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## Biopharmaceuticals: The Patent System and Incentives for Innovation

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<b>Citation</b>	Biopharmaceuticals: The Patent System and Incentives for Innovation (2004 Third Year Paper)
<b>Accessed</b>	June 24, 2018 7:54:57 PM EDT
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# **Biopharmaceuticals: The Patent System and Incentives for Innovation**

**April 6, 2004**

This paper is submitted in satisfaction of the Food and Drug Law Course Paper (Winter 2003) and the Third Year Written Work Requirement.

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## ABSTRACT

This paper discusses the requirements for patentability as applied to biotechnology and pharmaceutical inventions. Focusing on case law from the Court of Appeals for the Federal Circuit, as well as guidelines issued by the United States Patent and Trademark Office, the Paper describes the requirements of utility, novelty, nonobviousness, written description, and enablement. The Paper then goes on to summarize literature on the economics of patents and the structure of the biotechnology industry. The Paper argues that strong patent protection is vital in order to ensure innovation in the biotechnology industry. Finally, the Paper addresses issues in patenting recent developments in biotechnology.

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## I.

### Introduction

Between the years 2000-2003, over a quarter of all new drugs approved were biotechnology drugs or biopharmaceuticals.<sup>1</sup> Over 60 products in the United States and European Union were approved during these three years, as compared to 84 biopharmaceuticals approved prior to the year 2000.<sup>2</sup> The biopharmaceutical business has translated into big profits and economic opportunity for drug companies: the annual global market for biopharmaceuticals is estimated to be more than \$30 billion.<sup>3</sup>

Despite the great potential in the area of biopharmaceuticals, compared to the billions of dollars that pharmaceutical companies have been investing in research and development in recent years, the output in terms of new drug products has been minimal. While the large pharmaceutical companies have undergone a wave of mergers in recent years, the answer instead may be to turn to smaller biotechnology firms.<sup>4</sup> These firms can play an invaluable role in early drug discovery. Larger pharmaceutical companies can then play a role

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<sup>1</sup>Gene Walsh, *Biopharmaceutical Benchmarks—2003*, 21 *Nature Biotechnology* 865 (2003).

<sup>2</sup>*Id.*

<sup>3</sup>*Id.*

<sup>4</sup>*Bigger Isn't Always Better*, 418 *Nature* 353 (2002).

in later development of commercial products and drug marketing.<sup>5</sup>

Patents on early research are often the most valuable assets owned by small biotechnology firms, allowing these firms to obtain financing and attract venture capital. At the same time, recent advances in the field of biotechnology have challenged the application of traditional patent law doctrines. It is of vital importance that new developments in patent law address scientific advances in a way that promotes incentives for innovation in the field of biotechnology.

## II.

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<sup>5</sup>*Id.*

Biopharmaceuticals are drugs that are produced through genetic engineering, as opposed to traditional chemically-synthesized drugs. Biopharmaceuticals can be grouped into five basic categories: 1) recombinant proteins; 2) monoclonal antibody-based therapeutics; 3) antisense-based treatments; 4) gene therapy; and 5) tissue-engineering products.<sup>6</sup>

Genetic engineering methods take advantage of the relationship between the DNA sequence of a given gene and its corresponding protein or RNA molecule. Once the function of a DNA sequence is known, modern recombinant techniques allow scientists to manipulate the DNA sequence in vitro, and eventually to produce altered recombinant human proteins that can be used to treat specific diseases. Monoclonal antibody-based treatments can be produced in at least two ways. One common method is through hybridoma technology, which uses a cloned cell line to produce a single type of antibody;<sup>7</sup> a second method uses recombinant DNA technology. Antisense-based treatments aim to use small, synthetic oligonucleotides<sup>8</sup> to inhibit gene expression—and thus the production of a protein.<sup>9</sup> Gene therapy-based drugs attempt to change the expression of an individual's genes, by delivering a normal copy of a missing or defective gene, or by delivering a gene that will provide a special form of protection.<sup>10</sup> Finally, tissue engineering treatments include products such as injectable tissue matrices or substitute skin grafts.

The fields of genomics and proteomics will help to identify new targets for biotechnology drug therapy. While a comprehensive sequence of the human genome was completed in the spring of 2003, the functions of many

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<sup>6</sup>See Walsh, *supra* note 1.

<sup>7</sup>See *Chiron Corp. v. Genentech, Inc.*, Nos. 03-1158, 03-1159, 2004 WL 612854 (Fed. Cir. Mar. 30, 2004).

<sup>8</sup>Oligonucleotides are short polymers of 2-20 nucleic acids.

<sup>9</sup>Only one antisense product has been approved for market sale, “although a recent surge of interest in RNAi could fuel activity in this area.” Walsh, *supra* note 1, at 866.

<sup>10</sup>American Medical Association, *Gene Therapy*, available at <http://www.ama-assn.org/ama/pub/category/2827.html>. No gene therapy product has been approved for market sale to-date. See Walsh, *supra* note 1, at 866. While the traditional approach to gene therapy was plagued by dose and delivery problems, a U.S. Patent No. 6,225,290 issued on May 3, 2001 for a “gene pill” which claims to overcome these problems with a new method of delivering genes to intestinal cells. See Debra Robertson, *Gene Pill Patents a Surprise for Gene Therapy*, 19 *Nature Biotechnology* 604 (2001).

human genes remain undetermined.<sup>11</sup> There are an estimated 30,000 to 35,000 protein-encoding genes in an individual's DNA,<sup>12</sup> and there are much larger "non-coding" portions of the genome that are thought to be functionally important.<sup>13</sup> Thus, "[u]nderstanding, not 'simply' decoding, the operation, function, and coordination of genome information will be the next transforming phase in biology."<sup>14</sup>

Pharmacogenomics studies the interaction between genes and drug therapy and works toward understanding how individual genetic variation affects drug action.<sup>15</sup> One particularly promising prospect in pharmacogenomics is the study of single-nucleotide polymorphisms ("SNPs").<sup>16</sup> An SNP is a "polymorphism caused by the change of a single nucleotide. Most genetic variation between individual humans is believed to be due to SNPs."<sup>17</sup> The SNP Consortium for Biomedical Research, made up of 10 pharmaceutical companies and the Wellcome Trust, has discovered and characterized nearly 1.8 million SNPs to date.<sup>18</sup> SNPs can alter the way that proteins are made, but more frequently they are useful as markers to locate mutations in DNA and speed up the development of drug treatments for disease.<sup>19</sup>

Proteomics refers to "various technologies used to analyze collections of proteins produced by different cell types at different stages in development and the cell cycle."<sup>20</sup> By analyzing what proteins are present in diseased and healthy tissue samples, scientists are working to identify proteins that cause disease or that can be targeted in disease treatment.<sup>21</sup> While it used to take scientists years to fingerprint a protein fragment,

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<sup>11</sup>Francis S. Collins, et. al., *A Vision for the Future of Genomics Research*, 422 *Nature* 835 (2003) (discussing the landmark completion of the Human Genome Project).

<sup>12</sup>Human Genome Project Information, Facts About Genome Sequencing, available at [http://www.ornl.gov/sci/techresources/Human\\_Genome/faq/seqfacts.shtml](http://www.ornl.gov/sci/techresources/Human_Genome/faq/seqfacts.shtml).

<sup>13</sup>See Collins, supra note 11.

<sup>14</sup>Marvin E. Frazier, et. al., *Realizing the Potential of the Genome Revolution: The Genomes to Life Program*, 300 *Science* 290 (2003).

<sup>15</sup>Cheedy Jaja, *Foretelling Our Pharmacogenomic Future*, 21 *Nature Biotechnology* 487 (2003).

<sup>16</sup>Jeanette J. McCarthy & Rolf Hilfiker, *The Use of Single-Nucleotide Polymorphism Maps in Pharmacogenomics*, 18 *Nature Biotechnology* 505 (2000).

<sup>17</sup>Peer Bork & Richard Copley, *Genome Speak*, 409 *Nature* 815 (2001).

<sup>18</sup>See the SNP Consortium LTD, Website at <http://snp.cshl.org>.

<sup>19</sup>The SNP Consortium LTD, Single Nucleotide Polymorphisms: An Introduction, available at <http://snp.cshl.org/about/introduction.shtml>.

<sup>20</sup>Robert A. Bohrer, *Proteomics: The Next Phase in the Biotechnology Revolution and the Next Challenge for Biotechnology Law*, 22 *Biotechnology L. Rep.* 263 (2003).

<sup>21</sup>Robert F. Service, *High-Speed Biologists Search for Gold in Proteins*, 294 *Science* 2074 (2001).

this can now be done in a matter of minutes with the use of complex supercomputers.<sup>22</sup> A few years ago proteomics was touted as being “biology’s biggest boom industry.”<sup>23</sup> However, proteomics is much more complex than genomics; there are somewhere between 200,000 and 2 million proteins that are constantly changing throughout a person’s lifetime, and proteomics is “an attempt to capture the dynamics of a living system.”<sup>24</sup> Thus, progress in proteomics has been slower and more expensive than originally predicted.

### III.

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<sup>22</sup> *Id.* Researchers are able to translate a protein’s amino acid sequence into a DNA sequence and then search for this sequence in computer databases for the gene. *Id.* Assuming that it is known what protein the gene encodes for, researchers are able to identify the protein. *Id.*

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

<sup>24</sup> *Id.* at 2075 (quoting Ruedi Aebersold, co-founder of the Institute for Systems Biology in Seattle, Washington).

The Constitution gives Congress the power to create laws to “promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Rights to their respective Writings and Discoveries.”<sup>25</sup> A patentee has the right to exclude others from making, using, selling, or offering to sell the patented invention.<sup>26</sup> The term of a patent begins on the date of issuance and lasts up to 20 years from the date on which the application was filed.<sup>27</sup> There are five basic requirements for issuance of a patent: 1) utility, 2) novelty, 3) nonobviousness, 4) written description, and 5) enablement.

The landmark decision of *Diamond v. Chakrabarty*<sup>28</sup> paved the way for an explosion in the number of biotechnology patents granted during the past two decades. In *Chakrabarty* the Supreme Court determined for the first time that a live, human-made microorganism qualified as patentable subject matter.<sup>29</sup> The invention at issue consisted of genetically-engineered bacteria capable of breaking down components of crude oil, a property possessed by no naturally occurring bacteria.<sup>30</sup> Congress set forth the qualifications for patentable subject matter in 35 U.S.C. §101, which states “[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.”<sup>31</sup> Before *Chakrabarty*, it was well established that “the laws of nature, physical phenomena, and abstract ideas” were not patentable,<sup>32</sup> but it was unclear whether a living organism could be considered a “manufacture” or a “composition of

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<sup>25</sup>Art. I, §8, cl. 8.

<sup>26</sup>35 U.S.C. §154 (2002).

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

<sup>28</sup>447 U.S. 303 (1980).

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

<sup>30</sup>*See id.* at 305.

<sup>31</sup>35 U.S.C. §101 (2002) (emphasis mine).

<sup>32</sup>*Chakrabarty*, 447 U.S. at 309 (“Thus, a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that  $E=mc^2$ , nor could Newton have patented the law of gravity. Such discoveries are “manifestations of . . . nature, free to all men and reserved exclusively to none” (internal citations omitted)).

matter” under §101. Many argued that notwithstanding human intervention through genetic engineering, a living microorganism should be considered a product of nature and thus unpatentable under §101.<sup>33</sup>

Instead, the Court read §101 broadly, relying heavily on the legislative history which indicated Congress’s intent to include as patentable subject matter “anything under the Sun that is made by man.”<sup>34</sup> Finding Chakrabarty’s invention not “a hitherto unknown natural phenomena, but... a nonnaturally occurring manufacture or composition of matter—a product of human ingenuity ‘having a distinctive name, character and use,’”<sup>35</sup> the Court determined that the invention qualified as patentable subject matter under §101. Although the Court’s decision may now seem a matter of course, *Chakrabarty* stretched the boundaries of law at the time; the majority cast aside concerns that genetic research might be too risky a project to be supported by the federal government, while at the same time admitting that they, as judges, were without competence to evaluate many of the scientific and policy issues involved.<sup>36</sup>

The *Chakrabarty* decision highlights an important tension that courts often face in the area of patent law. While courts are charged with implementing the delicate balance that Congress has struck between competing economic and social interests, courts must also face the reality of rapid and unforeseen advances in science and technology. In other words, in an area where the law is designed to deal with unanticipated inventions, the most important of which “push back the frontiers of chemistry, physics and the like,”<sup>37</sup> it is simply implausible to expect Congress to provide in advance for every situation. Judge Pauline Newman has noted that “[t]he shaping of patent law is to an exceptional degree within the hands of the judiciary,

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<sup>33</sup> *See id.* at 306.

<sup>34</sup> *See id.* at 309 (citing S. Rep. No. 1979, 82d Cong., 2d Sess., 5 (1952)).

<sup>35</sup> *Id.* at 309-310.

<sup>36</sup> *Id.* at 316;

It is argued that this Court should weigh these potential hazards in considering whether respondent’s invention is patentable subject matter under §101. . . we are without competence to entertain these arguments—either to brush them aside as fantasies generated by fear of the unknown or to act on them. The choice we are urged to make is a matter of high policy resolution within the legislative process after the kind of investigation, examination, and study that legislative bodies can provide and courts cannot.

<sup>37</sup> *Id.* at 316, quoting *Great A. & P. Tea Co. v. Supermarket Corp.*, 340 U.S. 147, 154 (1950) (J. Douglas concurring opinion.)

for in patent cases a relatively simple statutory law is applied to an extraordinary complexity of factual circumstances.”<sup>38</sup>

The role courts play in shaping patent law is of central importance because the inconsistent application of patent law can lead to decreased incentives for innovation in those technologies which depend on legal certainty in order to invest in new research and development.<sup>39</sup> The Court of Appeals for the Federal Circuit (“Federal Circuit”) was established by Congress in 1982, in part, to address inconsistency among circuits in the application of patent law (and the resulting forum shopping) and to provide economic incentives for industry investment in research and development.<sup>40</sup> The Federal Circuit is a national appellate court with jurisdiction to hear a variety of cases including those that “arise under” patent law, in whole or in part.<sup>41</sup>

Not surprising given the history surrounding its creation, the Federal Circuit has been described by many as “pro-patent,” and some statistical studies seem to bear this claim out.<sup>42</sup> In a now-famous study, Dunner *et al.* found that between the years 1982 and 1994 the Federal Circuit was significantly more likely to affirm judgments in favor of patent owners than accused infringers in district court cases.<sup>43</sup> After the creation of

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<sup>38</sup>Pauline Newman, *The Federal Circuit: Judicial Stability or Judicial Activism?*, 42 Am. U. L. Rev. 683, 685 (1993).

<sup>39</sup>See Pauline Newman, *Celebrating the Tenth Anniversary of the Court of Appeals for the Federal Circuit*, 14 Geo. Mason U. L. Rev. 513, 515 (1992):

Although not all new technologies require the support of a patent in order to be economically viable, for those that do the degree of legal certainty, as to patentability and enforceability, is a significant factor in innovation decisions. And for those technologies that may not require patent support to be viable, any enhanced economic prospect that is available from a patent will favorably affect the risk/return calculation, and thus will weigh on the side of allocating resources toward innovation.

<sup>40</sup>*Id.* See also Josh Lerner, *Patent Policy Reform and Its Implications*, NBER Reporter: Research Summary (Winter 2003) (noting that before the creation of the Federal Circuit some appellate courts were more than twice as likely to uphold patent claims than others).

<sup>41</sup>See Newman, *supra* note 39. The Federal Circuit also has appellate jurisdiction over: monetary claims against the government; American Indian claims; disputes involving contracts with the federal government; Merit Systems Protection Board cases; cases from the Court of Veterans Appeals; the Court of Federal Claims; the Court of International Trade; the International Trade Commission; the Tax Court; and the Department of Agriculture; as well as cases dealing with the Economic Stabilization Act; the Natural Gas Policy Act; the Emergency Petroleum Allocation Act; and the Energy Policy and Conservation Act. See *id.*

<sup>42</sup>See Lerner, *supra* note 40 (arguing that the Federal Circuit is staffed with judges who are sympathetic to the patent system and that the court has significantly broadened patent holder’s rights).

<sup>43</sup>Donald R. Dunner *et al.*, *A Statistical Look at the Federal Circuit’s Patent Decisions: 1982-1994*, 5 Fed. Circuit B.J. 151 (1995).

the Federal Circuit there was a dramatic increase in the number of applications for U.S. patents: there were 62,098 utility patent applications (originating in the United States) in the year 1980 as compared to 164,795 applications in the year 2000.<sup>44</sup> The contribution of the Federal Circuit’s allegedly “pro-patent” policies to this increase has been widely debated.<sup>45</sup> At the very least, the Federal Circuit has developed a body of case law that: 1) is closely watched by those in the biotechnology industry and 2) on a continuous basis clarifies and refines the requirements for patentability set forth by Congress in the patent laws.

**A.**

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<sup>44</sup>U.S. DEPT. OF COMMERCE, UNITED STATES PATENT AND TRADEMARK OFFICE, NUMBER OF UTILITY PATENT APPLICATIONS FILED IN THE UNITED STATES, BY COUNTRY OF ORIGIN CALENDER YEAR 1965 TO PRESENT (2001).

<sup>45</sup>SAMUEL KORTUM & JOSH LERNER, STRONGER PROTECTION OR TECHNOLOGICAL REVOLUTION: WHAT IS BEHIND THE RECENT SURGE IN PATENTING? (Nat’l Bureau of Econ. Research, Working Paper No. 6204, 1997) (finding economic data supports the theory that the surge in U.S. patent applications was attributable to new firm formation and innovation in the high technology sector, not to changes in legal policy). *See also* Lerner, *supra* note 40 (noting that simultaneous changes occurred in the structure of the USPTO, with the agency “increasingly [defining] its mission as serving patent applicants”).

<sup>46</sup>35 U.S.C. §101 (2002) (emphasis mine).

<sup>48</sup>*See In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995).

The policy behind the utility requirement is that “the basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with *substantial* utility.”<sup>49</sup> Thus, an invention that is inoperable, frivolous, fraudulent, or against public policy would not be patentable for lack of utility.<sup>50</sup> Indeed, a process or product is not “useful” within the meaning of §101 merely because it is the subject of serious scientific investigation and its disclosure would help to advance that serious scientific investigation.<sup>51</sup>

With respect to biotechnology inventions, the most important line of cases addressing the utility requirement is that dealing with pharmaceutical inventions. In the context of pharmaceuticals, the Federal Circuit has stated that “knowledge of the pharmaceutical activity of any compound is obviously beneficial to the public” and that “adequate proof of any such utility constitutes a showing of *practical* utility.”<sup>52</sup> In addition, in order to provide a sufficiently *specific* utility, the patent applicant must disclose a particular disease against which the claimed compounds are alleged to be effective.<sup>53</sup>

The Federal Circuit has often considered the type of testing necessary to establish a practical utility for a compound. The court has held that “the test results need not absolutely prove that the compound is pharmacologically active. All that is required is that the tests be ‘reasonably indicative of the desired [pharmacological] response.’”<sup>54</sup> For example, in vitro test results,<sup>55</sup> if presented with a known correlation

<sup>49</sup>*Brenner v. Manson*, 383 U.S. 519, 534 (1966) (emphasis mine). The Court went on to state that “[u]nless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.” *Id.* at 534-535.

<sup>50</sup>U.S. DEPARTMENT OF COMMERCE, U.S. PATENT AND TRADEMARK OFFICE, *MANUEL OF PATENT EXAMINING PROCEDURE*, §706.03(a)(1) (2003).

<sup>51</sup>*Brenner v. Manson*, 383 U.S. at 533.

<sup>52</sup>*Cross v. Iizuka*, 753 F.2d 1040, 1046 (emphasis mine) (Fed. Cir. 1985) (quoting *Nelson v. Bowler*, 626 F.2d 853 (CCPA 1980)).

<sup>53</sup>*See In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995).

<sup>54</sup>*Fujikawa v. Wattanasin*, 93 F.3d 1559, 1564 (Fed. Cir. 1996) (quoting *Nelson v. Bowler*, 626 F.2d 853, 856 (CCPA 1980)). The court continued, “In other words, there must be a sufficient correlation between the tests and an asserted pharmacological activity so as to convince those skilled in the art, to a reasonable probability, that the novel compound will exhibit the asserted pharmacological behavior.” *Id.*

<sup>55</sup>In vitro refers to tests performed outside a living organism.

between the results and in vivo activity,<sup>56</sup> may be sufficient to establish practical utility.<sup>57</sup> The court has also indicated that sufficient structural similarity between the compound at issue and another compound known to possess a particular pharmacological activity will often be sufficient evidence of practical utility.<sup>58</sup> The Federal Circuit does not interpret the utility requirement of §101 as requiring a rigorous correlation between in vitro and in vivo activity<sup>59</sup> because of the “firm conviction that one who has taught the public that a compound exhibits some desirable pharmaceutical property in a standard experimental animal has made a significant and useful contribution to the art, even though it may eventually appear that the compound is without value in the treatment in humans.”<sup>60</sup> The same reasoning would explain why sufficient structural similarity between two compounds will often support a finding of practical utility. In both situations, the Federal Circuit has interpreted §101 as reflecting Congress’s desire to provide incentives to industry to pursue pharmaceutical research and development.<sup>61</sup> If the utility requirement were construed too narrowly and companies were not able to procure patent protection based on in vitro testing or structural homology, the costs of further research and development might simply be prohibitive.

The U.S. Patent and Trademark Office (“USPTO”) issued Utility Examination Guidelines (“Utility Guidelines”) in January 2001, which attempted to incorporate the Federal Circuit’s precedent and to strike a

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<sup>56</sup>In vivo refers to tests performed within a living organism.

<sup>57</sup>See *Fujikawa*, 93 F.3d at 1564. See also *Genentech v. Chiron*, 220 F.2d 1345 (Fed. Cir. 2000) (finding that there was sufficient evidence for the district court to find that practical utility existed in the case of a recombinant human insulin-like growth factor fusion protein).

<sup>58</sup>*Cross v. Iizuka*, 753 at 1048 (stating that “[t]his court, in *Rey-Bellet* and *Kawai*, has implied that a particular pharmacological activity identified with prior art compounds may have probative value as to the fact that the compound of the count possesses this particular pharmacological activity where there is a structural similarity between the prior art compounds and the compound of the count. *Rey-Bellet*, 493 F.2d at 1385-87; *Kawai* 480 F.2d at 890-91.”)

<sup>59</sup>*Cross v. Iizuka*, 753 at 1050.

<sup>60</sup>In *re Brana*, 51 F.3d at 1567. The court went on to state:

[u]sefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

*Id.* at 1568.

<sup>61</sup>See *supra* note 60.

compromise between two competing concerns expressed by the public.<sup>62</sup> On the one hand, members of the biotechnology industry were concerned that “an overly restrictive utility requirement [would chill] investment in the early stages of a company’s life, by withholding the promise of exclusivity associated with a patent for too long.”<sup>63</sup> On the other hand, several organizations, such as the American Society of Human Genetics and the Human Genome Organization, were concerned that an overly broad utility requirement for genetic patents would actually stifle innovation.<sup>64</sup>

The Utility Guidelines make clear that in order to survive a rejection for lack of utility, an invention must have a utility that is (1) specific, (2) substantial, and (3) credible.<sup>65</sup> First, a specific utility is a utility that would not be applicable to the broad class of the invention.<sup>66</sup> For example, one could not claim a polynucleotide to be used as a “gene probe” without disclosing a specific DNA target.<sup>67</sup> Second, an invention with substantial utility has practical use without requiring further research or experimentation.<sup>68</sup> In order for the gene probe in the above example to have a substantial utility, the DNA target itself must have a utility that is specific, substantial, and credible.<sup>69</sup> Finally, credible utility is a utility that is “believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided.”<sup>70</sup>

When the USPTO was originally considering revising the Utility Guidelines, sharp criticism was lodged by

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<sup>62</sup>Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan 5, 2001).

<sup>63</sup>ROBERT P. MERGES, PATENT LAW AND POLICY: CASES AND MATERIALS at 205-06 (2d ed. 1997).

<sup>64</sup>See Lawrence T. Kass & Michael N. Nitbach, *A Roadmap for Biotechnology Patents? Federal Circuit Precedent and the PTO’s New Examination Guidelines*, 30 AIPLA Q.J. 233 (2002). Noting “[i]n general, there has been support for criteria that would prevent the patenting of broad claims based upon partial DNA sequences and, in particular, those partial sequences for which no specific biological utility has been demonstrated.” *Id.* at 244.

<sup>65</sup>Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan 5, 2001). The Guidelines “do not constitute substantive rulemaking and hence do not have the force and effect of law.” *Id.* at 1098.

<sup>66</sup>U.S. Department of Commerce, U.S. Patent and Trademark Office, Revised Interim Utility Guidelines Training Materials 5-6, available at <http://www.uspto.gov/web/offices/pac/utility/utilityguide.pdf>.

<sup>67</sup>*Id.*

<sup>68</sup>*Id.* at 6-7.

<sup>69</sup>*Id.*

<sup>70</sup>*Id.* at 5. Note that “[c]redibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record (*e.g.*, test data, affidavits, declarations from experts in the art, patents or printed publications) that is probative of the applicant’s assertions.” Utility Examination Guidelines, *supra* note 65, at 1098.

many within the scientific community who argued that finding sequence homology required little scientific insight or invention.<sup>71</sup> Many expressed concern that once a patent is granted based solely on homology, “the patent holder will have little incentive to continue to a full characterization of the gene product –but could claim the rights to the results of other researchers who later did this.”<sup>72</sup> Similarly, Jack Spiegel, Director of the NIH’s Division of Technology Transfer and Development noted that “[m]inor changes in the nucleotide or amino acid sequences of . . . molecules may produce profound changes in biological activity. . . homology in an unpredictable art cannot, by itself, provide a specific utility.”<sup>73</sup> However, despite the concerns initially expressed, the USPTO and the Federal Circuit have made clear that the utility requirement can be met based on in vitro test results or DNA sequence homology.

## B.

A third requirement for patentability is novelty, as set forth in pertinent part, in 35 U.S.C. §102(a): a person shall be entitled to a patent unless “the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for the patent.”<sup>74</sup> The novelty requirement has often been called “technical” because a product or process is not considered to be anticipated under §102 unless all of the elements of the claimed invention are disclosed in a single prior art reference.<sup>75</sup> The Federal Circuit has formulated the novelty test

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<sup>71</sup>Paul Smaglik, *NIH Opposed Plans for Patenting ‘Similar’ Gene Sequences*, 405 *Nature* 2 (2000).

<sup>72</sup>*Id.*

<sup>73</sup>*Id.*

<sup>74</sup>35 U.S.C. §102(a) (2002).

<sup>75</sup>Rebecca S. Eisenberg & Robert P. Merges, *Opinion Letter as to the Patentability of Certain Inventions Associated with the Identification of Partial cDNA Sequences*, 23 *AIPLA Q. J.* 1, 20-21 (1995) (stating “[t]hus patent lawyers who have the relevant prior art references before them may often avoid novelty rejections by tinkering with the claim language to avoid covering subject matter that has been disclosed in the prior art.”)

as follows: “[a]n ‘anticipating’ reference must describe all of the elements and limitations of the claim in a single reference, and enable one of skill in the field of the invention to make and use the claimed invention.”<sup>76</sup> When a patent claim covers *several* different structures or compounds, the claim is considered anticipated if *any one* of the compounds is present in the prior art.<sup>77</sup> In addition, in order for a prior art reference to anticipate a claim, the reference must enable one of skill in the art to make and use the invention.<sup>78</sup>

It has long been established that there is some flexibility in the test of novelty; a prior art reference can anticipate a patent claim “without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference.”<sup>79</sup> In a recent and controversial case, *Schering Corporation v. Geneva Pharmaceuticals, Inc.*, the Federal Circuit arguably expanded this flexibility by holding that “this court sees no reason to modify the general rule for inherent anticipation in a case where inherency supplies the entire anticipatory subject matter.”<sup>80</sup>

The subject matter at issue in *Schering*, was a compound known as DCL, a metabolite<sup>81</sup> of loratadine that operates as a non-drowsy antihistamine.<sup>82</sup> The prior art disclosed the structure of loratadine and its use as a non-drowsy antihistamine, however it did not disclose DCL or refer to metabolites of loratadine.<sup>83</sup> The court found that the claims of the prior art patent inherently disclosed DCL, because “a patient ingesting loratadine would necessarily metabolize the compound to DCL.”<sup>84</sup>

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<sup>76</sup>*Merck v. Teva Pharmaceuticals*, 347 F.3d 1367, 1373 (Fed. Cir. 2003).

<sup>77</sup>*See Brown v. 3M*, 265 F.3d 1349, 1351 (Fed. Cir. 2001).

<sup>78</sup>*Elan Pharm., Inc. v. Mayo Found. for Med. Educ. and Research*, 346 F.3d 1051 (Fed. Cir. 2003). For discussion of requirements for enablement, see *infra*.

<sup>79</sup>*Schering Corp. v. Geneva Pharm., Inc.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003) (citing *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991)).

<sup>80</sup>*Id.* at 1379.

<sup>81</sup>A metabolite is “a compound formed in the patient’s body upon ingestion of a pharmaceutical.” *Id.* at 1375.

<sup>82</sup>*See id.*

<sup>83</sup>*See id.*

<sup>84</sup>*See id.* at 1380. The court later stated:

A skilled patent drafter, however, might fashion a claim to cover the metabolite in a way that avoids anticipation. For example, the metabolite may be claimed in its pure and isolated form...or as a pharmaceutical composition (e.g., with a

Prior to *Schering*, the doctrine of inherent anticipation was used to invalidate a claim when the relevant prior art was missing a feature of the claimed invention, but the missing feature was a “natural result flowing from the reference’s explicitly explicated limitations.”<sup>85</sup> However, in *Schering* the court found the subject matter of the claims anticipated even though no part of the structure of DCL was explicitly disclosed in the prior art. The court found that the entire structure of DCL was inherent in the prior art, and was thus placed within the public domain. The court also reaffirmed that inherent anticipation does not require recognition in the prior art—thus a person of ordinary skill in the art at the time need not have been able to recognize the inherent disclosure.<sup>86</sup>

The Federal Circuit denied petitions for a panel and an en banc rehearing of the *Schering* case. In a heated dissent to the denial of rehearing, Judge Pauline Newman found that the court “reached the correct result of no liability for infringement, but for the wrong reason.”<sup>87</sup> Judge Newman explained that “the panel strains to hold that this newly discovered, previously unknown product cannot be validly patented” under §102.<sup>88</sup> Judge Newman expressed concern that the panel’s new rule may have “particular impact on the discovery of biological products.”<sup>89</sup> For example, in any patentable biological organism there will necessarily be many products that are inherent, but which might not be “discovered” until a much later date.<sup>90</sup> The general rule of patent law has always been that a “previously unknown product does not become unpatentable simply because it existed before it was discovered.”<sup>91</sup> Judge Newman explained that the crucial move made by the court in *Schering* was to determine that the missing element in the prior art need not have been known to

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pharmaceutically acceptable carrier). The patent drafter could also claim a method of administering the metabolite or the corresponding pharmaceutical composition. The [prior art patent] would not provide an enabling disclosure to anticipate such claims because, for instance, the [prior art patent] does not disclose isolation of DCL.

*Id.* at 1381.

<sup>85</sup>Eli Lilly and Co. v. Barr Labs., Inc., 251 F.3d 955 (Fed. Cir. 2001).

<sup>86</sup>See *Schering Corp. v. Geneva*, 339 F.3d 1337.

<sup>87</sup>*Schering Corp. v. Geneva Pharm.*, 348 F.3d 992, 994 (Fed Cir. 2003) (denial of rehearing). Judge Newman explained that a finding of non-infringement was appropriate because the defendants were only practicing the technology of the expired loratadine patent. *Id.*

<sup>88</sup>*Id.*

<sup>89</sup>*Id.*

<sup>90</sup>*Id.*

<sup>91</sup>*Id.*

be present by a person of ordinary skill in the art. In the *Schering* case, Judge Newman noted that there was no evidence that a “person of ordinary skill would have known that DCL is formed *in vivo* upon the ingestion of loratadine.”<sup>92</sup>

Judge Lourie also dissented from the denial of rehearing in *Schering*. Judge Lourie noted that a pharmaceutical product patent typically issues before “clinical trials on the product have revealed the identity or nature of any metabolites, ” and the court’s holding in *Schering* mandates that “the mere issuance of the patent on the product—or any other publication of that product—inherently anticipates claims to the metabolite merely by disclosing that the product can be administered to a patient, on the theory that such administration would inevitably cause the human body to ‘make’ the metabolite.”<sup>93</sup>

### C.

A fourth requirement for patentability is nonobviousness, as set forth in 35 U.S.C. §103:

The obviousness determination is a question of law which depends in part on the factual inquiries set out by the Supreme Court in *Graham v. John Deere Co.*: (1) the scope and content of the prior art; (2) the differences between the claims and the prior art; (3) the level of ordinary skill in the pertinent art; and (4) secondary considerations, if any, of nonobviousness.<sup>95</sup> Since “[t]he genius of invention is often a combination

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<sup>92</sup> *Id.* at 995.

<sup>93</sup> *Id.* at 995.

<sup>95</sup> 383 U.S. 1 (1965). The phrase ‘secondary considerations’ refers to “evidence outside the intrinsic features of the invention. . . the real-world circumstances surrounding its origin and commercialization.” Robert P. Merges, *Commercial Success and*

of known elements which in hindsight seems preordained,”<sup>96</sup> the Federal Circuit has stated further that a showing of obviousness requires “a motivation or suggestion to combine or modify prior art references, coupled with a reasonable expectation of success.”<sup>97</sup>

The requirement of a reasonable expectation of success is especially important in the area of biotechnology, a relatively unpredictable art.<sup>98</sup> In the closely related area of chemical compounds, the Federal Circuit has held that a prima facie case of obviousness is established where there is “structural similarity” between the claimed and prior art subject matter and where the prior art gives “reason or motivation to make the claimed compositions.”<sup>99</sup> In the area of biotechnology, the chemical structure at issue will often be the structure of a DNA, cDNA, or RNA molecule. While prior art will often not disclose the structure of any relevant DNA molecules, for example, it will often disclose the structure of the protein encoded by the DNA molecule at issue.

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*Patent Standards: Economic Perspectives on Innovation*, 76 Cal. L. Rev. 803 (1988). Secondary or objective considerations include: commercial success of the invention, the extent of licensing, immediate copying by competitors, failure of others to make the same invention, and long-felt need for the invention. *Id.* at 817. Another especially important secondary or objective consideration is the presence of “unexpected results.” See *Richardson-Vicks Inc. v. Upjohn Co.*, 122 F.3d 1476 (Fed. Cir. 1997) (stating that evidence of unexpected results must be considered in evaluating the obviousness of a claimed invention). Note that objective evidence “such as commercial success, failure of others, long-felt need, and unexpected results must be considered *before* a conclusion on obviousness is reached and is not merely ‘icing on the cake.’” *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1986).

<sup>96</sup>*McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1352 (Fed. Cir. 2001).

<sup>97</sup>*Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 320 F.3d 1339 (Fed. Cir. 2003). In addition, both “the suggestion and the reasonable expectation of success must be found in the prior art, and not in the applicant’s disclosure.” In *re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). The case law has made clear that just because something is “obvious to try” this does not necessarily mean that the claimed subject matter is obvious under §103. In *re O’Farrell*, 853 F.2d 894 (Fed. Cir. 1988). An invention is “obvious to try” where “the prior art gives either no indication of which parameters are critical or no direction as to which of many possible choices is likely to be successful. *Merck & Co. v. Biocraft Inc.*, 874 F.2d 804, 807 (Fed. Cir. 1989). It has also been stated that “[a]n ‘obvious to try’ situation exists when a general disclosure may pique the scientist’s curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued.” In *re Eli Lilly & Co.*, 902 F.2d 943, 945 (Fed. Cir. 1990).

<sup>98</sup>*Eli Lilly & Co.*, 902 F.2d at 948 (stating that “[a]lthough we recognize and give weight to the unpredictability of biological properties, in *Raun’s* case the prior art teaches the claimed use with specificity”).

<sup>99</sup>In *re Dillon*, 919 F.2d 688, 692 (Fed. Cir. 1990). See also *Yamanouchi Pharm. Co., v. Danbury Pharm. Inc.*, 231 F.3d 1339 (Fed. Cir. 2000); In *re Deuel*, 51 F.3d 1552, 1558 (Fed. Cir. 1995) (noting that “a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties”).

In *In re Bell*, the Federal Circuit rejected the proposition that “just as closely related homologs, analogs, and isomers in chemistry may create a prima facie case [of obviousness]... the established relationship in the genetic code between a nucleic acid and the protein it encodes also makes a gene prima facie obvious over its correspondent protein.”<sup>100</sup> The court acknowledged that once the structure of a protein is known, it is possible to hypothesize structures of the gene encoding for that protein.<sup>101</sup> However, the court concluded that “because of the degeneracy of the genetic code, there are a vast number of nucleotide sequences that might code for a specific protein.”<sup>102</sup> Thus, unless the prior art suggested that a particular genetic sequence would be more likely than others to encode the protein disclosed in the prior art, subject matter relating to the structure of the corresponding gene would not be rendered obvious.<sup>103</sup>

Similarly, in *In re Deuel*, the Federal Circuit held that when the prior art did not disclose any relevant cDNA molecules,<sup>104</sup> the mere disclosure of corresponding proteins and the general idea, function, and chemical nature of the claimed cDNA molecules was not enough to render the subject matter obvious.<sup>105</sup> The court found that the “redundancy of the genetic code precluded contemplation of or focus on the specific cDNA molecules of [the claims],” and thus “any motivation that existed was a general one, to try to obtain a gene that was yet undefined and may have constituted many forms.”<sup>106</sup>

The Federal Circuit’s obviousness jurisprudence has been criticized as being based on the assumption that “biotechnology is as much a black art as a science, where the result of experimentation is largely out of

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<sup>100</sup>*In re Bell*, 991 F.2d 781, 783-784 (Fed. Cir. 1993).

<sup>101</sup>*Id.*

<sup>102</sup>*Id.*

<sup>103</sup>*Id.*

<sup>104</sup>A cDNA molecule has a sequence that is complementary to the mRNA corresponding to a particular protein. Thus the cDNA sequence is the same as the naturally occurring DNA sequence that encodes the protein.

<sup>105</sup>*In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995).

<sup>106</sup>*Id.* at 1558. However, the court did note that a “different result might pertain... if there were prior art, e.g., a protein of sufficiently small size and simplicity, so that lacking redundancy, each possible DNA would be obvious over the protein.” *Id.* at 1559.

the skilled artisan's hands."<sup>107</sup> Burk & Lemley have argued that instead of carving out a special law for obviousness and written description in biotechnology cases, the court should focus on the level of skill in the art:

Since the obviousness and enablement standards are inversely related, the court's assumptions about unpredictability in the field of biotechnology have made it easier for patent applicants to meet the obviousness requirement but more difficult for applicants to meet the written description and enablement requirements.<sup>109</sup> The end result is the issuance of numerous narrow patents on genes and DNA sequences.<sup>110</sup>

#### **D. Written Description, Enablement, and Best Mode: 35 U.S.C. §112**

Two final requirements for patentability are written description and enablement, as set forth in 35 U.S.C. §112, ¶ 1:

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<sup>107</sup>Dan L. Burk & Mark A. Lemley, *Is Patent Law Technology-Specific?*, 17 Berkeley Tech. L.J. 1155, 1193 (2002).

<sup>109</sup>*Id.* at 1181.

<sup>110</sup>*Id.* at 1193.

The written description requirement serves a “signaling function,” allowing others to read the patent and “understand with a substantial degree of certainty where the patentee’s proprietary boundaries lie.”<sup>112</sup> The basic policy rationale behind the two requirements is that in exchange for a period of exclusivity, the patentee must provide the public with enough information about the bounds of the invention and how to use the invention so that others can improve and build upon the invention—thus leading to further advances in the science.<sup>113</sup>

It should be noted that 35 U.S.C. §112 also requires that the specification set forth the “best mode” of the invention. This analysis has been interpreted as having two components: first, whether the inventor contemplated a best mode of practicing his invention, and second, whether he concealed that best mode from the public.<sup>114</sup>

## 1.

The legal test for the written description requirement ensures that “the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him.”<sup>115</sup> The disclosure must “clearly allow persons of ordinary skill in the art to recognize that [the applicant] invented what is

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<sup>112</sup>DONALD S. CHISUM ET AL., PRINCIPLES OF PATENT LAW: CASES AND MATERIALS 211-212 (2d ed. 2001). §112, ¶ also contains a requirement of definiteness. This requirement has been interpreted as requiring that the “claims, read in light of the specification, reasonably apprise those skilled in the art both of the utilization and scope of the invention” and the language must be “as precise as the subject matter permits.” *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385 (Fed. Cir. 1986).

<sup>113</sup>CHISUM, *supra* note 112, at 162.

<sup>114</sup>*Amgen, Inc., v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209 (Fed. Cir. 1991). The court went on the state that the best mode requirement is “a safeguard against the possible selfish desire on the part of some people to obtain patent protection without making a full disclosure. The requirement does not permit an inventor to disclose only what is known to be the second-best embodiment, retaining the best.” *Id.* at 1211.

<sup>115</sup>*In re Wertheim*, 541 F.2d 257 (CCPA 1976).

claimed.”<sup>116</sup> The question of whether a written description is adequate is a question of fact, that will “necessarily vary depending on the nature of the invention claimed.”<sup>117</sup>

The Federal Circuit has held generally that in a case where DNA or other nucleic acid is the subject matter of the claim, an adequate written description requires “a precise definition, such as by structure, formula, chemical name, or physical properties.”<sup>118</sup> In the important case of *The Regents of the University of California v. Eli Lilly & Co.*, the Federal Circuit reaffirmed this principle. In *Eli Lilly*, the patent at issue covered recombinant plasmids and microorganisms that produce human insulin.<sup>119</sup> Although the written description did not provide the nucleotide sequence of the human insulin-encoding gene, it did describe a method of obtaining the DNA sequence as well as the amino acid sequences of human insulin A and B chains.<sup>120</sup> The applicant also disclosed the rat proinsulin cDNA sequence.<sup>121</sup> However, relying on its decision in *In re Deuel* (finding that a claim to a specific DNA is not made obvious by knowledge of the protein sequence and methods for generating the DNA that encodes that protein), the court found the written description inadequate.<sup>122</sup> The court stated that a “description that does not render a claimed invention obvious does not sufficiently describe that invention for purposes of §112, ¶1.”<sup>123</sup> Notably, the court also went on to find claims to a broad class of vertebrate or mammalian insulin cDNA invalid, because they were based on a mere description of rat insulin cDNA.<sup>124</sup> Only by describing a representative number of cDNA’s within the genus (by disclosing their sequence) or by describing structural features common to the members

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<sup>116</sup>*In re Alton*, 76 F.3d 1168, 1172 (Fed. Cir. 1996).

<sup>117</sup>*Enzo Biochem v. Gen-Probe, Inc.*, 296 F.3d 1316, 1324 (Fed. Cir. 2002).

<sup>118</sup>*Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed Cir. 1992).

<sup>119</sup>*Id.*

<sup>120</sup>*Id.*

<sup>121</sup>*Id.*

<sup>122</sup>*Id.* The court went on to note that “a cDNA is not defined or described by the mere name ‘cDNA,’ even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the DNA.” *Id.*

<sup>123</sup>119 F.3d 1559 (Fed. Cir. 1997).

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

of the genus, could the University of California have provided adequate written description.<sup>125</sup> However, in *Enzo Biochem, Inc. v. Gen-Probe Inc.*, the Federal Circuit made clear that not all functional descriptions of genetic material fail to meet the written description requirement.<sup>126</sup> The court suggested that claimed nucleotide sequences may be adequately described by their ability to hybridize to a substrate identified in the specification.<sup>127</sup> The patent at issue related to nucleic acid probes that selectively hybridize to genetic material of the bacteria that cause *N. gonorrhoeae*, thus making the bacteria detectable.<sup>128</sup> Although the applicant did not disclose the full sequences of the nucleic acid probes, the applicant described the binding affinity of the sequences and made the sequences available at a public depository.<sup>129</sup> The court was “persuaded” that this description of binding affinity could be sufficient to meet the written description if it was coupled with 1) “a disclosed correlation between that function and a structure that is sufficiently known or disclosed;” and 2) a reference in the specification to the nucleotide sequence available in a public depository.<sup>130</sup> While the court made clear that the sequences themselves were adequately described, the court remanded the district court the determination as to whether claims to *mutated* variations of the deposited sequences, still within the hybridization ratio, were adequately described.<sup>131</sup> In addition, some of the claims covered a broad genus of nucleic acids. With respect to the issue of whether the disclosed species of nucleic acids were representative of the genus—either based on the functional description or the deposits of material—the court determined that this was an issue of fact that needed to be determined on remand.<sup>132</sup> In *Enzo Biochem*, the court cited with approval Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, “Written Description” Requirement (“Written Description Guidelines”) which were

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

<sup>126</sup> 323 F.3d 956 (Fed. Cir. 2002).

<sup>127</sup> *Id.*

<sup>128</sup> *Id.* at 1320-21.

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

<sup>130</sup> *Id.* at 1325.

<sup>131</sup> *Id.* at 1326-27

<sup>132</sup> *Id.* at 1327.

issued by the USPTO in January 2001.<sup>133</sup> The Written Description Guidelines explain how in certain cases an applicant may meet the written description requirement by disclosing merely the function, as opposed to the structure, of a genetic material:

The training materials based on the Written Description Guidelines provide as an example an isolated nucleic acid that specifically hybridizes under highly stringent conditions to a known DNA sequence that encodes a protein with a specific function.<sup>135</sup> Although only a single species within the scope of the claimed genus is disclosed, the materials find the claimed invention to be adequately described.<sup>136</sup> This determination is based on the fact that a person of skill in the art would not expect substantial variation among species within the claimed genus due to the “highly stringent” hybridization conditions which would limit the claims to structurally similar DNA.<sup>137</sup>

made clear that inquiry into the adequacy of written description is highly fact-specific and dependent on the level of skill in the art.<sup>138</sup> The patents at issue were related to the production of erythropoietin (“EPO”),

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<sup>133</sup>Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, “Written Description” Requirement, 66 Fed. Reg. 1099 (2001). The Written Description guidelines do not constitute substantive rulemaking and thus do not have the force and effect of law. *Id.* at 1104.

<sup>135</sup>U.S. Department of Commerce, U.S. Patent and Trademark Office, Synopsis of Application of Written Description Guidelines at 35-37, *available at* <http://www.uspto.gov/web/patents/guides.htm>.

<sup>136</sup>*Id.*

<sup>137</sup>*Id.*

<sup>138</sup>*Amgen Inc., v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313 (Fed. Cir 2003). Recently, in the case of *Noelle v. Lederman*, the court noted that each case involving the issue of written description, “must be decided on its own facts. Thus precedential value of cases in this area is extremely limited.” 355 F.3d 1343, 1349 (Fed. Cir. 2004).

a naturally occurring hormone that controls the formation of red blood cells in bone marrow.<sup>139</sup> Patent claims were directed to recombinant techniques of introducing human DNA encoding EPO into Chinese hamster ovary (“CHO”) cells and resulting in the production of EPO product with the capacity to cause bone marrow cells to increase the production of red blood cells.<sup>140</sup> Although the claims were directed to a method of producing recombinant EPO in a broad class of vertebrate or mammalian cells, the specification only disclosed examples utilizing monkey cells.<sup>141</sup> Despite this fact, the court affirmed the district court’s finding that the written description requirement had been met. In doing so, the court cited testimony that there would be only “minor differences” in applying the method of the disclosed examples to any vertebrate or mammalian cells, and that those of ordinary skill could “easily” figure out these differences in methodology.<sup>142</sup> Thus, the court found both “Eli Lilly and Enzo Biochem. . . inapposite to this case because the claim terms at issue here are not new or unknown biological materials that ordinarily skilled artisans would easily miscomprehend.”<sup>143</sup> The court further found that the words “vertebrate” and “mammalian” readily provide enough information for one of skill in the art to be able to recognize the members of the genus.<sup>144</sup>

The recent case of *Noelle v. Lederman* involved patent claims relating to the CD40CR antibody that represses the cell-to-cell signaling interaction between helper T-cells and B-cells, thus preventing the B-cell from producing antibodies which can be helpful for treating overactive immune system responses.<sup>145</sup> The applicant claimed mouse, human, and genus forms of the CD40CR and described their binding affinity to the CD40CR antigen. Yet the applicant failed to disclose any structural elements of the antibodies, and

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<sup>139</sup>*Id.* at 1319.

<sup>140</sup>*Id.* at 1321-22.

<sup>141</sup>*Id.* at 1331.

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

<sup>143</sup>*Id.* at 1332.

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

<sup>145</sup>355 F.3d 1343, 1345 (Fed. Cir. 2004). *Noelle v. Lederman* actually concerned an interference proceeding, but the written description requirement must be met in order for a patent to claim a priority filing date. *Id.*

disclosed structural elements of only the mouse CD40CR antigen.<sup>146</sup> The Federal Circuit stated:

The court thus held the claims to the human and genus forms of the antibody invalid because the applicant could not “define an unknown by its binding affinity to an unknown.”<sup>148</sup> The court determined that at the time of patent application there was too much unpredictability in the structure of antibodies from species other than the monkey to allow the applicant to claim the genus.

Another recent decision by the Federal Circuit on the written description requirement is *University of Rochester v. G.D. Searle & Co., Inc.*<sup>149</sup> Researchers at the University of Rochester discovered that unlike traditional anti-inflammatory treatments that inhibit prostaglandin synthesis catalyzed by both the PGHS-1 and PGHS-2 enzymes, a compound that inhibits only the PGHS-2 enzyme would have significantly fewer side effects.<sup>150</sup> The University of Rochester patent claimed a method of treatment using a compound that selectively inhibits PGHS-2 activity and a method of screening for such compounds.<sup>151</sup> Although the patent claimed a wide variety of compounds useful for treatment, including peptides, antibodies, and small inorganic compounds, the patent did not identify the compounds with any particularity by describing their structure or physical properties.<sup>152</sup> The court described the district court’s finding of the patent’s disclosure as follows:

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<sup>146</sup> *Id.* at 1349.

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

<sup>149</sup> 358 F.3d 916 (Fed. Cir. 2004).

<sup>150</sup> See Anne Y. Brody, *Rochester v. Searle: Complying with the Written Description and Enablement Requirements in Early-Stage Drug Discovery*, 22 *Biotechnology L. Rep.* 472 (2003).

<sup>151</sup> *Searle*, 358 F.3d at 918.

<sup>152</sup> See Brody, *supra* note 150, at 474.

The court affirmed the principle that “[a] description of what a material does, rather than of what it is, usually does not suffice. . . . The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described.”<sup>154</sup>

The *Searle* case has particular significance for the future of the drug industry. Before this case, it was standard practice to use method of treatment patents with “reach-through” claims in order to secure profits from commercial products resulting down the line from the identification of drug targets.<sup>155</sup> The Federal Circuit made clear that it will not allow a patent to issue too early in the research and development process and that researchers engaging in fundamental research will be able to secure only limited profits from later commercialization of products based on their discoveries.

## 2.

The legal test for enablement is whether there is “sufficient working procedure for one skilled in the art to practice the claimed invention without undue experimentation.”<sup>156</sup> Factors relevant to the determination of whether the required experimentation is reasonable include: 1) the quantity of experimentation necessary, 2)

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<sup>154</sup>*Id.* at 923 (citing *Lilly and Enzo*).

<sup>155</sup>See Brody, *supra* note 150 at 472.

<sup>156</sup>*In re Stephens*, 529 F.2d 1343, 1345 (CCPA 1976). See also *Elan Pharm. v. Mayo Found. for Medical Education and Research*, 346 F.3d 1051 (Fed. Cir. 2004).

the amount of direction or guidance presented, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims.<sup>157</sup> Although based on a factual inquiry, the determination of enablement is a legal one.<sup>158</sup>

In the context of biotechnology inventions that depend on the use of living materials, further steps may be necessary in order to satisfy the enablement requirement. In some cases, simply reading a description of the invention, if lacking the necessary starting materials, does not allow one to practice the invention. It is often necessary for the microorganisms or cultured cells to be deposited in a cell depository which will then make these samples available to the public.<sup>159</sup> The Federal Circuit has held that “[e]ven when starting materials are available, a deposit [is] necessary where it would require undue experimentation to make the cells of the invention from the starting materials.”<sup>160</sup>

The Federal Circuit has applied a more stringent enablement standard in the relatively “unpredictable” area of biotechnology. In the case of *In re Vaeck*, the Federal Circuit determined that “[w]here, as here, a claimed genus represents a diverse and relatively poorly understood group of microorganisms, the required level of disclosure will be greater than, for example, the disclosure of an invention involving a “predictable” factor such as a mechanical or electrical element.”<sup>161</sup> In the case of *Enzo Biochem, Inc. v. Calgene, Inc.*, the Federal Circuit similarly held that broad claims covering the practice of antisense technology in *all* prokaryotic and eukaryotic cells, by only describing the technology in *E. coli*, were invalid.<sup>162</sup>

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<sup>157</sup>In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

<sup>158</sup>Genentech, Inc. v. Novo Nordisk, A/S. 108 F.3d 1361, 1365 (Fed. Cir. 1997).

<sup>159</sup>*Id.* at 735. See also In re Lundak, 773 F.2d 1216, 1220 (Fed. Cir. 1985) (stating “[w]hen an invention relates to a new biological material, the material may not be reproducible even when detailed procedures and a complete taxonomic description are included in the specification”).

<sup>160</sup>*In re Wands*, 858 F.2d at 735.

<sup>161</sup>947 F.2d 488, 496 (Fed. Cir. 1991). In *Genentech, Inc. v. Novo Nordisk, A/S*, where the patent concerned a cleavable fusion expression process for producing human growth hormone, the Court stated “[w]hile every aspect of the generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. 108 F.3d 1361, 1366 (Fed. Cir. 1997).

<sup>162</sup>188 F.3d 1362 (Fed. Cir. 1999).

### 3.

In the case of *Plant Genetic Systems, N.V. v. DeKalb Genetics, Corp.*, the Federal Circuit rejected the contention that a “pioneer” patent was entitled to broad scope of coverage and a lower enablement standard.<sup>163</sup> The patent claims at issue covered plants, plant cells, and seeds that were genetically engineered to be herbicide-resistant (by producing a protein that prevents herbicides from blocking the function of glutamine synthetase.)<sup>164</sup> While the claims broadly covered any type of plant cell—which would include both monocots<sup>165</sup> and dicots<sup>166</sup>—the patent only disclosed working examples of how to transform dicots.<sup>167</sup> At the time the patent application was filed, “monocots existed... and stably-transformed monocot cells were highly desirable... But stably transformed monocot cells were difficult to produce, and the [patent] gave no instruction how.”<sup>168</sup>

The court reaffirmed that §112, ¶ requires that the scope of the claims bear a reasonable correlation to the scope of the enablement provided by the specification to persons of ordinary skill in the art.<sup>169</sup> When making this determination, enablement must be assessed as of the effective filing date of the patent.<sup>170</sup> In *Plant Genetic Systems*, the court distinguished the case of *In re Hogan*.<sup>171</sup> In *Hogan*, the patent claims covered

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<sup>163</sup>*Plant Genetic Systems, N.V. v. DeKalb Genetics Corp.*, 315 F.3d 1335 (Fed. Cir. 2003).

<sup>164</sup>*Id.* at 1337.

<sup>165</sup>A monocot is a flowering plant that initially develops with one leaf.

<sup>166</sup>A dicot is a flowering plant that initially develops with two leaves.

<sup>167</sup>*Plant Genetic Systems*, 315 F.3d at 1338.

<sup>168</sup>*Id.* at 1340.

<sup>169</sup>*Id.* at 1340 (citing *In re Fisher*, 447 F.2d 833, 839 (CCPA 1970)).

<sup>170</sup>*Id.*

<sup>171</sup>*In re Hogan*, 559 F.2d 595 (CCPA 1977).

a solid polymer of propylene.<sup>172</sup> Nine years after the patent application was filed, a method was discovered to produce amorphous polymers.<sup>173</sup> The court in *Plant Genetic Systems* explained that *Hogan* stood for the proposition that “the claims (albeit with a narrower scope) might be nevertheless enabled in view of the state of the art [at the time of filing.]”<sup>174</sup> However, the Federal Circuit made clear that the facts at issue in *Plant Genetic Systems* were quite different from those in *Hogan*:

The Federal Circuit affirmed the district court’s finding that the claims at issue were invalid for lack of enablement. Arguably, the court imposed a reasonable foreseeability standard when assessing the enablement requirement.<sup>176</sup> The court is likely to find claims invalid for lack of enablement when at the time of filing it is foreseeable that an improvement to an invention could have been made, but there is no disclosure in the application about how to achieve that improvement.<sup>177</sup>

The Federal Circuit’s most recent decision addressing the written description and enablement requirements is *Chiron Corp. v. Genentech, Inc.*<sup>178</sup> This case involved monoclonal antibody technology, specifically, a “monoclonal antibody that binds to human c-erbB-2 antigen.”<sup>179</sup> An antibody is a protein molecule generated by the immune system that is capable of recognizing and binding to a very specific antigen. The

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<sup>172</sup> *Id.*

<sup>173</sup> *Id.*

<sup>174</sup> *Id.*

<sup>176</sup> Brian v. Slater & Lucian C. Chen, *Enablement in the Spotlight: Federal Circuit Applied Foreseeability Standard for Biotech Patents, Which will Likely Restrict Broad Claims*, 25 Nat’l L.J. S1, Col. 2 (June 16, 2003).

<sup>177</sup> *Id.*

<sup>178</sup> *Chiron Corp. v. Genentech, Inc.*, Nos. 03-1158, 03-1159, 2004 WL 612854 (Fed. Cir. Mar. 30, 2004).

<sup>179</sup> *Id.*

antigen in this case, c-erbB-2 (or HER2) is associated with breast cancer cells. The court determined that the patent claims covering the antibody were invalid for failure to meet the written description and enablement requirements.

Murine antibodies are antibodies derived from mouse cells that have been produced using hybridoma technology. Chimeric and humanized antibodies, on the other hand, are produced using recombinant DNA techniques; both are derived from the DNA of more than one species, but humanized antibodies are derived primarily from human DNA. Chimeric and humanized antibodies have many advantages over murine antibodies, including reducing the likelihood of a deleterious immune response and activating beneficial secondary human immune responses.<sup>180</sup>

In *Chiron v. Genentech*, the patent in dispute claimed priority based on applications filed in 1984, 1985, and 1986. The 1984 application disclosed a murine antibody, known as 454C11, which was capable of binding to the antigen HER2. However, the application did not identify the structure, function, or molecular weight of the antigen. The application also did not disclose any chimeric or humanized antibodies. In fact, the first publication disclosing chimeric antibodies did not appear until four months after the 1984 filing date, and the first publication disclosing humanized antibodies did not appear until two years after the 1984 filing date.

The 1985 and 1986 applications each disclosed six additional monoclonal antibodies that bind to HER2 and both applications provided an approximate molecular weight of the antigen. However, neither application described the identity, structure, or function of the antigen, and neither application disclosed any information

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<sup>180</sup>*Id.*

about chimeric or humanized antibodies. The two applications defined the term “monoclonal antibody” as “an antibody composition having a homogenous antibody population. It is not intended to be limited as regards the source of the antibody or the manner in which it is made.”<sup>181</sup>

With respect to the 1984 application, the court noted that because the first mention of chimeric antibody technology appeared in the literature after the filing date of the application, chimeric antibody technology was by definition “outside the bounds of the enablement requirement.”<sup>182</sup> Thus, the inventors were under no obligation to enable the nonexistent technology of chimeric antibodies. However, Chiron could not claim priority based on the 1984 application because the application failed to satisfy the written description requirement.<sup>183</sup> The court found that the “Chiron scientists, by definition, could not have possession of, and disclose, the subject matter of chimeric antibodies that did not even exist at the time of the 1984 application.”<sup>184</sup>

With respect to the 1985 and 1986 applications, the court determined that at the time of their filings, chimeric antibodies could appropriately be characterized as a “nascent technology.” Evidence suggested that in 1985 and 1986 it was a difficult and unpredictable process to produce chimeric antibodies and that most laboratories did not have the necessary equipment. Thus, because “undue experimentation” would have been required in order to produce chimeric antibodies based on the provided disclosure, the district court appropriately concluded that Chiron could not claim priority based on the 1985 and 1986 applications because the applications failed to satisfy the enablement requirement.

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<sup>181</sup> *Id.* at \*3.

<sup>182</sup> *Id.* at \*5 (citing *Hogan*).

<sup>183</sup> *Id.* at \*6. The court explained that:

The written description requirement prevents applicants from using the amendment process to update their disclosures (claims or specifications) during their pendency before the patent office. Otherwise applicants could add new matter to their disclosures and date them back to their original filing date, thus defeating an accurate accounting of the priority of invention.

*Id.*

<sup>184</sup> *Id.* at 6.

In a thoughtful concurring opinion, Judge Bryson addressed the important interaction between the enablement requirement and claim construction. Judge Bryson agreed that as the claims were construed in *Genentech v. Chiron*, the 1984 application failed to satisfy the written description requirement, and thus that the patentee was not entitled to the priority date of the 1984 application. However, Judge Bryson believed that the law of enablement, as stated in *Plant Genetic Systems*, meant that a later-existing state of the art could not be used to invalidate a patent that met the enablement requirement at the time of filing. Thus, in *Genentech v. Chiron*, the later-developed chimeric antibody technology should not have been used to determine that the 1984 application failed to meet the enablement requirement. Instead, the claims of the Chiron patent should have been construed, if possible, not to reach the undeveloped chimeric antibody technology:

While patentees would like the best of both worlds: broad claim coverage and the earliest possible priority date; the broader the claim language the less likely the patent is to meet the enablement requirement. This is, of course, because the scope of enablement must be commensurate with the scope of the claims. In addition, in an area such as biotechnology, where science is rapidly advancing, patentees often attempt to secure broad claims that cover technology appearing only after the date of filing. Under the *Plant Genetic Systems* approach, these broad claims would still be enabled as long as the claims were construed to cover technology that was as of yet undiscovered at the time that the patent application was filed. However, as in *Chiron v. Genentech*, these broad claims will often be held invalid for failure to meet the written description

requirement. Judge Bryson's suggested approach would ensure that the patentee's claims (although more narrowly construed) would be more likely to meet the written description requirement and thus be upheld as valid.

The requirements of written description and enablement have caused more controversy in the biopharmaceutical community in recent years than have any of the other requirements for patentability. Many have hailed the heightened written description requirement set forth in the *Eli Lilly* line of cases as critical in order to protect incentives for innovation in the biotechnology industry. Steven Caltrider and James Kelly, members of the patent division at Eli Lilly and Company, have stated:

Others have criticized the Federal Circuit's general approach to treating DNA-based technology as a subset of chemistry, as being "misconceived."<sup>187</sup> Art Rai, for example, has argued that the Federal Circuit is well behind the technology in acknowledging the information containing nature of genetic sequences.<sup>188</sup> This argument implies that there may be less of a need for heightened disclosure requirements in the area of biotechnology because the field is really not as unpredictable as the Federal Circuit makes it out to be.

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<sup>187</sup>Arti K. Rai, *Intellectual Property Rights in Biotechnology: Addressing New Technology*, 34 Wake Forest L. Rev. 827, 835-36 (1999).

<sup>188</sup>*Id.*

IV.

Traditional thinking about the economics of patents provides four main justifications for the patent system: 1) incentive to invent, 2) incentive to disclose, 3) incentive to commercialize, and 4) incentive to design around.<sup>189</sup> Standard theory relies on the special characteristics of information and the resulting difficulty in enforcing property rights. Three notable characteristics of information are its non-appropriability, its non-excludability, and its non-rivalry.<sup>190</sup> Information is non-appropriable because the producer cannot sell it for its full value; once the producer discloses the information to a buyer, the buyer can then re-sell the information for only a fraction of the cost (the cost of transmission).<sup>191</sup> Likewise, information is non-excludable because it is very costly to prevent the transmission of information to those not purchasing from the original producer.<sup>192</sup> Finally, information is non-rivalrous because the value of the information to others is generally not decreased depending on how many other people use it.<sup>193</sup>

Through the patent system, the government intervenes in the market to create property rights in information and thus to provide an incentive for invention. Based on the characteristics of information explained above, economic theory suggests that some form of market regulation is necessary in order to avoid an underproduction of works embodying ideas.<sup>194</sup> Since a patent provides an exclusive right to one's invention, the patentee is able to secure monopoly profits on the invention for the length of the patent and can appropriate more of the economic value of the invention. Thus, traditional thinking about patents is that stronger patent

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<sup>189</sup>See CHISUM, *supra* note 112, at 70-76.

<sup>190</sup>ROBERT COOTER & THOMAS ULEN, LAW AND ECONOMICS, 126 (3d. ed. 2000).

<sup>191</sup>*Id.* In addition, it is difficult for buyers to determine the value of information until they have access to it—at which point they are no longer willing to pay for it. *Id.*

<sup>192</sup>*Id.* While this characteristic of information ensures that information will be optimally utilized, it provides no incentive for investment in research. See W. KIP VISCUSI, ET AL, ECONOMICS OF REGULATION AND ANTITRUST 800 (3d. ed. 2000).

<sup>193</sup>COOTER, *supra* note 190, at 126.

<sup>194</sup>*Id.* Two alternative forms of government intervention are the state supply of information (such as weather forecasts) and public subsidies for the private provision of information (such as government funding of scientific research by private universities). *Id.*

protection will induce more investment in research and development.<sup>195</sup> Of course, when the patentee prices products higher than marginal cost, this will mean that fewer consumers will be able to afford to purchase the product than under a more competitive system. This “deadweight loss” imposes costs on the public. Consequently, the patent system can be justified only if the benefits it produces in terms of innovation outweigh the costs to society.<sup>196</sup>

While the empirical evidence supporting the “reward theory” has been mixed, it has often been shown that in the pharmaceutical industry patents are an effective means of appropriating returns on investment in research.<sup>197</sup> This is due, in part, to the fact that in addition to preventing duplication, patents in the pharmaceutical industry have been effective in securing royalty income.<sup>198</sup> Of great importance, many small and medium sized biotechnology firms would not be able to exist without the prospect of patent protection.<sup>199</sup> Patents are often a small firm’s most valuable asset and enable the firm to attract investment capital.<sup>200</sup>

A second traditional justification for the patent system is that patents will induce the patentee to disclose valuable information to the public. At the most basic level, once the term of the patent expires, the invention can be practiced freely by the public and the benefits can become widespread. In addition, when a patent issues, the contents of the document become available to the public. Thus, the public has immediate access to information about the underlying technology and the public may be alerted to additional uses of the invention not foreseen by the patentee.<sup>201</sup> The patent system also ensures that the patentee does not have to expend valuable resources to keep the invention a trade secret.<sup>202</sup> The greater security and decreased

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<sup>195</sup>Nancy T. Gallini, *The Economics of Patents: Lessons from Recent U.S. Patent Reform*, 16 J. of Economic Perspectives 131 (2002).

<sup>196</sup>Mark A. Lemley, *The Economics of Improvement in Intellectual Property Law*, 75 Tex. L. Rev. 989, 997-97 (1997).

<sup>197</sup>Richard C. Levin, et al, *Appropriating the Returns from Industrial Research and Development*, 1987 Brookings Papers on Economic Activity 783, 795-96 (1987).

<sup>198</sup>*Id.* at 799.

<sup>199</sup>Roberto Mazzoleni & Richard R. Nelson, *The Benefits and Costs of Strong Patent Protection: A Contribution to the Current Debate*, 27 Research Policy 273 (1998).

<sup>200</sup>*See id.* at 276. *See also* Levin, *supra* note 197 at 797.

<sup>201</sup>Mazzoleni, *supra* note 199, at 278.

<sup>202</sup>WILLIAM M. LANDES & RICHARD A. POSNER, *THE ECONOMIC STRUCTURE OF INTELLECTUAL PROPERTY LAW* 328 (2003).

cost of licensing a patent as opposed to a trade secret allows for efficiency in manufacturing.<sup>203</sup> This ability to license inventions at low risk and low cost is especially important for small firms that are often unable to afford to develop and manufacture commercial products based on their inventions.

A third traditional justification for the patent system is that it provides an incentive for firms to commercialize products. Often, large investments must be made between the time that a patent is granted on an invention and the time that a marketable product is developed. This is especially true in the case of pharmaceutical products. More than 99.9% of drugs do not make it past preclinical testing or clinical trials, and the current cost of bringing a drug to market is estimated at \$800 million.<sup>204</sup> Small firms, which often play an invaluable role in early drug discovery, rely on patents in order to obtain financing to develop drug products.<sup>205</sup> This is because larger companies are unlikely to invest huge sums of money to develop a product unless they can secure monopoly profits to recoup their losses (at least in the case of the drugs that succeed and make it to market). In addition, in some cases it may be necessary for the original inventor to secure some of the rewards of later commercial development in order for the invention to occur in the first place.<sup>206</sup>

A fourth traditional justification for the patent system is that it provides an incentive to design around inventions. Often, the full benefits of an invention are only realized when competitors are able to imitate and improve the invention.<sup>207</sup> A common strategy in the pharmaceutical industry, known as “molecular modification,” involves development of a chemical compound distinct from the patented invention but which performs a similar function.<sup>208</sup> While this practice is “arguably wasteful,” it may result in the development of products without some of the deleterious side effects of the original drug.<sup>209</sup>

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<sup>203</sup> *Id.* at 329.

<sup>204</sup> *Bigger Isn't Always Better*, 418 *Nature* 353 (2002).

<sup>205</sup> Mazzoleni, *supra* note 199 at 277 (citing Rebecca Eisenberg).

<sup>206</sup> *Id.* at 276.

<sup>207</sup> See Levin, *supra* note 197, at 783.

<sup>208</sup> See VISCUSI, *supra* note 192, at 821.

<sup>209</sup> *Id.*

A.

Introduced by Edmund Kitch, the “prospect theory” offers an alternative conception of the way in which the patent system functions.<sup>210</sup> This theory recognizes that in the process of technological innovation, there are many different prospects, “each with [their] own associated sets of probabilities of costs and returns.”<sup>211</sup> Each technological prospect can be pursued by a number of different firms, because often “when technological developments bring something into the realm of the possible, it may be known to many and many may search.”<sup>212</sup> These different firms may use varying levels of resources and their activities may not be disclosed to each other.<sup>213</sup> Thus, this process can only be undertaken efficiently if a system is put in place that assures:

The patent system often functions in this manner by issuing patents for inventions long before a commercial product is developed.<sup>215</sup> Early grants of patents ensure efficient allocation of resources and investment in product development.<sup>216</sup> Even if the original inventor does not conduct additional research and development himself, no other parties are likely to invest significantly without first licensing the patent from the original inventor.<sup>217</sup>

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<sup>210</sup>Edmund W. Kitch, *The Nature and Function of the Patent System*, 20 J. of Law and Economics 265 (1977).

<sup>211</sup>*Id.* at 266.

<sup>212</sup>*Id.* at 269.

<sup>213</sup>*Id.* at 276 (noting that “subsequent investigation of the same prospect by other firms can neither build on the knowledge obtained by the first searcher nor determine the efficient level and strategy of search based upon his failure”).

<sup>215</sup>*Id.* at 267.

<sup>216</sup>*Id.* Note that early grants of patents also shorten the monopoly period of the patent. *See* LANDES, *supra* note 202, at 303.

<sup>217</sup>Kitch, *supra* note 210, at 276.

Thus, the patent system enables firms to signal each other and helps to prevent duplicative search efforts.<sup>218</sup> Since patenting of an invention often occurs early on in the road to commercial development of a product, disclosure of the invention also occurs at this stage. Disclosure functions differently under the prospect theory:

Therefore, under the prospect theory, a detailed disclosure of the invention is not necessary because the inventor can be relied on to disclose information about the invention in the most efficient way during product development.

Many commentators have expressed concerns about the prospect theory as a justification for the patent system. While the prospect theory may work well when there is only one important commercial product that can be developed as a result of each patented invention, in the case of biotechnology there are often many different treatments and innovations that may result from the initial patented invention, and a single entity might be interested in pursuing only a select few.<sup>220</sup> In addition, a single entity supervising research and development projects might easily overlook different avenues of research that would be pursued by a larger number of independent inventors.<sup>221</sup>

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<sup>218</sup> *Id.* at 278.

<sup>220</sup> See VISCUSI, *supra* note 192, at 813.

<sup>221</sup> *Id.* See also Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 Colum. L. Rev. 839 (1990) (noting that “[o]nce a firm develops and becomes very competent in one part of a ‘prospect,’ it may be very hard for it to give much attention to other parts, even though in the eyes of others, there may be great promise there”).

## B. Narrow v. Broad Patents

The breadth of the property rights granted by the patent system has important implications for innovation. Under the “reward theory,” strong, broad patent grants may be necessary in order to allow inventors to appropriate returns on fundamental research; this is especially the case if the fundamental research has little “stand alone value.”<sup>222</sup> A broad patent allows the original inventor to receive some of the value of later commercial applications and thus encourages more fundamental research.<sup>223</sup> Similarly, under the “prospect theory,” early issuance of broad patents ensures that the commercial development process will proceed efficiently.

In addition to those criticisms of the prospect theory already articulated, broad patent grants may give rise to two more problems. First, firms may be deterred from engaging in research “in the neighborhood” of the patented invention, and second, they may be deterred from searching for improvements in the patented invention.<sup>224</sup> A significant improvement on an original invention may be patented, as long as the improvement meets all of the requirements for patentability.<sup>225</sup> However, the situation of “blocking” patents arises when the owner of the improvement patent cannot practice his invention without infringing the original patent, and the original patent owner cannot practice the improvement technology without infringing the improvement patent.<sup>226</sup> In a situation of “blocking patents,” both parties must enter into a licensing agreement in order for either party to be able to practice the improvement.<sup>227</sup> As a consequence, the “more absolute the property right given to original authors and inventors, the more critical efficient licensing is to subsequent innovation,

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<sup>222</sup> See COOTER, *supra* note 190, at 132.

<sup>223</sup> *Id.* at 131.

<sup>224</sup> Mazzeloni, *supra* note 199, at 275. See also Lemley, *supra* note 196.

<sup>225</sup> See *supra* Section III.

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<sup>226</sup> See Lemley, *supra* note 196, at 1009-10.

<sup>227</sup> *Id.*

and the more sensitive the industry is to market failures in licensing.”<sup>228</sup>

The optimal breadth of patent scope may also depend on the particular nature of the technology. Merges and Nelson have suggested that in science-based technologies, such as biotechnology, there is a heightened danger associated with the award of broad patents.<sup>229</sup> A science-based technology is an industry that relies in large part on published scientific articles and general scientific advances; it “straddles the public world of science and the private world of intellectual property.”<sup>230</sup> Often, in a science-based industry, a patent is issued to the first person who can practically apply general scientific advancements, and there is a danger that the breadth of the patent will include much work of others and not just the contributions of the particular inventor.<sup>231</sup> The authors suggest that “scope limitations based on close adherence to the inventor’s disclosure and judicious use of the doctrine of equivalents provide the surest way around this danger.”<sup>232</sup>

There is reason to believe that overly broad patents in the biotechnology field may have greater potential to impede innovation than in other industries. While “molecular modification”<sup>233</sup> may be a common practice in the pharmaceutical industry, it may be much more difficult to “design around” treatments that depend on a gene sequence: “several applications of a gene, including diagnostics, rely on the use of the precise sequence of a gene and its mutations.”<sup>234</sup>

### **C. Biotechnology and the Patent Thicket**

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<sup>228</sup> See Lemley, *supra* note 196, at 998-99.

<sup>229</sup> See Merges & Nelson, *supra* note 221.

<sup>230</sup> *Id.* at 915.

<sup>231</sup> *Id.*

<sup>232</sup> *Id.*

<sup>233</sup> See VISCUSI, *supra* note 192, at 821.

<sup>234</sup> Sandy M. Thomas, *et al.*, *Shares in the Human Genome—the Future of Patenting DNA*, 20 *Nature Biotechnology* 1185 (2002).

Many commentators agree that crafting patent law in the area of biotechnology presents unique challenges. Heller and Eisenberg have suggested that patents can actually deter innovation in the area of biotechnology due to the “tragedy of the anticommons.”<sup>235</sup> As opposed to the more traditional tragedy of the commons (when too many individuals have access to a common, scarce resource), the tragedy of the anticommons refers to the following situation:

**The anticommons situation described above becomes a “tragedy” because of the transaction costs that must be incurred in order to negotiate use of the resource.<sup>237</sup> The greater the number of people owning rights of exclusion on a valuable resource, the less likely it is that the resource will be used in a socially optimal way.<sup>238</sup>**

The tragedy of the anticommons can occur in the area of biomedical research when “too many owners hold rights in previous discoveries that constitute obstacles to future research.”<sup>239</sup> As an example, take the case of Expressed Sequence Tags (“ESTs”). An EST is a short piece of DNA which corresponds to a fragment of cDNA and can often be patented as useful tools to search for full-length genes.<sup>240</sup> Later, if the full-length gene is discovered and characterized, it too could be patented as long as it is “novel and nonobvious” (i.e. as long as the patentee discloses a new use for the full-length gene).<sup>241</sup> However, in order to use the full-length

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<sup>235</sup>Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 *Science* 698 (1998).

<sup>237</sup>*Id.* at 673-74.

<sup>238</sup>*Id.*

<sup>239</sup>Heller & Eisenberg, *supra* note 235.

<sup>240</sup>*See* Bork & Copley, *supra* note 17.

<sup>241</sup>Molly A. Holman & Stephen R. Munzer, *Intellectual Property Rights in Genes and Gene Fragments: A Registration*

gene, the patentee would need to first obtain a license from the owner of the EST patent.<sup>242</sup> Since a typical EST is only 400 to 500 nucleotides in length, and a typical gene is 2,000 to 25,000 nucleotides in length,<sup>243</sup> many ESTs could be patented on the same gene, making licensing agreements for the use of the gene fragment potentially difficult.

**A similar situation has the potential to arise any time multiple patents were issued on individual, isolated fragments of the same gene. Strong, overlapping ownership could make the development of many downstream commercial products based on the gene sequences difficult.<sup>244</sup> Notably, protein-based therapies and many diagnostic tests require the use of multiple gene fragments.<sup>245</sup> Assuming that these gene fragments are all owned separately, then in order to develop many commercial products it is necessary to transact with each of the individual patent owners. This process of transacting is likely to be difficult and costly and could end up impeding biomedical innovation.**

Carl Shapiro has referred to this situation of overlapping licenses that arises as a result of cumulative innovation and blocking patents as a “patent thicket.”<sup>246</sup> Potential strategies for the private sector to address this patent thicket include cross-licensing and patent pools.<sup>247</sup> Cross-licensing is “an agreement

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*Solution for Expressed Sequence Tags*, 85 Iowa L. Rev. 735, 764 (2000). See also John J. Doll, *The Patenting of DNA*, 280 Science 689 (1998).

<sup>242</sup>*Id.* at 764.

<sup>243</sup>Holman & Munzer, *supra* note 241, at 749.

<sup>244</sup>Heller & Eisenberg, *supra* note 235, at 699.

<sup>245</sup>*Id.*

<sup>246</sup>Carl Shapiro, *Navigating the Patent Thicket: Cross Licenses, Patent Pools, and Standard-Setting*, Innovation, Policy, and the Economy, Vol. I (2001).

<sup>247</sup>*Id.*

between two companies that grants each the right to practice the other's patents."<sup>248</sup> A patent pool is an arrangement among multiple patent holders to aggregate their patents, typically making all pooled patents available to each member of the pool and offering standard licensing terms to licensees who are not members of the pool.<sup>249</sup> However, in addition to the increased transaction costs resulting from coordination, private companies must also contend with antitrust concerns.<sup>250</sup>

While it is well accepted today that the "intellectual property laws and the antitrust laws share the common purpose of promoting innovation and enhancing consumer welfare,"<sup>251</sup> patent pools pose unique problems under antitrust law. The Department of Justice and the Federal Trade Commission have issued *Antitrust Guidelines for the Licensing of Intellectual Property* ("Antitrust Guidelines").<sup>252</sup> These guidelines explain that patent pooling agreements may provide pro-competitive benefits in the following ways: 1) integrating complementary technologies; 2) reducing transaction costs; 3) clearing blocking positions; 4) avoiding costly infringement litigation; and 5) promoting the dissemination of technology.<sup>253</sup>

On the other hand, the Antitrust Guidelines make clear that patent-pooling agreements can have anti-competitive effects if: 1) collective price or output restraints do not contribute to an efficiency-enhancing integration of economic activity among participants; 2) patent pools are mechanisms to accomplish price-fixing or market division; 3) the effect of a settlement is to diminish competition among entities that would have been actual or likely potential competitors in a relevant market; 4) excluded firms cannot effectively compete in the relevant market for the good incorporating the licensed technologies; or 5) the arrangement

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<sup>248</sup> *Id.*

<sup>249</sup> Robert P. Merges, *Institutions for Intellectual Property Transactions: The Case of Patent Pools*, in EXPANDING THE BOUNDARIES OF INTELLECTUAL PROPERTY 123 (Rochelle Cooper Dreyfuss *et al.* eds., 2001).

<sup>250</sup> See Shapiro, *supra* note 246.

<sup>251</sup> Antitrust Guidelines for the Licensing of Intellectual Property, U.S. Department of Justice and Federal Trade Commission, April 6, 1995.

<sup>252</sup> *Id.*

<sup>253</sup> *Id.*

alters or discourages participants from engaging in research.<sup>254</sup>

Unless a patent pool is challenged as *per se* illegal (an agreement to fix prices or output, rig bids, or share or divide markets), the pool will be evaluated under the “rule of reason.”<sup>255</sup> Under the “rule of reason” analysis, the “central question is whether the relevant agreement likely harms competition by increasing the ability or incentive profitably to raise prices above or reduce output, quality, service, or innovation below what likely would prevail in the absence of the relevant agreement.”<sup>256</sup>

The Department of Justice (“DOJ”) has issued a series of business review letters pursuant to DOJ’s Business Review Procedure, 28 C.F.R. §50.6, which provide some guidance as to how the principles announced in the Antitrust Guidelines will be applied.<sup>257</sup> As summarized by Carl Shapiro, the essence of the DOJ’s approach is:

In sum, when evaluating patent pools under the antitrust laws, the DOJ determines: 1) whether the proposed licensing program is likely to integrate complementary patent rights; and 2) if so, whether the resulting competitive benefits are likely to be outweighed by competitive harm posed by other aspects of the program.<sup>259</sup>

The Federal Trade Commission has taken a similar approach when evaluating patent pools under the antitrust laws.<sup>260</sup>

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<sup>254</sup> *Id.*

<sup>255</sup> Antitrust Guidelines for Collaborations Among Competitors, Federal Trade Commission and the U.S. Department of Justice, April 2000.

<sup>256</sup> *Id.*

<sup>257</sup> Letter from Joel I. Klein to Gerrard R. Beeney, June 26, 1997 (“MPEG-2 Business Review Letter”); Letter from Joel I. Klein to Gerrard R. Beeney, December 16, 1998 (“Phillips-Sony-Pioneer DVD Business Review Letter”); Letter from Joel I. Klein to Ky P. Ewing, November 12, 2002 (“3G Partnership Business Review Letter”).

<sup>259</sup> Letter from Joel I. Klein to Ky P. Ewing, Nov. 12, 2002 (“3G Partnership Business Review Letter”).

<sup>260</sup> See Aug. 21, 1998 Press Release, Summit and VISX Settle FTC Charges of Violating Antitrust Laws, <http://www.ftc.gov/opa/1998/08/sumvisx.htm>.

While patent pools may help to alleviate patent thicket problems, few patent-pooling agreements have arisen thus far in the biotechnology sector. Despite the potential for benefit, patent-pooling agreements may be less likely to arise in the biotechnology industry as opposed to other sectors. Heller & Eisenberg note that “because patents matter more to the pharmaceutical and biotechnology industries than to other industries, firms in these industries may be less willing to participate in patent pools that undermine the gains from exclusivity. Moreover, the lack of substitutes for certain biomedical discoveries (such as patented genes or receptors) may increase the leverage of some patent holders, thereby aggravating holdout problems.”<sup>261</sup> Finally, Arti Rai has argued that patent pools are less likely to arise in the biotechnology industry because of the great number of heterogeneous parties with contradictory interests that would have to come to an agreement.<sup>262</sup>

There are some signals that the biotechnology industry may be more receptive to patent pools in the future. Lawrence Sung explains the ways in which the structure of the industry seems to be changing:

In addition to Sung, many other academics and commentators have suggested that the economic and social benefits of patent pools outweigh their costs in the biotechnology sector.<sup>264</sup> Finally, the USPTO has issued

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<sup>261</sup>Heller & Eisenberg, *supra* note 235.

<sup>262</sup>See Rai, *supra* note 187, at 840-41.

<sup>264</sup>See *e.g.*, David B. Resnik, *A Biotechnology Patent Pool: An Idea Whose Time Has Come?*, *J. of Philosophy of Science & Law*, Vol.3, Jan. 2003; Katherine Moore, *Sharing Genetic Research Tools—The Ethical Considerations*, *Endocrine Society News*, Vol. 24(6), Dec. 1999.

a white paper addressing patent pools in the area of biotechnology. This paper suggests that the benefits of patent pooling include: 1) the elimination of problems caused by “blocking” patents; 2) reduction of licensing transaction costs; 3) reduction in litigation costs; 4) distribution of costs; and 5) institutionalized exchange of technical information not covered by patents.<sup>265</sup>

V.

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<sup>265</sup>Jeanne Clark *et al.*, *Patent Pools: A Solution to the Problem of Access in Biotechnology Patents*, Working Paper, U.S. Department of Commerce, U.S. Patent and Trademark Office, 2000.

## A. Small Biotechnology Firms: An Argument for Strong Patent Protection

The pharmaceutical industry spent an estimated \$33 billion on research and development in 2003.<sup>266</sup> In an additional attempt to increase productivity, pharmaceutical companies have engaged in waves of mergers. For example, there were 100 company mergers in the year 1996.<sup>267</sup> However, despite this large investment and these vast structural changes, the number of drugs per unit of research and development spending is thought to be decreasing each year.<sup>268</sup> To make matters worse, the average cost of bringing a new drug to market is now estimated at close to \$800 million.<sup>269</sup> Kenneth Kaitin, director of the Tufts Center for the Study of Drug Development has stated in reference to the current situation in the pharmaceutical industry: “This is not sustainable. . . It’s going to force a complete restructuring of the industry.”<sup>270</sup>

As previously noted, one proposed solution to the problem is a greater reliance on small biotechnology companies.<sup>271</sup> The reasoning is as follows: it is incredibly difficult to predict which drugs (given the 99.9% of drugs that fail either preclinical testing or clinical trials) will be winners.<sup>272</sup> Smaller biotechnology companies should be relied on for fundamental research and early drug discovery, and then once a favorable prospect is discovered, the firms can turn to larger pharmaceutical companies to develop the drug and help it to clear the expensive and multiple regulatory hurdles on the way to market.<sup>273</sup>

However, in order for small biotechnology firms to innovate, they are in desperate need of strong patent

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<sup>266</sup>Robert F. Service, *Surviving the Blockbuster Syndrome*, 303 *Science* 1796 (2004) (citing the Pharmaceutical Research and Manufacturers of America).

<sup>267</sup>*Id.*

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

<sup>269</sup>*Bigger Isn't Always Better*, 418 *Nature* 353 (2002).

<sup>270</sup>Service, *supra* note 266.

<sup>271</sup>*Bigger Isn't Always Better*, *supra* note 269.

<sup>272</sup>*Id.*

<sup>273</sup>*Id.*

protection in order to attract financing.<sup>274</sup> As Mark Lemley notes:

Lemley argues that a possible explanation for the demonstrated link between venture capital and financing is that “people are patenting at a very early stage in the process . . . precisely in order to attract or appease venture capital.”<sup>276</sup>

In sum, strong patent protection is a necessary prerequisite to promoting innovation at the level of the small biotechnology firms. First, strong patent protection allows these firms to attract financing and venture capital. Second, strong patent protection allows small firms greater leverage in licensing negotiations with large pharmaceutical companies.<sup>277</sup> If Lawrence Sung’s predictions are correct, then many biotechnology firms may be working to achieve intermediate business cycles of their own instead of simply being bought out by larger companies.<sup>278</sup> These small firms will therefore be interested in licensing their technology to larger pharmaceutical companies who are better equipped to work on commercial product development and drug marketing. Strong patent protection will favor the smaller firms in these licensing negotiations, and will thus give smaller firms greater incentive to engage in fundamental research in the first place.

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<sup>274</sup>Mark A. Lemley, *Reconceiving Patents in the Age of Venture Capital*, 4 J. Small & Emerging Bus. L. 137 (2000). See also Mazzoleni & Nelson, *supra* note 199.

<sup>276</sup>*Id.* (citing Samuel Kortum & Josh Lerner, *Does Venture Capital Spur Innovation?*, 1 Nat’l Bureau of Econ. Res. Working Paper No. W6846 (1998), for evidence that there is a positive relationship between venture capital and patenting).

<sup>277</sup>Gallini, *supra* note 195, at 141.

<sup>278</sup>See Sung, *supra* note 263.

## B.

As described earlier, the biotechnology industry is increasingly turning to proteomics to identify new targets for drug therapy. Since defective proteins are often the culprits leading to disease, protein-based drug therapies offer great promise.

Commentators have noted that “there is not likely to be a single technology that will dominate the [field of proteomics]—as robotic gene sequencers did for genomics—not a single corporate juggernaut like Celera Genomics of Rockville, Maryland. That’s because unlike genes, proteins vary widely in their chemical behaviors, making it difficult to come up with one technique that works equally well on all proteins.”<sup>279</sup> Indeed, advancements in proteomics to date have been hit or miss, and many firms have been forced to adopt the strategy of focusing on one specific avenue of research.<sup>280</sup> This focused approach came about as a result, in part, of the expense of patenting early stage discoveries in proteomics. The cost of patenting an invention worldwide can run as high as a couple of hundreds of thousands of dollars.<sup>281</sup> Thus, it is simply too expensive for most companies to engage in large-scale patenting of proteomics discoveries, given that most discovered proteins can only be used as a diagnostic tool, not as more-profitable drug targets.<sup>282</sup>

The complex and difficult nature of proteomics research will make the contribution of small biotechnology firms even more important. In addition, the development of patent protection for the resulting discoveries will have serious implications for innovation in the industry. While patenting proteins is not in and of

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<sup>279</sup> See Service, *supra* note 21.

<sup>280</sup> David Cyranoski, *This Protein Belongs To...*, 426 *Nature* 10 (2003).

<sup>281</sup> *Id.*

<sup>282</sup> *Id.*

itself anything new, the practice is likely to come under heightened scrutiny and to be of ever-increasing importance to the biotechnology industry. One important issue is how broadly the Federal Circuit should interpret patent claims covering proteins.

Patent law will need to address the important connection between patents on genes and patents on the corresponding proteins. While there are approximately only 35,000 protein-encoding genes, there are as many as 2 million proteins in any given individual.<sup>283</sup> It is now known that the same gene can be used to produce many different proteins, due to post-transcriptional and post-translational modifications.<sup>284</sup> After the transcription of a DNA sequence into an mRNA sequence, the mRNA transcript can be “spliced”<sup>285</sup> by cell machinery to produce many different proteins.<sup>286</sup> In addition, other modifications can be made by cell machinery after the mRNA transcript is translated into an amino acid sequence and a protein is formed. These modifications include the attachment of new chemical groups to the protein that can cause a change in function.<sup>287</sup>

At the time most gene patents issued, their claims covered only the single protein for which the gene was thought to encode.<sup>288</sup> Theoretically, these DNA claims could be interpreted broadly to cover the production of any protein encoded by a given DNA sequence.<sup>289</sup> However, this is very unlikely to happen. According to John Doll, head of the USPTO biotechnology art unit, as long as a given protein variant meets the requirements for patentability, including novelty and nonobviousness, it can still be patented even if a patent

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<sup>283</sup> See Robert F. Service, *Gene and Protein Patents Get Ready to Go Head to Head*, 294 *Science* 2082 (2001).

<sup>284</sup> See Thomas, *supra* note 234, at 1188.

<sup>285</sup> Splicing refers to a process whereby portions of a transcribed mRNA are removed to produce different proteins. See Bork & Copley, *supra* note 17.

<sup>286</sup> See Service, *supra* note 283.

<sup>287</sup> *Id.*

<sup>288</sup> *Id.*

<sup>289</sup> See Thomas, *supra* note 234.

has already issued for the gene sequence encoding the protein (or for another version of the protein.)<sup>290</sup> Of course, assuming that production of the new protein variant, or any resulting treatments or commercial products, requires use of the gene sequence, a company will still be forced to pay royalties to owner of the gene patent.

The case of *Amgen Inc. v. Hoechst Marion Rouessel, Inc.* provides some insight into how the Federal Circuit views the written description requirement when it comes to protein technology. Generally, recombinant protein techniques are not considered to be new or unknown techniques that those of skill in the art are likely to miscomprehend. Thus, it will be relatively easy for broad claims covering recombinant methods of protein production to meet the written description requirement. In *Amgen*, a rival company was found to have infringed Amgen's patent by producing a slightly different variant of EPO protein via recombinant techniques using host human cells (whereas Amgen's patent claims were construed to cover the recombinant production of EPO in a broad class of mammalian cells). Some commentators have criticized the Federal Circuit's ruling in *Amgen* as construing protein claims too broadly. Robert Cook-Deegan, Director of the Center for Genome Ethics, Law, and Policy at Duke University, has argued that the case could "discourage companies from trying to make better version of protein-based drugs."<sup>291</sup>

In addition, as the *University of Rochester v. Searle* makes clear, "reach through" claims relating to proteins are likely to be held invalid under the written description requirement. For example, a patentee could not claim a method of treatment consisting of using a compound to inhibit or stimulate production of a particular protein and a method of screening for such compounds, without identifying the compound or explaining how it might be obtained.

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<sup>290</sup> See Service, *supra* note 283.

<sup>291</sup> Cyranoski, *supra* note 280.

A second issue that patent law will need to address is the how to handle claims directed to proteins based on 3-D structural analysis. In addition to claims directed to proteins, it is likely that claims will also be made to computerized data storage mediums, to computerized screening methods for identifying compounds that bind to the protein and are useful in therapeutic treatments, and to the compounds that are identified through this process.

In 2002, the USPTO, European Patent Office, and Japan Patent Office met in Austria to discuss the patentability of protein 3-D structure related claims. The meeting produced a report on a comparative study of patenting practices at the three offices.<sup>292</sup> The report attempted to address four main issues: 1) what types of claims are eligible subject matter; 2) what types of claims satisfy the utility requirements; 3) what types of claims satisfy the enablement and written description requirements; and 4) what types of claims satisfy the novelty and nonobviousness requirements.<sup>293</sup>

With respect to claims covering a protein defined by structural coordinates, the USPTO comments explain that the protein would meet the utility requirement if the application discloses a specific therapeutic use for the protein such as lowering blood pressure. Of course, based on Federal Circuit precedent, the application would also have to present credible evidence of pharmacological activity based on in vitro or in vivo test results or based on structural homology. In addition, the claims to the protein would likely meet the novelty requirement assuming that another protein is not present in the prior art having the same specific function and approximately the same molecular weight. Finally, the claims to the protein would likely meet the written description and enablement requirements if the specification discloses the 3-D structure of the protein including the coordinates, of the amino acid side chains, the source organism for the protein, and

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<sup>292</sup>See European Patent Office, Japan Patent Office, and United States Patent Office, Trilateral Project WM4: Comparative Studies in New Technologies (biotechnology, business methods, etc.), Report on Comparative Study on 3-dimensional (3-D) Structure Related Claims, Vienna, Austria, Nov. 4-8, 2002.

<sup>293</sup>*Id.*

the molecular weight of the protein.

Both a computer model of a protein or a data array comprising the atomic coordination of a protein would be considered merely descriptive material or a mere arrangement of data and therefore not patentable subject matter under §101.

With respect to computerized screening programs used to identify proteins and therapeutically useful compounds that bind to the protein, the USPTO comments suggest that a screening method would qualify as patentable subject matter as long as it produces a “useful, concrete, and tangible result.”<sup>294</sup> A computerized screening method would meet the requirements of patentable subject matter when the program provides a result set that includes a number of lead compounds with an increased probability of binding to a protein whose structure was input. The utility of the screening method would depend on the utility of the candidate compounds; for example, the compounds might be useful for the stimulation or inhibition of a protein that would result in a treatment for a specific disease. However, in order to establish a substantial and credible utility, there must also be evidence of a correlation between the binding of the compound and either activation or inhibition of the protein. Whether the application meets the enablement requirement would depend on the amount and nature of experimentation required to determine which of the candidate compounds would be useful—i.e. the binding identification programs would have to be shown to be highly predictive. In order for the application to meet the written description requirement, the specification would have to describe the structural coordinates of the protein which are required by the screening program. Novelty of the screening method will depend on whether the 3-D coordinates of the protein required by the screening program are found in the prior art. Finally, obviousness of the screening method will depend on whether the computer algorithm used to identify the compounds is obvious based on the prior art. Merely inputting

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<sup>294</sup>State Street Bank & Trust Co. v. Signature Financial Group Inc., 149 F.3d 1368, 1374 (Fed. Cir. 1998)).

new 3-D protein coordinates into the same computer system is not enough to render the screening system nonobvious.

Finally, with respect to any compounds identified by using a computerized screening method, the USPTO comments suggested that the written description requirement will not be met without identification of specific structural or functional characteristics of the compound. The enablement requirement would likely not be met; since the art of computerized screening for protein binding compounds is considered to be unpredictable, undue experimentation would be necessary in order to identify the desired compounds. In sum, “patents will not be granted if the experimental data for compounds are predicted only by computer analysis. Inventions described with *in vivo* or *in vitro* experimental results together with protein structural information or pharmacophores would most likely be as effective as a patent strategy.”<sup>295</sup>

Federal Circuit precedent and USPTO guidelines attempt to strike a balance between the benefits of the patent system in terms of increased innovation and the costs imposed on the public stemming from monopoly prices during the term of the patent. While strong patent protection is of vital importance to ensuring innovation in the field of biotechnology and biopharmaceuticals, it is of equal importance that the requirements of patentability, especially written description and enablement, be applied strictly. When there is a great deal of unpredictability in a given art, patents should only be granted to the extent that the inventor has actually made a contribution in the field. This will ensure that there are appropriate incentives for downstream research and development, and in the long run will ensure that patents actually promote, rather than impede, innovation.

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<sup>295</sup>Itsuki Shimno, et al., *Patent Protection for Protein Structure Analysis*, 22 *Nature Biotechnology* 109 (2004).

