invention that others can copy.”); *Ass’n for Molecular Pathology v. U.S. Patent & Trademark Office*, 689 F.3d 1303, 1324 (Fed. Cir. 2012) (“[P]atents on life-saving material and processes, involving large amounts of risky investment, would seem to be precisely the types of subject matter that should be subject to the incentives of exclusive rights.”).

¹¹ See, e.g., Rebecca S. Eisenberg, *The Shifting Functional Balance of Patents and*

indeed be the primary avenue through which incentives to innovate intersect with the legal system. But in the case of most health technologies, patent law is not the only, or even perhaps the most important area of law to consider. Food & Drug Administration (“FDA”) regulations typically dictate the conditions under which such technologies may enter the market, and healthcare regulations promulgated by the Centers for Medicare & Medicaid Services (“CMS”) govern whether to pay for a given technology as part of its role as insurer to more than one hundred million Americans.¹²

Each of these three systems — FDA regulation, patent law, and healthcare regulation — affects the market for health technologies, and as such they can most helpfully be understood as a unit. FDA regulations not only play a key gatekeeping function, but in doing so they necessarily drive the cost of developing a given innovation.¹³ CMS must decide whether medical technologies will be covered by Medicare or Medicaid, and in doing so CMS is frequently involved in setting reimbursement rates,¹⁴ regulating the ability of innovators to profit from their inventions. And patent law classically functions to enable innovators to protect their investment into a given technology. Thus, an array of policy choices, not simply those taking place within any one field, shape incentives to innovate.¹⁵

The relevant legal actors in control of each system do not formally possess shared regulatory authority over the innovation space,¹⁶ and

Drug Regulation, 19 HEALTH AFF. 119, 120-21 (2001) [hereinafter *The Shifting Functional Balance*]; Arti K. Rai, *The Information Revolution Reaches Pharmaceuticals: Balancing Innovation Incentives, Cost, and Access in the Post-Genomics Era*, 2001 U. ILL. L. REV. 173, 178 [hereinafter *Information Revolution Reaches Pharmaceuticals*].

¹² See DEP’T OF HEALTH & HUMAN SERVS., CTRS. FOR MEDICARE & MEDICAID SERVS., FISCAL YEAR 2016 JUSTIFICATION OF ESTIMATES FOR APPROPRIATIONS COMMITTEES 109-10 (2015), available at <https://www.cms.gov/About-CMS/Agency-Information/PerformanceBudget/Downloads/FY2016-CJ-Final.pdf>.

¹³ See Amy Kapczynski & Talha Syed, *The Continuum of Excludability and the Limits of Patents*, 122 YALE L.J. 1900, 1922 (2013).

¹⁴ See Mark Hall, *Institutional Control of Physician Behavior: Legal Barriers to Health Care Cost Containment*, 137 U. PA. L. REV. 431, 436 (1988); Kevin Outterson, *Pharmaceutical Arbitrage: Balancing Access and Innovation in International Prescription Drug Markets*, 5 YALE J. HEALTH POL’Y L. & ETHICS 193, 241 n.204 (2005).

¹⁵ As I will discuss later, the effects of these fields cannot truly be reduced to a single sentence. See, e.g., *infra* text accompanying note 216. But these explanations provide broad characterizations of the effect of a particular body of law.

¹⁶ See Stuart Minor Benjamin & Arti K. Rai, *Fixing Innovation Policy: A Structural Perspective*, 77 GEO. WASH. L. REV. 1, 5 (2008); Eisenberg, *The Shifting Functional Balance*, *supra* note 11, at 121; Jody Freeman & Jim Rossi, *Agency Coordination in Shared Regulatory Space*, 125 HARV. L. REV. 1131, 1138-45 (2012).

yet their decisions interact in complex ways to affect incentives for innovation. In many cases, supposed problems that are identified in one system may cease to be of real concern when considered in the fuller context of all three.¹⁷ Alternatively, problems caused by changes in one system may most fruitfully be solved by legislative or regulatory tweaks to one of the others.¹⁸ More negatively, though, in some cases problems caused by changes in one system may be exacerbated by tweaks in another. Yet the relationships between these three areas of law have been underappreciated and too often even ignored in the legal literature.¹⁹ This Article is the first to consider the intersystemic interactions of these three areas, illustrating them by focusing, as a case study, on the technology of diagnostic tests.

Until roughly 2010, the incentives to develop diagnostic tests were reasonably favorable to innovators. The cost of developing such tests was much lower than the cost of developing a new drug or medical device; patents on diagnostic methods and targets were easily available

¹⁷ See Yaniv Heled, *Patents vs. Statutory Exclusivities in Biological Pharmaceuticals — Do We Really Need Both?*, 18 MICH. TELECOMM. & TECH. L. REV. 419, 424 (2012) (discussing double layered protection for biologics of both patents and FDA exclusivity periods).

¹⁸ Most notably, FDA exclusivity periods for pharmaceuticals may perform many of the same functions as patents in assisting innovators in protecting their investments. See Eisenberg, *The Shifting Functional Balance*, *supra* note 11, at 122. See generally Heled, *supra* note 17, at 449-50 (considering the redundancies between patents and regulatory exclusivities).

¹⁹ Professors Rebecca Eisenberg and Arti Rai have written memorably about the relationship between FDA exclusivity periods and the role of patents in the context of pharmaceuticals. See, e.g., Eisenberg, *The Shifting Functional Balance*, *supra* note 11, at 122; Rai, *Information Revolution Reaches Pharmaceuticals*, *supra* note 11, at 183. But the relationship between FDA regulation and patent law deserves much greater scrutiny, particularly as it applies to other healthcare technologies and newly enacted FDA regulations. Further, the role of healthcare regulation in this scholarly space is essentially absent, with a few exceptions. See, e.g., Kevin Outterson, *The Legal Ecology of Resistance: The Role of Antibiotic Resistance in Pharmaceutical Innovation*, 31 CARDOZO L. REV. 613, 645-55 (2010); Benjamin N. Roin, *Intellectual Property Versus Prizes: Reframing the Debate*, 81 U. CHI. L. REV. 999, 1053 (2014). Other scholarship that considers the role of alternative mechanisms has focused on the roles of other policies that enable monetary transfers, like federal funding and tax incentives. See generally, e.g., Daniel J. Hemel & Lisa Larrimore Ouellette, *Beyond the Patents-Prizes Debate*, 92 TEX. L. REV. 303 (2013) (setting forth a taxonomy of innovation incentives and detailing tax incentives in particular); Lisa Larrimore Ouellette, *Patentable Subject Matter and Nonpatent Innovation Incentives*, 5 UC IRVINE L. REV. 1115 (2015) [hereinafter *Patentable Subject Matter*] (applying non-patent incentives to differing technological fields). Although these alternative mechanisms are surely important, I put them aside until Part V, as they have not experienced analogous recent developments.

and enforceable; such products typically enjoyed a healthy amount of insurance reimbursement. Profit margins for diagnostics companies were not at the level reaped by the pharmaceutical industry,²⁰ but scholars were primarily concerned with whether incentives in this area were too high, rather than too low. There were serious policy debates about whether patents were at all necessary to produce new diagnostic tests, given the low cost of development, availability of government funding, and noncommercial motivation of academic researchers.²¹

Just in the last few years, though, the incentives to develop diagnostic tests have shifted dramatically. The FDA has recently proposed to increase significantly the regulatory burdens it places on diagnostic tests, sharply raising the costs of developing those tests for academic researchers and corporations alike.²² Congress and CMS have cut reimbursement rates for diagnostic tests, occasioning a restructuring of the industry and making it more difficult for potential innovators to recoup their investments.²³ And the Supreme Court and Federal Circuit have recently interpreted various patent law provisions in ways that make it harder to both obtain and enforce patents on diagnostic methods, thus making it more difficult for diagnostic companies to protect the investments they make in diagnostic testing.²⁴ Each of these developments has taken place independently from the others, but when considered as a unit they have the potential to depress significantly incentives for innovation in diagnostic tests.²⁵

²⁰ See *infra* notes 110–11.

²¹ Compare 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 1 (2010) [hereinafter SACGHS REPORT ON GENE PATENTS] (“[T]he prospect of patent protection of a genetic research discovery does not play a significant role in motivating scientists to conduct genetic research.”), with PRESIDENT’S COUNCIL OF ADVISORS ON SCI. & TECH., PRIORITIES FOR PERSONALIZED MEDICINE 21 (2008) (“The ability to obtain strong intellectual property protection through patents . . . will continue to be[] essential for pharmaceutical and biotechnology companies to make the large, high-risk R&D investments required to develop novel medical products, including genomics-based molecular diagnostics.”).

²² See *infra* Part I.

²³ See *infra* Part II.

²⁴ See *infra* Part III.

²⁵ Like many other pieces of innovation scholarship, this Article by necessity grapples with empirical questions about what level of innovation is optimal, what range of policies will best promote that level of innovation, and other related inquiries. Cf. John F. Duffy, *Rules and Standards on the Forefront of Patentability*, 51 WM. & MARY L. REV. 609, 618 (2009) (noting that courts and policymakers lack sufficient empirical information to tailor the patent system to produce optimal innovation incentives and considering the pervasiveness of our empirical limitations). Ultimately, though, this Article is able to bracket many of these questions by

This Article proceeds in five Parts. Part I considers the FDA's recent proposal to begin regulating laboratory-developed tests. This proposal would increase the costs of developing diagnostic tests by imposing new regulatory burdens on academic laboratories and diagnostic testing companies who were previously subject only to a much less onerous regulatory system. Part II considers the impact of the Affordable Care Act ("ACA") and other recent cuts made to Medicare reimbursement rates for the performance of diagnostic tests. These rates, which have ripple effects throughout the private insurance market, affect the ability of innovators to recoup their investment into a given diagnostic test. Part III will consider recent patent law decisions from the Federal Circuit and Supreme Court that make it more difficult for diagnostic method innovators both to obtain patents and to enforce them. Part III also considers how the ACA and related statutes are restructuring the diagnostics industry in a way that exacerbates these difficulties.

Part IV synthesizes these recent developments, explaining the ways in which they combine to affect incentives for innovation. It considers how the combination of these areas of law may differentially affect various actors in the innovation ecosystem, or may differentially impact the types of diagnostic technologies that are produced. It uses these insights to illustrate the ways in which existing scholarship focusing on innovation incentives is often incomplete, as it considers the role one legal system plays while missing the impact of other, similarly relevant systems. Ultimately, it suggests that flipping all three of these policy levers simultaneously may have significantly depressed incentives to innovate in the diagnostic testing field. More optimistically, though, Part IV contends that switching other policy levers within these areas of law may be able to counteract these effects, with minimal concomitant damage.

Part V therefore considers potential interventions, canvassing a range of specific alternatives across all three systems — FDA regulation, patent law, healthcare regulation — and across all three incentive levers — cost to develop the product, ability to protect the technology, and ability to recoup the investment. In doing so, Part V presents a new perspective on a recent Supreme Court decision, a fuller understanding of the ACA's incentive effects, and a new recommendation regarding an ongoing FDA regulatory process. Ultimately, Part V suggests that a menu of interventions may be

grounding its central thesis in comparison to existing scholarly accounts of incentives in this space.

needed to restore an appropriate balance in incentives to innovate in diagnostic testing, suggesting tweaks to the FDA's regulatory proposal that would ease the burdens on academic researchers and small companies, and tweaks to CMS's reimbursement system that would benefit larger firms.

I. INCREASING THE COSTS OF DEVELOPMENT THROUGH FDA REGULATION

A key concern for innovators in any field is the cost to develop a new technology.²⁶ Until recently, the amount of investment needed to develop a new diagnostic test was estimated to be quite low, perhaps in the range of ten thousand dollars,²⁷ which is far less than the multi-billion-dollar investment estimated to be required for a new pharmaceutical.²⁸ One key reason for this disparity is the level of scrutiny that the FDA has applied to new diagnostic tests as compared to new drugs. Drugs are generally subject to an extensive and expensive clinical trial process, the completion of which can contribute hundreds of millions of dollars to the cost of developing a single drug.²⁹

Yet until July 2014, the FDA essentially exercised no regulatory authority over "laboratory-developed tests" or LDTs, those which are "designed, manufactured, and used within a single laboratory."³⁰ The

²⁶ See, e.g., LANDES & POSNER, *supra* note 10, at 294.

²⁷ See SACGHS REPORT ON GENE PATENTS, *supra* note 21, at 34, 94.

²⁸ The typical cost of developing a new drug is hotly contested. The Tufts Center for the Study of Drug Development recently estimated the cost at \$2.6 billion, a significant increase from their 2003 estimate of \$802 million. See Joseph A. DiMasi et al., *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 47 J. HEALTH ECON. 20, 20 (2016) (estimating pre-approval costs to be \$2.558 billion); Joseph A. DiMasi et al., *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 151, 151 (2003) (estimating pre-approval costs to be \$802 million). Another consulting group roughly contemporaneously estimated the cost at \$1.5 billion. Jorge Mestre-Ferrandiz, *The R&D Cost of a New Medicine*, OFF. HEALTH ECON. (Jan. 29, 2013), available at <http://www.slideshare.net/OHENews/rd-cost-of-a-new-medicine-mestre-ferrandiz-19-jan2013>. However, studies like these have been heavily criticized by public interest advocates, who report far lower numbers. See, e.g., Donald W. Light & Rebecca Warburton, *Demythologizing the High Costs of Pharmaceutical Research*, 6 BIOSOCIETIES 1, 14 (2011) (stating that "R&D costs companies a median of \$43.4 million per new drug").

²⁹ See Kapczynski & Syed, *supra* note 13, at 1922 n.62.

³⁰ FOOD & DRUG ADMIN., U.S. DEP'T OF HEALTH & HUMAN SERVS., FRAMEWORK FOR REGULATORY OVERSIGHT OF LABORATORY DEVELOPED TESTS (LDTs), DRAFT GUIDANCE 5-8 (2014) [hereinafter LDT DRAFT GUIDANCE], available at <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM416685.pdf>.

FDA had only exercised its authority over diagnostics where a testing company had decided to produce a test kit for sale and use in hospitals and laboratories around the country.³¹ Depending on the level of risk posed by the kit, this review might include premarket notification, approval requirements, adverse event reporting, and registration.³² Companies responded to the incentives created by this scheme,³³ and estimates suggest that the majority of genetic tests are currently offered as LDTs,³⁴ and that there are more than 11,000 diagnostic tests currently available as LDTs.³⁵ However, the FDA's recent proposal to impose new regulatory burdens on many thousands of LDTs has the potential to significantly increase the costs of developing diagnostic tests.³⁶

This Part will first lay out the way in which diagnostic testing is currently regulated in the United States, focusing on the oversight exercised by CMS, and briefly noting the oversight exercised at the state

Importantly, this does not mean that only one laboratory in the country performs a given test. It certainly can, but it often does not. Many of the most widely available tests are LDTs, precisely because they are simple for every lab to develop and perform independently. Routine laboratory tests like a complete blood count or Pap smear typically qualify as LDTs for this reason. These tests are performed in hundreds or even thousands of labs around the country, but they can still qualify as LDTs as long as there is no test manufacturer who sells a diagnostic product to other labs. *21st Century Cures: Examining the Regulation of Laboratory-Developed Tests: Hearing Before the Subcomm. on Health of the H. Comm. on Energy and Commerce*, 113th Cong. 4 (2014) (statement of Alan Mertz, President, The American Clinical Laboratory Association), available at <http://www.acla.com/acla-written-statement-for-21st-century-cures-hearing-on-ldt-regulation/>.

³¹ The Federal Food, Drug, and Cosmetic Act 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, or in the cure, mitigation, treatment or prevention of disease.” 21 U.S.C. § 321(h) (2012).

³² See *infra* text accompanying notes 62–63.

³³ PRESIDENT'S COUNCIL OF ADVISORS ON SCI. & TECH., *supra* note 21, at 38-39.

³⁴ SACGHS REPORT ON GENE PATENTS, *supra* note 21, at 61.

³⁵ Andrew Pollack, *F.D.A. Acts on Lab Tests Developed In-House*, N.Y. TIMES (July 31, 2014), <http://www.nytimes.com/2014/08/01/business/fda-to-regulate-lab-developed-test-kits.html>.

³⁶ Of course, patent law and healthcare regulation (the other two areas of law explored in this Article) also contribute to the cost of developing a diagnostic test. Innovators spend time and resources prosecuting patents before the PTO, and they may need to negotiate with insurers and providers to be sure their tests are covered. But these costs are 1) likely to be small relative to the costs imposed by the FDA regulatory process and 2) are relatively fixed, at present, unlike the FDA process. See David Fagundes & Jonathan S. Masur, *Costly Intellectual Property*, 65 VAND. L. REV. 677, 689-91 (2012) (explaining that “an average patentee will spend approximately \$22,000 to successfully prosecute a patent application”).

level and by private standard-setting organizations. It will then examine the ways in which the FDA's new proposal seeks to supplement CMS's oversight, considering carefully the new regulatory burdens being imposed on diagnostic manufacturers. Importantly, the FDA's reasons for imposing these additional regulatory burdens are compelling from a public health perspective. However, this Part will conclude by pointing out the primary ways in which the FDA's proposal will nevertheless raise costs for innovative diagnostic producers.

A. Current Regulatory Scheme

Currently, laboratories performing diagnostic tests are primarily regulated by CMS through the Clinical Laboratory Improvement Amendments of 1988 ("CLIA").³⁷ Such laboratories are required to obtain a certificate of compliance or accreditation under CLIA every two years.³⁸ Much of the approval and renewal process focuses on the laboratories themselves and their operations, including the physical facilities available and the credentials of the laboratory employees.³⁹ But CLIA does impose some regulations on the tests, requiring in the case of FDA-approved tests that laboratories meet the "performance specifications" set by the tests' manufacturers.⁴⁰ Where the tests have not been FDA-approved, though (as in the case of most LDTs), the laboratory is permitted to set its own performance specifications. For these tests, CMS requires only that laboratories set specifications for dimensions of accuracy, precision, analytical sensitivity and specificity, and reportable ranges.⁴¹

CLIA therefore ensures that diagnostic tests possess *analytical validity*, but it provides essentially no information about a test's *clinical validity*.⁴² These epidemiological terms are perhaps best

³⁷ Clinical Laboratory Improvement Amendments of 1988, Pub. L. No. 100-578, 102 Stat. 2903 (codified as amended at 42 U.S.C. § 263a (2006)); LDT DRAFT GUIDANCE, *supra* note 30, at 7.

³⁸ 42 U.S.C. § 263a(c)(2) (2012). Some laboratories, which only perform tests which the FDA and CDC have determined are "so simple that there is little risk of error[.]" are eligible for CLIA waivers. *Certificate of Waiver Laboratory Project*, CENTERS FOR MEDICARE & MEDICAID SERVICES (Feb. 27, 2014, 8:11 AM), http://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Certificate_of_-Waiver_Laboratory_Project.html.

³⁹ See, e.g., Facility Administration for Nonwaived Testing, 42 C.F.R. §§ 493.1100-.1105 (2015); Personnel for Nonwaived Testing, 42 C.F.R. §§ 493.1351-.1495 (2015).

⁴⁰ 42 C.F.R. § 493.1253(b)(1) (2015).

⁴¹ *Id.* § 493.1253(b)(2).

⁴² *CLIA Overview: What Is CMS' Authority Regarding Laboratory Developed Tests (LDTs) and How Does It Differ from FDA's Authority?*, CENTERS FOR MEDICARE & MEDICAID SERVICES

illustrated with an example of one of the most famous LDTs: Myriad's genetic test for mutations in the BRCA genes, which can predispose their holders to an increased risk of breast and ovarian cancer.⁴³ A woman with a familial history of these diseases might reasonably want to determine whether she has inherited such a genetic mutation. Myriad, who for many years was the only commercial provider of such a test in the United States,⁴⁴ advertises tests for a large number of possible mutations.⁴⁵ CLIA accreditation provides assurance to any woman seeking testing that Myriad's test accurately detects the presence or absence of those specific mutations in her genes — that is, the test possesses analytical validity. It finds what it's supposed to find.

However, under CLIA, whether or not the woman's genes contain any of the mutations covered by the test — whether the test finds what it's supposed to find — does not necessarily provide her with any information about the likelihood that she will develop breast or ovarian cancer. That is, CLIA does not assure that Myriad's test possesses *clinical* validity. Of course, there is no question that mutations in the BRCA genes are generally associated with an increased risk of breast and ovarian cancer.⁴⁶ But it might be that the many mutations Myriad tests for would each only increase her chance of developing cancer by a *de minimis* amount, and that there are many other mutations not tested for which could far more dramatically increase her risk.⁴⁷ Or it might also be that Myriad only tests for a subset of known mutations, giving women who may have untested mutations a false sense of security.⁴⁸ The question of how the

(2013), http://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/LDT-and-CLIA_FAQs.pdf [hereinafter *CLIA Overview*] (“[U]nlike the FDA regulatory scheme, CMS’ CLIA program does not address the clinical validity of any test.”).

⁴³ See Mary-Claire King, “*The Race*” to Clone BRCA1, 343 SCI. 1462, 1462 (2014).

⁴⁴ *Id.* at 1465.

⁴⁵ See MYRIAD, CLINICAL QUALITY ASSURANCE MEASURES AT MYRIAD GENETIC LABORATORIES 5 (2013), available at https://s3.amazonaws.com/myriad-library/mfap/MFAP+WhitePaper_QA+Measures.PDF.

⁴⁶ See, e.g., Jeff M. Hall et al., *Linkage of Early-Onset Familial Breast Cancer to Chromosome 17q21*, 250 SCI. 1684, 1684 (1990).

⁴⁷ See, e.g., TOM STRACHAN & ANDREW P. READ, HUMAN MOLECULAR GENETICS 230 (2d ed. 1999) (explaining why frameshifting mutations may be more pathogenic than nonframeshifting mutations).

⁴⁸ Scientists alleged that as late as 2006, more than ten years after it began operating, Myriad's test still did not detect a significant percentage of large genomic deletions or duplications. Robert Cook-Deegan et al., *Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Inherited Susceptibility to Cancer*, 12 GENETICS MED. S15, S16 (2010); see also Steve Benowitz, *French Challenge to BRCA1 Patent Underlies European Discontent*, 94 J. NAT'L CANCER INST. 80, 80 (2002).

biological marker involved in the test relates to the specific disease at issue is one of clinical validity, and CLIA is unable to measure it.⁴⁹

Of course, this is not to say that the regulatory process is incapable of eliciting any information about clinical validity. In particular, two additional regulatory systems function in at least some cases to produce such information. New York State's wide-ranging clinical laboratory certification program⁵⁰ requires review for clinical validity.⁵¹ The College of American Pathologists, a certified accrediting organization under CLIA,⁵² similarly requires such review (although the accreditation itself is voluntary).⁵³ In addition to such programs, health insurers may also demand information about clinical validity.⁵⁴

But review by these systems is typically based on the scientific literature or clinical practice guidelines, rather than on additional clinical trials.⁵⁵ This is particularly significant in cases like Myriad's risk assessment test, where the question of clinical validity is multifaceted. That is, the scientific literature is rife with evidence that mutations in the BRCA gene are, in general, related to an increased risk of developing breast or ovarian cancer.⁵⁶ But the literature

⁴⁹ See *CLIA Overview*, *supra* note 42.

⁵⁰ By some estimates, New York's program oversees roughly 75% of all genetic and cytogenetic specimens tested in the United States. SECY'S ADVISORY COMM. ON GENETICS, HEALTH & SOC'Y, U.S. DEP'T OF HEALTH & HUMAN SERVS., U.S. SYSTEM OF OVERSIGHT OF GENETIC TESTING 36, 100 (2008) [hereinafter SACGHS REPORT ON OVERSIGHT]. This is because New York exercises oversight not only of labs within New York, but also of any labs which receive samples for testing from New York. *Id.* at 3, 36.

⁵¹ *Comprehensive Test Approval Policy and Submission Guidelines*, ST. N.Y. DEP'T HEALTH (2013), http://www.wadsworth.org/sites/default/files/WebDoc/2141071292/Comprehensive%20Test%20approval%20Submission_Guidelines_Policy.pdf; see also SACGHS REPORT ON OVERSIGHT, *supra* note 50, at 99.

⁵² See *About the CAP Laboratory Accreditation Program*, C. AM. PATHOLOGISTS (2014), http://www.cap.org/apps/cap.portal?_nfpb=true&cntvwrPtl_t_actionOverride=%2Fportlet%2FcontentViewer%2Fshow&_windowLabel=cntvwrPtl_t&cntvwrPtl_t%7BactionForm.contentReference%7D=laboratory_accreditation%2Faboutlap.html&_state=maximized&_pageLabel=cntvwr; see also SACGHS REPORT ON OVERSIGHT, *supra* note 50, at 77.

⁵³ SACGHS REPORT ON OVERSIGHT, *supra* note 50, at 105.

⁵⁴ See, e.g., Julie Steenhuysen, *INSIGHT — As Sequencing Moves into Clinical Use, Insurers Balk*, REUTERS (June 19, 2014), <http://www.reuters.com/article/us-health-sequencing-insight-idUSKBN0EU16S20140619>. Sometimes insurers seek information that would be classified in the clinical validity category, but more commonly they seek information regarding clinical utility: that is, even if we know that this patient has or is likely to develop a certain disease, are there meaningful treatment interventions available? If not, the insurer may decline to pay. See, e.g., PRESIDENT'S COUNCIL OF ADVISORS ON SCI. & TECH., *supra* note 21, at 46.

⁵⁵ See, e.g., SACGHS REPORT ON OVERSIGHT, *supra* note 50, at 98-99.

⁵⁶ See, e.g., Hall et al., *supra* note 46, at 1684.

generally does not comment on specific mutations and the specific percentage increase in risk attributable to those mutations. Yet this information is highly relevant to physicians and patients — these diagnostics are serious tests, with serious implications. If a physician would counsel a patient to have a prophylactic double mastectomy on the basis of receiving a positive result on Myriad's test, a patient deserves relevant information about the risks and benefits of that personal choice.⁵⁷

B. *The FDA's Proposal*

The FDA's fall 2014 proposal⁵⁸ is designed to gather such information about clinical validity for the first time for many tests like Myriad's. Further, FDA involvement in this area has additional benefits that CLIA cannot provide. For example, CLIA does not require adverse event reporting or even the removal of unsafe diagnostics from the market.⁵⁹ CLIA's review of products is also necessarily retrospective, while the FDA is proposing to regulate many of these products before they enter the market.⁶⁰

More broadly, the FDA is aiming to impose on LDTs a risk-based framework much like the scheme it presently imposes on other diagnostic tests and medical devices.⁶¹ Under the FDA's current system, low-risk (designated as Class I) devices such as tongue depressors are subject only to "general controls,"⁶² such as reporting and adherence to good manufacturing practices. By contrast, high-risk (designated as Class III) devices such as artificial hearts are subject to more stringent controls, including premarket approval requirements.⁶³

⁵⁷ See, e.g., Laura Koontz, Dir. of Policy, Ovarian Cancer Nat'l Alliance, Remarks Delivered at Food & Drug Admin. (Jan. 9, 2015), available at <http://www.ovariancancer.org/wp-content/uploads/2015/01/2015-01-08-FDA-LDT-meeting-general-session-comments.pdf>.

⁵⁸ Framework for Regulatory Oversight of Laboratory Developed Tests, 79 Fed. Reg. 59776 (Oct. 3, 2014); see generally LDT DRAFT GUIDANCE, *supra* note 30.

⁵⁹ LDT DRAFT GUIDANCE, *supra* note 30, at 9; SACGHS REPORT ON OVERSIGHT, *supra* note 50, at 32.

⁶⁰ LDT DRAFT GUIDANCE, *supra* note 30, at 9. But see SACGHS REPORT ON OVERSIGHT, *supra* note 50, at 98-99 (noting that New York's regulatory system requires premarket approval of many tests).

⁶¹ LDT DRAFT GUIDANCE, *supra* note 30, at 11-12.

⁶² 21 U.S.C. § 360c(a)(1)(A) (2012); LDT DRAFT GUIDANCE, *supra* note 30, at 12; Tongue Depressor, 21 C.F.R. § 880.6230 (2015).

⁶³ § 360c(a)(1)(C); LDT DRAFT GUIDANCE, *supra* note 30, at 12-13; Replacement Heart Valve, 21 C.F.R. § 870.3925 (2015).

Analogously, for low-risk LDTs, the FDA plans to continue exercising enforcement discretion regarding full premarket review, although it intends to require general controls including registration and adverse event reporting.⁶⁴ These general controls will also be required for moderate and high-risk tests, but as Class II and III diagnostics, respectively, those tests will also be subject to premarket review, which may or may not include the need to conduct “extensive new studies to demonstrate clinical validity.”⁶⁵ This might be less significant for Class II diagnostics, as the FDA currently proposes to require only premarket notification (rather than approval) for most of these tests,⁶⁶ but Class III tests will typically be subject to a full premarket approval process.⁶⁷

These distinctions between Class II and III diagnostics, and between premarket notification and premarket approval, have significant fiscal consequences. One survey of medical device manufacturers found that the average total cost to develop a Class III device and obtain FDA approval was \$94 million, whereas the average total cost to develop a Class II device requiring only premarket notification was approximately \$31 million.⁶⁸ But even if these numbers overstate the potential fiscal burdens on manufacturers of diagnostics rather than devices, the average cost to develop an LDT (no matter the Class) will undoubtedly far exceed the \$8,000–\$10,000 recent estimate from the Secretary’s Advisory Committee on Genetics, Health and Society (“SACGHS”).⁶⁹ The standard application fee alone for premarket review of a medical device is just over \$250,000,⁷⁰ while the standard application fee for the premarket notification process is roughly \$5,000.⁷¹

⁶⁴ LDT DRAFT GUIDANCE, *supra* note 30, at 12.

⁶⁵ *Id.* at 13-14.

⁶⁶ Premarket notification will be carried out through the 510(k) process. *Id.* at 14; see also When a Premarket Notification Submission Is Required, 21 C.F.R. § 807.81 (2015).

⁶⁷ LDT DRAFT GUIDANCE, *supra* note 30, at 13.

⁶⁸ JOSH MAKOWER ET AL., FDA IMPACT ON U.S. MEDICAL TECHNOLOGY INNOVATION 28 (Nov. 2010), available at http://www.medtecheurope.org/sites/default/files/resource_items/files/01112010_FDA%20impact%20on%20US%20medical%20technology%20innovation_Backgrounder.pdf. Other sources breaking these larger numbers down by stage (preclinical development versus clinical testing) confirm the survey’s rough estimates. See, e.g., Aaron V. Kaplan et al., *Medical Device Development: From Prototype to Regulatory Approval*, 109 CIRCULATION 3068, 3069, 3072 (2004).

⁶⁹ See SACGHS REPORT ON GENE PATENTS, *supra* note 21, at 34, 94-95.

⁷⁰ FY2016 MDUFA User Fees, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/forindustry/userfees/medicaldeviceuserfee/ucm452519.htm> (last updated Sept. 29, 2015).

⁷¹ *Id.* These fees are reduced for small businesses, which pay just over \$65,000 for the premarket approval application and roughly \$2,600 for the 510(k) application. *Id.*

The risk-based framework has worked well in the medical device context, and it is quite simple to understand there. Intuitively, the risk differential between a tongue depressor and an artificial heart is clear. Determining the risks imposed by a given diagnostic test, however, is much more difficult. Most diagnostic tests typically involve a relatively simple procedure (taking a sample from the patient and evaluating it on a particular dimension), and it is the ramifications of the information resulting from that test rather than the test itself which pose risk to the patient.⁷²

The FDA understands these difficulties, and has thus far offered the following in explaining how it is likely to classify LDTs by risk:

In determining the risk an LDT poses to the patient and/or the user, FDA will consider several factors including whether the device is intended for use in high risk disease/conditions or patient populations, whether the device is used for screening or diagnosis, the nature of the clinical decision that will be made based on the test result, whether a physician/pathologist would have other information about the patient to assist in making a clinical decision (in addition to the LDT result), alternative diagnostic and treatment options available to the patient, the potential consequences/impact of erroneous results, number and type of adverse events associated with the device, etc.⁷³

More specifically, the FDA has suggested that tests that act like companion diagnostics, those that are intended for use in asymptomatic patients, and those for use in testing for certain infectious diseases are likely to be considered higher risk.⁷⁴

Yet because these high-risk diagnostics may be among the most important ones, the FDA is likely to impose the strictest requirements on the most-needed tests. Companion diagnostics help physicians determine whether a specific drug is likely to help or harm a given patient, and their availability can sometimes make the difference between the FDA approving a drug and denying its application. And prognostic tests like Myriad's, which are used in asymptomatic patients, not only bring people great peace of mind but may also have

⁷² See PRESIDENT'S COUNCIL OF ADVISORS ON SCI. & TECH., *supra* note 21, at 37.

⁷³ LDT DRAFT GUIDANCE, *supra* note 30, at 12; *see also id.* at 26-27 (giving examples of LDTs likely to be classified as high-risk).

⁷⁴ *Id.* at 26-27.

the potential to achieve great cost savings, a commonly sought goal in our healthcare system.⁷⁵

At present, it is far from clear that the FDA will achieve its goal of regulating all LDTs. Their power to do so will be challenged on at least two grounds, with industry groups already arguing that the FDA both lacks the jurisdiction to regulate as broadly as it aims to and that it has chosen an inappropriate administrative law avenue for doing so.⁷⁶ At this time it is not clear whether either challenge is likely to succeed.⁷⁷ As a backstop, however, there are several proposals circulating in Congress that would implement the broad contours of the FDA's plan by statute, obviating these legal concerns.⁷⁸ In either case, some companies will seek to evade the FDA's authority by restructuring their business models.⁷⁹

⁷⁵ For instance, even as Congress and the media focus on the high price of many prescription drugs, policymakers are at the same time asking whether such costs may nevertheless be justified based on the healthcare savings they achieve. See, e.g., Robert Langreth, *How Gilead Priced Its \$20 Billion Blockbuster*, BLOOMBERG BUS. (Dec. 10, 2015, 2:37 PM), <http://www.bloomberg.com/news/articles/2015-12-10/behind-the-1-000-pill-a-formula-for-profits-inside-gilead>; Margot Sanger-Katz, *\$1,000 Hepatitis Pill Shows Why Fixing Health Care Costs Is So Hard*, N.Y. TIMES (Aug. 2, 2014), <http://www.nytimes.com/2014/08/03/upshot/is-a-1000-pill-really-too-much.html>.

⁷⁶ The American Clinical Laboratory Association has hired Professor Laurence Tribe and former Solicitor General Paul Clement to represent it in its efforts to hamstring the FDA. The ACLA may first challenge the FDA on the theory that LDTs are a *service* rather than a *device*, and therefore lie outside the FDA's regulatory authority. Second, they may argue that the FDA should have proceeded through notice-and-comment rulemaking, rather than attempting to achieve the same result through the guidance process. PAUL D. CLEMENT & LAURENCE H. TRIBE, LABORATORY TESTING SERVICES, AS THE PRACTICE OF MEDICINE, CANNOT BE REGULATED AS MEDICAL DEVICES 2-3 (2015), available at <http://www.acla.com/wp-content/uploads/2015/01/Tribe-Clement-White-Paper-1-6-15.pdf>. In light of recent case law, physicians may also seek to use the First Amendment against FDA enforcement efforts. See generally, e.g., Aaron S. Kesselheim & Michelle M. Mello, *Prospects for Regulation of Off-Label Drug Promotion in an Era of Expanding Commercial Speech Protection*, 92 N.C. L. REV. 1539 (2014) (considering recent constraints on the FDA's ability to limit off-label speech).

⁷⁷ See Turna Ray, *Q&A: Lawyer John Conley Counters Lab Industry Arguments Against FDA Regulatory Authority over LDTs*, GENOMEWEB (Jan. 15, 2015), <https://www.genomeweb.com/regulatory-news/qa-lawyer-john-conley-counters-lab-industry-arguments-against-fda-regulatory>.

⁷⁸ Jamie K. Wolszon & Jeffrey N. Gibbs, *Back from Break: FDA Issues Letter to Pathway Genomics for Cancer Screening LDT; Proposed Legislative Alternatives to FDA Framework Continue to Emerge*, FDA LAW BLOG (Sept. 29, 2015), http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2015/09/back-from-break-fda-issues-letter-to-pathway-genomics-for-cancer-screening-ldt-proposed-legislative-.html.

⁷⁹ Some companies will seek to evade the FDA's requirements by dividing their business into one service for sequencing genes and another for interpreting the

But if the FDA is able to regulate as it hopes to, the effect of the added regulatory burden will undoubtedly be to increase the costs of developing these tests, perhaps by several million dollars in the case of Class III devices, multiplying by a factor of a hundred or more the present cost of developing such tests.⁸⁰ This added burden will not fall equally on all potential actors in the innovation ecosystem. Large diagnostic companies will likely be able to bear these costs, while researchers at academic medical centers or within small diagnostic companies may not have such resources readily available. But much, if not most, of today's innovative diagnostic developments are taking place in these latter settings.⁸¹ As a result, the FDA's proposal might go too far in stifling future innovation in its quest to confirm the safety and efficacy of existing diagnostics.

The FDA is certainly sensitive to the potential negative effects of its regulations on diagnostic innovation, and many of its proposed carve-outs and procedural accommodations can be viewed as an attempt to minimize the regulatory costs it will impose. In particular, the FDA's decision to carve out several categories of LDTs, including traditional LDTs, LDTs "for unmet needs," and LDTs for rare diseases from its premarket approval scheme and to simply require their laboratories to register the test and report adverse events⁸² is a key example. These are complex concessions made in an effort to balance the quest for clinical validity data against the need for future innovation. That is, these carve-outs in some ways limit the FDA's search for safety and efficacy data. However, in the case of truly harmful diagnostics, the new adverse event reporting requirements will serve as a backstop, allowing the FDA to intervene in any dangerous situation by taking

results, as 23andMe has recently done in the wake of their public confrontation with the FDA. See *Status of Our Health-Related Genetic Reports*, 23ANDME, <https://web.archive.org/web/20141010201202/https://www.23andme.com/health/> (archived Oct. 10, 2014) (accessed by searching for "www.23andme.com/health" in the Internet Archive); see also Andrew Pollack, *F.D.A. Orders Genetic Testing Firm to Stop Selling DNA Analysis Service*, N.Y. TIMES (Nov. 25, 2013), <http://www.nytimes.com/2013/11/26/business/fda-demands-a-halt-to-a-dna-test-kits-marketing.html>.

⁸⁰ Where the cost to develop an LDT is currently estimated to be between eight and ten thousand dollars, SACGHS REPORT ON GENE PATENTS, *supra* note 21, at 34, 94, but the cost to bring a medical device to market and carry it through the FDA regulatory process is in the tens of millions of dollars, MAKOWER ET AL., *supra* note 68, at 28, the potential cost increase is enormous.

⁸¹ See, e.g., James P. Evans & Michael S. Watson, *Genetic Testing and FDA Regulation*, 313 J. AM. MED. ASS'N 669, 669-70 (2015).

⁸² LDT DRAFT GUIDANCE, *supra* note 30, at 12, 20-23 (defining these classes of tests and carving them out from the premarket approval scheme).

action against the company or by releasing information to warn physicians and patients.

A perhaps more significant carve-out, though, is the FDA's decision to accept information from the literature, where possible, to establish clinical validity.⁸³ Practically, this means that in many cases diagnostic innovators will not be required to conduct their own clinical trials to demonstrate clinical validity, and instead will be permitted to rely on existing research. But since the FDA has not yet explained how it is likely to implement this workaround, its impact is unknown. In particular, it might be that the carve-out permits developers of true diagnostics — those that diagnose patients who are currently symptomatic — to meet the clinical validity requirement easily. However, as discussed earlier, predictive tools like Myriad's test for which the question of clinical validity is multifaceted may find it more difficult to meet this requirement.⁸⁴

In the end, the new regulatory burdens imposed on many if not most LDTs are likely to be significant, especially when compared to the cost of the basic research that typically underlies such tests. As a result, the costs of developing and approving such tests will undoubtedly increase⁸⁵, and innovators will want assurances that they will be able to recoup their investment in these areas. Unfortunately, just as the FDA has been preparing to implement its new regulatory system, Congress has simultaneously been reducing insurance reimbursement rates available for the performance of diagnostic tests.

II. REDUCING REIMBURSEMENT RATES FOR DIAGNOSTIC TESTS THROUGH HEALTHCARE REGULATION

In addition to development costs, innovators must also concern themselves with the size of the demand for their product. If a company concludes that the potential market for their diagnostic test is too small to justify the estimated required research and development investment, they are unlikely to move forward with the test. Yet there are different reasons that the market for a potential diagnostic innovation may be insufficient to spur its development relative to other potential investment opportunities. For some diseases, the number of prospective patients to be tested may be too small.⁸⁶ For others, a test may be needed just once in

⁸³ See *id.* at 13, 15, 28.

⁸⁴ See *supra* text accompanying notes 56–57.

⁸⁵ See *supra* text accompanying notes 69–71.

⁸⁶ When a similar concern arose in the context of drugs, Congress responded by passing the Orphan Drug Act, which provides large benefits — including a seven year

a patient's life rather than repeatedly, limiting its potential return.⁸⁷ These classic economic problems are well-known to innovation and patent law scholars.⁸⁸ Relatively unexamined in the patent literature, however, is another problem: when a regulator caps reimbursement rates for a given technology in a way that artificially constrains incentives to supply it. While less studied, this prospect can just as easily discourage companies from investing in new technologies as can a small number of patients.

Along these lines, the recent series of Congressional and regulatory cuts to the Clinical Laboratory Fee Schedule ("CLFS"), which specifies the rates at which Medicare will reimburse outpatient laboratory testing services,⁸⁹ may exacerbate the potential concerns raised by the recent actions of the FDA and Federal Circuit. This Part will first briefly explain the CLFS, discussing its influence over private insurance reimbursement as well as over Medicare. It will then discuss the series of several rate cuts made to the CLFS over the past five years, cuts which may have a large collective effect going forward. Finally, this Part will explain the ways in which the series of CLFS cuts has impacted the testing industry.

A. *The CLFS*

Since its enactment in 1984,⁹⁰ the CLFS has specified the rates at which Medicare will reimburse outpatient clinical laboratory services. These rates are designed to vary somewhat by geographic area with

period of market exclusivity — to companies who obtain FDA approval for a drug designated to treat certain conditions, typically for those affecting few patients. See Robert A. Bohrer & John T. Prince, *A Tale of Two Proteins: The FDA's Uncertain Interpretation of the Orphan Drug Act*, 12 HARV. J.L. & TECH. 365, 370-71 (1999).

⁸⁷ This need not be true theoretically, but it is typically true in reality. Payors often balk at paying large up-front costs as compared to paying similar (or greater) amounts over time. See, e.g., Sanger-Katz, *supra* note 75 ("Think about AIDS treatment as paying a mortgage. Sovaldi is like buying a house with cash."). A related concern exists in the context of vaccines, which provide relatively small returns on investment both because they are much more complex to produce than many small-molecule drugs and because they are typically administered only once in a lifetime. See John P. Wilson, *The Resolution of Legal Impediments to the Manufacture and Administration of an AIDS Vaccine*, 34 SANTA CLARA L. REV. 495, 505 (1994).

⁸⁸ For a few recent discussions of these issues, see Hemel & Ouellette, *supra* note 19, at 303, 378-79, and Benjamin N. Roin, *The Case for Tailoring Patent Awards Based on Time-to-Market*, 61 UCLA L. REV. 672, 752 (2014).

⁸⁹ See *Clinical Laboratory Fee Schedule*, CENTERS FOR MEDICARE & MEDICAID SERVICES, <http://www.cms.gov/Medicare/Medicare-Fee-For-Service-Payment/Clinicallabfeesched/index.html> (last updated Oct. 13, 2015) [hereinafter *CLFS*].

⁹⁰ Deficit Reduction Act of 1984, Pub. L. No. 98-369, § 2303, div. B. tit. III, 98 Stat. 494 (codified in scattered sections of 26 U.S.C. and 42 U.S.C.).

differences in labor and supply costs,⁹¹ but a national payment cap limits the potential upward variation for each test.⁹² While Congress initially established the CLFS and frequently makes system-wide adjustments, CMS is primarily responsible for overseeing the CLFS.⁹³ Most importantly, when new laboratory tests are developed, it is CMS that determines how those tests will be reimbursed (if at all) under the existing system, through one of two potential processes. For some tests, CMS pegs payment rates to those of older, comparable tests through a process known as cross-walking. For all other tests, CMS uses a gap-filling method to assign payment rates where no comparable diagnostics exist.⁹⁴

Since Medicare is the single largest payer for clinical laboratory services in the country,⁹⁵ the rates set by the CLFS are highly significant in influencing the behavior of diagnostic innovators and providers. Yet the CLFS has also exerted informal influence far beyond the Medicare population. State Medicaid programs⁹⁶ and private insurance companies⁹⁷ typically look to Medicare rates as benchmarks when they set their own reimbursement rates.⁹⁸ In many cases, private insurance

⁹¹ CTRS. FOR MEDICARE & MEDICAID SERVS., CLINICAL LABORATORY FEE SCHEDULE FACT SHEET 3 (2014), available at <https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNProducts/Downloads/Clinical-Laboratory-Fee-Schedule-Fact-Sheet-ICN006818.pdf>.

⁹² See OFFICE OF INSPECTOR GEN., DEP'T OF HEALTH & HUMAN SERVS., VARIATION IN THE CLINICAL LABORATORY FEE SCHEDULE, at i (2009) [hereinafter VARIATION IN THE CLFS], available at <http://oig.hhs.gov/oei/reports/oei-05-08-00400.pdf>. Most laboratory tests are reimbursed at this rate, known as the National Limitation Amount. *Id.* at 8.

⁹³ See CLFS, *supra* note 89.

⁹⁴ VARIATION IN THE CLFS, *supra* note 92, at 3-4. These processes introduce additional uncertainty into investment decisions made by diagnostic innovators, as they cannot know with certainty how their prospective diagnostic will be reimbursed.

⁹⁵ OFFICE OF INSPECTOR GEN., DEP'T OF HEALTH & HUMAN SERVS., COMPARING LAB TEST PAYMENT RATES 1 (2013) [hereinafter COMPARING LAB RATES], available at <https://oig.hhs.gov/oei/reports/oei-07-11-00010.pdf>.

⁹⁶ In general, 42 U.S.C. § 1396b(i)(7) prohibits state Medicaid programs from setting payment rates for lab tests that exceed Medicare's rates. 42 U.S.C. § 1396b(i)(7) (2012); see also COMPARING LAB RATES, *supra* note 95, at 3.

⁹⁷ AM. COLL. OF MED. GENETICS & GENOMICS, 2013 MOLECULAR PATHOLOGY RATE-SETTING GUIDE FOR LABORATORIES 10 (2013), available at https://www.acmg.net/docs/ACMG_2013_Molecular_Pathology_Rate-Setting_Guide.pdf.

⁹⁸ Even if the CLFS was in practice limited to Medicare rates, Medicare spending makes up roughly 20% of all national health expenditures. CTRS. FOR MEDICARE & MEDICAID SERVS., NATIONAL HEALTH EXPENDITURES 2014 HIGHLIGHTS (2014), available at <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/highlights.pdf>. Medicaid reimbursement, which in this case is by definition even lower than the CLFS, see *supra* note 96, makes up another 16% of national expenditures. Providers cannot simply ignore these programs.

rates are even lower than Medicare's. Perhaps most sharply, in 2013 Aetna cut its diagnostic reimbursement rates so that they equal just 45% or 50% of the CLFS rates, depending on the test.⁹⁹ And a comprehensive 2013 report from the U.S. Department of Health & Human Services's ("HHS") Office of Inspector General compared CLFS rates to those offered by Federal Employee Health Benefit plans, finding that the federal insurers paid less than the CLFS for 54–61% of all laboratory tests, depending on the particular federal plan.¹⁰⁰

B. Cuts to the CLFS

Although the CLFS was initially designed to include updates for inflation, these have not typically occurred. Instead, in most years reimbursement rates have either been frozen or cut.¹⁰¹ Some of these cuts have come from CMS itself,¹⁰² but most have come from Congress. Within the past five years alone, Congress has made four across-the-board cuts to the CLFS. In 2010, the ACA included annual 1.75% cuts to any potential CLFS update to help fund other provisions of the Act, with the cuts to continue until at least 2015.¹⁰³ In 2011, the Budget Control Act imposed a 2% cut to all of Medicare as part of sequestration, which then took effect in 2013.¹⁰⁴ The 2012 Middle Class Tax Relief and Job Creation Act made another 2% cut to help finance the continued postponing of the Medicare physician reimbursement rate cuts (known informally as the "doc fix" and

⁹⁹ *Aetna Slashes Its Lab Fee Schedule*, 8 LABORATORY ECON. 1, 1 (2013). Blue Cross Blue Shield BCBS was already contracting at this rate. Gary Tufel, *CLFS Reformed*, CLINICAL LAB PRODS. (May 19, 2014), <http://www.clpmag.com/2014/05/clfs-reformed/>.

¹⁰⁰ COMPARING LAB RATES, *supra* note 95, at 10. As a corollary, though, for 38–45% of all tests, the federal employee insurers paid more than the CLFS rates. *Id.*

¹⁰¹ Tufel, *supra* note 99.

¹⁰² See, e.g., Coll. of Am. Pathologists, *CMS Cuts 88305 TC by 52%*, STATLINE (Nov. 1, 2012), http://www.cap.org/apps/portlets/contentViewer/show.do?printFriendly=true&contentReference=statline%2Fspecial_report_final_2013_physician_fee_schedule.html. However, CMS's authority to make such adjustments is more limited. COMPARING LAB RATES, *supra* note 95, at 3.

¹⁰³ Section 3401(l)(2) of the ACA, Pub. L. No. 111-148, 124 Stat. 119 (2010), amended 42 U.S.C. § 1395l(h)(2)(A) for this purpose. Patient Protection and Affordable Care Act, Pub. L. No. 111-148, § 3401(l)(2), 124 Stat. 119 (2010). The ACA also included a potential "productivity adjustment" to the CLFS, but its magnitude cannot be known in advance. *Id.*

¹⁰⁴ Ctrs. for Medicare & Medicaid Servs., *Mandatory Payment Reductions in the Medicare Fee-for-Service (FFS) Program — "Sequestration,"* CMS MEDICARE FFS PROVIDER E-NEWS (Mar. 8, 2013), <http://www.cms.gov/outreach-and-education/outreach/ffsprovpartprog/downloads/2013-03-08-standalone.pdf>; see also Budget Control Act of 2011, Pub. L. No. 112-25, § 302, 125 Stat. 240.

formally as the “Medicare Sustainable Growth Rate”).¹⁰⁵ And the Protecting Access to Medicare Act of 2014 changed the way in which the CLFS will calculate reimbursement rates beginning in 2017,¹⁰⁶ a move which the Congressional Budget Office estimates will result in a savings of \$2.5 billion over the next decade.¹⁰⁷ Given that total CLFS outlays in 2010 were just \$8.2 billion,¹⁰⁸ the cuts occasioned by the new methodology are potentially significant, with Congress feeling the unusual need to cap the percentage by which CLFS rates may be *reduced* in any given year.¹⁰⁹

C. *The Impact of the CLFS Cuts*

These cuts matter. Unlike many large pharmaceutical companies, who enjoy profit margins in the range of 20–30%,¹¹⁰ even the largest independent diagnostics companies — Quest and LabCorp — have profit margins in the single digits.¹¹¹ As such, these cuts have had at least two major effects on diagnostic testing developers.

The first and more direct effect is to discourage both companies and academic medical centers from investing in diagnostic technologies by artificially capping the amount they can expect to recover for even their greatest innovations. Importantly, this is not to say that cuts to the CLFS can never be justified. Rate cuts targeted toward older diagnostics might indeed be warranted, where manufacturers have had

¹⁰⁵ See Middle Class Tax Relief and Job Creation Act of 2012, Pub. L. No. 112-96, § 3202, 126 Stat. 156 (amending 42 U.S.C. § 1395l(h)(2)(A)). Laboratories and diagnostic testing companies seem to lack the political power possessed by physicians, physician groups, and hospital systems, which were all able to forestall these physician reimbursement cuts for many years.

¹⁰⁶ *CLFS Reform*, AM. CLINICAL LAB. ASS'N, <http://www.acla.com/clfs-reform/> (last visited Jan. 31, 2016).

¹⁰⁷ CONG. BUDGET OFFICE, COST ESTIMATE FOR THE PROTECTING ACCESS TO MEDICARE ACT OF 2014, at 2 (Mar. 26, 2014), available at <http://cbo.gov/sites/default/files/cbofiles/attachments/House%20introduced%20Protecting%20Access%20to%20Medicare%20Act%20of%202014,%20March%2026,%202014.pdf>.

¹⁰⁸ COMPARING LAB RATES, *supra* note 95, at 1.

¹⁰⁹ Protecting Access to Medicare Act of 2014, Pub. L. No. 113-93, § 216, 128 Stat. 1040 (creating 42 U.S.C. § 1395m-1) (capping annual rate reductions at 10% through 2019 and 15% through 2022).

¹¹⁰ See, e.g., Richard Anderson, *Pharmaceutical Industry Gets High on Fat Profits*, BBC NEWS (Nov. 6, 2014), <http://www.bbc.com/news/business-28212223>.

¹¹¹ *Laboratory Corporation of America Holdings: Key Statistics*, YAHOO FIN., <http://finance.yahoo.com/q/ks?s=LH> (last visited Feb. 7, 2016) (reporting LabCorp's profit margin at 5.69%); *Quest Diagnostics: Key Statistics*, YAHOO FIN., <http://finance.yahoo.com/q/ks?s=DGX> (last visited Feb. 7, 2016) (reporting Quest's profit margin at 9.46%).

time to optimize their performance. Similarly, for diagnostics in widespread use, economies of scale can offset some of the cuts.¹¹² But Congress's cuts are across-the-board (in contrast to CMS's more scalpel-like cuts), meaning that reimbursement rates are being cut for all diagnostics, including both older, common diagnostics and also complex, innovative new diagnostics, even where they may be used for only small populations. As such, particularly in light of the cuts that appear to be coming in the next few years, potential innovators in this field might decide not to invest the time and resources required to bring badly needed diagnostics to market if they know that they cannot command a premium for newer, superior diagnostics as compared to older, less precise technologies.

A second effect of these cuts involves direct restructuring of the diagnostic testing industry. On the surface, the reorganization story is one of consolidation. The CLFS rate decreases have helped spur large diagnostic companies like Quest and LabCorp to purchase small diagnostic companies, enabling them to increase both economies of scale and the purchasing power they have over private insurers and provider networks.¹¹³ Just in the past few years, Quest and LabCorp have become even more dominant, with the two companies together commanding roughly 31% of total market share.¹¹⁴ This largely parallels the reorganization taking place in the context of hospitals and physician groups, where a host of provisions in the ACA and related statutes have encouraged provider consolidation for the purpose of controlling costs.¹¹⁵

¹¹² Similarly, in the context of pharmaceuticals, older generic drugs are typically less expensive than newer, innovative drugs.

¹¹³ For examples of recent deals by Quest and LabCorp, see *infra* notes 117–19.

¹¹⁴ *Major Companies*, IBISWORLD, <http://www.ibisworld.com/industry/default.aspx?indid=1575> (last accessed Mar. 7, 2016).

¹¹⁵ See, e.g., Leemore Dafny, *Hospital Industry Consolidation — Still More to Come?*, 370 NEW ENG. J. MED. 198, 198 (2014). See generally SUZANNE M. KIRCHHOFF, *PHYSICIAN PRACTICES: BACKGROUND, ORGANIZATION, AND MARKET CONSOLIDATION* (2013) (exploring recent consolidation of physician practices along a range of dimensions). The development of care-coordinating Accountable Care Organizations is one prominent example. See Abbe R. Gluck, *Intrastatutory Federalism and Statutory Interpretation: State Implementation of Federal Law in Health Reform and Beyond*, 121 YALE L.J. 534, 593 n.160, 619 (2011). Related laws such as the 2009 HITECH Act, which provides financial incentives and penalties for providers to use electronic medical records, similarly encourage consolidation so that providers can achieve economies of scale in purchasing and implementing such technologies. Health Information Technology for Economic and Clinical Health (HITECH) Act, Pub. L. No. 111-5, 123 Stat. 115 (2009) (codified in scattered sections of 42 U.S.C.); Barbara J. Evans, *Much Ado About Data Ownership*, 25 HARV. J.L. & TECH. 69, 108-13 (2011);

But scholars have failed to notice the relationship between the consolidation observed in the provider context and the consolidation observed in the diagnostics industry. That is, all hospitals and many independent physician practices have laboratory facilities of their own, and the ACA and other cuts to the CLFS are also changing the relationships between the hospitals and their own laboratory facilities. Specifically, there is evidence that provider systems are increasingly jettisoning various non-essential groups of diagnostic tests, farming them out to external diagnostic companies.¹¹⁶ Most notably, some provider networks have even begun to contract out all of their outpatient testing services, including those covered directly by the CLFS. The recent deal between the University of Massachusetts's health system and Quest Diagnostics¹¹⁷ is the most prominent, but certainly not the only, example of this phenomenon,¹¹⁸ which was called the “[m]ost significant lab industry M&A trend of 2013–2014.”¹¹⁹ More commonly, though, this division of services is taking place on a smaller scale, but much more frequently. For instance, when hospital systems purchase smaller physician practices, the

Efthimios Parasidis, *Patients over Politics: Addressing Legislative Failure in the Regulation of Medical Products*, 2011 WIS. L. REV. 929, 966-67.

¹¹⁶ Hospitals must, of course, maintain at least some amount of in-house laboratory capacity — hospitalized patients whose treatment depends on the rapid review of basic, well-known diagnostic tests like a comprehensive metabolic panel or a complete blood count cannot afford to wait while their blood is sent to an external laboratory.

¹¹⁷ *Quest Diagnostics Acquires UMass Memorial Medical Center's Clinical and Anatomic Pathology Outreach Laboratory Businesses*, QUEST DIAGNOSTICS (Jan. 2, 2013), <http://newsroom.questdiagnostics.com/2013-01-02-Quest-Diagnostics-Acquires-UMass-Memorial-Medical-Centers-Clinical-and-Anatomic-Pathology-Outreach-Laboratory-Businesses>.

¹¹⁸ See, e.g., *John Muir Health Sells Clinical Laboratory Outreach Services to LabCorp*, JOHN MUIR HEALTH (Sept. 4, 2013), <http://www.johnmuirhealth.com/about-john-muir-health/press-room/Press-releases/2013-09-04-john-muir-health-sells-clinical-laboratory-outreach-services-to-labcorp.html>; *Quest Diagnostics Completes Acquisition of Lab-Related Clinical Outreach Operations of Dignity Health*, QUEST DIAGNOSTICS (June 24, 2013), <http://newsroom.questdiagnostics.com/2013-06-24-Quest-Diagnostics-Completes-Acquisition-of-Lab-Related-Clinical-Outreach-Operations-of-Dignity-Health>; *Quest Diagnostics Extends Partnership with Steward Health Care System*, QUEST DIAGNOSTICS (Apr. 23, 2014), <http://newsroom.questdiagnostics.com/2014-04-23-Quest-Diagnostics-Extends-Partnership-with-Steward-Health-Care-System>.

¹¹⁹ See HAVERFORD HEALTHCARE ADVISORS, OVERVIEW OF 2013–2014 LABORATORY INDUSTRY TRANSACTIONS 1, 24 (Apr. 29, 2014), available at <http://www.haverfordhealthcare.com/wp-content/uploads/2012/01/Overview-of-2013-2014-Laboratory-Transactions-Deal-Values-and-Multiples-and-Forecasting-of-Anticipated-Trends1.pdf>.

hospital may absorb only a portion of any laboratory facilities the practice may have had, outsourcing the rest.

Perhaps most relevant to this Article, though, is the role novel diagnostic tests play in this consolidation. These tests are likely to be the focus of innovative activity, and whether hospitals continue to perform traditional diagnostic tests is of less relative importance. In the case of novel diagnostic tests, where hospitals may find it costly to create infrastructure or maintain economies of scale, particularly where the tests are not time-sensitive, provider networks may be even more likely to shunt such testing off to companies like Quest and LabCorp.

These two effects of the series of cuts to the CLFS impact innovation incentives to develop new diagnostics in different ways. Of course, the first effect is to discourage directly investment in new diagnostics by artificially capping potential rewards. The full import of the second effect, though, cannot be appreciated in isolation. Industry consolidation is important primarily not for its own sake, but for the impact it has on another aspect of innovation incentives: the ability of innovators to protect their investment through intellectual property law.

III. HINDERING INNOVATORS' ABILITY TO PROTECT THEIR PERSONALIZED MEDICINE INNOVATIONS

In the area of diagnostic tests and other information goods, innovators' ability to recoup their costs is often dependent on their ability to protect their investments using patents or other exclusive rights. Even if development costs are high and reimbursement opportunities are low, as in the case of orphan drugs,¹²⁰ ensuring an innovator's ability to protect their investment through the creation of an exclusive right can provide a sufficient incentive to spur innovation.¹²¹ Until recently, it was a relatively simple matter for most diagnostic test innovators to obtain method patents on their technologies and to enforce those patents against violators. However, simultaneous developments in both patent law and healthcare regulation have threatened the ability of diagnostic method innovators to both obtain and enforce patents on those methods.

This Part will begin by examining the recent case law from the Federal Circuit and Supreme Court on the question of subject-matter

¹²⁰ See *supra* notes 28, 86 (discussing various estimates of the cost to bring a drug to market and specific issues with developing orphan drugs).

¹²¹ See, e.g., LANDES & POSNER, *supra* note 10, at 294. *But see* SACGHS REPORT ON GENE PATENTS, *supra* note 21, at 20 (explaining "that biotechnology researchers have strong incentives to invent that are independent of patents").

eligibility under 35 U.S.C. § 101, as the courts have recently narrowed the kinds of method claims that are eligible to receive patent protection in a series of cases, several directly implicating diagnostic method patents. It will then analyze these courts' recent cases on the subject of divided infringement of method patents under 35 U.S.C. § 271, explaining how decisions that typically require a single actor to perform all the steps of a given method claim before infringement liability can be found may prevent innovators from enforcing their patents. Although none of the divided infringement cases have dealt explicitly with diagnostic testing methods, this Part will consider the ways in which the broadly applicable patent law would apply to such claims. Finally, this Part will explain the ways in which the just-described restructuring of the diagnostics industry implicates patentholders' ability to enforce their diagnostic method patents.¹²²

Unlike the previous Parts, this Part is more agnostic as to the effect of these developments on innovation incentives, when considered in isolation. The previous Parts described policy tradeoffs, between the production of safety and efficacy data and innovation in the FDA context and between cost control and innovation in the CMS context. This Part, however, recognizes that the role of patents in the diagnostic method context is complicated and highly contested. Scholars have debated for years whether increased patent protection will promote innovation by enabling innovators to protect their technologies, or will stifle innovation by blocking cumulative innovation.¹²³ As such, a discussion of whether these doctrinal developments are on balance salutary ones must wait until Part IV, when these three areas of law are considered in combination.

A. *Making It More Difficult to Obtain Patents on Diagnostic Methods*

Over the past few years, the Supreme Court and Federal Circuit have addressed fundamental questions about what kinds of

¹²² Developments in the FDA's regulation of LDTs, as discussed in Part I, may actually act as a partially countervailing factor. That is, if the FDA exercises its gatekeeping function and stringently regulates the companies that are permitted to conduct diagnostic tests, its behavior may create de facto monopolies or oligopolies.

¹²³ See, e.g., Rebecca S. Eisenberg, *Noncompliance, Nonenforcement, Nonproblem? Rethinking the Anticommons in Biomedical Research*, 45 HOUS. L. REV. 1059, 1060-63, 1080-84 (2008); Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698, 698 (1998); Mark A. Lemley & A. Douglas Melamed, *Missing the Forest for the Trolls*, 113 COLUM. L. REV. 2117, 2158 (2013); Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839, 881-82 (1990).

technologies are eligible for patent protection under 35 U.S.C. § 101,¹²⁴ considering cases involving business methods, software patents, diagnostic methods, and gene sequences. Although the precise contours of the doctrine remain uncertain, the overall trajectory of these cases has resulted in a narrowing of the scope of patent-eligible subject matter, particularly patent-eligible methods, over the past five years. As a result, diagnostic method innovators have begun to and will continue to find it more difficult to obtain method patent claims on their inventions.

The most relevant patent eligibility case to reach the Supreme Court was *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*¹²⁵ Prometheus had sued Mayo for infringing two of its patents, which covered methods for optimizing the drug dosage patients received for certain autoimmune conditions.¹²⁶ The asserted method claims were quite spare, a representative one claiming only “[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”¹²⁷ The Federal Circuit initially held that the asserted claims survived Mayo’s § 101 challenge, reasoning that both the “administering” and “determining” steps constituted transformations under the then-prevailing machine-or-transformation test evaluated in the Supreme Court’s opinion in *Bilski v. Kappos*.¹²⁸

¹²⁴ This section 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.” 35 U.S.C. § 101 (2012). The Supreme Court has articulated a number of specific exceptions to this broad text: “[l]aws of nature, natural phenomena, and abstract ideas” are not eligible for patent protection. *Alice Corp. Pty. v. CLS Bank Int’l*, 134 S. Ct. 2347, 2354 (2014); *see also Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1293 (2012); *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980).

¹²⁵ *Prometheus*, 132 S. Ct. 1289.

¹²⁶ *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 628 F.3d 1347, 1349-51 (Fed. Cir. 2010).

¹²⁷ *Id.* at 1350 (quoting U.S. Patent No. 6,355,623, col. 10 ll. 10-16 (filed Apr. 8, 1999)).

¹²⁸ *Id.* at 1355-57. In *Bilski v. Kappos*, 561 U.S. 593 (2010), the Supreme Court held that the “machine-or-transformation test,” under which “[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,” was merely a “useful and important clue” or “investigative tool” to be used, rather than being the “sole test” for patent-eligibility. *Id.* at 604 (citing *In re Bilski*, 545 F.3d 943, 954 (Fed.

The Supreme Court reversed.¹²⁹ Writing for a unanimous Court, Justice Breyer held that Prometheus's claims encompassed mere unpatentable "laws of nature — namely, relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm."¹³⁰ He went on, though, to hold that the claims also failed in transforming these mere relationships into patent-eligible applications of those laws, concluding that the "well-understood, routine, conventional" elements of the method claims added nothing to the correlation itself.¹³¹ Most bluntly, he described the claims as "simply tell[ing] doctors to gather data from which they may draw an inference in light of the correlations"¹³² — a description that seems to encapsulate the very essence of a diagnostic test.

The next § 101 case to involve diagnostic method claims, *Association for Molecular Pathology v. Myriad Genetics, Inc.*,¹³³ is perhaps best known as the case in which the Supreme Court decided whether (and if so, when) human DNA sequences are ever patent-eligible.¹³⁴ However, the Federal Circuit's disposition of the method claims involved in the case is also important. Myriad's patents covered not only claims on the DNA sequences of the offending genes, but also methods for analyzing those genes to determine a woman's genetic susceptibility to breast cancer.¹³⁵ Specifically, several of the claims at issue in the suit involved methods of "analyzing" or "comparing" gene sequences to locate mutations that might predispose their carriers to breast cancer.¹³⁶

Cir. 2008) (en banc)).

¹²⁹ *Prometheus*, 132 S. Ct. at 1305.

¹³⁰ *Id.* at 1296; *see also id.* at 1294 (describing the claims as containing "unpatentable natural laws").

¹³¹ *Id.* at 1298.

¹³² *Id.*

¹³³ 133 S. Ct. 2107 (2013).

¹³⁴ Justice Thomas' opinion for a unanimous Court split the difference on this question, holding that "a naturally occurring DNA segment" is a product of nature and therefore not patent-eligible, but that cDNA is patent-eligible, precisely because it is not naturally occurring. *Id.* at 2111.

¹³⁵ *Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office*, 689 F.3d 1303, 1309-10 (Fed. Cir. 2012).

¹³⁶ *Id.* 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." *Id.* at 1309.

On remand after *Prometheus*,¹³⁷ the Federal Circuit invalidated these claims, finding them to encompass mere “abstract mental processes”¹³⁸ to compare two gene sequences and noting that the claims’ limitation to particular genes failed to render the claims patent-eligible.¹³⁹ In an effort to prove that their claims involved activities in the physical world, Myriad argued that additional, implicit steps should be read into the claims — “extracting DNA from a human sample” and “sequencing the *BRCA* DNA molecule.”¹⁴⁰ The panel declined to read those steps into the claim, though it did not say whether such steps would alter the result in the case.¹⁴¹

Most recently, the Supreme Court applied *Prometheus* to invalidate a set of software method claims in *Alice Corporation, Ltd. v. CLS Bank International*, its fourth patent eligibility case in five Terms.¹⁴² CLS Bank sought a declaratory judgment that several of Alice’s patents, directed toward methods of mitigating settlement risk using computers,¹⁴³ were invalid under § 101.¹⁴⁴ Justice Thomas, in his majority opinion, agreed that Alice’s specific method claims were invalid.¹⁴⁵ More important, though, was the way Justice Thomas interpreted the Court’s past precedent, crystallizing out of *Prometheus* a two-step process for deciding § 101 cases. The process asks first whether “the claims at issue are directed to [a] patent-ineligible concept[],” and then determines whether there is an “inventive

¹³⁷ *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*, 132 S. Ct. 1794, 1794 (2012).

¹³⁸ *Ass’n for Molecular Pathology*, 689 F.3d at 1334.

¹³⁹ *Id.* at 1334-35. The Federal Circuit subsequently invalidated even more of Myriad’s method claims, which were structured essentially identically. *Univ. of Utah Research Found. v. Ambry Genetics Corp.*, 2014-1361, slip op. at 19 (Fed. Cir. Dec. 17, 2014).

¹⁴⁰ *Ass’n for Molecular Pathology*, 689 F.3d at 1335.

¹⁴¹ *Id.*

¹⁴² *See Alice Corp. Pty. Ltd. v. CLS Bank Int’l*, 134 S. Ct. 2347 (2014). The Supreme Court has become very interested in patent cases recently, deciding 20 patent cases between 2010 and 2016 alone, compared with just 7 cases in the 1980s (including two patent-eligibility cases) and just 8 cases in the 1990s (with no patent-eligibility cases). *See* Lisa Larrimore Ouellette et al., *Supreme Court Patent Cases*, WRITTEN DESCRIPTION (2015), <http://writtendescription.blogspot.com/p/patents-scotus.html>.

¹⁴³ *CLS Bank Int’l v. Alice Corp. Pty.*, 717 F.3d 1269, 1274 (Fed. Cir. 2013) (en banc) (Lourie, J., concurring) (per curiam).

¹⁴⁴ *Id.* at 1273-74. The en banc Federal Circuit splintered badly, with ten judges issuing seven opinions, none commanding a majority. *Id.* at 1269.

¹⁴⁵ *Alice Corp.*, 134 S. Ct. at 2352 (holding further that “merely requiring generic computer implementation fails to transform [Alice’s] abstract idea into a patent-eligible invention”).

concept” that nonetheless transforms the patent-ineligible natural law into a patent-eligible application thereof.¹⁴⁶ Applying this test to Alice’s claims, Justice Thomas first found that they were directed to an abstract idea, making it a patent-ineligible concept.¹⁴⁷ At step two, Justice Thomas found that merely reciting the existence of a generic computer was insufficient to convert Alice’s patent-ineligible abstract idea into a patent-eligible invention.¹⁴⁸

In its § 101 jurisprudence, the Supreme Court has largely claimed that it is moving only incrementally. As early as *Bilski v. Kappos* in 2010, Justice Kennedy stressed the need to avoid “adopting categorical rules that might have wide-ranging and unforeseen impacts,”¹⁴⁹ an approach the Court continued in *Prometheus* and *Myriad*. Yet the Court’s adherence to standards over rules in many § 101 cases fostered confusion among the lower courts and within the Federal Circuit, resulting in a great deal of uncertainty in the § 101 case law.¹⁵⁰ That uncertainty itself affects incentives to innovate, as scientists and investors may be reluctant to move forward with product development if they cannot determine whether they will be able to protect their investment.¹⁵¹ Yet by avoiding a definitive ruling on the patent-eligibility of software claims, Justice Thomas signaled that he viewed *Alice* as continuing in this incremental tradition.¹⁵²

The lower courts have not viewed *Alice* this way. The Federal Circuit has applied its holding to invalidate claims on § 101 grounds in eighteen of the nineteen § 101 cases it has heard since *Alice*.¹⁵³

¹⁴⁶ *Id.* at 2355 (citations omitted).

¹⁴⁷ *Id.* at 2356.

¹⁴⁸ *Id.* at 2358.

¹⁴⁹ *Bilski v. Kappos*, 130 S. Ct. 3218, 3229 (2010); see also *CLS Bank Int’l*, 717 F.3d at 1281 (“Bright-line rules . . . are often impractical and counterproductive when applied to § 101.”).

¹⁵⁰ See John M. Golden, *Flook Says One Thing, Diehr Says Another: A Need for Housecleaning in the Law of Patentable Subject Matter*, 82 GEO. WASH. L. REV. 1765, 1770-71 (2014) (examining the Supreme Court’s case law on patentable subject matter and explaining its lack of clarity).

¹⁵¹ PRESIDENT’S COUNCIL OF ADVISORS ON SCI. & TECH., *supra* note 21, at 14.

¹⁵² *Alice Corp.*, 134 S. Ct. at 2357 (“[W]e need not labor to delimit the precise contours of the “abstract ideas” category in this case.”). Yet as in *Bilski*, where several Justices would have concluded that business methods are categorically not patent-eligible, *Bilski*, 130 S. Ct. at 3232 (Stevens, J., concurring) (joined by Justices Ginsburg, Breyer, and Sotomayor), the same was true in *Alice*. See *Alice Corp.*, 134 S. Ct. at 2360 (Sotomayor, J., concurring) (joined by Justices Ginsburg and Breyer).

¹⁵³ Robert R. Sachs, *#AliceStorm for Halloween: Was It Trick or a Treat?*, BILSKIBLOG (Nov. 6, 2015), <http://www.bilskiblog.com/blog/2015/11/alicestorm-for-halloween-its-scary-out-there-.html> [hereinafter *#AliceStorm*]. For representative cases, see Ariosa

District courts have also followed this pattern,¹⁵⁴ to the point that more patents were invalidated in the seven months after *Alice* than in the five years prior.¹⁵⁵ As of the end of October 2015, district courts had invalidated claims on § 101 grounds in 70% of the 155 post-*Alice* cases to be decided so far.¹⁵⁶

The only three post-*Alice* cases (two in the Federal Circuit and one in the District of Delaware) to involve diagnostic methods have invalidated claims closely resembling those already invalidated in *Prometheus* and *Myriad*.¹⁵⁷ Because no diagnostic method claims have as of yet been affirmed as patent-eligible post-*Alice*, practitioners have begun searching for ways to craft diagnostic method claims that will pass through the § 101 filter, even as academics have wondered whether such a feat is possible.¹⁵⁸ At oral argument in *Prometheus*, Justice Kagan suggested that adding a “treatment step” to the method claim in question would have changed the case, as such a claim “clearly would have been patentable.”¹⁵⁹ To use *Prometheus*’ claim as

Diagnostics, Inc. v. Sequenom, Inc., 788 F.3d 1371, 1373 (Fed. Cir. 2015) (reh’g en banc denied); *Ultramercial, Inc. v. Hulu, LLC*, 772 F.3d 709, 712 (Fed. Cir. 2014).

¹⁵⁴ For a particularly thoughtful discussion of the issues relating to the uncertain doctrine governing § 101 claims, see *Loyalty Conversion Sys. Corp. v. Am. Airlines, Inc.*, No. 2:13-CV-655, 2014 WL 4364848, at *5-7 (E.D. Tex. filed Sept. 3, 2014) (Bryson, J., sitting by designation).

¹⁵⁵ Robert R. Sachs, *Twenty-Two Ways Congress Can Save Section 101*, BILSKIBLOG (Feb. 12, 2015), <http://www.bilskiblog.com/blog/2015/02/twenty-two-ways-congress-can-save-section-101.html>.

¹⁵⁶ Sachs, #*AliceStorm*, *supra* note 153.

¹⁵⁷ See *Ariosa*, 788 F.3d at 1373; *In re BRCA1- & BRCA2-Based Hereditary Cancer Test Patent Litig.*, 774 F.3d 755, 765 (Fed. Cir. 2014); *Genetic Techs. Ltd. v. Lab. Corp. of Am. Holdings*, No. CV 12-1736-LPS-CJB, 2014 WL 4379587, at *13-14 (D. Del. Sept. 3, 2014).

¹⁵⁸ See, e.g., Rebecca S. Eisenberg, *Diagnostics Need Not Apply*, 21.2 J. SCI. & TECH. L. (2015) [hereinafter *Diagnostics*], available at http://www.bu.edu/jostl/files/2015/12/EISENBERG_ART_FINAL-web.pdf (“[M]ost important advances in [diagnostic testing] lie outside the boundaries of patent-eligible subject matter.”); Rebecca S. Eisenberg, *Prometheus Rebound: Diagnostics, Nature, and Mathematical Algorithms*, 122 YALE L.J. ONLINE 341, 342 (2013) [hereinafter *Prometheus Rebound*]; Arti K. Rai, *Diagnostic Patents at the Supreme Court*, 18 MARQ. INTELL. PROP. L. REV. 1, 2 (2014). There is general agreement that if the method of detecting a biomarker itself is novel (such as in the development of the Polymerase Chain Reaction or other related techniques) that method could itself be patented. The concern here is about whether generic methods may be patented as they apply to a newly discovered biological relationship, such as the one involved in *Prometheus*. See *Ariosa*, 788 F.3d at 1377-78.

¹⁵⁹ See Transcript of Oral Argument at 47, *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289 (2012) (No. 10-1150). Practitioners have seized on statements like these, publishing guides to drafting patents post-*Prometheus*. See, e.g., Holly J. Atkinson et al., *Personalized Medicine Patents at Risk: Tips for Battling*

an example, rather than simply claiming (1) administering a drug and (2) determining the level of the resulting metabolite in the blood,¹⁶⁰ the claim would include a third step of altering the patient's treatment accordingly. The suggestion seems to be that such a step would take the claim from a mere law of nature to an *application* of such a law, thereby making it patent-eligible.¹⁶¹ Such a claim has not yet been tested in the courts, but for innovators seeking to patent their discoveries, it may be their best hope.

B. Making It More Difficult to Enforce Patents

At the same time that the courts were altering the scope of patentable subject matter doctrine, they were also producing change in another area of patent law: divided infringement. The Federal Circuit and Supreme Court have recently decided several cases involving divided infringement of method patents, considering whether and when a defendant may be held liable for patent infringement where no single entity has performed all the steps of a given method claim. Their opinions have largely limited the reach of this doctrine, making it more difficult for courts to assign liability in such circumstances.

Yet discussions of these cases have typically ignored two major points which complicate the analysis substantially. First, legal scholars and commentators have not examined the relationship between the subject-matter eligibility cases discussed above and these divided infringement cases. And second, there has been no attention to the ways in which divided infringement doctrine interfaces with recent developments in healthcare organization outlined in the previous Part to affect the ability of diagnostic method patent holders in particular to enforce their patents. After reviewing the relevant doctrinal developments, this Part will consider these two points.

1. Developments in Divided Infringement Doctrine

Primarily, plaintiffs seeking to hold a defendant liable for patent infringement will bring a suit for direct infringement under 35 U.S.C. § 271(a), under which “whoever . . . makes, uses, offers to sell, or sells

Prometheus and Myriad to Obtain Claims to Diagnostics, CIPA J. (Mar. 2013), <http://www.finnegan.com/resources/articles/articlesdetail.aspx?news=d71205da-cb48-4827-9a8c-fde729146046>; JAMES BRADY ET AL., HOW TO PROTECT PATENTS AFTER PROMETHEUS (May 2012), available at http://www.dicksteinshapiro.com/sites/default/files/Protect_Patents_Prometheus.pdf.

¹⁶⁰ See U.S. Patent No. 6,355,623 B2 (filed Apr. 9, 1999).

¹⁶¹ Golden, *supra* note 150, at 1791-92.

any patented invention . . . infringes the patent.”¹⁶² Section 271(a) is a strict liability offense, such that a defendant may be held liable for infringement even if they lacked intent to infringe and indeed lacked knowledge of the patent’s existence.¹⁶³ Partly as a result,¹⁶⁴ courts have historically required § 271(a) plaintiffs to show that a single actor has made or used their invention.¹⁶⁵

To find infringement in the context of method patents, this means that a single actor must have performed each and every step of the asserted claim.¹⁶⁶ Importantly, the single actor need not be the defendant — plaintiffs may bring an action under § 271(b), attributing liability to those who “actively induce[] infringement of a patent.”¹⁶⁷ This section has traditionally been dependent on § 271(a), in the sense that it requires an act of direct infringement under § 271(a),¹⁶⁸ but it then goes on to assign liability to someone other than the direct infringer. Where the defendant is not the one to have directly infringed the patent, courts have required the defendant to have “specific intent” to induce the direct infringement.¹⁶⁹

But these are relatively simple cases. Courts have recently been confronted with a more difficult question: who, if anyone, is liable where all the steps of a method claim have been performed — but *not* by a single actor? Where the actions of two parties combine to perform all the steps of the claim, can the actions of one party ever be imputed to the other or to a third party, allowing courts to assign liability to them? If so, when — and why? The Federal Circuit’s focus on this issue began in 2007 and 2008, with its opinions in *BMC*

¹⁶² 35 U.S.C. § 271(a) (2012).

¹⁶³ See *BMC Res., Inc. v. Paymentech, LP*, 498 F.3d 1373, 1381 (Fed. Cir. 2007); Roger D. Blair & Thomas F. Cotter, *Strict Liability and Its Alternatives in Patent Law*, 17 *BERKELEY TECH. L.J.* 799, 800 (2002); see also Jason A. Rantanen, *An Objective View of Fault in Patent Infringement*, 60 *AM. U. L. REV.* 1575, 1590 (2011).

¹⁶⁴ See *Akamai Techs., Inc. v. Limelight Networks, Inc.*, 692 F.3d 1301, 1307, 1347 (Fed. Cir. 2012), *rev’d*, 134 S. Ct. 2111 (2014).

¹⁶⁵ *Id.* at 1307.

¹⁶⁶ See, e.g., *Muniauction, Inc. v. Thomson Corp.*, 532 F.3d 1318, 1329 (Fed. Cir. 2008). This is distinct from the context of product patents, where the actor providing the final piece of a patented product has committed infringement. *BMC*, 498 F.3d at 1380.

¹⁶⁷ 35 U.S.C. § 271(b) (2012).

¹⁶⁸ See *BMC*, 498 F.3d at 1379.

¹⁶⁹ *Id.* at 1381; see also *Akamai*, 692 F.3d at 1308; Rantanen, *supra* note 163, at 1599. Precisely what knowledge is required to establish intent is a subject the Supreme Court considered most recently in 2015. See *Commil USA, LLC v. Cisco Sys., Inc.*, 135 S. Ct. 1920 (2015).

*Resources, Inc. v. Paymentech, L.P.*¹⁷⁰ and *Muniauction, Inc. v. Thomson Corp.*, respectively.¹⁷¹ In both cases, the defendant argued that because it had performed some but not all steps of the method claims, it was not liable for direct infringement under § 271(a).¹⁷² And in both cases, the Federal Circuit agreed.¹⁷³

The Federal Circuit concluded that where “multiple parties combine to perform every step of a claimed method, the claim is directly infringed only if one party exercises ‘control or direction’ over the entire process such that every step is attributable to the controlling party, i.e., the ‘mastermind.’”¹⁷⁴ Mere “arms-length agreements”¹⁷⁵ or “arms-length cooperation”¹⁷⁶ between the entities were held to be insufficient to demonstrate such involvement. In *Muniauction*, the court went so far as to state that the “control or direction” standard can only be satisfied “where the law would traditionally hold the accused direct infringer vicariously liable for the acts committed by another party.”¹⁷⁷ Because this demanding standard was not satisfied, neither defendant could be found liable under § 271(a).¹⁷⁸

BMC and *Muniauction* laid the foundation for the developments leading to the Federal Circuit’s recent en banc ruling in *Akamai Technologies, Inc. v. Limelight Networks, Inc.*¹⁷⁹ Akamai’s patents claim technology that permits internet content providers to outsource the storage of portions of their content.¹⁸⁰ Similar to the defendants in

¹⁷⁰ *BMC Res., Inc. v. Paymentech, LP*, 498 F.3d 1373 (Fed. Cir. 2007). BMC’s patents claimed a method for handling debit card transactions over the phone without a PIN. *Id.* at 1375.

¹⁷¹ *Muniauction, Inc. v. Thomson Corp.*, 532 F.3d 1318 (Fed. Cir. 2008). *Muniauction*’s patent covered methods for conducting “original issuer auctions of financial instruments” using the internet. *Id.* at 1321; U.S. Patent No. 6,161,099, col. 1 ll. 12-15 (filed May 29, 1998).

¹⁷² See *Muniauction*, 532 F.3d at 1328-29; *BMC*, 498 F.3d at 1377.

¹⁷³ *Muniauction*, 532 F.3d at 1330; *BMC*, 498 F.3d at 1381.

¹⁷⁴ *Muniauction*, 532 F.3d at 1329 (citing *BMC*, 498 F.3d at 1380-81).

¹⁷⁵ *BMC*, 498 F.3d at 1381.

¹⁷⁶ *Muniauction*, 532 F.3d at 1329.

¹⁷⁷ *Id.* at 1330.

¹⁷⁸ In particular, in *BMC* the Federal Circuit affirmed the district court’s grant of summary judgment for Paymentech where there was no evidence it had supplied “instructions or directions regarding the use of” the data it provided to the financial institutions who completed the remaining claim steps. *BMC*, 498 F.3d at 1381. And in *Muniauction*, the panel held that Thomson’s control over the access to its system and instructions to bidders on its use (actions beyond those taken in *BMC*) were still insufficient to satisfy this standard. See *Muniauction*, 532 F.3d at 1330.

¹⁷⁹ 797 F.3d 1020, 1024 (Fed. Cir. 2015) (en banc).

¹⁸⁰ *Akamai Techs., Inc. v. Limelight Networks, Inc.*, 629 F.3d 1311, 1315 (Fed.

both *BMC* and *Muniauction*, Limelight had not performed all steps of the asserted claims; its customers helped complete each process.¹⁸¹ In 2010, the initial Federal Circuit panel noted that while the presence of “control or direction” is certainly a “consideration,”¹⁸² there can only be liability for infringement if there is an “agency relationship” between the parties or if “one party is contractually obligated to the other to perform the steps.”¹⁸³ The panel held that even though Limelight had a contractual relationship with its customers, they were not specifically contractually obligated to perform the remaining claim steps.¹⁸⁴ Therefore, the contract did not establish “either Limelight’s control over its customers or its customers’ consent to Limelight’s control,”¹⁸⁵ so that Limelight could not be liable for infringement.

After a badly splintered en banc decision in which the Federal Circuit attempted to avoid the § 271(a) issue entirely¹⁸⁶ and a subsequent strong rebuke by a unanimous Supreme Court,¹⁸⁷ in 2015 the en banc Federal Circuit issued a unanimous per curiam opinion largely reaffirming its 2010 panel opinion and its opinions in *BMC* and *Muniauction*. The court again held that an entity may be held liable for others’ performance of steps of a method claim “in two sets of circumstances: (1) where that entity directs or controls others’ performance, and (2) where the actors form a joint enterprise.”¹⁸⁸

There was a key difference from the 2010 panel opinion, however: the Federal Circuit concluded that “on the facts of this case, [] liability under § 271(a) can also be found when an alleged infringer conditions participation in an activity or receipt of a benefit upon performance of a step or steps of a patented method and establishes the manner or

Cir. 2010) (reh’g en banc granted); U.S. Patent No. 6,108,703, col. 1, ll. 34-40 (filed May 19, 1999).

¹⁸¹ See *Akamai*, 629 F.3d at 1317.

¹⁸² *Id.* at 1319.

¹⁸³ *Id.* at 1320.

¹⁸⁴ *Id.* at 1321.

¹⁸⁵ *Id.*

¹⁸⁶ See *id.* The en banc ruling also included *McKesson Technologies, Inc. v. Epic Systems Corp.*, a related case involving allegations of induced infringement under § 271(b), rather than direct infringement under § 271(a). See *McKesson Techs. Inc. v. Epic Sys. Corp.*, 2010-1291, slip op. at 5 (Fed. Cir. Apr. 12, 2011). After the Federal Circuit issued its first en banc opinion, *McKesson* and *Epic* settled, and the case dropped out of the further court proceedings. Stewart Bishop, *McKesson, Epic End High Court Induced-Patent Infringement Fight*, LAW360 (Mar. 5, 2013), <http://www.law360.com/articles/420852/mckesson-epic-end-high-court-induced-infringement-fight>.

¹⁸⁷ *Limelight Networks, Inc. v. Akamai Techs., Inc.*, 134 S. Ct. 2111, 2115 (2014).

¹⁸⁸ *Akamai Techs., Inc. v. Limelight Networks, Inc.*, 797 F.3d 1020, 1022 (Fed. Cir. 2015) (en banc).

timing of that performance.”¹⁸⁹ When this “conditions participation . . . upon performance” clause is met, the third party’s actions will be attributed to the alleged infringer for purposes of assigning § 271(a) liability.¹⁹⁰ Finding that a jury could have concluded that Limelight’s behavior met the requirements of this new condition, the Federal Circuit reinstated the jury’s verdict of liability against Limelight.¹⁹¹

The possibility of assigning liability where an alleged infringer “conditions participation upon performance” may well serve to create liability in cases involving software or business method claims like those at issue in *Akamai*, *BMC*, or *Muniauction*. However, it is relatively unlikely to apply with equal force in the diagnostic method context. In practice, diagnostic testing laboratories do not condition physicians’ ability to order a diagnostic test on the physician using the test results to make specific treatment recommendations. Indeed, such conditioning might in many states be unlawful, as it could run afoul of the corporate practice of medicine doctrine, which broadly seeks to prevent corporations from exerting control over professional medical judgment.¹⁹²

Unfortunately, the question of when liability may be found in cases of divided infringement remains far from settled. The depth of disagreement among the judges of the Federal Circuit, evident in their sharply worded opinions in the first en banc ruling in *Akamai*,¹⁹³ will impede the court’s ability to create anything more than case-by-case determinations in the near future. Even in this second en banc opinion, the court noted that “[g]oing forward, principles of attribution are to be considered in the context of the particular facts presented.”¹⁹⁴ As such, although I cannot rule out the possibility that the Federal Circuit might craft a new condition that would apply to diagnostic method patents, for now it is likely that the holder of any diagnostic method claim sufficiently detailed to be granted would be largely unable to bring an action for divided infringement.

But these developments cannot be fully understood when examined in isolation. Instead, developments involving both § 101 and § 271

¹⁸⁹ *Id.* at 1023.

¹⁹⁰ *Id.*

¹⁹¹ *Id.* at 1024.

¹⁹² See William M. Sage & Kelley McIlhatten, *Upstream Health Law*, 42 J.L. MED. & ETHICS 535, 542 (2014).

¹⁹³ See, e.g., *Akamai Techs., Inc. v. Limelight Networks, Inc.*, 692 F.3d 1301, 1319 (Fed. Cir. 2012) (Newman, J., dissenting); *id.* at 1350 (Linn, J., dissenting).

¹⁹⁴ *Akamai Techs., Inc. v. Limelight Networks, Inc.*, 797 F.3d 1020, 1023 (Fed. Cir. 2015) (en banc).

must be examined together, as a unit. Synthesizing these two areas of the law reveals the following: In order to cross the § 101 filter, would-be method patent holders must now include more, innovative steps in their method claims. At least in some cases, this means that those claims will be written to involve more than one individual in their performance. This is likely to be true in the diagnostic method context, if the step to be added is a “treatment” step typically performed by a physician, when compared to the “determining” steps typically performed by laboratory professionals. However, the § 271 case law holds that all those steps must be performed by a single actor in order to assign liability, and the Federal Circuit has been extremely strict in imputing the actions of multiple parties to a single individual.¹⁹⁵ As a result, not only might it suddenly become much more difficult to obtain diagnostic method patents under § 101, but the § 271 developments will compound the difficulties companies face in assigning liability for them.

The relationship between § 101 and § 271 also helps explain why one common argument made in response to *Akamai* — that the § 271 cases concern only poorly drafted patents, and that patentees will be able to use clever claim drafting methods to circumvent these concerns¹⁹⁶ — is at best a partial solution to the problem.¹⁹⁷ Particularly in the diagnostic method context, one result of the interplay between § 101 and § 271 is likely to be that examiners will require the addition of treatment steps to diagnostic method claims during prosecution. Where treatment steps are by definition performed by physicians, rather than diagnostic laboratories, this is tantamount to requiring applicants to write divided method claims.¹⁹⁸

¹⁹⁵ The Federal Circuit has held that the conduct of the parties could not be attributed to a single actor even where there was an MOU between the relevant parties. See *Travel Sentry, Inc. v. Tropp*, 497 F. App'x 958, 965-66 (Fed. Cir. 2012).

¹⁹⁶ See, e.g., *Akamai*, 692 F.3d at 1325 (Newman, J., dissenting); *BMC Res., Inc. v. Paymentech, LP*, 498 F.3d 1373, 1381 (Fed. Cir. 2007); Keith Jaasma, *Finding the Patent Infringement “Mastermind”: The “Control or Direction” Standard for “Joint” Infringement*, 26 SANTA CLARA COMPUTER & HIGH TECH. L.J. 411, 451-52 (2010); Mark A. Lemley et al., *Divided Infringement Claims*, 33 AIPLA Q.J. 255, 272 (2005).

¹⁹⁷ See, e.g., W. Keith Robinson, *No “Direction” Home: An Alternative Approach to Joint Infringement*, 62 AM. U. L. REV. 59, 105 (2012) (“[F]urther consideration should be given to policy arguments in favor of enforcement of interactive method claims.”).

¹⁹⁸ See Brief for Biotechnology Indus. Org. as Amicus Curiae in Support of Respondent at 13, *Limelight Networks, Inc. v. Akamai Techs., Inc.*, 134 S. Ct. 2111 (2014) (No. 12-786) (“Some methods are simply not capable of being drafted in a manner that requires the practice to be performed by one entity.”); Brief for Myriad Genetics, Inc. and Genomic Health, Inc. as Amici Curiae in Support of Respondent at 15, 18, *Limelight Networks, Inc. v. Akamai Techs., Inc.*, 134 S. Ct. 2111 (2014) (No.

Additionally, in the § 101 context, the courts have expressed concern over what they view as “manipulation by patent applicants” in the claim drafting process,¹⁹⁹ a concern which may also prevent claim drafting from providing a viable solution to the § 271 problem.

2. Developments in Healthcare Organization

As patent lawyers were battling over the contours of divided infringement liability, statutes like the ACA²⁰⁰ and amendments to the CLFS²⁰¹ were encouraging a broad restructuring of the healthcare industry. Yet as discussed in the previous Part, scholars have largely overlooked the way in which the consolidation of provider groups and of laboratory testing services has been siloed. Hospitals have begun to contract out their outpatient diagnostic testing to large diagnostic companies like Quest and LabCorp.²⁰²

Importantly, for many diagnostic method claims, the result of this reorganization has been to separate more sharply the various aspects of many diagnostic tests, as a physician may order a test and send it to an externally-run lab for processing. Alternatively, a patient may present with results from an already-performed direct-to-consumer test. This division may compound the difficulties diagnostic method patent holders face in attributing infringement liability and thus in enforcing their patents.

a. *The Recent Reorganization in the Healthcare Industry*

The situation might be explained more easily using a visual taxonomy. In general, most²⁰³ of the diagnostic tests at issue fall into the following quadrants:

12-786) (“[P]atentees must include additional steps in diagnostic methods in order to make those method claims eligible for patenting.”).

¹⁹⁹ See, e.g., *CLS Bank Int'l v. Alice Corp. Pty.*, 717 F.3d 1269, 1281 (Fed. Cir. 2013) (en banc) (Lourie, J., concurring) (plurality opinion).

²⁰⁰ Patient Protection and Affordable Care Act, Pub. L. No. 111-148, 124 Stat. 119 (2010) (codified as amended in scattered sections of 26 U.S.C. and 42 U.S.C.).

²⁰¹ Deficit Reduction Act of 1984, Pub. L. No. 98-369, § 2303, 98 Stat. 494 (codified in scattered sections of 26 U.S.C. and 42 U.S.C.).

²⁰² See *supra* text accompanying notes 117–18.

²⁰³ This simple taxonomy is not exhaustive. In particular, it leaves out two significant categories of tests. First are tests which can be performed at home, whether they are direct-to-consumer (such as pregnancy tests or over-the-counter HIV tests) or require some amount of physician involvement (such as glucose monitoring for diabetes). In terms of its size, this is a non-trivial category, but in terms of its salience from an innovation perspective, the category is likely to be less important. Generally,

	<u>Tests Performed in a Hospital Laboratory</u>	<u>Tests Performed in an External Laboratory</u>
<u>Physician-prescribed</u>	Example: CBC, metabolic panel	Example: Myriad's BRCA test
<u>Direct-to-consumer</u>	Example: mobile screenings	Example: 23andMe

Consider a typical physician employed either in the hospital itself or whose practice group is affiliated with a hospital such that they process laboratory tests there. Some tests ordered by that physician will be performed in the hospital's laboratory, including routine tests like a basic metabolic panel or complete blood count. But for less common tests, such as Myriad's BRCA test, perhaps the test will be sent to an external (non-hospital) laboratory for testing.

On the other hand, some tests will be marketed directly to the consumer. There are a small number of organizations, like HealthFair, who provide mobile screening directly to the consumer but affiliate with particular hospitals.²⁰⁴ More commonly, though, there is a growing set of direct-to-consumer tests which are performed in external laboratories, with 23andMe being the most publicly salient example.²⁰⁵ This sector in particular is a locus of innovative activity, with companies seeking not only to disrupt the traditional laboratory testing model but also to put patients in greater control of their medical information.²⁰⁶

at-home tests are not what we mean when we talk about the future of diagnostic innovation, as usually such technologies begin by being performed in a laboratory, and only later do scientists translate the technology into the home. A second category is whole-genome sequencing. Although this type of sequencing is not yet affordable enough to be widespread, that day is fast approaching, see Erica Check Hayden, *Technology: The \$1,000 Genome*, NATURE (Mar. 19, 2014), <http://www.nature.com/news/technology-the-1-000-genome-1.14901>, and it poses a special case for infringement liability. Essentially, where at a given time a primary care physician recommends sequencing a patient's genome, and where that genome is not interpreted until later, perhaps by another physician, a divided infringement situation is likely to be present. See Price, *Unblocked Future*, *supra* note 5, at 1628 n.129.

²⁰⁴ For more information regarding HealthFair's mobile screening program, see *Hospital Partnerships*, HEALTHFAIR (2015), <http://healthfair.com/hospital-partnership/>.

²⁰⁵ See *supra* note 77 for a discussion of how the FDA's decision to regulate LDTs has affected 23andMe's corporate structure.

²⁰⁶ See, e.g., Ken Auletta, *Blood, Simpler*, NEW YORKER (Dec. 15, 2014), <http://www.newyorker.com/magazine/2014/12/15/blood-simpler> (profiling Theranos, a company that aimed to deliver blood testing more cheaply and easily to consumers). But see John Carreyrou, *Hot Startup Theranos Has Struggled With Its Blood-Test Technology*, WALL ST. J. (Oct. 16, 2015), <http://www.wsj.com/articles/theranos-has-struggled-with-blood-tests-1444881901>.

Now it is easy to see how the ACA and CLFS have changed the relative sizes of these quadrants. Fundamentally, the size of the external laboratory column is growing, for the two reasons highlighted previously. First, the shedding of diagnostic testing from hospitals to external laboratories has resulted in tests shifting from the first to the second column. And second, as innovators develop novel and ever-specialized tests, and as those tests are increasingly housed in specialized laboratories (either academic or industrial) rather than hospitals, the external laboratory column will grow independently of the hospital column.

b. The Legal Implications of Diagnostic Reorganization

Having explained how the provider and diagnostic industries are restructuring themselves in the wake of the ACA and related statutes, the ways in which this reorganization might affect patent law can now be described. Returning to the two-by-two taxonomy presented above, we might ask what the legal implications for method patents covering tests in each quadrant are, post-*Akamai*, in terms of the ability of patent holders to enforce those claims. Most likely, they are as follows:

	<u>Tests Performed in a Hospital Laboratory</u>	<u>Tests Performed in a Clinical Laboratory</u>
<u>Physician-prescribed</u>	Likely infringing	Likely not infringing
<u>Direct-to-consumer</u>	Likely not infringing	Likely not infringing

Patent holders bringing suits to enforce method claims covering diagnostic tests in the upper left quadrant — those that are prescribed by a physician and conducted in that physician’s hospital — are the most likely to succeed in attributing liability for performance of the test. The courts are likely to treat the physician and lab technician(s) as employees²⁰⁷ of the same company and attribute liability to the organization on that basis.

More germane to this Article, however, are claims covering tests in the upper right quadrant, which require the involvement of multiple actors.

²⁰⁷ Using the word “employee” to describe a physician is usually not proper — typically, they are technically classified as independent contractors. See Richard S. Saver, *Squandering the Gain: Gainsharing and the Continuing Dilemma of Physician Financial Incentives*, 98 NW. U. L. REV. 145, 177, 210 (2003). However, the Federal Circuit has not yet made or otherwise accepted this distinction, even though these terms seem directly related to the key doctrinal question of “direction or control.”

Since none of the methods of attributing infringement liability to a single actor that have been recognized by the Federal Circuit to date clearly read on this situation, patent holders will find it difficult to enforce these claims. Even if there is a contract between the provider group and diagnostic company, the courts would be likely to describe the relationship between the physician and the outside laboratory as an “arms-length business transaction,” in which there is no infringement.²⁰⁸ Here, doctors and laboratories will likely find it a simple matter to structure their relationships to avoid infringement liability.

In both direct-to-consumer situations, where the testing is in a meaningful sense initiated by the patient, the courts are not likely to attribute infringement liability, although in the context of tests performed within the hospital this conclusion is likely to depend more on the structure of the specific claim at issue. In the context of direct-to-consumer tests performed in external laboratories (which are subsequently interpreted and/or applied by a physician), however, the involvement of several additional actors will make it even more difficult for courts to attribute infringement liability to a single actor.

Notably, the direct-to-consumer context is the only area of health law in which the Federal Circuit has ever opined on the availability of infringement liability — although it did so largely in dicta in *McKesson Technologies Inc. v. Epic Systems Corp.*, a now-vacated panel opinion.²⁰⁹ *McKesson* dealt with a patent on electronic communication between physicians and their patients.²¹⁰ As a result, the Federal Circuit had occasion to consider how the doctor-patient relationship fits into the divided infringement paradigm. Judge Linn, in his panel opinion, concluded that “[a] doctor-patient relationship does not by itself give rise to an agency relationship or impose on patients a contractual obligation such that the voluntary actions of patients can be said to represent the vicarious actions of their doctors,”²¹¹ declining to attribute the patients’ actions to their physicians for purposes of assigning liability. Assuming that this logic would be reiterated going

²⁰⁸ See, e.g., *BMC Res., Inc. v. Paymentech, LP*, 498 F.3d 1373, 1380-81 (Fed. Cir. 2007) (quoting *BMC Res., Inc. v. Paymentech, LP*, No. 3-03-CV-1927-M, 2006 WL 306289, at *6 (N.D. Tex. Feb. 9, 2006)) (discussing situations where the parties’ “arms-length” relationship can affect whether there is infringement or not).

²⁰⁹ Judge Linn, who wrote the panel opinion in *McKesson*, did reprise some of his analysis in his dissent in *Akamai* at the first en banc stage. See *Akamai Techs., Inc. v. Limelight Networks, Inc.*, 692 F.3d 1301, 1351 (Fed. Cir. 2012) (en banc) (Linn, J., dissenting).

²¹⁰ *McKesson Techs. Inc. v. Epic Sys. Corp.*, No. 2010-1291, slip op. at 2 (Fed. Cir. Apr. 12, 2011).

²¹¹ *Id.* at 10.

forward, it is therefore unlikely that courts would assign liability in the direct-to-consumer context.

Because the ACA and related statutes are functioning to shift tests into the right-hand column of the taxonomy, the concomitant result is to shift diagnostic method patentees from a situation in which they are more likely to be able to establish infringement liability over their claims to a situation in which they are less likely to do so. Insofar as the health law developments function to divide the steps of many method claims, they will therefore compound the enforcement difficulties created by the Federal Circuit's and Supreme Court's recent patent law opinions.

IV. SYNTHESIZING THE SITUATION

As explained in the previous Parts, three important policy levers have recently been pulled in the diagnostic testing context. The FDA has proposed to increase the regulatory burdens it places on many diagnostic tests.²¹² Congress and CMS have reduced reimbursement rates paid by Medicare for diagnostic tests.²¹³ And the Federal Circuit and Supreme Court have tightened the scope of patent-eligible subject matter and limited the reach of divided infringement liability.²¹⁴

Each of these levers also acts on the market for new diagnostics, changing the ways in which academic scientists, investors, and diagnostic testing companies consider whether to move forward with developing innovative diagnostic tests. The FDA's actions have increased the cost and uncertainty of developing diagnostic tests and bringing them to market. The legislative and regulatory changes in reimbursement rates have diminished the returns innovators can expect from their efforts. And the changes in patent law and healthcare organization have made it more difficult for diagnostic innovators to protect their investment into such technologies.

As explicated in the previous three Parts, the ways in which these levers affect incentives are complex and multifaceted. Additionally, they affect different institutional actors in different ways. The FDA's proposed LDT regulation is a particularly striking example of these considerations. If fully implemented, the regulation has the potential to increase drastically the costs of developing new diagnostic tests. Yet these costs are likely to be more burdensome to academic institutions and to small diagnostic companies than to large diagnostic companies

²¹² See *supra* Part I.

²¹³ See *supra* Part II.

²¹⁴ See *supra* Part III.

or to large pharmaceutical companies developing companion diagnostics.²¹⁵ As a result, if the FDA ends up exercising more of a gatekeeping role in stringently regulating the individuals who are permitted to perform diagnostic testing, it may end up creating de facto monopolies.²¹⁶ This has the potential to counteract the decreased ability of patent law to accomplish the same function.

Relatedly, these areas of the law interact not only in additive ways, but also in synergistic ways. It is not necessarily the case that if decreased patent protection lowers incentives by x amount, and decreased reimbursement lowers incentives by y amount, the combination of the two lowers incentives by an amount equal to $x+y$. As explained in Part III, these two areas do not act independently of each other. The industry restructuring resulting from cuts to reimbursement rates *compounds* the enforcement problem observed in patent law. When viewed in combination, the effect of these two areas of the law is likely to be greater than the otherwise-observed sum of their individual parts. In contrast, if one effect of FDA regulation is to replicate a portion of patent law's exclusionary function,²¹⁷ the effect of those two combined changes may be smaller than the otherwise-observed sum.

These two conclusions — that each of these areas of the law acts on the market for healthcare technologies, and that the laws interact with each other in complex and often synergistic ways — indicate that a full understanding of the innovation ecosystem cannot be gained by examining a single area of the law. By extension, coherent policy proposals similarly cannot be advanced without starting from a broader, intersystemic perspective. Whether considering innovation problems or solutions, these three areas of law must all be considered, and considered as a unified whole. In turn, such consideration should cause us to think more fully about each individual area of the law.

²¹⁵ See *supra* notes 80–81 and accompanying text.

²¹⁶ See, e.g., Preliminary Transcript of *21st Century Cures: Examining the Regulation of Laboratory Developed Tests: Hearing Before the Subcomm. on Health, H. Comm. on Energy & Commerce*, 113th Cong. 25-26 (2014) (statement of Dr. Jeffrey Shuren), available at <http://docs.house.gov/meetings/IF/IF14/20140909/102625/HHRG-113-IF14-Transcript-20140909.pdf> (discussing the example of diagnostic testing for melanoma and noting that under the current regulatory system, if the FDA clears a particular test, other labs can simply enter the market and have no incentive to conduct their own trials).

²¹⁷ See Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345, 364-66 (2007) (discussing the advantages of using FDA exclusivity periods rather than patent law when it comes to pharmaceutical incentives).

Patent law provides a useful example here. Of the three legal developments chronicled in this Article, only the changes in patent law doctrine have been subject to extensive debate in the legal literature.²¹⁸ Legal scholars have criticized both the Federal Circuit and Supreme Court as their decisions relate to both § 101²¹⁹ and § 271.²²⁰ Much of the criticism, even when couched in doctrinal arguments, is fundamentally based in policy concerns.²²¹ Particularly in the § 101

²¹⁸ There is some legal literature discussing the FDA's regulation of LDTs, but in general it takes place within specialized fora. See, e.g., Gail H. Javitt, *In Search of a Coherent Framework: Options for FDA Oversight of Genetic Tests*, 62 FOOD & DRUG L.J. 617, 638-40 (2007). The CLFS makes essentially no appearances in the legal academic literature.

²¹⁹ See, e.g., Eisenberg, *Prometheus Rebound*, *supra* note 158, at 342-43 (arguing that the Court's approach in *Mayo v. Prometheus* "invite[s] patent challenges while offering only vague guidance for resolving them"); 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, 6-7 (2012) (criticizing the Supreme Court's decision in *Bilski* and arguing that the Court provided no direction or clarity on the law regarding patentable subject matter); Peter S. Menell, *Forty Years of Wondering in the Wilderness and No Closer to the Promised Land: Bilski's Superficial Textualism and the Missed Opportunity to Return Patent Law to Its Technology Mooring*, 63 STAN. L. REV. 1289, 1291, 1305 (2011) (criticizing the Supreme Court's inability to set clear standards for patentable subject matter jurisprudence as "ungrounded" and "incoherent").

²²⁰ See, e.g., Timothy R. Holbrook, *The Potential Extraterritorial Consequences of Akamai*, 26 EMORY INT'L L. REV. 499, 501, 510-11 (2012).

²²¹ For instance, in the § 271 context, scholars have considered the potential for a weak divided infringement doctrine to permit would-be infringers to structure their affairs to escape liability for infringement, debating whether this is a reasonable limit on liability that would otherwise ensnare many innocent actors, or whether this is instead an unintended end run around patent protection. Compare Lemley, et al., *supra* note 196, at 282 (arguing that the law should not enforce distributed patent claims, as the strict liability standard would affect many innocent parties), and Mark D. Janis & Timothy R. Holbrook, *Patent Law's Audience*, 97 MINN. L. REV. 72, 119 (2012) (approving of the Federal Circuit's approach to shifting liability for patent infringement in the first *Akamai* en banc opinion because it shields innocent actors who would have otherwise been liable), with Jaasma, *supra* note 196, at 411, 456 (asserting that the Federal Circuit created a loophole by permitting contracts with foreign jurisdictions to avoid infringement). The Federal Circuit and Supreme Court have both recognized this aspect of the doctrine, see, e.g., *Limelight Networks, Inc. v. Akamai Techs., Inc.*, 134 S. Ct. 2111, 2120 (2014); *Akamai Techs., Inc. v. Limelight Networks, Inc.*, 692 F.3d 1301, 1318 (Fed. Cir. 2012) (en banc) (per curiam), but neither court discussed the issue in detail, and the Federal Circuit explicitly resisted the idea that this issue had affected its doctrinal conclusion. The Federal Circuit generally tries to avoid policy discussions entirely, with the judges throwing the term "policy maker" at each other almost in a derogatory fashion. See, e.g., *Akamai*, 692 F.3d at 1337 (Linn, J., dissenting). But the Federal Circuit does occasionally consider policy concerns, most often referring to the role played by the settled expectations of

context, many scholars have debated the proper doctrinal approach by appealing to the underlying values to be served by the patent-eligibility filter. The Supreme Court (and to a lesser extent, the Federal Circuit²²²) has often considered § 101 to be motivated by concerns about preemption,²²³ under which upholding a patent “would pre-empt use of [the patent’s] approach in all fields, and would effectively grant a monopoly over an abstract idea.”²²⁴ On this view, because the § 101 exclusions (abstract ideas, laws of nature, and natural phenomena) are “the basic tools of scientific and technological work[,]”²²⁵ granting patents in such areas would impede, not promote, the progress of science.²²⁶ Scholars have roundly criticized the Court’s application of the preemption doctrine, arguing that its application is at best unhelpful and vague²²⁷ and at worst incoherent or simply irrelevant.²²⁸

the relevant industries in promoting innovative activity. *See, e.g., Ass’n for Molecular Pathology v. U.S. Patent & Trademark Office*, 689 F.3d 1303, 1333 (Fed. Cir. 2012); *In re Bilski*, 545 F.3d 943, 976-77 (Fed. Cir. 2008) (en banc) (Newman, J., dissenting) (discussing the reliance various industries have on current law and arguing that the majority’s approach will “disrupt” those expectations). More recently, in the guise of simply offering “additional reflections,” then-Chief Judge Rader spoke more candidly about the relationship between the court’s decisions and incentives for innovation. *CLS Bank Int’l v. Alice Corp. Pty.*, 717 F.3d 1269, 1335 (Fed. Cir. 2013) (en banc) (Rader, C.J., offering additional reflections). The Supreme Court is sometimes more explicit in its consideration of policy arguments. *See, e.g., Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1294 (2012). But even in these cases policy concerns are nearly always expressed in general terms, reflecting the formal one-size-fits-all nature of the patent laws. The courts’ rare discussions of technology-specific policy concerns have largely appeared in concurring or dissenting opinions, mitigating their legal force. *See, e.g., Ass’n for Molecular Pathology*, 689 F.3d at 1357 (Bryson, J., concurring in part and dissenting in part) (“Broad claims to genetic material present a significant obstacle to the next generation of innovation in genetic medicine — multiplex tests and whole-genome sequencing.”).

²²² *See, e.g., CLS Bank Int’l*, 717 F.3d at 1280 (discussing the Supreme Court’s concern about preemption in § 101 cases); *Ass’n for Molecular Pathology*, 689 F.3d at 1357.

²²³ *See Alice Corp. Pty. v. CLS Bank Int’l*, 134 S. Ct. 2347, 2358 (2014); *see also Bilski v. Kappos*, 561 U.S. 593, 658 (2010) (Breyer, J., concurring).

²²⁴ *Bilski*, 561 U.S. at 611-12.

²²⁵ *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2116 (2013) (quoting *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1293 (2012)); *see also Alice Corp.*, 134 S. Ct. at 2354.

²²⁶ *Lab. Corp. of Am. v. Metabolite Labs., Inc.*, 548 U.S. 124, 126-27 (Breyer, J., dissenting from dismissal of certiorari) (quoting U.S. CONST. art. I, § 8, cl. 8); *see also Prometheus*, 132 S. Ct. at 1293; *Bilski*, 561 U.S. at 658 (Breyer, J., concurring).

²²⁷ *See Rochelle C. Dreyfuss & James P. Evans, From Bilski Back to Benson: Preemption, Inventing Around, and the Case of Genetic Diagnostics*, 63 STAN. L. REV. 1349, 1350-52 (2011).

²²⁸ *See Katherine J. Strandburg, Much Ado About Preemption*, 50 HOUS. L. REV. 563, 566-68 (2012).

But these policy discussions miss the mark when they consider only the impact of one or another specific patent law doctrine on technological innovation. And in the case of diagnostic methods, which the courts addressed in both *Prometheus* and *Myriad*, this focus marginalizes not only the way in which other areas of regulation (such as the FDA's oversight scheme or Congress' adjustments to the CLFS) interact with patent law to impact the innovation environment, but also the ways in which other areas of patent law doctrine (either § 271 or § 101) may interact with each other.

The potential analytical power of a newly broadened focus is most easily illustrated by examining one version of the § 101 policy argument. When scholars consider what types of things ought to be eligible for patent protection, one of the most influential theories requires asking whether patents are necessary for an invention's development. As the Supreme Court has put it, judges want to know whether a patent is needed to "motivate the invention."²²⁹ If patents are not needed to motivate a particular class of inventions, perhaps patents should not be available for the class, allowing society to avoid the economic and social harms resulting from granting patents (such as the deadweight loss accruing from the imposition of monopoly pricing²³⁰) while still getting the benefit of the technology.

Many scholars and policymakers have argued that patents are not necessary to generate innovations in a range of technological areas,²³¹ including diagnostic methods. Perhaps most persuasively, an exhaustive report from the Secretary's Advisory Committee on Genetics, Health and Society ("SACGHS") concluded that "the prospect of patent protection of a genetic research discovery does not play a significant role in motivating scientists to conduct genetic research."²³² Since most relationships between diseases and genes are

²²⁹ *Bilski*, 561 U.S. at 650 (quoting *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 63 (1998)); see also *In re Bilski*, 545 F.3d 943, 1005 (Fed. Cir. 2008) (en banc) (Mayer, J., dissenting).

²³⁰ See SCOTCHMER, *supra* note 9, at 58.

²³¹ This is particularly true in the areas of business method and software claims. See, e.g., Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law*, 89 VA. L. REV. 1575, 1618-19, 1622-23 (2003) (discussing the characteristics of the business method and software industries which encourage them to innovate without the use of patents); Rochelle Cooper Dreyfuss, *Are Business Method Patents Bad for Business?*, 16 SANTA CLARA COMPUTER & HIGH TECH. L.J. 263, 275 (2000). Several jurists have expressed agreement with these sentiments in the context of business method claims. See, e.g., *Bilski*, 561 U.S. at 650-51 (Stevens, J., concurring); *In re Bilski*, 545 F.3d at 1006 (Mayer, J., dissenting).

²³² SACGHS REPORT ON GENE PATENTS, *supra* note 21, at 1.

identified by researchers at universities or other non-profit institutions, rather than in industry, SACGHS pointed to motivating factors such as career advancement, grant opportunities, and scientific curiosity as driving much of the basic research in this field.²³³

Importantly, SACGHS also rejected the contention that patents were needed to stimulate investment to bring those initial discoveries to market.²³⁴ In doing so, they relied in large part on the fact that the cost to create a laboratory-developed test for a genetic market is low, perhaps “between \$8,000 and \$10,000.”²³⁵ On this view, the contraction of patentable subject matter and tightening of divided infringement liability are salutary developments, as a general decrease in patent protection will be thought to lead to more innovation (or, at the very least, increased access to the same number of innovative tests), not less.

At the same time, other scholars and policymakers argued precisely the opposite.²³⁶ Roughly contemporaneously with the SACGHS report, the President’s Council of Advisors on Science and Technology argued that “[t]he ability to obtain strong intellectual property protection through patents . . . will continue to be[] essential for pharmaceutical and biotechnology companies to make the large, high-risk R&D investments required to develop novel medical products, including genomics-based molecular diagnostics.”²³⁷ As such, the Council expressed concern about recent court cases that were beginning to “shed doubt on the potential to patent diagnostic correlations,”²³⁸ even before the Supreme Court had considered *Prometheus* and *Myriad*. On this view, these cases are therefore harmful to the progress of diagnostic technologies.

But both of these positions, importantly, generally hold constant other areas of regulation. It very well might be that patents on diagnostic methods are not necessary to incentivize their development — as long as the cost to produce the test is low and the ability to recoup investment is high. The problem in this case is that all three

²³³ *Id.* at 22.

²³⁴ *See id.* at 30, 35 (noting that patents were not necessary for the development of genetic test kits or laboratory-developed genetic tests).

²³⁵ *Id.* at 34, 94.

²³⁶ *See, e.g.*, CHRISTOPHER M. HOLMAN, THE CRITICAL ROLE OF PATENTS IN THE DEVELOPMENT, COMMERCIALIZATION, AND UTILIZATION OF INNOVATIVE GENETIC DIAGNOSTIC TESTS 3 (2014) (arguing that the “most direct and effective means” of protecting diagnostic testing methods is by claiming the method through a patent).

²³⁷ PRESIDENT’S COUNCIL OF ADVISORS ON SCI. & TECH., *supra* note 21, at 21.

²³⁸ *Id.*

areas of regulation have changed at the same time, and as a result, patents may have suddenly become relatively more important as an innovation incentive. SACGHS did recognize the FDA aspect of the situation, noting that the low cost of developing genetic tests was in large part due to the absence of FDA oversight of LDTs²³⁹ and admitting that if the FDA did begin to regulate LDTs, “the cost of developing such tests . . . may become more substantial.”²⁴⁰ Yet it simply concluded that patents would still not be necessary in such an environment, without truly considering why that might be so.²⁴¹ Further, the analysis ignored other areas of patent law (including divided infringement concerns) as well as concerns about healthcare reimbursement.

Considering these areas in combination allows academics and policymakers to advance more robust policy conclusions. Relative to the previous baseline of low development costs, available patent protection, and higher reimbursement rates, flipping the policy levers in all three areas at once has likely decreased incentives to innovate in this space, at least in the aggregate. The effect of decreased patent protection may be to benefit innovators in academia or small firms, but they are disproportionately likely to be harmed by the actions of the FDA and CMS. Even the countervailing forces, like the FDA’s increased gatekeeping authority, would seem to redound only to the benefit of the most established institutional actors, again punishing academic institutions and smaller diagnostic companies who rely either on the low cost of production or on the availability of patent protection for their work.

The various policy changes will not only differentially impact various institutional actors, but they will also differentially impact various types of diagnostics. Companion diagnostic technologies that can be bundled with pharmaceutical interventions may become more valuable. For example, a test that examines a tumor’s genetic sequence for the presence of a particular mutation which, if present, would suggest the use of a particular chemotherapy drug might be developed rather than a test predicting a person’s risk of developing cancer to begin with. Similarly, clinical validity data may more easily be produced for “true” diagnostic tests — those that identify the disease affecting a symptomatic patient — rather than for prognostic tests, where the validity question is multifaceted, as previously

²³⁹ See SACGHS REPORT ON GENE PATENTS, *supra* note 21, at 95.

²⁴⁰ *Id.* at 94-95; see also PRESIDENT’S COUNCIL OF ADVISORS ON SCI. & TECH., *supra* note 21, at 37-38.

²⁴¹ See SACGHS REPORT ON GENE PATENTS, *supra* note 21, at 95-96.

considered.²⁴² The effect may be to bias innovation toward true diagnostics and treatment selection tools, and away from prognostic tests or tests that evaluate outcomes.

Considering these three areas of law as a unit changes the shape of the debate. Rather than simply considering whether patents are needed to motivate the development of diagnostic technologies, advocates on either side must now consider the role of FDA regulation and healthcare reimbursement. Those who previously argued that patents were necessary for the development of these technologies will likely conclude that developments in the FDA and reimbursement spaces have only further decreased incentives for innovation in a problematic way. Yet even those who previously supported the developments in patent law reducing protection for diagnostics may become concerned that incentives, particularly among academics, have become too low in light of these recent developments. Fortunately, just as each of these areas has contributed to creating an innovation problem in the diagnostics space, each of them may also provide potential policy solutions to the problem.

V. CONSIDERING POTENTIAL LEGAL INTERVENTIONS

If these three legal developments have combined to depress unacceptably incentives to innovate in diagnostics, the problem can be addressed by intervening in any one of the three areas of law — FDA regulation, healthcare regulation, or patent law — in a way that alters any one of the corporate incentives — cost to develop the product, ability to protect the technology, and ability to recoup the investment.²⁴³ The ultimate goal is to identify an intervention or set of interventions 1) with the potential to solve or at least improve the existing incentive situation, 2) which will achieve this result without significantly impacting other areas of law and technology in a negative way, and 3) which have a real possibility of being implemented in the current judicial and political climate. Each of these criteria requires further explication.

First, at a minimum, any potential intervention must actually work. But some interventions will be more efficacious than others, or may provide differential benefits to certain types of actors. As suggested above, if the FDA regulations impose the largest burdens on academic

²⁴² See *supra* text accompanying notes 55–57.

²⁴³ Cf. Ouellette, *Patentable Subject Matter*, *supra* note 19, at 1142–43 (arguing that the courts should recognize the existence of a range of non-patent incentives for innovation).

researchers, interventions in that area or that otherwise lower the cost of development may have a greater relative impact on this population. Additionally, given the synergistic relationship between several of these levers as described above, some interventions may have a multiplicative effect, while others have seemingly no effect if employed in isolation. Attempts to target potentially multiplicative interventions would likely be most efficient in solving any incentive problem.

Second, the external costs imposed by any intervention should be minimized, where possible. An intervention that improves incentives without imposing *any* concomitant costs would clearly be most preferable,²⁴⁴ but it is also most unlikely to exist. And the potential costs that might arise are of different kinds. An intervention which served a patent-like function might have negative effects on follow-on innovation into a given diagnostic method,²⁴⁵ while one that increased reimbursement rates and thereby increased costs for consumers could result in decreased access.²⁴⁶ There are policy-based tradeoffs to be made between these types of costs, but these are largely beyond the scope of this paper.

Finally, any serious intervention should be feasible. This criterion has two primary dimensions: practical and political. The ultimate incentive solution — one which perfectly tailored incentives for particular types of diagnostics as compared to each other, and as compared to other types of technologies — is impractical. We simply lack the information required to achieve it. Other potential interventions face more political obstacles. The likelihood of any intervention that relies on the current Congress is low, particularly if it requires them to amend the patent laws or to appropriate more money for basic research or for reimbursement.

This Part will canvass a range of potential policy interventions across areas of the law and across incentives, keeping in mind the intersystemic perspective advanced in Part IV. The key advantage of this perspective is that just as considering the three legal areas as a unit allows for a more nuanced exploration of the incentive situation in the diagnostic method space, such consideration also allows for more nuanced arguments to be made in each individual policy area.

²⁴⁴ Such a solution would be Pareto superior. However, as will become clear in the discussion of specific policy options, the search for such a solution may be futile.

²⁴⁵ See *supra* note 123 and accompanying text.

²⁴⁶ See, e.g., SACGHS REPORT ON GENE PATENTS, *supra* note 21, at 43 (giving the example of testing for an inherited predisposition to Alzheimer's disease, where the high cost of testing for consumers decreased access).

Each of the areas of law can be used to accomplish different incentive goals, and incentives even beyond these areas may also prove useful.

A. FDA Regulation

A broad range of potential tweaks might be made to FDA regulation to address innovation incentives. One set of promising avenues for intervention is inspired by the many ways in which the FDA attempts to incentivize drug companies to invest in new therapies. For instance, Congress might create a Priority Review Voucher-like system for neglected diagnostics,²⁴⁷ enabling innovators to decrease the length of premarket review and thus decrease their development costs. Alternatively, Congress might create a brief exclusivity period for novel diagnostic tests, much like the system it first created for pharmaceuticals in the Hatch-Waxman Act of 1984.²⁴⁸

Creating such a regulatory exclusivity period would allow diagnostic manufacturers to protect their investments even where patent protection is unavailable, and it would do so through a mechanism that is in many ways more powerful than patent protection. Statutorily-defined exclusivity periods are stronger than patent protection in that they are less susceptible to challenge. An FDA exclusivity period is both automatically enforced by the FDA's gatekeeping authority and is difficult to contest in the courts, while patentees seeking to enforce their rights against alleged infringers must typically invest significant resources in doing so, and their patent may be weakened or invalidated in the process.²⁴⁹

²⁴⁷ The FDA Amendments Act of 2007 created the "Priority Review Voucher," a transferable voucher that entitles its bearer to expedited FDA review on a future product, awarded to companies who obtain FDA approval for neglected tropical diseases. See 21 U.S.C. § 360n (2012). Given the high cost of the clinical trial process, vouchers can be worth hundreds of millions of dollars. See, e.g., Ed Silverman, *How Much? Gilead Pays \$125M for an FDA Priority Review Voucher*, WALL ST. J. (Nov. 19, 2014, 3:41 PM), <http://blogs.wsj.com/pharmalot/2014/11/19/how-much-gilead-pays-125m-for-an-fda-priority-review-voucher/> (reporting on the \$125 million voucher a pharmaceutical company paid for an FDA tropical disease voucher); see also Michael Mattioli, *Communities of Innovation*, 106 NW. U. L. REV. 103, 126-27 (2012); Jon D. Michaels, *Privatization's Progeny*, 101 GEO. L.J. 1023, 1078 (2013).

²⁴⁸ See 21 U.S.C. § 355(j)(5)(F)(ii) (2012). Since then, Congress has created many other exclusivity periods. See, e.g., 21 U.S.C. § 360cc(a) (2012) (Orphan Drug Act, conferring seven years of market exclusivity); 42 U.S.C. § 262(k)(7)(A) (2012) (Biologics Price Competition and Innovation Act, conferring twelve years of data exclusivity).

²⁴⁹ See Heled, *supra* note 17, at 430-32.

One possibly concerning effect of an exclusivity period would be the creation of silos of data. That is, diagnostic tests that are able to create and maintain a monopoly for a short period of time (say, two or three years) might create such a database of information that their first-mover advantage could not be easily surmounted by follow-on diagnostic manufacturers.²⁵⁰ This is particularly true for genetic diagnostics or diagnostics involving machine learning, for which large amounts of data may lead to increased predictive value.²⁵¹ If so, a short monopoly period might by default turn into a perpetual monopoly period, perhaps creating the kind of cost concerns that led to the development of a generic drug approval pathway decades ago.²⁵²

It is difficult, though, to say whether such silos are a feature or a bug of this system. Although a world in which all test providers have access to all such information may be most preferable, it may be difficult or impossible to create the Congressional action required for such an outcome. When faced with a host of suboptimal options, consolidating information might enable the development of a single exemplary test, rather than the development of several merely acceptable tests. Further, with Congress continuing to control reimbursement rates aggressively through the CLFS, the usual concerns about monopoly pricing may not be as salient.

It is true that the creation of an exclusivity period would require Congressional action, which poses concerns for feasibility. However, of all the possible legislative proposals that could be made in this space, this one seems comparatively likely to pass in the current Congressional environment. In particular, since many members of the House have publicly expressed unease with the burden on industry of the FDA's proposal to regulate LDTs,²⁵³ many Republicans might sign

²⁵⁰ See, e.g., John M. Conley et al., *Myriad After Myriad: The Proprietary Data Dilemma*, 15 N.C. J. L. & TECH. 597, 612 (2014) (observing that when Myriad opened a new lab in Germany, it had a competitive advantage over other diagnostic manufacturers due to its United States patent-based monopoly that gave it a "vast and unique interpretive database" to rely on); see also Barbara J. Evans, *Economic Regulation of Next-Generation Sequencing*, 42 J.L. MED. & ETHICS 51, 53-54 (2014) (discussing the importance of data in analyzing variants of unknown significance in the BRCA gene and noting that Myriad's patents enabled it to accumulate large amounts of data and provide more information to patients as a result).

²⁵¹ See W. Nicholson Price II, *Black-Box Medicine*, 28 HARV. J.L. & TECH. 419, 432, 434 (2015).

²⁵² See, e.g., H. REP. NO. 98-857, pt. I, at 14-15 (1984) ("The purpose of Title I of the bill is to make available more low cost generic drugs by establishing a generic drug approval procedure . . .").

²⁵³ See Preliminary Transcript of *21st Century Cures*, *supra* note 216, at 12, 32 (statement of Dr. Michael C. Burgess, Vice Chairman, Subcomm. on Health)

on to the measure as a way to protect innovative companies, while Democrats might sign on to a compromise bill that explicitly gave the FDA the authority to regulate LDTs, avoiding a potentially significant legal challenge.²⁵⁴ An exclusivity period would also be at least partially “off-budget,” in the sense that some of the resulting increased expenditures would be incurred by private actors, rather than the government.²⁵⁵ Since CMS operates as a primary purchaser of diagnostic tests, some of these costs would be borne directly by government actors. But in this political climate, interventions that are at least partially off-budget may require less political capital to enact when compared with on-budget interventions.

Another possible concern is that an exclusivity period would likely function to benefit companies who already possess the resources to pass through the FDA’s approval process, and as noted above, that process is likely to be the least burdensome for this group to begin with.²⁵⁶ Possibly more efficacious, therefore, would be a change to the FDA’s draft guidance that relieved some of the regulatory burdens on academic medical centers or small diagnostic companies.²⁵⁷ Such institutions might be permitted to partner with each other and submit a single application for review, pooling their resources to decrease their individual burdens. Alternatively, on the assumption that the FDA’s LDT review process is to be funded by user fees,²⁵⁸ the FDA might alter its existing tiered pricing system, which presently charges higher fees to large for-profit companies and lower fees to smaller companies, possibly even waiving the fee entirely for academic institutions.²⁵⁹ Interventions along these lines would decrease the costs of developing a given diagnostic. Further, the FDA could make these changes without any input from Congress, making them even more feasible.

(statement of Rep. Frank Pallone, Member, Subcomm. on Health).

²⁵⁴ See *supra* note 76 (discussing the potential legal challenges that could arise with FDA efforts to regulate LDTs).

²⁵⁵ See Robert P. Merges, *The Economic Impact of Intellectual Property Rights: An Overview and Guide*, 19 J. CULTURAL ECON. 103, 111 (1995).

²⁵⁶ See *supra* text accompanying notes 80–81.

²⁵⁷ As discussed in Part I, the FDA has already started down this path by carving out certain types of diagnostic tests from the most extreme of its LDT reforms, at least in the first few years of the program. See LDT DRAFT GUIDANCE, *supra* note 30, at 13, 20–24.

²⁵⁸ The FDA’s system of medical device regulation, on which LDT review will be based, is driven by user fees. See *supra* notes 70–71.

²⁵⁹ At present, the fee is waivable only for extremely small businesses submitting their first-ever medical device application. See *supra* note 71.

B. Healthcare Organization

The potential ways in which a financial incentive might be formulated to affect the healthcare organization piece of the puzzle are essentially endless. Incentives might encourage hospitals and provider groups to retain some or all of their diagnostic capacity, taking the form of direct payments, tax benefits, or other in-kind rewards. These incentives would be targeted at addressing the ability of diagnostic innovators to enforce any patents they may still be able to obtain post-*Prometheus*, mitigating the effects of *Akamai*.²⁶⁰ Alternatively, we might look to amend the CLFS in one of several ways to address the recoupment concern. Such an amendment might most simply increase reimbursement rates directly, or it might change the metric along which CMS reimburses diagnostics to include additional considerations such as value or whether the test addresses an unmet need.

Amending the CLFS in particular could have a doubly powerful effect. Essentially, it has the potential to address not only the recoupment concern, but also the related protection problem. As discussed above, the institutional reorganization hastened by the CLFS cuts has compounded the *Akamai* divided infringement problem by decoupling the patient's treating physician from the laboratory professionals performing other steps of the method claim.²⁶¹ But an amendment to the CLFS that enabled hospitals to maintain their existing diagnostic profit margins could reduce their incentives to spin off their outreach practices, making patent enforcement easier in such contexts.

However, the simplest way to accomplish this intervention is also the least feasible. An across-the-board spending increase would not only require Congress to act, but it would require Congress both to approve an on-budget expenditure of government funds in a way that increases Medicare costs and to refrain from cutting rates going forward (as it has consistently done with the CLFS).²⁶² Fortunately, though, there are more effective ways to amend the CLFS than to simply enact an across-the-board increase that affects uncommon,

²⁶⁰ See, e.g., Eisenberg, *Diagnostics*, *supra* note 158, at 2 (analyzing the various cases relating to patent protection for diagnostics and concluding that “diagnostic applications are not patent eligible” under current law); Golden, *supra* note 150, at 1791-92.

²⁶¹ See *supra* Part III.B.2.

²⁶² A law that would achieve this effect but would be limited to certain types of diagnostics — perhaps those using advanced genomic technology or those designed to be prognostic rather than truly diagnostic — might be able to gain support, but given our general inability to predict the course of technological development, it might be shortsighted.

innovative diagnostics to the same degree as common tests which have achieved economies of scale over time.

A system that is both more precise and more politically feasible might be imposed by CMS rather than by Congress itself. Perhaps ideally, Congress could task CMS with apportioning some overall percentage increase, instructing it to apportion those increases across the various sectors of the diagnostic industry in a way that would achieve the largest amount of impact from an innovation perspective. In reality, though, it might be the case that Congress simply allows CMS to apportion *cuts* across the industry, in a way that would spare novel tests and target out-of-date technologies. This would comparatively advantage novel diagnostic tests, even if testing as a whole is disfavored.

C. Patent Law

The foregoing analysis provides a novel argument against the Supreme Court's recent opinions in the patent law space. That is, it supports the conclusion of those scholars who argue that the Supreme Court's opinions in cases like *Prometheus* and *Akamai* were unsupported as a policy matter, but it provides a different reason — the depression of incentives to innovate in diagnostic methods, when coupled with other areas of law — for that conclusion. One such intervention, therefore, would be to reverse the effects of those decisions either by having the Federal Circuit attempt to circumvent them on remand or by encouraging Congress to intervene. The potential for the Federal Circuit to act in the § 271 context in particular is quite clear, given the fact that the Federal Circuit might be willing to expand further the reach of divided infringement after their opinion on remand in *Akamai*.²⁶³

Targeted toward improving innovators' ability to protect their investment in diagnostic testing, this potential solution has several benefits. First, because an emerging health technology company's possession of patents may contribute to the availability of investor funding,²⁶⁴ securing patents might be the simplest way to ensure a

²⁶³ Justice Alito's opinion in *Akamai* explicitly left open the possibility that on remand the Federal Circuit might revisit its § 271(a) precedent, the effect of which would be to render his own opinion of "no value" or "a nullity," as he and Justice Kagan respectively noted at oral argument. *Limelight Networks, Inc. v. Akamai Techs., Inc.*, 134 S. Ct. 2111, 2120 (2014); see also Transcript of Oral Argument at 13, 15, *Limelight Networks, Inc. v. Akamai Techs., Inc.*, 134 S. Ct. 2111 (2014) (No. 12-786), available at http://www.supremecourt.gov/oral_arguments/argument_transcripts/12-786_5he6.pdf.

²⁶⁴ See, e.g., Stuart J.H. Graham et al., *High Technology Entrepreneurs and the Patent*

diagnostic company has the resources to complete newly required clinical trials. Second, the very fact that it is implemented through the patent law, whose primary purpose is to promote innovation,²⁶⁵ means there may be fewer collateral consequences in other areas of law than might otherwise be expected. Third and more practically, it can potentially be accomplished without involving Congress.

But intervening through the patent law is not without its problems. Perhaps chief among them is that because patent law is formally one-size-fits-all and does not have different statutory requirements for different technological areas, the potential ripple effects in other areas of technology might be significant. If patent protection truly is unimportant in driving the development of business methods or software, changing the law in a way that would also increase the protection of these kinds of methods may be socially harmful, for the reasons articulated previously.²⁶⁶ Scholars do generally agree that the patent laws are not applied in a uniform fashion, and Professors Dan Burk and Mark Lemley have carefully analyzed the ways in which the Federal Circuit's opinions are uniform in theory, but technology-specific in practice.²⁶⁷ But because the Federal Circuit generally has not appropriately calibrated its application of the doctrine to the policy concerns underlying the technology in question,²⁶⁸ there is no guarantee that the differential application of various patent law doctrines would work out favorably in this particular instance to minimize the social harms of strengthening patent protection over business methods or software.

An attempt to avoid these problems by asking Congress to create a diagnostic method-specific doctrine would be both impractical and unwise. Such an intervention fails both aspects of the feasibility test, as it not only requires Congress to act, but requires them to act based upon information they do not possess. In addition, it would present an opportunity for rent-seeking behavior on behalf of the regulated

System: Results of the 2008 Berkeley Patent Survey, 24 BERKELEY TECH. L.J. 1255, 1280-83 (2009); Ted Sichelman & Stuart J.H. Graham, *Patenting by Entrepreneurs: An Empirical Study*, 17 MICH. TELECOMM. & TECH. L. REV. 111, 159 (2010).

²⁶⁵ Burk & Lemley, *supra* note 231, at 1580.

²⁶⁶ *See id.* at 1588-89.

²⁶⁷ *See id.* at 1576-78; Transcript of Oral Argument at 15, *Global-Tech Appliances, Inc. v. SEB S.A.*, 131 S. Ct. 2060 (2011) (No. 10-6), available at http://www.supremecourt.gov/oral_arguments/argument_transcripts/10-6.pdf (Roberts, C.J.: "But we might decide that it's more important to consider what's going to happen to the semiconductor industry in articulating our standard than what's going to happen to the deep-fryer industry").

²⁶⁸ *See* Burk & Lemley, *supra* note 231, at 1577-78.

industry. Finally, such an effort might ultimately be wasteful, as the pace of technological progress might make the specific terms of any such statute obsolete by the time of its passing.²⁶⁹ From a distributive perspective, an intervention through the patent law would also disproportionately benefit larger private entities, rather than university systems.

D. External Interventions

There are of course other ways in which the government might support incentives for diagnostic development that do not fall within any of these three areas. Most obviously, the government might devote more money to funding basic research with an eye toward supporting diagnostic test development, encouraging the National Institutes of Health (“NIH”) to award grants to projects that would translate basic science discoveries into diagnostic products ready for FDA approval²⁷⁰ or increasing research tax credits in these areas.²⁷¹ Alternatively, the government might establish a prize fund for the development of diagnostics in particularly underserved treatment areas.²⁷²

The provision of grants, tax credits, or prizes would accomplish the same goals as the above legal interventions, and it has great potential to do so without negatively affecting other areas of technology.²⁷³ However, the legislation providing for these awards would still be subject to rent-seeking behavior, and the idea of Congress passing a law that would increase the budget of the NIH without extracting

²⁶⁹ *Id.* at 1635-37; see also Rachel Sachs, *The New Model of Interest Group Representation in Patent Law*, 16 YALE J. L. & TECH. 344, 390 (2014).

²⁷⁰ See PRESIDENT’S COUNCIL OF ADVISORS ON SCI. & TECH., *supra* note 21, at 33-34; see also *Clinical and Translational Science Awards (CTSA) Program*, NAT’L CENTER FOR ADVANCING TRANSLATIONAL SCI., <http://www.ncats.nih.gov/research/cts/ctsa/ctsa.html> (last visited Jan. 31, 2016).

²⁷¹ See Hemel & Ouellette, *supra* note 19, at 321-23.

²⁷² Such a prize would not be without precedent. President Obama recently signed an executive order creating a \$20 million prize for a rapid point-of-care diagnostic for antibiotic-resistant bacteria, to be overseen by the NIH and Biomedical Advanced Research and Development Authority. Press Release, Office of the Press Sec’y, Fact Sheet: Obama Administration Takes Actions to Combat Antibiotic-Resistant Bacteria (Sept. 18, 2014), available at <http://www.whitehouse.gov/the-press-office/2014/09/18/fact-sheet-obama-administration-takes-actions-combat-antibiotic-resistan>.

²⁷³ This assumes that new money will be allocated for this goal, rather than reallocating existing grant funds. Unfortunately, this assumption is not always borne out in practice. See, e.g., Paula Park, *Funding Research in Africa*, SCIENTIST (Nov. 12, 2014), available at <http://www.the-scientist.com/?articles.view/articleNo/41427/title/Funding-Research-in-Africa/> (“[S]ome worry that increased funding for Ebola in the midst of the epidemic will actually draw funds away from other research programs.”).

concessions elsewhere in the regulatory process is, unfortunately, a remote possibility at the present time.

On balance, no single solution would perfectly increase incentives to innovate in this space across the relevant actors, especially without causing harms elsewhere. More likely, a menu of potential interventions will be needed to accomplish this goal. Encouraging the FDA to be more solicitous of the burdens its guidance process will place on academic medical centers, such as by permitting them to submit tandem applications, pool research results, or pay smaller fees, would seem to be most efficacious for this particular population. And an amendment to the CLFS that tasked CMS with apportioning rate adjustments could be a more efficient solution for private industry, as it addresses both the recoupment and patent protection concerns. By permitting the relevant expert agencies to tailor these interventions, these solutions could be structured to impose minimal concomitant harms. Both interventions are practically feasible, and the first is politically feasible, too. Although the difficulty of amending the CLFS is of course real, there is a dearth of effective solutions that do not require the involvement of Congress, and the potentially multiplicative effect of this intervention would seem to make it worth the political capital.

CONCLUSION

In this Article, I have examined the ways in which patent law, FDA regulation, and health law interact to affect incentives for innovation, largely considering the way in which this theory applies to a particular case: diagnostic technologies. Although the picture painted by recent developments in those three areas of the law is quite negative, I view this particular story as an optimistic one overall, because it provides a way forward through the identification of possible solutions.

But this Article aims not simply to present a case study of the diagnostic technology space. Its consideration of the way in which patent law, FDA regulation, and health law interact is generalizable more broadly. Contextualizing these interactions within a case study permits a detailed discussion of the complexities of one technological situation, but interactions between these areas of law exist with respect to a host of other healthcare technologies, including pharmaceuticals and medical devices. Further, the way in which aspects of these particular non-patent levers — FDA's role as gatekeeper, healthcare reimbursement, insurance design — contribute to the innovation ecosystem has been underspecified in the literature. As such, this Article opens up many avenues for further research.

This research must include not only studies of other technological areas and deeper examinations of each individual lever, but also higher-level consideration of the way in which the relevant institutional actors relate to each other. Each of the relevant actors should now realize that it has the capacity to affect the entire innovation system, for better and for worse. Although at present they formally lack shared regulatory authority over this space, further study will reveal superior ways to structure their relationships and alter the institutional architecture of these various innovation systems. For now, though, the ultimate takeaway is simply that each of these areas has great potential to rescue incentives for innovation in diagnostic testing, and therefore to preserve the future of personalized medicine.