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Biotechnology's Uncertainty Principle¹

Dan L. Burk² and Mark A. Lemley³

Patents have proven to be important to the growth and financing of the American biotechnology industry, but it remains unclear whether current patent standards are well suited to the needs of this industry. Patent law has a general set of legal rules to govern the validity and infringement of patents in a wide variety of technologies. With a very few exceptions, the statute does not distinguish between different technologies in setting and applying legal standards. Rather, those standards are designed to adapt flexibly to new technologies, encompassing "anything under the sun made by man."⁴ In theory, then, we have a unified patent system that provides technology-neutral protection to all kinds of technologies.

However, we have recently noticed an increasing divergence between the rules actually applied to different industries. Biotechnology provides one of the best examples.

¹ © 2003 Dan L. Burk & Mark A. Lemley. This chapter is derived in part from two other articles we have written: *Is Patent Law Technology-Specific?*, 17 BERKELEY TECH. L.J. 1155 (2002) and *Policy Levers in Patent Law*, __ VA. L. REV. __ (forthcoming 2003).

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⁴ *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980) (citing S.Rep.No.1979, 82d Cong., 2d Sess., 5 (1952); H.R.Rep.No.1923, 82d Cong., 2d Sess., 6 (1952)).

In biotechnology cases, the Federal Circuit has repeatedly held that uncertainty in predicting the structural features of biotechnological inventions renders them nonobvious, even if the prior art demonstrates a clear plan for producing the invention. At the same time, the court claims that the uncertain nature of the technology requires imposition of stringent patent enablement and written description requirements that are not applied to patents in other disciplines. Thus, as a practical matter it appears that although patent law is technology-neutral in theory, it is technology-specific in application. We provide evidence for this claim in Part I. While our paper focuses on biotechnology, which presents an extreme example, our findings have implications for other industries as well, notably small-molecule chemistry.

Part II begins by exploring how the application of the same legal standards can lead to such different results in diverse industries. Much of the variance in patent standards is attributable to the use of a legal construct, the “person having ordinary skill in the art” (PHOSITA), to determine obviousness and enablement. The more skill those in the art have, the less information a patentee has to disclose, but the harder it is to find an invention nonobvious. The level of skill in the art affects not just patent validity, but also patent scope. Because both claim construction and the doctrine of equivalents turn on the understanding of the PHOSITA in certain circumstances, judgments the court makes about those industries affect the scope of those patents that do issue.

One reading of the biotechnology cases is that the Federal Circuit believes that biotechnology experts know very little about their art – at least, this seems the clear implication of the court’s holdings and accompanying analysis. We do not challenge the idea that the standards in each industry should vary, nor the idea that that variation

depends in part on the level of skill in that industry. As we have explained elsewhere, patent law should be technology-specific, because the industries it affects are not homogenous.⁵ We think the use of the PHOSITA provides needed flexibility for patent law, permitting it to adapt to new technologies without losing its essential character. We fear, however, that the Federal Circuit has not applied that standard properly in biotechnology. The court has a static perception of the field that was set in its initial analyses of biotechnology inventions, but which does not reflect the realities of the industry.

In Part III, we offer a very preliminary policy assessment of these industry-specific patent cases. We suggest that the special rules the Federal Circuit has constructed for biotech cases are rather poorly matched to the specific needs of the industry. Indeed, in some ways the Federal Circuit cases have it exactly backwards. We offer a few suggestions as to what a consciously designed biotechnology patent policy may look like. In doing so, we hope to lay the groundwork for broader exposition of those ideas, and suggestions for implementing them.

I. Heterogeneity in the Patent Law

Intellectual property law generally aims to solve the “public goods” problem that arises in regard to creative activity. . Legal rights in the product of creative activity allow creators to control and profit from goods that are costly to produce but which are virtually costless to reproduce or to appropriate once they have been created. . A variety of intellectual property systems have been promulgated to deal with this problem for

⁵ Burk & Lemley, *Policy Levers*, *supra* note 1.

different, if occasionally overlapping, areas of subject matter. These various degrees and modes of legal protection carry different scopes and lengths of protection, hopefully roughly appropriate to their subject areas. Copyright is generally addressed to artistic or aesthetic works, although it now includes software in its ambit; patent law generally addresses industrial or technological inventions; trade secrecy covers a wide range of valuable business assets. Each of these modes of protection covers a wide swath of subject matter; specialized statutes, sometimes called “sui generis” laws, are relatively rare.⁶ As a practical matter, Congress cannot enact a new form of intellectual property statute each time a new technology arises.⁷ Nevertheless, there are drawbacks to encompassing many types of subject matter within one broad system, as demonstrated by patent law.

A. The History of the Uniform Patent System

⁶ At various times commentators have called for sui generis protection of specific subject matter. See, e.g., Peter S. Menell, *Tailoring Legal Protection for Computer Software*, 39 STAN. L. REV. 1329, 1364-65 (1987) (computer software); Pamela Samuelson, *Creating a New Kind of Intellectual Property: Applying the Lessons of the Chip Law to Computer Programs*, 70 MINN. L. REV. 471 (1985) (same); Dan L. Burk, *Copyrightability of Recombinant DNA Sequences*, 29 JURIMETRICS J. 469, 530-31 (1989) (biotechnology); Kenneth D. Crews, *Looking Ahead and Shaping the Future: Provoking Change in Copyright Law*, 49 J. COPYRIGHT SOC'Y USA 549, 564 (2001) (“One-size-fits-all’ ultimately fits few.”). Cf. Nancy Gallini & Suzanne Scotchmer, *Intellectual Property: When Is It the Best Incentive System?*, in INNOVATION POLICY AND THE ECONOMY 2 51, 53 (Adam B. Jaffe et al. eds., 2001) (“[I]ntellectual property regimes should be designed so that the subject matter of each one has relatively homogenous needs for protection.”). The Semiconductor Chip Protection Act of 1984 is one of the few examples where Congress heeded such encouragement. It created a unique form of intellectual property in the “mask works” embodying semiconductor chip circuit designs. See Semiconductor Chip Protection Act of 1984, 17 U.S.C. §§ 901-914 (2000)).

⁷ See Louis Kaplow, *The Patent-Antitrust Intersection: A Reappraisal*, 97 HARV. L. REV. 1813, 1819-20 (1984); Richard Stern, *The Bundle of Rights Suited to New Technology*, 47 U. PITT. L. REV. 1229, 1261 (1986).

A patent statute was one of the first laws Congress passed, in 1790. Since that time, a patent statute has been a constant feature of the U.S. legal landscape.⁸ While the nature of the patent system went through some rather dramatic changes in the first fifty years of the Republic—beginning with a requirement that two cabinet officials must personally review and sign off on any patent⁹ and swinging to the other extreme with an automatic registration system subject to caveats¹⁰—by 1836 the essential features of modern patent law were in place.¹¹ Despite periodic revisions, most recently in 1952, the basic structure of the patent system has remained unchanged for 165 years.

Technology, of course, has changed dramatically during that time. The “useful arts” envisioned by the Framers were mechanical inventions useful in a primarily agrarian economy. Since that time, the country has gone through several periods of dramatic innovation in a wide variety of fields. As late as 1950, though, most inventions were still mechanical in nature. It is only in the last half-century—and to a large extent in the last twenty-five years, as Allison and Lemley show¹²—that patent law has lost its

⁸ See, e.g., BRUCE BUGBEE, *THE GENESIS OF AMERICAN PATENT AND COPYRIGHT LAW* 126, 143 (1967); Edward C. Walterscheid, *To Promote the Progress of Useful Arts: American Patent Law and Administration, 1787-1836*, pts. 1 & 2, 79 J. PAT. & TRADEMARK OFF. SOC'Y 61, (1997); 80 J. PAT. & TRADEMARK OFF. SOC'Y 11, (1998). Even before that time, the U.S. colonies granted patent rights. See ROBERT P. MERGES ET AL., *INTELLECTUAL PROPERTY IN THE NEW TECHNOLOGICAL AGE* 109 (3d ed. 2003).

⁹ This was a feature of the short-lived Patent Act of 1790. See Walterscheid, *supra* note 8; Edward C. Walterscheid, *Charting a Novel Course: The Creation of the Patent Act of 1790*, 25 AIPLA Q.J. 445, 519-20 (1997).

¹⁰ The 1793 Act replaced the cumbersome cabinet-level review with a registration system. Under this system, patents were granted without examination unless a competitor or other interested party filed a “caveat”—essentially a request to be notified and given a chance to object if someone patented in a particular field. See Walterscheid, *supra* note 8, at 73.

¹¹ See MERGES ET AL., *supra* note 9, at 109-10.

¹² See John R. Allison & Mark A. Lemley, *The Growing Complexity of the United States Patent System*, 82 B.U. L. REV. 77, 87-90 (2002).

primarily mechanical character, branching out into biotechnology, semiconductors, computer hardware and software, electronics, and telecommunications.

What is notable about this history is that the fundamental rules of patent law were set in a world in which inventions were mechanical. Because inventions in the past were far more homogenous than they are today,¹³ it made sense to have a unified set of rules for dealing with those inventions. The application of those old rules to new technologies has not been free from controversy. Some have suggested that the unified rules suitable for the old, homogeneous world are no longer appropriate in today's increasingly complex innovative landscape.¹⁴ But without changing the rules themselves, in the last dozen years the Federal Circuit has applied those rules in a way that effectively creates different standards for different industries.¹⁵ In the sections that follow, we examine the legal treatment of one such industry — biotechnology -- in detail.

B. Biotechnology Patent Cases¹⁶

In stark contrast to the Federal Circuit decisions in other technologies,¹⁷ recent decisions involving genetic material have imposed a stringent disclosure standard for

¹³ *Id.* at 79-80.

¹⁴ See, e.g., S. Benjamin Pleune, *Trouble With the Guidelines: On Urging the PTO to Properly Evolve With Novel Technologies*, 2001 J. L., TECH. & POL'Y 365 (arguing for DNA-specific legislation). For a critical analysis of such proposals, see Dan L. Burk, *Biotechnology and Patent Law: Fitting Innovation to the Procrustean Bed*, 17 RUTGERS COMP. & TECH. L.J. 1 (1991).

¹⁵ Hodges observes that computers and biotechnology are treated differently in the written description cases, though he limits his focus primarily to biotechnology. Robert A. Hodges, Note, *Black Box Biotech Inventions: When a "Mere Wish or Plan" Should be Considered an Adequate Description of the Invention*, 17 GA. ST. U. L. REV. 831, 833 (2001). Others have complained that even within industries the standard may not be applied consistently. See, e.g., Glynn S. Lunney Jr., *E-Obviousness*, 7 MICH. TELECOMM. & TECH. L. REV. 363, 365 & n.13 (2001).

patenting macromolecules.¹⁸ The Court has placed particular emphasis on the “written description” requirement of section 112, which requires the patentee to specifically describe the claimed invention as part of the disclosure. The justification for such a detailed description is to demonstrate to others of ordinary skill that the inventor in fact has the invention in her possession; the assumption being that a sufficiently detailed description would not be possible if the inventor were speculating or guessing about its features.¹⁹ This requirement is separate from (and potentially more stringent than) the enablement requirement. Although the two are closely connected, satisfying one requirement does not necessarily satisfy the other. The classic example offered by one court is the situation in which the description of a particular chemical compound enables

¹⁶ For background on the science of biotechnology, see generally ROBERT P. MERGES, ET AL., *INTELLECTUAL PROPERTY IN THE NEW TECHNOLOGICAL AGE: 2002 CASE AND STATUTORY SUPPLEMENT* 501-16; Dan L. Burk, *A Biotechnology Primer*, 55 U. PITT. L. REV. 611 (1994).

¹⁷ For example, the Federal Circuit has articulated very loose, almost trivial standards for disclosure of computer software. See, e.g., *Northern Telecom, Inc., v. Datapoint Corp.*, 908 F.2d 931 (Fed. Cir. 1990) (holding that only minimal disclosure is needed for enablement, because implementation is “a mere clerical function to a skilled programmer”). For elaboration of how software cases differ from biotech cases, see Dan L. Burk & Mark A. Lemley, *Is Patent Law Technology-Specific?*, 17 BERKELEY TECH. L.J. 1155 (2002).

¹⁸ We acknowledge Lawrence Sung’s contrary view, that the Federal Circuit’s biotechnology cases are simply decided on their individual facts and do not reflect any patterns. See Lawrence M. Sung, *On Treating Past as Prologue*, 2001 U. ILL. J. L. TECH. & POL’Y 75, 107. See also John W. Schlicher, *Biotechnology and the Patent System: Patent Law and Procedures for Biotechnology, Health Care and Other Industries*, 4 U.BALT. INTELL. PROP. L.J. 121, 127 (1996) (“I do not understand the Court of Appeals for the Federal Circuit to have created a subset of patent law doctrines for biotechnology.”). But other commentators appear to recognize that something unusual is happening in the case of biotechnology. See, e.g., Hodges, *supra* note 15, at 832; Janice M. Mueller, *The Evolving Application of the Written Description Requirement to Biotechnological Inventions*, 13 BERKELEY TECH. L.J. 615 (1998); Harris A. Pitlick, *The Mutation on the Description Requirement Gene*, 78 J. PAT. & TRADEMARK OFF. SOC’Y 209 (1998); Margaret Sampson, *The Evolution of the Enablement and Written Description Requirements Under 35 U.S.C. § 112 in the Area of Biotechnology*, 15 BERKELEY TECH. L.J. 1233 (2000). It seems readily apparent to us, as to the majority of other commentators, that the biotechnology cases consistently depart from the standards applied in other industries.

¹⁹ Of course, in the case of constructive reduction to practice, or filing a “paper patent” without having actually made the invention, the inventor is in some sense speculating or guessing about the features of an invention not yet built. But even in that instance, the underlying assumption in patent law is that the inventor “has” the invention mentally, and so can give a sufficiently detailed description of that inventive conception—physically creating the invention is straightforward.

one of ordinary skill to make other, related, compounds, yet those other compounds are not described in the patent disclosure. The first compound is both enabled and described; the others are only enabled.²⁰

This venerable chemical patenting hypothetical has been brought to life by the Federal Circuit's biotechnology opinions. For example, in *Fiers v. Revel*,²¹ the court considered the decision of the Patent Office in a three-way interference over patent applications claiming the human DNA sequence that produces the protein fibroblast beta-interferon (β -IF).²² One of the applicants, Revel, relied for priority upon his Israeli patent application, which disclosed methods for isolating a fragment of the DNA sequence coding for β -IF and for isolating messenger RNA coding for β -IF. The court considered whether the disclosure in Revel's Israeli application satisfied the U.S. written description requirement and could therefore support a U.S. application. The Federal Circuit upheld a determination by the Board of Patent Appeals and Interferences that Revel's disclosure was not an adequate description, largely because it failed to disclose the actual sequence of the DNA molecule at issue. According to the court's reasoning, disclosing a method for obtaining the molecule was not the same as disclosing the molecule itself:

An adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself. . . . A bare reference to a DNA with a statement that it can be obtained by reverse transcription is not a description; it does not indicate that Revel was in possession of the DNA.²³

²⁰ *In re DiLeone*, 436 F.2d 1404, 1405 n.1 (C.C.P.A. 1971).

²¹ *Fiers v. Revel*, 984 F.2d 1164 (Fed. Cir. 1993).

²² In biotechnology terms, we say that the DNA sequence in question "codes for" the protein.

²³ *Id.* at 1170-71.

Since the Revel application did not disclose the sequence for the molecule claimed, the court characterized it as disclosing merely “a wish, or arguably a plan, for obtaining the DNA.”²⁴ Under *Fiers*, an inventor does not conceive of a DNA invention until she actually creates it.²⁵

A similar conclusion was reached in a subsequent case, *Regents of the University of California v. Eli Lilly*.²⁶ The patent at issue covered a microorganism carrying the DNA sequence coding for human insulin. The patentee supported this claim by disclosing a method for obtaining the human cDNA²⁷, as well as the amino acid sequences for the insulin protein and the corresponding insulin DNA sequence in rats. Relying on the *Fiers* opinion, the court concluded that the written description requirement again was not met: “Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the DNA itself.”²⁸

In reaching these results, the Federal Circuit has been adamant that the degree of specificity required for an adequate description of nucleic acids requires description of

²⁴ *Id.*

²⁵ See also *Adang v. Fischhoff*, 286 F.3d 1346 (Fed. Cir. 2002) (disclosure of genetically altered tobacco plant did not enable claim to genetically altered tomato plant); *Hitzeman v. Rutter*, 243 F.3d 1345 (Fed. Cir. 2001) (conception of biotechnology invention simultaneous with reduction to practice). To be sure, the court stopped short of creating an absolute rule, noting that “[t]here may be situations where an organism’s performance of certain intracellular processes might be reasonably predictable, and evidence of such predictability might be sufficient to support a finding of conception prior to reduction to practice.” *Id.* at 1357. But even here the court’s language focuses on organic processes, not DNA sequences.

²⁶ 119 F.3d 1559 (Fed. Cir. 1997).

“structure, formula, chemical name, or physical properties.”²⁹ In *Eli Lilly*, because “[n]o sequence information indicating which nucleotides constitute human cDNA appears in the patent . . . the specification does not provide a written description of the invention.”³⁰ The court in such cases seems particularly incensed by applicants who designate a macromolecule by generic or functional terms, such as “vertebrate insulin cDNA”:

A definition by function . . . is only an indication of what the gene does, rather than what it is. It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.³¹

Such failure to describe more than one or two nucleotides is a particular problem where the patent claims are drawn to a broad class of nucleotides. For example, Revel's claim covered all DNA molecules that code for β -IF, but “[c]laiming all DNAs that achieve a result without defining what means will do so is not in compliance with the description requirement; it is an attempt to preempt the future before it has arrived.”³²

The Federal Circuit's construction of the written description requirement as requiring precise sequence data gains particular significance whenever claims are drawn to an entire genus, or family, of molecules. The patent discussed in the *Eli Lilly* written description analysis claimed a broad family of DNA molecules coding for insulin in different mammalian species, but it disclosed only one species of DNA, that coding for

²⁹ *Id.* at 1171.

rat insulin. The court held this to be insufficient to describe the broad class of cDNAs coding for mammalian or vertebrate insulin.³³ Although declining to specify exactly what would be needed to support a broad claim, the court cited previous chemical cases dealing with related groups of small molecules. Based on these cases, the court declared that macromolecules should be treated in the same fashion: the patentee need not show every member of a claimed genus, but is required to show a “representative” number of cDNAs illustrating or defining the common structural features of a “substantial” portion of the genus.³⁴

A similarly broad claim was rejected in the *Amgen* case as failing the standard for enablement rather than written description.³⁵ There, the patentee claimed nucleic acid sequences coding for the protein erythropoietin or for other proteins with the same biological function. The trial judge concluded that because Amgen was unable to specify which analogs might have the biological properties claimed, the claims were not enabled.³⁶ The Federal Circuit panel, however, held that the district court had reached the right conclusion for the wrong reason. While the district court focused on the thousands of EPO analogs that could be created by substituting amino acid residues in the polypeptide chain, the appellate court focused on the patentee's failure to disclose the DNA molecules that would code for those analogs.³⁷ Since the claims were directed to

³³ *Eli Lilly*, 119 F.3d at 1567.

³⁴ *Id.* at 1569. *Cf.* *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69 (D. Mass. 2001) (patent for urinary erythropoietin preparations invalid under written description requirement because different preparations vary in glycosylation).

DNA sequences, the issue was not the enablement of the EPO analogs, but rather the enablement of the myriad DNA sequences, which the court held could not be made and used on the basis of a few examples.³⁸

In an important recent decision, the Federal Circuit backed off somewhat from its categorical insistence on structure in biotechnology disclosure cases. In *Enzo Biochem v. Gen-Probe*,³⁹ the court adopted the PTO's Guidelines on Written Description.⁴⁰ Those Guidelines provide that biotechnology inventions normally must be described by structure, but may also be described by "functional characteristics when coupled with a known or disclosed correlation between function and structure."⁴¹ The court specifically identified antibody claims as ones that might be described by function—i.e., by describing the antigen to which they bind.⁴² Its holding was more limited, however. It held that the deposit of three actual DNA sequences created a factual question as to whether the deposited sequences could satisfy the written description requirement for claims covering those sequences and a broader genus. Because the deposited sequences inherently included the structure of the gene, the court in *Enzo* had no opportunity to endorse claims based entirely on proof of function rather than structure. The court did not repudiate, and indeed relied upon, the *Eli Lilly* baseline rule that disclosure of structure was required.

³⁸ *Id.*

³⁹ 296 F.3d 1316 (Fed. Cir. 2002).

The same concerns that characterize the Federal Circuit's jurisprudence of biotechnology disclosure—the inadequacy of methodological disclosure, the requirement to specify sequence or structure, and uncertainty of selection within large classes of homologous molecules—have shaped the Federal Circuit's biotechnology obviousness cases. However, in the case of obviousness, the issue has been the presence of such factors in the prior art, rather than in the inventor's disclosure. Thus, the Federal Circuit held in *In re Bell* that a claim to DNA coding for human insulin-like growth factor (hIGF) was not obvious even though the prior art disclosed the amino acid sequence for the hIGF proteins and a method for using that information to obtain the corresponding DNA molecule.⁴³ Under similar facts in *In re Deuel*, the court found claims directed to DNA coding for heparin binding growth factors (HBGFs) were not obvious in light of prior art disclosure of a partial amino acid sequence and a method for using that information to obtain the corresponding DNA molecule.⁴⁴

Each decision rested largely upon the court's perception that the actual sequence of the claimed DNA molecules was uncertain or unpredictable from the prior art. In both cases the court dismissed as irrelevant the biological relationship between the molecules disclosed in the prior art and those claimed by the patent. The amino acid sequences of the proteins disclosed in the prior art are ultimately determined by the sequence of RNA nucleotides coding for the protein, which is in turn determinative of the cDNA claimed in the patent.⁴⁵ The correspondence of nucleotide sequences to amino acid sequences is

⁴³ See *In re Bell*, 991 F.2d 781, 784 (Fed. Cir. 1993).

⁴⁴ See *In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995).

⁴⁵ Neither *In re Bell* nor *In re Deuel* dealt with genomic DNA (gDNA) sequences, which are transcribed by cellular proteins to produce a messenger RNA molecule. See FREIFELDER & MALACINSKI, *supra* note 27 (describing the transcription process). Both cases considered non-naturally occurring cDNA sequences,

well known as key to the “central dogma” of molecular biology: the transfer of genetic information from DNA to RNA to protein chains. However, particular amino acids can correspond to more than one nucleotide sequence, introducing uncertainty into the inverse relationship: that of amino acid sequence to nucleotide sequence. Because of this redundancy or “degeneracy” in the genetic code, the court noted in *Bell* that a vast number of possible sequences—about 10^{36} —might code for the protein sequences disclosed in the prior art. The plaintiff claimed only one of these, in essence having searched among a large number of possibilities to select the particular cDNA sequence coding for hIGF.

Numerous commentators have pointed out that such a search is relatively routine using tried and true techniques of molecular biology.⁴⁶ But prior art disclosure of a method, even an admittedly obvious method, was held insufficient to cure such uncertainty of structure. In rejecting the DNA claims in *Bell* and *Deuel*, the court rejected “the PTO’s focus on known methods for potentially isolating the claimed DNA molecules” as “misplaced because the claims at issue define compounds, not methods.”⁴⁷ Prior to *Bell*, the opinion in *Amgen* had stressed the uncertainty of the methods for gene location available at the time of invention: while “it might have been feasible, perhaps obvious to try, to successfully probe a human gDNA library with a monkey cDNA probe,

which are reverse transcribed from messenger RNAs. The correspondence between gDNA and RNA may be very different than that of cDNA to RNA, especially in eukaryotic organisms where the processing of RNA transcripts may be extensive. *Id.*

⁴⁶ See, e.g., Anita Varma & David Abraham, *DNA is Different: Legal Obviousness and the Balance Between Biotech Inventors and the Market*, 9 HARV. J.L. & TECH. 53 (1996); PHILIPPE G. DUCOR,

it does not indicate that the gene could have been identified and isolated with a reasonable likelihood of success. . . . there was no reasonable expectation of success in obtaining the EPO gene by the method that Lin eventually used.”⁴⁸ The court arguably just got the science wrong; by the time of the research at issue in *Bell*, such methods for searching a large universe of molecules were perhaps painstaking and time-consuming, but had an established likelihood of success.

Yet the court defined the issue in *Bell* and *Deuel* not as a matter of the uncertainty of obtaining a particular sequence, but of the uncertainty of predicting or visualizing from the prior art what sequence would be found. Even in the *Amgen* opinion, the court hinted that the key to macromolecular obviousness lay in the prediction of an exact sequence, as “[n]either the DNA nucleotide sequence . . . nor its exact degree of homology with the [prior art] monkey EPO gene was known at the time.”⁴⁹ And in *Deuel*, the court explicitly held that “until the claimed molecules were actually isolated and purified, it would have been highly unlikely for one of ordinary skill in the art to contemplate what was ultimately obtained. *What cannot be contemplated or conceived cannot be obvious.*”⁵⁰ Thus a likelihood—or even a certainty—of finding a DNA molecule with particular properties was deemed essentially irrelevant to whether structural claims to that molecule are obvious.⁵¹

⁴⁸ *Amgen, Inc. v. Chugai Pharm. Co.* 927 F.2d at 1208-09.

⁴⁹ *Id.*

⁵⁰ 51 F.3d at 1558 (emphasis added).

⁵¹ *Cf. Rhone-Poulenc Agro v. DeKalb Genetics Corp.*, 272 F.3d 1335, 1357-58 (Fed. Cir. 2001) (holding that addition of second transit peptide to string of amino acids with transit peptide and fragment of a second transit peptide was not obvious because the amino acids were structurally different).

The corollary to this holding is that a molecule will be obvious if the sequence is discernible in the prior art, even if its function is not. Prior art description of the “general idea of the claimed molecules, their function, and their general chemical nature”⁵² is insufficient to render a molecule obvious. Some commentators have suggested that this formulation of obviousness stands some danger of collapsing into the standard for anticipation⁵³; under section 102 of the Patent Act, an invention lacks patentable novelty if its elements are fully described in a prior art reference, and the Federal Circuit’s obviousness requirement could be read to require such a prior art anticipation as the effective standard for obviousness.⁵⁴ But unlike the requirements for anticipation, the Federal Circuit’s biotechnology obviousness standard appears to require that the sequence of the DNA be predictable from the prior art, and not necessarily explicitly described. For example, the court in *Deuel* suggests that for “a protein of sufficiently small size and simplicity, . . . lacking redundancy, each possible DNA would be obvious over the protein.”⁵⁵ Although the Federal Circuit has not explicitly held so, one would also suspect that disclosure in the prior art of a substantial number of homologous sequences would render a new homologue predictable, and so render it obvious—just as the court has held that disclosure of a substantial number of homologues is enough to satisfy the written description requirement for a genus of homologues.

⁵² 51 F.3d at 1558.

⁵³ See Rebecca 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, 32 (1995).

The Federal Circuit's biotechnology obviousness cases are all of a piece with the court's earlier holdings, such as the rejection on disclosure grounds of Revel's claim to all DNA sequences coding for β -IF.⁵⁶ Due to degeneracy in the genetic code, Revel could not adequately describe the claimed invention as DNA coding for β -IF; an astronomically large number of possible sequences might do so. And if a functional or narrative description in a patent is insufficient to properly describe a DNA molecule coding for β -IF, the presence of a functional or narrative description of β -IF protein in the prior art would be insufficient to render the molecule obvious. According to the court, one cannot describe what one has not conceived, and what cannot be contemplated or conceived cannot be obvious. Just as disclosure in a patent of a method for obtaining a particular cDNA is inadequate to properly describe the invention, so disclosure in the prior art of a method for obtaining a particular cDNA cannot render the claimed invention obvious.

The conceptual linkage of obviousness and enablement to the depiction of macromolecular sequences in, respectively, the prior art or the patent disclosure, dictates a particular and predictable result for the availability and scope of such biotechnology patents. The expected outcome is that DNA patents will be numerous but extremely narrow. Under the Federal Circuit's precedent, a researcher will be able to claim only sequences disclosed under the stringent written description rules—the actual sequence in hand, so to speak. And as Judge Learned Hand observed long ago, a claim that covers

only the thing invented is a weak claim indeed.⁵⁷ At the same time, the inventor is shielded from obviousness by the lack of such explicit and detailed disclosure in the prior art. This lack of effective prior art seems to dictate that anyone who has isolated and characterized a novel DNA molecule is certain to receive a patent on it. But the inventor is certain to receive a patent only on that molecule, as the Federal Circuit appears to regard other related molecules as inadequately described until their sequence is disclosed.

The set of axioms underlying this set of results forms a logical framework that may be extended to certain other biotechnology inventions. For example, one would conclude from the Federal Circuit's analysis in these cases that a cDNA should be obvious in light of its corresponding mRNA⁵⁸, since the former is reverse transcribed from the latter, and there is no redundancy or degeneracy in the correspondence between the nucleotides in the two molecules.⁵⁹ However, an mRNA or corresponding cDNA need not render obvious the genomic DNA (gDNA) from which it is derived, since in many organisms, the gDNA will include intervening sequences, or introns, that are not predictable from the mRNA sequence.

Perhaps more important than the extension of the Federal Circuit's logic to other classes of molecules is the extension of its logic to other patent doctrines. For example, as we have indicated with regard to software, patent scope is a function of the

⁵⁷ See *Philip A. Hunt Co. v. Mallinckrodt Chem. Works*, 177 F.2d 583, 585-86 (2d Cir. 1949) (noting that it may be impossible to write claims of appropriate scope without using functional language to describe variants).

obviousness and written description requirements. Under the court's decisions, the literal scope of biotechnology patents will be quite narrow: patent claims are confined to the DNA sequences actually generated and disclosed, rather than those enabled by the patentee. While that scope may be broadened by the doctrine of equivalents⁶⁰, the recent trend to limit the scope of the doctrine of equivalents⁶¹ may mean that the biotechnology industry will be characterized by large numbers of narrow patents.

C. The Divergent Standards

Patent practitioners often focus on a single technology area, and so may tend to take the court's rules in that area for granted. Even a casual juxtaposition of the biotechnology and software cases, however, shows dramatic differences in applying what are nominally the same legal rules.⁶² District courts have recognized the difference,

⁶⁰ The very parsimonious reading that the Federal Circuit gives to obviousness in biotechnology cases seems to leave wide latitude for findings of equivalence in nucleotide infringement cases. *See Wilson Sporting Goods Co. v. David Geoffrey & Assoc.*, 904 F.2d 677 (Fed. Cir. 1990) (testing equivalence by inquiring whether a hypothetical claim encompassing the accused product would have been obvious at the time of invention).

⁶¹ The courts have recently strengthened other limits on the doctrine of equivalents, notably prosecution history estoppel and the doctrine of dedication to the public domain. *See, e.g., Festo Corp. v. Shoketsu*, 122 S. Ct. 1831 (2002) (prosecution history estoppel applies broadly, though not absolutely); *Johnson & Johnston Assoc. v. R.E. Serv. Co.*, 238 F.3d 1347 (Fed. Cir. 2001) (en banc) (equivalents disclosed in the patent but not claimed are dedicated to the public domain). *See also* Matthew J. Conigliaro, et al., *Foreseeability in Patent Law*, 16 BERKELEY TECH. L.J. 1045 (2001) (discussing both doctrines). Those limitations may prevent any patent from being read too broadly under the doctrine of equivalents.

⁶² Commentators have observed that the Federal Circuit's biotechnology written description cases apply a standard quite different from the written description precedent in other areas. *See, e.g., Mueller, supra* note 18; Sampson, *supra* note 18; Limin Zheng, Note, *Purdue Pharma L.P. v. Fausch Inc.*, 17 BERKELEY TECH. L.J. 95, 95 (2002). While there are a number of recent written description cases outside the biotechnology context, all of them involve patentees who changed their claims during prosecution to cover a competitor's product. *See, e.g., Turbocore Div. of Demag Delaval Turbomachinery Corp. v. Gen. Elec. Co.*, 264 F.3d 1111 (Fed. Cir. 2001); *Hyatt v. Boone*, 146 F.3d 1348 (Fed. Cir. 1998); *Gentry Gallery, Inc. v. Berkline Corp.*, 134 F.3d 1473 (Fed. Cir. 1998). *See also* Janice M. Mueller, *Patent Misuse Through the Capture of Industry Standards*, 17 BERKELEY TECH. L.J. 623, 639-40 (2002) (distinguishing the biotechnology cases from written description decisions in other areas, especially *Union Oil Co. of Cal. v. Atl. Richfield Co.*, 208 F.3d 989 (Fed. Cir. 2000)). *Cf.* Matthew L. Goska, *Of Omitted Elements and*

applying the Federal Circuit rules in different ways depending on the technology at issue.⁶³ The easiest way to see this may be to imagine the court's language from one discipline applied to another. In *Fonar*, for instance, the court said:

As a general rule, where software constitutes part of a best mode of carrying out an invention, description of such a best mode is satisfied by a disclosure of the functions of the software. This is because, normally, writing code for such software is within the skill of the art, not requiring undue experimentation, once its functions have been disclosed.⁶⁴

Replace software with DNA, though, and the following would result:

As a general rule, where [DNA] constitutes part of a best mode of carrying out an invention, description of such [DNA] is satisfied by a disclosure of the functions of the [DNA]. This is because, normally, [identifying such DNA] is within the skill of the art, not requiring undue experimentation, once its functions have been disclosed.

This is *exactly* antithetical to the actual rule in biotechnology cases, as stated by *Eli Lilly*:

A definition by function . . . is only an indication of what a gene does, rather than what it is. It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.⁶⁵

Overreaching Inventions: The Principle of Gentry Gallery Should Not Be Discarded, 29 AIPLA Q.J. 471, 484 (2001) (arguing that the written description requirement makes sense, but that it should not be applied to original claims as it has been in the biotechnology cases).

Other commentators have pointed out that the nonobviousness standard in biotechnology is lower than in other industries. See, e.g., Sara Dastgheib-Vinarov, *A Higher Nonobviousness Standard for Gene Patents: Protecting Biomedical Research from the Big Chill*, 4 MARQ. INTELL. PROP. L. REV. 143, 154 (2000); John Murray, Note, *Owning Genes: Disputes Involving DNA Sequence Patents*, 75 CHI.-KENT L. REV. 231, 247 (1999).

Conversely, of course, application of the biotechnology rule to software would radically change the law. The legal rules are the same, but the application of those rules to different industries produces results that bear no resemblance to each other.⁶⁶

Polk Wagner has argued that these differences need not concern us greatly, because they are merely case-specific differences rather than systematic variations by industry.⁶⁷ We simply disagree with that reading of the cases. The court's systematic conclusions in different cases, its reliance on industry-specific precedent from case to case, its focus on uncertainty in the biotechnological arts, and its emphasis in biotechnology cases on proof of structure – a discussion totally absent from the software cases – all point in the direction of industry-specific rather than fact-specific differences in legal rules.

II. Modulating Technology-Specificity

Besides divergent results, our survey of the biotechnology patent cases also highlights an important reciprocal relationship between obviousness and disclosure. In

⁶⁶ Nor are obviousness, disclosure, and patent scope the only doctrines which show such an industry-specific variation. The requirement that an invention have general utility, which has been all but eliminated in most fields of technology, see *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364 (Fed. Cir. 1999) (saying that a patented device is useful if there is a demand for it), is alive and well in the life sciences. The Supreme Court imposed a stringent requirement on pharmaceutical inventions in *Brenner v. Manson*, 383 U.S. 519 (1966). The Federal Circuit has relaxed that requirement, see *In re Brana*, 51 F.3d 1560, 1567 (Fed. Cir. 1995), but the court still requires more proof of experimentation in order to satisfy the utility requirement in biotechnology and pharmaceuticals than elsewhere. See U.S. Patent & Trademark Office, *Utility Examination Guidelines*, 60 Fed. Reg. 36263 (July 14, 1995) (describing the law as setting different standards for the life sciences); Timothy J. Balts, *Substantial Utility, Technology Transfer, and Research Utility: It's Time For a Change*, 52 SYRACUSE L. REV. 105 (2002) (describing and criticizing the higher utility standard applied to life sciences); Philippe Ducor, *New Drug Discovery Technologies and Patents*, 22 RUTGERS COMPUTER & TECH. L.J. 369, 431-33 (1996); cf. 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 (1995) (arguing that the utility doctrine may bar the patenting of "expressed sequence tags" that can be used to identify human gene sequences).

⁶⁷ R. Polk Wagner, *(Mostly) Against Exceptionalism*, cite book (2003). See also Sung, *supra* note 18 (making the same argument for the biotechnology cases).

biotechnology, where highly detailed disclosure is required to satisfy the enablement and written description standards, similarly detailed disclosure in the prior art is required to render the invention obvious. The Federal Circuit takes the patentability requirements of nonobviousness and disclosure as firmly tied to a common standard. The use and misuse of that common standard, then, is central to the development of technologically tailored patent rules.

A. The Role of the PHOSITA

The common standard connecting the requirements of obviousness and disclosure is the requirement in each statutory section that obviousness and the sufficiency of disclosure must be considered from the perspective of the "person having ordinary skill in the art," sometimes known by the acronym of PHOSITA.⁶⁸ Much of the case law concerning the PHOSITA arises out of the consideration of the obviousness standard found in § 103 of the patent statute.⁶⁹ Although originally developed as a common law doctrine, the nonobviousness criterion was codified in the 1952 Patent Act as a requirement that the claimed invention taken as a whole not be obvious to one of ordinary skill in the art at the time the invention was made.⁷⁰

The PHOSITA is equally central to calibrating the legal standard for patent disclosure. As the quid pro quo for her period of exclusive rights over an invention, the

⁶⁸ John O. Tresansky, *PHOSITA—The Ubiquitous and Enigmatic Person in Patent Law*, 73 J. PAT. & TRADEMARK OFF. SOC'Y 37 (1991); see also ROBERT L. HARMON, PATENTS AND THE FEDERAL CIRCUIT § 4.3 (5th ed. 2001); Joseph P. Meara, Note, *Just Who is the Person Having Ordinary Skill in the Art? Patent Law's Mysterious Personage*, 77 WASH. L. REV. 267 (2002). The first known use of the term PHOSITA

inventor must fully disclose the invention to the public. The first paragraph of section 112 requires that this disclosure enable “any person skilled in the art” to make and use the claimed invention.⁷¹ The parallel language suggests that the inventor’s compliance with the requirement of enablement should be measured with reference to a standard similar or identical to that in section 103; indeed, the language appears to tie the enablement requirement to nonobviousness via this shared metric.⁷²

This same language sets the metric for several related disclosure doctrines as well. First, the definition of enablement affects the patentability requirement of specific utility, as the invention must operate as described in the specification if the inventor is to enable one of ordinary skill to use it.⁷³ Additionally, compliance with the independent requirements of adequate written description and best mode disclosure is measured with reference to the understanding of a “person skilled in the art.”⁷⁴ And finally, the definiteness of patent claims, which must be written so as to warn members of the public just what is and is not covered by the patent, has traditionally been assessed with regard to the knowledge of one having ordinary skill in the art. If the terms of the claims would not be comprehensible to such a person, then they failed the requirements of section 112.⁷⁵

⁷¹ 35 U.S.C. § 112 ¶ 1 (2000).

⁷² The language of the two statutes is not identical, however, and one might draw a distinction between one of ordinary skill and “any person skilled,” on the theory that the latter standard includes those with less than ordinary skill. More on this *infra*.

The PHOSITA is nothing if not versatile, and may also show up as a convenient metric in other unexpected areas, including judicially created patent doctrines. Claim construction requires reference to how the PHOSITA would understand terms in the patent claims.⁷⁶ The PHOSITA reappears in some formulations of the standard for infringement by equivalents. In its germinal opinion on the doctrine of equivalents, *Graver Tank*, the Supreme Court indicated that the equivalence between elements of an allegedly infringing device and those of a claimed invention might be tested by determining whether the elements were known in the art to be substitutes for one another.⁷⁷ The Federal Circuit strengthened this use of the PHOSITA by making the “reasonable interchangeability” of elements—judged from the perspective of one of ordinary skill in the art—a fundamental test for equivalence.⁷⁸ A great deal of patent doctrine therefore rests upon the measurement of some legal parameter against the skill and knowledge of the PHOSITA.

This is not to say the PHOSITA has any actual skill or knowledge. Like her cousin, the reasonably prudent person in tort law,⁷⁹ the PHOSITA is something of a juridical doppelganger,⁸⁰ embodying a legal standard for patentability rather than the

burden in construing patent claims. See *Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1454-55 (Fed. Cir. 1998) (en banc).

⁷⁶ See Craig Allen Nard, *A Theory of Claim Interpretation*, 14 HARV. J. L. & TECH. 1, 6 (2000).

⁷⁷ See *Graver Tank Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 609 (1950).

⁷⁸ See *Hilton Davis Corp. v. Warner-Jenkinson*, 62 F.3d 1512, 1519 (Fed. Cir. 1995) (en banc), *aff'd in part & rev'd in part on other grounds*, 520 U.S. 17 (1997).

actual capability of any individual or group of individuals.⁸¹ Courts have on occasion equated the knowledge of a given individual, such as a patent examiner, with that of the PHOSITA.⁸² But courts walk a fine line between taking the skill of an examiner or other artisan as probative evidence of the level of skill in the art and equating the skill of such persons with the characteristics of the hypothetical PHOSITA.⁸³ Further, unlike any actual person of skill in the art, the PHOSITA is endowed with knowledge of all of the relevant prior art references.⁸⁴

This places the standard for patentability on a legally objective, rather than subjective, footing. The PHOSITA standard measures the inventor's achievements against a judicially determined external metric, rather than against an expectation based on whatever level of skill the inventor might actually possess. The standard also has the practical effect of avoiding the requirement that judges and other arbiters of patentability be experts in a given field. The PHOSITA standard is thus an ultimate conclusion of law based upon evidence,⁸⁵ not dictated by the capabilities or knowledge of the Patent Office examiner, a reviewing judge, or even that of the inventor:

Realistically, courts never have judged patentability by what the real inventor/applicant/patentee could or would do. Real inventors, as a class, vary in their capacities from ignorant geniuses to Nobel laureates; the

⁸¹ See, e.g., *Stewart-Warner Corp. v. City of Pontiac*, 767 F.2d 1563, 1570 (Fed. Cir. 1985); Michael H. Davis, *Patent Politics*, (visited Nov. 15, 2002) <http://papers.ssrn.com/sol3/papers.cfm?abstract_id=282056> (observing that the PHOSITA standard is "undeniably fictional"); David E. Wigley, *Evolution of the Concept of Non-Obviousness of the Novel Invention: From a Flash of Genius to the Trilogy*, 42 ARIZ. L. REV. 581, 598-99 (2000).

⁸² See Tresansky, *supra* note 126 at 58 (collecting cases).

⁸³ See, e.g., *In re Mahurkar Double Lumen Hemodialysis Catheter Patent Litigation*, 831 F. Supp. 1354, 1361-62 (N.D. Ill. 1993) (Easterbrook, J., sitting by designation) (taking the finding of the examiner, as a PHOSITA, to be probative of written description compliance).

⁸⁴ See *In re Winslow*, 365 F.2d 1017 (C.C.P.A. 1966).

⁸⁵ See *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561 (Fed. Cir. 1987).

courts have always applied a standard based on an imaginary worker of their own devising whom they have equated with the inventor.⁸⁶

The standard is thus objective in the sense that it does not inquire into a particular inventor or artisan's level of skill. But this does not mean that it is static or fixed. Courts consider a number of constituent factors that may be adjusted to modulate the requirements for patentability under different circumstances. The first of these is the definition of the particular "art" in which the PHOSITA is deemed to have ordinary skill. The PHOSITA is generally portrayed as having comprehensive knowledge of the references in the particular art.⁸⁷ But the parameters of the art are subject to fluctuation, and thus so is the size and depth of the library of references with which the PHOSITA is presumed to be familiar. For example, in the case of a DNA patent, would the relevant art be biochemistry or molecular biology, or cell biology, or biology in general? Courts have attempted to avoid drawing such boundaries by defining the PHOSITA's knowledge as that reasonably pertinent to the problem the inventor was trying to solve. But this requires that the court engage in the equally mercurial exercise of defining the problem that the inventor had under consideration.⁸⁸

A second PHOSITA variable that may be adjusted to different circumstances is the level of skill that would be considered "ordinary." Unlike the inventor, who almost

⁸⁶ *Kimberly-Clark Corp. v. Johnson & Johnson*, 745 F.2d 1437, 1454 (Fed. Cir. 1984). *See also In re Nilssen*, 851 F.2d 1401 (Fed. Cir. 1988) (noting that the Board of Patent Appeals and Interferences was not required to have ordinary skill in the art to apply the standard); *Hodosh v. Block Drug Co.*, 786 F.2d 1136 (Fed. Cir. 1986) (stating that actual inventors cannot be required to have the omniscience of the figurative person of ordinary skill).

by definition is presumed to be one of extraordinary skill,⁸⁹ the PHOSITA standard contemplates some median or common level of skill. In assessing that common level, courts may take into account a long list of factors, including the approaches found in the prior art, the sophistication of the technology involved, the rapidity of innovation in that field, and the level of education typical of those in the field.⁹⁰ The courts have also endowed the PHOSITA with mediocre personality traits; she is conceived of as an entity that adopts conventional approaches to problem solving, and is not inclined to innovate, either via exceptional insight or painstaking labor.⁹¹

Some care must be exercised in characterizing the PHOSITA, as it is tempting to do so on the basis of an unfounded presumption, which is that the PHOSITA remains constant from section to section of the patent statute. On the contrary, some commentators have recognized the possibility that the imaginary artisan found in these different statutory sections, though bearing the same denomination, might well display different and even inconsistent characteristics as between the different sections.⁹² The PHOSITA for purposes of obviousness may not necessarily be the PHOSITA for purposes of enablement, written description, definiteness, or equivalence. Because she is a legal construct designated to embody certain legal standards, the PHOSITA could well change depending on the purpose she is serving at the time. Understanding this difference

⁸⁹ *Standard Oil Co. v. Am. Cyanamid Co.*, 774 F.2d 448, 454 (Fed. Cir. 1995).

⁹⁰ *See, e.g., Bausch & Lomb Inc. v. Barnes-Hind, Inc.*, 796 F.2d 443 (Fed. Cir. 1986) (listing pertinent factors); *see also Helifix Ltd. v. Blok-Lok Ltd.*, 208 F.3d 1339 (Fed. Cir. 2000) (stating that district court erred by failing to consider these factors).

⁹¹ *Standard Oil Co. v. Am. Cyanamid Co.*, 774 F.2d 448, 454 (Fed. Cir. 1985).

⁹² *See Tresansky, supra* note 126 at 52-53.

is critical, because the Federal Circuit's linkage of obviousness and enablement depends on the easy equation of the PHOSITAs.

Some disparity of this sort does in fact appear in the judicial characterization of the PHOSITA in the contexts of obviousness and of enablement. The section 103 PHOSITA appears to be something of a problem solver, who the courts set to work hypothetically tackling the problem solved by the inventor.⁹³ To be sure, the obviousness PHOSITA is not an especially inspired problem solver, as she is imagined to remain stuck in the rut of conventional thinking.⁹⁴ But the obviousness PHOSITA is still someone who is trying to solve new problems. By contrast, the PHOSITA of the first paragraph of section 112 shows no such innovative tendency, but is simply a user of the technology. If the enablement PHOSITA shows any problem solving ability, it is in tapping the prior art to fill in gaps left by the inventor's disclosure—a rather different skill than that of the obviousness PHOSITA.⁹⁵

The two PHOSITAs also differ in the date at which knowledge is imputed to them. The knowledge of the obviousness PHOSITA is assessed as of the time of invention, while the enablement PHOSITA is aware of information available at the time a patent is filed. Due to the passage of time, the latter universe of references is likely to be larger. The temporal disparity is even stronger when the doctrine of equivalents PHOSITA is employed; this latter entity knows of all developments up to the date of

infringement.⁹⁶ But conversely, hidden or non-public references which may serve as prior art under section 103 are not necessarily imputed to the knowledge of the PHOSITAs who make or use the invention under section 112, as such references are not readily available to the public.⁹⁷

B. Misapplication of the PHOSITA Standard

The PHOSITA approach in general represents the proper standard for patent law. Basing the proof required on the level of skill in the art makes logical sense.⁹⁸ At the simplest level, this approach is intended to benefit the public; people who work in a given technology must understand the patent as it relates to the prior art, so it makes sense to take into account what that person knows in order to decide whether a patent is obvious or has been enabled. From a policy standpoint, the practicality of working in different technologies requires a flexible approach to determining disclosure or obviousness, and the PHOSITA approach gives a court that flexibility. In this sense, patent law is inherently technology-specific, in essence offering different and fact-sensitive standards of disclosure and obviousness for different technologies.

But even recognizing that the PHOSITA standard dictates that different technologies will be accommodated in different ways, the developments that we have described in biotechnology seem to us extraordinary and difficult to explain solely by

⁹⁶ See *Warner-Jenkinson Co., Inc. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 37 (1997) (holding that equivalence is tested at the time of infringement). Indeed, were it otherwise, the doctrine of equivalents could not feasibly be applied to later-developed technologies.

reference to the level of skill in these arts. Consider, for example, the extremely stringent disclosure standard developed in the biotechnology cases. If the PHOSITA analysis explains that requirement, it suggests that the Federal Circuit believes that biotechnology researchers need a very high degree of assurance before they are capable of replicating an invention. Computer programmers, on the other hand, apparently require very little assurance—simply an indication of function will do. Similarly, with regard to obviousness, the court appears to believe that computer programmers can fully envision working code from only a suggestion of function, whereas biotechnologists apparently need genetic sequences explicitly spelled out in the prior art to render a molecule obvious. As detailed below, we are not persuaded that the levels of skill in these arts are in fact so different, either for innovators or for users.

In this section, we seek to understand why the Federal Circuit's application of the PHOSITA standard has produced such incongruous results in the industries we studied. In order to identify the source of the anomalies in biotechnology, we look first to the Federal Circuit's application of this standard, rather than to the standard itself. One possibility, which has occurred to previous commentators as well as to us, is that the Federal Circuit application of the PHOSITA standard in these technologies is wrong as a matter of science.⁹⁹ One reading of these cases is that the Federal Circuit seems to have substituted caricature for a nuanced understanding of the technology. In the biotechnology cases, the court focuses repeatedly on the "uncertainty" inherent in the field, scoffing at claims drawn to molecular function rather than structure and demanding

precise disclosure of any embodiment.¹⁰⁰ The court seems to believe that biotechnology is as much a black art as a science, where the result of experimentation is largely out of the skilled artisan's hands. While the assumption that an art is uncertain may befit a new and undeveloped field, the court has maintained its assumption that biotechnology is an uncertain art long after the industry began to mature. The Federal Circuit has sidestepped the difficulty of determining the level of skill in the art in each case by grounding biotechnology patent standards in a doctrine of structural foreseeability. This solution is attractive to the court, as the requirement of foreseeable structure becomes an axiom from which other patent standards can be neatly derived. However, just as we are cautioned by the old maxim that when one has a hammer everything looks like a nail, it would seem that the Federal Circuit, having once crafted a solution based on structural foreseeability, begins to see every DNA patenting problem as a problem of structure. In *Bell* and *Deuel* the court's belief in uncertainty benefits the patentee, since it means that knowledge of a protein and a method for deriving the cDNA sequence did not render the cDNA sequence obvious without the disclosure of structure.¹⁰¹ By contrast, the same assumption about uncertainty hurts patentees in cases like *Enzo v. Calgene*, *Lilly* and *Amgen*, because it precludes them from claiming any DNA sequence they have not actually described in structural terms in the patent specification.¹⁰² All of these holdings are based on the

¹⁰⁰ See *supra* notes 44-51 and accompanying text (discussing the role of uncertainty in the Federal Circuit's biotechnology jurisprudence).

¹⁰¹ See *In re Deuel*, 51 F.3d 1552, 1559 (Fed. Cir. 1995); *In re Bell*, 991 F.2d 781 (Fed. Cir. 1993). Cf. *Fiers v. Revel*, 984 F.2d 1164 (Fed. Cir. 1993) (using the same standard in an interference proceeding to benefit one applicant at the expense of another). But cf. *In re Mayne*, 104 F.3d 1339 (Fed. Cir. 1997) (DNA sequence in prior art rendered obvious a claim to an altered version of that sequence that changed only one amino acid).

¹⁰² See *Enzo Biochem v. Calgene, Inc.*, 188 F.3d 1362, 1371 (Fed. Cir. 1999); *Regents of the Univ. of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997); *In re Goodman*, 11 F.3d 1046, 1052 (Fed. Cir. 1993); *Amgen Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200 (Fed. Cir. 1991).

assumption that one ordinarily skilled in biotechnology cannot move conceptually from a protein to a DNA sequence, or from the DNA sequence of one organism to the corresponding DNA sequence of another organism.

Arguably this understanding of the science of biotechnology is simply wrong. Robert Hodges has argued that “[T]he key event is the cloning of the first gene in a family of corresponding genes. Once a researcher accomplishes this very difficult task, the researcher can typically obtain other members of the gene family with much less effort.”¹⁰³ Indeed, today the process is largely automated. Such research is properly compared to searching a “black box” in which are contained molecules of known characteristics, if unknown structure; the search is conducted on the basis of what is known—the function—rather than on the basis of what is unknown— — the precise structure. The function of the molecule that will be found is predictable, as is the likelihood of finding such a molecule, even if the precise structure of the molecule cannot be predicted.¹⁰⁴

This explanation of the Federal Circuit’s jurisprudence in these areas is not altogether satisfactory, as (in biotechnology, at least) it fails to explain the court’s indifference to the technology subsequent to *Amgen*. The obviousness decision in *Amgen* clearly rested upon the uncertain likelihood of success in the particular probing

¹⁰³ Robert A Hodges, *Black Box Biotech Inventions: When a Mere “Wish or Plan” Should be Considered an Adequate Description of the Invention*, 17 GA. ST. U. L. REV. 831, 832 (2001). See also John M. Lucas, *The Doctrine of Simultaneous Conception and Reduction to Practice in Biotechnology: A Double Standard for the Double Helix*, 26 AIPLA Q.J. 381, 418 (1998) (“Making the inventions of *Amgen*, *Fiers* and *Lilly* today would be routine.”).

methodology used to find the EPO gene. Had the court adhered to this analysis in later cases, carrying forward into subsequent opinions a static impression of biotechnological techniques, the poor fit between patent doctrine and patent policy could be easily explained; indeed some commentators have offered this easy explanation.¹⁰⁵ But in those later cases, the court seems quite indifferent to the certainty or uncertainty of methodological success, fashioning instead a standard based on structural precision and foreseeability that ignores the state of technology, past or present. It seems not so much that the court misunderstood the changes in technology since *Amgen* as that the court simply ignored them.

We should here acknowledge an alternative explanation for the Federal Circuit's biotechnology decisions: that the court, rather than stumbling in its application of law to changing technology, is as a matter of law deliberately creating a unique enclave of patent doctrine for biotechnology, making patent law indeed technology specific. Yet this alternative explanation seems to us even less satisfactory than the first. If the court is taking the trouble of fashioning individual patentability standards for different areas of subject matter, one would expect that the standards fashioned would be suited to the needs of the different areas addressed. Yet as we discuss in Part III, the Federal Circuit's biotechnology cases are ill-considered as a policy matter.

C. Obstacles to Applying the PHOSITA Standard Properly

If, as we suggest, the concept of the PHOSITA makes sense, why has the Federal

there are several structural barriers that make it difficult for courts to accurately assess the level of skill in a complex technological art. As a practical matter, it is worth emphasizing that judges are at a rather serious disadvantage in trying to put themselves in the shoes of an ordinarily skilled scientist. Judges generally don't have any scientific background, and at the district court level at least, most law clerks don't either. Further, district court judges have extremely full dockets with many different types of cases. The average judge may hear no more than one patent case every few years.¹⁰⁶ Few of those will be biotechnology cases.¹⁰⁷ A very busy judge must therefore learn not only patent law but also some difficult science in a very short period of time. Expert witnesses can help, but the Federal Circuit has imposed some limits on the extent to which district courts can rely on such evidence.¹⁰⁸ In particular, courts must avoid the temptation to

¹⁰⁶ There are roughly 1700 patent cases filed per year. The exact data for the years 1995-1999 can be found in the Derwent Litalert database <<http://www.derwent.com/intellectualproperty/litalert.html>>. The data that follow were compiled as of June 1, 2000, and involve cases labeled "patent."

Year	Number of Cases Filed
1999	1,652
1998	1,730
1997	1,731
1996	1,514
1995	1,258

Id.

Most of these cases settle, however. Kimberly Moore's comprehensive study of all patent cases that went to trial found only 1,411 cases in the 17 years from 1983 to 1999, an average of less than 100 cases per year. Kimberly A. Moore, *Judges, Juries, and Patent Cases—An Empirical Peek Inside the Black Box*, 99 MICH. L. REV. 365, 380 (2000). Since there are over 600 district court judges in the United States, it is obvious that most judges get only a few filed patent cases a year, and well less than one patent trial a year. In fact, many judges get even fewer cases than this number would suggest (though others get more), since the concentration of innovation in certain regions and the permissibility of forum shopping in patent cases cause patent cases to be bunched in a few districts. See Kimberly A. Moore, *Forum Shopping in Patent Cases: Does Geographic Choice Affect Innovation?*, 79 N.C. L. REV. 889 (2001) (analyzing where patent suits are filed).

¹⁰⁷ See John R. Allison & Mark A. Lemley, *Empirical Evidence on the Validity of Litigated Patents*, 26 AIPLA Q.J. 185, 217 tbl.5 (1998) (demonstrating that between 1989 and 1996, only 3% of patent cases litigated to judgment involved biotechnology).

¹⁰⁸ See *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1584 (Fed. Cir. 1996) (stating that courts may rely on expert testimony in construing patent claims only in rare circumstances); *but see Pitney-Bowes v.*

assume that the expert witness is a person ordinarily skilled in the art.¹⁰⁹ Even the Federal Circuit, which does not suffer nearly so much from these limitations,¹¹⁰ is not in a position to fully understand all of the science it encounters.¹¹¹ Given these limitations, courts understandably won't get it right all the time.¹¹²

Second, the timing of the PHOSITA analysis complicates the court's task. While the court will determine the level of skill in the art during a pretrial hearing or at trial, the appropriate level of skill in the art is not what people know at the time of trial, but what people knew at the time of the invention (in the case of obviousness) or the filing of a

Hewlett-Packard Corp., 182 F.3d 1298, 1308 (Fed. Cir. 1999) (holding that judges may hear expert testimony on the meaning of patent claims, but may not normally *rely* on such testimony). This distinction between admitting testimony to help the judge understand the claims and reliance on such testimony may make conceptual sense, but courts reading this line of cases may be reluctant to hear such evidence at all. Plus, it will not help much in deciding pretrial motions.

More recently, the Federal Circuit has taken yet another tack on claim construction, emphasizing the importance of dictionary definitions over either the prosecution history or oral testimony. *Texas Digital Sys. v. Telegenix, Inc.*, 308 F.3d 1193 (Fed. Cir. 2002). In so doing, it seemed to denigrate the role of expert testimony in construing claims, perhaps signaling a return to a variant of the *Vitronics* approach.

¹⁰⁹ See, e.g., *Dayco Prods. v. Total Containment, Inc.*, 258 F.3d 1317, 1324 (Fed. Cir. 2001) ("Our objective is to interpret the claims from the perspective of one of ordinary skill in the art, not from the viewpoint of counsel or expert witnesses."); *Endress & Hauser v. Hawk Measurement Sys.*, 122 F.3d 1040, 1042 (Fed. Cir. 1997) ("The 'person of ordinary skill' in the art is a theoretical construct . . . and is not descriptive of some particular individual"; experts need not themselves be of ordinary skill in the art.).

¹¹⁰ While relatively few Federal Circuit judges have technology backgrounds, John R. Allison & Mark A. Lemley, *How Federal Circuit Judges Vote in Patent Validity Cases*, 27 FLA. ST. U. L. REV. 745, 751 n.23 (2000), many of their clerks do. Further, the Federal Circuit has more time to consider each case, has the full record before it, and gets many more patent cases, including software and biotechnology cases, than any district court judge would.

¹¹¹ Arti Rai argues that the Federal Circuit should defer to the PTO, because the PTO better understands biotechnology. Rai, *supra* note 104. We agree with her that the Federal Circuit makes mistakes in this area. We are not persuaded that the PTO can do any better, however, particularly given the minimal time examiners can spend on any one invention. See Mark A. Lemley, *Rational Ignorance at the Patent Office*, 75 NW. U. L. REV. 1495, 1500 (2001) (noting that examiners spend only eighteen hours per application on average).

¹¹² Cf. Stephen L. Carter, *Custom, Adjudication, and Petrushevsky's Watch: Some Notes From the Intellectual Property Front*, 78 VA. L. REV. 129, 132 (1992) (worrying that judges may not be particularly good at "judicial anthropology").

patent application (in the case of enablement).¹¹³ On average, it takes more than twelve years from the time a patent application is filed until final judgment on the merits; it takes even longer from the date of invention, of course.¹¹⁴ So courts trying to determine the level of skill in the art must learn not just science, but the history of that science. Courts and expert witnesses must shut out of their minds intervening developments in the field. This is notoriously hard to do. Empirical evidence has demonstrated that people in general, and judges in particular, are subject to a “hindsight” bias: they are likely to reason backwards from what did happen to make assumptions about what was likely to happen *ex ante*.¹¹⁵ The Federal Circuit has repeatedly recognized the problem of hindsight bias in its obviousness jurisprudence,¹¹⁶ and has built rules designed to cope with it there,¹¹⁷ but hindsight bias risks infecting the PHOSITA analysis in enablement

¹¹³ See *Arkie Lures, Inc. v. Gene Larew Tackle, Inc.*, 119 F.3d 953, 956 (Fed. Cir. 1997) (holding that PHOSITA analysis must “focus on conditions as they existed when the invention was made” in obviousness cases).

¹¹⁴ Allison & Lemley, *Empirical Evidence*, *supra* note 177, at 236 tbl.11 (12.3 years on average). This has been a particular problem in biotechnology cases, particularly because they spend longer in prosecution and because biotechnology patents are often most valuable at the end of their lives. See, e.g., *Enzo Biochem v. Calgene, Inc.*, 188 F.3d 1362, 1371 (Fed. Cir. 1999) (16 year-old invention); *Genentech, Inc. v. Novo Nordisk*, 108 F.3d 1361, 1367 (Fed. Cir. 1997) (18 year-old invention); Jeffrey S. Dillen, *DNA Patentability—Anything But Obvious*, 1997 WISC. L. REV. 1023, 1038 (noting this time lag).

¹¹⁵ There is an interesting empirical literature in the behavioral law and economics movement on hindsight bias. The existence of such a bias is well documented. In the behavioral science literature, see, e.g., Baruch Fischhoff, *Hindsight ? Foresight: The Effect of Outcome Knowledge on Judgment Under Uncertainty*, 1 J. EXPERIMENTAL PSYCHOL.: HUM. PERCEPTION & PERFORMANCE 288 (1975); Amos Tversky & Daniel Kahneman, *Availability: A Heuristic for Judging Frequency and Probability*, 5 COGNITIVE PSYCH. 207 (1973). In the legal literature, see, e.g., BEHAVIORAL LAW AND ECONOMICS (Cass Sunstein ed. 2000); Russell Korobkin & Thomas S. Ulen, *Law and Behavioral Science: Removing the Rationality Assumption from Law and Economics*, 88 CALIF. L. REV. 1051, 1095 (2000); Eric Talley, *Disclosure Norms*, 149 U. PA. L. REV. 1955, 2000 (2001). There is even empirical evidence that federal judges are subject to hindsight bias. See Chris Guthrie et al., *Inside the Judicial Mind*, 86 CORNELL L. REV. 777, 799-805 (2001).

¹¹⁶ See, e.g., *Al-Site Corp. v. VSI Int'l, Inc.*, 174 F.3d 1308, 1324 (Fed. Cir. 1999); *Monarch Knitting Mach. Corp. v. Fukuhara Indus. & Trading Co.*, 139 F.3d 877 (Fed. Cir. 1998).

¹¹⁷ See, e.g., *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999) (“Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous

and claim scope as well. Hindsight bias will normally lead factfinders to overestimate the level of skill in the art, since subsequent advances will suggest that the invention could not have been that difficult to do. This effect is likely to be the most pronounced in technologies that are familiar or readily understood by the trier of fact—that is, in the “predictable” arts. Occasionally, however, hindsight bias may have the opposite effect, notably where certain things known or believed at one time to be feasible turn out later to be more difficult than anticipated.¹¹⁸

Finally, the backward-looking nature of the legal system itself creates a problem that is in some sense the opposite of the hindsight bias. Legal rules are based on *stare decisis*. The law accumulates nuance over time by respecting and building on the body of existing precedent. Only rarely will courts expressly reject their prior decisions. This system has worked well over time in producing thoughtful legal rules.¹¹⁹ Judges trained in this process will naturally tend to apply it to factual issues they see repeatedly. Indeed, doing so seems economical as well, since revisiting those factual determinations appears redundant. Thus, once the Federal Circuit has ruled on the level of skill in a particular art, the temptation is strong for both that court and district courts to apply that

application of the requirement for a showing of the teaching or motivation to combine prior art references.”). Indeed, the Federal Circuit may have overcompensated, making it very difficult to combine references in order to prove obviousness. See Mark A. Lemley & David W. O'Brien, *Encouraging Software Reuse*, 49 STAN. L. REV. 255, 301 (1997) (making this argument). For an extremely strict statement of the legal standard on combining references, see *Winner Int'l Royalty Corp. v. Wang*, 202 F.3d 1340 (Fed. Cir. 2000).

¹¹⁸ For a detailed discussion of hindsight in biotechnology cases, see Lawrence M. Sung, *On Treating Past as Prologue*, 2001 U. ILL. J. L. TECH. & POL'Y 75.

¹¹⁹ For arguments suggesting the common law evolves towards efficiency over time, see RICHARD A. POSNER, *ECONOMIC ANALYSIS OF LAW* 23-27 (1st ed. 1979); George L. Priest, *The Common Law Process and the Selection of Efficient Rules*, 6 J. LEGAL STUD. 65 (1977); Paul H. Rubin, *Why is the Common Law Efficient?*, 6 J. LEGAL STUD. 51 (1977). Whether or not this controversial claim is correct, *stare decisis* is clearly entrenched in the legal mindset.

determination in subsequent cases. This tendency is evident in biotechnology cases. *In re Bell* concluded that knowledge of an amino acid sequence produced by a gene, coupled with a plan for identifying the DNA sequence of the gene, did not render the DNA sequence itself obvious.¹²⁰ *In re Deuel* relied on *Bell*'s conclusion, despite the fact that biotechnology had advanced somewhat between the two inventions.¹²¹ In *Regents of the University of California v. Eli Lilly & Co.*,¹²² the court expressly relied on its conclusions about the level of skill in the art in *Bell* and *Deuel* to determine its conclusions regarding written description.¹²³ *Fiers* is even more explicit in this regard, creating a firm rule that conception of a DNA sequence requires a listing of that sequence "irrespective of the complexity or simplicity of the method of isolation."¹²⁴

¹²⁰ *In re Bell*, 991 F.2d 781, 785 (Fed. Cir. 1993).

¹²¹ *In re Deuel*, 51 F.3d 1552, 1559 (Fed. Cir. 1995). In *Bell*, the prior art disclosed the amino acid sequence for the proteins of interest, and a method for cloning genes. By contrast, the art in *Deuel* disclosed only a partial amino acid sequence. Nonetheless, the passage of several years between the priority dates of the applications (*Deuel*'s application was first filed January 8, 1990, and *Bell*'s application was filed June 16, 1987) was ignored by the court, which did not focus on or even mention when the inventions occurred.

¹²² 119 F.3d 1559 (Fed. Cir. 1997).

¹²³

Example 6 provides the amino acid sequence of the human insulin A and B chains, but that disclosure also fails to describe the cDNA. Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention. *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966. We had previously held that a claim to a specific DNA is not made obvious by mere knowledge of a desired protein sequence and methods for generating the DNA that encodes that protein. *See, e.g., In re Deuel*, 51 F.3d 1552, 1558, 34 USPQ2d 1210, 1215 (1995) ("A prior art disclosure of the amino acid sequence of a protein does not necessarily render particular DNA molecules encoding the protein obvious because the redundancy of the genetic code permits one to hypothesize an enormous number of DNA sequences coding for the protein."); *In re Bell*, 991 F.2d 781, 785, 26 USPQ2d 1529, 1532 (Fed.Cir.1993). Thus, a fortiori, a description that does not render a claimed invention obvious does not sufficiently describe that invention for purposes of § 112 ¶ 1. Because the '525 specification provides only a general method of producing human insulin cDNA and a description of the human insulin A and B chain amino acid sequences that cDNA encodes, it does not provide a written description of human insulin cDNA.

Id. at 1567.

¹²⁴ *Fiers v. Revel*, 984 F.2d 1164, 1169 (Fed. Cir. 1993).

While apparently logical, the reliance on industry-specific precedent in determining the level of skill in the art is problematic. First, while both obviousness and enablement rely on the PHOSITA construct, the PHOSITA is not necessarily the same for obviousness and enablement even in a single case. Obviousness is tested at the time the invention was made, while enablement is tested at the time the application was filed. Clearly the application cannot be filed until after the date of invention, and in some cases several years elapse between the two.¹²⁵ Knowledge in the art can change during this period, sometimes dramatically. Second, and more important, the level of skill in the art will normally change between the dates of different inventions. It is hazardous, therefore, to rely on one court's statement of the level of skill in the art as determinative or even evidentiary of the level of skill in the same art at a different time. The level of skill in the art is a factual question that must be determined anew on the particulars of each case.¹²⁶

A related problem is the equally time-honored tradition of reasoning by analogy. If courts and lawyers can't find precedent directly on point, they will turn to the closest available analog. In the case of biotechnology, the court appears to have taken its understanding of DNA directly from its small-molecule chemistry cases of a generation before. But if reliance on precedent is bad in the case of the PHOSITA, reliance on analogy is worse. Expanding the search for the PHOSITA beyond a narrow definition of the field in question will almost certainly get it wrong, as indeed the court has done in the

¹²⁵ The law permits a one-year grace period between any public act and the filing of a patent application. See 35 U.S.C. § 102(b) (2000). But many inventors wait even longer between invention and the filing of an application. This is permissible, so long as they do not put the invention on sale or in public use in the interim, and do not abandon it. 35 U.S.C. § 102(c) (2000).

¹²⁶ For a detailed discussion, see Dillen, *supra* note 114, at 1039-44. The U.S. Court of Customs and Patent Appeals in *In re Driscoll*, 562 F.2d 1245, 1250 (C.C.P.A. 1977), and the Federal Circuit in *Enzo Biochem. v. Calgene, Inc.*, 188 F.3d 1362, 1374 n.10 (Fed. Cir. 1999), both recognized this. However, it has proven a hard rule to adhere to.

biotechnology cases. Given the fact-specific nature of the inquiry, the Federal Circuit may need to resist its tendency—well documented in other areas—to substitute its factual conclusions for those of the district court.¹²⁷ A clear signal by the Federal Circuit that identifying the PHOSITA is a fact-specific question that must be decided anew in each case (perhaps by reference to expert testimony) might go a long way towards solving the problem of substituting precedent and analogy for detailed analysis.¹²⁸ Courts should also spend more time and effort fleshing out the PHOSITA, who in many opinions seems to be mentioned only perfunctorily.¹²⁹ We offer more ideas for tailoring the treatment of the PHOSITA elsewhere.¹³⁰

III. Innovation, Invention and Uncertainty

The fact that the court has created technology-specific patent rules for biotechnology is not necessarily a bad thing. As we have suggested elsewhere, different

¹²⁷ See, e.g., William C. Rooklidge & Matthew F. Weil, *Judicial Hyperactivity: The Federal Circuit's Discomfort With Its Appellate Role*, 15 BERKELEY TECH. L.J. 725 (2000) (noting this problem); Arti K. Rai, *Engaging Facts and Policy: A Multi-Institutional Approach to Patent System Reform*, 106 COLUM. L. REV. — (June 2003) (arguing that the Federal Circuit's preoccupation with making factual determinations has prevented it from taking a leadership role in guiding legal rules). Empirical data suggests that the Federal Circuit is particularly unlikely to defer to district court rulings construing patent claims. See Christian Chu, *Empirical Analysis of the Federal Circuit's Claim Construction Trends*, 16 BERKELEY TECH. L.J. 1045 (2001); Kimberly A. Moore, *Are District Court Judges Equipped to Resolve Patent Cases?*, 15 HARV. J. L. & TECH. 1 (2001). Rai also argues that the Federal Circuit has not shown sufficient deference to factfinders in obviousness and disclosure cases. See Rai, *Facts*, *supra*.

¹²⁸ In this respect we agree with Wagner, who argues that improper determinations of the PHOSITA in one case should not bind courts in a later case. Wagner, *supra* note 67, at 6. But since the Federal Circuit has relied on such prior determinations, we see the current state of affairs as more problematic than he does.

¹²⁹ See Meara, *supra* note 68 (arguing that the existing factors for determining skill in the art do not work very well, and suggesting ways to refine the PHOSITA inquiry).

¹³⁰ Burk & Lemley, *Technology-Specific*, *supra* note 1, at 1202-05.

industries experience both innovation and the patent system in very different ways.¹³¹ Biotechnology is no different. We don't object, therefore, to the idea that courts treat biotechnology differently. Indeed, we embrace it. Existing law creates a variety of "policy levers" that permit and indeed may compel the courts to do so. Our concern is instead that courts do not seem to take the actual characteristics of the industry into account. As a result, the specific biotechnology rules the court has created don't work for the biotechnology industry. In this section, we talk briefly about the theories of patent law that fit the economics of biotechnology, and what those theories imply for optimal biotechnology patent policy.

A. Theories of Biotechnology Patents

There are a number of different economic theories of the patent system. These approaches exist in considerable tension. They make different and conflicting predictions about the effect of patents on industries, and dictate different and conflicting prescriptions for the parameters of patent law. We discuss five different theories in detail elsewhere;¹³² here we briefly review the two that apply most neatly to biotechnology.

1. Prospect Theory

In 1977, Edmund Kitch offered a new theory of the patent system, one which he said would "reintegrate[] the patent institution with the general theory of property

¹³¹ Burk & Lemley, *Policy Levers*, *supra* note 1.

¹³² *Id.* at Part II.A.

rights."¹³³ This prospect or property rights theory of intellectual property is rooted in many of the same economic traditions as the classic incentive-to-invent theory, but its focus is not on ex ante incentives to create as much as it is on the ability of intellectual property ownership to force the efficient use of inventions and creations through licensing once they are made.¹³⁴ The fundamental economic bases of this approach are the "tragedy of the commons" and the hypothetical Coasean world without transactions costs. The tragedy of the commons is a classic economic story, in which common property will be over-used by people who have access to it, since each individual reaps all of the benefits of his personal use, but shares only a small portion of the costs. Thus, lakes open to the public are likely to be over-fished, with negative consequences for the public (to say nothing of the fish!) in future years. Common fields will be over-grazed, with similarly unfortunate consequences. Any other exhaustible resource may be misallocated if publicly available.

The conventional economic solution to the tragedy of the commons is to assign resources as private property. If everyone owns a small piece of land (or lake), and can keep others out of it (with real or legal "fences"), then the private and public incentives are aligned. People will not over-graze their own land, because if they do they will suffer the full consequences of their actions.¹³⁵ Further, if deal-making between neighbors is

¹³³ Edmund Kitch, *The Nature and Function of the Patent System*, 20 J. L. & ECON. 265, 265 (1977).

¹³⁴ See *id.* at 276-78; Wendy J. Gordon, *Of Harms and Benefits: Torts, Restitution, and Intellectual Property*, 21 J. LEGAL STUD. 449, 473 (1992); Robert P. Merges, *Of Property Rules, Coase, and Intellectual Property*, 94 COLUM. L. REV. 2655 (1994).

¹³⁵ While in theory it is possible for cattle-owners to agree to limit their grazing in the public interest, any such effort at agreement is likely to run into insurmountable problems. Not only will organizing and policing such an agreement take effort that will not be rewarded, but individual grazers have an incentive to free ride, reaping the benefits of reduced grazing by others while refusing to reduce their own grazing. For more on these problems, see MANCUR OLSON, *THE LOGIC OF COLLECTIVE ACTION* (1961). One

costless, as Coase postulated but did not believe,¹³⁶ transactions will allow neighbors with large cattle herds to purchase grazing rights from others with smaller herds. Such transactions should occur until each piece of land is put to its best possible use.¹³⁷

In the context of intellectual property, Kitch's article remains one of the most significant efforts to integrate intellectual property with property rights theory.¹³⁸ Kitch argues that the patent system operates not (as traditionally thought) as an incentive-by-reward system, giving exclusive rights to successful inventors in order to encourage future inventors, but as a "prospect" system analogous to mineral claims. In this view, the primary point of the patent system is to encourage further commercialization and efficient use of as yet unrealized ideas by patenting them, just as privatizing land will encourage the owner to make efficient use of it.¹³⁹ Society as a whole should benefit from this equalization of private with social interests.

Fundamental to this conclusion are three assumptions. First, Kitch argues that

commentator views this internalization of (positive) externalities as a key function of property. Harold Demsetz, *Toward a Theory of Property Rights*, 57 AM. ECON. REV. 347, 348 (1967).

On the other hand, for a rejection of the tragedy of the commons approach in certain contexts, see Carol Rose, *The Comedy of the Commons: Custom, Commerce, and Inherently Public Property*, 53 U. CHI. L. REV. 711 (1986). Rose is surely correct that private division of land is not always efficient. Consider the problematic task walking through your neighborhood would be if every piece of sidewalk were privately owned by a different person, and you were required to obtain permission to take each step. Cf. Dan Hunter, *Cyberspace as Place and the Tragedy of the Digital Anticommons*, 91 CALIF. L. REV. ____ (forthcoming May 2003); Mark A. Lemley, *Place and Cyberspace*, 91 CALIF. L. REV. ____ (forthcoming May 2003) (both criticizing the excessive division of rights currently taking place online).

¹³⁶ See Ronald H. Coase, *The Problem of Social Cost*, 3 J.L. & ECON. 1 (1960).

¹³⁷ See Guido Calabresi & A. Douglas Melamed, *Property Rights, Liability Rules, and Inalienability: One View of the Cathedral*, 85 HARV. L. REV. 1089 (1972) (discussing this implication of Coase).

¹³⁸ For other property-based views of intellectual property, see, e.g., Kenneth W. Dam, *Some Economic Considerations in the Intellectual Property Protection of Software*, 24 J. LEGAL STUD. 321 (1995); I. Trotter Hardy, *Property (and Copyright) in Cyberspace*, 1996 U. CHI. L.F. 217; Edmund Kitch, *Patents: Monopolies or Property Rights?*, 8 RES. L. & ECON. 31 (1986).

¹³⁹ Kitch, *Nature*, *supra* note 133, at 270-71, 275 (making the analogy to land explicit).

a patent prospect increases the efficiency with which investment in innovation can be managed. . . . [T]echnological information is a resource which will not be efficiently used absent exclusive ownership. . . . the patent owner has an incentive to make investments to maximize the value of the patent without fear that the fruits of the investment will produce unpatentable information appropriable by competitors.¹⁴⁰

This is analogous to the tragedy of the commons argument that only with private ownership do private incentives match social incentives. In the tragedy of the commons, the private incentive to "invest" in a field or lake -- for example by letting it lie fallow, or limiting grazing, in order to permit it to grow -- is less than the social value of such an investment. In the patent context, Kitch makes an analogous argument: that the private incentive to improve and market an invention will be less than the social value of such efforts unless the patent owner is given exclusive control over all such improvements and marketing efforts.

Second, Kitch argues that "[n]o one is likely to make significant investments searching for ways to increase the commercial value of a patent unless he has made previous arrangements with the owner of the patent. This puts the patent owner in a position to coordinate the search for technological and market enhancement of the patent's value so that duplicative investments are not made and so that information is exchanged among the searchers."¹⁴¹ This is the Coase theorem at work. Under that theory, giving one party the power to control and orchestrate all subsequent use and

¹⁴⁰ *Id.* at 276.

¹⁴¹ *Id.*

research relating to the patented technology should result in efficient licensing, both to end users and to potential improvers -- assuming, that is, that information is perfect, all parties are rational, and licensing is costless.¹⁴²

Finally, for social benefit to be maximized, the property owner must make the invention (and subsequent improvements) available to the public at a reasonable price -- ideally, one that approaches marginal cost as much as is feasible.¹⁴³ But a property owner will have no incentive to reduce his prices toward marginal cost unless he faces competition from others. If the property owner is alone in the market, he may be expected to set a higher monopoly price for his goods, to the detriment of consumers (and social welfare). Kitch notes this problem, but does not resolve it. He merely points out that not all patents confer monopoly rights, and that in some cases the creators of intellectual property rights will face competition from the makers of other fungible goods, and therefore that their individual firm demand curves will be horizontal rather than downward-sloping.¹⁴⁴ If one assumes such competition, intellectual property owners may be expected to price competitively, just as producers of wheat do.

¹⁴² See Anastasia P. Winslow, *Rapping on a Revolving Door: An Economic Analysis of Parody and Campbell v. Acuff-Rose Music, Inc.*, 69 S. CAL. L. REV. 767, 780 (1996) (arguing that the Coase theorem suggests that initial assignment of property rights between original creators and improvers is irrelevant). For a discussion of what happens when we relax these unrealistic assumptions, see Mark A. Lemley, *The Economics of Improvement in Intellectual Property Law*, 75 TEXAS L. REV. 989, 1048-72 (1997). On the importance of efficient licensing to the case for intellectual property protection, see Wendy J. Gordon, *Asymmetric Market Failure and Prisoner's Dilemma in Intellectual Property*, 17 U. DAYTON L. REV. 853, 857 (1992).

¹⁴³ It is not possible to price intellectual property at its marginal cost and still stay in the business of producing new works, since developing those new works requires a fixed investment of resources (time, research money, etc.), one that frequently dwarfs the marginal cost of making and distributing copies of the idea once it has been developed.

¹⁴⁴ Kitch, *supra* note 133, at 274.

Kitch's prospect theory strongly emphasizes the role of a single patentee in coordinating the development, implementation, and improvement of an invention. The analogy to mining is instructive: Kitch's theory is that if we consolidate ownership in a single entity, that entity will have appropriate incentives to invest in commercializing and improving an invention. Indeed, on Kitch's theory one might think it appropriate to assign rights to prospect for inventions to companies even before they have invented anything, just as we do for the owners of prospecting rights, because doing so will give them the monopoly incentive to coordinate the search.

Kitch's prospect theory draws on economic literature in the Schumpeterian tradition, which in its strong form holds that companies in a competitive marketplace have insufficient incentive to innovate. On this view, only strong rights to preclude competition will effectively encourage innovation.¹⁴⁵ Prospect theory therefore suggests that patents should be granted early in the invention process, and should have broad scope and few exceptions.

Prospect theory is based on the premise that strong rights should be given into the hands of a single coordinating entrepreneur. Thus, prospect theory necessarily envisions invention as something done by a single firm, rather than collectively; as the result of significant expenditure on research, rather than the result of serendipitous or inexpensive research; and as only the first step in a long and expensive process of innovation, rather

¹⁴⁵ The classic argument cited in favor of monopolists coordinating innovation is JOSEPH A. SCHUMPETER, *CAPITALISM, SOCIALISM, AND DEMOCRACY* 106 (1st ed. 1942). For an application to patent law, see F. Scott Kieff, *Property Rights and Property Rules for Commercializing Inventions*, 85 MINN. L. REV. 697 (2001). Cf. Suzanne Scotchmer, *Protecting Early Innovators: Should Second-Generation Products Be Patentable?*, 27 RAND J. ECON. 322 (1996) (suggesting that incentives be weighted towards pioneers). Schumpeter's conclusions have been challenged, both in theoretical and empirical terms. See Burk & Lemley, *Policy Levers*, *supra* note 1, at II.A.2 (discussing this literature).

than as an activity close to a final product.¹⁴⁶ As a result, prospect theory suggests that patents should stand alone, should be broad, and should confer almost total control over subsequent uses of the product.¹⁴⁷

The prospect vision of patents maps most closely to invention in the pharmaceutical industry. Pharmaceutical innovation is notoriously costly and expensive. The pharmaceutical industry reports that it spends as much as \$800 million in R&D for each new drug produced.¹⁴⁸ While those numbers are almost certainly inflated,¹⁴⁹ there is also no doubt that R&D is extremely expensive in the pharmaceutical industry.¹⁵⁰ Further, inventing a new drug is only the beginning of the process, not the end. The Food and Drug Administration requires a lengthy and rigorous set of tests before drugs can be released to market.¹⁵¹ While imitation of a drug is reasonably costly in absolute terms, a generic manufacturer who can prove bioequivalency can avoid the R&D cost entirely, and can get FDA approval much more quickly than the first mover. The ratio of inventor

¹⁴⁶ We follow Joseph Schumpeter in distinguishing between the act of invention, which creates a new product or process, and the broader act of innovation, which includes the work necessary to revise, develop, and bring that new product or process to commercial fruition. See RICHARD R. NELSON & SIDNEY G. WINTER, *EVOLUTIONARY THEORY OF ECONOMIC CHANGE* 263 (1982) (distinguishing the invention of a product from innovation, a broader process of research, development, testing and commercialization of that product, and attributing that distinction to Schumpeter); WILLIAM KINGSTON, *DIRECT PROTECTION OF INNOVATION* (1987).

¹⁴⁷ See *supra* notes 133-44 and accompanying text.

¹⁴⁸ See Gardiner Harris, *Cost of Developing New Medicine Swelled to \$802 Million, Research Study Reports*, WALL ST. J., Dec. 3, 2001.

¹⁴⁹ Among other things, they include substantial marketing expenditures, which should not count as R&D.

¹⁵⁰ Estimates of the average cost of drug development and testing range from \$110 million to \$500 million; the latter is the industry's figure. Compare <http://www.phrma.org/publications/publications/profile01/chapter2.pdf> with <http://www.citizen.org/Press/pr-drugs33.htm>

¹⁵¹ Pharma estimates that the total time spent from the beginning of a research project to the marketing of a successful drug is 14.2 years, 1.8 years of which is due to the FDA approval process. See <http://www.phrma.org/publications/publications/profile01/chapter2.pdf>.

cost to imitator cost, therefore, is quite large in the absence of effective patent protection. As a result, it is likely that innovation would drop substantially in the pharmaceutical industry in the absence of effective patent protection.¹⁵² And as a general rule, the scope of patents in the pharmaceutical industry tends to be coextensive with the products actually sold. Patents do not merely cover small components that must be integrated into a marketable product.¹⁵³ On the other hand, if patents do not cover a group of related products, imitators can easily design around the patent by employing a close chemical analog to the patented drug.

All of these factors suggest that patents in the pharmaceutical industry should look like those prospect theory prescribes. There is in this industry no serious problem of either cumulative or complementary innovation. Strong patent rights are necessary to encourage drug companies to expend large sums of money on research years before the product can be released to the market. And because much of the work occurs after the drug is first identified, it is important to give patentees the right to coordinate downstream changes to the drug. Prospect theory fits the pharmaceutical industry.

2. Anticommons Theory

¹⁵² See, e.g., James W. Hughes et al., *Napsterizing Pharmaceuticals: Access, Innovation, and Consumer Welfare*, NBER Working Paper No. 9229 (2002) (finding that eliminating patent protection on pharmaceuticals would cost consumers \$3 in lost innovation benefits for every dollar saved in reduced drug prices).

¹⁵³ While pharmaceutical companies have tried to find ways to obtain multiple patents on the same basic invention in an effort to extend the life of their patents, these efforts are aberrations that represent a failure of the system, not its normal function. See Lara J. Glasgow, *Stretching the Limits of Intellectual Property Rights: Has the Pharmaceutical Industry Gone Too Far?*, 41 IDEA 227 (2001) (documenting efforts by pharmaceutical companies to obtain multiple patents on the same basic drug). The patent doctrine of "double patenting" is designed to prevent this sort of abuse. See, e.g., *Eli Lilly & Co. v. Barr Labs.*, 251 F.3d 955 (Fed. Cir. 2001).

While the economic literature on cumulative innovation has generally suggested the grant of divided entitlements as a means of encouraging innovation by both initial inventors and improvers, a more recent body of literature has pointed to the limits of divided entitlements in circumstances in which transactions costs are positive. Relying on Michael Heller's description of what he calls the 'anticommons,'¹⁵⁴ a number of patent scholars have argued that granting too many different patent rights can impede the development and marketing of new products where making the new product requires the use of rights from many different inventions.¹⁵⁵ Underlying this argument are concerns about transactions costs and strategic behavior, which these scholars argue will sometimes prevent the aggregation of the necessary rights.

The anticommons is characterized by fragmented property rights, the aggregation of which is necessary to make effective use of the property.¹⁵⁶ Aggregating such fragmented property rights entails high search and negotiation costs to locate and bargain with the many rights owners whose collective permissions are necessary to complete broader development. This type of licensing environment may quickly become dominated by "holdouts" who refuse to license their essential sliver of the pie unless bribed.¹⁵⁷ Because a given project will fail without their cooperation, "hold-outs" may be

¹⁵⁴ See Michael A. Heller, *The Tragedy of the Anticommons: Property in the Transition from Marx to Markets*, 111 HARV. L. REV. 621 (1998).

¹⁵⁵ See Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698 (1998). See also Arti Kaur Rai, *The Information Revolution Reaches Pharmaceuticals: Balancing Innovation Incentives, Cost and Access in the Post-Genomics Era*, 2001 U. ILL. L. REV. 173.

¹⁵⁶ Heller, *supra* note 154, at 670-72.

¹⁵⁷ On the holdout problem, see generally MANCUR OLSON, *THE LOGIC OF COLLECTIVE ACTION* (1961). On its specific application in patent law, see Rochelle Cooper Dreyfuss, *Is Pursuing the Steady Course in Genetic Patenting Taking Us Where We Want to Go?* book cite [draft at 4] (2003).

prompted to demand a bribe close to the value of the entire project.¹⁵⁸ And, of course, every property holder needed for the project is subject to this same incentive; if everyone holds out, the cost of the project will rise substantially, and probably prohibitively.

The “anticommons” problem is really a particular species of a more general problem in economics – the issue of complementarity of products. Complementarity exists where two or more separate components must be combined into an integrated system. Economists have noted the problem of double (or triple or quadruple) marginalization that can occur when different companies own rights to complementary goods.¹⁵⁹ The problem is this: If a product must include components A and B, and A and B are each covered by patents that grant different companies monopoly control over the components, each company will charge a monopoly price for its component. As a result, the price of the integrated product will be inefficiently high – and output inefficiently low – because it reflects an attempt to charge two different monopoly prices. The anticommons literature builds on this economic work, offering additional reasons to believe that the companies may not come to terms at all.¹⁶⁰

¹⁵⁸ Lloyd Cohen, *Holdouts and Free Riders*, 20 J. LEGAL STUD. 351 (1991).

¹⁵⁹ The double-marginalization theorem shows that it is inefficient to grant two monopolies in complementary goods to two different entities because each entity will price its piece without regard to the efficient pricing of the whole, resulting in an inefficiently high price. For a technical proof of this, see Carl Shapiro, *Setting Compatibility Standards: Cooperation or Collusion?*, in EXPANDING THE BOUNDARIES OF INTELLECTUAL PROPERTY 81, 97-101 (Rochelle Cooper Dreyfuss et al. eds., 2001) [Hereinafter Shapiro, *Cooperation or Collusion*]. For a description of the problem in practice, see Ken Krechmer, *Communications Standards and Patent Rights: Conflict or Coordination?* 3 (2002) (draft working paper, on file with author) (citing examples in which so many different IP owners claim rights in a standard that the total cost to license those rights exceeds the potential profit from the product); Douglas Lichtman, *Property Rights in Emerging Platform Technologies*, 29 J. LEGAL STUD. 615 (2000) (making a double-marginalization argument in favor of vertical integration in computer systems).

¹⁶⁰ There is some evidence casting doubt on whether patents in fact commonly have anticommons characteristics. See John P. Walsh, Ashish Arora, & Wesley M. Cohen, *The Patenting and Licensing of Research Tools and Biomedical Innovation* (working paper 2000) (conducting a survey and finding no

Complements or anticommons problems can arise either horizontally or vertically in an industry. The problem arises horizontally when two different companies hold rights at the same level of distribution – say, inputs into the finished product. It arises vertically if a product must be passed through a chain of independent companies (such as a monopoly manufacturer who must sell through an independent monopoly distributor), or if patents on research tools or upstream components must be integrated with downstream innovation in order to make a finished product.

The anticommons literature suggests that too many companies have patents on components or inputs into products.¹⁶¹ The problem is not so much the scope of those patents as it is the number of different rights with different owners that must be aggregated in order to participate in the marketplace. Thus, this literature addresses a dimension of patent rights not really considered in any of the theories discussed above. It is generally at odds with the divided entitlement proposals of cumulative innovation theory. There are two different ways to solve this problem: consolidate ownership of rights among fewer companies or grant fewer patents. Most legal scholars working in the anticommons literature have assumed that the solution is to grant fewer patents, particularly to developers of upstream products like research tools or DNA sequences.¹⁶² Economists, by contrast, tend to assume that the solution to vertical complementarity

evidence of anticommons problems in the biotechnology industry). But the theoretical problem certainly exists.

¹⁶¹ See Matthew Erramouspe, Comment, *Staking Patent Claims on the Human Blueprint: Rewards and Rent-Dissipating Races*, 43 UCLA L. REV. 961 (1996) (making this argument).

¹⁶² See, e.g., Arti K. Rai, *Fostering Cumulative Innovation in the Biopharmaceutical Industry: The Role of Patents and Antitrust*, 16 BERKELEY TECH. L.J. 813 (2001); Philippe Jacobs & Geertrui Van Overwalle, *Gene Patents: A Different Approach*, [2001] EUR. INTELL. PROP. REV. 505, 505 (arguing that patents should not be granted for DNA, but only for downstream medical products).

problems is to vertically integrate – that is, to consolidate rights in a single company.¹⁶³ Obviously, these two different solutions have very different implications for patent policy. As a result, the anticommons literature does not necessarily dictate particular policy results.

Anticommons theory emphasizes the problems of divided entitlements among complements. These problems can occur either horizontally or vertically, horizontally if patents cover different pieces that must be integrated into a product, and vertically if patents cover different steps in a cumulative innovation process. Anticommons theorists point to the risk of bargaining breakdown whenever the development of a product requires permission from the owners of two or more inputs. Different strands of anticommons theory suggest that the solution to this problem is either to consolidate ownership in a single owner – a result reminiscent of prospect theory – or to preclude patent protection altogether for certain types of inputs, particularly upstream research tools.

Anticommons theory maps very well onto the biotechnology industry. The biotechnology industry has some of the characteristics of the pharmaceutical industry, with which it indeed shares certain products.¹⁶⁴ In particular, the long development and testing lead time characteristic of pharmaceuticals is also evident in DNA-related innovation. These delays are due in part due to the stringent regulatory oversight

¹⁶³ Alternatively, anticommons licensing rights can be consolidated into a collective rights organization such as ASCAP or a patent pool, even if the rights themselves remain under separate ownership. For a discussion of collective rights organizations, see Robert P. Merges, *Contracting Into Liability Rules: Intellectual Property Rights and Collective Rights Organizations*, 84 CALIF. L. REV. 1293 (1996).

¹⁶⁴ Biotechnology products appear in a wide variety of economic sectors, from pharmaceuticals to foodstuffs to industrial processes. See Dan L. Burk, *A Biotechnology Primer*, 55 U. PITT. L. REV. 611 (1994). Much of our discussion will focus on a subset of biotechnology that includes gene sequences and gene therapy.

exercised over the safety of new drugs, foods, biologics, and over environmental release of new organisms. Another similarity between DNA and pharmaceuticals is that generics who wish to imitate an innovator's drug face substantially lower costs and uncertainty than do innovators in the industry. While the FDA does impose regulatory hurdles even on second-comers, the process is substantially more streamlined than it is for innovators. Indeed, the primary regulatory hurdle a generic company faces is to show that its drug is bioequivalent to the innovator's drug.¹⁶⁵ Assuming bioequivalency, the FDA allows the generic to rely on the innovator's regulatory efforts. The uncertainty associated with developing and testing a new drug is also completely absent for generic competitors; they need only replicate the drug the innovator has identified and tested. Similarly, the hard work involved in producing a cDNA sequence coding for a human protein is in identifying and isolating the right sequence; once the sequence is known a follow-on competitor can quite easily replicate it. And the existence of numerous functional equivalents to a particular DNA sequence means that patent protection must be broad enough to effectively exclude simple design-arounds, just as pharmaceutical patents must be broad enough to cover chemical analogs.

On the other hand, the total cost of sequencing a particular gene is significantly less than the cost of more traditional drug design, especially as computers have made it possible to automate much of the process.¹⁶⁶ And DNA, unlike pharmaceuticals, involves the use of both vertical and horizontal complements. Patentees have acquired

¹⁶⁵ For a discussion of this process, see, e.g., *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 676 (1990).

¹⁶⁶ See, e.g., Robert A. Hodges, *Black Box Biotech Inventions: When a Mere "Wish or Plan" Should be Considered an Adequate Description of the Invention*, 17 GA. ST. U. L. REV. 831, 832 (2001) (discussing the increasing automation of gene sequencing).

thousands of patents on DNA sequences that cover specific genes or in some cases fragments of genes.¹⁶⁷ Further, biotechnology companies have patented probes, sequencing methods, and other research tools. Any particular gene therapy requires the simultaneous use of many of these patents, leading to anticommons problems. The problem is exacerbated by “reach-through” licenses in which the owners of upstream research tools seek control of and royalties on the downstream uses of the tool.¹⁶⁸

Scholars have proposed several different ways of solving these aggregation problems. First, vertical integration of companies may make much of the problem disappear. If biotechnology companies are owned by or allied with pharmaceutical companies, the resulting company may own enough rights to research tools, gene sequences, and implementation methods to go it alone.¹⁶⁹ Alternatively, if the absolute cost of sequencing DNA is sufficiently low, or the existence of non-proprietary incentives sufficiently great, the anticommons problem could be solved by refusing to protect certain types of inventions – such as ESTs – at all.¹⁷⁰

In short, the structure of the biotechnology industry seems likely to run high anticommons risks. Product development times from creation to market are long and costly, but DNA patents are numerous and narrow. Production of any given product may require bargaining with multiple patent holders. The potential for divided patent

¹⁶⁷ See, e.g., S.M. Thomas et al., *Ownership of the Human Genome*, 380 NATURE 387, 387 (1996).

¹⁶⁸ See Rebecca S. Eisenberg, *Reaching Through the Genome* (working paper 2002).

¹⁶⁹ See Rai, *Cumulative Innovation*, *supra* note 162. Rai is critical of this form of integration, however.

¹⁷⁰ See *id.*; cf. 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 (1995).

entitlements to prevent efficient integration into products is particularly high. Anticommons theory fits DNA.

In the section that follows, we consider the implications the prospect and anticommons theories have for biotechnology patent policy. We then talk briefly about some implications of our reasoning for the related issue of pharmaceutical patent policy.

B. Designing Optimal Biotechnology Policy

If any technology fits the criteria of high cost, high-risk innovation, it is certainly biotechnology. Development of biotechnology products, particularly in the pharmaceutical sector, has been characterized by extremely long development times and high development costs. Such delays are due in part due to the stringent regulatory oversight exercised over the safety of new drugs, foods, biologics, and over environmental release of new organisms.¹⁷¹ Yet the onerous regulatory requirements to which biotechnology is subject may obscure a more fundamental uncertainty that justifies such oversight: biotechnology products arise out of living systems, and are typically intended to interact with other human or non-human living systems. Such interactions, whether physiological or ecological, are enormously complex and the systems involved poorly characterized. As a consequence, the functionality of biotechnology products is always unforeseeable, and always involves a high degree of uncertainty and risk.¹⁷² Thus, while we have argued that the Federal Circuit has been wrong to suggest that identifying and making biotechnological products – *invention* of those products – is

¹⁷¹ See *supra* notes 148-51 and accompanying text (discussing the delay and cost associated with pharmaceutical development)

always difficult and uncertain, it is also true that turning those research tools into medicines that can be sold in the market – *innovation* – is time-consuming, complex and risky.

At the same time, imitators, such as generic manufacturers, who wish to imitate an innovator's drug face substantially lower costs and uncertainty than do innovators in the industry. While the FDA does impose regulatory hurdles even on second-comers, the process is substantially more streamlined than it is for innovators. Indeed, the primary regulatory hurdle a generic company faces is to show that its drug is bioequivalent to the innovator's drug.¹⁷³ Assuming bioequivalency, the FDA allows the generic to rely on the innovator's regulatory efforts. The uncertainty associated with developing and testing a new drug is completely absent for generic competitors; they need only replicate the drug the innovator has identified and tested. Similarly, the hard work involved in producing a cDNA sequence coding for a human protein is in identifying and isolating the right sequence; once the sequence is known a follow-on competitor can quite easily replicate it.

Consistent with these characteristics and Merges' standard economic model, the current Federal Circuit jurisprudence lowers the obviousness barrier for biotechnology.¹⁷⁴ This lower barrier seems at odds with the modern science of biotechnology. The availability of research tools has made routine the isolation and characterization of biological macromolecules. As a result, considerable criticism has been directed against

¹⁷² For example, the Centocor sepsis antibody, a highly promising biotechnology treatment, succeeded in passing many years of costly trials, but failed in the last phase of FDA approval.

¹⁷³ Federal Food, Drug, and Cosmetic Act, § 505(j)(2)(A)(i), 21 U.S.C.A. § 355(j)(2)(A)(i).

¹⁷⁴ See Burk & Lemley, *Technology-Specific*, *supra* note 1, at 1178-79.

the Federal Circuit's biotechnology obviousness cases.¹⁷⁵ Given such tools, the outcome of a search for a particular nucleotide or protein seems relatively certain, and hence it is argued, obvious. But if patents are to drive innovation, rather than merely invention, in biotechnology, courts must take account of the cost and uncertainty of post-invention testing and development.¹⁷⁶ The availability or unavailability of a patent is expected to have little effect on the incentive to engage in preliminary research to, say, use the available tools to secure a macromolecule of interest.¹⁷⁷ But the ready availability of tools for finding a new biotechnology product does not change the high cost and uncertainty entailed in developing a marketable product using that macromolecule. Hence under Merges' framework a lowered standard of obviousness might seem to make sense from a policy standpoint not so much to encourage invention as a way to encourage the development of marketable products.¹⁷⁸

¹⁷⁵ KENNETH J. BURCHFIEL, *BIOTECHNOLOGY AND THE FEDERAL CIRCUIT* §6.2, at 84 (1995); Jonathan M. Barnett, *Cultivating the Genetic Commons: Imperfect Patent Protection and the Network Model of Innovation*, 37 SAN DIEGO L. REV. 987 (2000); Philippe Ducor, *New Drug Discovery Technologies and Patents*, 22 RUTGERS COMP. & TECH. L.J. 369 (1996); Arti K. Rai, *Intellectual Property Rights in Biotechnology: Addressing New Technology*, 34 WAKE FOREST L. REV. 827 (1999). See generally John M. Golden, *Biotechnology, Technology Policy, and Patentability: Natural Products and Invention in the American System*, 50 EMORY L.J. 101 (2001).

¹⁷⁶ See Robert P. Merges, *Uncertainty and the Standard of Patentability*, 7 HIGH TECH. L.J. 1 (1992); Robert P. Merges, *One Hundred Years of Solicitude: Intellectual Property Law, 1900-2000*, 88 CALIF. L. REV. 2187, 2225-27 (2000); Karen I. Boyd, *Nonobviousness and the Biotechnology Industry: A Proposal for a Doctrine of Economic Nonobviousness*, 12 BERKELEY TECH. L.J. 311 (1997).

¹⁷⁷ See, e.g., ROBERT P. MERGES, *PATENT LAW AND POLICY* 519 (2d ed. 1997).

¹⁷⁸ See ROBERT P. MERGES & JOHN FITZGERALD DUFFY, *PATENT LAW AND POLICY* 727-28 (3d ed. 2002) ("section 103 actually has a bigger effect on decisions regarding which technologies to *develop* than regarding which research projects to pursue in the first place."); see also Sirilli, *Patents and Inventors: An Empirical Study*, 16 RES. POL'Y 157, 164 (1987) (finding that patents give most inventors more incentive to commercialize than incentive to invent). One way to think of this is to conceive of patents as a financing mechanism: by providing definable rights, patents enable companies to obtain the funding they need to turn an invention into a product. See *Picard v. United Aircraft Co.*, 128 F.2d 632, 642-43 (2d Cir. 1942) (patents may serve as a "lure to investors"); Golden, *supra* note 175, at 167-172; Mark A. Lemley, *Reconceiving Patents in the Age of Venture Capital*, 4 J. SM. & EMERGING BUS. L. 137 (2000); Fritz Machlup, *Patents*, in 2 *ENCYCLOPAEDIA OF THE SOCIAL SCIENCES* 461, 467 (1968).

Yet in its current jurisprudence, what the Federal Circuit gives biotechnology with one hand, it takes away with the other. Although biotechnology patents are relatively easy to obtain under the obviousness standard, the accompanying enablement and written description standards dramatically narrow the scope of the resulting patents. By requiring disclosure of the particular structure or sequence in order to claim biological macromolecules, the Federal Circuit effectively limits the scope of a patent on those molecules to the structure or sequence disclosed.¹⁷⁹ This standard dictates that the inventor have the molecule “in hand” (so to speak) before being able to claim it. In other words, the inventor can have patent protection for any given molecule only after a substantial investment has already been made in isolating and characterizing the molecule. The result is that everyone who invests in discovering a new molecule will receive a patent, but one that is trivial to avoid infringing, at least literally. Under this standard, no one is likely to receive a patent broad enough to support the further costs of development.¹⁸⁰ Indeed, some promising lines of inquiry, such as the development of

¹⁷⁹ See, e.g., *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997) (describing rat insulin DNA did not justify claims to insulin DNA for any other mammals); *Plant Genetic Sys. v. DeKalb Genetics*, 315 F.3d 1335 (Fed. Cir. 2003) (holding a patent claim to a class of genetically engineered plants invalid for lack of enablement because only certain types of plants within the class were described, notwithstanding the pioneer nature of the invention). But see *Amgen v. Hoechst Marion Roussel*, 314 F.3d 1313 (Fed. Cir. 2003) (finding the written description requirement satisfied by a broad claim to cells used to produce EPO, where host cells, unlike DNA, were well-known in the art; the written description “requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.”). While *Amgen* certainly reads the written description requirement more laxly than *Lilly*, it appears to have limited its holding to cases in which those of skill in the art already know of a correspondence between function and structure before the invention, something that will not be true in the DNA patent cases.

¹⁸⁰ See Kenneth G. Chahine, *Enabling DNA and Protein Composition Claims: Why Claiming Biological Equivalents Encourages Innovation*, 25 AIPLA Q.J. 333 (1997) (arguing for a broader scope of biotechnology patents, extending to proteins with comparable biological activity).

Curiously, *Merges* doesn’t see this as a major problem, suggesting that in general “the Federal Circuit has overall been quite successful at integrating biotechnology cases into the fabric of patent law.” *Merges, Solicitude*, *supra* note 176, at 2228. We think the written description cases and the

drugs custom-tailored to individual DNA, may be foreclosed entirely if a biotechnology patent is not broad enough to cover the small structural variations that inhere in custom drugs.

Unfortunately, this proliferation of narrow biotechnology patents may be nearly impossible to avoid under the reciprocal structure of obviousness and enablement in current PHOSITA patent doctrine.¹⁸¹ In order for the invention to avoid obviousness, it must be deemed beyond the skill of the PHOSITA to construct given the level of disclosure in the prior art. Yet this means that in disclosing the invention, the inventor must tell those of ordinary skill a good deal more about how to make and use it, effectively raising the standard for enablement and written description. The Federal Circuit's insistence that the results of biotechnology research are unforeseeable or unpredictable avoids the problem of obviousness, but results in an extremely stringent standard for disclosure and description. Once again, the result is not optimal from the perspective of economic policy. We have suggested elsewhere a doctrinal solution to this

correspondingly narrow scope afforded biotechnology patents are a more serious problem than Merges acknowledges.

One might question why, if the written description requirement is producing such narrow DNA patents, the biomedical industries consistently cite patent protection as extremely important to them. See, e.g., Richard C. Levin et al., *Appropriating the Returns from Industrial Research and Development*, 1987 BROOKINGS PAPERS ON ECONOMIC ACTIVITY 783; Wesley M. Cohen, et al., *Protecting Their Intellectual Assets: Appropriability Conditions and Why U.S. Manufacturing Firms Patent (or Not)* (NBER Working Paper No. W7552, Feb. 2000). We think there are two answers. First, the industries that count patents as extremely valuable tend to be chemistry and pharmaceuticals, not biotechnology per se, and certainly not those in the business of discovering and using DNA sequences. Second, the biotechnology written description cases are relatively new, and the industry-specific studies are somewhat older, so their understanding of the value of patents may not reflect modern realities either because the survey is old or because those in the industry have not yet internalized the effect of these decisions.

¹⁸¹ See, e.g., Mark J. Stewart, *The Written Description Requirement of 35 U.S.C. § 112(1): The Standard After Regents of the University of California v. Eli Lilly & Co.*, 32 IND. L. REV. 537, 557-58 (1999) (noting the linkage between the Federal Circuit's view of biotechnology as an uncertain art and the narrowness of the patents that result).

particular problem, namely, treating the PHOSITA standards in obviousness and disclosure as separate policy based questions, rather than as a common standard.¹⁸²

But even given such doctrinal tools, courts must confront the policy question of the proper scope of patents in the biotechnology industry. The proper focus of biotechnology patent policy is a matter of some dispute. Merges' classic economic framework suggests that the standard of nonobviousness should be low to compensate for the high cost of innovation in the industry.¹⁸³ Both the need for effective protection and the anticommons literature suggest that the disclosure requirement should be less strict than it currently is, lest property rights be too disintegrated to permit effective licensing.¹⁸⁴ But if both the nonobviousness and disclosure requirements are lessened, the result will be more patents with broader scope. This in turn will likely produce a large number of blocking patents.¹⁸⁵ Blocking patents aren't necessarily bad, particularly when they are coupled with mechanisms like the reverse doctrine of equivalents that will relieve bargaining pressures in extreme cases.¹⁸⁶ And they will certainly give

¹⁸² Burk & Lemley, *Technology-Specific*, *supra* note 1, at 1202-05.

¹⁸³ Merges, *Uncertainty*, *supra* note 176.

¹⁸⁴ Heller & Eisenberg, *supra* note 155; Rebecca Eisenberg & Arti Rai, *The Public and the Private in Biopharmaceutical Research*, <http://www.law.duke.edu/pd/papers/raieisen.pdf>.

¹⁸⁵ For example, suppose a patentee isolates the DNA sequence for human beta-interferon, but because of the lowered disclosure requirement is entitled to claim all mammalian beta-interferon. The lowered obviousness requirement may mean that future inventors can patent rat, bat, and cat beta-interferon respectively if they discover those particular sequences; it is well established that a patent on a genus does not necessarily render obvious claims to a previously undisclosed species within that genus. *E.g.* In re Baird, 16 F.3d 380 (Fed. Cir. 1994); *Corning Glass Works v. Sumitomo Elec. U.S.A.*, 868 F.2d 1251 (Fed. Cir. 1989). Those later patents will be subservient to, but block, the original broad patent to mammalian beta-interferon.

¹⁸⁶ For detailed discussions, see Mark A. Lemley, *The Economics of Improvement in Intellectual Property Law*, 75 TEXAS L. REV. 989 (1997); Robert P. Merges, *Intellectual Property Rights and Bargaining Breakdown: The Case of Blocking Patents*, 62 TENN. L. REV. 75 (1994). There is some evidence that the reverse doctrine of equivalents may play a greater role in the biotechnology arena than elsewhere. *See, e.g.*, *Scripps Clinic & Res. Found. v. Genentech*, 927 F.2d 1565 (Fed. Cir. 1991).

biotechnology companies incentives to innovate, at least initially. But they do raise the specter of overlapping first-generation patents choking out innovation, particularly where those first-generation patents are granted on upstream research tools.¹⁸⁷ This is precisely the concern that anticommons theory identifies.

We suggest instead that courts should modify Merges' classic theory. Lowering the obviousness threshold is only one way to encourage investment in uncertain technologies. An alternative is to broaden the scope of the patents that do issue by reducing the disclosure requirement or by strengthening the doctrine of equivalents for a particular industry; doing either will encourage innovation in uncertain industries not by increasing the percentage chance of getting a patent, but by increasing the value of the patent once it is granted. In fact, it seems to us that while Merges is right to suggest that the standard of patentability should be responsive to the cost and uncertainty of innovation, obviousness is the wrong lever to use in biotechnology.¹⁸⁸ Lowering the obviousness threshold makes it more likely that marginal inventions will be patented, but does nothing to encourage inventions that would have met the (already rather modest) obviousness standard anyway. If getting from invention to market is the costly and uncertain part of the endeavor, it is these more significant inventions that we need to worry about rewarding.¹⁸⁹

¹⁸⁷ See, e.g., Eisenberg & Merges, *supra* note 53; Heller & Eisenberg, *supra* note 155.

¹⁸⁸ See also Rebecca S. Eisenberg, *Reaching Through the Genome* 26 (working paper 2002) (arguing that the Federal Circuit's low obviousness standard for biotechnology has aggravated the anticommons problem). Merges himself notes that increasing the scope of patents is an alternative to lowering the obviousness threshold. See Merges, *Uncertainty*, *supra* note 176, at 47. He doesn't pursue that alternative in his paper, however.

¹⁸⁹ Indeed, Hunt suggests that lowering the nonobviousness threshold actually creates a tradeoff, increasing the probability of acquiring a patent but reducing the value of any given patent, and therefore

This alternative approach – a fairly high obviousness threshold coupled with a fairly low disclosure requirement – will produce a few very powerful patents in uncertain industries. It will therefore solve the anticommons problem often identified with biotechnology, while at the same time boosting incentives to innovate.¹⁹⁰ This calibration of patent frequency and scope seems to us the proper response to the anticommons concern found in much of the biotechnology literature. We worry that the alternate solution proposed by certain commentators, of largely eliminating biotechnology property rights in favor of governmental control over inventions supported by public funds¹⁹¹, might unacceptably reduce the incentive for biotechnology companies to move beyond invention to innovation and product development.

Recalibrating patent scope through disclosure would seem to require a much more fundamental rethinking of the Federal Circuit's section 112 jurisprudence. The court currently requires *more* disclosure from patentees in uncertain arts, while our proposal would in fact require *less*. The key to understanding this seeming puzzle is the difference between uncertainty about invention *ex ante* and the uncertainty about innovation (getting the product to market) *ex post*. The court repeatedly intones the maxim that biotechnology is an "uncertain art."¹⁹² We think, however, that it is not so much invention as product development, production and regulatory approval that is uncertain in the biotechnology industry. From a policy perspective, the result is the same:

possibly weakening the incentive to innovate. Robert M. Hunt, *Nonobviousness and the Incentive to Innovate: An Economic Analysis of Intellectual Property Reform*, working paper 1999.

¹⁹⁰ Heller and Eisenberg, *supra* note 155; Eisenberg and Rai, *supra* note 184.

¹⁹¹ Eisenberg and Rai take this approach. *See id.*

¹⁹² *See, e.g., In re Vaeck*, 947 F.2d 488, 496 (Fed. Cir. 1991) (biotechnology less "predictable" than mechanics or electronics).

biotechnological inventions need more incentive than other types of inventions if they are actually to make it to market. But from a disclosure perspective, the difference is quite significant: there is no reason to require heightened disclosure of an invention – and correspondingly narrow its scope – if invention itself isn't uncertain in the art.

Biotechnology, then, is properly described in part by the anticommons theory (too many narrow patents must be aggregated to produce a viable product) and in part by prospect theory (a long and uncertain post-invention development process justifies strong control over inventions). A rational patent policy for DNA would seek to minimize the anticommons problems and give inventors sufficient control to induce them to walk the uncertain path towards commercial development. A variety of policy levers might be employed to this end. The utility and abstract ideas doctrines can restrict the anticommons problem in a few cases by preventing unnecessary upstream patents (for example on ESTs) that threaten to hold up downstream innovation. The written description and enablement doctrines need to be recalibrated to permit broader claiming of inventions. The doctrine of equivalents can play a similar role, perhaps by rejuvenating the doctrine of pioneer patents or by applying the notion of known interchangeability with an eye towards function, not structure. Experimental use may also have a role to play, ensuring that the long development time necessary in the biotechnology industry doesn't interfere with an inventor's ability to patent the ultimate product.¹⁹³

¹⁹³ Other policy levers may also be relevant to biotechnology. For example, arguments against injunctive relief may be stronger in biomedical cases than with other sorts of inventions. The levers we discuss in text are the most important for fashioning the incentive to innovate, however.

C. Designing Optimal Pharmaceutical Policy

Application of the uncertainty principle courts have used in biotechnology may have pernicious effects in other industries as well. For example, small-molecule chemistry has long had its own discrete set of patentability doctrines, developed in a long line of cases that attempt to accommodate the level of skill in that particular technology.¹⁹⁴ The rules articulated in this line of cases represent something of a compromise between the predictable similarities in the characteristics of molecular families and the difficulty in predicting the effect of structure in three dimensions. As a first approximation, structural relatedness between molecules disclosed in the prior art and a novel molecule claimed in a patent gives rise to a *prima facie* case of obviousness.¹⁹⁵ However, chemical structures depicted two-dimensionally on paper may not accurately reflect the properties of a physical structure that exists in three dimensions. Molecules react with one another in three dimensions, and the three dimensional configuration dictates the chemical characteristics of the molecule.

Thus, even in small molecules, the three-dimensional complexity arising from what appear on paper to be slight changes in structure may give rise to radically different properties in apparently related molecules. Even with three-dimensional modeling, the effects of such complexity have long been difficult to predict. Such unpredicted characteristics occurred with enough frequency that a rule developed allowing a *prima facie* case of obviousness in small molecules to be rebutted by evidence of unpredictable

¹⁹⁴ See *In re Dillon*, 919 F.2d 688 (1990) (recounting history of chemical obviousness cases).

¹⁹⁵ HAROLD WEGNER, CHEMICAL PATENT PRACTICE (1991).

or unexpected properties in the claimed molecule.¹⁹⁶ The technological assumption built into such a rule appears to be that the PHOSITA in small-molecule chemistry can generally predict the properties of a chemical or group of chemicals, or may occasionally be surprised by their properties, but either outcome is based on the molecules' structural depiction.

The rule in these small molecule cases appears closely related to that announced in Federal Circuit's biotechnology cases. The Federal Circuit has declared that DNA "is a chemical, albeit a complex one,"¹⁹⁷ and has articulated a desire to treat the patenting of macromolecules in the same fashion as the patenting of more traditional organic molecules. In focusing upon structural depiction as the linchpin of both obviousness and disclosure, the biotechnology cases rely upon, and appear to extend, the line of chemical cases summarized above. But just as we question the application of these rules to macromolecules, we are similarly uncertain that these special rules for obviousness in small molecule chemical cases are well suited to accommodate current chemical research practice, especially in light of the rules articulated by the Federal Circuit for macromolecules.

In particular, modern techniques of rational drug design and combinatorial chemistry seem to push against this traditional construction of chemical obviousness in much the same way that the routinization of DNA probing pushes against the rules of patentability in the biotechnology cases. For example, small-molecule chemists now

¹⁹⁶ In re Papesch, 315 F.2d 381 (C.C.P.A. 1963); see also Harold Wegner, *Prima Facie Obviousness of Chemical Compounds*, 6 AM. PAT. L. ASS'N Q.J. 271 (1978).

¹⁹⁷ In re Bell, 991 F.2d 781 (Fed. Cir. 1993); In re Deuel, 51 F.3d 1552 (Fed. Cir. 1995). *But see* Rai, *Addressing New Technology*, *supra* note 46, at 203 (arguing against treating biotechnology cases as analogous to earlier chemical cases).

search for useful compounds by first specifying the functions that they hope to find.¹⁹⁸ The characteristics of desirable molecules are represented mathematically, in equations depicting functionally equivalent chemical groups and side chains.¹⁹⁹ Based on the predictions of such mathematical models, chemists can then search through large panels of related molecules, selecting those with the closest match to predicted function.²⁰⁰

This methodology closely parallels the type of molecular "search" considered in most of the Federal Circuit macromolecule cases, where large libraries of DNA molecules are probed in order to identify those that correspond to an expected functional characteristic – e.g., the propensity to hybridize with probes of a particular nucleotide configuration, and concomitantly the capacity to code for cellular production of particular gene products.²⁰¹ Combinatorial chemistry, much like DNA probing, tends to focus upon the function of the end product, removing much of the uncertainty from the outcome of a search for a desired molecule but not necessarily from predicting the precise structure of the molecule that is ultimately found. Indeed, the role of chemical structure is to some extent marginalized, as dissimilar structures with similar functions may be treated as equivalent in narrowing the search. Just as in biotechnology, a focus on structure rather

¹⁹⁸ See generally Hugo Kubinyi, *The Quantitative Analysis of Structure-Activity Relationships* in 1 BURGER'S MEDICINAL CHEMISTRY AND DRUG DISCOVERY 497-571 (Manfred E. Wolff ed. 1995).

¹⁹⁹ RICHARD B. SILVERMAN, THE ORGANIC CHEMISTRY OF DRUG DESIGN AND DRUG ACTION 26-34 (1992) (describing the Hansch equation that correlates biological activity with physicochemical properties of drug candidates).

²⁰⁰ See Dinesh V. Patel et al., *Applications of Small-Molecule Combinatorial Chemistry to Drug Discovery*, 1 DRUG DISCOVERY TODAY 134 (1996); Jan J. Scicinski, *Chemical Libraries in Drug Discovery*, 134 TRENDS IN BIOTECHNOLOGY 246 (1995); Joseph C. Hogan Jr., *Directed Combinatorial Chemistry*, 384 NATURE 175 (1996).

²⁰¹ See generally J. WATSON ET AL., RECOMBINANT DNA 104-07 (2d ed. 1991) (describing techniques for probing libraries of cloned genes).

than function may render chemical patent protection ineffective because modern development tools render structure less important to the invention.

Consequently, the industry-specific patent prescriptions for small-molecule chemistry increasingly resemble those we have described for biotechnology. To the extent that such research is done in heavily regulated contexts, particularly for pharmaceutical applications, it faces much the same innovation profile as biotechnology. Other stringent regulatory oversight, such as EPA TSCA oversight,²⁰² may affect innovation outlooks similarly. Chemistry and pharmaceuticals, like biotechnology, seem to fit well into prospect theory. Fewer and broader patents, encouraged by relaxing the disclosure doctrines and strengthening the doctrine of equivalents, are most likely to provide the proper encouragement to innovation. A relatively robust utility doctrine can prevent anticommons problems in chemistry by preventing the patenting of numerous analogues to a successful chemical by “inventors” who don’t know what the chemical can do.²⁰³

One policy lever that will likely take on greater importance in the pharmaceutical industry than in biotechnology is patent misuse. Pharmaceutical companies have gone to great lengths to try to extend the lawful scope of their patents, by collusively settling disputes with generic companies,²⁰⁴ strategically delaying prosecution of patents, and

²⁰² Toxic Substances Control Act, 15 U.S.C.A. §§ 2601-2671.

²⁰³ Alternatively, Becky Eisenberg has suggested that FDA law can serve to encourage innovation in pharmaceuticals, not just regulate them, by granting industry-specific exclusive rights. The advantage of this industry-specific exclusivity is that it is applied downstream, to products as they enter the marketplace, and not upstream where anticommons problems are more likely. See Rebecca S. Eisenberg, *Reexamining Drug Regulation from the Perspective of Innovation Policy* (working paper 2003).

²⁰⁴ See, e.g., Herbert Hovenkamp et al., *Anticompetitive Settlement of Intellectual Property Disputes*, 87 MINN. L. REV. ____ (forthcoming 2003); Maureen A. O'Rourke & Joseph F. Brodley, *Antitrust Implications of Patent Settlement Agreements*, 87 MINN. L. REV. ____ (2003); Thomas F. Cotter, *Refining the*

obtaining multiple patents covering the same invention.²⁰⁵ The patent misuse doctrine can play a powerful role in deterring anticompetitive efforts to extend patent rights beyond the scope a rational pharmaceutical patent policy would give.²⁰⁶

Conclusion

Patent law is becoming technology-specific. The legal rules applied to biotechnology cases bear less and less resemblance to those applied in other industries, and particularly in the software cases. One can debate the wisdom of tailoring patent law to accommodate particular industries.²⁰⁷ But if the courts *are* to create a new set of legal rules for biotech cases, it only makes sense to try to design those special rules to fit the industry. While there are good policy reasons to treat biotechnology differently than other industries, the current legal rules are not expressly informed by the economics of the industry, but by an ad hoc combination of judicial policymaking and stare decisis. Not surprisingly, they don't reflect optimal patent policy in biotechnology. We have offered some explanations for this phenomenon, along with a sketch of how an optimal

"Presumptive Illegality" Approach to Settlements of Patent Disputes Involving Reverse Payments, 87 MINN. L. REV. ____ (2003).

²⁰⁵ On these latter strategies, see Glasgow, *supra* note 153, at 248-51.

²⁰⁶ Alternatively, the problem could be controlled to some extent using policy levers relating to obviousness. Pharmaceutical companies often engage in the practice of "double-patenting": seeking multiple patents on the same or only slightly different technologies in an effort to extend the effective life of their proprietary right. Strengthening the obviousness standard will make it harder to extend patent life through double-patenting, because the doctrine of "obviousness-type double patenting" precludes obtaining two patents that would be obvious in view of one another unless the patentee disclaims the longer patent term. See, e.g., *Ortho Pharmaceutical Co. v. Smith*, 959 F.2d 936 (Fed. Cir. 1992).

²⁰⁷ For a detailed discussion of the wisdom of both legislative and judicial industry-specificity, see Burk & Lemley, *Policy Levers*, *supra* note 1, at Part III.

biotechnology patent law might look. Unfortunately, the Federal Circuit's current trends in biotech won't get us there.