The Unblazed Trail: Bioinformatics and the Protection of Genetic Knowledge*

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INTRODUCTION

The history of the endeavor to understand the human condition, fueled in part by the desire to prolong or otherwise enhance the enjoyment of life, will mark this year with great significance. On February 12, 2001, the world awoke to the news sensation of the achievement of a milestone in genetic knowledge arguably unrivaled by any other previously.[1] The scientific research teams dedicated to

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1. *See, e.g.*, *Scientists Set to Announce Major Advances in Mapping the Human Genome* (*Early Edition*, CNN television broadcast, Feb. 12, 2001) ("[I]n just three hours, we're going to hear what could be the beginning of a revolution in the practice of medicine. An announcement regarding the mapping of all the genes in the human body will be made in Washington."); *Human Genome Decoded* (*Today*, NBC television broadcast, Feb. 12, 2001) ("This morning details on what may be the most amazing scientific accomplishment ever, the mapping of the human genome. Last June, scientists on competing teams announced they had done it, and today they are releasing their results, and it could revolutionize the future of medical care."); *Map of Human Genome Debuts with Some Big Surprises* (*World News This Morning*, ABC television broadcast, Feb. 12, 2001) ("History will have to judge, of course, but scientists say they may be at a turning point comparable to Copernicus figuring out the layout of the solar system or Darwin beginning to understand how plants and animals evolved."); *Two Rival Studies Offer the First Detailed Look at Most of the Human Genetic Code* (*The Early Show*, CBS television broadcast, Feb. 12, 2001).

> We've been trying in the 20th century to try to treat disease without even knowing what the parts were, without knowing what was wrong in diseases like diabetes or

the elucidation of the precise structural nature of the chemicals that encode the design of the human organism announced the release of their long anticipated findings—the nucleotide sequence of the human genome.[2]

For even the most casual observers, the accomplishment underlying this report was earthshaking.[3] Even for those who had closely monitored the progress of this project throughout its years of intensive effort, the publication of the human genome sequence was no less heralded. Indeed, the editors of *Science*, one of the two leading scientific journals to report this data, pronounced it a

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asthma or hypertension. It'd be like bringing your car to an auto mechanic who didn't know what was under the hood, didn't know the parts.

Id.; *see also* Clive Cookson, *A Glimpse of the Secrets of Life: The Results of the Human Genome Project Show Unexpected Layers of Complexity in our Genes*, FIN. TIMES (LONDON), Feb. 12, 2001, at 21.

Eight months ago, Bill Clinton and Tony Blair linked up to proclaim one of science's greatest achievements: decoding the human genome or "book of life." But that public relations spectacular was not supported by research data or conclusions. This week scientists get their first look at the evidence, with the official publication of the human genome sequence in the journals *Nature* and *Science*.

Id.; *China on Par With Developed Countries in Genome Research*, XINHUA DAILY NEWS SERVICE, Feb. 12, 2001.

The latest map and preliminary conclusion on the human genome by experts from China and five developed countries indicate China is on a par with the developed countries in this field . . . . [T]he progress, unveiled late Monday by international sciences news weekly *Science* and *Nature*, is the result of international cooperation. The research demonstrates the strength of China, the only developing country allowed to join the project, in this advanced research field . . . .

Id.

2. *See* Elizabeth Pennisi, *The Human Genome*, 291 SCIENCE 1177, 1178 (2001):

Just obtaining the sequence is a phenomenal achievement, one that many researchers did not believe possible 15 years ago . . . . Spelling out the entire sequence, all 3 billion or so chemical letters that make up DNA along each chromosome, would fill tomes equivalent to 200 New York City phone books . . . . Perhaps most humbling of all is the finding . . . that humans have 32,000 genes, give or take a few thousand.

3. *See* Leslie Roberts, *Controversial From the Start*, 291 SCIENCE 1182, 1182 (2001):

The human genome: the crown jewel of 20th century biology, heralded at the White House, plastered on the covers of countless magazines–and at last spelled out today in intricate detail in both *Science* and *Nature*. Deciphering this string of 3 billion A's, T's, G's, and C's is being hailed as an achievement that will usher in a new era of biology and even alter our understanding of who we are.

"historic moment for the scientific endeavor."[4] The message to the scientific community, however, also appeared to reflect a tenor of underlying concern.

> Humanity has been given a great gift. With the completion of the human genome sequence, we have received a powerful tool for unlocking the secrets of our genetic heritage and for finding our place among the other participants in the adventure of life . . . .
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> It should be no surprise that an achievement so stunning, and so carefully watched, has created new challenges for the scientific venture.[5]

To be sure, the process of discovering our genetic code, from its inception, has fostered coincident public scrutiny and concern, which included portents of privacy loss, genetic discrimination, and eugenics.[6] Perhaps most controversial, however, were the issues of ownership and exclusivity obtainable through patent protection to aspects of the human genome.[7] The public debate aside, the federal

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4. *See* Barbara R. Jasny & Donald Kennedy, *Editorial: The Human Genome*, 291 SCIENCE 1153, 1153 (2001) (commemorating the contemporaneous publications of the human genome sequence in *Science* by J. Craig Venter et al. of Celera Genomics, a private enterprise, and in *Nature* by the International Human Genome Sequencing Consortium, a publicly-funded international cooperative of laboratories led by Francis Collins).

5. *See id.* (indicating that "access to all the data needed to verify conclusions" and "protection against piracy [to] enable other proprietary data to be published after peer review" are important considerations).

6. *See* Jeremy A. Colby, *An Analysis of Genetic Discrimination Legislation Proposed by the 105th Congress*, 24 AM. J.L. & MED. 443, 443-44 (1998).

> [G]enetic information may also result in a world characterized by genetic discrimination and genetic determinism. Although genetic information will be used to develop revolutionary treatments, such as gene therapy and other molecular medicine, it will also bring genetic discrimination and heretofore unrealized invasions into the privacy of our genetic codes.

Id.

7. *See* Eliot Marshall, *Sharing the Glory, Not the Credit*, 291 SCIENCE 1189, 1191 (2001) (reporting the stern reaction by scientists to the negotiations between Celera and *Science* of "a balanced plan, requiring Celera to release data freely to academics but allowing the company to protect its database by requiring readers to obtain access at a company site and register as academic or commercial users"). Of course, the U.S. patent system has supporters and detractors alike as a general proposition. Nevertheless, its significance, positive or negative, to the business community appears clear. *See* John R. Allison & Mark A. Lemley, *Taking Stock: The Law and Economics of Intellectual Property Rights: Who's Patenting What? An Empirical*

courts, principally the Court of Appeals for the Federal Circuit,[8] and the U.S. Patent and Trademark Office (USPTO), attempted to provide guidance on the intellectual property rights that might impact such matters involving the human genome and other genetic data. These efforts, however, met with, at best, lackluster support from patent law practitioners and other commentators, as well as the general public.[9]

In recent days, public debate in this regard focused on the proper scope, if any, of patent protection for genetic discoveries generally and for expressed sequence tags (ESTs) and single nucleotide polymorphisms (SNPs) specifically. Two concerns prevail. The first relates to the challenge, pursuant to the written description requirement of the patent law, to patent coverage of inventions pertaining to genes or gene fragments where the applicant failed to disclose the corresponding nucleotide sequence information. The second involves whether isolated and purified nucleic acid fragments with no known association or other functionality can satisfy the patent law requirement of utility as well as written description.

Exploration of Patent Prosecution, 53 VAND. L. REV. 2099, 2100 (2000).

> Patents are big business. Individuals and companies are obtaining far more patents today than ever before. Some simple calculations make it clear that companies are spending over $5 billion a year obtaining patents in the U.S.–to say nothing of the costs of obtaining patents elsewhere, and of licensing and enforcing the patents. There are a number of reasons why patenting is on the rise; primary among them are a booming economy and a shift away from manufacturing and capital-intensive industries towards companies with primarily intellectual assets. But whatever the reason, it is evident that many companies consider patents important.

Id.

8. The Federal Circuit has exclusive jurisdiction of appeals in civil actions across the country that arise under the patent statutes. *See* 28 U.S.C. § 1295 (1994) (vesting the Federal Circuit with exclusive jurisdiction in patent appeals from final judgments and orders of the U.S. district courts and the U.S. Court of Federal Claims, from decisions of the Board of Patent Appeals and Interferences of the U.S. Patent and Trademark Office, from decisions of the Commissioner of Patents and Trademarks, and from decisions of the U.S. International Trade Commission); *see also* S. REP. NO. 275, at 2 (1981), *reprinted in* 1982 U.S.C.C.A.N. 11, 12 (describing the legislative rationale behind the establishment of the Federal Circuit with the enactment of the Federal Courts Improvement Act of 1982, Pub. L. No. 97-164, 96 Stat. 25, 37 (codified as amended at 28 U.S.C. § 1295 (1994)).

9. *See* Jerry Knight, *Biotech Stocks Tougher to Unravel Than Genome*, WASH. POST, Feb. 19, 2001, at E01 (warning about investment in biotechnology companies because "[t]heir science is so complex, their business strategies so unpredictable, their path to profitability so uncertain–to say nothing of so long–that it's impossible to calculate what each stock is worth or which is better to buy").

Given the reactive nature of the patent system, particularly in a technical art such as biotechnology, where the law today deals with the potentially decades old science, the legal issues center on early research work in recombinant protein production and genomics.[10] With the human genome sequence in hand now, scientists and other interested members of the public recognize that the practical applications will likely include better, faster, and cheaper routes to drug discovery and advances in medical practice.[11] This progress depends in large part on other scientific fields, that of bioinformatics (once better known as computational biology) and proteomics.[12] The

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10. *See* Courtney J. Miller, *Patent Law and Human Genomics*, 26 CAP. U. L. REV. 893, 984 (1997).

> The genomics industry is a complex and frustrating combination of philanthropy and commercialism, science and law. The basic premise of sequencing the human genome is that such a venture will benefit humankind, but the importance of protecting the significant financial and physical investments required to sustain the effort have resulted in the need for definitive federal legislative guidelines concerning the intellectual property generated as the genomics industry matures.

Id.

11. *See* Sara Dastgheib-Vinarov, *A Higher Nonobviousness Standard for Gene Patents: Protecting Biomedical Research from the Big Chill*, 4 MARQ. INTELL. PROP. L. REV. 143, 158-59 (2000).

> In the new millenium, computational and molecular techniques allow scientists to accomplish what was once deemed impossible. Some of these techniques include designing optimum DNA probes for PCR and comparing three-dimensional protein secondary structure of various species with their mRNA sequences on a computer. These techniques, which reduce experiment times from days to minutes, have made most traditional molecular biological procedures obsolete.

Id.; Lawrence M. Sung & Don J. Pelto, *Bioinformatics May Get Boost From "State Street,"* NAT'L L.J., Oct. 19, 1998, at C28.

> How quickly scientists achieve these goals thus may depend little on the breakneck pace at which they undertake to obtain new DNA sequence information by brute force. Indeed, the smart money is now focusing on how long it takes to understand what the exploding storehouses of genetic information actually teach. The true race is not to see who first maps every last stretch of human DNA, but who can most successfully identify candidates for effective drug and gene therapy based on genetic information with little, if any, known biological significance.

Id.

12. *See* 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, 555 n.153 (1999) ("The development of bioinformatics is beginning to manage the increasing amount of genetic sequence information that is becoming available. Bioinformatics provides ways to analyze DNA and protein sequences and make predictions regarding structure or

legal ramifications of intellectual property protection in this developing research area will probably take years to manifest, but might engender as much, if not more, public debate than that presently observable with biotechnology patents.[13]

This Article begins with a review of the legal treatment of biotechnology patents involving genetic information and addresses contemporary issues facing the federal courts and the USPTO. A consideration follows regarding the likely patent protection scenarios

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function relationships.") (citing ANDREAS D. BAXEVANIS & B.F. OUELLETTE, BIOINFORMATICS: A PRACTICAL GUIDE TO THE ANALYSIS OF GENES AND PROTEINS (1st ed. 1998)); Ronald Cass et al., *Advances in Biomaterials and Devices, and Their Financing*, 6 B.U. J. SCI. & TECH. L. 2, 6 (2000).

> How bioinformatics and genetic engineering become important is that one can use information from the human genome project. The idea is then to use this information to help predict what functions other proteins or other regions of proteins are involved in—not only cellular adhesion but also other cellular roles such as cell death, growth, and migration and differentiation.

Id.; David Malakoff & Robert F. Service, *Genomania Meets the Bottom Line*, 291 SCIENCE 1193, 1201 (2001) ("Toolmakers, information suppliers, and discovery companies are already looking beyond genomics to proteomics, the latest effort to demystify the functions of the proteins coded for by all those genes. Surveying genes is a good way of finding possible drug targets, the reasoning goes."); Stanley Fields, *Proteomics in Genomeland*, 291 SCIENCE 1221, 1221 (2001) ("In the wonderland of complete sequences, there is much that genomics cannot do, and so the future belongs to proteomics: the analysis of complete complements of proteins.").

13. *See* Rebecca S. Eisenberg, *Genetics and the Law: The Ethical, Legal, and Social Implications of Genetic Technology and Biomedical Ethics: Intellectual Property at the Public-Private Divide: The Case of Large-Scale cDNA Sequencing*, 3 U. CHI. L. SCH. ROUNDTABLE 557, 565 (1996).

> Despite the growth of the public database, the private databases remain significantly larger. Inasmuch as all the information that enters the public database promptly becomes available in the private databases as well, the public database can never contain more information than the private databases. The private database owners also claim to offer superior products in that they have assembled contiguous fragments into longer sequences, they provide more complete annotations for the sequences, including information about expression in different types of tissue, they provide sequence information from customized cDNA libraries derived from tissue types of interest to their subscribers, and their sequence information comes with high-powered bioinformatics capabilities and user-friendly software. Ironically, Merck's investment in enhancing the public database may have enhanced the value of the private databases as a resource for discovery, not only by contributing further data to make the information in the private databases more complete, but also by creating a deluge of information that enhances the value of the complementary proprietary bioinformatics capabilities that the private database owners offer to their clients.

Id. (internal citations omitted).

surrounding bioinformatics and proteomics. The Article concludes with various proposals for the enhancement of progress in bioinformatics and proteomics, and other beneficiary research fields of genomics, through the securing of intellectual property rights.[14]

I

The protection of genetic information under patent law raises several issues. A prominent issue concerns the characterization of nucleic acids as basic research tools, to which easy access is considered vital to the progress of science.[15] With knowledge of a particular nucleotide sequence, a scientist can engage in further experimentation, including a determination of whether that sequence is physically present in a sample, as well as whether transcription or translation products corresponding to that sequence are produced. In addition, nucleic acids of consequence can be used to construct recombinant proteins. In this sense, as structural components, nucleic acids can be used to facilitate further discovery. There is another facet to the character of nucleic acids.

Beyond its nature as a chemical compound, a nucleic acid serves as a storage medium for biological information.[16] The nucleotide sequence alone can provide an understanding of the relative significance of the specific nucleic acid and the products it encodes. As such, the genetic knowledge a nucleic acid contains can be as

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14. *See* Emanuel Vacchiano, *It's A Wonderful Genome: The Written-Description Requirement Protects The Human Genome From Overly-Broad Patents*, 32 J. MARSHALL L. REV. 805, 830 (1999).

> Congress and the biotech community must consider implementing a special patent category for patents to human DNA segments where a medical or industrial utility is not demonstrated. This special patent category would award a limited term based on a diminished examination process. For example, a five-year term can be appropriate for these patents, although such a determination requires considerable comment from the biotech community before implementation.

Id.

15. *See* Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 698 (1998).

16. *See* R.C. Lewontin, *In the Beginning Was the Word*, 291 SCIENCE 1263, 1263 (2001) (reviewing LILY E. KAY, WHO WROTE THE BOOK OF LIFE? (2000), and noting her examination of "how the view that DNA is 'information' that is 'written' in a 'language' whose 'words' are in 'code' has driven the research program and claims of molecular biology").

inseparable from the discrete chemical compound as a personality is from the human individual.

This knowledge creates a problem, however, because intellectual property law is not intended to vest ownership in information per se. The essence of nucleic acids as both chemical compounds and information reservoirs, therefore, fosters a dichotomy that the patent law, in particular, is ill-equipped to reconcile. If patent protection to nucleic acids was accorded based solely on their chemical character, for example, claims might be issued that would be arguably overbroad.[17] The fundamental inquiry remains whether the discoverer of a certain isolated and purified nucleic acid provides the public with knowledge worthy of the reward of a temporary right of exclusivity.

The USPTO and federal courts have addressed the patentability of genetic discoveries.[18] Until relatively recently, all were situations in which the patent applicant disclosed the genetic knowledge in conjunction with the chemical structure.[19] In these cases, the public

17. Assuming arguendo the inevitability of such unreasonable patent claims, then various remedies can be proposed to ameliorate the detrimental effects. Among such notions are an expanded infringement exemption for pure academic, or otherwise non-commercial, research similar to the fair use defense under copyright law. *Cf.* Julie E. Cohen & Mark A. Lemley, *Patent Scope and Innovation in the Software Industry*, 89 CAL. L. REV. 1, 18 (2001) (recognizing that presently the "patent statute includes no express provision allowing reverse engineering, nor is there any judicially-developed exception akin to copyright's fair use doctrine that might permit it"). Another possibility is a broader infringement exemption for experimental use. *Cf. id.* at 29 (noting that although the "patent statute itself contains only a narrow experimental use defense . . . [under 35 U.S.C. § 271(e)] there is also a non-statutory exception for experimental uses"). A third option is compulsory licensing. In recent days, compulsory licensing issues have arisen in the international context of government-sanctioned generic substitutes for patented AIDS medicines. *See* Jon Jeter, *Trial Opens in South Africa AIDS Drug Suit*, WASH. POST, Mar. 6, 2001, at A01 (reporting on the lawsuit brought by thirty-nine foreign drug manufacturers in Pretoria High Court to block any action pursuant to the 1997 South African statute, the Medicines Control Act, which authorizes South Africa's health minister to control the import and pricing of AIDS medications, irrespective of existing patent rights).

18. *See, e.g.*, *In re* Mayne, 104 F.3d 1339 (Fed. Cir. 1997); *In re* Alton, 76 F.3d 1168 (Fed. Cir. 1996); *In re* Goodman, 11 F.3d 1046 (Fed. Cir. 1993); *In re* Bell, 991 F.2d 781 (Fed. Cir. 1993); *In re* Vaeck, 947 F.2d 488 (Fed. Cir. 1991); *In re* O'Farrell, 853 F.2d 894 (Fed. Cir. 1988).

19. *See, e.g.*, Monsanto Co. v. Mycogen Plant Science, Inc., 261 F.3d 1356 (Fed. Cir. 2001) (concerning claims reciting the introduction into plants of recombinant DNA known to make them more resistant to insects by genetic modification to express a *Bacillus thuringiensis* protein, which is toxic to various insects); Singh v. Brake, 222 F.3d 1362 (Fed. Cir. 2000) (involving the appellate review of an interference proceeding before the USPTO Board of Patent Appeals and Interferences concerning a DNA construct known to relate to alpha-factor,

benefit rationale underlying the patent system is arguably satisfied—the public is taught the what, why, when, where, and how of the biological significance as well as the chemical structure of the patented nucleic acid. By contrast, more recent patent applications to some genetic discoveries, such as ESTs and SNPs, disclose little, if any, corresponding genetic knowledge.[20] The present controversy over patenting genes generally appears to center on these certain inventions that are accompanied by minimal disclosure of associative or functional biological relevance.

In any event, the advent and increasing precision of technologies like bioinformatics and proteomics might better facilitate the patentability of gene fragments randomly isolated from samples. Even where no known association or function can be ascribed to it upon isolation, a nucleic acid might begin to impart such knowledge with the aid of predictive modeling available through bioinformatics and proteomics.[21] Accordingly, perhaps the controversy over patenting genes that derive from concerns over ESTs and SNPs will subside as the state of the art progresses, allowing scientists to recognize meaning in the otherwise bare nucleotide sequences.[22]

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also known as alpha-mating factor, which is a peptide released by the budding yeast *Saccharomyces cerevisiae* when a haploid cell is prepared to mate); Schering Corp. v. Amgen Inc., 222 F.3d 1347 (Fed. Cir. 2000) (involving recombinant DNA molecules known to encode specific types of human interferon).

20. *See infra* note 115.

21. Of course, fans and critics alike can find support in their positions on the relative success of computer predictive modeling, as evidenced in many other fields such as seismic and weather forecasting. *See More Quakes Ahead for Pacific Northwest?* (Mar. 1, 2001), *at* http://www.cnn.com/2001/TECH/science/03/01/quake.folo/index.html. ("Will another powerful earthquake rip through western Washington State or the region after Wednesday's big one? Despite considerable improvements in seismology, no one knows for sure . . . . The more we learn about earthquakes, the more elusive real predictions seem to be."). *Compare Major Storm Poised to Unload Snow on U.S. East Coast* (Mar. 4, 2001), *at* http://www.cnn.com/2001/WEATHER/03/03/weather.storm.02/. ("U.S. East Coast residents with travel plans for Monday are being warned of a powerful storm moving into the region that has the potential to be the worst so-called "nor'easter" in 50 years."), *with Snow Across the Northeast* (Mar. 6, 2001), *at* http://www.cnn.com/2001/WEATHER/03/06/winter.storms.02/index.html ("A major snow-storm traveling on the strength of a howling nor'easter crept into New England overnight Monday into Tuesday morning, but the storm didn't pack the punch officials had expected.").

22. *Cf.* David S. Roos, *Bioinformatics-Trying to Swim in a Sea of Data*, 291 SCIENCE 1260, 1261 (2001):

> The 'postgenomic era' holds phenomenal promise for identifying the mechanistic bases of organismal development, metabolic processes, and disease, and we can

In the meantime, the development of the legal authority trails years, if not decades, behind.[23] Given the history of such resolutions, the federal courts will have many years before needing to confront patents granted on nucleic acid discoveries with little, if any, corresponding genetic knowledge. Thus, no applicable precedent exists today. Instead, the extant decisions focus on the aspect of genes or gene fragments as chemical entities, and not on their coincidental information content.[24] Indeed, a review of the most recent Federal Circuit cases, for example, reveals the straightforward consideration of genetic discoveries as chemical inventions.[25]

> confidently predict that bioinformatics research will have a dramatic impact on improving our understanding of such diverse areas as the regulation of gene expression, protein structure determination, comparative evolution, and drug discovery. The availability of virtually complete data sets also makes negative data informative: by mapping entire pathways, for example, it becomes interesting to ask not only what is present, but also what is absent. As the potential of genomics-scale studies becomes more fully appreciated, it is likely that genomics research will increasingly come to be viewed as indistinguishable from biology itself. But such research is possible only if data remain available not only for examination, but also to build upon.

23. *See* Lawrence M. Sung, *Stranger in a Strange Land: Biotechnology and the Federal Circuit*, 2 Wash. U. J.L. & Pol'y 167, 170 (2000) (noting a potential failure to appreciate the significant temporal distortion that exists with the decisions of the Federal Circuit in appeals involving biotechnology inventions and the attendant possibility that the casual observer might conclude the court's biotechnology judgments are senseless, because they rest on anachronistic notions of the science). The author explains:

> The effective date of the filing of a patent application often dictates what prior art the invention must overcome to qualify for patent protection. In addition, the breadth and depth with which applicants must describe their inventions in patent applications can depend upon the respective filing dates. The judicial consideration of the patentability of the subject matter in a patent application, or the validity of an issued patent, therefore must focus on the state of the art at the time of the patent application rather than the time of the dispute.
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> The disparity between the filing of the patent application and the conclusion of the patent infringement lawsuit is perhaps more pronounced in the field of biotechnology than in the electrical, mechanical, or even chemical arts. The prosecution of biotechnology patent applications in the U.S. Patent & Trademark Office (USPTO) and the litigation of issued biotechnology patents both commonly exhibit a lengthier duration than that with most other types of inventions. In biotechnology matters, it is not uncommon for the Federal Circuit to apply the patent laws to decades-old science.

Id.

24. *See infra* Part II.

25. *See* Ajinomoto Co. v. Archer-Daniels-Midland Co., 228 F.3d 1338 (Fed. Cir. 2000) (standing, oath, enablement, best mode, claim construction, infringement, importation,

II

To obtain a patent, the applicant must be able to demonstrate that the claimed invention is useful.[26] The utility of an invention, in concert with its novelty and nonobviousness, merits the reward of patent protection.[27] Whether a claimed invention lacks utility is a question of fact, which the Federal Circuit reviews under the clearly erroneous standard.[28] In any event, an alleged inventive act is not legally cognizable unless the inventor conceived of the specific utility of the claimed invention.[29]

In *Kridl v. McCormick*,[30] the Federal Circuit addressed the utility requirement in the context of a patent interference proceeding.[31] The court reviewed the determination of the USPTO Board of Patent Appeals and Interferences (Board), which considered two competing patent applications claiming the same, or substantially the same, biotechnology subject matter.[32] The interference count related to the use of antisense technology to produce plants or plant cells with

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damages); SIBIA Neurosciences, Inc. v. Cadus Pharm. Corp., 225 F.3d 1349 (Fed. Cir. 2000) (obviousness); Life Techs., Inc. v. Clontech Labs., Inc., 224 F.3d 1320 (Fed. Cir. 2000) (inequitable conduct, prior inventorship); Singh v. Brake, 222 F.3d 1362 (Fed. Cir. 2000) (conception, written description, enablement); Schering Corp. v. Amgen Inc., 222 F.3d 1347 (Fed. Cir. 2000) (claim construction); Genentech, Inc. v. Chiron Corp., 220 F.3d 1345 (Fed. Cir. 2000) (conception); Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362 (Fed. Cir. 1999) (enablement, experimental use).

26. *See* 35 U.S.C. § 101 (1994) ("Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.").

27. Brenner v. Manson, 383 U.S. 519, 534 (1966) ("The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility."); Cross v. Iizuka, 753 F.2d 1040, 1044 (Fed. Cir. 1985).

28. *See* Raytheon Co. v. Roper Corp., 724 F.2d 951, 956 (Fed. Cir. 1983).

29. *See* Rey-Bellet v. Engelhardt, 493 F.2d 1380, 1385 (C.C.P.A. 1974) ("[C]onception of an invention is not complete absent a conception of its utility.").

30. 105 F.3d 1446 (Fed. Cir. 1997).

31. *Id.* at 1447. The USPTO may declare an interference where a patent application claims the same, or substantially the same, subject matter as another application or as an unexpired patent. *See* 35 U.S.C. § 135 (1994). In this proceeding, the USPTO determines which party has priority of invention, or in other words, who was the first to invent. Because the first to invent is the only true inventor entitled to patent protection, the outcome of an interference proceeding typically leaves the winner with a patent and the loser without.

32. 105 F.3d at 1448 (reporting the interference declared between a patent application assigned to Agracetus, Inc., and another assigned to Calgene, Inc.).

resistance to certain viruses.[33] McCormick, having filed a patent application before Kridl, was the first to reduce the invention to practice, albeit constructively.[34] To establish priority of invention, however, McCormick also needed to prove a date of conception before that of Kridl.[35]

McCormick sought to rely upon the pages of Marcia Vincent's laboratory notebook.[36] These pages described an experiment in January 1984 in which a gene fragment encoding a viral protein was inserted into a cloning vector in both the sense and antisense orientations.[37] The Board applied a "rule of reason" analysis to evaluate this evidence and found that McCormick conceived of the invention before Kridl.[38] The Board thus awarded priority of invention to McCormick.[39]

In reaching its decision, the Board also concluded that McCormick conceived of the utility of the claimed invention in January 1984.[40] The Board did so based solely on the uncorroborated testimony of one of the inventors, Dr. William Swain.[41] Kridl contended that antisense had more than one substantial use, and thus, McCormick might have used it for a different purpose in January 1984.[42] According to Kridl, McCormick could have used antisense as an experimental control or as a mere template for the production of recombinant DNA in the sense orientation.[43]

The Federal Circuit considered the state of the biotechnology art in 1984 to refute Kridl's arguments and affirm the Board's

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33. *See id*. An interference count establishes the scope of the interference by defining the invention common to the parties. The interpretation of an interference count is analogous to claim construction.

34. *See id.* at 1449.

35. *See id.*

36. *See id.* at 1448.

37. *See id.* at 1448-49.

38. *See id.* at 1449; *see also* Price v. Symsek, 988 F.2d 1187, 1195 (Fed. Cir. 1993) ("A 'rule of reason' analysis is applied to determine whether the inventor's prior conception testimony has been corroborated . . . . An evaluation of *all* pertinent evidence must be made so that a sound determination of the credibility of the inventor's story may be reached.").

39. *See Kridl*, 105 F.3d at 1449, 1688.

40. *See id.*

41. *See id.* at 1450.

42. *See id.*

43. *See id.*

determination.[44] There was no dispute that the use of antisense in plants was not known in 1984.[45] The Federal Circuit thus reasoned that it would have been illogical for McCormick to use such novel material as an experimental control, which usually involves tried and true compounds.[46] In addition, because sense constructs could be produced at that time by more established methods, the Federal Circuit stated that it would have been "wasteful" for anyone to use antisense to generate recombinant DNA in the sense orientation.[47]

Accordingly, the Federal Circuit held that an individual skilled in the art in 1984 would have seen no other substantial use for the antisense constructs described in Ms. Vincent's laboratory notebook than as a means for imparting viral resistance to plants or plant cells.[48] The court stated that under a rule of reason analysis, explicit corroboration of the inventor's recognition of utility might not always be necessary.[49] For example, in certain situations, utility might be implicit in the evidence presented.[50]

Similar to the biotechnology cases involving obviousness inquiries, the Federal Circuit in *Kridl* was forced to rely on its hindsight analysis of the state of the art as the context for the parties' conduct. Indeed, in *Kridl*, the look backwards crossed almost a decade and a half. This practice only further complicates the already difficult task before the Federal Circuit in parsing unfamiliar technology. The genomics, bioinformatics, and proteomics arts will likely face similar difficulties.

To receive patent protection, an invention must be nonobvious at the time of the invention to one of ordinary skill in the relevant art.[51] Nonobviousness is a question of law that the Federal Circuit reviews de novo.[52] The conclusion of nonobviousness, however, is subject to underlying factual findings, which the Federal Circuit reviews for

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44. *See id.*
45. *See id.*
46. *See id.*
47. *See id.*
48. *See id.*
49. *See id.* at 1451.
50. *See id.*
51. *See* 35 U.S.C. § 103 (1994) (defining conditions for patentability, including nonobvious subject matter).
52. *See In re* Donaldson Co., 16 F.3d 1189, 1192 (Fed. Cir. 1994) (en banc).

clear error.[53]

During patent prosecution, the patent examiner bears the burden of establishing a prima facie case of obviousness.[54] Once the examiner meets this initial burden, the burden shifts to the applicant to provide rebuttal evidence to overcome the examiner's rejection.[55]

In *In re Deuel*,[56] the Federal Circuit reversed the Board's decision, which upheld the patent examiner's final rejection of the claims as obvious.[57] The subject matter of the application involved DNA encoding heparin-binding growth factor (HBGF) of bovine and human origins.[58] Deuel first isolated bovine uterine HBGF protein and determined the amino acid sequence of a small beginning portion of the protein.[59] Next, Deuel chemically synthesized a single strand of DNA (oligonucleotide) corresponding to this short amino acid sequence.[60] Using this oligonucleotide, Deuel isolated the naturally occurring bovine HBGF gene from a collection of DNAs (cDNA library) encoding bovine uterine proteins in general.[61] Deuel then determined the entire nucleotide sequence of the bovine uterine HBGF gene and predicted the amino acid sequence of the remaining unknown portion of the bovine uterine HBGF protein.[62] These bovine sequences constituted part of the claimed invention.[63]

In addition, Deuel used the oligonucleotide to isolate the naturally occurring human HBGF gene from the human placental cDNA library.[64] Similarly, Deuel then determined the entire nucleotide

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53. *See In re* Woodruff, 919 F.2d 1575, 1577 (Fed. Cir. 1990); *see also In re* Beattie, 974 F.2d 1309, 1311 (Fed. Cir. 1992) (discussing what the prior art teaches as a question of fact reviewable under the clearly erroneous standard).

54. *See In re* Rijckaert, 9 F.3d 1531, 1532 (Fed. Cir. 1993).

55. *See id.*; *see also In re* Dillon, 919 F.2d 688, 692-93 (Fed. Cir. 1990) (en banc) ("Such rebuttal or argument can consist of . . . any other argument or presentation of evidence that is pertinent."), *cert. denied*, 500 U.S. 904 (1991).

56. 51 F.3d 1552 (Fed. Cir. 1995).

57. *In re* Deuel, 51 F.3d 1552, 1554 (Fed. Cir. 1995), *rev'g ex parte*, 33 U.S.P.Q.2d (BNA) 1445 (Bd. Pat. App. & Interferences 1993).

58. 51 F.3d at 1554. The application at issue was U.S. Application Serial No. 07/542,232. *Id.* at 1553.

59. *Id.* at 1555.

60. *Id.*

61. *Id.*

62. *Id.*

63. *Id.*

64. *Id.*

sequence of the human placental HBGF gene and predicted the amino acid sequence of the complete human placental HBGF protein.[65] These human sequences also constituted part of the claimed invention.[66]

The patent examiner asserted that the claimed invention would have been prima facie obvious in view of the prior art.[67] The prior art upon which the examiner relied included a reference (Maniatis) describing gene cloning methods and a reference (Bohlen) disclosing the partial amino acid sequences of proteins composing a subclass of human and bovine HBGF.[68] The examiner maintained that Bohlen would have motivated one skilled in the art to clone the respective human and bovine HBGF genes according to Maniatis to produce human and bovine HBGF protein.[69]

In rebuttal, Deuel contended that the prior art taught away from the claimed invention. According to Deuel, Bohlen suggested that one skilled in the art would not have been motivated to use the same oligonucleotide to isolate the genes for human and bovine HBGF.[70] The examiner rejected Deuel's "teaching away" argument, apparently relying on the unfounded notion that HBGF genes were homologous across species.[71] The Board upheld the examiner's rejection, focusing instead on the allegedly routine nature of cloning.[72]

In reversing the rejection of Deuel's claims, the Federal Circuit relied on precedent stating that, absent prior art suggesting the specific claimed DNA, a particular DNA sequence is not obvious simply because the prior art discloses general methods for isolating DNA.[73] The court further applied precedent regarding chemical inventions stating that the prior art disclosure of a broad genus does not necessarily render obvious a specific compound within the genus.[74] Because many different DNA sequences can encode the

65. *Id.*
66. *Id.*
67. *Id.* at 1555.
68. *Id.* at 1555-56.
69. *Id.* at 1556.
70. *Id.*
71. *Id.*
72. *Id.* at 1556-57.
73. *Id.* at 1559 (*affirming In re* Bell, 991 F.2d 781, 785 (Fed. Cir. 1993)).
74. 51 F.3d at 1559 (citing with approval *In re* Baird, 16 F.3d 380 (Fed. Cir. 1994)).

identical protein, the court concluded that the simple disclosure of the protein does not render any particular one of those DNA sequences obvious, absent prior art specifically pointing to one sequence.[75] The Federal Circuit also discounted the Board's contentions regarding the routine nature of Deuel's work as mere speculation and impermissible hindsight reconstruction of the claimed invention.[76]

Obviousness inquiries in all technologies risk corruption from the hindsight analysis method.[77] The long time-lapse between patent application filing and litigation with biotechnology inventions can exacerbate the problem.[78] The often unsettled nature of science, compounded with the natural deterioration of reliable accounts of that context, make invalidity challenges to biotechnology patents based on obviousness unpredictable, notwithstanding the statutory presumption of validity. When considering genomics, bioinformatics, and proteomics inventions in the future, the courts will likely confront similar problems in resolving obviousness questions.

As an additional requirement for patent protection, an inventor must set forth an adequate written description of the invention.[79] In short, a patent must describe an invention in sufficient detail that one skilled in the art could clearly conclude that the inventor had possession of the claimed subject matter.[80] For biotechnology inventions, an adequate written description of nucleic acids, such as DNA or RNA, requires a precise definition, including the pertinent structure, formula, chemical name, or physical properties.[81] A mere statement that a nucleic acid is part of the invention, and a reference

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75. 51 F.3d at 1558-59.

76. *Id.* at 1558.

77. *See In re* Dembiczak, 175 F.3d 994, 999 (Fed. Cir. 1999).

> Measuring a claimed invention against the standard established by section 103 requires the oft-difficult but critical step of casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field.

Id.

78. *See, e.g.*, *supra* note 23 and accompanying text.

79. *See* 35 U.S.C. § 112 (1994).

80. *See* Lockwood v. Am. Airlines, Inc., 107 F.3d 1565, 1572 (Fed. Cir. 1997); *In re* Gosteli, 872 F.2d 1008, 1012 (Fed. Cir. 1989).

81. *See* Fiers v. Revel, 984 F.2d 1164, 1171 (Fed. Cir. 1993).

to a potential method for isolating it, will not suffice.[82]

In *In re Brana*,[83] the Federal Circuit reversed the Board's decision that upheld the patent examiner's final rejection of the claims of the application for failure to satisfy the written description requirement.[84] The subject matter of the application involved pharmaceutical compositions having antitumor activity in humans.[85] In the final office action, the examiner rejected the claims of the application, "because the specification failed to describe any specific disease against which the claimed compounds were active and did not establish a reasonable expectation that the claimed compounds had a practical utility."[86] The Board upheld the patent examiner's rejection under § 112, first paragraph, but stated that a rejection under § 101 would likewise have been proper.[87]

Regarding the examiner's written description, the Federal Circuit noted that the applicants tested the claimed compounds on tumor cell lines derived from animals suffering from lymphocytic leukemias.[88] The court thus concluded that the disclosed ameliorative activity of the claimed compounds on tumor cells constituted a proper allegation of sufficiently specific use.[89] As for the utility rejection, the Federal Circuit held that the examiner failed to satisfy the initial burden of challenging a presumptively correct assertion of utility in the disclosure.[90] The court noted that the prior art references upon which the Board relied did not question the usefulness of any related compound as an antitumor agent.[91] Moreover, one of the references disclosed compounds that were structurally similar to those of the claimed invention and possessed proven *in vivo* effectiveness as chemotherapeutics against various types of tumors.[92] The Federal

82. *See id.* at 1170. The adequacy of a written description is a question of fact that the Federal Circuit reviews for clear error. *See* Ralston Purina Co. v. Far-Mar-Co, Inc., 772 F.2d 1570, 1575 (Fed. Cir. 1985).

83. 51 F.3d 1560 (Fed. Cir. 1995).

84. *Id.* at 1569.

85. *See id.* at 1562 (citing the U.S. patent application as Serial No. 533,944).

86. *See id.* at 1563-64.

87. *See id.* at 1564.

88. *See id.* at 1565.

89. *See id.*

90. *See id.* at 1566.

91. *See id.*

92. *See id.*

Circuit held that even if the USPTO satisfied its initial burden, the applicant's evidence of statistically significant results from animal tests was sufficient to convince one skilled in the art of the inventions' asserted utility.[93]

In *Fiers v. Revel*,[94] the Federal Circuit affirmed the Board's decision toward priority of invention to Sugano et al.[95] The interference amongst three foreign inventive entities (Fiers, Revel, and Sugano) related to the DNA that coded for human fibroblast beta-interferon (β-IF), a protein that promotes viral resistance in human tissue.[96] The Board based its decision on the findings that (i) Sugano was entitled to the benefit of the March 19, 1980 filing date of its Japanese patent application; (ii) Fiers was entitled to the benefit of the April 3, 1980 filing date of its British patent application, but failed to prove conception of the subject matter before that date; and (iii) Revel was not entitled to the benefit of the November 21, 1979 filing date of its Israeli patent application.[97]

The Federal Circuit upheld the Board's determinations, noting that

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93. *See id.* at 1567. The court also noted that to require *in vivo* human testing akin to Phase II clinical studies conducted by the Food and Drug Administration would place a higher standard § 112, ¶ 1, compliance on applicants seeking patent protection for pharmaceuticals for humans.

94. 984 F.2d 1164 (Fed. Cir. 1993).

95. *Id.* at 1166.

96. *See id.* at 1166 (reporting the interference count defined as "[a] DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide").

97. *See id.* at 1167.

> Sugano's Japanese application disclosed the complete nucleotide sequence of a DNA coding for β-IF and a method for isolating that DNA. Revel's Israeli application disclosed a method for isolating a fragment of the DNA coding for B-IF as well as a method for isolating messenger RNA (mRNA) coding for β-IF, but did not disclose a complete DNA sequence coding for β-IF. Fiers, who was working abroad, based his case for priority on an alleged conception either in September 1979 or in January 1980, when his ideas were brought into the United States, coupled with diligence toward a constructive reduction to practice on April 3, 1980, when he filed a British application disclosing the complete nucleotide sequence of a DNA coding for β-IF. According to Fiers, his conception of the DNA of the count occurred when two American scientists, Walter Gilbert and Phillip Sharp, to whom he revealed outside of the United States a proposed method for isolating DNA coding for β-IF brought the protocol back to the United States . . . . On February 26, 1980, Fiers' patent attorney brought into the United States a draft patent application disclosing Fiers' method, but not the nucleotide sequence for the DNA.

Id.

"when an inventor is unable to envision the detailed chemical structure of the gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated."[98] The court thus held that "irrespective of the complexity or simplicity of the method of isolation employed, conception of a DNA, like conception of any chemical substance, requires a definition of that substance other than by its functional utility."[99]

The Federal Circuit concluded that Fiers' proof of conception of a method that enabled one of ordinary skill in the art to make the DNA of the count was insufficient to establish conception of the DNA count.[100] In addition, the court held that Revel failed to prove that its Israeli patent application contained a written description of a DNA coding for β-IF because it did not disclose the nucleotide sequence or "an intact complete gene."[101] By contrast, Sugano's Japanese patent application set forth the complete and correct nucleotide sequence of a DNA coding for β-IF, thus satisfying the written description

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98. *See id.* at 1168-69 (quoting Amgen Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1206 (Fed. Cir. 1991)).

99. *See id.* at 1169.

100. *See id.*

> Before reduction to practice, conception only of a process for making a substance, without a conception of a structural or equivalent definition of that substance, can at most constitute a conception of the substance claimed as a process. Conception of a substance claimed per se without reference to a process requires conception of its structure, name, formula, or definitive chemical or physical properties.

Id.

101. *See id.* at 1170-71.

> 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. Revel's specification does not do that. Revel's application does not even demonstrate that the disclosed method actually leads to the DNA, and thus that he had possession of the invention, since it only discloses a clone that might be used to obtain mRNA coding for β-IF. 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. Revel's argument that correspondence between the language of the count and language in the specification is sufficient to satisfy the written description requirement is unpersuasive when none of that language particularly describes the DNA.

Id.

requirement and entitling Sugano to the benefit of that foreign filing date.[102]

In *University of California v. Eli Lilly & Co.*,[103] the Federal Circuit affirmed the district court's judgment that the asserted patent claims were invalid because the patent failed to provide an adequate written description of the claimed subject matter.[104] The patented technology involved human insulin produced by recombinant DNA methods.[105]

The patent claims were directed to the use of human insulin cDNA, but the specification provided a written description only regarding rat insulin cDNA.[106] Although the patent recited a general method for obtaining human cDNA, along with the amino acid sequences for human insulin, the Federal Circuit noted that enablement was not the issue.[107] This disclosure provided no structural information or physical characteristics, such as a nucleotide sequence, of any of the human cDNAs in the claimed genus.[108]

Absent such identification, the generic references to vertebrate or mammalian insulin cDNA were inadequate written descriptions, which could not be used to distinguish the claimed genus from others, except by function.[109] The Federal Circuit stated that a proper written description of a cDNA genus, for example, might be the nucleotide sequences of a representative number of cDNAs, or the recitation of structural features common to the members of the genus.[110] Generic references alone indicate only what one might achieve and provide no information about the resulting claimed material.[111]

The pronouncements on written description by the Federal Circuit

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102. *See id.* at 1172 (stating that Sugano's Japanese patent application "convey[s] with reasonable clarity to those skilled in the art that, as of the filing date sought, [Sugano] was in possession of the [DNA coding for β-IF]").

103. 119 F.3d 1559 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998).

104. Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1562 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998).

105. *See id.* (identifying the patents-in-suit as U.S. Patents No. 4,652,525 (issued Mar. 24, 1987) and No. 4,431,740 (issued Feb. 14, 1984)).

106. *See id.* at 1562-63.

107. *See id.* at 1567.

108. *See id.*

109. *See id.*

110. *See id.* at 1568.

111. *See id.*

arguably garnered more criticism than any other statutory compliance issue in recent days. With biotechnology subject matter involving molecular genetic information, the Federal Circuit has clearly taken an extreme position in requiring the disclosure of actual nucleotide sequences as claim support.[112] The ideological controversy about the origins and justifications of the written description requirement aside, the Federal Circuit holding in *Eli Lilly* creates a serious question as to the continuing vitality of prophetic patent claims, certainly with respect to biotechnology inventions, if not others as well.

Since *Eli Lilly*, the Federal Circuit seems to have opened the door to a more liberal interpretation of the written description requirement vis-à-vis the state of the relevant technology.[113] In *Union Oil*, the Federal Circuit arguably refines the written description inquiry to shift the focus of the determination away from the isolated disclosure and closer to what those skilled in the art could understand from that disclosure.[114] Accordingly, even if the Federal Circuit were to stand firmly behind its earlier pronouncements on written description in other respects, the rapidly changing state of biotechnology should eventually alleviate the seemingly harsh results possible from the *Eli Lilly* standard alone. Following the reasoning of *Union Oil*, the

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112. *See, e.g.*, Janice M. Mueller, *The Evolving Application of the Written Description Requirement to Biotechnological Inventions*, 13 BERKELEY TECH. L.J. 615, 617 (1998).

> The *Lilly* decision establishes uniquely rigorous rules for the description of biotechnological subject matter that significantly contort written description doctrine away from its historic origins and policy grounding. The *Lilly* court's elevation of written description to an effective 'super enablement' standard of uncertain scope and applicability will likely chill development in this critically important technological field and frustrate the United States patent system's policy goal of encouraging prompt disclosure of new inventions.

Id.

113. *See* Union Oil Co. of Cal. v. Atlantic Richfield Co., 208 F.3d 989, 997 (Fed. Cir. 2000).

> Appellant refiners assert that the specification does not describe the exact chemical component of each combination that falls within the range claims of the '393 patent. However, neither the Patent Act nor the case law of this court requires such detailed disclosure. Rather, the Patent Act and this court's case law require only sufficient description to show one of skill in the refining art that the inventor possessed the claimed invention at the time of filing.

Id. (internal citations omitted).

114. *Id.*

disclosure of actual nucleotide sequences should not be required as claim support once the state of biotechnology advances to the point at which those skilled in the art could understand that, in the absence of such disclosure, the inventor was in possession of the claimed invention at the time of application filing.

III

As the foregoing section indicated, the existing legal authority provides little guidance regarding the genomics, bioinformatics, and proteomics inventions that the USPTO faces today. Indeed, if the time from filing a patent application, to federal court judgments, with respect to past biotechnology patent cases, is any indication, it will be several years before the Federal Circuit sees such matters. Accordingly, because Federal Circuit precedent does not answer the question of whether nucleic acid discoveries with little, if any, corresponding genetic knowledge are patentable, the USPTO is forced to consider the issue first, without guidance."

In February 1997, the USPTO adopted a controversial position when it announced the likely grant of patent claims to ESTs and SNPs, despite minimal disclosure of their biological significance by the patent applicant.[115] The patent claims receiving the preliminary approval of the USPTO seemed of such broad scope that even the use of products derived from genetic material, of which only a fraction of the sequence is patented, could constitute an infringement under the patent law.[116] The patent applicant ultimately withdrew these claims.[117] Nonetheless, such claims fueled already mounting public outcry over gene patenting, which spurred the USPTO into action.[118]

On January 5, 2001, the USPTO issued examination guidelines on the patentability requirements of utility and written description.[119] This action marked a significant retreat from the questionable policy

115. *See* Ed Susman, *U.S. PTO to Allow Patents on Gene Fragments called ESTs*, BIOTECHNOLOGY NEWSWATCH, Mar. 3, 1997, at 1; Lynn Pasahow & Andrew Kumamoto, *Human Genome Project Raises Patenting Issues*, NAT'L L.J., Oct. 20, 1997, at C31.

116. *See* Susman, *supra* note 115, at 1.

117. *See id.*

118. *See* Pasahow & Kumamato, *supra* note 115, at C31.

119. *See infra* notes 120-23.

decision by the USPTO in 1997. Moreover, this consideration appears to end an almost four-year moratorium on the issuance of patent claims to ESTs and SNPs.

At the outset, the utility examination guidelines provided responses to comments generated by earlier proposed versions of the guidelines.[120] Although generally applicable to all technologies, these guidelines reacted to public concerns about the patenting of ESTs and SNPs.

The USPTO acknowledged that patent claims to ESTs and SNPs, or any other nucleic acids, are unpatentable for lack of utility where the supporting disclosure fails to provide any information regarding a biological association or function corresponding to the claimed nucleic acid.[121] According to the USPTO, only in conjunction with such a teaching would a claimed nucleic acid have a specific, substantial, and credible utility.[122]

Like the utility examination guidelines, the revised written description guidelines provided responses to comments generated by earlier proposed versions.[123] As with the utility examination guidelines, the written description guidelines promulgated in reaction to public concerns about the patenting of ESTs and SNPs, despite the disclaimer of their general applicability to all technologies.

Arguably less provocative than the utility examination guidelines

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120. *See* Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 6, 2001) ("This revision supersedes the Revised Interim Utility Examination Guidelines that were published at 64 FR 71440, Dec. 21, 1999; 1231 O.G. 136 (2000); and correction at 65 FR 3425, Jan. 21, 2000; 1231 O.G. 67 (2000).").

121. *See id.* at 1093.

> If a patent application discloses only nucleic acid molecular structure for a newly discovered gene, and no utility for the claimed isolated gene, the claimed invention is not patentable. [W]here the application discloses a specific, substantial, and credible utility for the claimed isolated and purified gene, the isolated and purified gene composition may be patentable.

Id.

122. *Id.*

123. *See* Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement, 66 Fed. Reg. 1099 (Jan. 6, 2001) ("These Guidelines supersede the "'Revised Interim Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 'Written Description' Requirement" that were published in the Federal Register at 64 FR 71427, Dec. 21, 1999, and in the Official Gazette at 1231 O.G. 123, Feb. 29, 2000.").

with respect to the patenting of ESTs and SNPs, the written description guidelines tracked Federal Circuit precedent closely.[124] In this regard, the USPTO reiterated that patent claims to a nucleic acid drawn only by reference to its biological association or function, where the supporting disclosure provides no understanding of the chemical structure of the nucleic acid (such as the nucleotide sequence), would be unpatentable for lack of adequate written description.[125] In short, patent protection would extend only to those inventions involving nucleic acids for which the patent applicants provided the public with both a proper understanding of the structure of the claimed nucleic acids, and the corresponding genetic knowledge they contained.[126]

IV

The Federal Circuit and its predecessor court expressed the necessity of those seeking a patent grant to provide the public with appropriate notice of the metes and bounds of their inventions and attendant exclusive rights.[127] Similarly, the courts demanded that patent applicants be clear about their claimed inventions with respect to their required disclosures.[128]

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124. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence. For example, even though a genetic code table would correlate a known amino acid sequence with a genus of coding nucleic acids, the same table cannot predict the native, naturally occurring nucleic acid sequence of a naturally occurring mRNA or its corresponding cDNA. The Federal Circuit pointed out that under U.S. law, a description that does not render a claimed invention obvious cannot sufficiently describe the invention for the purposes of the written description requirement of 35 U.S.C. § 112. *See* Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112, 711, "Written Description" Requirement, 66 Fed. Reg. at 1108 n.14.

125. *Id.*

126. *Id.*

127. *See* Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd., 234 F.3d 558, 575 (Fed. Cir. 2000) ("[T]he notice function of patent claims has become paramount, and the need for certainty as to the scope of patent protection has been emphasized."), *cert. granted*, 69 U.S.L.W. 3779 (No. 00-1543) (U.S. June 18, 2001); *see also infra* note 128 and accompanying text (describing the significance of notice and guidance with respect to the written description requirement).

128. "It is an old custom in the woods to mark trails by making blaze marks on the trees. It is no help in finding a trail . . . to be confronted simply by a large number of unmarked trees."

Promulgated in view of these Federal Circuit precedents, the recent rules set forth by the USPTO on the patentability standards of utility and written description, establish the need for the analogous degree of clarity in genetic discoveries and other biotechnology inventions.[129] However, the USPTO appears to recognize that inventions involving nucleic acids possess distinct characteristics or structure and function that cannot be easily divorced from one another.[130]

Although the forecast for judicial treatment of this technology might not be an optimistic one, it might be fair to say that any stormy weather should pass. Indeed, the resolution might owe as much to the progress of the science as it will to action by the USPTO and federal courts in governing the science.

The likelihood exists that as increased competency in computer predictive modeling develops in bioinformatics and proteomics, a bare nucleotide sequence can reveal its biological significance. We should have every reason to trust that the isolation today of an otherwise nonsensical sequence of nucleotides will soon be supplanted by technology that simultaneously identifies a multiplicity of inherent characteristics that can perhaps indicate, inter alia, origin, function, and evolutionary lineage. As the state of the art achieves this hope, the patent system might find its treatment of such inventions in the future easier to reconcile than suspected today.

In re Ruschig, 379 F.2d 990, 994-95 (C.C.P.A. 1967), *quoted in* Fujikawa v. Wattanasin, 93 F.3d 1559, 1570 (Fed. Cir. 1996).

129. *See supra* notes 120-23 and accompanying text (discussing USPTO guidelines).

130. A DNA sequence—i.e., the sequence of base pairs making up a DNA molecule—is simply one of the properties of a DNA molecule. Like any descriptive property, a DNA sequence itself is not patentable. A purified DNA molecule isolated from its natural environment, on the other hand, is a chemical compound and is patentable if all the statutory requirements are met. An isolated and purified DNA molecule may meet the statutory utility requirement if, e.g., it can be used to produce a useful protein or it hybridizes near and serves as a marker for a disease gene. Therefore, a DNA molecule is not per se unpatentable for lack of utility, and each application claim must be examined on its own facts. Utility Examination Guidelines, 66 Fed. Reg. 1092, 1094 (Jan. 6, 2001).

CONCLUSION

The release of the completed nucleotide sequence of the human genome represents the culmination of extraordinary efforts to demystify a fundamental question of who we are. The close of this phase of scientific endeavor, however, finds itself at the dawn of new progress towards comprehending the daunting volumes of genetic data the Human Genome Project uncovered. Bioinformatics and proteomics are such fields of research that will rise with the wave that the genomics surge started.

Ownership of genetic discoveries is not a new occurrence. However, what is troubling for many is the developing possibility of patent protection for inventions involving nucleic acids with minimal, if any, teaching regarding the biological significance. The present controversy over patenting genes and gene fragments seems more principled where a patent applicant fails to couple genetic knowledge with the disclosure of the chemical structure of the claimed nucleic acid.

The legal authority that will likely frame these issues focuses on the utility and written description requirements under the patent law. Applying existing case law, the USPTO and Federal Circuit should take the position that a patent claim to a bare nucleotide sequence, devoid of any indication of biological association or function, lacks utility. Similarly, a patent claim to a desired biological association or function, without the disclosure of a specific nucleic acid as defined by its nucleotide sequence, is not supported by an adequate written description. Under this interpretation of the statutory scheme, the patentability of a nucleic acid would depend upon a proper disclosure reflecting the merger between its characteristics as a chemical compound and a storage medium for biological information.

As the fields of bioinformatics and proteomics develop, the separation between strategies of the past in patenting genes and gene fragments, and the agendas of the present and future in patenting ESTs and SNPs might begin to close. Where computer predictive modeling through bioinformatics and proteomics can provide meaning in the sense of biologic significance based on the nucleotide sequence alone, the public can begin to obtain the clearer knowledge benefit it demands in exchange for granting a temporary right of

exclusivity to the discoverer of the claimed nucleic acid. To the extent this convergence fails to occur, the USPTO and the federal courts must be mindful of the problematic consequences that can arise from approving or upholding patent claims where the supporting disclosure teaches only the nucleotide sequence of the nucleic acid, or only the biological association and function of the nucleic acid, but not both. Allowing and enforcing such claims in those circumstances would constitute an unreasonable extension of the patent right.