

## BRCA1 AND BRCA2 MUTATIONS HIGHLIGHT THE NEED FOR IMPROVED REGULATION OF LABORATORY-DEVELOPED TESTS

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### I. INTRODUCTION

Through recent advances in molecular biology and the Human Genome Project, genetic testing is becoming more available and increasing in demand.<sup>1</sup> The fact that one can determine if he or she has a genetic propensity toward a certain disease makes obtaining this information desirable to many.<sup>2</sup> This information renders making a “preemptive strike” in treating a disease a possibility.<sup>3</sup> In the case of the BRCA1 or BRCA2 genetic mutations, for example, which heightens one’s susceptibility to breast cancer,<sup>4</sup> a patient may choose to begin early chemopreventative treatments or to remove some of the tissue that is at-risk for developing the cancer.<sup>5</sup> One may also have a greater motivation to avoid certain high-risk activities in an effort to not compound the genetic propensity toward the disease

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<sup>1</sup> Temitope Keku et al., *Gene Testing: What the Health Professional Needs to Know*, 144 J. NUTRITION 3754S, 3754S (2003), available at <http://jn.nutrition.org/content/133/11/3754S.full>.

<sup>2</sup> See *id.*

<sup>3</sup> See *id.*

<sup>4</sup> Bernard Friedenson, *The BRCA1/2 Pathway Prevents Hematologic Cancers in Addition to Breast and Ovarian Cancers*, 7 BMC CANCER 152, 153, available at <http://www.biomedcentral.com/content/pdf/1471-2407-7-152.pdf>.

<sup>5</sup> *BRCA1 and BRCA2: Cancer Risk and Genetic Testing*, NAT’L CANCER INST. AT THE NIH (May 29, 2009), <http://www.cancer.gov/cancertopics/factsheet/Risk/BRCA>.

with unhealthy activities or issues, such as alcohol consumption, poor diet, and obesity.<sup>6</sup> Many companies developing these genetic tests desire a patent on both the gene sequence utilized, as well as the test itself, which often consists of comparing the results of the test to a standard value or sequence.<sup>7</sup> The patentability of these tests has recently come under fire by the courts, hinting toward an anti-gene sequence patent and anti-“comparative” test patent sentiment.<sup>8</sup>

Genetic tests are often available through what are known as “laboratory-developed tests,” or LDTs.<sup>9</sup> These tests have not been highly scrutinized by the Food and Drug Administration (FDA), but that seems to be changing.<sup>10</sup> The FDA desires higher regulations of LDTs because they are becoming more and more prominent and may pose a risk to the patient if the tests’ efficacy are not properly validated.<sup>11</sup>

Because LDTs have become more prevalent, are often supplied directly to the consumer without a health-care provider’s professional opinion, and pose possible serious consequences if incorrect, some sort of regulation is necessary. However, the current FDA mechanism toward regulating medical devices may not be the preferred scheme for regulating LDTs, especially since genes and “comparative” genetic test patents are susceptible to litigation.

This paper will discuss why regulation is necessary and why the

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<sup>6</sup> *Id.*

<sup>7</sup> See *Ass’n for Molecular Pathology v. U.S. Patent & Trademark Office*, 702 F. Supp.2d 181, 185 (S.D.N.Y. 2010) (deciding whether isolated human genes and the comparison of their sequences are patentable); *cf.* *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 628 F.3d 1347 (Fed. Cir. 2010) (method claimed for determining proper dosage of thiopurine drugs to treat autoimmune diseases, involving comparison of patients’ metabolite levels to predetermined levels is patent-eligible); *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 370 F.3d 1354 (Fed. Cir. 2004), *cert. dismissed*, 548 U.S. 124 (2006) (company granted injunction to protect their patent for measuring levels of an amino acid to predict future vitamin deficiency).

<sup>8</sup> See generally *Ass’n for Molecular Pathology*, 702 F. Supp.2d 181.

<sup>9</sup> See Dan Vorhaus, *Breaking: FDA Moves to Broadly Regulate LDTs*, GENOMICS LAW REPORT (June 16, 2010), <http://www.genomicslawreport.com/index.php/2010/06/16/breaking-fda-moves-to-broadly-regulate-ldts>.

<sup>10</sup> See *id.*; see also Notice of Pub. Meeting & Request for Comments, 75 Fed. Reg. 34,463 (June 17, 2010).

<sup>11</sup> See *supra* note 10.

current FDA regulatory process is not ideal in light of current court decisions. This paper will also propose a more cost- and time-efficient regulatory mechanism. Part II will explain the science of genetics and genetic testing, the BRCA gene, and why genetic tests are needed. Part III will explore the current mechanism through which LDTs are regulated and why this must change. Part IV will discuss the current process by which medical devices are regulated, the courts' recent decisions on "comparative" tests and "abstract ideas," and why the current regulatory mechanism of medical devices is not an appropriate pathway for genetic LDTs. Part V will propose a new regulatory scheme for genetic LDTs.

## II. GENETIC TESTING

### A. The Science of Genetics

Deoxyribonucleic acid (DNA) is the building block of life. DNA is composed of four different bases: thymine (T), guanine (G), adenine (A), and cytosine (C).<sup>12</sup> Each base is then attached to a phosphate group and a sugar, forming a single nucleotide.<sup>13</sup> Genetic information is encoded in the sequence of nucleotides in the strand;<sup>14</sup> therefore, the quantity and sequence of nucleotides in a strand of DNA differs depending upon the organism.<sup>15</sup> Each base's chemistry renders it specifically complementary with one other base (A-T and C-G).<sup>16</sup> When two complementary strands of DNA come together base-pairs form between the nucleotides, resulting in the familiar double-stranded double helix structure.<sup>17</sup> The sequence of nucleotides codes for genetic information through what is known as the "central dogma" of molecular biology (DNA → RNA →

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<sup>12</sup> Nat'l Library of Med., *What is DNA?*, GENETICS HOME REFERENCE (Oct. 4, 2011), <http://ghr.nlm.nih.gov/handbook/basics/dna>.

<sup>13</sup> BRUCE ALBERTS ET AL., *MOLECULAR BIOLOGY OF THE CELL* 193 (4th ed. 2002).

<sup>14</sup> *Id.* at 195.

<sup>15</sup> *Id.* at 195.

<sup>16</sup> *Id.* at 194-95.

<sup>17</sup> *Supra* note 10.

protein).<sup>18</sup> This process, in which the sequence of a strand of DNA (a "gene") is translated into a protein is known as "gene expression."<sup>19</sup> Ribonucleic acid (RNA), a single-stranded molecule, is formed inside the nucleus where bases complementary to the nucleotide sequence within the strand of DNA are coded.<sup>20</sup> This process is known as "transcription" because the RNA molecule, through its complementary sequence, is essentially transcribing the nucleotide sequence of the gene located on that specific section of the DNA strand.<sup>21</sup> The RNA strand then exits the nucleus into the cytoplasm of the cell, taking the DNA sequence information along with it.<sup>22</sup> Once outside the nucleus, the RNA strand codes for the formation of a protein.<sup>23</sup> Each group of three nucleotide bases in the RNA sequence codes for one amino acid.<sup>24</sup> Amino acids are the building blocks of protein.<sup>25</sup> The amino acids bind in sequence to the RNA molecule and, in the process, bind to each other.<sup>26</sup> After formation along the RNA strand, the protein is then released.<sup>27</sup> The sequence of amino acids in the protein determine whether it will function as an enzyme, antibody, hormone, or structural molecule.<sup>28</sup>

Mutations in DNA can occur through several mechanisms. Nucleotides can be deleted from or added to the sequence, or they

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<sup>18</sup> Francis Crick, *Central Dogma of Molecular Biology*, 27 NATURE 561, 561 (1970), available at <http://profiles.nlm.nih.gov/ps/access/SCBCCH.pdf>.

<sup>19</sup> *Supra* note 11, at 196.

<sup>20</sup> Nat'l Ctr. for Biotech. Info., *What is a Genome?*, [http://www.ncbi.nlm.nih.gov/About/primer/genetics\\_genome.html](http://www.ncbi.nlm.nih.gov/About/primer/genetics_genome.html) (last visited Jan. 23, 2011).

<sup>21</sup> Alberts, *supra* note 12, at 336.

<sup>22</sup> Ann Smith & Kenna Shaw, *Discovering the Relationship Between DNA and Protein Production*, NATURE EDUCATION (2008), available at <http://www.nature.com/scitable/topicpage/Discovering-the-Relationship-Between-DNA-and-Protein-27699>.

<sup>23</sup> *Id.*

<sup>24</sup> Alberts, *supra* note 12, at 336.

<sup>25</sup> Nat'l Ctr. for Biotech. Info., *supra* note 19.

<sup>26</sup> Alberts, *supra* note 12, at 342.

<sup>27</sup> *Id.* at 350.

<sup>28</sup> Nat'l Ctr. for Biotech Info., *supra* note 19.

can be in the incorrect order.<sup>29</sup> These mutations can either be hereditary<sup>30</sup> or caused by environmental factors resulting in DNA damage.<sup>31</sup>

## B. Genetic Testing

The presence of certain genes can be detected via gene-specific tests. These tests are performed by first manufacturing a molecule with nucleotides complementary to the gene sequence being tested for (known as a “probe”).<sup>32</sup> A DNA sample is procured from the patient, often in the form of a blood draw, and then the probe is introduced into the sample, flagging the presence of the gene.<sup>33</sup>

### 1. The Need for Genetic Tests

One example of a genetic test that is available is the test for a mutation in the BRCA1/2 genetic sequences. BRCA1 and BRCA2 are known as “tumor suppressor genes,” meaning the proteins for which they code repair damaged DNA.<sup>34</sup> Certain mutations in tumor suppressor genes lead to a higher susceptibility to cancer in the damaged DNA that is not repaired. This leads to unrestrained replication of the damaged DNA.<sup>35</sup> Specifically, one recent study has shown that a mutation in the BRCA1 gene results in a 55% chance of developing breast cancer and a 39% chance of developing ovarian cancer by age 70.<sup>36</sup> For a mutation in the BRCA2 gene, the risk for breast cancer is 47% and the risk for ovarian cancer is 17%.<sup>37</sup> A

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<sup>29</sup> *Id.*

<sup>30</sup> Alberts, *supra* note 12, at G:23.

<sup>31</sup> *Id.* at 268.

<sup>32</sup> Human Genome Project Info., *Gene Testing*, [http://www.ornl.gov/sci/techresources/Human\\_Genome/medicine/genetest.shtml](http://www.ornl.gov/sci/techresources/Human_Genome/medicine/genetest.shtml) (last visited Jan. 23, 2011).

<sup>33</sup> *Id.*

<sup>34</sup> Nat'l Cancer Inst., *supra* note 4.

<sup>35</sup> *Id.*

<sup>36</sup> Sining Chen & Giovanni Parmigioni, *Meta-Analysis of BRCA1 and BRCA2 Penetrance*, 25 J. CLINICAL ONCOLOGY 1329, 1332 (2007).

<sup>37</sup> *Id.*

mutation in the BRCA1 gene can also lead to an increase risk of cervical, uterine, pancreatic, and colon cancers.<sup>38</sup>

The ability to detect the presence of mutated BRCA1 and BRCA2 genes is desirable in order to determine one's susceptibility to breast cancer. Upon discovering the presence of one of these mutations, the patient has several options available to her to manage or prevent the manifestation of the disease.<sup>39</sup> Once a patient knows she has a genetic disposition toward breast cancer, she may want to begin early surveillance methods.<sup>40</sup> These methods include mammography and clinical breast exams.<sup>41</sup> The American Cancer Society recommends women with a BRCA1 or BRCA2 mutation should begin receiving mammograms at age thirty.<sup>42</sup> A patient may also choose to remove the at-risk tissue through a bilateral prophylactic mastectomy, the removal of the healthy breasts, or a prophylactic salpingo-oophorectomy, the removal of healthy fallopian tubes and ovaries.<sup>43</sup> However, removal of this tissue only reduces the chance of developing cancer, and is not a complete protection against it.<sup>44</sup> Discovering one has a genetic propensity toward developing breast or ovarian cancer may motivate the individual to avoid or manage certain conditions or behaviors that may compound the risk of developing these types of cancer, such as alcohol consumption, obesity, and a high-fat diet.<sup>45</sup>

A standard way of categorizing a patient's prognosis is through a

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<sup>38</sup> Nat'l Cancer Inst., *supra* note 4 (citing L. Kadouri et al., *Cancer Risks in Carriers of the BRCA1/2 Ashkenazi Founder Mutations*, 44 J. MED. GENETICS 467, 467-69 (2007); Deborah Thompson, *Cancer Incidence in BRCA1 Mutation Carriers*, 94 J. AM. CANCER INST. 1358, 1358-65 (2002)).

<sup>39</sup> Nat'l Cancer Inst., *supra* note 4.

<sup>40</sup> *Id.*

<sup>41</sup> *Id.*

<sup>42</sup> AM. CANCER SOC'Y, *Cancer Prevention & Early Detection Facts & Figures 2010*, available at <http://www.cancer.org/Research/CancerFactsFigures/CancerPreventionEarlyDetectionFactsFigures/acs-cancer-prevention-early-detection-facts-figures-2010>.

<sup>43</sup> Nat'l Cancer Institute, *supra* note 4.

<sup>44</sup> *Id.* (citing N.D. Kauff, et al., *Reducing Risk-Reducing Salpingo-Oophorectomy for the Prevention of BRCA1 and BRCA2-Associated Breast and Gynecologic Cancer: A Multicenter, Prospective Study*, 26 J. CLINICAL ONCOLOGY 1331, 1331 (2008)).

<sup>45</sup> *Id.*

statistic known as a “survival rate.”<sup>46</sup> For example, a five-year survival rate is the percentage of patients who live at least five years after being diagnosed with cancer.<sup>47</sup> Recent studies have shown if the cancer is detected when it is still in its localized stage, the five-year survival rate is 98%.<sup>48</sup> The 2001–2002 statistics from the National Cancer Data Base indicate late-stage detection of breast cancer results in a five-year survival rate of 41% in early stage 3 and 15% in stage 4.<sup>49</sup> These statistics indicate early detection of cancer is highly desirable in that the earlier the cancer is detected, the higher the probability of survival. Genetic testing can help ensure cancer is detected at an early stage. Those who have the BRCA1/2 mutation can begin surveillance early and will possibly be able to detect the presence of cancer before otherwise detected (i.e. visible lump on the breast). BRCA1/2 indicates a propensity toward a particular disorder or disease and is just one example of a genetic mutation for which a test is available.

## 2. *Laboratory-Developed Tests (LDTs)*

A laboratory-developed test (LDT) is a medical procedure that is “developed, validated, and offered within a single laboratory.”<sup>50</sup> The patient submits a fluid sample (blood or saliva) to the laboratory to be tested.<sup>51</sup> The laboratory does not distribute a test kit, but rather a laboratory report of the test results.<sup>52</sup> These tests can be used for a

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<sup>46</sup> AMERICAN CANCER SOCIETY, *Breast Cancer Survival Rates By Stage*, available at <http://www.cancer.org/cancer/breastcancer/detailedguide/breast-cancer-survival-by-stage> (last visited Feb. 26, 2011).

<sup>47</sup> *Id.*

<sup>48</sup> Am. Cancer Soc’y, *supra* note 42 (citing L. Ries, D. Melbert, and M. Krapcho, *SEER Cancer Statistics Review, 1975-2006* (2009), available at [http://seer/cancer/gov/csr/1975\\_2006/](http://seer/cancer/gov/csr/1975_2006/).) The American Cancer Society notes in 2001–2002, the five-year survival rate of early-detection was 93%. *Supra* note 45.

<sup>49</sup> Am. Cancer Soc’y, *supra* note 46.

<sup>50</sup> *Id.*; Vorhaus, *supra* note 10.

<sup>51</sup> Dept. Health & Human Servs., U.S. Food & Drug Admin., Laboratory Tests, <http://www.fda.gov/medicaldevices/productsandmedicalprocedures/invitrodiagnostics/labtest/default.htm> (Last updated June 18, 2009).

<sup>52</sup> Gail H. Javitt, In Search of a Coherent Framework: Options for FDA Oversight of Genetic Tests, 62 *FOOD & DRUG L.J.* 617, 624 (2007).

wide variety of things, including testing for the presence of a particular disease<sup>53</sup> as well as the presence of a particular gene sequence.<sup>54</sup> LDTs are available either direct-to-consumer (DTC)<sup>55</sup> or require the patient's physician to order the test and analyze the results.<sup>56</sup> Examples of DTC LDTs offered in 2008 include tests for diabetes, atrial fibrillation, myocardial infarction, osteoporosis, Alzheimer's disease, breast cancer (BRCA), skin cancer, and a range of other common diseases.<sup>57</sup>

### III. REGULATION OF LDTs

The United States Food and Drug Administration (FDA) has traditionally exercised its enforcement discretion over LDTs.<sup>58</sup> Laboratories in which LDTs are manufactured are currently certified by the Centers for Medicare and Medicaid Services (CMS).<sup>59</sup> Because of the higher prevalence in the marketplace of LDT genetic tests that detect genetic propensity toward more serious diseases (i.e. breast cancer), the FDA is taking steps to increase regulation of these LDTs.<sup>60</sup> In setting forth its reasoning for taking these steps, the FDA has noted many good reasons for requiring more stringent regulation

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<sup>53</sup> Adam Bonislowski, ASU Biodesign Scientists Hope to Apply Direct-to-Consumer Model to Proteomics Testing, *PROTEOMONITOR* (Feb. 4, 2011), <http://www.genomeweb.com/proteomics/asu-biodesign-scientists-hope-apply-direct-consumer-model-proteomics-testing>.

<sup>54</sup> See, e.g., BRACAnalysis, Myriad Genetics, [www.bracnow.com](http://www.bracnow.com) (last visited Feb. 27, 2011).

<sup>55</sup> Kathy Hudson et al., ASHG Statement on Direct-to-Consumer Genetic Testing in the United States, 81 *AM. J. HUM. GENETICS* 635, 635 (2007).

<sup>56</sup> See, e.g., BRACAnalysis, *supra* note 54.

<sup>57</sup> David Melzer, et al., *Genetic Tests for Common Diseases: New Insights, Old Concerns*, 336 *BMJ* 590, 592 (2008), available at <http://www.bmj.com/content/336/7644/590.full>.

<sup>58</sup> U.S. Food & Drug Admin., FDA/CDRH Public Meeting: Oversight of Laboratory Developed Tests (LDTs), Date July 19-20, 2010, <http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm212830.htm> (last visited Feb. 27, 2011).

<sup>59</sup> Am. Ass'n Clinical Chem., *Genetic and Laboratory-Developed Tests*, [http://www.aacc.org/resourcecenters/resource\\_topics/tests/pages/default.aspx](http://www.aacc.org/resourcecenters/resource_topics/tests/pages/default.aspx) (last visited Jan. 23, 2011).

<sup>60</sup> U.S. Food & Drug Admin., *supra* note 10.

of LDTs.<sup>61</sup>

### A. Current Regulation of LDTs

As of today, the FDA does not oversee the production and marketing of LDTs.<sup>62</sup> The use of LDTs marketed directly to the consumer (DTC) are mainly regulated by state legislatures.<sup>63</sup> As of 2007, roughly half of the states allowed the use of DTCs.<sup>64</sup> LDTs are currently regulated by the CMS under the 1988 Clinical Laboratory Improvement Amendments (CLIA '88),<sup>65</sup> which establishes "quality standards for all laboratory testing to ensure the accuracy, reliability and timeliness of patient test results."<sup>66</sup> The CMS is mainly responsible for certifying both the laboratories in which LDTs are developed and manufactured and the analytical validity of the tests.<sup>67</sup>

These guidelines, contained in 42 C.F.R. § 493, define a "laboratory" as any facility that examines human material for "the purpose of providing information for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of, human beings."<sup>68</sup> The FDA places in vitro diagnostic tests into one of three CLIA regulatory categories: waived tests, tests of moderate complexity, and tests of high complexity.<sup>69</sup> To obtain a

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<sup>61</sup> *Id.*

<sup>62</sup> Dan Vorhaus, *Why 23andMe's Sample Swap is actually an Argument In Favor of DTC Genetic Testing*, Genomics Law Report (June 9, 2010), <http://www.genomicslawreport.com/index.php/2010/06/09/23andme-sample-swap/>.

<sup>63</sup> Hudson, *supra* note 55.

<sup>64</sup> *Id.* at 635.

<sup>65</sup> Am. Ass'n Clinical Chemistry, *supra* note 59.

<sup>66</sup> U.S. Food & Drug Admin., *Clinical Laboratory Improvement Amendments (CLIA)*, available at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/IVDRegulatoryAssistance/ucm124105.htm>.

<sup>67</sup> Dep't Health & Human Servs., Report of the Secretary's Advisory on Genetics, Health, and Society, *U.S. System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health and Human Services* (April 2008), 3, available at [http://oba.od.nih.gov/oba/SACGAS/reports/SACGAS\\_oversight\\_report.pdf](http://oba.od.nih.gov/oba/SACGAS/reports/SACGAS_oversight_report.pdf) [hereinafter *Oversight*].

<sup>68</sup> 42 C.F.R. § 493.2 (2010).

<sup>69</sup> *Supra* note 62.

certificate of waiver, the test must have been approved by the FDA, be relatively simple to use with a low likelihood of error, and pose no reasonable risk to the user if the test is used incorrectly.<sup>70</sup> Examples of these tests include urinalysis tests for glucose, hemoglobin, and protein levels, ovulation tests, and urine pregnancy tests.<sup>71</sup> Other tests are ranked as “high” or “moderate” complexity based on the complexities of the knowledge and training required to use the test, the reliability of the chemicals, and the sophistication required for interpretation of the results, among others.<sup>72</sup> Each laboratory must satisfy certain “CMS requirements relating to quality control, personnel qualification, records maintenance, and proficiency testing.”<sup>73</sup> The Secretary’s Advisory Committee on Genetics, Health, and Society (SACGHS) has expressed its concern that CLIA’s proficiency testing is insufficient, because it is not required for all tests.<sup>74</sup>

CMS sees that laboratories are complying with CLIA standards through inspections in which the laboratories are required to verify performance characteristics of their tests.<sup>75</sup> A key issue is that the CLIA standards only enforce analytical validity, and not clinical utility.<sup>76</sup> Analytical utility refers to the ability to detect the analyte or genotype itself, whereas clinical utility refers to the ability of the test to predict the disorder associated with the presence of an analyte or genotype.<sup>77</sup>

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<sup>70</sup> 42 C.F.R. § 493.15 (2010).

<sup>71</sup> *Id.*

<sup>72</sup> 42 C.F.R. § 493.17 (2010).

<sup>73</sup> Dan Vorhaus, *supra* note 59.

<sup>74</sup> Dep’t Health & Human Servs., report of the Secretary’s Advisory on Genetics, Health, & Society, US System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health & Human Services (April 2008), 4.

<sup>75</sup> *See supra* note 63.

<sup>76</sup> *Id.*

<sup>77</sup> *Id.*

## B. The Need for Heightened Regulation of LDTs

Because of the recent advances in molecular biology, LDTs are able to perform genetic tests.<sup>78</sup> The FDA has not engaged in regulating LDTs because it has traditionally considered them to be low risk.<sup>79</sup> The FDA has taken notice of these becoming more widespread and has expressed interest in regulating these tests.<sup>80</sup> It began with the FDA's warning letter to Pathway Genomics,<sup>81</sup> which had just entered into an agreement with Walgreens to sell its LDT genetic tests.<sup>82</sup> Walgreens promptly cancelled the deal after this warning.<sup>83</sup> One month later, the FDA sent warning letters to five other companies producing DTC LDTs, informing them that they are producing a device without FDA approval.<sup>84</sup> While these early

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<sup>78</sup> See Andrea Ferreira-Gonzalez & Carleton T. Garrett, *Laboratory-Developed Tests in Molecular Diagnostics*, in *MOLECULAR DIAGNOSTICS*, 247 (William Coleman ed., 2006); see *infra* Part II.B.

<sup>79</sup> Britt E. Erickson, *Lab-Developed Tests Come Under Fire*, *CHEMICAL & ENGINEERING NEWS* (Aug. 9, 2010), <http://pubs.acs.org/cen/analytical/88/8832gov1.html>.

<sup>80</sup> See *supra* note 8.

<sup>81</sup> Letter from James Woods, Office of *In Vitro* Diagnostic Device Evaluation and Safety, FDA, to James Plante, Founder and CEO Pathway Genomics Corp. (May 10, 2010), *available at* <http://www.fda.gov/downloads/MedicalDevices/ResourcesforYou/Industry/UCM211875.pdf>.

<sup>82</sup> Dan Vorhaus, *FDA Puts the Brakes on Pathway-Walgreens Pairing; What's Next for DTC?*, *GENOMICS LAW REPORT* (May 13, 2010), <http://www.genomicslawreport.com/index.php/2010/05/13/fda-puts-the-brakes-on-pathway-walgreens-pairing-whats-next-for-dtc/>.

<sup>83</sup> *Id.*

<sup>84</sup> Letter from Alberto Gutierrez, Office of *In Vitro* Diagnostic Device Evaluation and Safety, FDA, to Anne Wojcicki, President 23andMe, Inc. (June 10, 2010), *available at* f; Letter from Alberto Gutierrez, Office of *In Vitro* Diagnostic Device Evaluation and Safety, FDA, to Vance Vanier, President, Navigenics (June 10, 2010), *available at* <http://www.fda.gov/downloads/MedicalDevices/ResourcesforYou/Industry/UCM215243.pdf>; Letter from Alberto Gutierrez, Office of *In Vitro* Diagnostic Device Evaluation and Safety, FDA, to Earl Collier, CEO, deCODE Genetics (June 10, 2010), *available at* <http://www.fda.gov/downloads/MedicalDevices/ResourcesforYou/Industry/UCM215241.pdf>; Letter from Alberto Gutierrez, Office of *In Vitro* Diagnostic Device Evaluation and Safety, FDA, to Jorge Conde, CEO, Knome, Inc. (June 10, 2010), *available at* <http://www.fda.gov/downloads/MedicalDevices/ResourcesforYou/Industry/UCM215239.pdf>; Letter from Alberto Gutierrez, Office of *In Vitro* Diagnostic Device Evaluation and Safety, FDA, to Jay Flatley, President & CEO, Illumina, Inc. (June 10, 2010), *available at* <http://www.fda.gov/downloads/MedicalDevices/ResourcesforYou/Industry/UCM21524>

warnings were targeted only to the DTC LDTs, the FDA has since taken a more aggressive stance toward the possibility of regulating all LDTs; those marketed directly to the consumer as well as those required to be ordered by a health care provider.<sup>85</sup> In July 2010, the FDA issued a notice of proposed rulemaking regarding more stringent regulation of all LDTs.<sup>86</sup> Through its notice for the invitation of public comment, the FDA presents several arguments for proposing the increase in regulations.<sup>87</sup> First, as LDTs have become more complex, they are beginning to use components that are not approved by the FDA.<sup>88</sup> Second, the FDA believes that a competitive disadvantage is created because some manufacturers' tests are approved and others are not.<sup>89</sup> Finally, because doctors and patients are relying more and more on the results of LDTs in treatment, prevention, and management decision-making, the FDA believes that LDTs that have not been properly validated are putting patients at risk.<sup>90</sup>

At a House of Representatives Energy & Commerce subcommittee hearing in July 2010, Jeffrey Shuren, director of FDA's Center for Devices & Radiological Health, stated that "[f]ailure to validate the accuracy, reliability, and clinical implications of a test can result in patient harm from misdiagnosis, failure to treat, delay in treatment, inappropriate treatment, or avoidable adverse events."<sup>91</sup> Tests that have not been properly validated may result in false positives or false negatives resulting from a lack of knowledge of the genetic sequence variations, faulty equipment or reagents, inappropriate reference materials, and lack of method optimization.<sup>92</sup> The SAGHS report notes that false positive test results can lead to

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<sup>85</sup> See *supra* note 7.

<sup>86</sup> See *supra* note 8.

<sup>87</sup> *Id.* at 34,463–64.

<sup>88</sup> *Id.* at 34,463.

<sup>89</sup> *Id.* at 34,464.

<sup>90</sup> *Id.* at 34,464.

<sup>91</sup> Erickson, *supra* note 75.

<sup>92</sup> Oversight, *supra* note 63, at 109.

several social and psychological harms including altered self-image, stigmatization, impact on family relationships, and exclusion from health insurance.<sup>93</sup> A false positive result could also result in unnecessary prophylactic surgery.<sup>94</sup> Additionally, a false negative result may lead to false assurance of health, as well as delayed diagnosis, screening, and treatment.<sup>95</sup> Furthermore, a false assurance of health could cause the patient to ignore important prevention measures, such as diet and exercise.<sup>96</sup> The SAGHS report also notes that even correct genetic results could be misapplied due to poorly-trained physicians or a lack of understanding of the result.<sup>97</sup>

A concrete example of harm that resulted from a test with low clinical validity included the HLA-B27 test, which is useful in diagnosing axial spondyloarthritis, a genetic disorder leading to inflammatory back pain.<sup>98</sup> Several harms resulted from the administration of this test, including “exposure of patients without axial spondyloarthritis to anti-inflammatory therapies with less benefit and an increased harm from adverse drug events, and exposure to additional diagnostic tests.”<sup>99</sup>

#### IV. LDTs SHOULD NOT BE REGULATED UNDER THE CURRENT FDA MEDICAL DEVICE REGULATORY MECHANISM

Although LDTs should be regulated more closely, the current FDA system of regulating mechanical devices is not an appropriate pathway for the regulation of genetic LDTs. Because genes and genetic tests that simply compare a gene sequence to another do not provide strong patentable subject matter, it would be difficult for

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<sup>93</sup> *Id.*

<sup>94</sup> See Melzer, *supra* note 53, at 592 (citing J. Lenzer, *Advert for Breast Cancer Gene Test Triggers Inquiry*, 335 *BRITISH MED. J.* 579 (2007)).

<sup>95</sup> See *id.*

<sup>96</sup> *Id.*

<sup>97</sup> Oversight, *supra* note 63, at 109.

<sup>98</sup> *Id.* at 110 (citing M. Rudwaleit et al., *How To Diagnose Axial Spondyloarthritis Early*, 63 *ANN. RHEUMATIC DISEASES* 592-600 (2004)).

<sup>99</sup> *Id.*

laboratories developing and manufacturing these tests to afford the traditional FDA regulatory path.

## A. Medical Device Regulation Under the FDA

### 1. FDA Regulation Process for Medical Devices

The Federal Food, Drug, and Cosmetic Act establishes regulations to ensure the safety of various substances for the American public.<sup>100</sup> A medical “device” is 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

(1) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,

(2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or

(3) intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.<sup>101</sup>

The Medical Device Amendments of 1976 established three regulatory classes of medical devices, with Class III falling under the most stringent regulation, and Class I falling under the least.<sup>102</sup> A Class III device is one that “is purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, or presents a potential unreasonable risk of illness or injury.”<sup>103</sup> Class I

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<sup>100</sup> See generally Chapter 9, 21 U.S.C. (2006).

<sup>101</sup> 21 U.S.C. § 321(h) (2009).

<sup>102</sup> See Food & Drug Admin., FDA.GOV, *PMA Approvals*, <http://www.fda.gov/medicaldevices/productsandmedicalprocedures/deviceapprovalsandclearances/pmaapprovals/default.htm> (last visited Sep. 1, 2011).

<sup>103</sup> 21 U.S.C. § 360c(a)(1)(C)(ii)(I)-(II) (2009).

and Class II devices are those with a lower perceived risk.<sup>104</sup>

Medical devices are regulated by the Center for Devices and Radiological Health (CDRH) segment of the FDA.<sup>105</sup> Any manufacturer who wishes to produce a medical device must comply with several requirements, including “[e]stablishment registration, [m]edical [d]evice [l]isting, [p]remarket [n]otification 501(k) [Classes I and II] or premarket approval [Class III], [i]nvestigational [d]evice [e]xemption . . . for clinical studies, [q]uality [s]ystem[sic] regulation, [l]abeling requirements, and [m]edical [d]evice [r]eporting[sic].”<sup>106</sup>

The regulation process differs considerably depending on the device’s class placement.<sup>107</sup> Class I devices are subject to basic “general controls,” which means that they are held to basic standards of proper labeling, and proper manufacturing processes and conditions.<sup>108</sup> These types of devices are also subject to post-market surveillance and reporting by the FDA.<sup>109</sup> In most cases, these devices may be produced and sold without obtaining prior FDA approval.<sup>110</sup>

Class II devices are held subject to higher standards than Class I devices in that they are required to meet specific design and performance standards.<sup>111</sup> These devices must also be tested for safety and efficacy before introduction into the market.<sup>112</sup> Class III devices also require clinical data on safety and efficacy before entry into the market.<sup>113</sup> “Examples of Class III devices include implantable

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<sup>104</sup> See Aaron Kaplan et al., *Medical Device Development: From Prototype to Regulatory Approval*, 109 CIRCULATION 3068, 3069 (2004).

<sup>105</sup> *Id.* at 3069.

<sup>106</sup> Food & Drug Admin., *Overview of Device Regulation*, <http://www.fda.gov/MedicalDevices/DeviceRegulationandguidance/Overview/default.htm> (last visited Jan. 23, 2011) [hereinafter *Regulation Overview*].

<sup>107</sup> See Kaplan, *supra* note 100, at 3069.

<sup>108</sup> *Id.*

<sup>109</sup> *Id.*

<sup>110</sup> *Id.* (citing 21 U.S.C. § 360).

<sup>111</sup> *Id.*

<sup>112</sup> See Kaplan, *supra* note 100, at 3069.

<sup>113</sup> *Id.*

pacemakers and breast implants.”<sup>114</sup>

If the FDA decides to regulate LDTs under its current medical device regulatory mechanism, they will most likely be classified as Class II or Class III, based on interviews concerning this issue. In an interview with the Wall Street Journal, Jeffrey Shuren stated that the FDA considers DTC LDTs to be “high risk.”<sup>115</sup> Also, in a recent interview, Alberto Gutierrez, the director of the Office of *In Vitro* Diagnostics of the FDA, stated that DTC LDTs could potentially be classified as either low risk or “high risk.”<sup>116</sup>

The FDA seems to be more concerned with whether or not the DTC LDT manufacturer is making medical claims about the data resulting from their tests.<sup>117</sup> Gutierrez, in an interview with USA Today, stated that initially LDT manufacturers offering tests directly to the consumers began making low-risk claims but are now making claims that the FDA “would consider more high-risk, medical-device type claims.”<sup>118</sup>

## 2. Time and Financial Costs of Current Medical Device Regulation

Regulating LDTs under the current FDA medical device regulation scheme would have a significant impact on the laboratories developing the tests and will increase the regulatory cost of these tests.<sup>119</sup> Laboratories will be affected by both the direct cost

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<sup>114</sup> FDA, *Learn if a Medical Device has been Cleared by FDA for Marketing*, FDA.GOV, <http://www.fda.gov/MedicalDevices/ResourcesforYou/Consumers/ucm142523.htm> (last visited Jan. 23, 2011)[hereinafter *Cleared for Marketing*].

<sup>115</sup> Jennifer C. Dooren, *FDA Weighs Rules for Consumer Genetic Tests*, WALL STREET JOURNAL (July 19, 2010), available at <http://online.wsj.com/article/SB10001424052748704875004575374960528395530.html>.

<sup>116</sup> Mary Carmichael, *DNA Dilemma: The Full Interview with the FDA on DTC Genetic Tests*, NEWSWEEK (August 5, 2010), available at <http://www.newsweek.com/blogs/the-human-condition/2010/08/05/dna-dilemma-the-full-interview-with-the-fda-on-dtc-genetic-tests.html>.

<sup>117</sup> See Rita Rubin, *FDA Groups Genetic Tests With Medical Devices; Those About Drug Metabolism, Risk May Need Approval*, USA TODAY, June 15, 2010, at D.7.

<sup>118</sup> *Id.*

<sup>119</sup> Jeffrey N. Gibbs, *The Cost of Regulating LDTs*, GENOMICS LAW REPORT (August 25, 2010), <http://www.genomicslawreport.com/index.php/2010/08/25/the-cost-of-regulating-ldts/#more-4300>.

of the regulation process, and the indirect cost of the delay of introducing the tests onto the market. Premarket Notification 510(k) clearance, required by all Class II devices and a few Class I devices,<sup>120</sup> requires support by sufficient data.<sup>121</sup> Data that is sufficient for submission to peer-review journals and that is required for CLIA certification is not necessarily sufficient to meet the FDA requirements.<sup>122</sup> Therefore, the laboratories must spend more time and money on obtaining this data in order to make the submission.<sup>123</sup> Once the submission is made, more waiting is required.<sup>124</sup> The FDA has 90 days to review the submission, after which, it will likely submit a set of questions to the laboratory.<sup>125</sup> The FDA then has another 90 days to review the subsequent responses.<sup>126</sup>

Those LDTs classified as Class III devices will require submission to premarket authorization (PMA).<sup>127</sup> This is a much more complicated system in which the laboratory must demonstrate the safety and effectiveness of the test, a much more demanding standard.<sup>128</sup> The laboratory must submit manufacturing information showing that the tests are manufactured in accordance with the Quality System Regulation (QSR), and the FDA also performs its own inspection to ensure QSR compliance.<sup>129</sup> Overhauling laboratories from CLIA-certification standards to QSR standards will be a daunting task, both in time and expense, because the laboratories will have to develop new protocols and procedures.<sup>130</sup>

A recent study revealed that the average total cost of developing a new 501(k) device (Class I and II) was approximately \$31 million,

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<sup>120</sup> *Regulation Overview*, *supra* note 102.

<sup>121</sup> Gibbs, *supra* note 115.

<sup>122</sup> *Id.*

<sup>123</sup> *See id.*

<sup>124</sup> *Id.*

<sup>125</sup> *Id.*

<sup>126</sup> Gibbs, *supra* note 115.

<sup>127</sup> *See Cleared for Marketing*, *supra* note 110.

<sup>128</sup> Gibbs, *supra* note 115.

<sup>129</sup> *Id.*

<sup>130</sup> *See id.*

with \$24 million (more than 77% of the total cost) being spent on the FDA approval process.<sup>131</sup> Getting a Class III device through the required premarket approval (PMA) requires an even higher cost: \$94 million, with \$75 million spent on the FDA approval process.<sup>132</sup>

However, cost is not the only issue to consider. It also takes a long time to obtain FDA approval for a medical device. The same study found that it takes approximately 46 months after beginning the regulatory process to obtain approval for a 501(k) device and about 73 months to obtain approval for a PMA device.<sup>133</sup>

## **B. Possibility of Non-patentability of Genetic Tests Compounds The Need for an Alternate Regulatory Mechanism**

Recent court decisions have hinted that a genetic test consisting of merely comparing one gene sequence (i.e. that of a patient) to a standard gene sequence (i.e. BRCA1), and correlating the presence of a mutation in the patient's gene sequence to the presence of a disease, may be unpatentable subject matter. This is significant because if a laboratory cannot obtain a patent on its newly-developed test, it may not be able to afford undergoing the traditional FDA regulatory process.

### ***1. Genetic Tests are Possibly Non-Patentable Subject Matter***

The Patent Act defines patentable subject matter as "any new and useful process, machine, manufacture, or composition of matter."<sup>134</sup> In defining the statutory term "process," the courts have held that there is a "products of nature" exception to the definition of patentable subject matter in that "laws of nature, natural phenomena,

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<sup>131</sup> Josh Makower, et al., FDA IMPACT ON U.S. MEDICAL TECHNOLOGY INNOVATION: A SURVEY OF OVER 200 MEDICAL TECHNOLOGY COMPANIES (Nov. 2010), at 28, available at <http://www.advamed.org/NR/rdonlyres/040E6C33-380B-4F6B-AB58-9AB1C0A7A3CF/0/makowerreportfinal.pdf>.

<sup>132</sup> *Id.* at 28.

<sup>133</sup> *Id.* at 29-30.

<sup>134</sup> 35 U.S.C. § 101.

and abstract ideas” are nonpatentable.<sup>135</sup> This section will explore how under this reasoning, recent court decisions suggest genetic tests may soon be unpatentable subject matter. Both gene sequences themselves,<sup>136</sup> as well as methods of comparing one numerical value<sup>137</sup> to another or one DNA sequence to another,<sup>138</sup> have come under fire both by the Federal Circuit and the Supreme Court as being a law of nature or an abstract idea.

#### a. Method Patents

The statutory definition of a patentable “process” was most recently discussed in the *Bilski* decisions.<sup>139</sup> The invention at issue concerned a method for hedging risks in the field of commodities trading.<sup>140</sup> In its decision, the Federal Circuit introduced the “machine-or-transformation test” as the test for patentability of a process claim.<sup>141</sup> The court stated that a process is surely patentable if it is (1) “tied to a particular machine or apparatus,” or (2) “it transforms a particular article into a different state or thing.”<sup>142</sup> Upon appeal, the Supreme Court stated that while the machine-or-transformation test is useful in informing whether or not a particular process is patentable, it is not the only test.<sup>143</sup> While it rejected the test the Federal Circuit had so confidently put forth as being supported by Supreme Court precedent, it still upheld the nonpatentability of the process patent at issue due to its being merely an abstract idea.<sup>144</sup> While the court purposefully left open the possibility of medical

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<sup>135</sup> *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980).

<sup>136</sup> *Ass’n for Molecular Pathology v. U.S. Patent and Trademark Office*, 702 F.Supp.2d 181, 185 (S.D.N.Y. 2010).

<sup>137</sup> *Laboratory Corp. of Am. Holdings v. Metabolite Laboratories, Inc.* 548 U.S. 124, 137 (2006).

<sup>138</sup> *Ass’n for Molecular Pathology*, 702 F.Supp.2d at 185.

<sup>139</sup> *In re Bilski*, 545 F.3d 943, 949 (Fed. Cir. 2008); *Bilski v. Kappos*, 130 S.Ct. 3218, 3226 (2010).

<sup>140</sup> *In re Bilski* at 949.

<sup>141</sup> *Id.* at 954, 955 n.8.

<sup>142</sup> *Id.* at 954.

<sup>143</sup> *Kappos*, 130 S.Ct. at 3226.

<sup>144</sup> *Id.* at 3222.

diagnostic assays,<sup>145</sup> the decisions hint toward a more rigorous definition of what is and is not an “abstract idea.”

The post-*Bilski* world is almost identical to the pre-*Bilski* world in that the only process claims that remain non-patentable are laws of nature, abstract ideas, or natural phenomena. The case merely introduced another test by which to consider whether a process is an abstract idea. After the Supreme Court’s issuance of the *Bilski* decision, the USPTO issued a set of guidelines to its patent examiners laying out factors to consider when weighing whether or not the invention is an abstract idea.<sup>146</sup> The fact that a claimed method “involves or is executed by a particular machine or apparatus” or that the “performance of claimed method results in or otherwise involves a transformation of a particular article” weighs toward the method not merely being an abstract idea.<sup>147</sup> Apart from the machine-or-transformation test, the fact that a claimed method “involves an application of a law of nature,” even without being tied to a machine or involved in transformation of an article, weighs toward not being an abstract idea.<sup>148</sup> On the other hand, the presence of a “general concept” (i.e. a theory or natural principle) as a step of the method weighs toward the method being an abstract idea.<sup>149</sup> Relevant factors to be considered are listed among these categories.<sup>150</sup>

Another opinion to consider is Justice Breyer’s dissent in *Laboratory Corp. of America Holdings v. Metabolite Laboratories, Inc.*<sup>151</sup> The Federal Circuit had found this patent to be valid and the Supreme Court granted a writ of certiorari, which it then dismissed as improvidently granted.<sup>152</sup> The patent in that case claimed the process of using any test to measure the level of homocysteine in a

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<sup>145</sup> See *id.* at 3227.

<sup>146</sup> Interim Guidance for Determining Subject Matter Eligibility for Process Claims in View of *Bilski v. Kappos*, 75 Fed. Reg. 43,922, 43,923–43,926 (July 27, 2010).

<sup>147</sup> *Id.* at 43,925.

<sup>148</sup> *Id.*

<sup>149</sup> *Id.*

<sup>150</sup> *Id.* at 43,295–96.

<sup>151</sup> *Laboratory Corp.*, 548 U.S. at 124.

<sup>152</sup> *Id.* at 125.

patient's body fluid and then comparing that level to the normal level.<sup>153</sup> If the level is higher than the normal level, then a vitamin deficiency is likely to be present.<sup>154</sup> Justice Breyer, with whom Justices Stevens and Souter joined, took the opportunity in his dissent to express his belief that this process is not patentable.<sup>155</sup> His main reasoning is that this patent attempts to claim a "natural phenomena" – the fact that a vitamin deficiency results in an elevated level of homocysteine in the blood.<sup>156</sup>

These decisions reveal a strong sentiment on the Federal Circuit that a process must either be tied to a machine or transform an article. Whether a genetic test would meet these tests is questionable. Even though the Supreme Court rejected the machine-or-transformation test as the "sole" test, the Federal Circuit will most likely require a process to meet that test to some extent. The *Prometheus* dissent reveals sentiment on the Supreme Court that a test that merely compares one value to another is unpatentable subject matter. Genetic tests would most likely be categorized this way and therefore subject to being deemed unpatentable subject matter.

#### **b. Genetic Test Patents**

The Southern District of New York recently ruled that Myriad Genetics' patents concerning tests for the presence of the BRCA1 and BRCA2 are invalid.<sup>157</sup> Specifically, these patents related to the isolated DNA sequence coding for the BRCA1 and BRCA2 genes as well as the method of comparing the results of the test to the BRCA1 and BRCA2 gene sequence.<sup>158</sup> The Court invalidated the gene sequence patents as unpatentable subject matter under 35 U.S.C. § 101 because it's not "markedly different" from a product of nature.<sup>159</sup>

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<sup>153</sup> *Id.*

<sup>154</sup> *Id.*

<sup>155</sup> *Id.* at 135.

<sup>156</sup> *Id.*

<sup>157</sup> *Ass'n for Molecular Pathology v. U.S. Patent and Trademark Office*, 702 F.Supp.2d 181 (S.D.N.Y. 2010).

<sup>158</sup> *Id.* at 185.

<sup>159</sup> *Id.* at 227-32.

Also, importantly, the Court invalidated the patent claims toward a genetic test comparing one gene sequence to another as merely consisting of “laws of nature, physical phenomena, and abstract ideas.”<sup>160</sup> Granted, the Court did invalidate the test under the machine-or-transformation test, since this decision was issued before the Supreme Court’s *Bilski* decision.<sup>161</sup> However, in light of the sentiment on the courts regarding “comparing” tests, it is questionable whether this test would remain valid otherwise.

## ***2. Patent Protection Provides Ability to Afford the FDA Regulatory Process***

A patent grants the patent-owner, whether inventor or assignee, the right to exclude others from making, using, or selling the patented invention.<sup>162</sup> The patent term extends twenty years from the date of filing the patent application.<sup>163</sup> The constitutional purpose behind granting a short-term monopoly on an invention is to “promote the progress of science and useful arts.”<sup>164</sup> Whether the patent system has this desired effect on innovation is not discussed in this paper, but instead the fact that the direct results of patent protection—short-term monopoly and capital gains—are by-products of the patent system required for a small company or laboratory to afford FDA regulation.

One benefit of a strong intellectual property portfolio to small and medium-sized companies, like most laboratories producing LDTs, is the potential to attract venture capital investors.<sup>165</sup> This is due to the potential profits obtained by the company over the recovered costs of research and development as a result of the

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<sup>160</sup> *Id.* at 218–222 (quoting *Diamond v. Chakrabarty*, 477 U.S. 303, 309 (1980)).

<sup>161</sup> *Id.* at 233–37.

<sup>162</sup> 35 U.S.C. § 154(a)(1).

<sup>163</sup> 35 U.S.C. § 154(a)(2).

<sup>164</sup> U.S. Const. art. I, § 8, cl. 8.

<sup>165</sup> Mario W. Cardullo, *Intellectual Property – The Basis for Venture Capital Investments*, WORLD INTELLECTUAL PROPERTY ORGANIZATION, [http://www.wipo.int/sme/en/documents/venture\\_capital\\_investments.htm](http://www.wipo.int/sme/en/documents/venture_capital_investments.htm) (last visited Feb. 27, 2011).

exclusionary rights given by a patent.<sup>166</sup> Investment is most likely if the patent is strong, meaning not susceptible to litigation.<sup>167</sup>

If small and medium-sized companies are not given the ability to “corner the market” on a diagnostic test through a patent, it will be difficult if not impossible for that company to afford FDA approval through the traditional medical device regulatory mechanism. Because genetic test patents seem to be prone to litigation in the future, these patents are not viewed as “strong,” and are therefore not as attractive to investors.

## V. PROPOSED REGULATORY SCHEME FOR GENETIC LDTs

This paper has discussed why the need for regulation of laboratory-developed tests is necessary.<sup>168</sup> The regulatory mechanism for these tests must be both time- and cost-efficient, neither of which describes the current FDA regulatory scheme for medical devices.<sup>169</sup> The danger in LDTs results from an inaccurate interpretation of the test results.<sup>170</sup> The regulatory scheme should effectively establish the tests’ clinical, as well as analytical, validity and focus on education of health care providers in correctly interpreting the test results.

First and foremost all genetic tests must be required to undergo testing to ensure clinical validity as well as analytical validity. The fact that a particular gene sequence is related to a propensity toward a certain disease must be validated as well as the ability of the test to merely detect the presence of the gene sequence. Due to the important role that genetic testing will most likely play in the future of medicine, it will be necessary for a separate regulatory entity within the FDA to be dedicated only toward genetic testing. Once a gene sequence-disease correlation is discovered, it would be reported

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<sup>166</sup> Gene Quinn, *BIO and AUTM Defend Patentability of DNA-Based Inventions*, IPWATCHDOG (Nov. 1, 2010), <http://ipwatchdog.com/2010/11/01/bio-and-autm-defend-patentability-of-dna-based-inventions/id=13072/>.

<sup>167</sup> *Ass’n for Molecular Pathology*, 702 F.Supp.2d at 191.

<sup>168</sup> See *supra* Part III.

<sup>169</sup> See *supra* Part IV.A.

<sup>170</sup> See *supra* Part III.

to this entity. When the correlation is confirmed by this entity, it would then be added to a database storing this type of information. The storage of this information would allow faster assessment of new tests coming in.

An online database for all laboratories supplying genetic tests should be established.<sup>171</sup> The goal would be to decrease gaps in information as to which laboratory offers which test for which disease. This database would be kept up to date by the aforementioned FDA sub-entity as gene sequence-disease correlations are confirmed. The upkeep of this database as well as the assessment of the tests should be run by the FDA, but be more transparent and similar to the peer-review system, encouraging more input from the scientific community.

The final proposal is to provide more education for health care providers. Those who offer these tests and counsel their patients to use them should undergo genetic test-specific training in order to ensure competency in interpreting test results and accuracy in choosing the correct treatment options upon obtaining those results. They should be fully educated on the clinical and analytical validities of all genetic LDTs, including those marketed directly to the consumer.

## VI. CONCLUSION

Due to the increasingly important role LDTs are playing in clinical decision-making, they should be more highly regulated than they are currently in order to ensure clinical validity with less false positive and negative test results. However, because genes and gene tests may not be patentable, the current FDA regulatory process for medical devices is not the ideal mechanism for regulating LDTs. There needs to be a more cost- and time-efficient system including more input from the scientific community, an up-to-date informative database of confirmed gene sequence-disease correlations, and health care provider education.

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<sup>171</sup> This idea is a common theme among those proposing a change to the current regulation of LDTs. See *e.g. supra* note 48, at 646; *supra* note 63, at 112-13.