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Hugh McTavish

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When drafting patent claims, inventors and their attorneys attempt to obtain the broadest patent protection possible. Samuel Morse, the inventor of the telegraph, claimed not just the telegraph, but all means of communicating electronically at a distance.[1] An inventor of a new chemical discovered to have useful properties wants to claim not just that particular chemical, but the whole class of chemicals structurally related to it, particularly if there is reason to believe that the other chemicals in the class will have the same properties.[2] A claim

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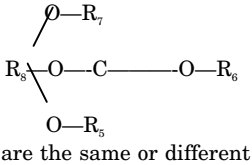
* J.D. candidate, University of Minnesota, 2001. B.A. Biology, Carleton College, 1984. Ph.D. Biochemistry, University of Minnesota, 1992. I wish to thank Dan Burk and Jan Embretson for offering comments on earlier versions of this note.

1. *See* O'Reilly v. Morse, 56 U.S. 62 (1854) (holding that Morse's claim for a patent on all communication made electronically at a distance was invalid because it was too broad).

2. *See, e.g., In re* Dillon, 919 F.2d 688, 690 (Fed. Cir. 1990). Claim two of the patent at issue in Dillon stated that:

> A composition comprising: a hydrocarbon fuel; and a sufficient amount of at least one orthoester so as to reduce the particulate emissions from the combustion of the hydrocarbon fuel, wherein the orthoester is of the formula:
>
> 
>
>
> wherein R_5, R_6, R_7, and R_8, are the same or different monovalent organic radical comprising 1 to about 20 carbon atoms.

Id. at 690.

This claims a very large class of chemicals. In fact, it claims almost an infinite number of particular chemical structures. The only restriction on the R groups is they contain 1-20 carbon atoms. They can have the carbon atoms arranged in any way (i.e., in a straight chain or a branched chain, with branches at different possible locations. They may or may not contain any number of atoms of other elements, such as Cl, N, O, S, Br, H, etc., in any possible combination. *See* THERALD MOELLER ET AL., CHEMISTRY: WITH INORGANIC QUALITATIVE ANALYSIS, CHAPTER 33 (2nd ed. 1984).

to a single composition of matter, machine, article of manufacture, or process is called a *species* claim.[3] A claim to a whole class of the above listed, for instance, one containing multiple related species, multiple related chemicals, or multiple related processes, is a *genus* claim or *generic* claim.[4]

In determining whether an inventor is entitled to a genus claim or merely a species claim, the courts traditionally first determine whether the written specification, which describes the invention and how to practice it, *enables* others to practice the invention as broadly as it has been claimed.[5] This is the enablement requirement, mandated by 35 U.S.C. section 112, paragraph 1.[6] An additional requirement for patentability,

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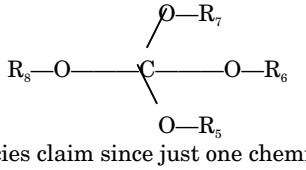
Furthermore, each R group can be different from each other. Obviously the inventor could not have synthesized every chemical falling within this class. However, she presumably synthesized and tested a few, and therefore had reason to believe that any chemical containing the core structure shown, four ester bonds to a single carbon atom, would have the recited property of reducing particulate emissions from the combustion of hydrocarbon fuel.

3. *See* MANUAL OF PATENT EXAMINING PROCEDURE § 806.04(e) (2000). The manual states that: "[c]laims may be restricted to a single disclosed embodiment (i.e., a single species, and thus be designated a *specific species claim*), or a claim may include two or more of the disclosed embodiments within the breadth and scope of the definition (and thus be designated *a generic or genus claim*)." *Id*. "Species are always the specifically different embodiments." *Id*. In *Dillon*, if the claim had been to the orthoester of the formula:



it would have been a species claim since just one chemical is being claimed.

4. *See*, *e.g.*, *Dillon* 919 F.2d at 690 (explaining that the claim at issue was a genus claim because it encompasses a whole class of species; in this case a class of chemicals united by a structural feature); *O'Reilly*, 56 U.S. at 112 (illustrating that Samuel Morse's claim to all means of communicating electronically at a distance, is a genus claim because it encompasses many means); MANUAL OF PATENT EXAMINING PROCEDURE § 806.04(d) ("[A] generic claim should include no material element additional to those recited in the species claims, and must comprehend within its confines the organization covered in each of the species."). *See also supra* note 3 (presenting the chemical structure of one of the species the claim in *Dillon* encompasses).

5. *See* 35 U.S.C. § 112 (2000); *In re* Angstadt, 537 F.2d 498, 504 (C.C.P.A. 1976) (explaining that if those seeking patents have sufficiently enabled others skilled in the applicable art, then the claim is valid).

6. 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,

found in 35 U.S.C. section 112, paragraph 1, is the written description requirement.[7] In several recent recombinant DNA cases, the Federal Circuit interpreted the written description requirement in a way that led it to strike down generic claims, notwithstanding that they were enabled.[8] The Federal Circuit has held that claimed DNA must be described by specification of its nucleotide sequence,[9] and that compositions of matter (specifically DNA) can never be described by its function or method of isolation, but must be described by its structure.[10] Interestingly enough, the second holding, though phrased generally, has not been applied to a similar major area of biotechnology patent subject matter—monoclonal antibodies.[11] These additional requirements make generic claims to recombinant DNA inventions difficult, if not impossible.

This Note will argue that these additional requirements for recombinant DNA patents should be eliminated and that the Federal Circuit should instead return to a focus on the enablement requirement. The Note will then describe the enablement and written description requirements and how these statutory requirements apply to biotechnology cases. Finally, this Note will argue that the court's current approach is flawed and propose that the court's evaluation of DNA patents should return to an emphasis on the enablement requirement.

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and shall set forth the best mode contemplated by the inventor of carrying out his invention. 35 U.S.C. § 112, ¶ 1 (2000).

7. *See* Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1560-64 (Fed. Cir. 1991), *cert. denied*, 454 U.S. 1055 (1981).

8. *See* Regents of Univ. Calif. v. Eli Lilly & Co., 119 F.3d 1559, 1566-71 (Fed. Cir. 1997); Fiers v. Revel, 984 F.2d 1164, 1170-71 (Fed. Cir. 1993); and Amgen v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 1200-13 (Fed. Cir. 1991).

9. *See Eli Lilly & Co*., 119 F.3d at 1567.

10. *See Fiers*, 984 F.2d at 1169 ("[I]rrespective of the complexity or simplicity of the method of isolation employed, conception of a DNA, like conception of any chemical substance, requires a definition of that substance other than by its functional utility.").

11. *See In re* Wands, 858 F.2d 731 (Fed. Cir. 1988); *infra* notes 75-79 and accompanying text (discussing the *Wands* case).

I. BACKGROUND

A. ENABLEMENT REQUIREMENT

To receive a patent, an inventor must describe the invention well enough for one skilled in the art to understand, make, and use it.[12] That requirement is codified in 35 U.S.C. section 112, paragraph 1:

> The specification [of a patent] 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, and shall set forth the best mode contemplated by the inventor of carrying out his invention.[13]

The patent specification must be sufficiently detailed to enable others skilled in the art to practice the claimed invention without "undue experimentation."[14] The specification need not be so detailed as to enable a layperson to practice the invention.[15] Rather, it must enable a person skilled in the art, which in biotechnology is a Ph.D.-level scientist, who also is knowledgeable in the subdiscipline of the invention and skilled in that subdiscipline's routine techniques.[16]

The other key aspect of the enablement requirement is that it only requires that others will not have to perform "undue experimentation" to reproduce it. Enablement is not precluded by the necessity of some experimentation, "[t]he key word is 'undue,' not experimentation."[17] The court in *In Re Wands* stated a test for what would constitute "undue experimentation": "The test [for 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

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12. "To be enabling under § 112, a patent must contain a description that enables one skilled in the art to make and use the claimed invention." Atlas Powder Co. v. E.I. duPont de Nemours & Co., 750 F.2d 1569, 1576 (Fed. Cir. 1984).

13. 35 U.S.C. § 112, ¶ 1 (2000).

14. *See In re* Angstadt, 537 F.2d 498, 504 (C.C.P.A. 1976); PPG Industries, Inc. v. Guardian Industries, Corp., 75 F.3d 1558, 1564 (Fed. Cir. 1996) (holding that to satisfy the enabling requirement, a patent must show those skilled in the art how to make and use the invention).

15. *See* Enzo Biochem., Inc. v. Calgene, Inc., 188 F.3d 1362, 1372-74 (Fed. Cir. 1999).

16. *See id*.

17. *Angstadt*, 537 F.2d at 504.

guidance with respect to the direction in which the experimentation should proceed . . . ."[18]

Enablement is generally considered to be the most important factor for determining the scope of claim protection allowed.[19] The scope of enablement must be commensurate with the scope of the claims.[20] However, enablement does not require that an inventor disclose every possible embodiment of his invention.[21] Additionally, there is a policy to reward pioneer inventions with broad protection. [22] Since a pioneer inventor may have enabled a broad new range of inventions, courts consider that the inventor should be rewarded for it.[23]

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18. *In re* Wands, 858 F.2d 731, 737 (Fed. Cir. 1988), (quoting *In re* Jackson, 217 U.S.P.Q. 804, 807 (BNA)).

19. *See* ROBERT P. MERGES, PATENT LAW AND POLICY: CASES AND MATERIALS 660 (2nd ed. 1997).

20. *See Amgen, Inc*., 927 F.2d at 1212; *O'Reilly*, 56 U.S. at 62. In *O'Reilly*, the inventor, Samuel Morse, had claimed "the use of . . . electromagnetism, however developed for marking or printing intelligible characters . . . at any distance . . ." *Id*. at 112. Morse had not taught how to practice or even imagined all possible means of communicating at a distance via electromagnetism. *See id*. at 112-14. He had only enabled one means—the telegraph—others later invented other means. *See id*. at 68-74. *See also In re* Hyatt, 708 F.2d 712, 714-15 (Fed. Cir. 1983) (holding that a means plus function claim, claiming all means for achieving a given function, was invalid for lack of enablement where only a single means was disclosed).

21. *See* Clark Blade & Razor Co. v. Gillette Safety Razor Co., 194 F. 421, 423 (3rd Cir. 1912), (quoting Deering v. Winona Harvester Works, 155 U.S. 286, 302 (1894)). The court stated that:

> [F]or if such were the law, patentability must have been denied to Elias Howe for the "grooved and eye-pointed needle," . . . of which it was said [by the Supreme Court] in *Deering v. Winona,* 155 U.S. 286, 15 Sup. Ct. 118, 39 L.Ed. 153*:* 'The invention of a needle with the eye near the point is the basis of all the sewing machines used, but the methods of operating such a needle are many; and if Howe had been obliged to make his own method a part of every claim in which the needle was an element, his patent would have been practically worthless.

Id. at 423.

22. *See*, *e.g.*, *In re* Hogan, 559 F.2d 595 (C.C.P.A. 1977). The *Hogan* court expressed this policy stating that:

> To restrict [a patentee] to the . . . form disclosed . . . would be a poor way to stimulate invention, and particularly to encourage its early disclosure. To demand such restriction is merely to state a policy against broad protection for pioneer inventions, a policy both shortsighted and unsound from the standpoint of promoting progress in the useful arts, the constitutional purpose of the patent laws.

Id. at 606.

23. *See id.*

The enablement requirement is stricter for "unpredictable arts" than predictable ones. Thus, "[i]f an invention pertains to an art where the results are predictable, . . . a broad claim can be enabled by disclosure of a single embodiment."[24] Courts consider, for instance, that the field of electronics is a predictable art.[25] From the invention of a single type of circuit, courts presume that one skilled in the art may be able to create other, similar circuits and know with a reasonable certainty that they will perform predictably.[26] In contrast, chemistry and biology are often classified as unpredictable arts.[27] Courts are hesitant to allow a claim encompassing a broad class of chemicals from the synthesis of one or a few chemicals of the class:[28] though one can make reasonable predictions about the characteristics of similar chemicals, one is not entirely certain until the new species are actually synthesized and characterized.[29] In unpredictable arts, enablement of generic claims is considered lacking because the undescribed embodiments cannot be made without undue experimentation.[30]

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24. Spectra-Physics, Inc. v. Coherent, Inc., 827 F.2d 1524, 1533 (Fed. Cir. 1987) (citing In re Cook, 439 F.2d 730, 735 (CCPA 1971); In re Vickers, 141 F.2d 522, 527 (CCPA 1944)).

25. *See In re* Fisher, 427 F.2d 833, 839 (C.C.P.A. 1970) ("In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment 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.").

26. *See id.* Because of the complexity of circuits in many modern semiconductor chips, that presumption is no longer valid. Developers often do not know how a circuit will perform until it is tested. *See* Christine Gorman, *Hacking the Cell's Circuitry*, TIME, Aug. 7, 2000, at 75.

27. *See e.g.*, *Fisher*, 427 F.2d at 839. *See also In re* Cook, 439 F.2d 730, 734 (C.C.P.A. 1971) (deciding that in lieu of labeling an entire art predictable or unpredictable; a case by case inquiry determining whether the factors involved in the art are predictable or not is more proper).

28. *See In re* Marzocchi, 439 F.2d 220, 223-24 (C.C.P.A. 1971); *In re* Smythe, 480 F.2d 1376, 1383 (C.C.P.A. 1973).

29. *See Marzocchi*, 439 F.2d at 223-24; *Smythe*, 480 F.2d at 1383.

30. *See Smythe*, 480 F.2d at 1383 ("In . . . chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus . . . .").

B. WRITTEN DESCRIPTION

In biotechnology cases, the Federal Circuit has given prominence to another requirement for patentability that in other fields has rarely been invoked to invalidate patent claims: the written description requirement. The written description requirement, like the enablement requirement, is derived from 35 U.S.C. § 112, paragraph 1.[31] It is a requirement that the patent application provide "adequate support" for the claims at issue.[32] The standard is that an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date, the applicant was in possession of the invention.[33] The requirement most often arises in disputes over whether claims can relate back to the specification of an earlier application to gain the benefit of that earlier filing date.[34]

The purpose of the written description requirement is to guard "against the inventor's overreaching by insisting that he recount his invention in such detail that his future claims can be determined to be encompassed within his original

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31. *See Vas-Cath, Inc.*, 935 F.2d at 1560-64.

32. *See id.* at 1560.

33. *See In re* Gosteli, 872 F.2d 1008, 1012 (Fed. Cir. 1989).

34. *See* 35 U.S.C. §§ 120 and 132 (2000). Section 120 provides: "An application for a patent for an invention disclosed in an application previously filed . . ., which is filed by an inventor or inventors named in the previously filed application, shall have the same effect as to such invention as though filed on the date of the prior application . . . ." Section 132 addresses the limitations on the amendment of a patent after it has been rejected. It provides that "[n]o amendment shall introduce new matter into the disclosure of the invention." Thus, under § 132, if an inventor wishes to introduce new claims during the consideration of her patent or the specification of the patent, the written description of the invention, must provide "adequate support" for the new claims. *See Vas-Cath, Inc*., 935 F.2d at 1560. Otherwise, she must file a new patent, with a later filing date, wherein the invention might no longer be patentable because of prior art arising between the two filing dates. Likewise, under § 120, an inventor can file a new patent, but relate it back to the filing date of an earlier application (again so as to antedate certain prior art that arose in the meantime) if the earlier application's written description of its invention provides support for the claims of the new patent. *See id*.

In *Vas-Cath*, the inventor filed a utility patent for a catheter claiming a lumen that is "substantially greater than one-half but substantially less than a full diameter." *See id*. at 1566. An earlier design application by the same inventors for the same or similar catheter had included drawings of the catheter, but the earlier application had said nothing about the range of diameter for the lumen. *See id*. The defendants argued, and the court agreed, that one of ordinary skill in the art would have been able to derive the claimed range from the earlier drawing, and so the earlier application had provided an adequate written description to support the new claims. *See id*.

creation."[35] This formulation suggests that the written description requirement is only relevant to determine whether claims can relate back to an earlier specification. Another expression of the purpose is that the requirement prevents inventors from practicing "upon the credulity or the fears of other persons, by pretending that his invention is more than what it really is."[36] This implies that courts are concerned about deception and want proof that the inventor actually invented what he has claimed.

C. BIOTECHNOLOGY CASES

1. Written Description Requirement

The Federal Circuit has used the written description requirement to strike down the claims in a key biotechnology case. In *Regents of Univ. Calif. v. Eli Lilly & Co.,*[37] the University of California ("UC") had cloned and determined the nucleotide sequence of the rat insulin cDNA.[38] From that

35. *See Vas-Cath Inc.*, 935 F.2d at 1561 (quoting Rengo Co., Ltd. v. Molins Mach. Co., 657 F.2d 535, 551 (3rd Cir.)).

36. *See id*. (quoting Evans v. Eaton, 20 U.S. 356, 434 (1822)).

37. 119 F.3d 1559 (Fed. Cir. 1997).

38. DNA is composed of four nucleotides: A, C, G, and T. The structure of a DNA can be defined by the sequence of these nucleotides, e.g., AAGTCCAGT. The term cDNA can be thought of as synonymous with *gene* for our purposes. It is a stretch of DNA created by recombinant DNA techniques that codes for one, or sometimes a few, proteins. DNA is double stranded, with the nucleotides of one strand binding to the complementary nucleotides of the other strand. A is complementary to T, and C is complementary to G. The two strands of a gene are called the template strand and the non-template strand. Thus, the sequence of the two strands of a portion of a gene would look like this:

non-template ACGTTCCAA
template TGCAAGGTT

When the gene is expressed, the template strand is "read," or used as a template for the synthesis of a complementary strand of RNA. That process is called *transcription*. The resultant RNA has the same sequence as the non-template strand, except that RNA uses nucleotides called uridine, or U, instead of the thymidine, or T, of DNA. The RNA strand is called messenger RNA, or mRNA. Thus, the template DNA and mRNA would have these sequences:

mRNA ACGUUCCAA
DNA template TGCAAGGTT

discovery, UC claimed generic patents for cDNA encoding any vertebrate insulin and cDNA encoding any mammalian insulin.[39] The court ruled those broad claims invalid for lack of an adequate written description.[40] It reasoned that a description of rat insulin cDNA is not a description of vertebrate or mammalian cDNA.[41] Likewise, the court reasoned that the mere name "mammalian insulin cDNA" is not an adequate description because it describes the function of the gene, but not the structure.[42] It is a description of what the gene does, which is encode insulin, not of what it is made.[43] An adequate description "requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA."[44]

To enable generic claims, applicants "are not required to disclose every species encompassed by their claims, even in an unpredictable art."[45] However, disclosure of one species' gene sequence, such as rat insulin cDNA, was held not enough to claim the gene sequence for the entire genus of mammalian

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The mRNA dissociates from the DNA to become a single-stranded mRNA, and the template DNA strand reassociates with the non-template DNA to reform double-stranded DNA. Next the mRNA is "translated" by cellular enzymes into a protein. That is, the sequence of nucleotides in the RNA will determine the sequence of amino acids in the protein whose synthesis it directs. One mRNA codes for the synthesis of one or a few proteins. A gene is defined as a sequence of DNA that codes for one protein. So sometimes an mRNA corresponds to one gene, sometimes to a few genes. *See* WILLIAM B. WOOD, BIOCHEMISTRY: A PROBLEMS APPROACH, CHAPTERS 17, 18, 20 (2nd ed. 1981).

The DNA at issue in *Eli Lilly* was a complementary DNA, or cDNA. A cDNA is synthesized from a mRNA. Enzymes are used that will copy a single-stranded mRNA into a double-stranded DNA, and the double-stranded DNA that results is called a cDNA. The cDNA will have the same sequence as the genomic DNA (genomic DNA is the DNA naturally present in the cell) that was originally used in the cell to direct transcription of the mRNA, with one difference. Genomic DNA contains sequences of varying sorts that do *not* encode proteins and are not transcribed into RNA. In fact, in mammals, including humans, the overwhelming majority of DNA is not transcribed into RNA. Thus, a cDNA corresponds to only the DNA that is transcribed into RNA, most of which encodes the amino acid sequences of proteins. *See* JAMES DARNELL ET AL., MOLECULAR CELL BIOLOGY 249-55 (1986).

39. *See Eli Lilly & Co.*, 119 F.3d at 1562-63.
40. *See id.* at 1566-69.
41. *See id.* at 1568.
42. *See id.*
43. *See id.*
44. *See id.* at 1569.
45. *Id.* (quoting *In re* Angstadt, 537 F.2d 498, 502-03 (C.C.P.A. 1976)).

insulin cDNAs.[46] The court suggested that enumeration of cDNAs for a plurality of species may provide an implicit description of the genus.[47]

In *Eli Lilly*, UC also claimed human insulin cDNA, supported in the patent specification by a protocol for isolating the human cDNA, which was based on the procedure used for isolating rat insulin cDNA and the known amino acid sequence of human insulin.[48] The court said that "whether or not [this] provides an enabling disclosure, it does not provide a written description of the cDNA encoding human insulin."[49] Apparently the nucleotide sequence would be required in order to provide an adequate written description of the claim.[50]

Such strict written description requirements indicate that the enablement requirement is inadequate in recombinant DNA inventions. Taken literally, it means that no matter how routine it may become to clone and sequence DNA, and no matter how complete the enablement of a recombinant DNA invention, the DNA cannot be claimed without a specification of its nucleotide sequence.

The Federal Circuit took the same position in one of the cases cited in *Eli Lilly*. *Fiers v. Revel*[51] involved a priority dispute over a recombinant DNA invention. In *Fiers,* the court denied priority to the party that first conceived of the successful procedure for isolating the gene, even though it found that the procedure was routine to one skilled in the art.[52] Instead, it awarded priority to the party that first determined the gene's nucleotide sequence.[53] The court stated that "[i]rrespective of the complexity or simplicity of the method of isolation employed, conception of a DNA, like conception of any chemical substance, requires a definition of that substance other than by its functional utility."[54] The court went on to hold that conception of a process for making a substance, i.e. for cloning a gene, does not constitute conception of the gene

46. *See id.* at 1567-69.
47. *See id.* at 1569.
48. *See id.* at 1567.
49. *See id*.
50. *See id.*
51. 984 F.2d 1164 (Fed. Cir. 1993).
52. *See id.* at 1167-69.
53. *See id.* at 1172.
54. *See id.* at 1169.

itself.[55] Conception for a substance claim, i.e. to the gene itself, requires conception of the nucleotide sequence of a gene, which is the substance's physical structure.[56]

2. Breadth of Enablement in Recombinant DNA Cases

Two Federal Circuit cases directly addressed the scope of enablement provided in recombinant DNA inventions. In each case, the court concluded that the breadth of enablement provided by the specification was too narrow for the generic claims at issue. In *Amgen v. Chugai Pharmaceutical Co.*,[57] Amgen had cloned the gene for human erythropoietin ("EPO"), a hormone that stimulates red blood cell production.[58] Claim 7 of the patent claimed all DNA sequences "encoding a polypeptide having an amino acid sequence sufficiently duplicative of . . . EPO to allow possession of the biological property of causing bone marrow cells to increase production of . . . red blood cells . . . ."[59] The court ruled the claim invalid for lack of an enabling disclosure, based on the fact that the patent specification taught only how to prepare a few analogs of the EPO gene, whereas it claimed any DNA encoding a protein with EPO biological activity and an amino acid sequence similar to EPO.[60] The court ruled that the scope of enablement was not as broad as the scope of the claims.[61]

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55. *See id*.

56. *See id.* The court cites *Amgen v. Chugai Pharmaceutical Co*., 927 F.2d 1200 (Fed. Cir. 1991), for this view. However, this is actually a departure from *Amgen*. In *Amgen*, the court focused on the uncertain success of the conceived method for isolating the gene as the reason it ruled that conception of the gene did not occur until it was actually isolated. *See Amgen*, 927 F.2d at 1207. For "conception of a purified and isolated DNA sequence encoding human EPO, . . . Fritsch's conception of a process had to be sufficiently specific that one skilled in the relevant art *would* succeed in cloning the EPO gene." *Id*. (emphasis added). That certainly implies that if success were guaranteed, conception of a process for obtaining the gene would constitute conception of the gene.

57. 927 F.2d 1200 (Fed. Cir. 1991).

58. *See id.* at 1212.

59. *Id.* at 1204.

60. *See id*. at 1213. The court stated that the "[d]etails for preparing only a few EPO analog genes are disclosed. This 'disclosure' might justify a generic claim encompassing these and similar analogs, but it represents inadequate support for Amgen's desire to claim all EPO-type products." *Id.*

61. *See Amgen,* 927 F.2d at 1213-14.

The court asserted that it is theoretically possible for a genus claim to genetic sequences to be valid.[62] One has to wonder about that assertion, since the Federal Circuit has never upheld a genus claim to DNA sequences.

The second case that directly addresses scope of enablement in recombinant DNA patents is *Enzo Biochem, Inc. v. Calgene, Inc.*,[63] a case dealing with a patent on antisense technology. Antisense technology is a means of controlling gene expression by reducing the production of particular proteins inside a cell.[64] In this case, Calgene used the technology in its *flavr savr* tomato to slow the ripening process in tomatoes.[65] They used antisense to reduce the production of an enzyme that promotes ripening.[66]

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62. *See id*. at 1214. The court reasoned that:

> [We] do not intend to imply that generic claims to genetic sequences cannot be valid where they are of a scope appropriate to the invention disclosed by an applicant. That is not the case here, where Amgen has claimed every possible analog of a gene containing about 4,000 nucleotides with a disclosure only of how to make EPO and a few analogs.

Id.

In addition the court stated that:

> [I]t is not necessary that a patent applicant test all the embodiments of his invention. [W]hat is necessary is that he provide a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of his claims. For DNA sequences, that means disclosing how to make and use enough sequences to justify grant of the claims sought. Amgen has not done that here.

Id. at 1213.

63. 188 F.3d 1362 (Fed. Cir. 1999).

64. *See Enzo Biochem, Inc.*, 188 F.3d at 1362. The idea of antisense technology is rather simple. In gene expression, an enzyme called RNA polymerase copies one strand of the segment of DNA making up a gene or group of genes, the template strand, into a complementary RNA strand. This single stranded RNA, called a messenger RNA (mRNA) is "translated" into protein. Enzymes in the cell "read" the single-stranded mRNA and translate it into protein.

In antisense technology, a DNA construct is created so that the *nontemplate* strand of some gene, rather than the template strand, is transcribed into RNA. This single-stranded antisense RNA binds to the complementary mRNA for that gene that exists naturally in the cell. This makes the RNA double stranded instead of single stranded, so that it cannot be read by the cellular enzymes and translated into protein. Thus, in theory at least, that particular protein is not created as the long as the antisense RNA is present. *See id.* at 1366-67.

65. *See Enzo Biochem, Inc.*, 188 F.3d at 1368.

66. *See id*.

Enzo had a patent that claimed antisense technology in all organisms including bacteria, plants, animals, fungi, and viruses.[67] The inventor only succeeded in regulating three genes in one organism; the *E. coli* bacterium.[68] He failed in attempts to regulate some other genes in *E. coli*.[69] There were no examples of success in any other organisms.[70] Despite these failures, the claims were drawn very broadly.

In evaluating whether the disclosure enabled the generic claims, the court considered the list of factors set forth in *In re Wands*:

> (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.[71]

The issue for the court was whether these broad generic claims were enabled by the disclosure. The court found that: the claims were extraordinarily broad, covering an infinite number of cell types;[72] antisense technology was highly unpredictable;[73] the quantity of experimentation necessary to adapt the technology to plants or to any species other than *E. coli* was quite high;[74] and that the amount of direction and number of examples provided in the specification were very narrow compared to the breadth of the claims.[75]

The court invalidated the claims, holding that the breadth of enablement was not commensurate with the breadth of the claims.[76] It did, however, leave the door open for generic claims in biotechnology, stating:

It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art. However, there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the

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67. *See id.* at 1367-68.
68. *See id.* at 1372-73.
69. *See id.*
70. *See id.*
71. *See id.* at 1371 (quoting *In re* Wands, 858 F.2d 731, 737 (Fed. Cir. 1998)).
72. *See id.* at 1372.
73. *See id.*
74. *See id*. at 1372-73.
75. *See id.* at 1374-75.
76. *See id*. at 1372-75.

invention as broadly as it is claimed.[77]

The court also said that with advances in science, what was unpredictable at one time may become predictable and, at that time, broader generic claims are more likely to be allowed.[78]

A third recombinant DNA case, *In re Bell*,[79] was decided based on whether the prior art made the claimed invention obvious. The court's analysis also sheds some light on the enablement requirement. An obviousness inquiry has two parts: first, whether the prior art suggests the claimed invention, and second, whether the prior art demonstrates a reasonable expectation of success in attempting to practice the claimed invention.[80] The second part of the inquiry asks whether the prior art enables one skilled in the art to practice the invention. In *Bell*, the inventors claimed the genes for human insulin-like growth factors I and II.[81] The complete amino acid sequences of both proteins were already known from the prior art.[82] The question for the court was whether this and the prior art in recombinant DNA cloning made the genes obvious to one of ordinary skill in the art.[83] The court first considered whether the method used to select the clone, hybridization with degenerate oligonucleotide primers, would have been obvious to one skilled in the art.[84] The court found it would not—a finding that is clearly in error. The method of using degenerate oligonucleotide primers to select DNA clones was in the prior art. That method was, at the time, and, still is today, the preferred method to select a gene based on knowledge of the full or partial amino acid sequence of the protein it encodes[85] and would have been the obvious method to try.

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77. *Id*. at 1374 (quoting *In re* Vaeck, 947 F.2d 488, 496 & n.23 (Fed. Cir. 1991)).

78. *See Enzo Biochem, Inc.,* 188 F.3d at 1374 n.10.

79. 991 F.2d 781 (Fed. Cir. 1993).

80. *See In re* O'Farrell, 853 F.2d 894, 903-04 (Fed. Cir. 1988); Anita Varma and David Abraham, *DNA is Different: Legal Obviousness and the Balance Between Biotech Inventors and the Market*, HARV. J.L. & TECH. 53, 81 (1996). *See also* MANUAL OF PATENT EXAMINING PROCEDURE § 2142 (2000).

81. *See In re* Bell, 991 F.2d 781, 782 (Fed. Cir. 1993).

82. *See id*. at 783.

83. *See id.*

84. *See id.* at 784-85.

85. *See* Varma and Abraham, *supra* note 80, at 61-62 and 82.

Whether the method, at that time, would have had a reasonable expectation of success is a closer question, which the court did not reach. Today, success would be nearly assured without undue experimentation.[86] At the time of *Bell*, in 1981, the method was new, and perhaps, a person of ordinary skill in the art would not have felt so certain that it would succeed.[87] If we assume, though, that there was a reasonable expectation of success in cloning the gene, then from an enablement standpoint, the prior art made the invention of the cloned gene obvious. We could say that the prior art enabled one of ordinary skill in the art to practice the invention.

The court did not find the genes obvious for the following reasons. First, because it wrongly concluded that the method to isolate the genes was not obvious.[88] Second, regardless of the obviousness of the method, "the issue is the obviousness of the compositions, not of the method by which they are made."[89] Because of the degeneracy of the genetic code, the court asserted that 10^{36} nucleotide sequences could encode the known amino acid sequence, and thus, the structure of the gene was not obvious.[90] If the focus instead had been on the obviousness of the method used to isolate the gene, along with a reasonable expectation of success (in other words, whether or not the prior art enabled the practice of the invention) the genes should have been ruled obvious.

The Federal Circuit declined to consider, in *Eli Lilly,*[91] whether the claims at issue were enabled, but it is useful for the purposes of this note to determine whether they were. The University of California researchers had discovered and cloned the nucleotide sequence of the rat insulin cDNA.[92] From this, they generically claimed vertebrate and, more narrowly, mammalian insulin cDNAs, as well as specifically human

86. Even the author was able to use the procedure to clone a gene. *See* H. McTavish et al., *Sequence of the Gene Coding for Ammonia Monooxygenase from Nitrosomonas europaea*, 175 J. BACTERIOL. 2436 (1993).

87. *See* Varma and Abraham, *supra* note 80, at 61-62 (arguing that the procedures made reasonably certain, even at the time the experiments were initiated in *Bell*).

88. *See Bell*, 991 F.2d at 784.

89. *Id.* at 785.

90. *See id*. at 784.

91. Regents of Univ. Calif. v. Eli Lilly & Co., 119 F.3d 1559 (Fed. Cir. 1997).

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

insulin cDNA, which they had not yet cloned.[93] Their specification described methods to isolate these cDNAs by reference to the method used to isolate the rat insulin cDNA.[94] First, one would make a cDNA library from the appropriate tissue of the organism—the islet cells of the pancreas.[95] Then one would screen the library with the rat insulin cDNA.[96] The creation of cDNA libraries was fairly new but becoming routine in the art by the time of the UC application in 1977.[97] Screening that library with the cloned cDNA from a homologous gene was also routine and would be virtually certain to succeed.[98] Proteins performing the same function in any two species of mammals are certain to have very similar amino acid sequences.[99] Likewise, the genes for those proteins are certain to be homologous. It follows that there was at least a reasonable expectation that the screening of mammallian cDNA libraries with rat insulin cDNA would succeed in isolating the insulin cDNA from any desired mammallian species, including humans. Even though UC only knew the sequence of rat insulin cDNA, its specification of that invention enabled anyone skilled in the art to isolate any other mammallian insulin cDNA. The procedure, while lengthy and time consuming, all but assured success.[100] Thus, the

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93. *See id*.

94. *See* U.S. Pat. No. 4,652,525, W.J. Rutter et al., *Recombinant Bacterial Plasmids Containing the Coding Sequences of Insulin Genes.*

95. *See id.*

96. *See id. See also* U.S. Pat. No. 4,431,740, G. Bell et al., *DNA Transfer Vector and Transformed Microorganism Containing Human Proinsulin and Pre-Proinsulin Genes*.

97. *See* T. Maniatis et al., *Amplification and Characterization of a -Globin Gene Synthesized in Vitro*, 8 CELL 163 (1976).

98. *See* W. David Benton & Ronald W. Davis, *Screening gt Recombinant Clones by Hybridization to Single Plaques in situ*, 196 SCIENCE 180-81 (1977) (describing both the process and accuracy of the screening methods.)

99. *See*, *e.g*., THOMAS E. CREIGHTON, PROTIENS: STRUCTURES AND MOLECULAR PROPERTIES, Ch. 3 (2nd ed. 1993). The same protein in closely related species, such as insulin in rats and humans, usually differs by relatively few amino acids. For instance, the human hemoglobin -chain differs in amino acid sequence from the analogous protein in Rhesus monkey by 3% and from cow by 12%. Additionally, these differences in amino acid sequence occur in regions of the protein that do not play an essential role in its function.

100. After obtaining a rat cDNA, the UC researchers required two years to clone the human cDNA. *See Eli Lilly & Co*., 119 F.3d at 1562-63. Today this task would not take as long.

The obvious counterargument would suggest that the disclosure was not enabling of the human cDNA because cloning the human gene would require undue experimentation. A finding of undue experimentation could be

specification enabled the generic claims.

However, the court never reached that question, disposing of the case instead on its rule that a written description of a claimed gene must include its specific nucleotide sequence. Thus, these generic claims were disallowed. The focus on both the written description requirement and structure meant that otherwise enabled claims were invalid.

3. Enablement in a Monoclonal Antibody Case

The Federal Circuit's holdings regarding another major area of biotechnology have differed from its holdings regarding recombinant DNA patents. The court has allowed monoclonal antibodies,[101] unlike genes or DNA molecules, to be described by their function and conceived by their method of isolation without structural description. In *In re Wands,*[102] the

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supported by the length and recent development of the procedure. At the time the UC patent at issue in *Eli Lilly* was filed, the procedures used to clone both the rat and human insulin genes were relatively new and researchers did not have a great deal of experience with the techniques. *See id.* On that basis, perhaps one could argue that someone who attempted to clone the human insulin gene using the patent disclosing the rat gene would not have been certain of success. The certainty of success had not yet been established. Nonetheless, we know that the method disclosed in the patent would have led to successfully cloning the human gene. UC, in fact, did enable the cloning of the human gene. Furthermore, the methods of creating a cDNA library and screening it for a particular clone have not changed a great deal since the UC patent application. *Compare* Maniatis, *supra* note 97, at 163 ("develop[ing] a method for gene purification and amplification which could be applied to any . . . gene whose mRNA could be obtained."), *with* T. MANIATIS, E.F. FRITSCH, AND J. SAMBROOK, MOLECULAR CLONING: A LABORATORY MANUAL (1982), *and* T. MANIATIS, E.F. FRITSCH, AND J. SAMBROOK, MOLECULAR CLONING: A LABORATORY MANUAL (2nd ed. 1989) (describing essentially the same cloning techniques, respectively, six and thirteen years later).

101. *See In re* Wands, 858 F.2d 731, 733-34 (Fed. Cir. 1988) (providing an insightful general description of monoclonal antibodies). Antibodies are a class of proteins that help defend the body against invaders. Antibodies bind tightly to other molecules, present on the invaders, called antigens. The tightness of the antibody-antigen binding is called *affinity*. Each antibody binds to just one antigen, and in fact to just one part of the antigen molecule, called a *determinant*. In an immune response, many different antibodies — that is, proteins with different amino acid sequences — binding to the same antigen are produced. Different antibodies binding to the same determinant on the antigen are even produced. From this diversity of antibodies binding to a single antigen, scientists can select one of these antibodies and make large amounts of it. These identical antibodies produced from a single cell type are called monoclonal antibodies. *See also* BRUCE ALBERTS ET AL., MOLECULAR BIOLOGY OF THE CELL, 181-84, 951-1012 (1983).

102. *See Wands,* 858 F.2d at 734.

appellants claimed an immunoassay method for detecting hepatitis-B surface antigen using any IgM monoclonal antibody with a binding affinity constant of greater than 10^9 moles/liter.[103] The issue before the court was whether the disclosure enabled this broad claim.[104] The inventors disclosed a method for isolating IgM monoclonal antibodies meeting those binding affinity specifications.[105] This disclosure of a procedure to isolate a monoclonal antibody sufficiently satisfied the enablement requirement, because it was routinely used by those skilled in the art and, more importantly, it had a high rate of success in producing monoclonal antibodies fitting the claims.[106] Thus, the disclosure did not require undue experimentation.[107] This ruling came despite the fact that the method was lengthy and was difficult enough that even the inventors had trouble in their first few attempts.[108]

Interestingly, each time a scientist isolated monoclonal antibodies to produce this invention, he would isolate a different monoclonal antibody.[109] Although the antibody isolated would have the same functional characteristic — binding hepatitis B surface antigen with high affinity — it would have a different amino acid sequence.[110] By the logic of *Eli Lilly* and *Fiers*, each isolation would be a different invention.

The court here, unlike in the DNA cases, focused on enablement, not structure.[111] It did not address the issue, perhaps because it was not raised, of whether the amino acid sequence of the monoclonal antibody used was not specified. Nor was the court bothered (again perhaps because the argument was not raised) by the fact that anyone attempting to practice this invention would isolate a monoclonal antibody with a different amino acid sequence.

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103. *See id.* at 734-35. Antibodies can be used for sensitive diagnostic tests called immunoassays that detect the presence of the antigen to which an antibody binds, such as hepatitis-B surface antigen.

104. *See id*. at 735.

105. *See id*. at 736.

106. *See id.* at 739-40.

107. *See id*. at 740.

108. *See id.*

109. *See* T.D. BROCK & M.T. MADIGAN, BIOLOGY OF MICROORGANISMS 437-46 (6th ed. 1991).

110. *See id*.

111. *See Wands*, 858 F.2d at 735-40.

D. AN ECONOMIC ARGUMENT AGAINST GENUS PATENTS

The Federal Circuit seems to have erected special barriers to generic or broad claims in biotechnology, particularly in recombinant DNA. Presumably, the court is concerned with allowing broad areas of a new field of technology to be blocked from competition. An economic basis for those concerns was articulated by Robert Merges and Richard Nelson.[112]

A broad patent can give the patent holder rights not just over the invention, but also over some improvements on the invention when those improvements are considered obvious.[113] Merges and Nelson argue that this is economically inefficient.[114] When a single rightholder controls the rights to future improvements on a current technology, it can be expected that the rightholder will underdevelop the improvements.[115] The single entity will have less imagination and take a less wide-ranging approach to exploring possible improvements than would multiple actors.[116] Second, when a firm has rights to the improvements, it will move more slowly in developing the improvements, because it need not fear that others will develop them first and obtain a monopoly over the improvements.[117] The ultimate concern here is not the firm, but rather, the possible lack of incentive to improve technology in the field.

E. BLOCKING PATENTS

When broad patent claims are awarded, as this note advocates, it intrinsically increases the possibility of nonobvious improvements falling within the scope of the claims. Blocking patents arise when an inventor claims a nonobvious patentable improvement that literally infringes an earlier patent.[118] An example of how this can arise is when a

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112. *See* Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839 (1990) (arguing that the breadth of a patent influences its economic significance).

113. *See id*. at 845-49.

114. *See id.* at 844. In many industries the efficiency gains from the pioneer's ability to coordinate are likely to be outweighed by the loss of competition for improvements to the basic invention. *See id.*

115. *See* Merges & Nelson*, supra* note 112, at 873-74.

116. *See id.* at 873-75.

117. *See id.* at 872.

118. *See* MERGES, *supra* note 19, at 697-701. Blocking patents arise because of point in time at which enablement is judged. Enablement is judged

new use is found for a pre-existing, patented compound. Minoxidil, for instance, was a patented compound, with its known usefulness being as a drug for relieving hypertension.[119] When it was discovered that it was also useful for treating baldness, those who discovered the new use obtained a patent for a method of treating baldness with Minoxidil.[120] However, practicing that invention would infringe the earlier composition of matter patent claim to the compound Minoxidil.[121] The later patent is a subservient patent. The subservient patent cannot be practiced without a license from the holder of the dominant patent. Likewise, the holder of the dominant patent cannot infringe the subservient patent without a license. Thus, each patent effectively blocks the other. The holder of the patent on

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as of the time of filing. *See* U.S. Steel Corp. v. Phillips Petroleum Co., 865 F.2d 1247, 1251 (Fed. Cir. 1989). An inventor can claim material that later turns out to be beyond her research, as long as the disclosure enables others to make use the claimed invention as it was understood at the time of filing. *See id.* at 1251. An example is a claim of Phillips Petroleum Co. to crystalline polypropylene. *See id.* Phillips, at the time of the patent application, had only synthesized low molecular weight crystalline polypropylenes. *See id.* at 1249-50. However, the essence of Phillips' invention was crystyllinity, and at the time of filing they enabled making the only known crystalline polypropylenes. *See id.* at 1249. That Phillips did not enable the production of higher molecular weight polypropylene was irrelevant to the validity of the claim, because "[a] patent applicant is not . . . required, however, to predict every possible variation, improvement, or commercial embodiment of his invention." *Id.* at 1250 (citing Phillips Petroleum Co. v. U. S. Steel Corp., 673 F.Supp. 1278, 1292 (D. Del. 1987)). The court further stated that:

> Defendants' misdirected approach here is the same as that improperly relied upon by the PTO in Hogan. Defendants do not, as they cannot, argue that the 1953 specification fails to enable one skilled in the art to practice the *claimed invention*. That the [Phillips] claim may cover a later version of the claimed composition (crystalline polypropylene with higher intrinsic viscosity and average molecular weight) relates to infringement, not patentability. To hold differently would "impose an impossible burden on inventors and thus on the patent system."

Id. at 1251-52 (citations omitted).

Because enablement is evaluated at the time of filing, a later improvement invention can be non-obvious over the previous patent, and thus patentable, yet infringe the previous patent.

119. *See generally* U.S. Pat. No. 4,871,839, W.T. Gibson, *Skin Treatment Composition*.

120. *See* U.S. Pat. No. 4,139,619, C.A. Chidsey III, *6-Amino-4-(substituted amino)-1,2-dihydro-1-hydroxy-2-iminopyrimidine, Topical Compositions and Process for Hair Growth*.

121. A patent claim to a composition of matter conveys the exclusive right to make, use, or sell the composition for any purpose. *See* 35 U.S.C. § 271(a). It is irrelevant that the purpose in this case is one that was unknown at the time the composition of matter was claimed.

a method of treating baldness cannot practice his invention at all without a license from the holder of the patent claiming Minoxidil as a composition. Likewise, the holder of the composition patent cannot use it to treat baldness without a license from the holder of the patent claiming a method to treat baldness.[122]

II. ANALYSIS

With respect to recombinant DNA patents, the Federal Circuit has generally focused on rules that, taken literally, would make generic claims to more than one specific DNA impossible. First, it has created a written description rule that DNA must be described by its nucleotide sequence.[123] Second, in what is really the rationale of the previous rule, it has ruled that DNA, and any claimed composition of matter, can only be described by its structure, not its function.[124] It has held that genes and DNA cannot be conceived by their functional utility, i.e., what proteins they encode,[125] nor by the method for isolating them,[126] but only by their structure (nucleotide sequence).

Amgen shows how these rules for recombinant DNA patents thwart genus claims in that field. In *Amgen*, the inventors, after having cloned and sequenced the gene for erythropoietin, attempted to claim DNA sequences encoding

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122. *See* Cantrell v. Wallick, 117 U.S. 689, 694 (1886). When one patent is an improvement on another "neither of the two patentees can lawfully use the invention of the other without the other's consent." *Id*. *See also* MERGES, *supra* note 19, at 697-701.

123. *See Eli Lilly & Co*., 119 F.3d at 1568-69 (Fed. Cir. 1997) ("[A] cDNA . . . requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA."); *Fiers*, 984 F.2d at 1170-71 (Fed. Cir. 1993) ("An adequate 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.").

124. *See Eli Lilly & Co.*, 119 F.3d at 1568 ("A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.").

125. *See Fiers*, 984 F.2d at 1169 ("[C]onception of a DNA, like conception of any chemical substance, requires a definition of that substance other than by its functional utility.").

126. *See id*. ("[C]onception only of a process for making a substance . . . can at most constitute a conception of a substance claimed as a process. Conception of a substance claimed per se without reference to a process requires conception of its structure, name, formula, or definitive chemical or physical properties.").

proteins homologous to and having the same function as erythropoietin.[127] It was the prototypical recombinant DNA generic claim, claiming not just one nucleotide sequence, but also the other nucleotide sequences that would encode the same protein or closely related proteins that function in the same way. These variant nucleotide sequences encoding the same protein would be obvious not just to one of skill in the art, but arguably to anyone familiar with the degeneracy of the genetic code.[128] The inventors in *Amgen* tried to claim not just the composition of matter they had actually discovered or invented, but also other compositions that are closely related to the discovered species, that are obvious from knowledge of the species, and that are expected to function the same as the species.[129] However, under the rules the Federal Circuit has created for recombinant DNA inventions, it is impossible to claim related species of DNA until their sequences have been determined.[130] The sequences could not be claimed by their

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127. *See* Amgen, Inc. v. Chugai Pharmuceutical Co., 927 F.2d 1200, 1203-04 (Fed. Cir. 1991).

128. *See generally* BRUCE ALBERTS ET AL., MOLECULAR BIOLOGY OF THE CELL, 199-232 (1983) (outlining DNA structure, synthesis, and replication). The structure of any DNA molecule can be specified by the sequence of the four nucleotides within it. A typical recombinant DNA molecule is composed of a few thousand nucleotides. Each set of three nucleotides in the coding region of a gene is known as a codon and specifies one amino acid in a protein, as indicated below.

DNA: GCC-TAC-CCT-ACT

amino acids for which it codes:Ala-Tyr-Pro-Thr

Proteins are polymers of 20 different types of amino acids. Thus, when one knows the nucleotide sequence of a cDNA, one knows the amino acid sequence of the protein it encodes. But the converse is not true. Most amino acids are specified by more than one codon. For instance, GCT, GCC, GCG, and GCA all code for the amino acid alanine, designated above by its three letter abreviation Ala. The fact that more than one codon encodes the same amino acid is called the *degeneracy* of the genetic code. Because of the degeneracy of the genetic code, it would be obvious to one skilled in the art that one could circumvent a claim to a single nucleotide sequence by altering the nucleotide sequence in such a way that the DNA would still encode the same amino acid sequence. A variant nucleotide sequence encoding the same amino acid sequence would be expected to function the same in the invention. Likewise, even if the claims were limited to DNAs encoding a single amino acid sequence, it would be obvious to one skilled in the art how to circumvent the claims. One could alter the nucleotide sequence so that one or a few amino acids in the encoded protein were changed, because a small number of amino acid changes are usually tolerated biologically. Usually the resultant protein's utility would be unchanged. *See also supra* note 38 and accompanying text (providing a more general description of DNA structure and sequencing).

129. *See* CREIGHTON, *supra* note 99.

130. *See supra* notes 44, 49, 54-56 and accompanying text.

function.[131] The court also emphasized the large number of possible nucleotide sequences encoding a protein with an amino acid sequence closely homologous to EPO.[132] The court implied that Amgen also would not have been allowed to claim the genus structurally — for instance, the class of nucleotide sequences encoding an amino acid sequence 95% or more identical to the amino acid sequence of EPO — because there are too many members of that class.[133] It seems, under the rules of the Federal Circuit, there is no way to claim a genus of DNA.

The requirements created for recombinant DNA patents have the effect of being an *a priori* ban on generic claims. There is no reason generic claims to this area of technology should be *a priori* precluded, especially when generic claims have been permitted in related areas, such as chemistry[134] and monoclonal antibodies.[135] To avoid this illogical result, the court should return to a focus on enablement in determining whether generic claims are justified, as it does in other chemical cases and as it has done in the recent recombinant DNA case *Enzo Biochem, Inc*.[136] If the specification enables the invention to be practiced as broadly as it is claimed, those claims should be allowed. They should not be thwarted by erecting a requirement that description of a claimed DNA requires specification of its nucleotide sequence, or that a composition of matter can never be claimed by its function (encoding a particular protein, in the case of a gene) or the process for its isolation.

Why has the Federal Circuit erected special barriers to genus or broad claims in recombinant DNA? The court has never articulated a reason for what seems to be special treatment given this field, but some speculation is possible. The court is probably concerned that it would stifle innovation in a new field if it allowed broad patents to block off

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131. *See Amgen, Inc.*, 927 F.2d at 1212-14 (encoding a protein that behaves like EPO is an insufficient patent specification).

132. *See id.* (describing that after five years of testing, the inventor still could not identify precisely which of more than fifty analogs had the biological properties of EPO).

133. *See id.* at 1213-14. (The court notes that over a million analogs with changes in only 3 amino acids could be made, and "Amgen has told how to make and use only a few of them.").

134. *See supra* notes 2, 4 and accompanying text.

135. *See supra* notes 101-11 and accompanying text.

136. 188 F.3d 1362 (Fed. Cir. 1999).

competition. Broad patents deter further innovation within their scope.[137] First, others have less incentive to develop improvements knowing their improvements will be subject to a blocking patent.[138] Second, the rights holder has less incentive to develop improvements, knowing that it will retain a blocking patent even if another develops them first.[139]

However, while broad patent rights should hinder future innovation within the scope of that patent, a refusal to grant justified patent rights should also deter innovation. Others will not develop technologies at all if they cannot get a return on their investment, and sometimes the only way to get a return is to be awarded patent rights commensurate with what they have developed. If courts simply refuse to enforce broad patent rights, the incentives have been diminished for developing the significant, pioneer inventions that merit broad patent protection.

Second, concern that a broad patent will block the incentive to develop improvements is partially addressed by the option of improvement patents or subservient patents.[140] If improvements are obvious, there is no need for concern, because the rightsholder would see them and would have the incentive to develop them. If an improvement is not obvious, then it is not true that the rightsholder holds complete rights to it. The inventor of a nonobvious improvement covered by a broader patent is entitled to a subservient or improvement patent.[141] If the invention falls within the claims of the dominant patent, she cannot practice it without a license from the dominant patent rightsholder.[142] But neither can the dominant patent rightsholder practice the improvement without a license from the improvement patent holder.[143] Ordinarily, one would expect the two parties to reach an economically beneficial agreement, so that the improvement patent holder will receive some return for her contribution.[144]

Third, even if it is accepted that it would be economically wise to disallow broad patent claims in general because of their

137. *See supra* notes 112-17 and accompanying text.
138. *See supra* notes 118-22 and accompanying text.
139. *See supra* note 117 and accompanying text.
140. *See generally supra* notes 121-22 and accompanying text.
141. *See generally supra* notes 118-22.
142. *See id.*
143. *See id.*
144. *See* MERGES, *supra* note 19, at 945-47.

effect of stifling further innovation in the field, that policy should apply uniformly to all fields of technology, not just to recombinant DNA claims. There is no apparent reason why broad patent rights are more economically deleterious in recombinant DNA than in chemistry or other fields. With the written description requirement of a specific nucleotide sequence, it appears that unique barriers have been set up against generic claims to DNAs. Returning the focus to enablement would put DNA claims on the same footing as other claims.

Despite the possible effect of deterring innovation within the scope of a genus patent once the patent has been granted, genus patents in biotechnology should be granted and evaluated under the same standards as genus patents in other fields. This means they should be evaluated on the basis of enablement. The issues in an enablement inquiry are whether the scope of enablement matches the scope of the claims, and whether the invention can be practiced as broadly as it is claimed without undue experimentation.[145] The additional requirements the Federal Circuit has erected that seem designed specifically to deter broad claims to DNAs — that a composition of matter cannot be claimed by its function or method of isolation, and that the nucleotide sequence of any claimed DNA must be specified — should be dropped.

Some of the reasons for focusing exclusively on enablement in determining the breadth of claims allowed in recombinant DNA inventions are that it: (1) would create consistency with precedent on simultaneous conception and reduction to practice; (2) would create consistency with precedent in chemistry and monoclonal antibody claims; (3) would fulfill the purposes of the written description requirement and the general rule that compositions of matter should be described by structure; (4) is essential to avoiding easy circumvention of recombinant DNA patents; (5) allows for sensible assigning of inventorship; (6) would promote early disclosure; (6) would avoid economic waste; and (7) would be a rule that would not be made obsolete by advances in technology, as the current rules have been.

145. *See supra* notes 12-30 and accompanying text.

A. CREATING CONSISTENCY WITH PRECEDENT ON SIMULTANEOUS CONCEPTION AND REDUCTION TO PRACTICE

The written description requirement that DNAs can only be described by their complete nucleotide sequence creates a doctrine of simultaneous conception and reduction to practice for DNA inventions.[146] This leads to inconsistencies with the prior jurisprudence on simultaneous conception and reduction to practice. Reduction to practice occurs when an inventor has produced the actual working invention. It occurs when "the embodiment . . . actually work[s] for its intended purpose."[147] Conception occurs when the inventor has completed "the mental part of the inventive art."[148] In the past, courts have held that "conception is complete when one of ordinary skill in the art could reduce the invention to practice without undue experimentation."[149] This is the exact language of the enablement test.[150]

The Court of Customs and Patent Appeals ("C.C.P.A."), the predecessor to the Federal Circuit, explained the requirement for invoking simultaneous conception and reduction to practice in stronger terms in 1974. It stated that the doctrine applied "only in cases where conception is followed by extensive research characterized by perplexing and intricate difficulties arising every step of the way."[151] The doctrine was applied only once between 1974 and 1988.[152]

Now, however, the written description requirement for a nucleotide sequence in DNA inventions has created a situation where the doctrine of simultaneous conception and reduction to practice applies automatically to all claims for recombinant DNAs. In fact, under this requirement conception is held not to occur until *after* reduction to practice. Suppose one claims a cDNA clone that produces insulin. That invention is reduced to

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146. *See* John M. Lucas, *The Doctrine of Simultaneous Conception and Reduction to Practice in Biotechnology: A Double Standard for the Double Helix*, 26 A.I.P.L.A. Q.J. 381, 402-03 (1998).

147. Newkirk v. Lulejian, 825 F.2d 1581, 1582 (Fed. Cir. 1987).

148. Townsend v. Smith, 36 F.2d 292, 295 (C.C.P.A. 1929) (citing Mergenthaler v. Scudder, 11 App. D.C. 264, 276 (D.C. Cir. 1897)).

149. *Mergenthaler*, 11 App. D.C. at 276.

150. *See supra* notes 12-18 and accompanying text.

151. Alpert v. Slatin, 305 F.2d 891, 894 (C.C.P.A. 1962).

152. *See* Lucas, *supra* note 146, at 397 n.113 (citation omitted).

practice when it is cloned and the inventor has determined that the bacterium containing the cloned DNA is producing insulin. Yet at that point, the inventor may not know the nucleotide sequence of the clone. He has already reduced the invention to practice but still, under the written description rule, cannot patent it and therefore has not conceived it. Consistency with the precedent of conception and reduction to practice requires that conception be held to occur when an inventor can enable one of ordinary skill in the art to practice the invention, or to isolate and create the claimed recombinant DNA. In many cases, that occurs long before the DNA sequence is determined.

B. CONSISTENCY WITH MONOCLONAL ANTIBODY AND CHEMICAL CASES

DNA molecules and antibodies have very close parallels that should lead to similar treatment under patent law, but the Federal Circuit has treated them differently. The function of a gene is to encode a protein — to direct production of that protein and specify the amino acid sequence of the protein. Because of the redundancy of the genetic code, many possible nucleotide sequences can encode the same amino acid sequence.[153] Thus, many genes could encode the same protein. But from a functional standpoint, the only thing we are interested in is what protein a gene encodes. Nevertheless, the Federal Circuit in *Eli Lilly* and *Fiers* has held that for the purpose of obtaining patent protection for a gene, the claims cannot recite the gene's function — which protein it encodes — and that conception of the gene is not complete with development of a method for isolating the gene.[154] Conception and description of the gene is satisfied only by the gene's nucleotide sequence.[155]

The rule is the opposite for monoclonal antibodies.[156] The

153. *See supra* text accompanying note 128. The amino acid sequence of a protein gives one considerable information about the nucleotide sequence of the cDNA encoding it, but it does not completely determine that nucleotide sequence.

154. *See supra* notes 37-56 and accompanying text.

155. *See id*.

156. Antibodies are a class of proteins that help defend the body against invaders. Antibodies bind tightly to other molecules, present on the invaders, called antigens. *See* Alberts, *supra* note 128, at 34. The tightness of the antibody-antigen binding is called affinity. *See id*. at 970. Each antibody binds to just one antigen, and in fact to just one part of the antigen molecule,

function of antibodies is to bind to particular substances called antigens.[157] The only reason we are interested in genes is because of what they do: encode proteins; and the only reason we are interested in antibodies is because of what they do: bind antigens. If two genes encode the same protein (the same amino acid sequence) and direct production of the same amount of that protein, then they are identical for virtually any purpose.[158] Likewise, if two monoclonal antibodies bind the same determinant on the same antigen and bind it equally tightly, then they are identical for virtually any purpose. As with genes, many monoclonal antibodies could perform the same function — binding the same determinant with the same affinity. This is so because these functionally identical monoclonal antibodies (as with functionally identical genes, encoding the same amino acid sequence) could have different structures — different amino acid sequences.[159]

Despite these virtually exact parallels between monoclonal antibodies and genes, the Federal Circuit has allowed monoclonal antibodies to be described by their function and conceived by their method of isolation, without any structural description.[160]

Dropping the rules that description of a DNA invention requires specification of its nucleotide sequence, and that compositions of matter can never be claimed by their function or method of isolation, and returning the focus to enablement would restore consistency of the DNA cases with monoclonal antibody cases. As discussed above, the relevant characteristics of monoclonal antibodies and DNA sequences

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called a determinant. *See id*. at 972. In an immune response, many different antibodies — that is, proteins with different amino acid sequences — binding to the same antigen are produced. *See id*. at 183. Different antibodies binding to the same determinant on the antigen are even produced. *See id*. From this diversity of antibodies binding to a single antigen, scientists can select one of these antibodies and make large amounts of it. *See id*. These identical antibodies are called monoclonal antibodies because they come from a single clone of cells. *See id*. A good explanation of monoclonal antibodies is found in *In re* Wands, 858 F.2d 731, 733-34 (Fed. Cir. 1988).

157. *See supra* note 101.

158. *See id.*

159. *See* BROCK & MADIGAN, *supra* notes 109-10 and accompanying text.

160. *See generally Wands*, 858 F.2d at 731 (reversing the rejection of an inventor's claims for lack of enablement where the monoclonal antibodies needed to make and use the invention (immunoassays) could be made from readily available materials using methods well known in the monoclonal antibody art – the mere availability of such monoclonal antibodies satisfied the enablement requirement).

are exactly parallel. The only reason we are interested in either is because of their function — binding antigens (monoclonal antibodies) or encoding proteins (DNAs) — not their inherent structure. For either, a tiny change in structure could drastically change its function. A single amino acid change in an antibody could entirely eliminate its binding to the same antigen;[161] a single nucleotide change in a gene could entirely eliminate its ability to encode any protein.[162] Conversely, for either, numerous structures could perform the same function. Many different antibodies could bind the same antigen or even the same determinant with equal affinity; many different nucleotide sequences could encode the same protein.[163] Yet the Federal Circuit has allowed antibodies to be described and claimed by their function but not DNAs.[164] This inconsistency should be eliminated. Courts addressing recombinant DNA inventions should ask whether the specification enables the claims as broadly as they are drawn, not whether the sequence is specified.

Consistency with precedent in chemical patents also demands that genus claims to recombinant DNAs be obtainable. As the Federal Circuit emphasized in *Amgen*,[165] there are a large number of possible nucleotide sequences encoding the same or very similar proteins. The court implied that this alone justified denying claim to all the sequences

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161. *See* ALBERTS, *supra* note 128, at 976 (describing that only 5-10 amino acid residues on each polypeptide chain of an antibody make contact with the antigen). If one of those key residues is changed, antigen-antibody binding could be eliminated. Certain single amino acid changes in other parts of the polypeptide could totally change the conformation of the antibody polypeptide at the binding site, so that the antibody no longer recognizes antigen.

162. The easiest way for this to happen is that a single nucleotide change could change a codon encoding an amino acid to a stop codon, signaling that synthesis of the polypeptide is to stop. *See supra* note 92. TGA, TAA, and TAG are stop codons, signaling termination of polypeptide synthesis.

163. *See supra* note 92.

164. *See Wands*, 858 F.2d at 731; *Eli Lilly & Co.*, 119 F.3d at 1559; *Fiers*, 984 at 1164.

165. Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd., 927 F.2d 1200 (Fed. Cir. 1991). "The district court found that over 3,600 different EPO [erythropoietin] analogs can be made by substituting at only a single amino acid position, and over a million different analogs can be made by substituting three amino acids. The patent indicates that it embraces means for preparation of 'numerous' polypeptide analogs of EPO. Thus, the number of claimed DNA sequences that can produce an EPO-like product is potentially enormous." *Id.* at 1213.

encoding erythropoietin.[166] But the large number of possible nucleotide sequences encoding the same protein is not particularly relevant to whether or not a genus claim is justified. There are a large number of variants on a specific chemical compound, but courts allow generic claims to a family of compounds when the related compounds have the same properties as the original species and are obvious variants of it.[167] Often, claims encompassing a nearly infinite number of compounds are allowed. The Manual of Patent Examining Procedure states that the Examiner must come forward with an affirmative reason to reject a claim on grounds of a lack of utility.[168] In the case of recombinant DNAs, there is little reason to doubt that sequences encoding the same or very similar amino acid sequences would have similar utility. There appears no reason to have, in effect, an *a priori* ban on genus claims to recombinant DNAs when such claims are allowed for other chemicals.

C. FULFILLING THE PURPOSES OF THE GENERAL RULE THAT COMPOSITIONS OF MATTER SHOULD BE DESCRIBED BY STRUCTURE

Valid reasons exist for the general requirement that, for claims to chemical compounds, the compounds must recite their structures. Those reasons do not apply, however, to genes and proteins. The purposes of the requirement can be better satisfied by claiming genes and proteins by function.

The first purpose of requiring a description of the common structural features of a class in genus claims to chemical

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166. *See id.* at 1213-14. The court stated:

> Details for preparing only a few EPO analog genes are disclosed. . . . This 'disclosure' might well justify a generic claim encompassing these and similar analogs, but it represents inadequate support for Amgen's desire to claim all EPO gene analogs. There may be many other genetic sequences that code for EPO-type products. Amgen has told how to make and use only a few of them.

Id. at 1213-14.

167. *See generally In re* Baird, 16 F.3d 380 (Fed. Cir. 1994). A prior generic patent had claimed developer compositions comprised of the esterification product of any chemicals from two generic families — dicarbaxylic acids and phenols. The issue was whether Baird's patent for a product involving a particular species of phenol was obvious in view of that generic patent.

168. *See* MANUAL OF PATENT EXAMINING PROCEDURE § 706.03(a)(1) (7th ed. 1998). *See also id*. § 2164.04 (describing the burden placed on the examiner to establish a reason to question enablement).

compounds is that it clearly defines the boundaries of the claims.[169] If one claims all linear saturated alkanes, for instance, one of ordinary skill in the chemical arts knows whether or not a compound falls within that class.[170] For DNAs, however, that purpose can be met without a precise nucleotide sequence. Mammallian insulin cDNAs, for instance, can be defined as cDNAs derived from a mammal that encode insulin, with insulin being defined as a hormone that acts to decrease glucose levels in the blood.[171] That description by function clearly defines for one skilled in the art what cDNAs fall within the class.[172] Alternatively, the class could be defined by a structural description, but one that falls short of an exact nucleotide sequence for every member of the class. For instance, it could be defined as cDNAs that encode a protein that has an amino acid sequence at least 80% identical to the amino acid sequence of rat insulin. That definition would probably include every natural insulin cDNA, and no other naturally occurring genes. Thus, the purpose of clearly defining the boundaries of the claims to recombinant DNA is achievable without requiring an exact nucleotide specification of every member of the class, or even any nucleotide sequence information.

A second purpose of requiring a structural description for a claim to an ordinary chemical or chemicals is that structure gives a chemist skilled in the art good information about how to synthesize the chemical. For DNA, however, while a complete

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169. *See Eli Lilly & Co*., 119 F.3d at 1568 ("In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass.").

170. A linear saturated alkane is a compound containing only carbon and hydrogen, no branches on the chain, and no double or triple bonds. It has the structure CH_4, CH_3-CH_3, or CH_3-$(CH_2)_N$-CH_3, where N is any number from one to infinity. *See* MOELLER ET AL., *supra* note 2, at 896-99.

171. *See* DARNELL ET AL., *supra* note 38, at 693-95.

172. The court in *Eli Lilly & Co.* held that with a functional description of genes (what proteins they encode), "one skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus." *Eli Lilly & Co.*, 119 F.3d at 1568. This is incorrect. If one wishes to determine the function of a protein a gene produces, one can isolate the protein and test it in biochemical assays to see, for instance, if it acts like insulin. In the alternative, merely from the amino acid sequence of a protein, which is known from the DNA sequence of the gene, one could predict with a high degree of certainty that it performs the same function as another protein if the two proteins have very closely related sequences. *See* CREIGHTON *supra* note 99.

structure would allow one to synthesize the DNA by the polymerase chain reaction, the same purpose could be served by, for instance, description of a process for isolating a cDNA from a library based on knowledge of the amino acid sequence of the protein it encodes. In that case, specification of the nucleotide sequence is not necessary to enable preparation of the DNA. Thus, the purpose can be served in other ways.

A third purpose in requiring a structural description of chemicals is that their structure is assumed to be closely related to their characteristics and functional properties. That assumption is wrong when applied to DNA. The function of DNA is to encode proteins and a single nucleotide change could abolish production of the protein.[173] Conversely, many nucleotides could be changed in a DNA while allowing it to still encode exactly the same protein.[174] Thus, this purpose is better served by a functional, as opposed to a structural description.

D. FULFILLING THE PURPOSES OF THE WRITTEN DESCRIPTION REQUIREMENT

The purposes of the written description requirement can be fulfilled without a requirement that a claim to recombinant DNAs must be supported by listing a particular nucleotide sequence. The purposes courts have asserted for the written description requirement are: to prove that the inventor was in possession of the invention on the filing date; to ensure that new claims are adequately supported by an earlier filed specification; and to guard against deception or "pretending that an invention is more than what it really is."[175] The written

173. Codons are sequences of three nucleotides in the coding sequence of a gene that encode an amino acid or other information for the synthesis of a protein. *See supra* note 128. Most codons encode amino acids. But three codons — TAA, TAG, and TGA — are stop codons. They direct that no amino acid is to be inserted and synthesis of the protein is to stop at this point. *See* WOOD, *supra* note 38, at 433-37. Thus, if CAA, for instance, encoding glutamine, is found near the beginning of a gene, a single base change in that trinucleotide codon, to TAA, would change the codon to a stop codon. The result, although every other nucleotide in the gene remained the same, would be that synthesis of the entire protein would be stopped at that point. Only a greatly shortened, nonfunctional, version of the protein would be produced, which would be quickly degraded in the cell.

174. *See* ALBERTS ET AL., *supra* note 128.

175. *See* Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1561 (Fed. Cir. 1991), *cert. denied*, 454 U.S. 1055 (1981); *see also supra* notes 31-36 and accompanying text.

description requirement makes sense when an inventor attempts to relate back claims to an earlier application, because it may be that the earlier specification had enabled the practice of the newly claimed invention, but at that time, the inventor did not realize it. In that case, there may be policy reasons for asserting that the technology has been surrendered to the public, so that the inventor cannot reclaim exclusive possession of it. Or there may be reasons for awarding priority to an intervening claimant who first realized the presence of an invention intrinsically present in the first specification, rather than to the initial inventor. When we are looking at the specification and claims in the same patent application, however, it is difficult to see why the written description requirement is needed in addition to the enablement requirement. If the person is claiming the invention, and if his specification enables its practice, then there is no question that he is in possession of it. The enablement requirement is sufficient to guard against deception and fraudulent claims of inventorship, because enabling others to practice an invention necessarily implies that the inventor also has the ability to practice it. In addition, if the claim at issue is present in the originally filed application, then there is no doubt the inventor recognized the claimed invention by the time of filing.

E. AVOIDING EASY CIRCUMVENTION OF PATENTS

Another consequence of the requirement that claimed DNA be specified by nucleotide sequences is that it leads to easy circumvention of patents. Taken literally, this requirement means potential infringers could get around the claim by changing one nucleotide in the DNA. It is possible to change a large number of nucleotides in a DNA and have no effect on the amino acid sequence of the protein it encodes. Thus, infringers could change numerous nucleotides and still know that the invention will function exactly as it functioned previously. In *Amgen*, the claim drafters tried to encompass this obvious type of circumvention within their claim, but the court invalidated it. Amgen tried to claim other nucleotide sequences encoding the same, or closely related, amino acid sequences. Amgen claimed all DNA sequences "encoding a polypeptide having an amino acid sequence sufficiently duplicative of . . . erythropoietin to allow possession of the biological property of causing bone marrow cells to increase production of . . . red

blood cells . . . ."[176] The court invalidated this claim for lack of an enabling disclosure.[177] It would be obvious to one of ordinary skill to mutate the claimed DNA in *Amgen* so as to make a single amino acid change in the encoded EPO protein. One would expect that the resultant protein would probably function just as well as EPO, yet it would fall outside the literal claims. It would be even more obvious to change the nucleotide sequence in a way that does not change the amino acid sequence of the encoded protein. Then it is certain that the protein will function the same: it will be the same protein. The inventors tried to draft their claims to encompass these obvious ways to circumvent the claims, but the court rejected their attempts. That is a bad result.[178] Although the court made this ruling based on a mistaken enablement analysis, the same result would flow automatically from a rule that claimed DNAs must be specified by their nucleotide sequences.

F. PROMOTING EARLY DISCLOSURE

One of the main rationales of the patent system is promoting disclosure of technical advances.[179] Evaluating

176. *See Amgen, Inc.*, 927 F.2d at 1204 (describing the Amgen '008 patent, claim 7).

177. *See supra* notes 57-61 and accompanying text. At least the court was looking at enablement rather than a blanket rule that the nucleotide sequence of all claimed DNAs must be specified, but its ruling of lack of enablement seems debatable. Methods of making mutations in DNAs (changing their nucleotide sequences) are well known in the art. *See* J. SAMBROOK ET AL., MOLECULAR CLONING: A LABORATORY MANUAL, Chapter 15 (2nd ed. 1989). Likewise, it is well known in the art that a single amino acid change in a protein will usually have little or no effect on the protein's function. *See* CREIGHTON *supra* note 99.

178. *See* Ex parte Dubbs, 119 U.S.P.Q. 440, 441 (Bd. App. 1958) (holding that an applicant is entitled to claim variables of the invention in terms sufficiently broad to afford protection of the invention against easy circumvention).

179. *See* Paul A. David, *Intellectual Property Institutions and the Panda's Thumb: Patents, Copyrights, and Trade Secrets in Economic Theory and History*, *in* GLOBAL DIMENSIONS OF INTELLECTUAL PROPERTY RIGHTS IN SCIENCE AND TECHNOLOGY 20, 46 (Michael B. Wallerstein et al., eds., 1993) (describing that in the patent system of medieval Venice, it was not even essential that the applicant be the inventor). The important thing was that the inventor disclosed a technology not present in Venice. *See id*. Patents were a government grant of a temporary monopoly in exchange for importing and disclosing a foreign technology. *See id*. The enablement requirement of 35 U.S.C. § 112, ¶ 1, is really a requirement of full disclosure, requiring that the invention be set out in "such full, clear, concise, and exact terms as to

patents through a fact-based enablement inquiry would promote this goal. Rules stating that compositions of matter may never be claimed by their function or method of isolation thwart this goal. Once an inventor has determined the function of a gene by isolating, characterizing, and determining the amino acid sequence of a protein (which must be encoded by some gene) the isolation of the corresponding gene is often routine and obvious.[180] The quickest advancement of the nation's technical capacity occurs if inventors reveal their discoveries at that time so that others can build upon it. But under the Federal Circuit's doctrine they may not file for a patent on the gene at that time, because they do not know the nucleotide sequence of the gene. They would be well advised to withhold that information until they can complete the time consuming yet routine steps of isolating the gene and sequencing it. In *Eli Lilly*, for example, the inventors who isolated the rat insulin cDNA should have withheld that information from the public and used it secretly to complete the relatively routine steps of cloning the human insulin cDNA, which was the more economically valuable cDNA.

G. AVOIDING ECONOMIC WASTE

The current Federal Circuit requirements for patent claims to recombinant DNA promote economic waste. If a group of inventors publicly reveal discoveries which make it obvious how to isolate a cDNA, as the inventors in *Eli Lilly* did, under current doctrine others may race them to perform the isolation and file a patent application if they do so first.[181] It is economically wasteful to have multiple firms racing to accomplish a routine step that is achievable in roughly the same time by any one firm that attempted it. In contrast, if the court eliminated the rules that DNAs may not be claimed by their function or method of isolation, and just focused on whether the specification enables one skilled in the art to practice the invention without undue experimentation, the

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enable any person skilled in the art . . . to make and use the same. . . ." 35 U.S.C. § 112, ¶ 1 (2001). The requirement that the inventor not have disclosed his invention more than one year prior to filing also shows that the reason patents are granted in the U.S. is to promote disclosure. *See* 35 U.S.C. § 102 (b) (2001). If the inventor has already disclosed (more than one year earlier), he is not granted a patent. *See id*.

180. *See supra* notes 79-90 and accompanying text.

181. *See supra* notes 48-56 and accompanying text.

inventor who made the subsequent steps obvious could file for a patent and avoid this waste.

H. WRITING LAWS THAT WILL NOT BE MADE OBSOLETE BY ADVANCES IN TECHNOLOGY

Courts and legislatures should strive to write laws that endure and are adaptable to changing times. Advancements in technology should not render patent law doctrines obsolete. Perhaps when the Federal Circuit first announced in *Bell*[182] that a prior art protein amino acid sequence did not make the cDNA encoding it obvious, the court was correct in the sense that at the time the experimentation was done in that case, it was not routine enough to clone a cDNA from the knowledge of the protein sequence. Today, that procedure is clearly routine.[183] The Federal Circuit's invariant legal rule that DNA

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

183. The procedure has been widely used with few changes for the last 15 years. Amino acids are encoded by codons, a sequence of three nucleotides. There is more than one codon for most amino acids, but in most cases only the third nucleotide varies among them. Alanine, for instance, is encoded by four codons, but all of them begin with GC. The third nucleotide in the sequence could be any one of the four nucleotides — A, C, G, or T. A polypeptide having the sequence Ala-Lys-His-Ala, would be encoded by a DNA with the sequence GC(A,C,G,T)-AA(A,G)-CA(C,A)-GC(A,C,G,T), where the nucleotides in parentheses indicate the possible third nucleotides of each codon. *See* W.B. WOOD ET AL., BIOCHEMISTRY: A PROBLEMS APPROACH 433-37 (2nd ed. 1981). To find the DNA encoding the protein containing that stretch of four amino acids, one would synthesize a DNA having the sequence indicated above. For each position where the nucleotide is uncertain one would synthesize a mixture of DNA containing all possible nucleotides in that position. Thus one would synthesize a family of short pieces of DNA, and one member of the family would correspond to the exact DNA sequence of the gene encoding this protein. The mixture of short DNA is labeled with radioactivity or a fluorescent label and then allowed to hybridize to the DNA contained in a library of clones. The clone containing the DNA of interest is then identified by the radioactive or fluorescent label attached to it. In practice, the short DNAs used must contain at least 18 nucleotides, corresponding to a sequence encoding at least six amino acids. If more amino acids are known, the DNA can be made longer, producing more desirable results. *See* T. MANIATIS, ET AL., MOLECULAR CLONING: A LABORATORY MANUAL 224-28 (1982).

This procedure is described in a "recipe book" of standard molecular biology procedures. *See* T. MANIATIS ET AL., MOLECULAR CLONING: A LABORATORY MANUAL (2nd ed. 1989). It was also described in that manual's first edition in 1982 and it has been used in identical form since at least that time. The author has used the procedure to clone one gene and map two others; thousands of genes have been cloned in the same manner.

The procedure is time consuming. It takes at least two or three weeks and often a few months to clone a gene. There are many steps involved, and

can never be claimed without specification of their nucleotide sequence or that compositions of matter can never be claimed by their function or method of isolation has been overtaken by technology. It results in a bar to claiming DNA inventions until obvious steps are taken.[184] Legal rules should be crafted to be adaptable to advances in technology. The enablement requirement, that the patent specification must enable one skilled in the art to construct or perform the invention without undue experimentation, is flexible and adaptable to changes in technology. It is flexible because enablement is judged by the standard of technology at the time of filing. It has been a patent requirement since the first United State Patent Act of 1790.[185] It has been adaptable and useful in evaluating patentability through more than 200 years of technological advancement and it should be the central focus in evaluating the validity of generic biotechnology patent claims. The Federal Circuit's new rules are inflexible and have already been overtaken by technology. For these reasons, the Federal Circuit should rescind them.

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difficulties can arise at each step, particularly for the novice. But the procedures involved at each step have been worked out and have been used for years, and in the end success is virtually assured.

Is an undue amount of experimentation required to clone a gene from knowledge of the corresponding protein sequence? Not by the standard followed in *Wands*. *See supra* notes 102-108 and accompanying text. The procedure is lengthy and time consuming, but so was the procedure for isolating the monoclonal antibody at issue in *Wands*. *See id.* Success with the procedure is virtually assured, as it was in *In re Wands. See id*. Difficulties do arise in the procedure, but they did also arose in *Wands*. *See id*. In fact, the *Wands* inventors failed in their first three attempts at isolating the monoclonal antibody, until they gained the requisite experience of one of ordinary skill in the art. *See id*. In biotechnology cases, a court has defined one of ordinary skill in the art as a junior faculty member (presumably possessing a doctorate degree in biochemistry or a related discipline) with one or two years of relevant experience, or a postdoctoral student with several years of experience. *See Enzo Biochem., Inc*., 188 F.3d at 1373. With that level of skill, it is expected that one can carry out a lengthy but routine procedure, and overcome the sorts of difficulties that are routinely overcome by others of skill in the art. Thus, cloning a gene from the amino acid sequence of the protein it encodes is obvious and does not require undue experimentation.

184. *See supra* notes 48-56, 91-100, 182-83 and accompanying text.

185. *See* Donald S. Chisum, *Comment*: *Anticipation, Enablement and Obviousness: An Eternal Golden Braid*, 15 AM. INTELL. PROP. L. ASS'N. Q. J. 57, 59 (1987).

I. USING BLOCKING PATENTS TO REWARD THE CONTRIBUTIONS OF ALL PARTIES

Granting a genus patent to an inventor who enables the cloning and sequencing of a genus of genes does not necessarily mean the contributions of others who later clone and sequence particular species cannot also be rewarded with patents. Blocking patents accommodate this.[186] Cloning a gene and determining its nucleotide sequence requires a significant amount of work — even if the protein encoded by the gene and the amino acid sequence of the protein are known, or if a homologous gene in a different species has been cloned and sequenced.[187] Since cloning and sequencing genes does take a significant amount of work, it behooves society to encourage it by awarding patents. Furthermore, it is true that, as the Federal Circuit has observed, the exact nucleotide sequence of a gene is not obvious merely from the amino acid sequence of the protein it encodes.[188] For those reasons, the individual or group who clones and sequences a gene may deserve a patent on that nucleotide sequence and its close homologs. That does not mean, however, that the party who isolated the protein and determined its amino acid sequence, or who cloned the same gene in a different species, does not also deserve patent rights over the genes whose isolation they enabled. Both contributions can be recognized by the patent system. Blocking patents allow this arrangement.[189] One who clones the rat insulin cDNA, for example, should be able to claim all mammalian insulin cDNAs, since she has enabled their isolation by methods that are obvious and routine to one of skill in the art. The party that then clones and sequences the human insulin cDNA perhaps should also have a patent on recombinant DNAs comprising that particular nucleotide sequence and its close homologs, since the particular nucleotide sequence was nonobvious.

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186. *See supra* notes 118-22 and accompanying text.

187. *See* Eli Lilly & Co., 119 F.3d at 1562-63 (stating that while the patent application claiming the rat prosinsulin cDNA was filed in May of 1977, the application on the human proinsulin cDNA was not filed until September of 1979).

188. *See supra* notes 88-90 and accompanying text.

189. *See* In re Kaplan, 787 F.2d 1574, 1577-78 (Fed. Cir. 1986) (stating that an improvement is patentable if it meets the same three requirements for patentability all inventions must meet — novelty, nonobviousness, and utility, 35 U.S.C. §§ 101-103, even if it falls within the scope of a previous patent).

Both parties should be able to claim a range of nucleotide sequence variations, since those variations would be obvious to one of skill in the art and would not be expected to alter the utility of the invention. However, if another party finds that one of the obvious variations on the nucleotide sequence has useful and unexpected properties, he can also get a patent on that sequence.[190] Blocking patents are common in the patent system allowing all interests to be accommodated, and are appropriate under these circumstances.

CONCLUSION

The Federal Circuit is apparently hesitant to uphold broad patent rights in the new field of recombinant DNA. It is probably concerned that it should not choke off development in a new field of technology by granting excessively broad patent rights. It does not want to reduce incentives for others to continue to advance the field. That undoubtedly is a valid concern. But the court has addressed the concern in the wrong way. It has erected special barriers that make genus claims not merely difficult, but virtually impossible. A better way to address the concern would be to stringently examine recombinant DNA patents with the enablement requirement. That approach could still be used to strike down patents that are broader than justified, but would not have the effect of banning all genus claims in the field and would involve the use of a requirement that is adaptable and need not be changed as technology evolves.

190. *See* MANUAL OF PATENT EXAMINING PROCEDURE § 706.02 (a) (7th ed. 1998) (establishing that an unexpected property is evidence which may rebut a prima facie case of obviousness).