Vanderbilt Law Review

Volume 58 | Issue 3 Article 7

4-2005

Protecting the Frontiers of Biotechnology Beyond the Genome: The Limits of Patent Law in the Face of the Proteomics Revolution

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I. INTRODUCTION

Scientific knowledge and invention rapidly accelerated in the past few decades, resulting in an untold number of broken barriers and realized benefits. In 2001, scientists announced that the human genome, consisting of 30,000 to 40,000 genes, had been fully characterized.[1] Arguably one of the most important scientific breakthroughs in history, this accomplishment came far sooner than anyone could have anticipated.[2] Fueled by the enormous marketing potential in finding causes and cures for many diseases, the

1. *See, e.g.*, Robert F. Service, *High Speed Biologists Search for Gold in Proteins*, 294 SCIENCE 2074, 2074 (2001); Lawrence M. Sung, *The Unblazed Trail: Bioinformatics and the Protection of Genetic Knowledge*, 8 WASH. U. J.L. & POL'Y 261, 261-63 (2002) (discussing the significance of the announcement that research teams had figured out the nucleotide sequence of the human genome). The sequence was actually a "working draft" of the human genome, but the project was expected to be completed in its entirety in 2003. U.S. Dep't of Energy, Human Genome Research, *at* http://www.science.doe.gov/ober/hug_top.html (last visited May 25, 2005).

2. *See* Sung, *supra* note 1, 261-263 & nn.2-3 (citing the complexity of the achievement and the publicity it obtained).

biotechnology industry invested heavily in the project with the hope of maximizing control of genetic intellectual property and its potential downstream value.[3]

While the genomic revolution has steadily progressed, the ability of researchers to identify and characterize proteins has increased exponentially thanks to technological advancements.[4] The culmination of the Human Genome Project only added to this advancement and shifted the focus from genetic characterization to the proteins they express.[5] The research effort to characterize completely all proteins normally and abnormally expressed in the human body is roughly known as proteomics.[6] Proteins hold vastly more promise than even genes for drug discovery and medical research, and proteomics has quickly "become the new darling of the investment community."[7] As with genomics, the biomedical industry is rapidly attempting to claim as much patent territory in proteomics as possible.[8]

Protein characterization is much more complex than gene characterization, however, and proteomics projects are much less certain to result in realized value.[9] Further, proteomics patents raise their own unique issues and are almost certain to clash with genomics patents that may or may not cover the same claims.[10] Patent law currently leaves those wishing to maximize their investment in biological molecules uncertain of their ability to obtain sufficient protection for their efforts.[11] Once decided, however, the resolution of certain issues of patentability may give proteomics patent owners

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3. *See, e.g.*, Robert F. Service, *Gene and Protein Patents Get Ready to Go*, 294 SCIENCE, 2082, 2082 (2001) (discussing the race to patent genes thought to cause disease); Symposium, *Bioinformatics and Intellectual Property Law April 27, 2001 – Boston, Massachusetts: Molecules vs. Information: Should Patents Protect Both?*, 8 B.U. J. SCI. & TECH. L. 190, 202-07, 212-13 (2002) [hereinafter *Molecules v. Information*] (discussing biotech patenting in the pharmaceutical industry); *see also* discussion *infra* Part II. (discussing downstream value).

4. *See* Service, *supra* note 1, at 2075 (citing use of rapid computerization and improvement in techniques associated with protein identification, such as 2-D Gel Electrophoresis and X-ray crystallography).

5. *Id.* at 2074-75.

6. *Id.*

7. *Id.* at 2074 (internal quotation marks omitted).

8. *Id.*; *see also* David Cyranoski, *Intellectual Property: This Protein Belongs To. . .*, 426 NATURE 10, 10 (2003) (reporting that Oxford GlycoSciences announced in 2001 that it expected to patent over 4,000 proteins resulting from its disease research).

9. *See, e.g.*, Cyranoski, *supra* note 8, at 10-11 (discussing the great costs associated with patenting proteins which might deter experimentation if commercial value cannot be assured).

10. *See, e.g.*, Service, *supra* note 3, at 2082-83 (citing the "confusing landscape of competing gene and protein patent claims, perhaps setting the stage for legal battles for control over the future of genetic medicine").

11. *See infra* Part III.

more protection than is warranted under the traditionally accepted patenting policy espoused in the Constitution of the United States.[12] Increased incentive for private industry also threatens the time-honored research practices of scientific research, which supports the open exchange of ideas and information throughout the scientific community.[13]

The future of biotechnology patents, therefore, is ripe for litigation and may become a significant problem if not approached in a distinctive manner. Due to the vast potential of discovery in proteomics, its increasing industrial and academic value, and the uncertainty of whether patent law will cover or allocate proper incentives for these discoveries, adoption of patent protection may not be the best approach to organize this field. Rather, some sort of sui generis protection necessary to achieve the balance traditionally envisioned by the patent laws.

Part II of this Note offers a brief overview of genomics, proteomics, and the current state of biotechnology and information technology in the field. This Part also provides a brief examination of the requirements necessary to obtain a patent. Next, the Note discusses current patent law as it applies to biotechnology and genomic patents. The United States Patent and Trademark Office, as well as the federal court system, has begun to recognize the complexity and uniqueness of the field of biotechnology, but the lag time between the development of technology and court decisions has cast a large amount of uncertainty over the field. Part IV examines the major problems and potential conflicts that may arise with this nascent technology and the reasons why current patent law may never be adequate for the proteomics industry. Finally, Part V argues that, while other fields may have survived infancy under a general patent law system, the proteomics field is better served by unique protection that recognizes the special problems inherent in the field but preserves the balance anticipated by the Constitution.

II. BACKGROUND OF PATENT LAW, BIOTECHNOLOGY, AND PROTEOMICS

The Constitution of the United States grants Congress the power "[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."[14] Congress

12. *See infra* Part IV.
13. *See infra* Part IV.B.
14. U.S. CONST. art. I, § 8, cl. 8.

responded by enacting the first Patent Act in 1790, which built upon but changed in several important respects its English counterparts.[15] Since then, Congress has revised the Act many times to fit the evolving interpretations of patent law and to respond to the many changes in technology.[16]

Congress and the courts have taken steps independent of the Act itself to encourage technological innovation in the United States by improving and stimulating the patent system.[17] A primary example is Congress' formation of the Court of Appeals for the Federal Circuit ("Federal Circuit") in 1982, which is responsible for adjudicating all appeals that primarily involve patents.[18] Congress hoped that a single appeals court would reduce uncertainty in patent claim construction and increase the worth of obtaining a patent, thereby promoting invention and disclosure of innovation.[19] Court decisions have also stimulated the patent system by broadening the traditional scope of patentable subject matter. In addition, the United States Patent and Trademark Office ("USPTO") guidelines have evolved in response to emerging issues and to judicial interpretations of the Patent Act.[20] These judicial and administrative changes affect the patentability of new and developing technology prevalent in the biotech fields and impact the industry both positively and negatively.

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15. *See generally* Edward C. Waltersheid, *To Promote The Progress of Useful Arts: American Patent Law and Adminstration, 1787-1836 (Part I)*, 79 J. PAT. & TRADEMARK OFF. SOC'Y 61, 71-72 (1997) (discussing the inception and evolution of the Patent Act of 1790). Specifically, the Act required an examination of the invention to determine if it was useful enough to be granted protection, and a consideration of whether the invention was anticipated even outside the borders of the country. *Id.*

16. Indeed, six Patent Acts were passed between 1793 and 1836 alone. *Id.* at 63. The latest incarnation of the Patent Act was enacted in 1952. *See* Kathleen N. McKereghan, *The Nonobviousness of Inventions: In Search of a Functional Standard*, 66 WASH. L. REV. 1061, 1062 (1991) ("The 1952 Patent Act enunciates the current requirements of patentability: utility, novelty, and nonobviousness.").

17. *See* HERBERT F. SCHWARTZ, PATENT LAW AND PRACTICE 4-5 (3d ed. 2001) (noting the "legislative and judicial action" in the 1980s taken in response to the "relative increase in technological innovation throughout the rest of the world as compared with that in the United States").

18. ROBERT P. MERGES ET AL., INTELLECTUAL PROPERTY IN THE NEW TECHNOLOGICAL AGE, 110-11 (3d ed. 2003). This jurisdiction includes patent related appeals from all U.S. District Courts and appeals from the Board of Patent Appeals and United States Patent and Trademark Office. 28 U.S.C. § 1295 (2003). Since patents are exclusively federal in origin, federal courts have jurisdiction "exclusive of the courts of the states in patent," and there is no state patent law. 28 U.S.C. § 1338(a) (2003).

19. *See* SCHWARTZ, *supra* note 17, at 4-5 (discussing the reasoning behind the 1982 establishment of the Court of Appeals for the Federal Circuit to hear all patent appeals).

20. *Id.* at 5.

A. Genomics, Proteomics, and Bioinformatics: The Unique Interrelationship Between Living Organisms and Technical Information

To understand the impact patents have had and may have on biotechnology in the future, it is necessary to describe briefly the structure and function of genes and proteins and to explain exactly what proteomics entails. Further, it is beneficial to understand the importance of biological information collectively stored in public and private databases and computer software processes that predict and model proteins, methods together referred to as "bioinformatics," to the further advancement of biotechnology.[21] All of these fields interact with one another and will become further enmeshed in the future. This makes application of traditional patent laws to biotechnology increasingly problematic.

A genome is "an organism's complete set of DNA."[22] DNA, or deoxyribonucleic acid, is a biological molecule made up of building blocks called "nucleotides" (named by the particular nitrogenous bases they contain) that pair up distinctly to make two long chemical chains.[23] "Sequencing" of a DNA molecule, therefore, is the complex process of discovering the arrangement of the nucleotides in the molecule and listing them in exact order.[24] The arrangement of the nucleotides "spells out" the instructions that the particular DNA gives to the living cell and makes up the genetic traits of an organism.[25]

Human DNA is arranged into 24 chromosomes, which range from about 50 million to 250 million of the base pairs.[26] Chromosomes contain many different genes, which are "specific sequences of bases

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21. *See, e.g.*, Dov S. Greenbaum, *The Database Debate: In Support of an Inequitable Solution*, 13 ALB. L.J. SCI. & TECH. 431, 445-48 (2003) (describing the rise of the importance of database information to scientific discovery).

22. Human Genome Project, U.S. Dep't of Energy, From the Genome to the Proteome [hereinafter Genome to Proteome], *available at* http://www.ornl.gov/sci/techresources/Human_Genome/project/info.shtml (last visited May 25, 2005)

23. *Id.*; *see also* M. Scott McBride, *Bioinformatics and Intellectual Property Protection*, 17 BERKELEY TECH. L.J. 1331, 1335-36 (2002) (detailing the composition of DNA). The four bases are adenine ("A"), guanine ("G"), cytosine ("C"), and thymine ("T"). An A base will always pair up with a T base, and a G base will always pair up with a C base. *See, e.g.*, KATHLEEN TALARO AND AUTHOR TALARO, FOUNDATIONS IN MICROBIOLOGY, 229-30 (1993) (detailing the makeup of DNA).

24. *See, e.g.*, Genome to Proteome, *supra* note 22 (explaining the genome sequencing process in detail).

25. *Id.*

26. *Id.*

that encode instructions on how to make proteins."[27] Genes are only a small part of the total genome; much of the DNA comprising chromosomes serves other important functions in a living cell, such as regulating protein production, and some genes may have unknown functions or possibly no function at all.[28]

Genetic information flows from DNA to RNA (ribonucleic acid) through a process called transcription.[29] The information from the genes contained in the RNA molecule is then deciphered by other processes in the cell by a process called translation.[30] From these processes, proteins are produced.[31] The publicly funded Human Genome Project and its industry based competitors, therefore, have sought to produce DNA sequence data for all of the chromosomes in the human body and, from that information, have created a potential road map to all of the proteins produced by human cells.[32]

Deciphering proteins is a much more daunting task than deciphering genes, however. Unlike DNA, which is made up of four base pairs that only match up with one other pair, proteins are made up of twenty different amino acids in a multitude of complex combinations.[33] Proteins can range in size from 5,000 daltons[34] to over a million Daltons; their electrical charges differ and can change based on their bonding; and, in many cases, they exist either in very small amounts in a cell or for only a miniscule amount of time.[35] Since many proteins are homologous,[36] scientists typically categorize proteins by general function in the cell.[37] However, any change in structure or binding of the protein may drastically alter its function

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27. *Id.*

28. *Id.*

29. *See* TALARO, *supra* note 23, at 234 (describing the processes of transcription and translation).

30. *Id.*

31. *Id.*

32. Service, *supra* note 3, at 2082-83.

33. TALARO, *supra* note 23, at 52-54, 230.

34. The unit for atomic mass, named after the prominent English chemist, John Dalton. WEBSTER'S COLLEGIATE DICTIONARY 291 (10th ed. 1995).

35. Robert F. Service, *Public Projects Gear Up to Chart the Protein Landscape*, 302 SCIENCE 1316, 1317 (2003); Stanley Fields, *Proteomics in Genomeland*, 291 SCIENCE 1221, 1221 (2001).

36. Chemical compounds share the same homology if their physical structure differs only very slightly, often by placement or character of only one carbon group. *See, e.g.*, PHILLIPPE G. DUCOR, PATENTING THE RECOMBINANT PRODUCTS OF BIOTECHNOLOGY AND OTHER MOLECULES 24-25 & n.112 (1998) (discussing "structural similarity" of chemical compounds). This similarity potentially can cause difficulty in protein patents failing for obviousness. *Id.*; *see also* discussion *infra* Parts II.B, III.

37. *C.f.* Service, *supra* note 3, at 2083 (discussing the similarity in function of certain 'splice variants'); Fields, *supra* note 35, at 1221-22 (discussing the characterization of proteins by function).

and potentially cause the expression of disease.[38] Further, a single gene may code for several different proteins through different processes in a cell.[39] In all, it is now estimated that up to two-million distinct proteins are produced by human cells at some point in a given person's lifetime.[40]

The term "proteome" can be defined in several different ways but is generally thought to be the "total set of proteins expressed during the lifetime of a cell."[41] Proteomics encompasses the various methods of obtaining the complete information about the proteins that make up the proteome and involves all levels of analysis, such as structural determinations of the proteins, functional analyses and, cell modeling.[42]

While advances in technology have enabled protein researchers to expand their focus and have greatly sped up the protein characterization process, research is still time-consuming, and there are no guarantees of profits or success.[43] Determination of the structure of a protein alone involves deciphering four levels of composition.[44] Determination of the function of a given protein is much more difficult, since protein expression may change dramatically with gene mutation, environmental disturbances or simple metabolic fluctuations.[45] Because of the complexity currently inherent in the field, it is estimated that protein structure determination may cost up

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38. *See, e.g.*, Service, *supra* note 1, at 2074 ("Defective proteins are responsible for the chemistry that leads to a range of diseases from cancer to Alzheimer's.").

39. McBride, *supra* note 23, at 1336-37.

40. *E.g.*, Service, *supra* note 1, at 2074.

41. Keala Chan & Dennis Fernandez, *Patent Prosecutions in Proteomics*, 19 SANTA CLARA COMPUTER & HIGH TECH. L.J. 457, 461 (2003) (quoting P.C. TURNER, ET AL., INSTANT NOTES IN MOLECULAR BIOLOGY (2d ed. 2000)). Proteomics, as the study of proteins on a massive scale, is such a new field that the term was only coined in 1995. *See, e.g.*, Michael Quinon, World Wide Words, Proteomics, *at* http://www.worldwidewords.org/turnsofphrase/tp-pro3.htm (last visited May 25, 2005).

42. Quinon, *supra* note 41.

43. For example, one technique, 2-D Gel electrophoresis, which separates proteins by both weight and isoelectric point, has difficulty separating out key smaller weight and membrane proteins, and requires much replication of experiments to reach a level of confidence with the results. Service, *supra* note 1, at 2075-77; *see also* Service, *supra* note 35, at 1318 (discussing the various research techniques used to discover the function of different proteins and the fact that there is still "a long way to go" before the medical benefits of the research can be realized).

44. *See, e.g.*, Chan & Fernandez, *supra* note 41, at 461-62 (explaining that these levels include primary structure (chemical bonds and amino acid sequences), secondary structure (typical formations), tertiary structure (the three dimensional folding patterns of the secondary structures) and quarternary structure (organization of polypeptide chains)); *see also* TALARO, *supra* note 23, at 52-54 (discussing the four structural layers of a protein).

45. Chan & Fernandez, *supra* note 41, at 461-62; *see also* Service, *supra* note 1, at 2074 (whereas genes "remain essentially unchanged through life, proteins are constantly changing, depending on the tissues they are in, a person's age, and even what someone ate for breakfast.").

to $100,000 dollars per protein with a discovery period that may extend for years.[46]

Nevertheless, the promises of finding proteins that directly relate to major pharmaceutical breakthroughs, such as specific drug targets, have fueled industry demand for extensive protein research.[47] Several companies have merged or been created to rapidly characterize bulk amounts of protein data or to sell the technology to enable others to do so.[48] Other companies, even genomic-oriented companies, are setting up labs to avoid being left behind by the industry.[49] Publicly funded projects, such as the Human Proteome Organization ("HUPO"), also have been created as academic researchers try to make sure they are not shut out of this scientific avenue.[50]

As with genomics in the 1990s, the race to identify proteins, define their function, and patent them in the hope that immense value may eventually be extracted from them may fuel proteomics research at a heavier pace, especially in private industry.[51] Determining who should receive the downstream value of protein promises to be a viable and contentious issue far into the future.[52]

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46. Chan & Fernandez, *supra* note 41, at 462.

47. Service, *supra* note 1, at 2074 (discussing how the complexity and ubiquity of proteins is what makes them more promising and attractive than gene research: "proteomics reveals the nuts and bolts [of life]. . . . And blocking or boosting these proteins offers the straightest shot to finding the next blockbuster drug."). The potential for medical benefits is enormous. *See, e.g., Gynecological Cancer: Proteomics is the Newest, Most Promising Direction for Gynecologic Cancer*, CANCER WKLY., Jan. 6, 2004, *available at* 2004 WL 55262326 ("Proteomic technology is the newest and most promising direction for translational developments in gynecologic cancers, researchers report.").

48. *See, e.g.*, Tim Adams, *Celera, Inpharmatica Join For Drug Discovery*, BIOTECHNOLOGY NEWSWATCH, Nov. 19, 2001, at 2 (describing how Celera, a leading genomic company, has integrated through cooperation with other companies to enter part of the proteomic market); Sally Lehrman, *Mergers, Acquisitions Seen as Fundamental to Growth*, BIOTECHNOLOGY NEWSWATCH, Feb. 4, 2002, at 1 (describing how Biotech companies look to expansion into proteomic science and its technology through mergers).

49. *See, e.g.*, Adams, *supra* note 48, at 1 (discussing how the pharmaceutical industry alone has invested hundreds of millions of dollars in the first year after tbe complete draft of the human genome was completed).

50. *See* Service, *supra* note 35, at 1316-18 ("HUPO helps set priorities, coordinate research, set standards for handling and processing samples, and arrange for the use of common bioinformatics tools to ensure that researchers can directly compare their results.").

51. *See, e.g.*, Service, *supra* note 1, at 2075 ("The driving force is to crank through as many proteins as possible to patent them."). Representatives of the pharmaceutical industry have stated that patents in proteins, even if they have no present value, are obtained in mass quantities because all other companies are doing the same thing and the company needs property to trade. *See Molecules vs. Information*, *supra* note 3, at 212 ("[U]ltimately, someone is going to hold a patent on every important drug target.").

52. In biomolecule patenting, downstream value may include all of the products derived directly or indirectly from the protein, such as drugs which increase or decrease the level of the

Further clouding the mix of patent law and biotechnology is the burgeoning field of bioinformatics. Bioinformatics is "the research, development, or application of computational tools and approaches for expanding the use of biological . . . data."[53] As genomics and proteomics have generated volumes of information, bioinformatics has grown to help decipher the data and generate predictions, statistics and models to aid the process.[54] It has become a multi-million dollar industry, and many of the tools and methods used in the field have been patented. Private industry also has charged licensing fees for the use of genome and proteome information, actions that some see as contrary to the principles of science. [55]

Although courts would probably hold abstract biological information, such as the raw sequence data of proteins and DNA, to be non-patentable,[56] biological molecules and bioinformatics pose unique issues for patent law now and will continue to do so in the future.[57] Biological molecules are both compositions of matter and informational molecules, and the patentability of the former may prevent the use of the latter.[58] Further, as computers and biotechnology continue to form closer relationships, computers likely will begin to use biological molecules as storage media.[59] These developments, which are beyond the scope of this Note, will stretch

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protein in the system, or use the protein or byproduct to perform some other therapeutic function. One of the problems with determining control of value-generating products is that the genes that encode for the proteins are likely also patented, giving the owner, who may not be the same as the protein patent owner, a viable claim to the products downstream of the gene, the same "stream" as the protein. *Molecules vs. Information*, *supra* note 3, at 202-07.

53. McBride, *supra* note 23, at 1332 (quoting National Institutes of Health, Office of Extramural Research, Bioinformatics at the NIH, *available at* http://grants1.nih.gov/grants/bistic/bistic.cfm (last visited May 5, 2002)).

54. *See* Charles Vorndran & Robert L. Florence, *Bioinformatics: Patenting the Bridge Between Information Technology and the Life Sciences*, 42 IDEA 93, 93-95 (2002) (discussing how bioinformatics can help manage biological information).

55. *See infra* Part III & n. 114; *see also* McBride, *supra* note 23, at 1332 n.7 (noting that bioinformatics is expected to generate a worldwide revenue of over $2 billion in 2001 alone).

56. *See* McBride, *supra* note 23, at 1342 (explaining that the subject matter requirement of patentability dictates that only a "process, machine, apparatus, or composition" may be patented and thus suggesting that the abstract biological sequence may not be patentable subject matter).

57. *See* Vorndran & Florence, *supra* note 54, at 95 (noting that in 2000, the bioinformatics industry raked in $700 million making it "one of the fastest growing areas of all life sciences related markets").

58. *See, e.g.*, *Molecules vs. Information*, *supra* note 3, at 199-202 (discussing the drawbacks of patenting bioinformation).

59. *See* Vorndran & Florence, *supra* note 54, at 130 ("Bioinformatics inventions are unique, however, because they combine the use of a computer and/or software with biological information."). This enmeshing goes the opposite direction as well. Researchers have already been successful in attempts to get a volume of DNA to solve a mathematical equation.

patent law beyond its current limits and will warrant a new look at the system in additions to the problems posed here.

B. General Requirements for Patenting an Invention

For the USPTO to approve an invention for patent protection, the invention must meet several general requirements: (1) the subject matter of the invention must be patentable; (2) the invention must be useful, new and nonobvious;[60] (3) the patent specification must disclose the invention such that another person in the field would be able to make and use it; and (4) the invention must be distinctly claimed, so others in the field will be able to ascertain the bounds of the protection.[61] Obtaining a patent on an invention entitles the owner to a presumption of validity in infringement actions and a possible award of injunctive relief or monetary damages if a court finds infringement has occurred.[62]

1. Statutory Subject Matter

According to the Patent Act, an invention may be eligible for patenting if it is a "new and useful process, machine, manufacture, or composition of matter."[63] The Federal Circuit has stated that the subject matter inquiry should focus upon whether the claim as a whole is directed to that which is patentable, and that claims should not be defeated simply because they contain elements that may not be patentable.[64] This interpretation, along with other judicially interpreted expansions,[65] has greatly lowered the threshold for meeting the subject matter requirement.[66]

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60. Chan & Fernandez, *supra* note 41, at 449.

61. *See* Fiers v. Revel, 984 F.2d 1164, 1169-71 (Fed. Cir. 1993) ("We hold that 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.").

62. 35 U.S.C. §§ 282-284 (2003).

63. 35 U.S.C. § 101.

64. State St. Bank & Trust Co. v. Signature Fin. Group, 149 F.3d 1368, 1375 & n.10 (Fed. Cir. 1998) (citing *In re* Shrader, 22 F.3d 290, 298 (Fed. Cir. 1994) (Newman, J., dissenting)).

65. *See, e.g.*, Diamond v. Diehr, 450 U.S. 175, 192-93 (1981) (expanding recognition to certain types of software that involve the use of a mathematical formula); Diamond v. Chakrabarty, 447 U.S. 303, 317-18 (1980) (extending patentability to isolated microorganisms). These cases are discussed in more detail *infra* Part III.

66. *See infra* Part III for further discussion of the Federal Circuit's approach to subject matter qualifications and its impact on biotechnology patents.

2. Utility

Similarly, there is an extremely low standard for usefulness generally required for obtaining a patent. The invention must merely be "capable of providing some identifiable benefit."[67] The policy behind this requirement is simple: an invention must show at the very least that it works in order to be granted the patent monopoly.[68] The courts have expressed a reluctance to expand the requirement further, fearing insertion of their own policy judgments on the function of a particular patent.[69] There have been certain circumstances in which a patent has been rejected for lack of utility,[70] however, and it is more likely to occur in groundbreaking technologies such as biotechnology.[71] Utility considerations, therefore, are paramount in the successful crafting of a patent based on proteomics.[72]

3. Novelty

The invention claimed in the patent application must also be new: a single portion of an older reference ("prior art") must not incorporate all of the claimed elements of the invention.[73] The novelty requirement prevents a patent from issuing on an invention that was known or used by others prior to the date of the invention or that was disclosed in a publication in sufficient detail to enable someone to understand and make the invention.[74] This requirement exists simply because it would be inequitable to reward someone a monopoly on an

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67. Juicy Whip, Inc. v. Orange Bang, Inc., 185 F.3d 1364, 1365 (Fed. Cir. 1999) (overturning the district court's ruling that the invention had lacked utility due to its deceptive nature and imitation). "The fact that one product can be altered to make it look like another is in itself a specific benefit sufficient to satisfy the statutory requirement of utility." *Id.* at 1367.

68. Merges, *supra* note 18, at 141-42.

69. *Cf. id.* at 141-45 (discussing the decline of the "moral utility" doctrine).

70. *See, e.g.*, Brenner v. Manson, 383 U.S. 519, 523 (1966) (rejecting a process which produced a steroid in which there was no known use, even though homologues of the structure had a definite function).

71. *See infra* Part III. This occurrence is of particular concern in biotechnology considering the wealth of information being generated by research which may or may not produce anything sufficiently "useful," and also in light of the increased standards for utility in biotechnology patents adopted by the USPTO. Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001).

72. Lawrence M. Sung, *IP Horizons in the Protection of Genetic Knowledge*, AAPS NEWSMAGAZINE, June 2001, at 20, 21-22.

73. Kalman v. Kimberly-Clark Corp., 713 F.2d 760, 772 (Fed. Cir. 1983). Novelty requirements are described in 35 U.S.C. § 102 (a), (e) and (g). Schwartz, *supra* note 17, at 66.

74. 35 U.S.C. § 102(a) (2003). The requirement can at times be harsh. *See In re* Hall, 781 F.2d 897 (Fed. Cir. 1986) (denying an inventor a patent on his invention due to a single doctoral dissertation publicly accessible in one library in Germany.).

invention's use when another person had previously conceived of the idea.[75]

Statutory bars also preclude patentability of inventions that were publicly used or sold by the inventor more than one year prior to the filing of the patent application.[76] The date the invention was created is generally considered the filing date, but in interference actions, earlier dates may be established through evidence of reduction to practice.[77] All of these requirements reward the diligence of an inventor over his competitors.[78] The hard-working inventor who first conceives of the idea but takes longer to implement the concept or file the application than a competitor is still able reap the benefit.[79]

4. Nonobviousness

The standard for showing that a claimed invention was not obvious to those in the relevant community is more stringent than the standards for usefulness and novelty.[80] Congress wrote this requirement into the 1952 Patent Act to codify a judicial requirement of comparing the invention to its background skill of the art.[81] Therefore, inventions not only have to be new, but also have to exhibit some "inventive leap" beyond the background art.[82] This requirement is again in response to the policy that something "extra" must be

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75. *See* Cherylyn A.P. Esoy, *The PTO's 2001 Revised Utility Examination Guidelines For Gene Patent Applications: Has the PTO Exceeded the Scope of Authority Delineated by the Court's Interpretation of a "Useful" Invention?*, 33 SETON HALL L. REV. 127, 139-140 (2002) (discussing how § 102 ensures that patents are only awarded to inventors for only novel inventions); Merges, *supra* note 18, at 147 ("Section 102 . . . embodies the principle that only truly new inventions deserve patents.").

76. 35 U.S.C. § 102(b).

77. 35 U.S.C. § 102(g). An interference action occurs when two inventors claim the same patented invention. *E.g.*, Schwartz, *supra* note 17, at 28-29.

78. *See* 35 U.S.C. § 102(g) ("In determining priority of invention under this subsection, there shall be considered . . . the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.").

79. Merges, *supra* note 18, at 166-71. The "reasonable diligence" standard has been interpreted as a balance between increasing the incentive to invent and the public interest in "earliest possible disclosure," thus certain gaps in practice will cause the first inventor to lose the right to the invention. Merges, *supra* note 18, at 168-69 (citing Griffith v. Kanamaru, 816 F.2d 624 (Fed. Cir. 1987)).

80. *See* 35 U.S.C. § 103(a) (2003) ("A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102. . ., if the differences . . . are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. . . .").

81. Graham v. John Deere Co., 383 U.S. 1, 3 (1966).

82. Merges, *supra* note 18, at 183.

shown in order for it to be equitable to others to grant the inventor such strong protection.[83]

The nonobvious standard is particularly important in the biotechnology field, considering that volumes of molecular information generated in research cumulate in the public domain,[84] and the many parallels in structure and function of similar biological molecules.[85] Further, scientific publications tend to speculate about the potential ramifications of their research and the directions in which they foresee the specific issue developing. The increase in publicly available research information decreases the chances that several different sources will not anticipate any given biotechnology invention.[86]

5. Written Description Requirements

Finally, for an invention to be patented, the application must include a written description in its specification section "in such full, clear, concise, and exact terms" that would enable someone skilled in the art to create and use the invention, and it must disclose the "best mode [of creation] contemplated" at the time the patent application is filed.[87] Disclosure of the invention itself is one of the essential parts of the patent system—a quid pro quo for governmental protection—and is expected to accomplish the goals set forth in the Constitution.[88] The description requirement also ensures that the inventor was in fact in possession of the invention at the time the patent application was filed and not merely attempting to patent a potential future innovation before a competitor.[89]

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83. *Id.*

84. For example, a National Institutes of Health project seeks to reduce the cost and time spent in determining protein structures by grouping them into structural families in databases, and anticipates up to 200 protein structures solved annually by 2005. Chan & Fernandez, *supra* note 41, at 462-64. This is in addition to the mass of genetic and protein sequences already publicly available in databases for many species, including humans. *See, e.g.*, McBride, *supra* note 23, at 1337-1340 & n.51 (2002) (citing one often used database, BLAST, which compares a typed in biological sequence to known sequences in the database).

85. *E.g.*, Merges, *supra* note 18, at 209-11.

86. *Molecules vs. Information*, *supra* note 3, at 215-216.

87. 35 U.S.C. § 112 (2003). The claims listed in the patent must also be distinct in describing the subject matter that the patent covers, or be expressed in a "means or step for performing a specified function" that covers the corresponding description and its equivalents. *Id.*

88. *See, e.g.*, Eldred v. Ashcroft, 537 U.S. 186, 216 (2003) (acknowledging the importance of this exchange concept in patent law, but not in copyrights).

89. Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F. 3d 1316, 1329 (Fed. Cir. 2002). See *infra* Part III.A.-B. for further discussion of the importance of this requirement in biotechnology applications.

The written description requirement also serves to convey the scope of the patent's protection to the public.[90] Claim drafters attempt to craft language broad enough to anticipate future developments of the invention but not so broad as to be declared indefinite by the courts or the USPTO.[91] Therefore, most patent litigation involves disagreements between patent owners and potential infringers concerning the interpretation of particular claims.[92]

III. THE STATE OF CURRENT PATENT LAW AND ITS APPLICATION TO BIOTECHNOLOGY AND PROTEOMICS

A. The Interaction of Patent Law, Biology, and Biotechnology

Like many other technological and scientific fields, biotechnology has progressed at a much faster rate than the prevailing patent law. Patent law concepts have only very slowly incorporated or adjusted to the biotechnology field. However, because of the economic impact of the pharmaceutical industry and the vastly untapped potential of biological research, more attempts are being made to recognize the issues unique to biotechnology. These changes have both positive and negative aspects on scientific research. Regardless, the problems of proteomic research probably cannot be addressed within the confines of the current system.

1. Early Biological Patent Issues

For much of the nation's history, the concept of patents covering biological molecules such as DNA was foreign and contrary to the principles of patent law and popular ethics.[93] Any products of nature were commonly thought to be unpatentable, and many argued

90. Schwartz, *supra* note 17, at 89.

91. *See, e.g.*, Chan & Fernandez, *supra* note 41, at 468 (describing broad language used in the patent for the drug Viagra).

92. As discussed *infra*, a major issue in patentability in the field of proteomics is the scope of claims due to the time that is necessary to fully understand the potential functions of the newly discovered protein. *See also* Chan & Fernandez, *supra* note 41, at 462-63, 468 ("Obtaining FDA approval for a drug often takes substantially longer than patent prosecution, effectively reducing the term of the patent once issued.").

93. *See Molecules vs. Information*, *supra* note 3, at 191-96 (discussing the development of patenting DNA sequences); Diamond v. Chakrabarty, 447 U.S. 303, 318-320 (1980) (Brennan. J., dissenting) ("The Acts [do] not include living organisms."). Indeed, many people remain opposed to this type of patenting, seeing it as treating life as a commodity. *See, e.g.*, Human Genetics Alert, The Human Genome Gold Rush, *at* http://www.hgalert.org/topics/lifePatents/Patents2.html (last visited Oct. 15, 2005) (citing numerous arguments against gene patenting).

that living things were beyond the scope of the written requirements for patenting.[94] Courts very early on recognized subject matter products isolated and purified by man, such as proteins, as patentable.[95] From this beginning has come a tendency to expand the patentability of modified living matter. For example, Congress passed the Plant Patent Act of 1930, which extended patent protection to various asexually produced plants, and the 1970 Plant Variety Protection Act, which extended patent protection to certain sexually reproduced plants.[96]

The issue of whether living organisms could be patented without the express approval of Congress came to the forefront in *Diamond v. Chakrabarty*.[97] The USPTO granted a patent to Chakrabarty covering genetically altered bacteria specially designed to break down the components of crude oil.[98] The United States fought this approval on several grounds, including the argument that granting incentives to create genetically altered material would possibly "spread pollution and disease, that it may result in a loss of genetic diversity, and that its practice may depreciate the value of human life."[99] The Supreme Court, choosing a broad interpretation of the Patent Act's subject matter requirements, held that Congress intended to extend patent protection to "anything under the sun made by man."[100] Since the invention was man-made and not occurring naturally in nature, it qualified for protection.[101]

The *Chakrabarty* decision significantly altered the pace and path of biotechnology development, since biotechnology researchers were given another tool by which they could claim value for their works.[102] In the years since the decision, patent procurement has

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94. *Chakrabarty*, 447 U.S. at 311-12.

95. *See, e.g.*, Parke-Davis & Co. v. H.K. Mulford Co., 189 F. 95, 103-04 (C.C.S.D.N.Y. 1911) (accepting the patentability of purified adrenalin).

96. *Chakrabarty*, 447 U.S. at 310-11.

97. 447 U.S. at 303. The petitioner, representing the United States, argued unsuccessfully that since bacteria were excluded from the 1970 Plant Act, Congress did not in general believe that living things were patentable. *Id.* at 311.

98. *Id.* at 305-06.

99. *Id.* at 316.

100. *Id.* at 309. This broad interpretation of subject matter has been extended in subsequent cases by the Federal Circuit. *E.g.*, State St. Bank & Trust Co. v. Signature Fin. Group, 149 F.3d 1368, 1373 (Fed. Cir. 1998) (citing *Chakrabarty*, 447 U.S. at 309); AT&T Corp. v. Excel Communications, Inc., 172 F.3d 1352, 1355 (Fed. Cir. 1999) (same).

101. *Chakrabarty*, 447 U.S. at 315-16.

102. *See generally* FOOD AND AGRICULTURAL ORGANIZATION, UNITED NATIONS, IPRS IN THE FIELD OF BIOTECHNOLOGY FOR FOOD AND AGRICULTURE (discussing the path of biotechnology development), *available at* http://www.fao.org/biotech/C6doc.htm (last visited Feb. 25, 2005).

been one of the major resources of biotechnology innovators.[103] Patents are used for their own value, for their leverage in licensing negotiations, and for possible "reach through" to recoup on the improvements of the patent's successors.[104] "Reach-through" licenses are particularly contentious since they involve charging fees on the sales of products developed through the patented technology but not included in the claim and likely not foreseen by the patentee.[105]

2. The Human Genome Project and the Race to Patentable Information

The United States Department of Energy ("DOE") and National Institutes of Health ("NIH") founded the Human Genome Project in the early 1990s for the purpose of coordinating a global effort of sequencing the entire human genome and cataloging all of the genes found in human chromosomes.[106] The project was supposed to take well over a decade to complete.[107] However, advances in technology, fueled partially by the fears that research corporations would attempt to patent all of the sequence information they generated, resulted in the project's early completion. [108]

The experience of the genomics industry may be illustrative of the positive and negative impacts that the possibility of patents will cause as the focus of biotechnology shifts from the genome to the proteome. The NIH originally set out to patent gene expressed sequence tags ("ESTs") in its research but backed away from this effort when it faced opposition from the USPTO and controversy in the public.[109] At the time of this action, the majority of biotechnology

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103. Patents in the molecules and the technology themselves are ubiquitous and offer investments that are both attractive and legally dangerous to investors. *See* Donald R. Ware, *Research Tool Patents: Judicial Remedies*, 30 AIPLA Q.J. 267, 269-70 (2002) (listing potential research tool patents that an innovator may have to confront when searching for drug targets with genomics or proteomics).

104. *See generally* Reid Adler, *Corporate Strategies in the Genomics Industry*, 3 YALE SYMP. L. & TECH. 1 (2000) (providing "an overview of the various corporate patent strategies available to genomics companies attempting to secure an influx of capital"). Indeed, there has been so much of an increase in biotechnology patent applications that the USPTO has begun to craft ways to limit their procurement. Esoy, *supra* note 75, at 128-30.

105. *E.g.*, Ducor *supra* note 36, at 156-57; *see also infra* Part IV.

106. Human Genome Project, U.S. Dep't of Energy, About the Human Genome Project, *at* http://www.ornl.gov/sci/techresources/Human_Genome/project/about.shtml (last visited May 25, 2005); *see, e.g.*, Esoy, *supra* note 75, at 132.

107. Esoy, *supra* note 75, at 132.

108. *Id.*

109. Cyranoski, *supra* note 6, at 10. ESTs are fragments of DNA which of themselves may have no function, but they can provide information about corresponding genes. *See* Human Genome Project, U.S. Dep't of Energy, Genome Glossary, *at* http://www.ornl.gov/sci/techresources

research was "not-for-profit," conducted in universities, and established by unique funding.[110] Many feared that the "scientific and medical advances promised by the human genome sequence would be restricted by overarching patent claims."[111]

However, members of the original research laboratories did not give up on the possibility. As USPTO guidelines changed in the late 1990s,[112] corporations such as Celera began securing patents on these types of biological information. Celera became the major competitor of the Human Genome Project.[113] In 2000, Celera announced that it had finished sequencing and applied for over 6,500 provisional patent applications.[114] Further, it planned to release the genomic information it did not patent via a patented computer database available to researchers only by subscription and attached to a non-disclosure agreement.[115] Other companies quickly followed suit.[116]

/Human_Genome/glossary/ (last visited May 25, 2005). Single nucleotide polymorphisms ("SNPs"), which are sequence variations occurring when a single base pair is altered, are another form of biological matter which has proven contentious under patent law. *Id.; see also, e.g.*, Sung, *supra* note 72, at 21.

110. Symposium, *Bioinformatics and Intellectual Property Law April 27, 2001 – Boston, Massachusetts: The Proper Scope of IP Rights in the Post-Genomics Era*, 8 B.U. J. SCI. & TECH. L. 233, 242 (2002) [hereinafter *Proper Scope*].

111. Cyranoski, *supra* note 6, at 10. "A proliferation of intellectual property rights upstream may be stifling life-saving innovations further downstream . . . ." Michael A. Heller and Rebecca Eisenberg, *Can Patents Deter Innovation? The Anti-commons in Biomedical Research*, 280 SCIENCE 698, 698 (1988). This argument is further developed in *infra* Part IV.

112. "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." Sung, *supra* note 1, at 282. Since this time, the USPTO has completely reversed its guidelines causing considerable confusion as to the validity of these types of patents. *See* Esoy, *supra* note 74, at 153-54, 163-64 (arguing that the standards are contrary to the relatively lax position adopted by the Federal Circuit).

113. *See* Celera, Our History [hereinafter Our History] (describing Celera milestones in mapping the human genome), *available at* http://www.celera.com/celera/history (last visited Feb. 23, 2005).

114. Jennifer Doran, *Celera Genomics to Complete DNA Map*, 28 J. L. MED. & ETHICS 188, 188 (2000). Provisional patents give inventors a set time to determine if full patent protection is justified. *Id.*; *e.g.*, 35 U.S.C. § 111(b) (2003).

115. *Our History*, *supra* note 113; Amol Pachnanda, Comment, *Scientific Databases Should Be Protected Under a Sui Generis Regime*, 51 BUFFALO L. REV. 219, 219-220 (2003); McBride, *supra* note 23, at 1338.

116. For example, Genomics Solutions, Inc. and Affymetrix Corp., two of the leaders in genomics and proteomics research, require use of their products system to access their rapidly expanding databases of molecular information. *See* Genomics Solutions, Inc., Home (important notices on sign-in), *at* http://bioinformatics.genomicsolutions.com/index.html (last visited May 25, 2005); Affymetrix Corp, NETAFFX Analysis Center (same), *at* http://www.affymetrix.com/analysis/index.affx (last visited Feb. 23, 2005). Of course, the expenses in developing systems such as these may justify restricting access to certain information obtained in the research process.

Today, just two of the major genomics companies have filed over 25,000 DNA-based patent applications.[117]

While Celera and other private industry giants justifiably seek to maximize profits extracted from their labor, their actions are threatening to the traditional, academically-oriented scientific community, which has long operated on the proposition of freely transferred information and data, peer review, and publication.[118] The race to patent resulted in a backlash that caused an influx of publicly generated information designed to create prior art to defeat patent claims.[119] Public scientific research has managed to survive and compete with private industry in the field of biotechnology. Recent developments in patent law interpretation, however, threaten to shut out universities from anything but basic research in the field and potentially may alter the dynamics of scientific research as a whole.[120]

B. The USPTO and the Federal Circuit's Patent Act Interpretations and Their Implication on Proteomics Patents

Biotechnology patent applications are generally evaluated like any other patent by both the courts and the USPTO.[121] This evaluation can cause problems because the biotechnology field does not lend itself to traditional patent law concepts.[122] Recently, however, there has been some recognition of the unique aspects of biotechnology reflected in both the USPTO's guidelines and the Federal Circuit's interpretation of those guidelines. This equal treatment of biotechnology with respect to some patent requirements and special treatment with respect to others has and will continue to

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117. These are Human Genome Sciences and Incyte Genomics. Service, *supra* note 3, at 2082.

118. Pachnanda, *supra* note 115, at 220. Indeed, peer review and publication of scientific data are so pervasive that they have long been instrumental factors in whether expert scientific testimony is admissible in courts. *See, e.g.*, Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579, 594 (1993) ("The fact of publication (or lack thereof) in a peer reviewed journal thus will be a relevant, though not dispositive, consideration in assessing the scientific validity of a particular technique or methodology on which an opinion is premised.").

119. *Molecules vs. Information*, *supra* note 3, at 201.

120. *E.g.*, Cyranoski, *supra* note 6, at 10. For example, a company who owns a patent on a gene and a patent for a target protein resulting from that gene may theoretically be able to claim any process or product downstream from the protein as within their claim, resulting in total control over a specific drug target and its homologs. *See, e.g.*, *Molecules vs. Information*, *supra* note 3, at 94 ("They patent what they can, and they hope that some of those patents will some day help them make a profit, maybe by allowing them to capture a share of the profits on future drugs."). This problem is discussed *infra* Part IV.

121. It is precisely this equal treatment that this Note argues against.

122. *See supra* discussion in Parts II., III.A.1.

cause confusion and legal controversy. Of particular importance are these institutions' interpretations of subject matter, the written description requirement, the utility requirement, the scope of patent claims, and, recently, the experimental use exception.

1. Further Extension of Subject Matter to Include Business Methods and Software Directly Impacts Bioinformatics

Several Federal Circuit decisions have reinterpreted the scope of a patent's subject matter and written description requirements.[123] These sections of the patent statute appear to have been the "principal sites in which the U.S. Federal Circuit's structural conception of modern biotechnology has been reflected"[124] and where the most change with respect to biotechnology in the patent law has occurred. First, with respect to statutory subject matter, the Federal Circuit rejected limitations on patentability of an invention, so long as it "falls within at least one of the four enumerated categories" of section 101.[125] The court abandoned several traditional "judicially-created" exceptions to patentability and, instead, focused simply upon whether the methods or processes claimed in the invention, as a whole, produce "useful, concrete and tangible results" and whether they meet the other requirements of the patent statute.[126] The decision opened the way to increased acceptance of the patentability of software applications.[127]

In *AT&T Corp. v. Excel Communs., Inc.*,[128] the Federal Circuit reiterated its focus on the claim's usefulness in satisfying the broad principles of section 101. Excel, defending an allegation that they infringed on a software patent, contended that claims involving mathematical algorithms as part of their function could only meet the patentable subject matter requirements of section 101 if the process

123. *See* 35 U.S.C. § 101 (setting forth the subject matter requirements); 35 U.S.C. § 112 (setting forth the written description requirements) .

124. Justine Pila, *Bound Futures: Patent Law and Modern Biotechnology,* 9 BU. J. SCI. & TECH. L. 326, 345 n.57 (2003).

125. State St. Bank & Trust Co. v. Signature Fin. Group, 149 F.3d 1368, 1372 (Fed. Cir. 1998). The categories permissible for patenting are "any new and useful process, machine, manufacture, or composition of matter." 35 U.S.C § 101 (2003).

126. *State St. Bank*, 149 F.3d at 1373-76. Specifically, the court rejected the "business method" exception as it categorically distinguished between business and other processes, and the "mathematical algorithm" exception, to the extent that it was used to exclude any kind of invention making use of mathematical subject matter and not limiting its use to inventions that represented abstract ideas standing alone. *Id.*

127. *See* Vorndran & Florence, *supra* note 54, at 108 ("The result . . . is that pure software patents are here to stay . . . .").

128. 172 F.3d 1352 (Fed. Cir. 1999).

"physically transformed" the data it used into another form.[129] The court stated that, while a claimed transformation of data sufficiently satisfied section 101, it was not due to the transformation but rather because a change in form demonstrated the production of a "useful, concrete tangible result."[130] Therefore, any claim that utilizes unpatentable subject matter[131] to produce a useful result should at least satisfy the low threshold of section 101 for patentability. Decisions such as *AT&T* are profoundly important in the proteomics field, since the use of biological databases for identifying and assessing results is essential to the efficiency of the industry.[132] Since databases can now be patented and the information contained in them secured by agreements not to disclose, another traditional publicly available route to research data is now protected through the patent monopoly.[133]

2. Relaxation of the Written Description Requirement

With its decision in *Enzo Biochem, Inc.*, the Federal Circuit has also responded to the unsettled nature of biotechnology by altering its interpretation of the patent statute's written description requirement.[134] Just five years before the *Enzo* decision, the court applied its traditional written description analysis to reject a claim for human insulin cDNA based on the successful cloning at the University of California of a similar sequence in rats.[135] The court stated that, to be adequate, a written description of a biological molecule " 'requires a precise definition, such as by structure, formula, chemical name, or

129. *Id.* at 1358-60.

130. *Id.* at 1358-59.

131. These include "laws of nature, natural phenomena, and abstract ideas." Diamond v. Diehr, 450 U.S. 175, 185 (1981).

132. *See generally* Vondran & Florence, *supra* note 54 (discussing the role of bioinformatics in the pharmaceutical industry for the efficient development of drugs based on proteins discovered through proteomic techniques).

133. Further, scientists who wish to start genomic or proteomic research will have to license from the company the database, the information contained in the database, and all of the technology necessary to generate their own data in a total package. *See, e.g.*, Genomic Solutions, Proteomics (exhibiting their full range of researching tools and data integration), *at* http://www.genomicsolutions.com/showPage.php?cachevar=&menuID=361 (last visited Feb. 23, 2005).

134. "The specification shall contain a written description of the invention . . . in such, full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains . . . to make and use the same . . . ." 35 U.S.C. § 112 (2003).

135. *See generally* The Regents of the Univ. of Cal. v. Eli Lily & Co., 119 F.3d 1559, 1562-69 (Fed. Cir. 1997) ("[A] cDNA is not defined or described by the mere name 'cDNA'. . .but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA.").

physical properties,' not a mere wish or plan for obtaining the claimed chemical invention."[136] Therefore, under *Lilly*, one has to know the exact structure, not simply the functions of the molecule, in order to patent a claim successfully.[137] The decision was steeply criticized as heightening standards for the biological industry in comparison to other fields.[138]

The Federal Circuit appeared to affirm this decision in *Enzo Biochem, Inc. v. Gen-Probe Inc.*,[139] when it affirmed that nucleic acid probes, which were defined by biological activity and deposited publicly, did not satisfy section 112 with respect to written description.[140] Enzo received a patent for its invention of molecular probes that reacted exclusively with the DNA of the bacteria that cause gonorrhea.[141] To meet the written specification requirements of the Patent Act, it deposited a sample of the actual recombinant DNA molecule at the American Type Culture Collection ("ATCC").[142] The court stated that describing a molecule by its function and sequence "fails to distinguish it from other molecules that can perform the same function."[143] The written description requirement must not only enable one skilled in the art to "make and use" the invention but must also show with "reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention."[144]

On rehearing, the court vacated and reversed the judgment[145] and signaled that it may be more tolerant of the unique and uncertain qualities possessed by biological inventions.[146] The court, adopting the

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136. *Id.* at 1566 (quoting Fiers v. Revel, 984 F2d 1164, 1171 (Fed. Cir. 1993)).

137. *Id.* at 1568. A description of one type of mammalian DNA is not a description of the genus. *Id*; *see also* John C. Stolpa, *Toward Aligning the Law With Biology? The Federal Circuit's About Face in* Enzo Biochem, Inc. v. Gen-Probe, Inc., 4 MINN. INTELL. PROP. REV. 339, 350 (2003) (discussing the ramifications of *Eli Lilly* on those pursuing patents in DNA technology).

138. Stolpa, *supra* note 137, at 350-351.

139. 285 F.3d 1013, 1020 (Fed. Cir. 2002).

140. *See id.* at 1018-20 ("We also conclude that Enzo's claims do not meet the written description requirement..[and] § 12, ¶ 1 is not met.").

141. *Id* at 1015-16.

142. *Id.* at 1016. The ATCC is a non-profit organization that collects, preserves and distributes biological materials and information to industry and academia for the purposes of furthering research. It has grown to be one of the world's largest warehouses of biological materials. *See* ATCC, The Global Bioresource Center, About ATCC, *at http://www.atcc.org/About/AboutATCC.cfm* (last visited Feb. 25, 2005) (providing an overview of the organization).

143. *Enzo*, 285 F.3d at 1019.

144. *Id.* at 1020 (quoting Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563 (Fed. Cir. 1991)).

145. Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F. 3d 1316, 1320 (Fed. Cir. 2002).

146. The court's reasoning was based "[i]n light of the history of biological deposits for patent purposes, the goals of the patent law, and the practical difficulties of describing unique biological materials in a written description." *Id.* at 1325; *see also* Stolpa, *supra* note 137, at 357 (stating that the decision appears to be a "concession" to biologists).

guidelines used by the USPTO, refused to accept that *all* biological material described in functional terms fell short of the written requirements if the claim incorporated a "disclosed correlation" with a "sufficiently known" structure.[147] Therefore, since "words alone" are often not satisfactorily enabling or demonstrative of possession of the invention claimed, the court was willing to accept that a deposit of claimed material in a publicly accessible depository and incorporation by reference in the specification adequately described the claim for purposes of section 112.[148] This broadening of statutory interpretation represents an alternative method by which biological researchers may be granted protection without expending valuable time and money racing for the exact sequence or structure of the molecule they have isolated or cloned.[149] The court also believed that a materials deposit properly referenced in the invention's specifications represented an adequate exchange of information for the patent monopoly. [150]

The decision in *Enzo* has important ramifications to the proteomics field. As previously stated, proteins are likely to be discovered and isolated initially by structure and afterwards by function, and an exact written description alone may not have been enough to satisfy the requirements of section 112.[151] Further, even if a structural or chemical description of the invention may be adequate, the level of disclosure of the invention is of crucial importance.[152] It is only much later in the research and development of isolated proteins that their complete functionality can be comprehensively understood.[153] An inventor may be left with patent protection for a particular protein function that has no value after the disclosure of the information results in a multitude of different applications impossible to anticipate at the time of the initial discovery.[154]

While *Enzo* potentially has broadened the scope of biological patent protection, it has left many questions unanswered and has been the subject of criticism due to the uncertainty it has generated in

147. *Enzo*, 296 F.3d at 1324-25. The PTO guidelines are discussed in greater detail, *infra* Part III.

148. *Id.* at 1325-26 (quoting MPEP § 2402 (8th ed. Aug. 2001). This assumes that all other requirements for patentability are also satisfied. *Id.*

149. *See* Stolpa, *supra* note 137, at 357 ("Enzo II purports to provide additional means by which inventors might also meet [the written description requirement].").

150. *Enzo*, 296 F.3d at 1330.

151. Chan & Fernandez, *supra* note 41, at 461-62.

152. *Id.* at 468.

153. *Id.* at 462.

154. *See, e.g.*, *Molecules vs. Information*, *supra* note 3, at 205-06 (arguing that drugs ultimately produced from protein discoveries may never be considered infringing uses of that particular patent).

claim crafting.[155] The decision does not render all functional descriptions, or even all deposits of biological material, adequate for section 112 requirements.[156] While a broadened written description possibly may allow a researcher to claim more within his limited area of innovation, such as downstream products or unforeseen functions, inventors may still be confined to the sequence that must be disclosed.[157] Simply "establishing goals does not a patent make," [158] and courts remain adamant that there must be enough referencing or description to enable others skilled in the art to recognize possession of the invention and to reproduce it.[159] Some analysts believe, therefore, that *Enzo* still does not allow for a biological innovation to "reach through" to subsequent, but initially unrecognizable, uses.[160]

3. Utility – USPTO and the Federal Circuit Currently Have Different Standards for Biotechnology

As stated previously,[161] the Federal Circuit has developed a very relaxed standard in considering utility. However, the USPTO recently has adopted specific guidelines addressing the requirement of utility with respect to gene patent applications.[162] This occurred in response to the controversy engendered from relaxing the guidelines to allow the patentability of EST fragments and SNPs.[163] The previous guidelines were designed to "give proper deference" to biotechnologists and required only that an invention show "specific" and "credible" utility.[164] The relaxed guidelines had allowed EST

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155. *See generally* Harold C. Wegner, *When a Written Description is Not a "Written Description": When* Enzo *Says it's Not*, 12 FED. CIR. B.J. 271 (2002) (attacking the decision on several grounds).

156. *See, e.g.*, Stolpa, *supra* note 137, at 358-62 ("Making a biological deposit may now be used to demonstrate possession, but this is contingent on the accession number of the deposit being recited in the specification."); *see also* Univ. of Rochester v. G.D. Searle & Co., 249 F. Supp. 2d 216, 219-235 (W.D.N.Y. 2003) (holding that a claim for two related human enzymes that could potentially be used to produce a stomach pain reliever did not meet § 112 because, while providing a function for the enzymes, the claim did not disclose the organic compounds necessary to provide that function).

157. Stolpa, *supra* note 137, at 360; Merges, *supra* note 18, at 139-41.

158. *Univ. of Rochester*, 249 F. Supp. 2d at 218.

159. *Id.*

160. *See generally* John R. Thomas, *Formalism at the Federal Circuit*, 52 AM. U. L. REV. 771, 800-01 (2003) (discussing the relative flexibility of claim constructions in biotechnology versus other scientific industries). "Reach-through" licenses are defined *supra* in Part II.A.

161. *See supra* Part II.B.

162. Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001).

163. *See supra* note 111 and accompanying text.

164. Esoy, *supra* note 75, at 150-51 (discussing Utility Examination Guidelines, 60 Fed. Reg. 36323 (July 14, 1995)).

patents to be approved without failing for lack of utility during the late 1990s.[165]

The new utility guidelines establish that biotechnological patents must possess a "specific, substantial and credible" utility in order to be patentable.[166] The specificity requirement ties the utility to the subject matter claimed.[167] This means that gene fragments would have to be able to state a specific function or connection that corresponded to the claimed nucleic acid.[168] Further, the "substantial" language may be interpreted as requiring a "real world use," rather than simply the ability to predict or identify other biological molecules and data.[169]

Strengthening the utility requirement for biotechnology inventions may be a step in the right direction towards the recognition of the unique problems in the field.[170] The prevention of broad-reaching biotechnology patent claims at least demands that more functional research be conducted before intellectual property territory can be claimed.[171] However, the new rules are in direct opposition to the Federal Circuit's broad interpretation of the utility requirement and may meet with some consternation if challenged in court.[172] The Federal Circuit repeatedly has held the statutory requirement of utility is met if "it is capable of providing some identifiable benefit."[173] The Federal Circuit is not bound by the USPTO policy determinations and only uses them as a guide to its interpretation of the law.[174] Therefore, the court may, and at least one paper has argued it should, decide that the policy is too restrictive under the language of the statute.[175] Either way, Congress arguably is in a better position to address the issue.

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165. *See* Esoy, *supra* note 75, at 150 (citing, for example, U.S. Patent No. 5, 817, 479 issued to Incyte, Inc. with the EST's stated utility of being able to "generate kinase homologs").

166. *Id.* at 152.

167. *Id.*

168. Claimed nucleic acid structure, which can easily be obtained from these fragments, are unpatentable without a claimed utility for the gene they disclose. Sung, *supra* note 1, at 283 & n.121.

169. Esoy, *supra* note 75, at 153.

170. The new guidelines were met with general approval in the scientific community. *Id.* at 152.

171. Chan & Fernandez, *supra* note 18, at 469-70.

172. *Id.*

173. Juicy Whip, Inc. v. Orange Bang, Inc., 185 F.3d 1364, 1366 (Fed. Cir. 1999).

174. *See, e.g.*, Esoy *supra* note 75, at 156 ("It is clear that the PTO does not have unfettered discretion on these matters.") (citing Enzo Biochem, Inc. v. Gen-Probe, Inc., 296 F.3d 1316, 1324 (Fed. Cir. 2002)).

175. *See id.* at 157-65 ("By judging patent applications against the 'specific, substantial, and credible' utility standard, the PTO is effectively denying patents to inventions that should

4. Claim Breadth: Interpretations Lead To Patenting Uncertainty

Industry and individual researchers who wish to obtain any profit from biological molecule patents must try to craft them as broadly as possible.[176] Navigating the fine line between claims that are too broad to be accepted and too narrow to produce value is not unique to biotechnology patents.[177] This tension, however, is of particular importance in the patenting of biological molecules because of the existence of a multitude of structurally and potentially functionally equivalent molecules that may not be discovered until after the patent is issued.[178] A functionally equivalent protein, for example, that was adjudged not to be covered by the patent would completely undercut the patent's value.[179] For this reason, much of the patent prosecution process involves the fine-tuning of claims.[180]

The judicially created doctrine of equivalents has allowed patentees to stake claim to certain "insubstantial variations" that are beyond the literal bounds of the claim.[181] However, the Supreme Court recently stated that an applicant who surrenders subject matter during the prosecution process due to the USPTO's rejection of the patent's specification is estopped from reclaiming the same subject matter under the doctrine of equivalents.[182] The decision has led prospective patentees to fear that protein patents would have to "meticulously and individually disclose and claim each and every functionally equivalent homolog" in order to protect the value of the

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receive patent protection"). Another potential argument, however, with respect to protein patents and utility is that, despite the Federal Circuit's relaxation of the standards for other patents, proteins must meet the substantial utility standard of *Brenner*. *See* Brenner v. Manson, 383 U.S. 519 (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.").

176. Merges, *supra* note 18, at 144-149.

177. *See, e.g.*, Jacob S. Wharton, Festo *and the Complete Bar: What's Left of the Doctrine of Equivalents?*, 20 ST. LOUIS U. PUB. L. REV. 281, 282-83 (2001).

178. *See, e.g.*, Mark L. Hayman & Lisa E. Stahl, *Homology Claims Face New Equivalents Hurdles; Variations on DNA and Protein Molecules May Be Harder to Protect*, 26 NAT'L L.J. S4 (2003) (discussing the impact of the Supreme Court's narrowing of doctrine of equivalents claims on biological molecule patents due to the existence of many functional homologs of patented proteins).

179. *Id.*

180. *Id.* "The actual effect on activity of a given alteration in amino acid sequence can be unpredictable," resulting in frequent rejection of homolog claims by the USPTO for claims that could not be replicated without undue experimentation. *Id.* This leads frequently to amended claims with respect to homology. *Id.*

181. *Id.*

182. Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushki Co., Ltd., 535 U.S. 722 (2002); Hayman & Stahl, *supra* note 178, at S4.

patent.[183] The total effect of the Supreme Court's interpretations is unclear as cases on the issue have been remanded for further trial court proceedings.[184] Uncertainty as to the potential value of the multitude of protein patents currently being filed or in effect presumably will lead to greater protective efforts by private industry to recoup profits.[185]

On the opposite end of the spectrum are judicial and USPTO decisions that uphold broadly drafted patents. For example, the Federal Circuit upheld a number of patents for the protein erythropoietin ("EPO") which were produced through recombinant DNA technology.[186] The patents' claims were broadly drafted as covering any EPO protein that was "vertebrate," "mammalian," and "non-naturally occurring."[187] The court has enforced the patents to cover any use of mammalian cells for the production of EPO, which effectively gives the patent owner complete control over the production and distribution of this valuable protein, since all potential variations would likely fall within the claims.[188]

Another example is DuPont's patent on its genetically altered "OncoMouse," which the company exclusively licenses.[189] The patent potentially covers inserting any oncogene into any mammalian species.[190] Transgenic mice patents such as this have had some chilling effect on scientific research.[191] The acceptance of broadly reaching patents such as these encourages broadly drafted patents on all fronts.[192]

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183. Wharton, *supra* note 177, at 290.

184. Hayman & Stahl, *supra* note 178, at S4.

185. *See e.g., Molecules v. Information*, *supra* note 3, at 204-05, 212 (describing one company's efforts to maximize profits by patenting every discovery possible, using roadblocks and trading rights to proteins because of tbe uncertainty of the market).

186. *See, e.g.,* Amgen, Inc. v. Hoechst Marion Roussel, 314 F.3d 1313, 1324-25 (Fed. Cir. 2003).

187. *Id.* at 1324-25.

188. Cyranoski, *supra* note 8, at 11.

189. Richard Stallman, *Are U.S. Patents Too Broad?*, SCIENCE., July 19, 2002, at 336.

190. *Id.* An "oncogene" is a "gene thought to be capable of producing cancer." BIOTECanada, Biotech Classroom–What is Biotechnology?–Glossary, *at http://www.biotech.ca/EN/glossary.html.*

191. John P. Walsh et. al, *Working Through the Patent Problem*, SCIENCE, Feb. 14, 2003, at 1021.

192. For example, patent 6,647,341, issued in November 2003, covers the use of an algorithm to distinguish samples in a gene expression array, and is broadly drafted such that it may cover "pretty much any application of gene-expression arrays for clinical data.'" Jocelyn Kaiser, *Patent Sprawl: From Genes to Gene Interpretation*, SCIENCE, Dec. 12, 2003, at 1878. The NIH is so concerned about this issue that it recently has awarded a $1.2 million grant to determine the consequences of judicially accepted broad patents covering biological molecules. Cyranoski, *supra* note 8, at 11.

5. The Experimental Use Exception—No Longer a Safe Haven for Academic Research

Finally, and perhaps most importantly in terms of the free exchange and use of research information, is judicial re-interpretation of the experimental use exception. The experimental use exception is a narrowly construed doctrine that "protects alleged infringers who use patented inventions solely for experimental purposes, such as testing whether a device functions as claimed or re-creating a process to observe its effects from a scientific perspective."[193] Many, if not most, academic researchers believe that this exception covers all academic research, so they have no reason to worry about broad reaching industry patents.[194]

In *Madey v. Duke University*,[195] however, the Federal Circuit made it clear that the experimental use doctrine does not exempt academic researchers from patent infringement.[196] The argument centered on the potentially infringing use of laser technology that Madey had developed and patented at Duke University.[197] The district court granted summary judgment in favor of Duke, believing the experimental use exception applied to institutions using patents with no commercial purpose.[198] The Federal Circuit reversed, stating that the exception only encompasses use for "amusement, to satisfy idle curiosity, or for strictly philosophical inquiry." [199]

The court stated that the University may be using the patented technology for research that would result in direct commercial gain from its own patentable inventions.[200] Further, even if the uses were not for direct commercial gain, the court concluded that if the experimentation was to "further the institution's legitimate business objectives," it would not be subject to the exception.[201] Under this interpretation, any educational research that utilizes patented

193. Tom Saunders, *Renting Space on the Shoulders of Giants:* Madey *and the Future of the Experimental Use Doctrine*, 113 YALE L.J. 261, 261 (2003).

194. Cyranoski, *supra* note 8. at 11.

195. 307 F.3d 1351 (Fed. Cir. 2002), *cert. denied*, 123 S. Ct. 2639 (2003).

196. *See id.* at 1360-63 ("The correct focus should not be on the non-profit status of Duke but on the legitimate business Duke is involved in.").

197. *Id.* at 1352-53.

198. *Id.* at 1354-55. Madey also successfully argued that the District Court in effect shifted the burden of proof to the patent holder to prove that the use was not experimental, an argument that the Federal Circuit rejected. *Id.* at 1360-61.

199. *Id.* at 1362. The use does not qualify when "it is undertaken in the 'guise of scientific inquiry' but has 'definite, cognizable, and not insubstantial commercial purposes.' " *Id.* (quoting Roche Products, Inc. v Boler Pharm. Co., 733 F.2d 858, 863 (Fed. Cir. 1984)).

200. *Id.*

201. *Id.*

material is potentially infringing if unauthorized by the patent's owner.[202] University research is conducted to aid in education, to maintain or to obtain status as a quality research facility and to obtain funding through grant programs.[203] All of the above reasons are more than enough to bring public research out of the experimental exemption.

It is unclear what impact the *Madey* decision will have on future academic research. *Madey* was undoubtedly a "unique" decision involving a disgruntled former employee suing to restrict the use of patents he developed while working at the University.[204] Private industry has, on a whole, been very tolerant of infringing uses by research institutions, since additional research can potentially increase the value of their patents and lawsuits can cause more damage than they are worth.[205] However, private industry is business, and where value is being threatened, such as infringing use of diagnostic tests in clinical research, companies may be more willing to litigate.[206] The proteomics field is a very high risk investment because of the uncertainty and large front-end cost in uncovering major profit-producing proteins, such as drug targets.[207] Thus, the economic nature of the industry may also lend this field to an increased willingness to litigate.[208]

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202. *See, e.g.*, Saunders *supra* note 193, at 263 (arguing that the decision effectively destroyed any use of the exception).

203.

> Major research universities, such as Duke, often sanction and fund research projects with arguably no commercial application whatsoever. However, these projects unmistakably further the institution's legitimate business objectives, including educating and enlightening students and faculty participating in these projects. These projects also serve, for example, to increase the status of the institution and lure lucrative research grants, students and faculty.

Id.; *see also* Cyranoski, *supra* note 8, at 11 (noting that "the university was using the technology in the business of teaching and getting grants, not to satisfy idle curiosity").

204. *Madey*, 307 F.3d at 1352-53. Madey was removed as the head of Duke's reputable free electron laser laboratory after disagreements with the institution and resigned his position the next year. *Id.*

205. *See* Walsh et al., *supra* note 191, at 1021 (reporting survey results indicating that intellectual property holders "tolerat[e] academic research infring[ment] . . . because it can increase the value of the patented technology"; additionally, "the small prospective gains from a lawsuit [a]re not worth the legal fees, the risk of the patent being narrowed or invalidated, and the bad publicity from suing a university").

206. *See id.* (noting that the tolerance of academic infringement does not extend to patents on diagnostic tests used in clinical research).

207. *See* Service, *supra* note 3, at 2083 (noting that the interaction between competing protein and gene patents is far from settled, and, accordingly, the value of both is extremely uncertain).

208. *Id.*

IV. TRADITIONAL PATENT LAW MAY NOT ADEQUATELY OR EFFICIENTLY COVER THE NATURE AND ECONOMICS OF PROTEOMICS

There are several benefits and drawbacks to the current aggressive market in biotechnology patents, in particular proteomics. The economic market in which private industry operates is in direct conflict with the public sector and will continue to cause uncertainty and tension as long as current patent law is in play.[209] Several biotechnology-specific alterations have been proposed, but they may not adequately address the potential problems and the resulting potential backlog of litigation proteomics may engender as it comes to fruition in the next few decades.

A. Private Industry, Research and Development, and Incentives to Innovate

The private biotechnology industry as a whole has highly supported the broad patenting of biological methods and molecules.[210] A key element of the patent theory is to provide protection for innovation as an incentive to promote more innovation.[211] This incentive is particularly important in biotechnology, where outcome uncertainty provides for exceptionally risky investments and start-up capital for new research and development reach staggering amounts.[212] Biotechnology companies argue that limiting or altering the patent law with respect to biological molecules will be a strong disincentive for investment and invention.[213]

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209. *See supra* Part III.B.5. (discussing the evolution of the experimental use exception).

210. *See e.g.*, Laurie L. Hill, *The Race to Patent the Genome: Free Riders, Hold Ups, and the Future of Medical Breakthroughs*, 11 TEX. INTELL. PROP. L.J. 221, 239-40 (2003). For example, the Biotechnology Industry Organization has been a strong lobbyist for traditional patent protection of biotechnology in Congress. *Id.* at 240-41.

211. This theory is embodied in the Constitution. *See* U.S. CONST. art. I. § 8. cl. 8 ("To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries.").

212. *See* Hill, *supra* note 210, at 239-40 ("Biotechnology industrialists forcefully maintain that strong patent protection is essential to protect risky investments in biology-based research because of the unusually high failure rate of products.")

213. The argument can be persuasive. The U.S. currently has over 1,400 biotechnology companies, with revenues over $20 billion annually and over 9,000 patents granted per year. *Id.* at 236-37. The industry has also tripled in size since 1992. *Id.* The relaxation of certain aspects of the patent law has appeared to have spurred at least part of this growth. *Id.*

1. Potential Benefits of Strong Patent Protection to Biotechnology

Supporters of current or more relaxed standards of patentability disparage arguments that biotechnology should have its own specific set of laws, and dismiss most of the public sector's fears as purely theoretical and highly improbable.[214] These entities pose several arguments in favor of maintaining the status quo. Drawing examples from other rapidly advancing industries, such as informational technology, biotech companies say that genes and proteins are not so different from any other inventions that have successfully developed under the current Patent Act.[215] They further argue that lack of patent protection may completely remove any value in the research, since much time, effort and money has to be expended in the front-end to reap any further value that free riders could easily take and exploit.[216] In fact, some supporters claim that more patent protection may be necessary in this area because of the many techniques available to defeat or work around patents.[217] Private patent holders rarely enforce patents against academic institutions for non-commercial uses.[218] If private industry resorts to this type of patent enforcement, supporters of the current system argue that the use of cross-licensing will alleviate most of the conflicts between the sectors.[219]

2. Counterarguments

Conventional patent theory completely supports a strong protection regime for fields that need incentives for private research and development.[220] However, biotechnology is unlike most other

214. *Id.* at 240.

215. *See id.* ("According to those in biotechnology, gene patents represent real invention and, therefore, should be treated as any other technology within the current patent system.").

216. *See, e.g.*, Arti K. Rai & Rebecca S. Eisenberg, *The Public Domain: Bayh-Dole Reform and the Progress of Biomedicine*, 66 LAW & CONTEMP. PROB. 289, 295 (2003) ("[W]ithout patents to permit pricing in excess of marginal cost, no one would be motivated to incur R&D expenses that were vulnerable to appropriation by free riders").

217. For some specific examples, see *infra* Part IV.B.

218. *See, e.g.*, Rai & Eisenberg, *supra* note 216, at 296 ("Some commentators have also argued that patents rarely impose high costs on academic research because patent holders practice an informal regime of price discrimination in favor of nonprofit researchers, primarily by not enforcing their patents against such researchers for non-commercial uses.").

219. The biotechnology industry has argued that the current product licensing system that occurs between companies and with university researchers creates an ideal partnership which acts to increase "improvements in medical diagnosis and treatment." Hill, *supra* note 210, at 240-41.

220. *See id.* at 238-41 (discussing economic theories supporting biotechnology patents).

technology and defies many comparisons. Arguments that the proper incentives will not exist without strong patent protection are diminished by the fact that a great number of the biotechnology discoveries result from direct or indirect public funding.[221] Basic scientific research has continued to progress at an increasing pace without the promise of profit or the assumption that downstream protection of inventions exists.[222] Public resources, often in very large amounts, are frequently expended by many different sources in order to answer specific limited issues.[223] For example, when using proteomics research to discover the cause and potential cure for a disease, researchers may look to abnormalities in genetic coding for a particular protein, examine protein expression through comparisons between diseased and normal tissue, or use computer modeling to predict where abnormal proteins will occur.[224] Approaching the problem from multiple directions allows many different researchers to work on solving similar issues and provides reinforcement for discoveries.[225]

Further, as stated previously,[226] the narrowing of the experimental use exception has left academic institutions that use patented technology or molecules at the mercy of the patent holders. Protein patents have the potential to protect not only the molecule and its functionality, but the information it contains.[227] Therefore, in the case of proteomics, a company may claim many thousands of proteins and all the information they contain.[228] In addition, broad claim

221. For example, 71.6% of the scientific references cited by biotechnology patents are derived from publicly funded basic science research. *Id.* at 242.

222. *Id.* at 242-43. The driving force in basic science is publication and peer acceptance. Public recognition for making a large contribution towards his or her field of study, obtaining grant funding, and disclosing their discoveries to other members of the scientific community make the opportunity for patent protection much less important to most biology researchers. *Id.* Obtaining a patent, while always attractive from a financial security standpoint, remains a secondary goal.

223. *See id.* at 243-45 (discussing "the norm[s] in scientific progress").

224. *See, e.g.*, National Cancer Institute, Questions and Answers: OvaCheck, *at* http://www.cancer.gov/newscenter/pressreleases/ProteomicsOvarian (last visited Oct. 15, 2005) (discussing proteomic methods used to aid in detecting ovarian cancer at earlier stages); *see also* Adler, *supra* note 104, at 1 (discussing patent strategies of certain firms).

225. *See* Hill, *supra* note 210, at 243-44 ("[W]ithin the scientific community, the validation and extension of a scientific finding by other researchers is essential in searching for the 'scientific truth' among various research models and approaches.").

226. *See supra* Part III.B.5 (discussing the current status of the experimental use exception).

227. *See, e.g.*, Stolpa, *supra* note 137, at 362-63 (criticizing one court's decision to focus on "technical possession and description, neither of which is an accurate description of the invention's scope").

228. *See, e.g.*, Cyranoski *supra* note 8, at 11 (describing fears that companies will "attempt to claim ownership of any approach to knocking out" proteins).

interpretation, causing protection of downstream molecules or methods, gives a potentially unbreakable monopoly and would allow the holder to elevate unreasonably the cost of licensing crucial elements of research.[229]

By inhibiting or threatening future innovations, increased biotechnology patent protection has "the exact opposite" effect intended by the policies behind a strong patent system.[230] Since current patent laws benefit the few institutions with the power to mass patent molecules, very little cooperation in cross-licensing may be necessary.[231] Even if companies are willing to offer reasonable licensing fees for their products, uncertainty in the system and the law, "imperfect information, disparate assessments of value, and the danger that pioneer patent holders will simply misappropriate the confidential research plans of follow-on researchers" may cause prohibitive transaction costs in license negotiations.[232]

B. The Public Sector, Open Research, and the Future of Scientific Knowledge

As made clear in the previous sections, academics and other publicly funded researchers in placed in a precarious position under current law. The incentives provided under the current patent system are shifting scientific emphasis from the open exchange of knowledge to guarded information doled out only if profitable.[233] Public databases of knowledge still exist for biomolecules and may be adequate for some research, but public databases pale in comparison to the periodically-updated and intensively researched databases from

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229. *See* Rai & Eisenberg, *supra* note 216, at 295-303 (discussing proprietary barriers to biomedical research and development). "Reach-through" rights, by which companies attempt to license downstream products if patent coverage of the gene or protein molecule fails, is the subject of great contention in the scientific community. *See, e.g.*, Hill, *supra* note 210, at 244-45 ("[N]egotiating patent licenses and valuing the risk of reach-through royalty or invention right agreements result in high transaction costs for basic science research and will quickly interfere with the norms of research.").

230. *See, e.g.*, Cyranoski, *supra* note 8, at 10 (noting that the fear surrounding some of the early gene patents was that their potentially huge reach would provide "a major disincentive to investment in research and development – the exact opposite of what the patent system is supposed to achieve"). Hill argues that, by threatening academic research, strong patent protection acts to reduce the disclosure of information in the public sector from fear of discoveries being improved upon and then patented by those with greater resources. Hill, *supra* note 210, at 244.

231. Larger firms may work out agreements among each other or continue the pattern of merger, thus eliminating their need to cross-license with smaller firms or universities.

232. Rai & Eisenberg, *supra* note 216, at 297.

233. *C.f. Proper Scope*, *supra* note 110, at 242 (describing the shift from "open science" to increasing corporate influence on basic research).

the private sector.[234] University and other publicly-funded researchers are, of course, able to and encouraged to patent the discoveries they make that qualify under the current system.[235] In the fast-paced world of protein patenting, however, strength lies with the resources, workers, and capital of private industry.

Nevertheless, there remain some avenues to engage in proteomic research for those who do not hold patents in proteins. The Supreme Court's interpretation of the doctrine of equivalents based on amended claims[236] may allow the use of homologous proteins with similar function.[237] Further, the USPTO's increased utility standards, to the extent they are good law, allow competing researchers more time to uncover "specific, substantial and credible" uses for proteins before they are claimed.[238] Biotechnological methods and processes, as well as bioinformatics databases, share many features with other machine and software patents, thus enabling creative competitors leeway to design around their claims.[239]

As a whole, however, the current patent law encourages the patent races occurring in the proteomics field, leaving those with the most resources obtaining the most territory and the most downstream control of the industry. Without special considerations for proteomics (and probably genomics as well) that fine tune the particular problems

234. *See* Pachnanda, *supra* note 115, at 230-46 (arguing for sui generis reform legislation for databases in the United States similar to that adopted by the European Union). The decrease in government funding over the past few years has further promoted aggressive tactics from the private sector to capture the important bioinformatics market. *Id.* at 237. "[S]everal non-profit biotech databases have been forced to shut-down." *Id.* at 234.

235. The Bayh-Dole Act of 1980 was enacted to increase the number of patents resulting from government-sponsored biotechnology research, and has been very successful at increasing university presence in the patent race. *See, e.g.*, Consumer Project on Technology, Health Care and Intellectual Property (providing information and internet links regarding the Bayh-Dole Act), *at* http://www.cptech.org/ip/health/bd/ (last visited Feb. 23, 2005); 35 U.S.C. §§ 200-212 (2005).

236. *See supra* Part III.B.4 (discussing judicial interpretations that have led to patent uncertainty).

237. *See* Hayman & Stahl, *supra* note 178, at S4 (analyzing recent federal case law interpreting the doctrine of equivalents). Of course, the response to the threat of lost profits from inadequate patents is to re-double their efforts to find, isolate and patent any similar proteins as well. *See* Service, *supra* note 3, at 2083 (noting that two of the major players in this industry have collectively filed more than 25,000 DNA-based patent applications).

238. *See supra* Part III.B.3 (contrasting the USPTO's utility standards with those applied by federal courts).

239. Broadly interpreted machine and process claims in biotechnology patents, however, have the potential to disrupt research in the field as much as broad patents in biomolecules such as proteins. *See* Kaiser, *supra* note 192, at 1878 (quoting one researcher who described the trend towards patenting biomedical research tools as "destructive for science"). As there are much stronger arguments for these types of patents to remain a part of the traditional patent system, further discussion on this point is beyond the scope of this Note.

presented, the future direction of scientific research and the allocation of scientific resources may rest in the hands of a select few. In a field where publicly funded research has played such a critical role in development and discovery, this at least is cause for concern and study.[240]

C. Other Considerations

Beyond the issue of whether biological informational molecules should be patented at all, there are several other factors in proteomics and genomics which will likely generate much future litigation. For example, there are thousands of gene and protein patent applications applied for and accepted every year by the USPTO, all with multiple potential functions.[241] It is highly likely that situations will arise where a gene patent owner will not hold the patent for the protein the gene encodes.[242] Assuming the particular function has enough potential value, such as in the pharmaceutical field, both parties are sure to litigate who has control over the uses for the proteins.[243] Again, the broadness of patent claims and the length of the reach of gene patents are very important issues in the proteomics industry.

To summarize, patenting the products of the proteomics industry raises many distinct problems and conflicts. Considerable front-end expense may be necessary to reap any future rewards, so some degree of intellectual property protection is required to encourage investment by private industry.[244] Patent protection of

240. Doomsday scenarios aside, in the absence of new regulations the ability to control mass amounts of intellectual property territory in this field will enable the relatively few biotechnology companies to operate with the public sector on essentially their own terms.

241. *See, e.g.*, Service, *supra* note 3, at 2082-83 (noting that two of the major players in this industry have collectively filed more than 25,000 DNA-based patent applications).

242. *See id.* (positing that because of the great uncertainty as to the interaction of gene and protein patents, "showdowns may be inevitable").

243. Considerable research and development money would have been invested in both the gene patent and the protein patent. For the owner to recoup any real value from their efforts, they would have to be able to claim control over the functional aspects of the protein or protein-products. Therefore, at the very least, negotiation will have to occur to determine whose patent, the gene owner or the protein owner, will cover the end uses. *See id.* (predicting that "people will work out a deal" to cross-license each other's patents in order to resolve these gene versus protein patent disputes). Considering the stakes involved and the substantial amount of uncertainty that remains in this area of the law, however, these disputes will likely be litigated frequently. *Id.*

244. Several treatises have discussed the possible benefits of other types of intellectual property protection for biomolecules, such as copyright and trade secret protection, and have concluded that these sources are very inadequate. *See, e.g.*, DUCOR, *supra* note 36, at 139-41 (discussing the reasons the U.S. Copyright Office "seems currently to exclude the copyrightability of genetic sequences and proteins" and arguing that trade secret law "does not

proteins may inhibit downstream innovation by giving too much control over end-products to the patentee, however, given the judiciary's relaxation of the written description and utility requirements.[245] Uncertain interpretation of the scope of claims and inconsistency in guidelines by the USPTO and Federal Circuit is not enough to impede investment where there are resources and potential reward, but they may lead to increased future litigation.[246] Further, current patent interpretation threatens to alter the traditional function of scientific research if patent holders strictly enforce their rights against academically or publicly funded researchers.[247]

V. UNIQUE LEGAL PROTECTION FOR BIOLOGICAL MOLECULES—THE BEST ALTERNATIVE TO REESTABLISHING BALANCE WITHIN THE BIOTECHNOLOGICAL SCIENCES

Scholars have suggested many distinct alterations that could be made to the existing patent system to improve the Patent Act with respect to biotechnology; many of these ideas remain viable alternatives.[248] Separate legislation designed to protect biological molecules may be the best alternative, however, for several reasons.

First, significant alterations made by the USPTO specifically for biological molecules may meet resistance from the Federal Circuit and possibly the Supreme Court, since the 1952 Patent Act, its revisions and the courts' relaxed precedents are binding.[249] Recent history has shown a general movement away from restrictions on patentability that would more reasonably control the problems raised

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provide enough protection"); McBride, *supra* note 23, at 1345-56 (explaining the shortcomings of both copyright and trade secret protection as applied to biomolecule discoveries).

245. This phenomenon is partly due to the uniqueness of biomolecules as having both functional and informational aspects.

246. This uncertainty may ultimately be a deterrent to those who do not have the resources to compete with those established in the field.

247. *See supra* Part III.B.5 (discussing the judicial re-interpretation of the experimental use exception).

248. *See* Hill, *supra* note 210, at 246-58 (suggesting shorter and possibly renewable patent terms, fair use exceptions, stringent licensing control, stricter limitations on the boundary of a gene patent or some combination of these ideas as possible improvements); Sung, *supra* note 1, at 268 & n.17 (recognizing an expanded infringement exemption for pure academic or otherwise non-commercial research similar to the fair use defense under copyright law, a broader infringement exemption for experimental use, and compulsory licensing as attractive alternatives). Others have suggested scaling back the heightened utility and written description requirements to bring biotechnology back "into the fold" of current patent law. *See* Esoy, *supra* note 75, at 163-64 (proposing less stringent utility requirements); Stolpa, *supra* note 137, at 361-66 (arguing that the heightened written description requirement should be pruned back).

249. The Federal Circuit has stated that the USPTO's guidelines do not bind the court when interpreting patent law. *See supra* text accompanying note 174.

by patenting biological molecules.[250] A stronger patent system may be necessary to encourage technology that has less interest or less potential to produce great returns on investment.[251] Proteomics has sufficient interest and support from both private and public investment, however, especially due to the medical advancements that the field promises.[252] Therefore, the innovations produced by proteomics would very likely continue to occur under a more restricted and specifically tailored system.

Second, proteomics is a burgeoning field that is developing rapidly but with much uncertainty and risk; this has resulted in the "land grab" of protein territory.[253] The court system is restrained in its ability to reform the patent system by the cases it receives. Since the greatest value of the biological molecule patents being currently issued likely will not be fully realized for several years,[254] issues raised in litigation will likely not be addressed before much of the available territory is claimed by private industry. By the time the courts take decisive action to correct the existing imbalances, the damage may by too severe to remedy[255] In other words, proteomics technology may so far out-pace adaptation of the Patent Act that a separate system set up earlier would better balance competing policies and would better adapt to such rapid changes.

Third, the existing system of patent law may never be able to appreciate fully the dual nature of biological molecules and the potentially devastating monopolies these patents create.[256] Even assuming that the judiciary will approve of any reformatory actions by

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250. *See supra* Part III.B.

251. *See supra* Part IV.A.

252. *See e.g.*, Jonathon M. Barnett, *Cultivating the Genetic Commons: Imperfect Patent Protection and the Network Model of Innovation*, 37 SAN DIEGO L. REV. 987, 990-94 (2000) (arguing that the normal theories for patent protection do not explain the pharmaceutical industries' investment in uncertain biotechnology).

253. *See* Service, *supra* note 1, at 2074 (explaining why proteomics has become a field in which both "money and hype are flowing fast and furious").

254. *See Molecules v. Information*, *supra* note 3, at 205-06 (noting that the holders of such patents are essentially making long-term bets that their patents will be used in the development of highly profitable drugs at some point in the future).

255. *See, e.g.*, Hill, *supra* note 210, at 246:

> It is true that the Federal Circuit will likely craft a more workable framework that fully appreciates and balances the unique nature of genes and the contributions of the inventors and basic science researchers. However, the question is whether there is time to wait for the courts to resolve the ongoing debate as more gene patents issue and basic science research grapples with increasing tolls on their research.

See also Sung, *supra* note 1, at 270 ("[T]he development of the legal authority trails years, if not decades, behind").

256. *See, e.g.*, Stolpa, *supra* note 137, at 362-63 (criticizing the Federal Circuit Court's myopic analysis of the written description requirement with respect to biological molecules).

the USPTO and will distinguish precedent to control the scope of these patents, the policies of *Chakrabarty* and the statutory requirements for patentability were not equipped to handle the power a person who holds a patent in a biological molecule may possess.[257] Thus, for proteomics and other biotechnology, the current system may unnecessarily inhibit innovation as compared to another system that properly recognizes that control of the underlying information in a biological molecule may, in theory, prevent any further use without approval of the patent owner.

Finally, Congress, with its political accountability and ability to respond relatively quickly to crucial issues, is best suited for ensuring that proper incentives are maintained in the industry.[258] The Patent Act as a whole seems to work properly for the innovations for which it was designed.[259] A complete overhaul of the Patent Act therefore seems unnecessary for most patented technology, but would likely have to occur to address the biotechnology issues raised in this Note. Sui generis legislation would be able to address all foreseeable aspects of biological molecule patents while leaving the existing patent system more or less intact.

Examples illustrate that some fields are better protected by legislation other than the Patent Act. These include the plant patenting acts, the Semiconductor Chip Protection Act ("SCPA") and the Orphan Drug Act ("ODA").[260] Congress designed the plant patenting acts to address specific aspects of non-patentability with respect to modified plant species, but these modifications are now considered, with the relaxation of patent requirements, to be separately patentable under the Patent Act.[261] Similarly, the SCPA was enacted in 1984 to grant limited protection to chip designs since they were not considered patentable or copyrightable.[262] Congress

257. *See, e.g., Molecules v. Information*, *supra* note 3, at 196 (asserting that the fundamental problem with the current jurisprudence is that it continues to view DNA sequences as molecules, and not information, when these sequences clearly share characteristics of both).

258. Of course, accountability also subjects congressional reform to greater influence by special interests groups, thus making it more likely that the direction of proteomics legislation will be shaped primarily by the pharmaceutical companies, which have the most to gain and to lose from any patent law alterations.

259. Examples include mechanical and engineering innovations.

260. Semiconductor Chip Protection Act, 17 U.S.C. §§ 901-914 (2005); Orphan Drug Act, 21 U.S.C. § 360aa-ee (2005). The Plant Protection Act and Plant Variety Protection Act are discussed briefly *supra* in Part II.A.

261. *See* Ducor, *supra* note 36, at 144-45 (explaining that the Plant Patenting Act and the Plant Variety Protection Act "are examples of intellectual property rights created because plant varieties doubtfully met the requirements of section 101 (patentable subject matter), 103 (non obviousness), and 112 (description, reproductibility) of the Patent Act").

262. *Id.* at 148-49.

enacted the ODA to encourage development of drugs for rare diseases, where the risks of investing may significantly outweigh the potential rewards in production.[263] That Act, however, also addresses specific issues in drug manufacturing that have caused problems and conflicts in the industry, thus demonstrating a correlation to proposed proteomics-specific legislation.[264]

Congress enacted the above measures to grant protection to otherwise unprotected inventions or to provide incentives for innovation.[265] Separate legislation for proteomic patents, however, would ideally provide different and well-defined, not necessarily less, protection for protein products while maintaining the proper incentives for innovation.[266] The goal of any new legislation that would specially protect proteomics and biological molecules would be to ensure that no one group will be able to assume too much broad-reaching control of all research aspects by limiting the downstream reaches of protein innovations or reach-through licenses. Any legislation should still provide incentives to non-publicly funded entities to invest in further research and development through limited protection of their discoveries. Moreover, legislation that specifically addresses the issues raised by proteomics, such as the dualistic informational and functional aspects or the importance of traditional scientific research in this field, will only add clarity and promote compromises which will further encourage investment and innovation.

VI. CONCLUSION

Every legal system has the capacity for improvement, and the Patent Act has been adapted over two centuries to incorporate many diverse fields and issues. The courts have been very adept at interpreting and re-interpreting statutory language to accommodate emerging technologies, such as the shift towards an information-based economy; and, for the most part, the "useful arts" have adapted well in

263. *Id.* at 145.

264. *Id.* at 145-48.

265. *Id.* at 149.

266. Ideally, the legislation would be preceded by intensive scientific and business study partnerships that could share and balance concerns from both the private and the academic sectors to craft working legislation. The importance of proteomics to future medical and other scientific breakthroughs makes the issue much more salient to the public at large, if given the opportunity, in comparison to other intellectual property expansions (such as copyright and trademark law). Patent protection in biological material also brings forth ethical issues and has met with some opposition from religious organizations and the public at large. *See, e.g., Molecules v. Information*, *supra* note 3, at 208-09 (discussing some of the concerns that have been advanced thus far, such as the theory that using genetic materials as commercial products is "playing God").

response to the changing requirements. An existing system can only be stretched so far, however, without a complete overhaul. Science is constantly pushing boundaries farther than the previous generation imagined that it could. Proteomics represents the latest boundary and one that will dominate the biotechnological landscape for decades to come. In order to accommodate this revolutionary system, as well as to anticipate the further merger of biology and the technological arts, something beyond tinkering with the existing system may be necessary. Sui generis protection represents the best scenario for encompassing this constantly expanding science and for providing a check to the potential volumes of litigation this area will surely engender.

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* I am in great debt to those who assisted in the editing of this Note. Thank you for your comments and suggestions.

From "Predominance" to "Resolvability": A New Approach to Regulating Class Actions

Allan Erbsen *58 Vand. L. Rev. 995 (2005)*

This Article develops normative and doctrinal innovations to cope with a pivotal yet undertheorized question in most proposed class actions: assuming that a class has adequate representatives, how much variance among class members' circumstances should courts tolerate? Class actions seeking monetary damages would be much less controversial if the factual circumstances of every class member were exactly alike. In an imagined world of perfect homogeneity, shifting from an individualized to an aggregative mode of adjudication would promote efficiency, mitigate collective action problems, and counterbalance defendants' inherent economies-of-scale without sacrificing accuracy or redistributing entitlements among class members. In the real world, however, most classes encompass at least partially heterogeneous claims spread across a spectrum of merit and economic value. This diversity creates opportunities for strategic behavior that can distort the outcome of trials or of settlements negotiated in the shadow of trial. The Article defines and explores three phenomena that create such distortions: "cherry-picking," "claim fusion," and "ad-hoc lawmaking."

The potentially mischievous consequences of heterogeneity in class actions suggest that courts should have a normative theory and doctrinal mechanism to distinguish between acceptable and excessive diversity among proposed class members. The Article addresses the normative question by introducing and justifying three principles to structure certification criteria: "finality," "fidelity," and "feasibility." The Article then applies these principles to assess the forty-year-old "predominance" standard that currently governs how courts decide whether to certify diverse damages classes. This analysis reveals that the predominance standard is

conceptually incoherent and that widely-cited doctrine applying it is normatively unsound.

To fill the gatekeeping function that the predominance standard ineffectively attempts, the Article proposes a new "resolvability" test for courts to apply when deciding if a class action would be an appropriate procedural vehicle for adjudicating diverse claims and defenses. The proposed test would permit certification of class actions seeking money damages only when: "The court has a feasible plan to answer all disputed questions of law and fact that must be resolved before entering judgment for or against class members under the law governing each class member's claim and applicable defenses." The Article then discusses broader implications of its proposal that highlight a dynamic relationship between substantive and procedural constraints on regulation of mass risks.