Stanger in a Strange Land: Biotechnology and the Federal Circuit

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Originally Published in WASHINGTON UNIVERSITY OF LAW & POLICY
2 WASH. U. J. L. & POL'Y 167 (2000)

Part II: Judicial Issues

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INTRODUCTION

The United States Court of Appeals for the Federal Circuit must engage in many diverse technical disciplines when rising to meet its legislative mandate of facilitating the nationwide uniformity and the improved administration of the patent laws.[1] Of these fields of study, biotechnology arguably occasions the most intellectual criticism and public debate regarding the court's efforts. In part, such challenges might reflect moral or ethical concerns over biotechnology patent protection *per se*.[2] A frustration also appears to exist, however, with

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

2. *See, e.g.*, Thomas D. Mays, *Biotech Incites Outcry*, NAT'L L.J., June 22, 1998, at C1 (Rick Weiss, *Patent Sought on Making of Part-Human Creatures; Scientist Seeks To Touch off Ethics Debate*, WASH. POST, Apr. 2, 1998, at A12; Rick Weiss, *What Is Patently Offensive? Policy on 'Immoral' Inventions Troubles Legal, Medical Professionals*, WASH. POST, May 11,

the perceived inability of courts, at times, to appreciate adequately the impact, or lack thereof, of certain biotechnology inventions for which patent protection has been sought.[3]

Are the members of the federal judiciary qualified to adjudicate such technology disputes? In patent cases the legal issues must be viewed through the eyes of the hypothetical person of ordinary skill in the art. With respect to biotechnology, the skilled artisan often holds a Ph.D. and has significant laboratory experience.[4] In this regard, those laypersons charged with the task of resolving biotechnology disputes would seem somewhat ill-prepared to assume such an esoteric perspective when applying the patent laws to this complex subject matter.[5]

In biotechnology cases, therefore, the casual observer might be more likely to point out incongruity between the jurisprudence of the

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1998, at A21).

3. The Federal Circuit does not stand alone as a target of such public scrutiny. Arguably, the U.S. Patent & Trademark Office (PTO) bears the brunt. In recent days the biotechnology industry, for example, has expressed grave concerns at the proposed guidelines that the PTO seeks to promulgate for use by its patent examiners to assess an application's compliance with various patentability standards. *See, e.g.*, Janice M. Mueller, *Examination Guidelines*, NAT'L L.J., Jan. 24, 2000, at B7 (commenting on the reaction to the first proposed written description examination guidelines published by the PTO in June 1998, and its impact on the second proposed written description examination guidelines published by the PTO in December 1999). The issue of the patentability of genetic elements known as expressed sequence tags (ESTs) and single nucleotide polymorphisms (SNPs) has attracted the media spotlight in recent days. *See, e.g.*, Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698 (1998); Lawrence M. Sung & Don J. Pelto, *Greater Predictability May Result in Patent Pools*, NAT'L L.J., June 22, 1998, at C2.

4. *See, e.g.*, Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1373 (Fed. Cir. 1999) (citing Enzo Biochem, Inc. v. Calgene, Inc., 14 F. Supp. 2d 536, 567 (D. Del 1998)) (stating that the district court did not abuse its discretion in finding that "a person of ordinary skill in the art would be 'a junior faculty member with one or two years of relevant experience or a postdoctoral student with several years of experience'").

5. At present, only two of the sixteen active and senior judges of the Federal Circuit hold advanced technical degrees, namely, Circuit Judge Pauline Newman (Ph.D. Chemistry) and Circuit Judge Alan D. Lourie (Ph.D. Organic Chemistry). In addition, Circuit Judge Arthur J. Gajarsa and Circuit Judge Richard Linn hold undergraduate degrees in electrical engineering. However, the court's human resources also include judicial clerks and the staff of the Office of the Senior Technical Assistant. In typical years, almost all of these personnel hold technical undergraduate, if not graduate, degrees that cover a wide range of disciplines. In a superficial examination, Judge Lourie appears to have authored most of the Federal Circuit opinions in biotechnology cases, a somewhat disproportionately high amount given the court's practice of random panel assignment.

Federal Circuit and the underlying scientific realities.[6] An ignorance of the procedural guidelines and substantive legal precedent, to which the appellate court must remain faithful in rendering its judgments, in general can only exacerbate the public's varying degrees of dissatisfaction over Federal Circuit pronouncements on biotechnology.[7] A more balanced consideration of these contributing factors might ameliorate the discontent that can accompany the biotechnology patent opinions of the Federal Circuit. Accordingly, this Article surveys recent Federal Circuit decisions regarding biotechnology-related subject matter from the combined perspectives of science and the law.[8]

In Part I this Article considers those cases dealing with biotechnology patents and patent applications that implicate the statutory conditions for patentability and disclosure requirements. The issues of utility, obviousness, written description, and enablement are most important here. Part II discusses inventorship and priority disputes involving biotechnology inventions. In particular, it examines the effect of the corroboration requirements on research and development activities. This Article concludes in Part III with a review of patent litigation that concerns biotechnology products and processes. This section focuses on the treatment of biotechnology inventions in interference proceedings before the United States Patent and Trademark Office (PTO) and in patent infringement actions before the federal courts.

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6. *See, e.g.*, Lawrence M. Sung, *Echoes of Scientific Truth in the Halls of Justice: The Standards of Review Applied by the U.S. Court of Appeals for the Federal Circuit in Patent-Related Matters*, 48 AM. U. L. REV. 1233, 1235-36 (1999) (noting scrutiny over the judicial treatment of technological matters and questions raised by the public about the accuracy of this treatment from a purely technical perspective).

7. *See id.* at 1237-38 (discussing the potential misunderstanding of the court's decisions in the absence of an appreciation of the degree of deference the Federal Circuit must show to the findings and conclusions of its lower tribunals on various substantive patent law issues).

8. This Article provides neither an exhaustive consideration of biotechnology patent law nor a critical jurisprudential analysis of the Federal Circuit patent law decisions addressing biotechnology. To accommodate an interest in these topics, however, it refers to available treatises or other published commentaries whenever appropriate. *See, e.g.*, HAROLD C. WEGNER, PATENT LAW IN BIOTECHNOLOGY CHEMICALS & PHARMACEUTICALS (2d ed. 1994); KENNETH J. BURCHFIEL, BIOTECHNOLOGY AND THE FEDERAL CIRCUIT (1995).

I.

Several common misapprehensions come to the forefront with respect to the decisions of the Federal Circuit in appeals involving biotechnology inventions. Perhaps the most insidious misapprehension is the failure to appreciate the existence of a significant temporal distortion. Absent recognition of the proper context, the casual observer might understandably conclude that the court's biotechnology judgments are senseless, because they rest on anachronistic notions of the science.

The effective date of the filing of a patent application often dictates what prior art the invention must overcome to qualify for patent protection. In addition, the breadth and depth with which applicants must describe their inventions in patent applications can depend upon the respective filing dates. The judicial consideration of the patentability of the subject matter in a patent application or the validity of an issued patent, therefore, must focus on the state of the art at the time of the patent application rather than at the time of the dispute.

The disparity between the filing of the patent application and the conclusion of the patent infringement lawsuit is perhaps more pronounced in the field of biotechnology than in the electrical, mechanical, or even chemical arts. The prosecution of biotechnology patent applications in the PTO and the litigation of issued biotechnology patents both commonly exhibit a lengthier duration than most other types of inventions. In biotechnology matters it is not uncommon for the Federal Circuit to apply the patent laws to decades-old science.[9]

Even forgiving this temporal distortion, however, leaves an unsatisfactory state of affairs. If a pronouncement by the Federal Circuit in a biotechnology case can only fairly reflect the proper application of the patent laws to our primitive understanding of biotechnology twenty years ago, what meaningful guidance has the

9. *See, e.g.*, Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1371 (Fed. Cir. 1999) (considering the state of the biotechnology art 16 years earlier); Genentech, Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1367 (Fed. Cir. 1997) (18 years earlier); Kridl v. McCormick, 105 F.3d 1446, 1448, 41 (Fed. Cir. 1997) (18 years earlier).

court provided for today's realities, and perhaps more importantly, for tomorrow's possibilities? The passage of such time in a rapidly developing art can witness progress through several next-generation technologies.[10] Accordingly, any reasoned extrapolation of applicable patent law principles from recently issued court decisions might seem to border on mere prognostication.[11] Of course, any hint of a legal quandary can create fits among those involved in the costly business of trying to navigate biotechnology research and development programs, whether commercial or academic, through patented seas.

An examination of the recent Federal Circuit decisions regarding biotechnology-related subject matter nevertheless provides a glimpse of the fundamental patent law principles to which the Federal Circuit will most likely continue to adhere. The remainder of this section considers the cases dealing with biotechnology patents and patent applications that implicate the statutory conditions for patentability and disclosure requirements.[12] In particular, this section discusses the issues of utility, obviousness, written description and enablement.

A. Utility

To obtain a patent the applicant must demonstrate that the claimed invention is useful.[13] The utility of an invention, in concert with its novelty and nonobviousness, merits the reward of patent protection.[14] Whether a claimed invention lacks utility presents a question of fact,

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10. *See* Lila Feisee, *Are Biotechnology Patents Important? Yes!*, 1 PTO TODAY 9, 9 (2000) (reporting the PTO perspective that "[b]iotechnology is one of the most research intensive and innovative industries in the global economy today.").

11. Of course, the Federal Circuit has acknowledged that in a rapidly advancing science like biotechnology, "what may be unpredictable at one point in time may become predictable at a later time." *See Enzo*, 188 F.3d at 1374 n.10 (citing *In re* Vaeck, 947 F.2d 488, 496 (Fed. Cir. 1991)).

12. An issued patent carries a statutory presumption of validity. *See* 35 U.S.C. § 282 (1994). A party must overcome this presumption by proving invalidity by clear and convincing evidence of noncompliance with 35 U.S.C. §§ 101-103 or 112.

13. 35 U.S.C. § 101 (1994) ("Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.").

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

which the Federal Circuit reviews under the clearly erroneous standard.[15] In any event, an alleged inventive act is not legally cognizable unless the inventor conceived of the specific utility of the claimed invention.[16]

In *Kridl v. McCormick* the Federal Circuit addressed the utility requirement in the context of a patent interference proceeding.[17] The court reviewed the determination of the PTO Board of Patent Appeals and Interferences ("Board"), which considered two competing patent applications that claimed the same, or substantially the same, biotechnology subject matter.[18] The interference count related to the use of antisense technology to produce plants or plant cells with resistance to certain viruses.[19] Having filed a patent application before Kridl, McCormick was the first to reduce the invention to practice, albeit constructively.[20] To establish priority of invention, however, McCormick also needed to prove a date of conception before that of Kridl.[21]

McCormick sought to rely upon the dated and witnessed pages of Marcia Vincent's laboratory notebook.[22] These pages described a January 1984 experiment in which a gene fragment encoding a viral protein was inserted into a cloning vector in both the sense and antisense orientations.[23] The Board applied a "rule of reason" analysis to evaluate this evidence and found that McCormick had

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

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

17. 105 F.3d 1446, 1447 (Fed. Cir. 1997). The PTO may declare an interference where a patent application claims the same, or substantially the same, subject matter as another application or as an unexpired patent. *See* 35 U.S.C. § 135 (1994). In this proceeding the PTO determines which party has priority of invention, or in other words, who was the first to invent. Because the first to invent is the only true inventor entitled to patent protection, the outcome of an interference proceeding typically leaves the winner with a patent and the loser without a patent.

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

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

20. *Id.* at 1449.

21. *Id.*

22. *See Kridl*, 105 F.3d at 1448.

23. *Id.* at 1448-49.

conceived of the invention before Kridl.[24] The Board thus awarded priority of invention to McCormick.[25]

In reaching its decision the Board also concluded that McCormick conceived of the utility of the claimed invention in January 1984.[26] The Board did so based solely on the uncorroborated testimony of one of the inventors, Dr. William Swain.[27] Kridl contended that antisense had more than one substantial use, and thus McCormick might have used it for a different purpose in January 1984.[28] According to Kridl, McCormick could have used antisense as an experimental control or as a mere template for the production of recombinant DNA in the sense orientation.[29]

The Federal Circuit considered the state of the biotechnology art in 1984 to refute Kridl's arguments and affirm the Board's determination.[30] There was no dispute that the use of antisense in plants was not known in 1984.[31] The Federal Circuit thus reasoned that it would have been illogical for McCormick to use such novel material as an experimental control, which usually involves tried and true compounds.[32] In addition, because sense constructs could be produced at that time by more established methods, the Federal Circuit stated that it would have been wasteful for anyone to use antisense to generate recombinant DNA in the sense orientation.[33]

Accordingly, the Federal Circuit concluded that one skilled in the art in 1984 would have seen no substantial use for the antisense constructs described in Ms. Vincent's laboratory notebook other than as "a means for imparting viral resistance to plants or plant cells."[34]

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

25. *Kridl*, 105 F.3d at 1449.

26. *Id.*

27. *Id.* at 1448-49.

28. *Id.* at 1450.

29. *Id.*

30. *See Kridl*, 105 F.3d at 1450.

31. *Id.*

32. *Id.*

33. *Id.*

34. *Id.*

The court stated that under a rule of reason analysis explicit corroboration of the inventor's recognition of utility might not always be necessary.[35] For example, in certain situations utility might be implicit in the evidence presented.[36]

B. Obviousness

To receive patent protection an invention must be nonobvious at the time of the invention to one of ordinary skill in the relevant art.[37] Nonobviousness is a question of law that the Federal Circuit reviews de novo.[38] The conclusion of nonobviousness, however, is subject to underlying factual findings, which the Federal Circuit reviews for clear error.[39] These facts include the scope and content of the prior art, the level of ordinary skill in the art at the time of the invention, objective evidence of nonobviousness, and differences between the prior art and the claimed invention.[40] Certain secondary considerations might also be pertinent, and include "commercial success, long felt but unsolved needs, [and] failures of others."[41]

During patent prosecution the examiner bears the burden of establishing a prima facie case of obviousness.[42] When the references cited by the patent examiner fail to establish such a case of obviousness, the rejection is improper and will be overturned.[43] Once the patent examiner meets this initial burden, however, the burden shifts to the applicant to provide rebuttal evidence to overcome the rejection.[44]

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35. *See Kridl*, 105 F.3d, at 1451.

36. *Id.*

37. *See* 35 U.S.C. § 103 (1994) (defining conditions for patentability, including nonobvious subject matter).

38. *See In re* Donaldson Co., 16 F.3d 1189, 1192 (Fed. Cir. 1994) (en banc).

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

40. *See* Monarch Knitting Mach. Corp. v. Sulzer Morat GMBH, 139 F.3d 877, 881 (Fed. Cir. 1998).

41. *See* Graham v. John Deere Co., 383 U.S. 1, 17-18 (1966).

42. *See In re* Rijckaert, 9 F.3d 1531, 1532 (Fed. Cir. 1993) (citing *In re* Oetiker, 977 F.3d 1443, 1445 (Fed. Cir 1992)).

43. *See In re* Fine, 837 F.2d 1071, 1074 (Fed. Cir. 1988).

44. *See In re* Dillon, 919 F.2d 688, 692-93 (Fed. Cir. 1990) (en banc) ("Such rebuttal or argument can consist of . . . any other argument or presentation of evidence that is pertinent.").

The Federal Circuit reversed the decision of the Board, which upheld the patent examiner's final rejection of the claims as obvious.[45] The subject matter of the patent application in *Deuel* involved DNA encoding heparin-binding growth factor ("HBGF") of bovine and human origins.[46] Deuel achieved the claimed invention by first isolating bovine uterine HBGF protein and determining the amino acid sequence of a small beginning portion of the protein.[47] Next, Deuel chemically synthesized a single strand of DNA, known as an oligonucleotide, corresponding to this short amino acid sequence.[48] Using this oligonucleotide, Deuel isolated the naturally occurring bovine HBGF gene from a collection of DNAs, referred to as a cDNA library, encoding bovine uterine proteins in general.[49] Deuel then determined the entire nucleotide sequence of the bovine uterine HBGF gene and predicted the amino acid sequence of the remaining unknown portion of the bovine uterine HBGF protein.[50] These bovine sequences constituted part of the claimed invention.[51]

In addition, Deuel used the oligonucleotide to isolate the naturally occurring human HBGF gene from the human placental cDNA library.[52] Similarly, Deuel then determined the entire nucleotide sequence of the human placental HBGF gene and predicted the amino acid sequence of the complete human placental HBGF protein.[53] These human sequences also constituted part of the claimed invention.[54]

The patent examiner asserted that the claimed invention would have been prima facie obvious in view of the prior art.[55] The prior art upon which the examiner relied included a Maniatis reference describing gene cloning methods and a Bohlen reference disclosing

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45. *In re* Deuel, 51 F.3d 1552, 1553-54 (Fed. Cir. 1995), *rev'g Ex parte* Deuel, 33 U.S.P.Q.2d 1445 (Bd. Pat. App. Int. 1993).
46. *Id.* at 1553-54 (referring to U.S. patent application Serial No. 07/542,232).
47. *Id.* at 1555.
48. *Id.*
49. *Id.*
50. *In re* Deuel, 51 F.3d at 1555.
51. *Id.*
52. *Id.*
53. *Id.*
54. *Id.*
55. *In re* Deuel, 51 F.3d at 1555-56.

the partial amino acid sequences of proteins composing a subclass of human and bovine HBGF.[56] The examiner maintained that Bohlen would have motivated one skilled in the art to clone the respective human and bovine HBGF genes as taught by Maniatis to produce human and bovine HBGF protein.[57]

In rebuttal, Deuel contended that the prior art "taught away" from the claimed invention; that is, Bohlen suggested that one skilled in the art would not have been motivated to use the same oligonucleotide to isolate the genes for human and bovine HBGF, as Deuel ultimately did.[58] The examiner rejected Deuel's teaching away argument, however, relying on the unfounded notion that HBGF genes may be homologous across species.[59] The Board upheld the examiner's rejection, focusing instead on the allegedly routine nature of cloning.[60]

In reversing the rejection of Deuel's claims, the Federal Circuit relied on precedent stating that, absent prior art suggesting the specific claimed DNA, a particular DNA sequence is not obvious simply because the prior art discloses general methods for isolating DNA.[61] The court further applied precedent regarding chemical inventions, which stated that the prior art disclosure of a broad genus does not necessarily render obvious a specific compound within the genus.[62] Because many different DNA sequences can encode the identical protein, the court concluded that the simple disclosure of the protein does not render any particular one of those DNA sequences obvious, absent prior art specifically pointing one out.[63] The Federal Circuit also discounted the Board's contentions regarding the routine nature of Deuel's work as mere speculation and "impermissible hindsight reconstruction of the claimed invention."[64]

Two years later in 1997, the Federal Circuit reached the opposite

56. *Id.*
57. *Id.* at 1556.
58. *Id.*
59. *Id.*
60. *In re* Deuel, 51 F.3d at 1556-57.
61. *Id.* at 1558-59 (reaffirming *In re* Bell, 991 F.2d 781, 785 (Fed. Cir. 1993)).
62. *Id.* (citing with approval *In re* Baird, 16 F.3d 380 (Fed. Cir. 1994)).
63. *Id.*
64. *Id.* at 1558.

conclusion on the obviousness issue with respect to another biotechnology invention. The Federal Circuit affirmed the Board's decision with *In re Mayne*,[65] which upheld the patent examiner's final rejection of claims to proteins produced by recombinant genetic technology.[66] Specifically, the patent application claimed proteins comprising the amino acid methionine connected to an enterokinase cleavage site and coupled to either human growth hormone (hGH) or bovine growth hormone (bGH).[67]

The Federal Circuit held that the PTO met its burden of establishing a prima facie case of obviousness.[68] The compounds, hGH and bGH, were well known.[69] In addition, the prior art taught the use of fusion proteins and identified possible cleavage sites for enterokinase.[70] The claimed invention recited a hGH or bGH fusion protein, including a region containing enterokinase cleavage site, that was structurally similar and functionally equivalent to that taught in the cited prior art references.[71] Moreover, the references suggested the interchangeability of these amino acid substitutions.[72]

Having the burden of providing rebuttal evidence to overcome the patent examiner's rejection, Mayne attempted to show that the "claimed fusion proteins possess an unexpected property over the prior art."[73] Mayne argued that both the low immune response induced after intravenous administration and the biological activity of the protein before cleavage of the initial peptide chain were surprising results.[74] However, the Federal Circuit discounted the evidence submitted in support of these assertions.[75] The absence in the patent specification of comparative data or any explanation of the significance of the data appeared fatal.[76]

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65. 104 F.3d 1339 (Fed. Cir. 1997).
66. *Id.* at 1340.
67. *Id.*
68. *Id.* at 1343.
69. *Id.* at 1342.
70. *In re* Mayne, 104 F.3d 1339, 1342 (Fed. Cir. 1997).
71. *Id.* at 1342-43.
72. *Id.*
73. *Id.* at 1343 (citing *In re* Soni, 54 F.3d 746, 750 (Fed. Cir. 1995)).
74. *Id.*
75. *In re* Mayne, 104 F.3d at 1343-44.
76. *Id.* at 1344.

C. Written Description

To obtain patent protection an inventor must set forth an adequate written description of the invention.[77] To comply with the written description requirement, a patent must describe an invention in sufficient detail that one skilled in the art could clearly conclude that the inventor had possession of the claimed subject matter.[78] As it pertains to biotechnology inventions, an adequate written description of nucleic acids, such as DNA or RNA, requires a precise definition, including the pertinent "structure, formula, chemical name, or physical properties."[79] A mere statement that a nucleic acid is part of the invention and "a reference to a potential method for isolating it," will not suffice.[80] The adequacy of a written description is a question of fact that the Federal Circuit reviews for clear error.[81]

The Federal Circuit reversed the Board's decision with *In re Brana*, which upheld the patent examiner's final rejection of the claims of the application for failure to satisfy the requirements of the first paragraph of 35 U.S.C. § 112.[82] The subject matter of the application involved pharmaceutical compositions having antitumor activity in humans.[83] In the final office action the examiner rejected the claims of the application, because the specification failed to (1) disclose a "specific disease against which the claimed compounds were active" and (2) "establish a reasonable expectation that the claimed compounds had a practical utility."[84] The Board upheld the patent examiner's rejection under the first paragraph of § 112 but stated that a rejection under § 101 would likewise have been proper.[85]

Regarding the examiner's first ground for rejection, the Federal Circuit noted that the applicants tested the claimed compounds on

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77. *See* 35 U.S.C. § 112 (1994).

78. *See* Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 (Fed. Cir. 1997); *In re* Gosteli, 872 F.2d 1008, 1012 (Fed. Cir. 1989) (citing *In re* Wertheim, 541 F.2d 257, 262 (C.C.P.A. 1976)).

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

80. *See id.* at 1170.

81. *See* Ralston Purina Co. v. Far-Mar-Co, Inc., 772 F.2d 1570, 1575 (Fed. Cir. 1985).

82. 51 F.3d 1560, 1569 (Fed. Cir. 1995).

83. *Id.* at 1562 (reporting the U.S. patent application at issue as Serial No. 533,944).

84. *Id.* at 1563-64.

85. *Id.* at 1564.

tumor cell lines derived from animals suffering from lymphocytic leukemias.[86] The court thus concluded that the disclosed ameliorative activity of the claimed compounds on tumor cells constitutes a proper allegation of sufficiently specific use.[87] As for the second ground for rejection, the Federal Circuit held that the patent examiner failed to satisfy "the initial burden of challenging a presumptively correct assertion of utility in the disclosure."[88] The court noted that the prior art references upon which the Board relied did not "question the usefulness of any [related] compound as an antitumor agent."[89] Moreover, one of the references disclosed compounds structurally similar to those of the claimed invention, possessing proven in vivo effectiveness as chemotherapeutics against various types of tumors.[90] The Federal Circuit determined that even if the PTO satisfied its initial burden, the applicants provided evidence of statistically significant animal tests sufficient to convince one skilled in the art of the inventions' asserted utility.[91] To require *in vivo* human testing akin to Phase II clinical studies conducted by the Food and Drug Administration would place a higher standard for the first paragraph of § 112, compliance on applicants seeking patent protection for pharmaceuticals for humans.[92]

In *In re Alton*,[93] the Federal Circuit vacated the Board's decision, which upheld the patent examiner's final rejection of the claims of the application for failure to provide an adequate written description.[94] The Federal Circuit did not decide whether or not the specification contained an adequate written description.[95] However, the court held that the patent examiner and the Board erred in dismissing a declaration submitted by the applicants concerning what

86. *In re* Brana, 51 F.3d at 1565.
87. *Id.*
88. *Id.* at 1566.
89. *Id.*
90. *Id.*
91. *In re* Brana, 51 F.3d at 1567-68.
92. *Id.* at 1568.
93. 76 F.3d 1168 (Fed. Cir. 1996).
94. *Id.* at 1170.
95. *Id.* at 1174 (citing Fiers v. Revel, 984 F.2d 1164, 1171 (Fed. Cir. 1993)) ("We express no opinion on the factual question of whether the specification adequately describes the subject matter of claim 70").

one skilled in the art would have known when the patent application was filed.[96]

The claimed technology related to an analog of human gamma interferon (IFN-γ).[97] The patent specification contained twelve examples of IFN-γ analogs, but none was identical to the claimed IFN-γ analog.[98] The closest example, example five, recited an asparagine as the eighty-first amino acid in an IFN-γ polypeptide sequence, whereas the claimed analog contained a lysine at that position.[99] The patent examiner noted this difference, stating that despite its similarity to the claimed analog, example five did not "constitute a description of the claimed analog."[100]

In response, the applicants offered the declaration of Randolph Wall as evidence of what one of ordinary skill in the art would have known in 1983.[101] Dr. Wall testified that the skilled artisan would have understood the asparagine-lysine difference as insignificant because the main thrust of the invention, as described in the specification, was the deletion of the first three amino acids of natural IFN-γ to achieve the claimed analog.[102] In other words, according to Dr. Wall, the skilled artisan would have interpreted example five to describe the claimed analog as well, given the irrelevance of the asparagine-lysine difference.[103] The patent examiner dismissed this declaration as merely an opinion stating a legal conclusion.[104]

The Federal Circuit did not address whether or not Dr. Wall was correct.[105] Instead, the court vacated the Board's decision on the ground that the patent examiner should not have refused to consider the substance of Dr. Wall's declaration.[106] The Federal Circuit held that the declaration, although couched in opinion terms, provided

96. *Id.* at 1176.
97. *Id.* at 1170 (describing the claimed subject matter of U.S. patent application Serial No. 06/483,451).
98. *Id.* at 1171.
99. *In re* Alton, 76 F.3d at 1171.
100. *Id.*
101. *Id.* at 1172.
102. *Id.* at 1173.
103. *Id.*
104. *In re* Alton, 76 F.3d at 1173-74.
105. *Id.* at 1174.
106. *Id.* at 1176.

factual bases attempting to explain why one of ordinary skill in the art would construe example five to also cover the claimed IFN-γ.[107]

In *Regents of University of California v. Eli Lilly & Co.*, the Federal Circuit affirmed the district court's judgment that the asserted patent claims were invalid, because the patent failed to provide an adequate written description of the claimed subject matter.[108] The patented technology involved human insulin produced by recombinant DNA methods.[109] The patent claims concerned the use of human insulin cDNA, but the specification provided a written description only regarding rat insulin cDNA.[110] Although the patent recited a general method for obtaining human cDNA along with the amino acid sequences for human insulin, the Federal Circuit noted that enablement was not the issue.[111] This disclosure provided no structural information or physical characteristics, such as a nucleotide sequence, of any of the human cDNAs in the claimed genus.[112]

Absent such identification, the generic references to vertebrate or mammalian insulin cDNA were inadequate written descriptions, which could not distinguish the claimed genus from others, except by function.[113] The Federal Circuit stated that a proper written description of a cDNA genus, for example, might be the nucleotide sequences of a representative number of cDNAs or the recitation of structural features common to the members of the genus.[114] Without more, generic references indicate only what one might achieve and provide no information about the resulting claimed material.[115]

In *Johns Hopkins University v. CellPro, Inc.*, the Federal Circuit considered a case presenting a written description question but did not decide the issue of compliance.[116] The claims of U.S. Patent No. 4,965,204 encompassed a broad genus of monoclonal antibodies that could bind specifically to antigens expressed on the surface of

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107. *Id.*
108. 119 F.3d 1559, 1562 (Fed. Cir. 1997).
109. *Id.* (identifying the patents-in-suit as U.S. Patents No. 4,652,525 and No. 4,431,740).
110. *Id.* at 1562-63.
111. *Id.* at 1567.
112. Regents of Univ. of California v. Eli Lilly & Co., 119 F.3d at 1567.
113. *Id.* at 1567-68.
114. *Id.* at 1568-69.
115. *Id.* at 1568.
116. 152 F.3d 1342, 1361-62 (Fed. Cir. 1998).

immature stem cells but not on the surface of mature cells.[117] The patent disclosed only one monoclonal antibody, anti-My-10, as an embodiment of the claimed invention.[118]

On appeal CellPro contended that an application of the Federal Circuit's holding in *Lilly* required the conclusion that the '204 patent lacked adequate written description to support its claims.[119] In *Lilly* the Federal Circuit ruled that claims to a genus of vertebrate or mammalian insulin cDNA were unsupported by the patent specification's disclosure of a single species of rat insulin cDNA.[120] CellPro sought to argue by analogy that the disclosure of anti-My-10 in the '204 patent did not provide adequate written description to support its claims to a broad genus of monoclonal antibodies.[121] The Federal Circuit, however, never reached the merits of CellPro's *Lilly* argument, which the court admonished as having been raised seriously for the first time only on appeal.[122]

D. Enablement

To obtain a patent the applicant must provide a sufficient disclosure to enable any person skilled in the art to practice the invention.[123] The patent specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.[124] A party seeking to invalidate a patent based on a lack of enablement must prove such by clear and convincing evidence.[125] Enablement is a question of law that the Federal Circuit reviews de novo.[126] The Federal Circuit reviews the

117. *Id.* at 1347.

118. *Id.*

119. *Id.* at 1361.

120. Johns Hopkins Univ. v. CellPro, Inc., 152 F.3d at 1361; Regents of Univ. of California v. Eli Lilly & Co., 119 F.3d at 1568.

121. 152 F.3d at 1361.

122. *Id.* at 1362 (citing Singleton v. Wulff, 428 U.S. 106, 120 (1976); Braun, Inc. v. Dynamics Corp. of Am., 975 F.2d 815, 821 (Fed. Cir. 1992)).

123. *See* 35 U.S.C. § 112 (1994).

124. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384 (Fed. Cir. 1986) (specifying that no amount of experimentation is preclusive if merely routine in nature).

125. *See* Morton Int'l Co. v. Cardinal Chem. Co., 5 F.3d 1464, 1469 (Fed. Cir. 1993).

126. *See* PPG Indus., Inc. v. Guardian Indus., Corp., 75 F.3d 1558, 1564 (citing *In re Vaeck*, 947 F.2d 488, 495 (Fed. Cir. 1991)) (Fed. Cir. 1996) (providing the court's standard of

underlying facts found by a lower tribunal for clear error.[127]

In *Enzo Biochem, Inc. v. Calgene, Inc.*,[128] the Federal Circuit considered whether patent claims to use antisense nucleic acids to regulate gene expression in prokaryotic and eukaryotic cells broadly were invalid.[129] The patents provided working examples limited to only one prokaryote, *Escherichia coli*.[130] The Federal Circuit affirmed the judgment of the district court that the patent claims were invalid for failure to satisfy the enablement requirement of the first paragraph of § 112.[131]

In this case the patented technology related to regulation of gene expression through antisense nucleic acid.[132] For example, the incorporation of antisense technology in the accused Calgene FLAVR SAVR tomato permitted better control of when the fruit ripens.[133] Specifically, the product relied upon antisense nucleic acid to block the expression of the polygalacturonase gene, which encodes an enzyme that promotes the ripening of tomatoes.[134]

Following a bench trial, the district court ruled that Calgene did not infringe the asserted claims of the Enzo patents and that, in any event, those patent claims were invalid.[135] With respect to the invalidity determination, the district court held that undue experimentation would have been "necessary to practice antisense

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review on the enablement issue); *In re* Wands, 858 F.2d 731, 735-37 (Fed. Cir. 1988) (citing Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 1268 (Fed. Cir. 1986)).

127. *See* Gould v. Quigg, 822 F.2d 1074, 1077 (citing Fregeau v. Mossinghoff, 776 F.2d 1034, 1037 (Fed. Cir. 1985)); FED. R. CIV. P. 52(a); Atlas Powder Co. v. E.I. Dupont De Nemowis & Co., 750 F.2d 1569, 1573 (Fed. Cir. 1984).

128. 188 F.3d 1362 (Fed. Cir. 1999).

129. *Id.* at 1372. The court noted that the critical date for the enablement inquiry is the date that the patent application was filed, which was the same for both patents-in-suit, namely, October 20, 1983. *Id.* at 1371.

130. *Id.* at 1367-68 (teaching the application of the patented technology to the *lpp* (lipoprotein), *ompC* (outer membrane protein C), and *ompA* (outer membrane protein A) genes of *E. coli*).

131. *Id.* at 1371.

132. *Id.* at 1366-67 n.4 (providing a working knowledge of antisense technology and recognizing that no universally accepted mechanism of action for gene expression regulation by antisense exists).

133. Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d at 1368.

134. *Id.*

135. *Id.* at 1365 (identifying the patents-in-suit as U.S. Patents No. 5,190,931, and No. 5,208,149).

technology in cells other than *E. coli*."[136] The Federal Circuit concluded that the district court did not clearly err in its findings on this issue.[137]

The Federal Circuit agreed with the district court's assessment that, in 1983, antisense was a highly unpredictable technology.[138] In addition, the Federal Circuit acknowledged the extensive amount of experimentation required to adapt antisense technology to cells other than *E. coli*.[139] Perhaps the clearest examples of this were the numerous instances of the inventor's own failed attempts to achieve antisense regulation of the expression of other prokaryotic or eukaryotic genes.[140] The Federal Circuit rejected Enzo's assertions that these failed attempts should be disregarded because the inventor did not possess the appropriate level of skill in the relevant field, namely, genetic engineering.[141]

In view of the absence of guidance, direction, working examples of antisense in eukaryotes, or even any prokaryote other than *E. coli*, the Federal Circuit held that the patent provided no more than a plan or invitation to practice antisense in those cells.[142] Such minimal disclosure was insufficient to support the broad scope of the patent claims.[143]

In *Genentech, Inc. v. Novo Nordisk A/S*, the Federal Circuit vacated the district court's preliminary injunction enjoining Novo from importing, marketing, using, selling, offering for sale, or distributing its Norditropin® brand recombinant human growth hormone (hGH) product.[144] Initially, Genentech had sued Novo for patent infringement.[145] The district court ruled that Genentech would likely overcome Novo's defense that Genentech's patent was invalid for lack of enablement.[146] The Federal Circuit held that the district

136. *Id.* at 1369.
137. *Id.* at 1372.
138. Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d at 1368.
139. *Id.*
140. *Id.* at 1372-73.
141. *Id.* at 1373.
142. *Id.* at 1374-75.
143. Enzo Biochem, Inc. v. Calgene, Inc. 188 F.3d at 1375.
144. 108 F.3d 1361 (Fed. Cir. 1997).
145. *Id.* at 1363.
146. *Id.*

court erred in reaching this conclusion and thus abused its discretion in granting Genentech's preliminary injunction motion.[147]

The patent claims were directed to a process for cleavable fusion expression.[148] This methodology involved the expression of DNA encoding a conjugate protein, and the use of an enzyme to cleave off the undesired portion of the correspondingly produced protein.[149] Novo argued that Genentech's patent was invalid because it failed to provide a disclosure commensurate with the scope of its claims.[150] Specifically, Novo pointed to the paucity of teaching, which included only statements about the possibility of cleavable fusion expression, the DNA sequence of hGH, the use of a single enzyme (trypsin) for cleaving undisclosed conjugate proteins, and the possibility of amino acid extensions conjugated to hGH as enzyme cleavage sites.[151]

The Federal Circuit agreed with Novo.[152] The court noted that the patent provided no description of any specific cleavable conjugate proteins or any reaction conditions under which cleavable fusion expression would work, with hGH or otherwise.[153] The patent merely described several applications for which cleavable fusion expression is generally well suited, and identified trypsin and its cleavage sites.[154] Accordingly, the Federal Circuit held that the limited disclosure constituted the "mere germ of an idea," which would not have enabled a person of ordinary skill in the art at the time of patent application filing to use cleavable fusion expression to make hGH without undue experimentation.[155]

In reaching this conclusion the Federal Circuit discounted the testimony offered by Genentech that one skilled in the art would have had sufficient knowledge to determine all the missing information and thus to achieve the claimed invention.[156] The court deemed the

147. *Id.* at 1362-63.
148. *Id.* at 1363 (indicating the patent-in-suit as U.S. Patent No. 5,424,199).
149. Genentech, Inc. v. Novo Nordisk A/S, 108 F.3d at 1363.
150. *Id.* at 1364.
151. *Id.*
152. *Id.* at 1366.
153. *Id.* at 1365.
154. Genentech, Inc. v. Novo Nordisk A/S, 108 F.3d at 1365.
155. *Id.* at 1366.
156. *Id.*

evidence irrelevant.[157] Indeed, the Federal Circuit stated that the patent specification was "so lacking . . . that providing testimony regarding the skill in the art has been an exercise in futility."[158]

Furthermore, the Federal Circuit reasoned that despite the motivation in the art to do so, no one was able to produce any human protein by use of the cleavage fusion expression method at the time of patent application filing, and for nearly a year afterwards.[159] From this consideration, the Federal Circuit reasoned that the claimed invention was "an application of an unpredictable technology in the early stages of development."[160] In such circumstances, an even higher judicial vigilance to the issue of compliance with the enablement requirement might be warranted.[161]

In *Johns Hopkins University v. CellPro, Inc.*, the Federal Circuit affirmed the district court's summary judgment in favor of Johns Hopkins that the claims of U.S. Patent No. 4,965,204 were not invalid for lack of enablement.[162] The patented technology related to monoclonal antibodies specific for antigens expressed on the surface of immature stem cells, but not on the surface of mature cells.[163] These antibodies could be used in cell separation methods to prepare enriched stem cell populations that are substantially free of mature myeloid and lymphoid cells.[164] The absence of mature cells would help minimize the risk of a potentially fatal condition known as Graft Versus Host Disease that can occur during bone marrow transplants.[165]

The claims of the '204 patent encompassed a broad genus of monoclonal antibodies that could bind specifically to "an antigen on nonmalignant, immature human marrow cells, wherein said antigen is stage specific and not lineage dependent, and said antigen is also specifically bound by the antibody produced by the hybridoma

157. *Id.* at 1366-67.
158. *Id.* at 1367.
159. Genentech, Inc. v. Novo Nordisk A/S, 108 F.3d at 1367.
160. *Id.*
161. *Id.* at 1368.
162. 152 F.3d 1342, 1361 (Fed. Cir. 1998).
163. *Id.* at 1347.
164. *Id.* at 1347 & n.4 (describing fluorescence-activated cell, or coating, separation).
165. *Id.* at 1346.

deposited under ATCC Accession No. HB-8483."[166] The recited antigen would be recognizable by those skilled in the art as the CD34 antigen, which was a designation that arose in custom after the filing of the patent application.[167] The '204 patent disclosed one monoclonal antibody, anti-My-10, as an embodiment of the claimed invention.[168] The parties did not dispute that anti-My-10, as well as the accused CellPro 12.8 antibody, would bind specifically to the CD34 antigen.[169]

CellPro charged that the '204 patent violated the first paragraph of § 112, because the disclosure of anti-My-10 was insufficient to enable one of ordinary skill in the art to make and use other antibodies within the claimed genus without undue experimentation.[170] To establish lack of enablement CellPro carried the burden of proof at trial by clear and convincing evidence.[171] The district court, however, concluded that the evidence upon which CellPro relied in opposition to Johns Hopkins' summary judgment motion did not raise a genuine issue of material fact necessary to avoid judgment against CellPro on the enablement issue as a matter of law.[172] The Federal Circuit agreed, even when the court properly viewed the evidence in the light most favorable to CellPro as the nonmoving party.[173]

The record showed that the method disclosed in '204 patent was used by others to produce over forty additional CD34 antibodies.[174] Moreover, the preferred immunogen, namely the KG-1a cell line, described in the patent for producing the claimed monoclonal antibodies was the same as CellPro used to make its accused 12.8 antibody.[175] This notwithstanding, CellPro pointed to instances of alleged failures to obtain an anti-CD34 antibody after following the

166. Johns Hopkins Univ. CellPro, Inc., 152 F.3d at 1347 (emphasis removed) (reciting claim 1 of the '204 patent).
167. *Id.* at 1350 & n.13.
168. *Id.* at 1347.
169. *Id.* at 1350-51 & n.13.
170. *Id.* at 1351.
171. Johns Hopkins Univ. v. CellPro, Inc., 152 F.3d at 1359.
172. *Id.* at 1361.
173. *Id.* at 1359.
174. *Id.*
175. *Id.*

disclosed method.[176]

After scrutinizing CellPro's evidence the Federal Circuit concluded that the inability of the inventor's own laboratory to produce another anti-CD34 antibody according to the method disclosed in the patent was of no moment.[177] In particular, the Federal Circuit noted that these specific laboratory personnel were undergraduate students with no previous experience in monoclonal antibody production.[178] The Federal Circuit held that CellPro failed to establish that anyone of ordinary skill in the art had failed to create an anti-CD34 antibody in the described fashion.[179]

Perhaps most importantly, the Federal Circuit discounted the testimony of CellPro's experts, which the court found to lack the required nexus between failure or difficulty in achieving the claimed antibodies and the method described in the '204 patent.[180] One expert indicated that he did not use the screening technique disclosed in the patent specification.[181] Another expert admitted that he did not attribute his problems to any shortcoming in the disclosure, but instead to the probabilistic nature of antibody production generally.[182] On this point, the Federal Circuit reiterated that if it is merely routine, even a considerable amount of experimentation is not undue.[183]

II.

The legal status of inventorship rests upon the core tenet that "[c]onception is the touchstone of inventorship."[184] From the earliest cases courts have uniformly held that an inventor is a person who conceived the patented invention.[185] However, the relatively static

176. Johns Hopkins Univ. v. CellPro, Inc., 152 F.3d at 1360.
177. *Id.*
178. *Id.*
179. *Id.*
180. *Id.*
181. Johns Hopkins Univ. v. CellPro, Inc. 152 F.3d at 1360.
182. *Id.*
183. *Id.*
184. *See* Burroughs Wellcome Co. v. Barr Labs., Inc., 40 F.3d 1223, 1227-28 (Fed. Cir. 1994) (citing Sewall v. Walters, 21 F.3d 411, 415 (Fed. Cir. 1994)).
185. *See* Collar Co. v. Van Dusen, 90 U.S. (23 Wall.) 530, 563-64 (1874). Indeed, one need not personally reduce to practice his or her complete conception to remain an inventor. Acts by others in certain circumstances can inure to the inventor's benefit. *See* Cooper v. Goldfarb, 154

nature of the patent law principles underlying inventorship belies the long-standing discontent with their practical application.[186]

The legal standard of conception can be thought of as the "formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention."[187] The courts have further explained that an idea is sufficiently "definite and permanent" when "only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation."[188] Of the positive indicia of inventorship, the ability to articulate the inventive concept is an important starting point.[189] "Invention" and "inventorship" are often at the heart of patent interference proceedings before the PTO to determine priority, i.e., who invented first.

In *Barton v. Adang* the Federal Circuit reversed the Board's entry of judgment against Barton in a three party interference.[190] The PTO declared an interference between the Barton patent application, the

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F.3d 1321, 1332 (Fed. Cir. 1998) ("In order to establish inurement, an inventor must show, among other things, that the other person was working either explicitly or implicitly at the inventor's request. . .. While derivation focuses on the communication of information between two parties, inurement focuses on the nature of the relationship between them. Communication of the conception by the inventor to the other party is not required to establish inurement." (internal citations omitted)).

186. *See, e.g.*, Mueller Brass Co. v. Reading Indus., Inc., 352 F. Supp. 1357, 1372-73 (E.D. Pa. 1972), *aff'd mem.*, 487 F.2d 1395 (3d Cir. 1973) (The exact parameters of what constitutes joint inventorship are quite difficult to define. It is one of the muddiest concepts in the muddy metaphysics of the patent law."). *Id.* at 1372.

187. *See* Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1376 (Fed. Cir. 1986) (quoting 1 ROBINSON ON PATENTS 532 (1890) Coleman v. Dines, 754 F.2d 353, 359 (Fed. Cir. 1985)).

188. *See id.*

189. *See* Burroughs Wellcome Co. v. Barr Labs., Inc., 40 F.3d 1223, 1228 (Fed. Cir. 1994).

> [T]he test for conception is whether the inventor had an idea that was definite and permanent enough that one skilled in the art could understand the invention; the inventor must prove his conception by corroborating evidence, preferably by showing a contemporaneous disclosure. An idea is definite and permanent when the inventor has a specific, settled idea, a particular solution to the problem at hand, not just a general goal or research plan he hopes to pursue.... The conception analysis necessarily turns on the inventor's ability to describe his invention with particularity. Until he can do so, he cannot prove possession of the complete mental picture of the invention.

Id. (citations omitted). These rules ensure that patent rights attach only when an idea is so far developed that the inventor can point to a definite, particular invention.

190. 162 F.3d 1140, 1141 (Fed. Cir. 1998).

Fischoff patent application, and the Adang issued patent. The respective assignees of the issued patent were Agracetus, Monsanto, and Mycogen Plant Science, Inc.[191] The patent applications and patent claimed methods for expression in plants of *Bacillus thuringiensis* genes encoding insecticidal proteins.[192]

Shortly after the declaration of the interference, Monsanto bought Agracetus, which eliminated the adversity between the Barton and Fischoff patent applications.[193] When it notified the PTO of this ownership change, Monsanto asserted that good cause existed for the continuation of the interference because the content of the count had not been firmly established.[194] Furthermore, Monsanto contended that the complexities of the priority determination in biotechnology cases "made it impossible for Monsanto to choose the best application with which to defend the interference."[195]

The Board issued a show cause order why judgment should not be entered against Monsanto given the commonly owned applications.[196] Monsanto responded that the indefiniteness of the count precluded a rational election between the applications.[197] When the Board issued an order that Monsanto had not shown good cause to continue the interference, Monsanto elected to proceed with the Fischoff application and moved to have judgment entered immediately against the Barton application.[198] The Board granted this motion and Monsanto appealed the original order.[199]

The Federal Circuit held that at the stage of the proceedings when the Board issued its show cause order, "Monsanto could not determine which application . . . would be the best evidence to establish priority" of invention to defeat the Adang patent.[200] If the

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191. *Id.* (identifying the patent applications and patent at issue as U.S. patent applications Serial No. 07/827,906 (Barton), No. 08/434,105 (Fischoff), and U.S. Patent No. 5,380,831 (Adang)).

192. *Id.*

193. *Id.* at 1142.

194. Barton v. Adang, 162 F.3d at 1142 (noting that "the precise content of the count in an interference is subject to change following preliminary motions").

195. *Id.*

196. *Id.*

197. *Id.*

198. *Id.* at 1143.

199. Barton v. Adang, 162 F.3d at 1143.

200. *Id.*

final interference count excluded subject matter disclosed in the Barton application but not the Fischoff application, Monsanto would lose patentable subject matter by the early dismissal of the Barton application.[201] Accordingly, the Federal Circuit remanded the case to the Board to continue the interference on both its applications until the Board decided the preliminary motions to finalize the count and the parties completed discovery.[202]

In *Schendel v. Curtis* the Federal Circuit reviewed the Board's summary judgment awarding priority of invention to Curtis in a patent interference proceeding.[203] The subject matter of the interference count involved a fusion protein of interleukin-3 (IL-3) and a hematopoietin, which could be granulocyte colony stimulating factor (G-CSF) or granulocyte-macrophage colony stimulating factor (GM-CSF).[204] Schendel alleged priority of invention based on his alleged "actual reduction to practice of an IL-3/G-CSF fusion protein" before Curtis' effective patent application filing date.[205]

The Federal Circuit upheld the Board's ruling that Schendel's evidence failed to show that he obtained an IL-3/G-CSF fusion protein.[206] Although the scientific evidence and declarations apparently indicated that Schendel had isolated material having the respective biological activities of IL-3 and G-CSF, there was no showing that this material constituted an actual fusion protein.[207] In particular, the absence of any chemical composition or structural data, such as a relatively simple molecular weight determination, appeared significant to the ultimate resolution of this case.[208]

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201. *Id.*

202. *Id.*

203. 83 F.3d 1399, 1400-02 (Fed. Cir. 1996) (reporting the interference declared between U.S. patent application Serial No. 08/057,198 and U.S. Patent No. 5,073,627).

204. *Id.* at 1400 & n.3.

205. *Id.* at 1401.

206. *Id.* at 1404.

207. Schendel v. Curtis, 83 F.3d at 1404.

208. *Id.* ("[W]ithout any molecular weight or other probative data relevant to the composition or structure of the molecule he allegedly prepared, there is insufficient evidentiary support for Schendel's conclusory assertion that he made . . . [a] fusion protein.").

III.

Patent infringement liability arises with the unauthorized manufacture, use, offer for sale, or sale in the United States of a patented invention, or the importation of that invention into the United States.[209] The determination of infringement is a two-step inquiry, the first step being a proper claim construction.[210] The second step of the infringement analysis involves the comparison of the accused product or process to the properly construed claim.[211]

A patent holder alleging infringement has the burden of proving by a preponderance of the evidence at trial that the accused infringer's product or process contains every limitation of at least one of the asserted claims of the patent, either literally or by equivalence.[212] Infringement is a question of fact that the Federal Circuit reviews for substantial evidence to support the jury's verdict or for clear error where the trial judge sits as the fact-finder.[213]

A literal infringement results when every exact limitation recited in a patent claim is present in an accused product or process.[214] A finding of infringement does not, however, require that the accused

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209. *See* 35 U.S.C § 271(a) (1994). For a statistical study of the Federal Circuit's dispositions in appeals from infringement findings, see Donald R. Dunner et al., *A Statistical Look at the Federal Circuit's Patent Decisions: 1982-1994*, 5 FED. CIR. B.J. 151, at tbl. 5 (1995) (covering period from Oct. 1, 1982 to Mar. 15, 1994).

210. Carroll Touch, Inc. v. Electro Mechanical Sys., 15 F.3d 1573, 1576 (Fed. Cir. 1993) (stating that "the claim must be properly construed to determine scope and meaning") (citations omitted).

211. Lemelson v. General Mills, Inc., 968 F.2d 1202, 1206 (Fed. Cir. 1992).

212. Conroy v. Reebok Int'l Ltd., 14 F.3d 1570, 1573 (Fed. Cir. 1994) (noting that [t]o support an infringement determination, an accused device must embody exactly each claim limitation or its equivalent); Key Mfg., Inc. v. Microdot, Inc., 925 F.2d 1444, 1449 (Fed. Cir. 1991) (citing Julien v. Zerrigue, 864 F.2d 1569, 1571 (Fed. Cir. 1989)) (stating that the patentee must prove that the accused device embodies every limitation in the claim, either literally or by a substantial equivalent).

213. *See Lemelson*, 968 F.2d at 1207 ("[The substantial evidence test] requires us to decide for ourselves whether reasonable jurors viewing the evidence as a whole could have found the facts needed to support the verdict in light of the applicable law."). *See also* United States v. United States Gypsum Co., 333 U.S. 364, 395 (1948) ("A finding is 'clearly erroneous' when although there is evidence to support it, the reviewing court on the entire evidence is left with the definite and firm conviction that a mistake has been committed.").

214. Mannesmann Demag Corp. v. Engineered Metal Prods. Co., 793 F.2d 1279, 1282 (Fed. Cir. 1986) (citing Stewart-Warner Corp. v. City of Pontiac, 767 F.2d 1563, 1570 (Fed. Cir. 1985)).

product or process embody every limitation of the claim literally.[215] Even when a patent holder cannot prove literal infringement, a finding of infringement may be appropriate under the doctrine of equivalents.[216]

In *Regents of University of California v. Eli Lilly & Co.*, the Federal Circuit affirmed the district court's judgment that Lilly did not infringe the asserted patent claims either literally or under the doctrine of equivalents.[217] The patented technology involved recombinant genetic constructs and microorganisms that express human proinsulin.[218] The Federal Circuit held that the proper interpretation of the patent claims in this case must recognize the effect of a disclaimer by the patent applicants during prosecution.[219]

The applicants surrendered coverage of human proinsulin production using a fusion protein.[220] The prior art cited by the patent examiner taught the use of recombinant eukaryotic and prokaryotic fusion proteins to produce a eukaryotic protein, including insulin, in a bacterial host.[221] The applicants amended their claims to distinguish this prior art.[222] This same action resulted in both a claim interpretation that precluded a finding of literal infringement and a prosecution history estoppel that precluded a finding of infringement under the doctrine of equivalents.[223]

In its nonprecedential disposition in *Evans Medical Ltd. v. American Cyanamid Co.*,[224] the Federal Circuit affirmed the district

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215. Graver Tank & Mfg. Co., Inc. v. Linde Air Prods. Co., 339 U.S. 605, 607-08 (1950).
216. *Id.*
217. 119 F.3d 1559 (Fed. Cir. 1997).
218. *Id.* at 1562 (discussing U.S. Patent No. 4,431,740).
219. *Id.* at 1572-73 & n.6.
220. *Id.*
221. Regents of Univ. of California v. Eli Lilly & Co., 119 F.3d at 1572-73.
222. *Id.* at 1573.
223. *Id.* at 1573-74.
224. 52 U.S.P.Q.2d (BNA) 1455, 1455-56 (Fed. Cir. 1999). All dispositions of the Federal Circuit are precedential unless otherwise noted. FED. CIR. R. 47.6(a). The holdings of a precedential decision are binding on a subsequent panel unless overruled by the court en banc. South Corp. v. United States, 690 F.2d 1368, 1370 n.2 (Fed. Cir. 1982) (en banc) (stating appropriateness of adopting body of law established by Court of Claims and Court of Customs and Patent Appeals in Federal Circuit decisions); *cf.* Johnston v. IVAC Corp., 885 F.2d 1574, 1579 (Fed. Cir. 1989) (citing Newell Cos., Inc. v. Kenney Mfg. Co., 864 F.2d 757, 765 (Fed. Cir. 1988)) ("Where conflicting statements . . . appear in our precedent, the panel is obligated to review the cases and reconcile or explain the statements, if possible. If not reconcilable and if

court's summary judgment of noninfringement.[225] The patented technology involved purified *Bordetella pertussis* antigen and its use as a vaccine.[226] The crux of the infringement analysis was the proper construction of the claim term "purified."[227]

The Federal Circuit noted that the claim term purified inherently required a characterization of degree in order to be defined precisely.[228] The court acknowledged that no consensus had emerged on the plain meaning of the term to one of ordinary skill in the art.[229] Upon examination of the patent specification, the Federal Circuit concluded that the claim term purified meant that the recited antigen must comprise greater than fifty percent of the 69kD antigen.[230]

In view of the statement in the specification that the 69kD antigen preparation contemplated as the invention for use in vaccines "may, if desired, contain minor quantities of other antigenic compounds," the Federal Circuit reasoned that "other components" could not comprise more than fifty percent of the contemplated 69kD antigenic preparation as used in a vaccine.[231] However, these statements did not necessarily set a higher, upper bound on the degree of purity required.[232] In any event, because the parties did not dispute that the accused antigen product contained no more than four percent of the 69kD antigen, the Federal Circuit concluded as a matter of law that no infringement, either literally or under the doctrine of equivalents,

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not merely conflicting dicta, the panel is obligated to follow the earlier case law which is the binding precedent."). The assigned panel, however, may unanimously determine at the time of issuance that an opinion would not significantly add to the law and therefore designate the opinion or order as nonprecedential. FED. CIR. R. 47.6(b). An opinion or order so designated may not be employed or cited as precedent but may be relied upon for assertions of claim preclusion, issue preclusion, judicial estoppel, law of the case, or the like. *Id.* Furthermore, in certain circumstances the Federal Circuit may affirm the judgment of a trial court or administrative agency without opinion. FED. CIR. R. 36.

225. *Id.* at 1456 (table).

226. *Id.* at 1456-57 (identifying the patents-in-suit as U.S. Patents No. 5,237,052, No. 5,438,120, and No. 5,648,080).

227. *Id.* at 1459.

228. *Id.*

229. Evans Med. Ltd. v. American Cyanamid Co., 52 U.S.P.Q. 2d (BNA) at 1459.

230. *Id. See also id.* at 1457 & n.4 (describing the 69 kD antigen as an outer membrane *B. pertussis* protein with a molecular weight of 69 kilodaltons, which was also known in the art as P.69 and pertactin).

231. *Id.* at 1459.

232. *Id.*

could exist.[233]

Patent litigation regarding biotechnology inventions can also arise in the context of interference proceedings before the PTO.[234] The losing party can appeal an adverse Board decision by filing either a civil action in the federal district court, or a notice of appeal directly to the Federal Circuit.[235] Even if a party chooses the district court route, the Federal Circuit is the exclusive appellate forum for any appeal in such an action.[236]

In *Genentech, Inc. v. Chiron Corp.* the Federal Circuit reversed the district court's summary judgment that Genentech's claimed invention was not within the scope of the interference count for purposes of determining priority of invention.[237] The PTO declared an interference between two patent applications, one assigned to Genentech and the other to Chiron.[238] The sole count of the interference related to a recombinant genetic construct containing DNA encoding human insulin-like growth factor-I (hIGF-I) in proper reading frame with *Saccharomyces* alpha-factor secretory leader and processing signal sequence.[239]

The Genentech application claimed a DNA construct that, upon insertion into a yeast expression plasmid and transformation into a yeast cell, would facilitate secretion of a fusion protein, i.e., a modified IGF-I consisting of a collagenase cleavage site at the carboxy terminal of hIGF-I.[240] The Board rejected Chiron's argument that this subject matter fell outside the scope of the interference count.[241] Nevertheless, the Board awarded priority of invention to Chiron based on its determination that Genentech failed to prove any practical, therapeutic utility of its fusion protein.[242]

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233. *Id.* at 1460.
234. 35 U.S.C. § 135 (1994).
235. *Id.* § 146.
236. 28 U.S.C. § 1291 (1994).
237. 112 F.3d 495, 496-97 (Fed. Cir. 1997).
238. *Id.* at 497 (indicating the interference between U.S. patent applications Serial No. 06/506,078 and No. 06/922,199).
239. *Id.* (describing the interference count as reciting "[a] DNA construct comprising a sequence coding for human insulin-like growth factor-I joined in proper reading frame with *Saccharomyces* alpha-factor secretory leader and processing signal sequence").
240. *Id.* at 497-98.
241. Genentech, Inc. v. Chiron Corp., 112 F.3d at 498.
242. *Id.*

Genentech appealed the Board's decision by filing a civil action in district court.[243] Chiron filed a motion for summary judgment that Genentech's claimed invention of a DNA construct encoding modified IGF-I was not within the scope of the interference count as properly interpreted.[244] The district court granted this motion and thus affirmed the Board's award of priority on different grounds.[245]

In so ruling, the district court interpreted the interference count's recitation of a DNA sequence coding for hIGF-I to mean that mature IGF-I, or the specific seventy amino acid protein, must be ultimately secreted from the transformed yeast cell containing the DNA construct of the count.[246] The district court also construed the count term "comprising," which typically allows additional elements to be present as long as the named elements are present, to exclude additional DNA between the alpha-factor processing sequences and the hIGF-I sequence.[247] Furthermore, the district court applied a common dictionary definition of the count term "joined" instead of one tailored to the biotechnical discipline.[248]

The Federal Circuit noted that the interference count specifically defined a DNA construct, not the protein that is produced by expression from the construct.[249] The count specified that the recited DNA construct included a DNA sequence coding for the secretory leader, a processing signal sequence, and hIGF-I.[250] No dispute existed as to whether the Genentech DNA construct contained the complete DNA sequences for these three proteins.[251] The issue, therefore, was whether the addition of nine codons encoding the collagenase cleavage site inserted between the sequences coding for hIGF-I and the alpha-factor processing sequences somehow removed the Genentech DNA construct from the scope of the interference

243. *Id.*
244. *Id.*
245. *Id.* at 498-99.
246. Genentech, Inc. v. Chiron Corp., 112 F.3d at 499.
247. *Id.* at 499-500.
248. *Id.*
249. *Id.* at 501 ("Although a close relationship exists between a DNA construct and the protein it encodes, the two are not equal.").
250. *Id.*
251. Genentech, Inc. v. Chiron Corp., 112 F.3d at 501.

count.[252] The Federal Circuit reasoned that this depended upon the interpretation of the count phrase "joined in proper reading frame."[253]

The Federal Circuit concluded that a proper construction of the phrase "in proper reading frame" meant that the nucleotides must be read in such a way that the seventy amino acids of hIGF-I are incorporated in the proper sequence in the expressed protein.[254] The court thus ruled that the count did not exclude nucleotides coding for additional amino acids at the beginning of the seventy amino acid IGF-I sequence.[255] The Federal Circuit further noted that such an interpretation of the count was consistent with the open-ended term comprising.[256]

In addition, the Federal Circuit determined that count term joined did not foreclose the possibility of additional nucleotides being inserted between the two joined elements, the alpha-factor processing sequences and hIGF-I sequence.[257] The Federal Circuit rejected that district court's interpretation of the count to require that the alpha-factor processing sequences and hIGF-I sequence must be directly joined with no intervening nucleotides.[258] The Federal Circuit held that when viewed properly through the broadest, reasonable interpretation, the count did not necessitate a direct joining or connection.[259]

CONCLUSION

A survey of the Federal Circuit decisions in biotechnology patent cases reveals certain informative guidelines. First, because the consideration of various standards for patentability and disclosure centers on the level of skill in the art at the time of patent application filing, the technical underpinnings of a Federal Circuit decision on

252. *Id.*
253. *Id.*
254. *Id.*
255. *Id.*
256. Genentech, Inc. v. Chiron Corp., 112 F.3d at 501 ("'Comprising' is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.").
257. *Id.*
258. *Id.*
259. *Id.*

these matters should be viewed in the proper time frame. Appreciation of this temporal distortion is particularly important where the issue involves whether the patent disclosure of specific species supports the scope of broad genus claims. This genus-species relationship is inherently a moving target. As biotechnology matures, an otherwise unpredictable art can become more predictable and thus might permit increasingly broader claims based upon limited examples.

Second, procedurally speaking, the Federal Circuit accomplishes its appellate task by a closed review of the evidence presented by the parties. Accordingly, the Federal Circuit's conclusions might not reflect the true state of the art from an objective perspective but typically track the record developed in the trial court precisely. In this regard the documentary evidence and witness testimony is as key in a biotechnology patent case as in any other lawsuit. Indeed, the record of the state of the art or the inventor's own research activities, which can be found in the patent application, its file history, and the cited prior art, as well as any laboratory notebooks, research grant materials or commercial information relating to the patented technology, often form the factual focus of the case.

Finally, the decisions of the Federal Circuit in biotechnology patent cases should be viewed with an eye towards the applicable standards of review. The court remains faithful to the established principles of deference to the factual findings of its lower tribunals on certain issues. This practice can result in an appellate disposition that rests less on an agreement with statements regarding the true state of the technology and more on the approval of conclusions drawn from evidentiary reflections of that technology.