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ABSTRACT

This Comment focuses on the current trend of the Federal Circuit to heighten both the enablement and written description requirements for biotechnological inventions under 35 U.S.C. § 112. It explores the history of the enablement requirement through a series of opinions by the Federal Circuit and the evolution of this requirement in case law. The Federal Circuit has interpreted the enablement requirement such that it is not satisfied if undue experimentation is required to practice the claimed invention. Likewise, the use of a heightened written description requirement by the Federal Circuit requiring the use of exact nucleotide sequences, allows definition and limitation of the scope of claimed genetic inventions. An analysis of the Revised Interim Guidelines on the written description requirement recently issued by the PTO is also made, concluding that the Interim Guidelines are not entirely consistent with the trend set forth by the Federal Circuit. The Comment suggests that although the Federal Circuit has been repeatedly criticized for the standards it has set in the area of biotechnology, to date the court’s analysis has been reasoned and has solved many problems involving the potential for overly broad patents in this complex field. It argues that this approach is workable and concludes that the power of biotechnology to benefit humankind will withstand the disadvantages that it suffers under the current patent system.

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I. INTRODUCTION

As the twentieth century draws to a close, the field of biotechnology has exploded with the completion of the human genome project, the success of animal cloning, and the development of human embryonic stem cells. These recent advances promise to further improve our standard of living by benefiting medicine, agriculture, and industry. While the academic and industrial research institutions in the United States are worldwide leaders in the development of biotechnology, inventions generated by these entities must be adequately protected to ensure continued innovation. However, this desire to encourage innovation must be balanced with a recognition that biological materials have properties that pose unique challenges to the U.S. patent law system. The Federal Circuit and the Patent and Trademark Office ("PTO") face the difficult task of balancing the interests of inventors and scientists to create an environment that encourages innovation by adequately protecting inventions without granting overly broad patent rights.

The policy behind the U.S. patent law system is to promote the progress of science and technology by offering limited monopolies to inventors for their inventions.\(^1\) Today this goal is embodied in the Patent Act of 1952,\(^2\) which attempts to promote innovation while avoiding "monopolies which stifle competition without any concomitant advance in the Progress

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of Science and useful Arts.'" Soc. grants an inventor a limited patent monopoly for twenty years from the date a patent application is filed. A patent allows the inventor to exclude all others from making, using, or selling the invention. In return, the public receives a full disclosure of a new and useful invention that enters the public domain after the patent term expires.

Inventors will obtain a patent from the PTO if their invention is useful, novel, nonobvious, and sufficiently described and enabled in the patent application. While all of these patentability requirements have evolved unique characteristics in the area of biotechnology, perhaps the most dramatic development has occurred under 35 U.S.C. § 112, first paragraph.

This Comment focuses on the current trend of the Federal Circuit to heighten both the enablement and written description requirements for biotechnological inventions under 35 U.S.C. § 112. In addition, this Comment examines how the PTO has responded to this trend. While the Federal Circuit has dealt extensively with biotechnological issues for patenting DNA sequences, these unique issues are quietly emerging in other important areas of biotechnology as the number of pioneering patent applications increases. The court's response to biotechnology patents has also made it clear that many of the issued biotechnology patents will not withstand the current scrutiny of the Federal Circuit. Therefore, proper understanding of the evolution and consequences of the enablement and

4. In 1994, Congress passed the Uruguay Round Agreements Act, Pub. L. No. 103-465, 108 Stat. 4809 (Dec. 8, 1994), which amended 35 U.S.C. § 154 to provide for a patent term of twenty years from the filing date of the patent application, rather than seventeen years from the date the patent issued. This amendment helped to address the problem of so-called "submarine patents" (the use of continuation applications to claim previously disclosed but unclaimed features of an invention many years after the patent application was originally filed).
10. A discussion of these other patentability requirements is beyond the scope of this Comment.
written description requirements are necessary to best protect biotechnology inventions.

Part II of this Comment is a general introduction to the fundamental properties and general interactions of the biological materials that form the foundation of biotechnology. Part III explores the remarkable history of the enablement requirement through a series of opinions issued by the Federal Circuit, as well as the adaptability of this requirement to the ever-increasing sophistication of biotechnology. Part IV introduces the written description requirement, examines its evolution in the case law of the Federal Circuit, and analyzes the Revised Interim Guidelines on the written description requirement recently issued by the PTO.

This Comment argues that although the Federal Circuit has been repeatedly criticized for the standards it has set in the area of biotechnology, to date the court has appropriately analyzed and solved many of the problems it has encountered in this complex field. The approach taken by the Federal Circuit toward biotechnological inventions is workable, and the power of biotechnology to benefit humankind will withstand the disadvantages it suffers under the current patent law system. This Comment also concludes that the Interim Guidelines issued by the PTO are not entirely consistent with the trend set by the Federal Circuit’s opinions.

II. GENERAL OVERVIEW OF BIOLOGICAL MATERIALS

Biotechnology involves the use of cellular processes and biological materials to generate therapeutically valuable products. Specifically, the principles of “cell and tissue culture, cell fusion, molecular biology, and . . . recombinant deoxyribonucleic acid (“DNA”) technology [are used] to generate unique organisms with new traits or organisms that have the potential to produce specific products.”12 There are three fundamental biological materials: deoxyribonucleic acid, ribonucleic acid (“RNA”), and proteins. A working understanding of these biological materials and how they interact is necessary to understand many of the concepts the Federal Circuit must address when examining the validity of biotechnology patents.13

Scientists define a "gene" as a functional unit composed of DNA that controls the transmission of one or more traits through inheritance. In a gene is composed of two complementary strands of DNA in a double helix structure. These two strands are composed of four building blocks called nucleotides or bases (abbreviated A, G, C, and T). DNA strands are complementary because A always pairs with T, and G always pairs with C. This complementary structure plays a key role in the replication of DNA and the transmission of genetic information to future generations. The identity of a gene is defined by its DNA sequence (the particular order of the nucleotides), much like the structure and meaning of a sentence is defined by the order of its words.

In a process called transcription, the DNA of a gene is transcribed into a carrier material called messenger RNA ("mRNA"). mRNA is composed of slightly modified nucleotides that allow a cell to distinguish between mRNA and DNA. mRNA is essentially a copy of the DNA sequence encoding a gene, with all unnecessary information for constructing the protein encoded by the gene snipped out. Scientists can generate stable copies of mRNA using the original DNA nucleotides (A, G, C, and T). These condensed copies of genes, called complementary DNA ("cDNA"), have been crucial in the development of recombinant DNA technology.

After mRNAs are transcribed in the nucleus they are directed out of the nucleus into the cytoplasm, where most are used as templates for con-
structing proteins in a process called translation. The sequence of a protein is determined by the linear sequence of the translated mRNA. An mRNA transcript is read in sequential units composed of three nucleotides, called codons, with each codon encoding a specific amino acid. Therefore, the order of the codons in the mRNA transcript directly determines the content and order of the amino acids in the protein. This story is complicated by the fact that a single amino acid may be encoded by multiple codons. Since the four nucleotides of DNA can form sixty-four possible codon triplets, and there are only twenty amino acids, there is redundancy or degeneracy in the genetic code. The primary implication of this fact for patent law is that knowing the amino acid sequence of a particular protein does not enable a person of ordinary skill in the art to determine the exact sequence of the gene that encodes the protein. However, the opposite is not true; knowing the DNA sequence of a gene does enable a person to determine the exact sequence of the encoded protein.

Recombinant DNA technology creates new and useful DNA sequences by joining pieces of DNA with different functions in novel ways. DNA sequences from any two organisms, from bacteria and viruses to yeast and humans, can be combined. cDNA sequences are extremely useful in recombinant DNA technology because they contain the genetic information

20. Proteins include enzymes, hormones, and structural materials of the cell, and regulate physiological functions. The identity of a cell depends on the genes it expresses, which in turn encode proteins that cause the cell to function in a particular manner.

21. For example, the codon CCG instructs the cell to insert the amino acid proline into a protein sequence, while the codon AGC instructs the translation machinery to insert the amino acid serine.

22. Once again, this concept can be illustrated as words making up a sentence. If three nucleotides make up a codon, the codon can be thought of as a word, such as “see,” “dog,” and “run.” Each of these codons in turn directs the machinery of the cell to get individual amino acids (for example, His, Trp, and Met, respectively). If the order of the codons in the mRNA transcript is “see-dog-run,” the resulting protein would be three amino acids in length in the order of “His-Trp-Met.” Likewise, if the mRNA transcript reads “dog-run-see,” the resulting protein would be “Trp-Met-His.”

23. Since only four nucleotides are available for each of the three nucleotides in a codon, \(4 \times 4 \times 4 = 64\) possible codons.

24. For example, both of the amino acids Leucine (Leu) and Serine (Ser) are encoded by six different codons. Therefore, thirty-six possible DNA sequences can encode the protein “Leu-Ser.” Since proteins can be hundreds of amino acids in length, the number of DNA sequences that can encode a single protein may be astronomical. See also Kenneth G. Chahine, Enabling DNA and Protein Composition Claims: Why Claiming Biological Equivalents Encourages Innovation, 25 AM. INTELL. PROP. L. ASS’N Q. J. 333, 354-56 (1997).

25. Endonucleases and ligases are bacterial enzymes that allow scientists to respectively cut and paste specific DNA sequences together.
of a gene in a relatively small and compact unit. A unique protein encoded by a recombinant DNA sequence and expressed in a host cell or organism allows scientists to learn about the functions of different regions of genes. In addition, this technology enables the generation of large quantities of proteins such as insulin or human growth hormone, which can be used for therapeutic treatments. Thus, recombinant DNA technology allows scientists to produce large quantities of proteins in various biological hosts, generate new and useful organisms, and treat genetic diseases through gene therapy. Recombinant DNA technology has the potential to generate limitless benefits for humankind.

III. THE EVOLUTION OF THE ENABLEMENT REQUIREMENT IN BIOTECHNOLOGY


35 U.S.C. § 112, first paragraph, sets forth the statutory basis of the enablement requirement for patentability:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same . . .

The crucial language of § 112 mandates that the specification of a patent teach a person skilled in the art how to make and use the full scope of the invention without "undue experimentation." While some experimentation may be necessary to make and use the disclosed invention, determining whether that experimentation is undue "requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art." In addition, the claims of the patent application must be enabled by the specification at the time the application

29. In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988) (citing Ansul Co. v. Uniroyal, Inc., 448 F.2d 872, 878-79 (2d Cir. 1971)).
was first filed.\textsuperscript{30} The issue of enablement is ultimately a matter of law for the courts.\textsuperscript{31}

The vague definition of “undue experimentation” led the Federal Circuit in \textit{In re Wands} to set forth a number of factors that courts might consider when determining whether a disclosure requires undue experimentation.\textsuperscript{32} While the court later clarified that a review of all the factors is not mandatory when determining whether a disclosure is enabling\textsuperscript{33} and then abandoned their use for a number of years, the court recently returned to utilizing these factors.\textsuperscript{34} One \textit{Wands} factor, the predictability of the art at issue, is particularly important for determining the scope of enablement.\textsuperscript{35} The mechanical and electrical arts are considered to be predictable because “a single embodiment [of the invention] provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws.”\textsuperscript{36} In contrast, the chemical and biotechnological arts are considered unpredictable because scientists are not yet able to predict how simple chemical changes will affect chemical reactions or physiological activities.\textsuperscript{37} Consequently, the scope of enablement in the chemical and biotechnological arts varies inversely with the level of unpredictability in the art.\textsuperscript{38}

**B. The Development of the Enablement Requirement in Federal Circuit Case Law**

1. \textit{DNA Sequences and Analogs}

The story of the evolution of the enablement requirement in biotechnology begins with the Federal Circuit’s decision in \textit{Amgen, Inc. v. Chugai}

\textsuperscript{30} See Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384 (Fed. Cir. 1986).

\textsuperscript{31} See Johns Hopkins Univ. v. CellPro, Inc., 152 F.3d 1342, 1354 (Fed. Cir. 1998) (citing \textit{In re Wands}, 858 F.2d 731, 735, 736-37 (Fed. Cir. 1988)).

\textsuperscript{32} See \textit{In re Wands}, 858 F.2d at 737 (The factors are: “(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.”).


\textsuperscript{34} See discussion \textit{infra}, Part III.C.


\textsuperscript{36} Id.

\textsuperscript{37} See id.

\textsuperscript{38} See id.
The patents at issue in *Amgen* involved technology relating to the production of human erythropoietin ("EPO"), a protein used to stimulate therapeutically the production of red blood cells for treatment of anemia and other blood disorders. Amgen owned a patent to the DNA sequence of human EPO, while Genetics Institute, Inc. ("GI"), a codefendant, held a product patent for EPO compositions. Amgen sued GI and Chugai for patent infringement, and the defendants counterclaimed that Amgen's patent was invalid. The Federal Circuit affirmed the district court's finding that Amgen's patent was invalid for lack of enablement.

Amgen's patent claimed all possible DNA sequences for functional substitutes or "analogs" of the natural human EPO protein. Amgen defined an EPO analog as a protein with the biological properties of normal EPO, but encoded by a DNA sequence different than the normal EPO DNA sequence. Thus, an EPO analog is structurally similar but not identical to the human EPO protein.

To enable this broad claim, Amgen's specification would have had to provide a disclosure sufficient to allow a person skilled in the art to produce predictably DNA sequences that encode EPO analogs with EPO-like activity. The problem with Amgen's claim to all EPO analogs is that it encompasses an astronomical number of possible DNA sequences without any ability to predict the biological activity of their encoded proteins. For example, over 3,600 analogs are possible if only a single amino acid in the EPO protein is substituted, while over a million analogs are possible if just three amino acids are substituted. Amgen argued that its generation of fifty to eighty EPO analogs was sufficient to show enablement of its claim. However, after five years of experimentation Amgen could not state whether any of these analogs had the same biological properties as

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40. *Amgen*, 927 F.2d at 1203-04.
41. *Id.* at 1203.
42. *Id.* at 1204.
43. *Id.* at 1203.
44. *Id.* at 1204.
45. *Id.* at 1212-14.
46. *Id.* at 1212-13.
47. *Id.* at 1213.
48. *Id.*
human EPO. Therefore, the court found that Amgen’s claim to all EPO-like analogs was not enabled because the specification only disclosed how to make “the gene and a handful of analogs whose activity has not been clearly ascertained," rather than a large set of analogs with EPO-like activity.

The court’s decision in Amgen significantly limits the ability of an inventor to protect a patented gene by claiming all possible biologically active variations of the gene’s DNA sequence. Thus, although an inventor may be able to write down the possible variations of a gene’s DNA sequence, unless the inventor can reliably predict the effect of the variations on the activity of the encoded protein, the inventor has no right to claim all biologically significant analogs of a gene.

2. Recombinant DNA Technology

The Federal Circuit next turned its attention to a series of cases involving recombinant DNA technology. In re Vaeck involved a patent application that broadly claimed the expression of endotoxin proteins, which are toxic to insects when in cyanobacterial hosts. When insects such as mosquitoes and black flies consume these recombinant cyanobacteria they also consume the toxic endotoxins. The PTO Board of Patent Appeals and Interferences (“Board of Appeals”) rejected the patent application for lack of enablement because it broadly claimed expression of the endotoxin genes in all strains of cyanobacteria. In contrast, the patent’s specification only described the transformation of a single strain of cyanobacteria.

The Federal Circuit affirmed the rejection of the application for lack of enablement, noting that people skilled in the art had a limited understanding of the biology of cyanobacteria at the time the patent application was filed. The court stated that there “is no reasonable correlation between the narrow disclosure in appellants’ specification and the broad scope of protection sought in the claims encompassing gene expression in any and all cyanobacteria.” The court noted that when dealing with an unpredictable factor such as a group of poorly understood microorganisms, the required level of disclosure necessary to meet the enablement requirement is

49. Id.
50. Id. at 1214.
52. Id. at 489-90.
53. Id. at 489-90.
54. Id. at 492-93.
55. Id. at 490.
56. Id. at 495.
57. Id. at 495 (citing In re Fisher, 427 F.2d 833, 839 (C.C.P.A 1970)).
greater than when dealing with a "'predictable' factor such as a mechanical or electrical element." In this manner, the Federal Circuit extended its reasoning in *Amgen* to another area of biotechnology: recombinant DNA technology.

The Federal Circuit reached the same conclusion in two cases that involved inventors who enabled their invention in a single species, and yet claimed the invention in all related organisms. *In re Goodman* involved a specification that disclosed a single example of one species of tobacco plant expressing a mammalian protein called gamma-interferon using a specialized plant vector. Instead of limiting the claims of the application to this single embodiment, the claimed invention was a general method of producing any mammalian protein in any plant. The court found that there was great "unpredictability" in the art of recombinant DNA expression in plants. Therefore, Goodman's claims would require undue experimentation by persons skilled in the art to achieve the expression of any desired mammalian protein in any plant.

Similarly, in *In re Wright*, the patent application enabled a single example of a recombinant vaccine that immunizes chickens against a specific RNA tumor virus. Nevertheless, Wright claimed processes for producing live, nonpathogenic vaccines against any pathogenic RNA virus, and for using these vaccines to protect all living organisms against that RNA virus. The Federal Circuit recognized the inappropriateness of granting these nonenabled claims to Wright when it noted that the proposed claims were so broad that they would "encompass vaccines against AIDS viruses." Today it is clear that "no one has yet, years after [Wright's] invention, developed a generally successful AIDS virus vaccine." In this case, the court demonstrated lack of enablement by using an obvious example of the disclosure's failure to meet the scope of the claimed invention.

The court also rejected Wright's narrower claims to vaccines against all avian RNA tumor viruses. The Federal Circuit stated that a person

58. *Id.* at 496.
59. 11 F.3d 1046, 1048-49 (Fed. Cir. 1993); *see also* Todaro, *supra* note 39, at 36-39.
60. *See In re* Goodman, 11 F.3d at 1048-49.
61. *See id.* at 1050.
62. 999 F.2d 1557, 1559 (Fed. Cir. 1993).
63. *See id.*
64. *Id.* at 1562.
65. *Id.*
66. *See id.* at 1564.
skilled in the art would not have reasonably believed that Wright’s limited success in chickens against a single avian RNA virus could be extrapolated to all other avian RNA viruses. Thus, the court recognized that avian RNA tumor viruses are not experimentally interchangeable, and the enablement of a technique with one virus does not constitute enablement with all viruses.

3. Fusion Proteins

The Federal Circuit examined progress in fusion protein technology to determine whether the claims in *Genentech, Inc. v. Novo Nordisk* were enabled. In *Genentech*, the Federal Circuit vacated an injunction granted by the district court to Genentech against Novo Nordisk, and held that Genentech’s patent for the human growth hormone (“hGH”) was invalid for lack of enablement. Genentech had alleged that sales by Novo Nordisk of recombinant hGH generated by cleavable fusion expression infringed Genentech’s patent. To generate a protein by cleavable fusion expression, a recombinant DNA construct encoding a short amino acid sequence is linked to the desired protein, and expressed in a host cell. The resulting fusion protein is cleaved using an enzyme that recognizes and removes the short sequence, leaving only the desired protein. While examining Genentech’s specification, the court asked “whether the specification would have enabled a person having ordinary skill in the art at the time of filing to use cleavable fusion expression to make hGH without undue experimentation.”

Interestingly, Genentech’s specification suggested that cleavable fusion expression could be used to produce hGH, and even proposed trypsin as a possible cleavage agent, as well as the amino acid sequence cleaved by trypsin. Thus, while Genentech theoretically described a method for generating hGH by cleavable fusion expression, at the time Genentech filed its patent application it had never actually reduced its suggestion to practice. In fact, it took five years of further experimentation to produce hGH successfully using this theoretical cleavable fusion expression sys-

67. See id.
68. 108 F.3d 1361 (Fed. Cir. 1997).
69. See id. at 1368.
70. See id. at 1363.
71. See id.
72. See id.
73. Id. at 1365.
74. Id. at 1365.
Therefore, Genentech’s disclosure required undue experimentation to reduce the invention to practice. The Federal Circuit, in response to Genentech’s argument that a person skilled in the art would know how to apply the suggestions in the specification to generate hGH from cleavable fusion expression, stated: “Tossing out the mere germ of an idea does not constitute enabling disclosure.” Genentech also illustrates the situation where the inventor arguably had written description of the invention in the specification, but the written description did not enable the invention.

4. Antisense RNA Technology

Recently, the Federal Circuit addressed the issue of enablement under § 112 in Enzo Biochem, Inc. v. Calgene, Inc. In Enzo Biochem, the Federal Circuit affirmed the district court’s finding that two patents exclusively licensed to Enzo relating to genetic antisense technology were invalid due to lack of enablement. Genetic antisense technology involves the expression of an “antisense” mRNA transcript from a specially designed DNA construct. This antisense mRNA transcript is complementary to mRNA naturally expressed in a cell, which allows the transcript to bind to the naturally expressed mRNA, thereby preventing the cellular machinery from translating the natural mRNA into a protein. This technology is used to either reduce or eliminate the expression of a naturally expressed protein in a cell.

The two patents at issue in Enzo Biochem had identical specifications and claimed various fundamental aspects of genetic antisense technology. The specification taught the use of antisense technology to regulate the expression of three genes in the prokaryote E. coli. Despite this limited disclosure, the patents broadly claimed the use of antisense technology in “any organism containing genetic material which is capable of be-

75. The court found that the use of trypsin for cleaving proteins was not known at the time the application was filed, and a reference cited by Genentech to teach otherwise suggested that trypsin would not be appropriate for cleaving hGH. See id. at 1365-67.
76. Id.
77. Id. at 1366.
78. See discussion infra, Part IV.
79. 188 F.3d 1362 (Fed. Cir. 1999).
80. Id. at 1381.
81. Id. at 1367.
82. Id.
83. Id.
84. Id. at 1366.
85. Id. at 1367.
86. Id. at 1367-68.
ing expressed,” including all prokaryotic and eukaryotic organisms. Enzo accused Calgene of infringing its patents because Calgene used antisense technology to produce the FLAVR SAVR tomato. The FLAVR SAVR tomato expresses antisense RNA to an mRNA that encodes a protein that promotes ripening in tomatoes. Thus, by blocking the expression of this protein the FLAVR SAVR tomatoes ripen more slowly. Calgene counterclaimed that Enzo’s patents were invalid for lack of enablement.

The district court found, and the Federal Circuit affirmed, that the claims at issue were “extraordinarily broad, encompassing an infinite number of cell types.” Antisense technology was also found to be highly unpredictable because the inventor, as well as other scientists, had failed multiple times to reduce the expression of other genes using the patented antisense technology in both prokaryotes and eukaryotes. Therefore, while the specification “set forth the basic blueprint for the manner in which the invention might be practiced in all types of cells,” the specification in reality did not enable the broad claims of the patents. The court concluded that the mere “germ of the idea” disclosed in Enzo’s patents would have required undue experimentation to develop into Calgene’s unique tomato.

C. Analysis of the Federal Circuit’s Approach to Enablement

The Federal Circuit uses the enablement requirement in the area of biotechnology to prevent inventors from obtaining or enforcing overly broad patent rights. In all of the cases summarized in this section, the Federal Circuit uniformly found that, based on the inventor’s disclosure,

87. U.S. Patent No. 5,190,931 (issued Mar. 2, 1993); see also MONROE W. STRICKBERGER, GENETICS 9 (3d ed. 1985) (Prokaryotes and eukaryotes are fundamentally different types of organisms. In “prokaryotes (“before the nucleus”), the nuclear material is not separated from the cytoplasm by a discrete membrane,” and include all “bacteria and blue-green algae (cyanobacteria).” “In the cells of the more complex eukaryotes (“true nucleus”), which include the majority of living species and multicellular organisms, a nuclear membrane separates the genetic material from the cytoplasm which is then further subdivided by other distinct membranous structures.”).
88. See Enzo Biochem, 188 F.3d at 1368.
89. See id.
90. See id.
91. Id. at 1369.
92. Id. at 1372.
93. Id.
94. Id. at 1375.
95. Id.
96. See id. at 1375.
scope of the claimed invention would require “undue experimentation” by a person skilled in the art. Therefore, the Federal Circuit uses a strict enablement requirement to limit inventors to the scope of their actual inventions.

Wright demonstrates the logic of the Federal Circuit’s approach. First, Wright has no right to claims that broadly encompass technologies he did not invent, and technologies that would take great amounts of experimentation to achieve. Second, Wright’s overly broad claims, if held valid, would function to chill research in the area of RNA virus vaccines. For example, Wright’s claims were so broad that they would cover all future vaccines to the virus that causes AIDS. If Wright’s claims had issued, many researchers and companies would have been deterred from investing time and resources into developing a vaccine to the HIV virus in humans because if they were successful, they inevitably would have encountered Wright’s blocking patent. This would give Wright power over an invention he never conceived, and he would likely receive royalties for work he did not do. Neither the goals of our patent system nor society would be served by this result.

Enzo Biochem also clearly supports the necessity of a strict enablement requirement. The Enzo patents disclosed working examples for controlling the expression of three genes in a single bacterial organism, E. coli. Based on this disclosure, Enzo did not broadly enable the use of genetic antisense technology in all organisms. A specification must do more than offer a “plan” or an “invitation” to those skilled in the art to experiment with the proposed technology. Calgene invented the FLAVR SAVR tomato by determining which protein to eliminate in order to preserve the freshness of a tomato, and then practically applying antisense technology to achieve that result. Enzo’s patents worked with the prokaryote E. coli, which is a far cry from tomatoes. To give Enzo rights over Calgene’s product would vest Enzo with rights to an invention it did not create and consequently would discourage innovation.

97. See Todaro, supra note 39, at 37-38.
98. If Wright owns a patent to all vaccines against RNA viruses in any organism, and another researcher invents a vaccine to HIV (a RNA virus), then each patent would block the practice of the other patent. In essence, “blocking patents disclose interdependent parts of the same product.” Int’l Mfg. Co. v. Landon, Inc., 336 F.2d 723, 730 (9th Cir. 1964).
99. Enzo Biochem, 188 F.3d at 1374.
100. See id. at 1374; see also Genentech, Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366 (Fed. Cir. 1997).
101. Enzo Biochem, 188 F.3d at 1368.
All of the enablement cases discussed in the previous section focused on the issue of undue experimentation. The Federal Circuit clarified the enablement requirement in *Wands* by listing eight factors a court may consider when determining whether a disclosure requires undue experimentation.\(^{102}\) The *Wands* factors are: (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims.\(^{103}\)

The court subsequently backed away from the *Wands* factors in *Amgen* when it stated that it is not necessary for a court to review all of the factors because they are "illustrative, not mandatory."\(^{104}\) In fact, the court seemingly ignored the *Wands* factors for many years.\(^{105}\) The trend away from the *Wands* factors led to the criticism that without clear guidance from the Federal Circuit about which patents are enabled, uncertainty regarding patent validity increases, which reduces the value of patents and increases litigation.\(^{106}\) The court recently returned to utilizing the *Wands* factors in *Enzo Biochem*.\(^{107}\)

Although the Federal Circuit did not explicitly use the *Wands* factors for many years, the spirit of the factors was present in the court’s opinions during that time. As the cases illustrate, one significant factor in determining whether an invention requires undue experimentation is the unpredictability of the technology, and recent developments in biotechnology are often unpredictable. Consequently, although a specification may outline the theoretical application of a technique in a wide variety of organisms, practical application of the technique may involve many variables that scientists do not yet understand, thereby making the actual practice of the technique unpredictable. For example, in *Enzo Biochem* one scientific expert testified that although the fundamental concept of genetic antisense technology was clear, the technology "is not universally applicable, it hasn’t proven to be, and that’s why it’s such an interesting area of research, because scientists don’t understand the rules."\(^{108}\) Thus, scientific

\(^{102}\) In re *Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

\(^{103}\) See id.


\(^{105}\) The *Wands* factors were not mentioned in the enablement discussion of *Wright, Goodman*, or *Novo Nordisk*.


\(^{108}\) Id.
understanding of the "rules" determines the predictability of an area in science.

In several cases reviewed in this section the Federal Circuit examined the progress in the claimed technology by both the inventor and others skilled in the art when determining whether a claim requires undue experimentation. In *Amgen*, the court noted that after five years Amgen had not determined whether its analogs had EPO-like activity, while in *Wright* the court pointed out that the claims would encompass a vaccine to AIDS that has yet to be developed. In *Genentech*, the court noted that it took five years of experimentation to produce hGH using Genentech’s cleavable fusion expression system, while in *Enzo Biochem* the court found that the inventor failed to reduce the invention to practice in any organism other than *E. coli*. While the *Wands* factors were not mentioned in three out of four of the above cases, several of these factors were inherently considered when the court analyzed the delay in reduction to practice.

When analyzing the length of time necessary to reduce a broadly claimed invention to practice, the Federal Circuit inherently considered the following issues, which correspond with certain *Wands* factors: (1) the large quantity of experimentation required to obtain the claimed invention; (2) the lack of guidance and direction in the disclosure that required extensive experimentation; (3) the minimal number of examples compared to the breadth of the claimed invention; (4) the lack of ability of persons skilled in the art to fill in the technical gaps in the disclosure; (5) the unpredictability of the technological area; and (6) the breadth of the claims.109

The length of time for reduction to practice after a patent application is filed should not be the decisive factor in the enablement analysis.110 A person skilled in the art will consider a certain amount of experimentation, as well as the use of personal knowledge and skills, routine when establishing a successful protocol outlined in a disclosure. However, if the protocol takes an excessive amount of experimentation or innovation, i.e., the person must significantly alter the disclosed protocol to use it successfully, then the experimentation is undue. The *Wands* factors help guide courts to ask the right questions about why reduction to practice was delayed.111


110. The test of undue experimentation is "not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Wands*, 858 F.2d at 737.

111. The opportunity to analyze the enablement of a disclosure using this approach is often possible due to the long delay most parties must tolerate before a trial. This oppor-
Although the Federal Circuit stated in Amgen that "it is not necessary that a court review all the Wands factors to find a disclosure enabling,"
112 a court would be well served by analyzing and balancing all of the Wands factors. Consistent use of the Wands factors will allow enablement analysis to become more uniform and reliable, which in turn will strengthen confidence in enabled patents, as well as aid courts as enablement cases become more difficult to resolve.

Thus far, the issue of enablement in the Federal Circuit cases has been relatively straightforward because the applicants uniformly asserted very broad claims, but disclosed only a single embodiment of the invention. Cases will become more difficult to resolve as applicants enable multiple embodiments for a broad claim. Presently, there is great uncertainty about the number of working examples that must be provided in a specification to enable a wide breadth of claims, especially when the "subject matter concerns biological materials or reactions, which are generally considered to be unpredictable."113

Would multiple embodiments suddenly entitle an inventor to claim broadly an invention to all recombinant DNA techniques in all species of a particular bacterium, all mammalian proteins expressed in plant cells, all vaccines to RNA viruses, or all genetic antisense techniques in all organisms? To preserve innovation in the area of biotechnology, the answer must be no. Patent law must limit patentees to their actual inventions; otherwise their rights will encompass the true inventions of others, thus reducing incentives to innovate.

However, this answer does not prevent an applicant from obtaining broad claims to a revolutionary invention because the inventor would still be limited to the actual invention. For example, suppose that Enzo had successfully demonstrated the use of antisense RNA technology to block protein expression in E. coli, yeast, flies, and mouse cells by discovering how to compensate for the unknown "rules" in antisense RNA technology,114 such that the method enabled in Enzo's specification could be used reliably to limit the expression of proteins in a wide range of organisms. In this situation, Enzo would be entitled to the broad patent claims it sought. While the unpredictability of biotechnology makes inventions of this

113. 3 DONALD S. CHISUM, CHISUM ON PATENTS § 7.03[4][d][i], at 7-58 (2000).
114. See Plimier, supra note 106, at 155.
magnitude rare, if an inventor has a revolutionary invention, that inventor should be rewarded with a broad patent. Entities such as Calgene that spend the time and effort to determine how to produce a commercially preferable product by reducing the expression of a specific protein in a particular organism will still be rewarded with a patent, they will just have to license Enzo’s blocking patent to use their invention. This result is fair if Calgene uses the technique disclosed by Enzo to generate its commercial product.

Finally, the cases reviewed in this section illustrate the shortsightedness often found when patents are prosecuted to the PTO. For example, the PTO issued the Enzo patents after the patent application had been rejected ten times for lack of enablement. The Enzo patents were allowed after an Enzo consultant submitted a declaration filled with conclusive assertions of enablement. The end result of this effort is that the Federal Circuit gave little weight to the PTO’s allowance of the claims. Therefore, even if an applicant is able to persuade the PTO to issue overly broad and nonenabled claims, the patentee does not benefit because the issued patent may be invalidated in court. Consequently, inventors and their attorneys should be aware of the trend in the area of biotechnology of subjecting patents to strict scrutiny under the enablement requirement in order to protect their inventions.

116. See id.
117. See id.
118. The recent Supreme Court decision in Dickinson v. Zurko, 527 U.S. 150 (1999), does not change the likelihood of this result. In Zurko, the Supreme Court ruled that the Federal Circuit must review all cases appealed from the PTO under the less stringent “arbitrary and capricious” or “substantial evidence” standards of review set forth under the Administrative Procedure Act (APA). See Zurko, 527 U.S. at 152-53; Administrative Procedure Act § 10(e), 5 U.S.C. § 706 (1994). However, the Federal Circuit will still use the “clearly erroneous” standard of review when reviewing a district court's findings of fact in cases where the validity of a patent is litigated. For a detailed discussion of Zurko and the standards of review applied by the Federal Circuit, see Lawrence M. Sung, Echoes of Scientific Truth in the Halls of Justice: The Standards of Review Applied by the United States Court of Appeals for the Federal Circuit in Patent-Related Matters, 48 AM. U. L. REV. 1233 (1999).
IV. THE EVOLUTION OF THE WRITTEN DESCRIPTION REQUIREMENT IN BIOTECHNOLOGY

A. Written Description and 35 U.S.C. § 112, First Paragraph

The role of the written description requirement under 35 U.S.C. § 112 has been the subject of much debate. Many patent experts, researchers, and even judges argued that written description was not a separate requirement under § 112. Indeed, before the creation of the Federal Circuit, the precedent was inconsistent as to whether written description was distinct from the enablement and best mode requirements. The Third Circuit presented a policy-based rationale for having separate enablement and written description requirements under § 112 in Rengo Co. v. Molins Mach. Co., stating that although the two requirements were complementary, they approached the problem of claiming an invention from different directions. The court explained that the written description requirement functions to prevent the inventor from overreaching the boundaries of the invention by claiming more than the actual invention, while the enablement requirement ensures that persons other than the inventor will have adequate notice of the scope of the patented invention.

The story of the modern written description requirement began in In re Ruschig. The Federal Circuit's predecessor, the Court of Customs and Patent Appeals ("CCPA"), announced in Ruschig a separate written description requirement designed to ensure that the applicant was in possession of the claimed invention at the time the patent application was filed. The CCPA went on to state in In re DiLenoe that "it is possible for a specification to enable the practice of an invention as broadly as it is claimed, and still not describe that invention." As an example the court posited a hypothetical where the specification discusses compound A.

119. See In re Barker, 559 F.2d 588, 594-95 (C.C.P.A. 1977) (Markey, J., dissenting); see also In re Ruschig, 379 F.2d 990, 995 (C.C.P.A. 1967) (inventor argued that § 112 requires only enablement of the invention); Laurence H. Pretty, The Recline and Fall of Mechanical Claim Scope Under "Written Description" in the Sofa Case, 80 J. PAT. & TRADEMARK OFF. SOC'Y 469, 470 (1998).
122. Id. at 551.
123. Id.
124. Id.
125. 343 F.2d 965 (C.C.P.A. 1965).
126. Id.
127. 436 F.2d 1404, 1405 (C.C.P.A. 1971).
without any broadening language.\textsuperscript{128} While the specification may also enable one skilled in the art to make and use compounds B and C, a class consisting of A, B, and C is not described, and therefore cannot be claimed.\textsuperscript{129}

The written description requirement had a shaky start in the Federal Circuit, but the court finally laid the controversy to rest in \textit{Vas-Cath, Inc. v. Mahurkar}, when it affirmatively stated that written description and enablement are separate and distinct requirements.\textsuperscript{130} The court clarified that while the enablement requirement teaches how to make and use an invention without undue experimentation, the written description requirement serves "to put the public in possession of what the party claims" as its invention.\textsuperscript{131} Specifically, the disclosure must clearly demonstrate that the applicant was in possession of the invention at the time the patent application was filed.\textsuperscript{132} In addition, unlike enablement, adequate written description is a question of fact.\textsuperscript{133} Therefore, under § 112 the applicant must enable all subject matter claimed, as well as "describe some subset of the disclosed information with more particularity in order to preserve the right to later claim some or all of the information in that subset."\textsuperscript{134}

Generally, patent law allows an inventor to patent an invention that has not yet been reduced to practice by regarding the filing of the patent application as a constructive reduction to practice.\textsuperscript{135} However, the Federal Circuit has essentially disallowed this practice in the "unpredictable art" of biotechnology by using a heightened written description requirement.\textsuperscript{136} "In the experimental sciences of chemistry and biology . . . [the] element of unpredictability frequently prevents a conception separate from actual experiment and test."\textsuperscript{137} Therefore, an inventor must first make or use the invention before a patent application is filed on a biotechnological inven-

\begin{itemize}
\item \textsuperscript{128} \textit{Id.} at 1405 n.1.
\item \textsuperscript{129} \textit{Id.}
\item \textsuperscript{130} 935 F.2d 1555, 1563 (Fed. Cir 1991).
\item \textsuperscript{131} \textit{Id.} at 1561 (quoting Evans v. Eaton, 20 U.S. (7 Wheat.) 356 at 434 (1822)).
\item \textsuperscript{132} \textit{Id.} at 1564.
\item \textsuperscript{133} \textit{Id.} at 1563.
\item \textsuperscript{134} ROBERT P. MERGES, PATENT LAW AND POLICY 713 (2d ed. 1997). For a general discussion of the development of the written description requirement, see Janice M. Mueller, \textit{The Evolving Application of the Written Description Requirement to Biotechnological Inventions}, 13 BERKELEY TECH. L.J. 615 (1998).
\item \textsuperscript{135} See Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1376 (Fed. Cir. 1986). The inventor must exercise due diligence while reducing the invention to practice in order to retain rights as the "first to invent."
\item \textsuperscript{136} One commentator has referred to the written description requirement as a "super-enablement" standard. See Mueller, supra note 134, at 633.
\item \textsuperscript{137} Smith v. Bousquet, 111 F.2d 157, 159 (C.C.P.A. 1940).
\end{itemize}
tion, i.e., reduce it to a physical form.\textsuperscript{138} If a claimed invention is insufficiently described in the original application, then it will be deemed "new matter,"\textsuperscript{139} and will not receive the benefit of the initial filing date.\textsuperscript{140}

Courts have consistently emphasized the fact-sensitive nature of the written description requirement.\textsuperscript{141} However, because the Federal Circuit has greatly expanded the scope of the written description requirement in biotechnology cases, there is great uncertainty about the breadth of the requirement, as well as the amount of disclosure necessary to satisfy the requirement. The following sections of Part IV examine the evolution of the written description requirement in the Federal Circuit case law and analyze the Revised Interim Guidelines on the written description requirement issued by the PTO that attempt to clarify the requirement in light of the court's decisions.

B. The Evolution of the Written Description Requirement in Biotechnology Case Law

1. Amgen, Inc. v. Chugai Pharmaceutical, Co.

In the field of biotechnology, the Federal Circuit has focused on defining the written description requirement with regard to claiming genes and cDNAs. Amgen, Inc. v. Chugai Pharmaceutical, Co. serves as the starting point for delineating the scope of the written description requirement.\textsuperscript{142} In this case, Amgen alleged that Genetics Institute (GI) and Chugai infringed its patent to the DNA sequence of human \textit{EPO}\textsuperscript{143} because GI used the human DNA sequence of EPO to produce recombinant \textit{EPO}.\textsuperscript{144} However, GI owned a patent for homogenous human EPO and pharmaceutical composi-

\textsuperscript{138} The written description is in essence corroborating evidence of conception. \textit{See} Burroughs Wellcome Co. v. Barr Laboratories, Inc., 40 F.3d 1223 (Fed. Cir. 1994).

\textsuperscript{139} Rules of Practice in Patent Cases, 37 C.F.R. § 1.118(a) (1997) ("No amendment shall introduce new matter into the disclosure of an application after the filing date of the application.").

\textsuperscript{140} \textit{See} 3 DONALD S. CHISUM, CHISUM ON PATENTS § 7.04 (Supp. 1997). The filing date is the prima facie date of invention for determining novelty, priority, nonobviousness, and enablement. The applicant may also provide evidence of an earlier date of invention; however, the filing date is the prima facie evidence of the latest date of invention. \textit{See} 1 IRVING KAYTON, PATENT PRACTICE § 2.6 (Patent Resource Inst., Inc. 6th ed. 1995).

\textsuperscript{141} \textit{See}, e.g., \textit{In re Smith}, 458 F.2d 1389, 1395 (C.C.P.A. 1972) (determining compliance with § 112 is a case-by-case inquiry); \textit{see also In re Dileone}, 436 F.2d 1404 (C.C.P.A. 1971) (what is necessary to fulfill the written description requirement depends on the nature of the invention).

\textsuperscript{142} 927 F.2d 1200 (Fed. Cir. 1991).

\textsuperscript{143} \textit{Id} at 1204.

\textsuperscript{144} \textit{Id}.
tions containing EPO that issued shortly before Amgen’s patent. The specification of GI’s patent also disclosed a method for isolating the EPO DNA sequence using the EPO protein.

In Amgen, the Federal Circuit proposed that sometimes an inventor must reduce an invention to practice before the inventor can adequately establish a conception of the invention. Using this theory the court found that since GI had not yet cloned the DNA sequence of the EPO gene when it filed its patent application, and the specification only suggested a possible method by which to isolate the DNA sequence, GI could not have had a mental conception of the EPO DNA sequence at the time the application was filed. The court reasoned that an inventor can only sufficiently distinguish a gene’s DNA sequence from other sequences after it is isolated. Thus, the court held that in some cases conception of a gene requires reduction to practice.

In addition, GI’s proposed method for isolating the EPO DNA sequence was not enabled because the method required actual knowledge of the EPO protein sequence, which GI did not yet have. Therefore, GI’s prospect of actually “cloning the gene was mere speculation,” even though GI later used the strategy disclosed to clone the human EPO gene. The unique facts of this case allowed the Federal Circuit to invalidate GI’s patent for lack of enablement and give new meaning to the written description requirement. Namely, an inventor claiming a DNA sequence must have an adequate conception of the DNA sequence before filing a patent application, which is achieved upon actual reduction to practice. Although the Federal Circuit left open the alternative of defin-

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145. Id. at 1203.  
146. Id. at 1205.  
147. “This situation results in a simultaneous conception and reduction to practice.” Id. at 1206 (citing 3 DONALD CHISUM, PATENTS § 10.04[5] (1990)). The court used chemical case law precedent to analyze the DNA claims because DNA is a complex chemical compound. Id. (citing Oka v. Youssefyeh, 849 F.2d 581, 583 (Fed. Cir. 1988)) (“Conception requires (1) the idea of the structure of the chemical compound, and (2) possession of an operative method of making it.”).  
148. Amgen, 927 F.2d at 1206.  
149. Id.  
150. Id. (A DNA sequence cannot be defined “solely by its principle biological property, e.g., encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.”).  
151. Id. at 1207.  
152. Id. at 1206.  
153. Id. at 1205.  
154. Id. at 1207.
ing the sequence "in terms of other characteristics sufficient to distinguish it from other genes," this alternative was significantly narrowed by subsequent case law.

2. Fiers v. Revel

In Fiers v. Revel, the Federal Circuit applied its holding in Amgen to an interference proceeding involving three foreign inventors, Fiers, Revel, and Sugano. Each of the parties claimed patent rights to DNA encoding human fibroblast beta-interferon ("β-IF"). Fiers asserted priority based on his conception of a method for isolating the DNA, coupled with due diligence towards a constructive reduction to practice. Fiers had disclosed this method to two American scientists before he isolated the DNA, both of whom submitted affidavits that Fiers' method would have allowed a person of ordinary skill in the art to isolate the β-IF DNA sequence without undue experimentation.

Fiers asserted that the stringent written description requirement set forth in Amgen only applies when the disclosed method for isolating a DNA sequence could not be easily carried out by one of ordinary skill in the art. In addition, Fiers asserted that Amgen allows conception of a DNA sequence by its method of isolation. The Federal Circuit rejected both of these arguments, stating that Fiers focused inappropriately on the issue of enablement rather than written description. The court asserted that if people are allowed to patent the mere idea of a compound or DNA sequence, would-be inventors would file patent applications before they could actually describe the invention. To allow applicants to file such applications would go against the policy of promoting the disclosure of inventions, not research plans.

Similarly, the Federal Circuit rejected Revel’s claim of priority based on the filing date of his Israeli patent application because the application did not contain a written description of the DNA sequence for β-IF. The

155. Id. at 1206.
156. 984 F.2d 1164 (Fed. Cir. 1993).
157. Id. at 1166.
158. Id.
159. Id.
160. Id.
161. Id. at 1169.
162. Id.
163. Id.
164. Id.
165. Id.
166. Id. at 1170.
court stated that “adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself.”\textsuperscript{167}

Ultimately, Sugano established priority for the invention because his application was the first disclosure that contained “the complete and correct sequence of the DNA which codes for [β]-IF, along with a detailed disclosure of the method used by Sugano to obtain that DNA.”\textsuperscript{168} Thus, after Fiers, an inventor must disclose a specific characteristic of the claimed DNA sequence sufficient to convey to one skilled in the art that the inventor was in possession of the invention at the time the patent application was filed.

3. \textit{Regents of the University of California v. Eli Lilly \& Co.}

The Federal Circuit most recently addressed the issue of the written description requirement for DNA inventions in \textit{Regents of the University of California v. Eli Lilly \& Co.}\textsuperscript{169} This decision has created a great deal of controversy as well as uncertainty with regard to the scope and validity of biotechnology patents.\textsuperscript{170} \textit{Eli Lilly} involved a dispute over the human insulin gene.\textsuperscript{171} Before the breakthroughs of recombinant DNA technology, insulin was purified from animals and used to treat diabetics.\textsuperscript{172} However, this insulin was expensive to produce and carried a risk of allergic response.\textsuperscript{173} Recombinant DNA technology promised a safer and more economical way of commercially producing insulin for the treatment of diabetics,\textsuperscript{174} but required that researchers first clone the human insulin gene.

In 1977, researchers at the University of California (“UC”) cloned the rat insulin gene and filed a patent application claiming the rat and human insulin genes, as well as all other mammalian and vertebrate insulin genes.\textsuperscript{175} After a patent issued to UC on the insulin genes (the ‘525 patent), UC filed suit against Eli Lilly for patent infringement because Eli

\begin{itemize}
\item \textsuperscript{167} \textit{Id.}
\item \textsuperscript{168} \textit{Id.} at 1171.
\item \textsuperscript{169} 119 F.3d 1559 (Fed. Cir. 1997).
\item \textsuperscript{171} See \textit{Eli Lilly}, 119 F.3d at 1562.
\item \textsuperscript{172} \textit{Id.}
\item \textsuperscript{173} \textit{Id.}
\item \textsuperscript{174} \textit{Id.}
\item \textsuperscript{175} \textit{Id.} at 1562-63.
\end{itemize}
Lilly sold synthetic human insulin.\textsuperscript{176} Eli Lilly responded that its product did not infringe the '525 patent, and that the '525 patent was invalid and unenforceable.\textsuperscript{177} The district court agreed with Eli Lilly and held that the '525 patent was invalid for failing to provide adequate written description of an entire genus of insulin genes.\textsuperscript{178}

The Federal Circuit, relying on its reasoning in Fiers, held that the '525 patent was invalid because adequately describing a cDNA in a patent specification “requires the kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA.”\textsuperscript{179} The court stated that while the '525 patent specification contained adequate written description of the rat insulin cDNA, this description did not give UC a right to also claim the cDNA encoding human insulin because describing one member of a genus does not give the inventor a right to claim the entire genus, only that one member.\textsuperscript{180}

The Federal Circuit rejected UC’s argument that the disclosure contained sufficient written description of the human insulin cDNA because the examples in the disclosure described how to isolate the cDNA.\textsuperscript{181} The court, echoing Fiers, stated that simply enabling a person skilled in the art to obtain a DNA sequence does not sufficiently describe that sequence.\textsuperscript{182} The court explained that unless an inventor possesses the complete sequence of a gene or cDNA, that inventor cannot visualize or recognize its identity.\textsuperscript{183} In fact, the court stated that even if a disclosure is sufficient to render an invention obvious, it still may be insufficient to satisfy the written description requirement.\textsuperscript{184}

C. Analysis of the Federal Circuit’s Approach to Written Description

The Federal Circuit’s decisions regarding the written description requirement in the area of biotechnology have led to a great deal of interest and debate on the wisdom of the court’s direction.\textsuperscript{185} Clearly, these cases impact the ability of inventors to obtain and enforce patents for DNA se-
quences and proteins. While many commentators have criticized the Federal Circuit's approach to patenting DNA and genes, the unique nature of genetic material necessitates a heightened written description requirement.

Some commentators believe *Eli Lilly* will have a broad impact on biotechnology by "compelling gene hunters to spell out the exact sequence of all the DNA they hope to claim, rather than just the function of the genes." Others argue that it is an overstatement of the court's holding to suggest that an inventor must provide the sequence of every cDNA that is claimed in order to meet the written description requirement. However, this is not an overstatement if the reasoning behind a heightened written description requirement is followed to its logical conclusion.

The Federal Circuit's reliance on the written description requirement to invalidate overly broad DNA patent claims centers on the argument that an applicant cannot patent a DNA sequence until the applicant demonstrates possession of the claimed invention by describing the exact DNA sequence. Thus, the primary goal of the Federal Circuit in biotechnology cases is to limit inventors to their actual inventions. This goal is uniquely illustrated in *Eli Lilly* by the characteristics of the technology at issue.

When examining the holding of *Eli Lilly*, it is important to remember that DNA and RNA are simple molecules composed of four different nucleotides in sequential order. The same nucleotides are used to build DNA and RNA in organisms from bacteria to yeast to humans. Therefore, a clear distinction between DNA and RNA produced by various organisms does not exist. Because of the inter-relatedness of genetic material, as explained below, the heightened written description requirement employed by the Federal Circuit in the area of biotechnology is arguably a reasonable way to handle patenting this material.

In *Eli Lilly*, UC cloned the rat insulin gene and claimed patent rights to the human insulin gene, even though UC did not clone the human insulin cDNA until two years after its patent application was filed. The rat and human insulin genes are homologs of each other, which means that they are in the same gene family (insulin) but are found in different species

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186. See generally Stewart, supra note 170, and Mueller, supra note 134. See also Harris A. Pitlick, *The Mutation on the Description Requirement Gene*, 80 J. PAT. & TRADEMARK OFF. SOC'Y 209, 222 (1998) (calling the *Eli Lilly* decision "an unmitigated disaster that if followed, has the potential for causing untold havoc in the biotechnology field").


188. Stewart, supra note 170, at 554.
(rat and human). Often, homologs from different organisms have a high degree of similarity or DNA sequence identity. Thus, if two cDNA homologs are isolated from rat and human, and each cDNA is 1000 nucleotides in length, it is likely that anywhere from 800 to 1000 of those nucleotides will be identical between the two DNA sequences (80% to 100% sequence identity). This high degree of homology exists between the genes of these species, even though rats appear very different from humans.\textsuperscript{189}

In fact, many mammals have genes with a high degree of sequence identity with their human homologs. For example, the chimpanzee genome is approximately 99% identical to the human genome.\textsuperscript{190} While some regions between homologs are highly conserved among species, other regions differ significantly, even if the species are closely related.\textsuperscript{191} The impact of these differences on the function of proteins from different organisms will range from significant to minor or nonexistent.

Within a single species, gene families consist of alleles, polymorphisms, and isoforms. Alleles are alternate forms of the same gene that code for proteins with identical or nearly identical biological properties. Polymorphisms describe members of a particular gene family whose DNA nucleotide sequences vary by one or more bases. Isoforms are genes in the same family that have similar basic functions but unique individual characteristics. The amazing diversity we see among organisms of a single species is largely due to the natural variations of alleles, polymorphisms, and isoforms in a single organism.\textsuperscript{192}

Since genes between and within species vary so dynamically, yet are so closely related, any alternative approach to patenting genes, cDNAs, or mRNAs other than disclosing exact nucleotide sequences risks granting overly broad patent rights to a single inventor. Without a heightened written description requirement, inventors could receive patent rights to se-

\textsuperscript{189} For example, the baboon and human EPO DNA sequences are ninety percent homologous, which means that nine out of every ten nucleotides of the baboon EPO DNA sequence are identical to the human EPO DNA sequence. See Amgen v. Chugai Pharm. Co., 927 F.2d 1200, 1208 (Fed. Cir. 1991).

\textsuperscript{190} Luke O’Neill et al., \textit{What are we? Where did we come from? Where are we going?}, 263 SCIENCE 181 (1994).

\textsuperscript{191} The DNA or protein sequences of homologs and families of genes can be compared to determine regions of the sequence that have been highly conserved over millions of years of evolution, and therefore, are important to the survival of the organism. If these regions were not critical to survival, they would have acquired random mutations over time from species to species, thus reducing homology in these regions. See Chahine, supra note 24, at 359-60.

\textsuperscript{192} For example, all humans have the same set of genes for generating eye color, but polymorphisms in those genes determine the color of an individual’s eyes.
quences of which they have no knowledge, in organisms with which they have never worked. If an inventor is given rights to a gene without disclosing the exact nucleotide sequence, that inventor may be able to claim the right to prevent others from using homologs, alleles, polymorphisms, and isoforms found in the same gene family, all of which have a high degree of sequence identity with the gene, but not 100% identity. If the line is not drawn at 100% sequence identity, these claims become a slippery slope with boundaries that must be individually defined. Therefore, the Federal Circuit's approach to the written description requirement in the area of biotechnology has prevented nucleotide sequence claims from becoming a Pandora's box that the patent law is unable to control.

One criticism of the holding in *Eli Lilly* is that "[p]ersons skilled in the art of recombinant DNA technology were very likely to have understood that by making the rat insulin cDNA, the UC inventors conceptually possess the human insulin cDNA (if not all mammalian cDNAs)." That, however, is not true. A person skilled in the art would have understood after cloning the rat cDNA that it is likely that the human cDNA would have a high degree of sequence identity with the rat cDNA. However, the person would not know which nucleotides the two sequences had in common or the biological significance of the variations until after sequencing the human cDNA. Thus, the person would not conceptually possess the human cDNA until after identifying its exact nucleotide sequence.

If the Federal Circuit had upheld UC's claim to the human insulin gene, any subsequent inventor that isolated and characterized a single gene would have been able to claim any related mammalian gene as long as an enabling protocol was included in the disclosure. Applicants would have been encouraged to submit applications for every related mammalian gene with potential commercial value, as well as all potential homologs, alleles, polymorphisms, and isoforms in the gene family. However, if a patentee obtained these broad patent rights, researchers and industry would be discouraged from continuing to invest time and effort into researching applications involving any member or related member of this gene family. Even if a patentee was willing to license broadly its invention, the patentee may condition the license on a right to inventions derived from the research, thus making the license unappealing for researchers and the industry. The patentee would gain all of these rights without having directly isolated any of the related mammalian genes or a significant number of the members of the gene family. The end result would be few patentees with very powerful patent rights. This would discourage innovation.

The primary argument against the Federal Circuit’s heightened written description requirement for biotechnological inventions is that while a bright-line rule is attractive in its certainty, it also “reduces incentives to invest in innovation by depriving potential patentees of the opportunity to fully benefit from their research.” The argument continues that the current written description requirement “dramatically reduce[s] the value of the [patent] by enabling competitors to easily avoid infringement through minor variation.” This argument has merit because under the heightened written description requirement, the patent law will not protect an inventor that claims a gene and its corresponding protein from competitors that generate slight variations in the nucleotide sequence of the gene, which result in a structurally different but still biologically equivalent protein. However, this shortcoming is preferable to granting overly broad patent rights, and may be minimized by using alternative strategies.

The Food and Drug Administration (“FDA”) encountered a problem similar to the above argument when it faced the “same vs. different” problem under the Orphan Drug Act. In 1985, Genentech was granted market exclusivity for genetically-engineered hGH under the Orphan Drug Act. A short time later, the FDA also granted Eli Lilly orphan drug market exclusivity for hGH protein that differed from Genentech’s hGH protein by a single amino acid. Genentech sought a temporary injunction to the FDA’s approval of Eli Lilly’s hGH, but the U.S. District Court for the District of Columbia held that the two versions of hGH were not the “same” drug under the Orphan Drug Act. Thus, the “same vs. different” problem can occur when “the FDA considers two structurally very similar drug variants to be ‘different,’ [because] it may approve both drugs,” which reduces the incentive to develop orphan drugs.

194. Id. at 651.
195. Id.
198. See Bohrer & Prince, supra note 196, at 387.
200. See id. at 383.
Given the danger of what this "narrow reading of the Orphan Drug Act would do to the incentives of the Act," the FDA subsequently promulgated regulations to define "sameness" under the Orphan Drug Act. The FDA found that large biological molecules with the "same principal molecular structure" are not considered different under the Orphan Drug Act, and that "FDA Orphan Drug regulations make a 'presumption of sameness' even when differences occur in protein structure." The FDA also decided that a second sponsor of a large biological molecule would always be able to establish the difference between two similar molecules.

201. See id. at 415.
202. See id. at 389 (citing Gina M. Cavalier, Note, Pushing Parentless Pharmaceuticals: Toward an International Home for 'Orphan Drugs' and a Cure for 'Zebra' Diseases, 27 LAW & POL'Y INT'L BUS. 447, 450 (1996)).
203. See Bohrer & Prince, supra note 196, at 389 (citing 21 C.F.R. § 316.3(b)(13)(ii) (1999)).

Same drug means ... if it is a drug composed of large molecules (macromolecules), a drug that contains the same principal molecular structural features (but not necessarily all of the same structural features) and is intended for the same use as a previously approved drug, except that, if the subsequent drug can be shown to be clinically superior, it will not be considered to be the same drug. This criterion will be applied as follows to different kinds of macromolecules:

(A) Two protein drugs would be considered the same if the only differences in structure between them were due to post-translational events or infidelity of translation or transcription or were minor differences in amino acid sequence; other potentially important differences, such as different glycosylation patterns or different tertiary structures, would not cause the drugs to be considered different unless the differences were shown to be clinically superior.

(B) Two polysaccharide drugs would be considered the same if they had identical saccharide repeating units, even if the number of units were to vary and even if there were postpolymerization modifications, unless the subsequent drug could be shown to be clinically superior.

(C) Two polynucleotide drugs consisting of two or more distinct nucleotides would be considered the same if they had an identical sequence of purine and pyrimidine bases (or their derivatives) bound to an identical sugar backbone (ribose, deoxyribose, or modifications of these sugars), unless the subsequent drug were shown to be clinically superior.

(D) Closely related, complex partly definable drugs with similar therapeutic intent, such as two live viral vaccines for the same indication, would be considered the same unless the subsequent drug was shown to be clinically superior.

Id.

based on significant clinical differences, particularly clinical superiority.\textsuperscript{205} Thus, the general principle of the FDA regulations under the Orphan Drug Act is that structurally similar drugs, such as those with a minor genetic alteration, will be considered identical and therefore ineligible for FDA marketing approval unless the second drug is clinically superior to the first.

The approach of the FDA under the Orphan Drug Act demonstrates that there are solutions to the concerns regarding incentives to research raised by a heightened written description requirement in the area of biotechnology.\textsuperscript{206} Although a competitor may design around an invention by generating a biological molecule with a slightly different chemical structure, the competitor will have no way to predict how minor variations, even in a single amino acid, will affect a protein's activity.\textsuperscript{207} The competitor cannot be certain of the molecule's resulting activity until the molecule is clinically tested. Given the current expense of clinically testing a biological molecule,\textsuperscript{208} a competitor would be hesitant to enter the FDA approval process unless the market offers significant economic rewards, particularly if approval may be withheld because the molecule is equivalent to a patented FDA approved drug. If the slightly modified molecule offers a clinically significant improvement over the FDA approved drug, the molecule should be eligible for marketing approval, as well as protected under the patent system.

While the above example does not answer all of the potential problems associated with a heightened written description requirement, it signals that these problems can be dealt with in a way that preserves the goal of promoting innovation. It is important to recognize that the heightened written description requirement even protects innovation in the above ex-


\textsuperscript{206} For a detailed discussion of the advantages and disadvantages of the FDA's approach to "same vs. different" problem under the Orphan Drug Act, see Bohrer & Prince, supra note 196, supra at 383-95.

\textsuperscript{207} A generic drug is chemically identical to the original pioneer drug and can rely on the safety and efficacy studies done with the pioneer drug. Therefore, the process of generic drug approval is simpler and less costly than with new drugs. See id. at 412-13. In contrast, an analog will have a slightly different chemical structure than the pioneer drug, which may result in new and unexpected biological activities in vivo. Therefore, independent clinical studies for FDA approval must be performed with the analog.

\textsuperscript{208} See Duff McDonald et al., Investing's New Frontier, MONEY, Sept. 1998, at 82 (reporting that "it can cost [up to] $350 million to develop a drug"). Although the cost of clinically testing an analog may be less due to reduced research and development costs, the cost will still be significant.
ample. Under a less stringent written description requirement, a patent claim to a single mutation that generates remarkably beneficial improvements in a protein may be within the scope of a previously issued claim to the protein, even though the first patentee did not conceive of the second patentee's invention. In contrast, under a heightened written description requirement, the scope of the first patentee's claim will be limited to the invention of the protein, and the second patentee will obtain rights to the remarkably improved protein without being subject to the rights of a prior patent. Thus, while restricting the scope of patents through a heightened written description requirement is not without problems, granting patentees overly broad patent rights will have an even greater negative impact on innovation than granting restrictive patent rights.

1. The PTO's Revised Interim Written Description Guidelines

The PTO recently proposed "Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. § 112(1) 'Written Description' Requirement" ("Revised Interim Guidelines"). The Revised Interim Guidelines present the PTO's approach to the written description requirement, and supercede a set of Interim Written Description Guidelines ("Interim Guidelines") previously published by the PTO. While the earlier proposed Interim Guidelines were "directed primarily to written descriptions of biotechnological inventions," the Revised Interim Guidelines reflect "the current understanding of the PTO regarding the written description requirement of 35 U.S.C. § 112, ¶ 1 and [are] applicable to all technologies." In addition, the PTO sets forth that the Revised Interim Guidelines are "fully consistent with binding precedent of the U.S. Supreme Court and the U.S. Court of Appeals for the Federal Circuit." It is important to note that these Revised Interim Guidelines do
"not constitute substantive rulemaking and hence [do] not have the force and effect of law."\textsuperscript{214}

The Revised Interim Guidelines suggest that inventors may face a less stringent written description requirement as the knowledge and skill in biotechnology improve. However, the PTO should be wary of backing away from the heightened requirements for genetic sequences because granting broader claims to inventors may function to chill technological innovations. In addition, the PTO’s proposal that an inventor may demonstrate possession with a written description that “sufficiently describes relevant identifying characteristics,” as well as the PTO’s approach to claiming a genus, are problematic.

The Revised Interim Guidelines emphasize that in order to satisfy the written description requirement, “a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention.”\textsuperscript{215} The PTO reiterates that this requirement will promote “the progress of the useful arts by ensuring that patentees adequately describe their inventions in their patent specifications in exchange for the right to exclude others from practicing the invention for the duration of the patent’s term.”\textsuperscript{216}

The Revised Interim Guidelines state that determining whether an inventor is in possession of the claimed invention “is a conclusion reached by weighing many factual considerations.”\textsuperscript{217} These factual considerations “include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.”\textsuperscript{218} The Revised Interim Guidelines conclude that satisfaction of the written description requirement is a question of fact, and must be resolved on a case-by-case basis.\textsuperscript{219}

The first set of Interim Guidelines issued by the PTO proposed that there is an inverse relationship “between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement.”\textsuperscript{220} However, several comments objected to the use of

\textsuperscript{214. Id. at 71434.}
\textsuperscript{215. Id.}
\textsuperscript{216. Id.}
\textsuperscript{217. Id. at 71436.}
\textsuperscript{218. Id.}
\textsuperscript{219. Id. at 71434.}
\textsuperscript{220. Interim Guidelines, supra note 210, at 32640.}
"predictability as a touchstone for written description" because it is an inquiry associated with the enablement requirement.\textsuperscript{221} To reduce confusion, the Revised Interim Guidelines state that "there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement."\textsuperscript{222} However, statements in the Revised Interim Guidelines indicate that the PTO is still inappropriately using predictability as a touchstone for written description.

The Revised Interim Guidelines suggest that, with regard to biotechnological inventions, as the general knowledge and skill in this art improves, the PTO will allow increasingly broader claims.\textsuperscript{223} The Revised Interim Guidelines also maintain that "in emerging and unpredictable technologies, more evidence is required to show possession."\textsuperscript{224} This position reflects the argument that while the state of DNA inventions was once unpredictable, today the state of the art has advanced to the point where isolating nucleotide sequences is routine to persons skilled in the art, and therefore predictable.\textsuperscript{225} The argument continues that since this area of biotechnology is now predictable, the "sliding scale" should permit the PTO to issue broad claims to a nucleotide sequence without requiring actual disclosure of the nucleotide sequence.

However, this argument does not change the fact that a scientist today trying to clone an unknown nucleotide sequence cannot predict its exact sequence until after it is isolated. Although improvements in a technology may affect the enablement requirement, predictability of an art should not be a factor under the written description requirement. Therefore, given Federal Circuit precedent, the PTO should continue to require the disclosure of the exact nucleotide sequence claimed and the written description requirement should continue to have broad implications in biotechnology, even as some areas become increasingly predictable.\textsuperscript{226}

\textsuperscript{221} Revised Interim Guidelines, supra note 209, at 71430; see also In re Fisher, 427 F.2d 833, 839 (C.C.P.A. 1970) ("In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.").

\textsuperscript{222} Revised Interim Guidelines, supra note 209, at 71435.

\textsuperscript{223} Id. at 71430.

\textsuperscript{224} Id. at 71436.


\textsuperscript{226} See id. at 141.
Under the Revised Interim Guidelines, an inventor can demonstrate possession of the invention by: (1) actual reduction to practice, (2) clear depiction in detailed drawings, or (3) written description that sufficiently describes relevant identifying characteristics of the invention such that a person skilled in the art would recognize possession. \(^{227}\) "Sufficiently detailed relevant identifying characteristics" of the claimed invention suggested by the Revised Interim Guidelines include "complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." \(^{228}\) The Revised Interim Guidelines also offer examples of identifying characteristics, including: sequence, structure, binding affinity and specificity, molecular weight, length, unique cleavage by particular enzymes, isoelectric points of fragments, detailed restriction maps, a comparison of enzymatic activities, and antibody cross-reactivity. \(^{229}\) The factors proposed by the Revised Interim Guidelines reveal information that identifies certain characteristics of a claimed invention. The Revised Interim Guidelines presume that the more factors an applicant can identify, the more likely the applicant is in possession of the claimed invention at the time of filing.

However, the alternative of using "sufficiently detailed relevant identifying characteristics" proposed by the Revised Interim Guidelines for fulfilling the written description requirement may be problematic in the area of biotechnology because of current case law, as well as the nature of genetic material. For example, identifying the molecular weight, length, and detailed restriction enzyme maps \(^{230}\) of a claimed nucleotide sequence does not fulfill the intent of the Federal Circuit's construction of the written description requirement because an applicant may be able to identify these characteristics without possessing the actual sequence of the claimed invention.

In fact, allowing such claims would discourage applicants from sequencing a claimed nucleotide sequence before filing a patent application

\(^{227}\) Revised Interim Guidelines, \textit{supra} note 209, at 71435.
\(^{228}\) \textit{Id.}
\(^{229}\) \textit{Id. at} 71439 n.39.
\(^{230}\) A restriction enzyme map of a nucleotide sequence outlines the locations where enzymes that recognize specific nucleotide sequences cut (usually 6 nucleotides in length). Specific points where the enzymes cut can define an individual nucleotide sequence. Thus, "[o]ne skilled in the art may be able to determine when the gene disclosed is the same as or different from a gene isolated by another by comparing the restriction enzyme map." \textit{Id.} at 71435.
because the applicant would obtain broader claims without disclosing an exact sequence. By using sufficiently detailed relevant identifying characteristics, the applicant's claims may potentially capture homologs, alleles, polymorphisms, and isoforms of the claimed nucleotide sequence. This incentive would directly contradict the purpose of the patent system, which is to encourage inventors to disclose the complete invention, not avoid it. Thus, if the PTO allows inventors to claim genes, cDNAs, or mRNAs without fully disclosing the claimed nucleotide sequences, the PTO will discourage inventors from possessing their inventions before filing, as well as allow inventors to claim more than the inventions they possess.

The following example illustrates this point: An inventor isolates and files a patent application on the healthy version of the hemoglobin gene that is linked to the disease sickle cell anemia. The inventor discloses only the size, detailed restriction enzyme map, source, and method for isolating the cDNA. The length and restriction maps of a gene outline general characteristics of the gene, but lack the exact nucleotide sequence of the gene. If the PTO allows this claim, the claim would likely encompass the cDNA later discovered by a second researcher of the same hemoglobin gene with a single mutated nucleotide, which causes sickle cell anemia. Thus, the first inventor's patent rights would include the mutant cDNA, even though the second inventor discovered the commercially significant cDNA with the mutation that causes sickle cell anemia. This situation would discourage innovation, because the second researcher would hesitate to continue research on the hemoglobin gene after becoming aware of the first researcher's patent. In addition, unless the patentee is willing to license broadly its invention to the hemoglobin gene, researchers and the industry will not continue to invest time and effort into finding a cure for sickle cell anemia. Requiring disclosure of complete nucleotide sequences avoids this scenario.

For these same reasons the PTO and courts should carefully limit the availability of genus claims in biotechnology. In *Eli Lilly*, the Federal Circuit suggested that "[a] description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by

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231. Although, like most polymorphisms, a single nucleotide mutation will usually have little or no effect on a protein's function, occasionally a single mutation will have a significant impact on the function of a protein, leading to disease.
232. The two inventors would end up with blocking patents.
233. Although the patentee may continue to research the hemoglobin gene family, the patentee will have a single perspective from which to pursue the research, and will not be under the pressure of competition, which is a significant motivator of innovation.
nucleotide sequence." 234 The Revised Interim Guidelines reflect this position by stating that the written description requirement for a genus may be met if a representative number of species are disclosed. 235 "A 'representative number of species' means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus." 236

The Federal Circuit has not yet addressed the issue in biotechnology of how many species must be disclosed to claim a genus. 237 However, the practical realities of claiming a genus of genes, cDNAs, or mRNAs present the same problems as claiming a single member of a genus. Until all of the members of a genus are known, there is no way to predict if there are widely varying characteristics among the members. In addition, an inventor with a patent to a genus of hemoglobin genes may inappropriately claim patent rights to all members of the genus, including all polymorphisms, alleles, isoforms, and homologs of the genes, whether or not they encode for proteins with novel functions (or lack thereof). Genus claims could also discourage other researchers from investigating genes in the patented genus, which would chill innovation. A possible solution to the problems posed by genus claims is if the PTO only allows claims that include enough universal characteristics of the genus to demonstrate that the inventor is in possession of the claimed invention. This approach would also protect any future inventor that identifies a closely related species with significantly varying characteristics because that species would fall outside the scope of the genus claim.

As stated earlier, the Revised Interim Guidelines suggest that an inventor may demonstrate possession by sufficiently describing relevant identifying characteristics, including "functional characteristics when coupled

235. Revised Interim Guidelines, supra note 209. "The Revised Interim Guidelines follow Federal Circuit case law which requires a representative number of species to satisfy the written description requirement for a genus. Written description is a question of fact, and what constitutes a representative number for a genus is a factual determination left to a case-by-case analysis by the examiner." Id. at 71432.
236. Id. at 71436. This language is more open then language in the first set of Guidelines, which stated: "[I]f the members of the genus are expected to vary widely in their identifying characteristics, . . . written description for each member within the genus may be necessary." Interim Guidelines, supra note 210, at 32642.
237. Thus far, cases have invalidated genus claims based on the disclosure of only a single species.
with a known or disclosed correlation between function and structure."\textsuperscript{238} The Revised Interim Guidelines clearly recognize the difficulty of using a purely functional claim to a nucleic acid sequence to meet the written description requirement: "A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence."\textsuperscript{239} "In such instances, the alleged conception fails not merely because the field is unpredictable or because of the general uncertainty surrounding experimental sciences, but because the conception is incomplete due to factual uncertainty that undermines the specificity of the inventor's idea of the invention."\textsuperscript{240}

While the PTO does not offer guidance on how to use functional claims as areas in biotechnology become more scientifically predictable, it is important that the PTO and courts continue to utilize a heightened written description requirement. Although areas of biotechnology will become more predictable over time, such as isolating specific cDNAs from organisms, this factor should only affect the amount of disclosure required to enable the invention, not the written description requirement. It is important to distinguish the roles each requirement plays in limiting inventors to their actual inventions.

2. The Future of the Written Description Requirement

Many commentators thought that the Federal Circuit's approach of using a heightened written description requirement would be limited to the unpredictable arts, in particular the more unpredictable areas of biotechnology.\textsuperscript{241} However, a recent decision by the Federal Circuit suggests that the court will no longer draw the line for a heightened written description at the unpredictable arts. In Gentry Gallery, Inc. v. Berkline Corp., the court invalidated a genus claim to a mechanical patent on a reclining sofa because the specification lacked adequate written description.\textsuperscript{242} While the Federal Circuit's reasoning in Gentry Gallery raises several concerns,\textsuperscript{243}

\textsuperscript{238} Revised Interim Guidelines, supra note 209, at 71435.
\textsuperscript{239} Id. at 71437 n.13.
\textsuperscript{240} Id. at 71429 (citing Burroughs Wellcome Co. v. Barr Laboratories Inc., 40 F.3d 1223, 1229 (Fed. Cir. 1994)).
\textsuperscript{241} See Patent & Trademark Office Society, supra note 225, at 141.
\textsuperscript{242} 134 F.3d 1473, 1480 (Fed. Cir. 1998).
\textsuperscript{243} For a detailed discussion of the court's reasoning, see Pretty, supra note 119, at 476-77.
the Revised Interim Guidelines issued by the PTO adopt the Federal Circuit’s approach by stating that the written description guidelines are intended to be equally “applicable to all technologies.” Therefore, it appears that the heightened written description requirement that the court previously used to evaluate claims in unpredictable arts will also apply in the predictable mechanical and electrical arts. This approach is consistent with the argument that the predictability of an art should only be considered under the enablement requirement, and should not be a factor under the written description requirement.

V. CONCLUSION

The enablement and written description requirements for biotechnological inventions have evolved over time as the Federal Circuit used these requirements to invalidate overly broad patents in biotechnology. Recently, the Federal Circuit indicated its willingness to start relying on these heightened requirements in traditionally predictable arts as well. A driving force in the evolution of these requirements appears to have been biotechnological inventions that progressed to a point where they were no longer “unpredictable” because the specification enabled overly broad claims. The Federal Circuit’s solution was to expand the written description requirement to invalidate these claims. While this approach has been widely criticized as reducing the value of biotechnology patents, the Federal Circuit’s approach is appropriate given the unique characteristics of biological materials, and will continue to encourage innovation in this important area.

The Federal Circuit uses a strict enablement requirement to prevent inventors from obtaining overly broad patent rights, thereby encouraging innovation. A key concept of enablement is whether the disclosure requires “undue experimentation” to make and use the invention. The Fed-

The opinion raises several concerns including:
(i) its reasoning is hard to reconcile with its earlier precedent in Utter concerning the predictable arts which it ignores, (ii) it fails to recognize that the predictability of mechanical and electrical principles makes many variations of the disclosed embodiments apparent to the skilled person addressed by paragraph one, (iii) it imposes an inquiry into the inventor’s subjective belief as to what was ‘essential’ concerning the hitherto objective evaluation of written description, and (iv) it casts doubt over the ability of patent applicants to obtain claim protection any broader than the originally filed broadest claim.

Id.
244. Revised Interim Guidelines, supra note 209.
eral Circuit in *Wands* provided eight factors that courts may consider when determining whether experimentation is undue. The *Wands* factors provide courts with a logical framework for analyzing the enablement requirement, as well as guidance on the right questions to consider when analyzing the issue. One key factor under this analysis is the predictability of an art. In unpredictable arts, although an inventor may understand the theory behind a broadly claimed invention, the inventor may not know or understand the subtle variations that practically enable the invention. The *Wands* factors are an important source of guidance because they lend certainty to the enablement analysis.

Similarly, the use of a heightened written description requirement by the Federal Circuit to define and limit the scope of claimed inventions preserves incentives for continued innovation. Given the inter-relatedness of genetic materials, requiring the disclosure of exact nucleotide sequences is a reasonable approach. Without a heightened written description requirement, great uncertainty about the scope of a patent would exist, and patent claims would be analyzed on a case-by-case basis. Broadly construed claims would allow patentees to obtain rights to genetic sequences they have no knowledge of in organisms they have never worked with, which would function to chill innovation in this area by giving a few inventors overly broad patent rights. A heightened written description requirement allows an inventor to claim only what the inventor possesses, and although this requirement does have some shortcomings, there are alternative strategies available to ensure that incentives and innovation are preserved in this revolutionary area.

The Revised Interim Guidelines issued by the PTO in 1999 for the written description requirement do not fully comply with a heightened written description requirement. For example, the Revised Interim Guidelines suggest that in unpredictable technologies, more evidence will be needed to demonstrate possession. However, predictability is not a factor under the written description requirement because the predictability of an art does not affect whether an inventor can demonstrate actual possession of the invention. In addition, the PTO should be cautious about the use by applicants of “sufficiently detailed relevant identifying characteristics” to demonstrate possession of a claimed invention. These characteristics may not adequately demonstrate possession by the applicant of the claimed invention, and therefore may result in overly broad patent rights, which discourage innovation.

Although this Comment primarily focuses on how the enablement and written description requirements have evolved with respect to genetic sequences, it is important to recognize that this case law lays the foundation
for approaching similar issues in other areas of biotechnology. The evolution of the limitations set by these requirements must be evaluated to understand the Federal Circuit's approach to biotechnological inventions, as well as its future approach to other technologies. The pioneering area of biotechnology will continue to evolve with the heightened enablement and written description requirements because these requirements serve to preserve rather than hinder innovation.