ON TREATING PAST AS PROLOGUE

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Over the years, the Federal Circuit has drawn much criticism for its jurisprudence regarding biotechnology cases because of seeming incongruities between its decisions and scientific realities. In this Article, Dr. Lawrence Sung undertakes to abate that criticism by surveying some of those cases and explaining the reasoning behind the court's decisions. Dr. Sung contends that the court was often bound by procedural guidelines and substantive legal precedent to reach the conclusions it did. It is the author's hope that better understanding of these cases will increase confidence in the Federal Circuit's jurisprudence and aid in predicting future outcomes so that conduct can be ordered accordingly.

Dr. Sung begins by pointing out the common failure to appreciate the inevitable temporal distortion that occurs between filing a patent application and interpreting the patent's claims and how that distortion, coupled with rapid evolutions in biotechnology, can result in an apparent shift in legal rights. Specifically, the author examines the impact upon issues such as claim interpretation, utility, obviousness, written description, and enablement. The author then moves to examine how the deterioration over time of evidence of invention and inventorship can affect the outcome of invalidity challenges and inequitable conduct charges. Dr. Sung concludes with a review of patent interference proceedings and infringement actions that illustrate how biotechnology inventions have been treated by the United States Patent and Trademark Office and the courts. Unfortunately, the small number of biotechnology cases, their widely differing facts, and the rapid development of the field does not facilitate the identification of a trend that would permit one to predict with reasonable accuracy the outcome of the application of the patent laws to future biotechnology cases.

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INTRODUCTION

Time-honored tradition is a tenet shared by science and the law. Both fields of endeavor acknowledge the wisdom of the critical study of historical observations and actions to facilitate the creation of new doctrines and to refine the scope and content of established ones. In the scientific method, data serves as a foundation for new hypotheses. In the rule of law, *stare decisis* embodies a similar dynamic.

The U.S. Court of Appeals for the Federal Circuit is no exception in its faithful application of legal precedent. The Federal Circuit, however, has a unique role as compared to other courts. Given its exclusive subject matter jurisdiction, the Federal Circuit sits as the ultimate arbiter in most instances of controversies over certain intellectual property rights. In so doing, the Federal Circuit not only parses the impact of science in a specific legal dispute, but also frames the governance of scientific development by our system of laws.

Indeed, 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. 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*. However, a frustration also appears to exist with the perceived inability of the courts to adequately

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1. 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 the body of law established by the 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) ("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 not merely conflicting dicta, the panel is obligated to follow the earlier case law which is the binding precedent."). The assigned panel, however, unanimously may 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)*. Furthermore, in certain circumstances, the Federal Circuit may affirm the judgment of a trial court or administrative agency without opinion. *Fed. Cir. R. 36.*


appreciate at times the impact, or lack thereof, of certain biotechnology inventions for which patent protection has been sought.\textsuperscript{4}

One concern, for example, is whether the members of the federal judiciary are 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.\textsuperscript{5} 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.\textsuperscript{6}

In biotechnology cases, therefore, the casual observer might be more likely to point out incongruity between the jurisprudence of the Federal Circuit and the underlying scientific realities.\textsuperscript{7} 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 varying degrees of dissatisfaction by the public over Federal Circuit pronouncements on biotechnology.\textsuperscript{8} A more balanced consideration of these contributing factors to the outcome of patent appeals might thus ameliorate the discontent that can accompany

\textsuperscript{4} To be sure, the Federal Circuit does not stand alone as a target of such public scrutiny. Arguably, the U.S. Patent & Trademark Office ("USPTO") bears the brunt. In recent days, the biotechnology industry, for example, has expressed grave concern at the proposed guidelines the USPTO 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 USPTO in June 1998 and its impact on the second proposed written description examination guidelines published by the USPTO 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. Petlo, Greater Predictability May Result in Patent Pools, NAT'L L.J., June 22, 1998, at C2.

\textsuperscript{5} See, e.g., Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1373 (Fed. Cir. 1999) (holding 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.'").

\textsuperscript{6} 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 have held technical undergraduate, if not graduate, degrees that cover a wide range of disciplines as a whole. In a superficial examination, Judge Lourie appears to have authored most of the Federal Circuit opinions in biotechnology cases, a somewhat disproportionately high number given the court's practice of random panel assignment.


\textsuperscript{8} 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).
the biotechnology patent opinions of the Federal Circuit. Accordingly, this Article surveys the recent Federal Circuit decisions regarding biotechnology-related subject matter from these combined perspectives of science and the law.9

In Part I, this Article considers those cases dealing with biotechnology patents and patent applications in which the statutory conditions for patentability and disclosure requirements are implicated. Taking center stage here are the issues of claim interpretation, utility, obviousness, written description, and enablement. In Part II, this Article continues with a discussion of inventorship and priority disputes involving biotechnology inventions. In particular, the impact of the corroboration requirements on research and development activities is examined. The Article concludes in Part III with a review of patent litigation that concerns biotechnology products and processes. The focus of this section is on the treatment of biotechnology inventions in interference proceedings before the United States Patent and Trademark Office ("USPTO") and in patent infringement actions before the federal courts.

I

Several common misapprehensions appear to come to the fore with respect to the decisions of the Federal Circuit in appeals involving biotechnology inventions. Perhaps the most insidious is the failure to appreciate the existence of a significant temporal distortion. Absent recognition of the proper context, it would be no wonder that the casual observer might 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, must therefore focus on the state of the art at the time of the patent application rather than 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 USPTO and the litigation of issued

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9. The purpose of this Article is to provide 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, this Article 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. Burchfield, Biotechnology and the Federal Circuit (1996).
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.\textsuperscript{10}

Even forgiving this temporal distortion as a matter of understanding leaves an unsatisfactory state of affairs, however. 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 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.\textsuperscript{11} Accordingly, any reasoned extrapolation of applicable patent law principles from recently issued court decisions might seem to border on mere prognostication.\textsuperscript{12} Of course, any hint of a legal quandary is capable of creating fits among those involved in the costly business of trying to navigate biotechnology research and development programs, whether commercial or academic, through patented seas.

Still, an examination of the recent Federal Circuit decisions regarding biotechnology-related subject matter provides a glimpse of the fundamental patent law principles to which the Federal Circuit will likely continue to adhere. What follows in the remainder of this section is a consideration of the cases dealing with biotechnology patents and patent applications in which the statutory conditions for patentability and disclosure requirements are implicated.\textsuperscript{13} In particular, the issues of claim interpretation, utility, obviousness, written description, and enablement are discussed.

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

12. Of course, the Federal Circuit has acknowledged that in a rapidly advancing science, like biotechnology, what might be unpredictable at one point in time might 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)).

A. Nomenclature and Claim Interpretation

Every patent concludes with at least one numbered paragraph called a "claim." The claim defines the patented invention. Moreover, the claim sets forth the scope of the patent holder's legal right to exclude others, during the patent term, from making, using, offering for sale, selling the patented invention throughout the United States, or importing that invention into the United States. The correct interpretation of a claim is paramount in virtually all patent-related matters. Indeed, judicial determinations regarding the patentability, validity, or infringement of a patent claim all rely on the same claim interpretation.

What happens when the terminology used in a patent claim does not comport with the commonly accepted meaning of that nomenclature in the scientific community? In Schering Corp. v. Amgen, Inc., the Federal Circuit considered a case where the evolving standards of scientific classification created an issue regarding the scope of patent protection to which an inventor was entitled. Here, the nomenclature relied upon by the scientific community to describe a certain class of proteins had changed following the filing of a patent application claiming a specific member of that class.

The patent claims recited recombinant DNA molecules containing sequences coding for interferon-alpha ("IFN-α"). However, in the original patent application, the claims referred to leukocyte interferon,
instead of IFN-α.23 Six months after the patent application filing, a scientific committee adopted new terminology to describe interferons.24 The committee abolished the term “leukocyte interferon” in favor of “IFN-α” because new data revealed that leukocytes produced other types of interferon beyond the type originally designated leukocyte interferon.25

In view of the scientific nomenclature change, the patent applicants amended the pending claims to substitute IFN-α for leukocyte interferon.26 Almost twenty years later, the crux of the patent dispute was whether the term “polypeptide of the IFN-α type”27 encompassed sequences that code generally for all IFN-α polypeptides or was limited to sequences coding for the IFN-α-1 subtype, which the patent disclosed.27 The Federal Circuit held that it was the latter.28

Although the court’s conclusion might seem unremarkable at first blush, perhaps the more meaningful observation rests with the fact that it took years of litigation to resolve this issue. Indeed, this case highlights the susceptibility of legal rights to the rapidly evolving nature of the biotechnology arts, a matter which the lengthy period to judicial definition clouds only more. Still, a focus on the fact that a change in scientific nomenclature can raise colorable concerns over the meaning and scope of a patent claim might be too narrow a perspective on the matter.

Arguably, a more informed view is that fears over the seemingly broad language of the claims of an otherwise pioneering patent can be ill-founded in certain instances, particularly where “after-arising” technology is considered.29 In such situations, the Federal Circuit has repeatedly demonstrated its willingness to tailor the scope of patent claims to the appropriate degree of the invention’s disclosure and distinctions over the prior art, irrespective of the apparent breadth of the claim terms. This scrutiny might allay fears about the effect of patents on newly developing fields of research.

Still, it can also raise concerns over the potential abdication of the proper perspective of one skilled in the art at the time of the claimed invention. The apparent attention of the Federal Circuit in Schering to a

23. Id. at 1352 (reporting that “scientific experiments showed that the old terminology did not accurately differentiate between species of interferon” and that “[t]he term ‘IFN-α’ more specifically identified a particular polypeptide by its physical properties—molecular weight, binding affinity for highly specific antibodies, and amino acid sequence.”).
24. Id.
25. Id.
26. Id.
27. Id. at 1353-54 (noting that IFN-α-1 was the only interferon subtype that the patent described).
28. Id. (indicating the Federal Circuit’s holding that “[b]ecause, at the time of the ’901 application, neither [the inventor] nor others skilled in the art knew of the existence of, let alone the identity of, the specific polypeptides now identified as subtypes of IFN-α, those subtypes cannot be within the scope of the claims”).
29. The reference to “after-arising” technology reflects subject matter invented or discovered after the earliest filing date to which the patent application at issue might be entitled.
post-filing event is one cause for such questions. A reliable trend in the Federal Circuit's biotechnology patent decisions in this regard, however, is not easily found.

B. Utility

To obtain a patent, the applicant must be able to demonstrate that the claimed invention is useful.30 The utility of an invention, in concert with its novelty and nonobviousness, merits the reward of patent protection.31 Whether a claimed invention lacks utility is a question of fact, which the Federal Circuit reviews under the clearly erroneous standard.32 In any event, an alleged inventive act is not legally cognizable unless the inventor conceived of the specific utility of the claimed invention.33

In Kridl v. McCormick,34 the Federal Circuit addressed the utility requirement in the context of a patent interference proceeding.35 The court reviewed the determination of the USPTO Board of Patent Appeals and Interferences ("Board"), which considered two competing patent applications that claimed the same, or substantially the same, biotechnology subject matter.36 The interference count related to the use of antisense technology to produce plants or plant cells with resistance to certain viruses.37 Having filed a patent application before Kridl, McCormick was the first to reduce the invention to practice, albeit constructively.38 To establish priority of invention, however, McCormick also needed to prove a date of conception before that of Kridl.39

McCormick sought to rely upon the dated and witnessed pages of Marcia Vincent's laboratory notebook.40 These pages described an experiment in January 1984 in which a gene fragment encoding a viral

30. See 35 U.S.C. § 101 (1994) ("Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.").
31. 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).
33. See Rey-Bellet v. Engelhardt, 493 F.2d 1380, 1385 (C.C.P.A. 1974) ("[C]onception of an invention is not complete absent a conception of its utility.").
34. 105 F.3d 1446 (Fed. Cir. 1997).
35. Id. at 1447. The USPTO may declare an interference where a patent application claims the same, or substantially the same, subject matter as another application or as an unexpired patent. See 35 U.S.C. § 135 (1994). In this proceeding, the USPTO determines which party has priority of invention, or in other words, who was the first to invent. Because the first to invent is the only true inventor entitled to patent protection, the outcome of an interference proceeding typically leaves the winner with a patent and the loser without.
36. See id. at 1448 (reporting the interference declared between a patent application assigned to Agracetus, Inc., and another assigned to Calgene, Inc.).
37. See id. An interference count establishes the scope of the interference by defining the invention common to the parties. The interpretation of an interference count is analogous to claim construction.
38. See id. at 1449.
39. See id.
40. See id. at 1448.
protein was inserted into a cloning vector in both the sense and antisense orientations. The Board applied a "rule of reason" analysis to evaluate this evidence and found that McCormick had conceived of the invention before Kridl. The Board thus awarded priority of invention to McCormick. In reaching its decision, the Board also concluded that McCormick conceived of the utility of the claimed invention in January 1984. The Board did so based solely on the uncorroborated testimony of one of the inventors, Dr. William Swain. Kridl contended that antisense had more than one substantial use, and thus, McCormick might have used it for a different purpose in January 1984. 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.

The Federal Circuit considered the state of the biotechnology art in 1984 to refute Kridl’s arguments and affirm the Board’s determination. There was no dispute that the use of antisense in plants was not known in 1984. 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. 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.

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

41. Kridl, 105 F.3d at 1448-49.
42. See id. at 1449. See also Price v. Symsek, 988 F.2d 1187, 1195 (Fed. Cir. 1993) ("A ‘rule of reason’ analysis is applied to determine whether the inventor’s prior conception testimony has been corroborated. An evaluation of all pertinent evidence must be made so that a sound determination of the credibility of the inventor’s story may be reached.").
43. See Kridl, 105 F.3d at 1449.
44. See id.
45. See id.
46. See id.
47. See id.
48. See id. at 1450.
49. See Kridl, 105 F.3d at 1450.
50. See id.
51. See id.
52. See id. at 1450-51.
53. See id. at 1451.
54. See id.
Not unlike that in the cases involving obviousness inquiries, discussed infra, the Federal Circuit in Kridl was forced to rely on its hindsight analysis of the state of the art as the context for the parties' conduct. Indeed, in Kridl, the look backwards crossed almost a decade and a half. This reaching back in time can only further complicate the already difficult task before the Federal Circuit in parsing unfamiliar technology.

C. 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. The conclusion of nonobviousness is a question of law that the Federal Circuit reviews de novo. The conclusion of nonobviousness, however, is subject to underlying factual findings, which the Federal Circuit reviews for clear error. 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. Certain secondary considerations might also be pertinent, and include commercial success, long felt but unsolved needs, failures of others, and copying.

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

In In re Deuel, the Federal Circuit reversed the decision of the Board, which upheld the patent examiner's final rejection of the claims as obvious. The subject matter of the patent application in Deuel involved DNA encoding heparin-binding growth factor ("HBGF") of bovine and human origins. Deuel achieved the claimed invention by first isolating bovine uterine HBGF protein and determining the amino

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56. See In re Donaldson Co., 16 F.3d 1189, 1192 (Fed. Cir. 1994) (en banc).
57. 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).
59. 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.").
60. See In re Fine, 837 F.2d 1071, 1074 (Fed. Cir. 1988).
61. See In re Fine, 837 F.2d 1071, 1074 (Fed. Cir. 1988).
62. See In re Rijckaert, 9 F.3d 1531, 1532 (Fed. Cir. 1993).
63. See In re Deuel, 51 F.3d 1552 (Fed. Cir. 1995).
acid sequence of a small beginning portion of the protein. Next, Deuel chemically synthesized a single strand of DNA, known as an oligonucleotide, corresponding to this short amino acid sequence. 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. 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. These bovine sequences constituted part of the claimed invention.

In addition, Deuel used the oligonucleotide to isolate the naturally occurring human HBGF gene from the human placental cDNA library. 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. These human sequences also constituted part of the claimed invention.

The patent examiner asserted that the claimed invention would have been prima facie obvious in view of the prior art. The prior art upon which the examiner relied included a Maniatis reference describing gene cloning methods and a Bohlen reference disclosing the partial amino acid sequences of proteins composing a subclass of human and bovine HBGF. 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.

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. The examiner rejected Deuel’s “teaching away” argument, however, apparently relying on the unfounded notion that HBGF genes were homologous across species. The Board upheld the examiner’s rejection, focusing instead on the allegedly routine nature of cloning.

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.80 The court further applied precedent regarding chemical inventions that the prior art disclosure of a broad genus does not necessarily render obvious a specific compound within the genus.81 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.82 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.83

Two years later, in 1997, the Federal Circuit reached the opposite conclusion on the obviousness issue with respect to another biotechnology invention. In In re Mayne,84 the Federal Circuit affirmed the Board’s decision, which upheld the patent examiner’s final rejection of claims to proteins produced by recombinant genetic technology.85 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”).86

The Federal Circuit held that the USPTO met its burden of establishing a prima facie case of obviousness.87 The compounds, hGH and bGH, were well known.88 In addition, the prior art taught the use of fusion proteins and identified possible cleavage sites for enterokinase.89 The claimed invention recited an hGH or bGH fusion protein including a region containing an enterokinase cleavage site that was structurally similar and functionally equivalent to that taught in the cited prior art references.90 Moreover, the references suggested the interchangeability of these amino acid substitutions.91

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.92 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.93

80. See id. at 1559 (reaffirming In re Bell, 991 F.2d 781, 785 (Fed. Cir. 1993)).
81. See id. (citing with approval In re Baird, 16 F.3d 380 (Fed. Cir. 1994)).
82. See Deuel, 51 F.3d at 1558-59.
83. See id. at 1558.
84. 104 F.3d 1339 (Fed. Cir. 1997).
85. Id. at 1340.
86. See id.
87. See id. at 1343.
88. See id. at 1342.
89. See id.
90. See id. at 1342-43.
91. See In re Mayne, 104 F.3d at 1343.
92. See id.
93. See id.
However, the Federal Circuit discounted the evidence submitted in support of these assertions.94 The absence in the patent specification of comparative data or any explanation of the significance of the data appeared fatal.95

The Federal Circuit's admonishment in Deuel and Mayne regarding the respective agency and applicant burdens in a patentability context alludes to the inherent difficulty in assessing nonobviousness from the perspectives of proper timeframe and skill in the art. The susceptibility to criticism of such analytical efforts is even greater when assessing nonobviousness in an invalidity challenge. The danger of hindsight distortion is exacerbated.

In SIBIA Neurosciences, Inc. v. Cadus Pharmaceutical Corp.,96 the Federal Circuit held that the asserted patent claims were obvious as a matter of law and reversed the district court judgment.97 The technology at issue in this patent infringement suit was a cell-based screening method useful for the identification of compounds associated with signal transduction pathways.98 At trial, Cadus alleged that the asserted patent claims would have been obvious in view of the prior art, namely the Stumpo reference.99

The parties did not dispute that the Stumpo reference taught the identical recombinant cells used in the claimed methods, and their use in a transcription-based assay to detect cell surface receptor activation.100 However, the apparent purpose of the assays described in the Stumpo reference was the characterization of certain aspects of the genetic material of the recombinant cell, not drug screening to which the claimed methods were directed.101 In other words, the Stumpo reference disclosed experimental methods to study known interactions, whereas the claimed methods were designed to discover new compounds.102

In view of the jury verdict that the patent claims were not invalid for obviousness, the Federal Circuit necessarily presumed that the jury found no requisite motivation to modify the teachings of the Stumpo

94. See id. at 1343-44.
95. See id.
97. SIBIA Neurosciences, No. 99-1381, slip op. at 1.
98. See id. at 2 (describing the subject matter of U.S. Patent No. 5,401,629 and noting that the effectiveness of the claimed methods in facilitating rapid and reliable screening of large numbers of compounds for agonist and antagonist activity).
99. See id. at 6-7 (identifying the Stumpo reference as Deborah J. Stumpo et al., Identification of c-fos Sequences Involved in Induction by Insulin and Phorbol Esters, 263 J. BIOL. CHEM. 1611 (Feb. 1988)).
100. See id. at 12-13 (stating that the Stumpo reference described "recombinant cells engineered to have both a heterologous cell surface receptor and a responsive reporter gene construct").
101. See id. at 13 (establishing that the Stumpo reference disclosed transcription-based assays with insulin, which was already known to interact with the cell surface receptors of Stumpo's recombinant cells).
102. See id. ("Claim 1 of the '629 patent, on the other hand, claims a method using recombinant cells identical to Stumpo's in transcription-based assays with compounds not previously known to interact with the cell surface protein of the recombinant cell.").
The majority's focus on the known attractiveness of cells having heterologous cell surface proteins to drug screening applications arguably missed the mark as to whether one of ordinary skill in the art would have been motivated to modify the transcription-based assays of the Stumpo reference to achieve the claimed invention. The majority's position that "the Stumpo paper leads one to within a hairsbreadth of anticipation" of the patent claims perhaps colored its inquiry. The majority holding arguably suggests that evidence of a weaker motivation or suggestion to combine might suffice where the claimed invention's distinction over the prior art seems minor. Indeed, the dissent expressed vehement concern over such hindsight reconstruction.

In any event, obviousness inquiries in all technologies risk corruption from hindsight perspectives. The passage of time between patent application filing and litigation with biotechnology inventions can exacerbate the problem. The often unsettled nature of science, compounded with the natural deterioration of reliable accounts of that context, make invalidity challenges to biotechnology patents based on

103. See SIBIA Neurosciences, No. 99-1381, slip op. at 13.
104. See id.
106. See id. at 13, 18 (citing In re Rouffet, 149 F.3d 1350, 1358 (Fed. Cir. 1998), for the proposition that "the motivation to modify a reference can come from the knowledge of those skilled in the art, from the prior art reference itself, or from the nature of the problem solved").
107. See id. at 18.
108. See id. at 20 (Mayer, C.J., dissenting) ("The court is making an end-run around the requirement that there must be a motivation to modify the reference along the path taken by the '629 patent. It combines a series of references not specifically argued to the jury to conclude that no reasonable jury could possibly find the absence of motivation in the prior art to modify the Stumpo paper to render the '629 patent obvious. . . . It opens the door for accused infringers to string together a series of references, which collectively contain the elements of an apparatus (here, the cell with a heterologous cell surface protein and reporter gene construct) and various suggestions for the use of those separate references. It then would allow an inference of motivation to modify a single reference to render obvious a method claim for utilizing the apparatus." (internal citations omitted)).
109. See In re Dembicznak, 175 F.3d 994, 999 (Fed. Cir. 1999) ("Measuring a claimed invention against the standard established by [Section 103 requires the oft-difficult but critical step of casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field.").
obviousness most unpredictable, notwithstanding the statutory presumption of validity.

D. Written Description

To obtain patent protection, an inventor must set forth an adequate written description of the invention.\(^{110}\) 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.\(^{111}\) 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.\(^{112}\) 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.\(^{113}\) The adequacy of a written description is a question of fact that the Federal Circuit reviews for clear error.\(^{114}\)

In *In re Brana*,\(^{115}\) the Federal Circuit reversed the Board’s decision, 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.\(^{116}\) The subject matter of the application involved pharmaceutical compositions having anti-tumor activity in humans.\(^{117}\) In the final office action, the examiner rejected the claims of the application because the specification failed to (1) “disclose any specific disease against which the claimed compounds were useful” and (2) “establish a reasonable expectation that the claimed compounds had a practical utility.”\(^{118}\) The Board upheld the patent examiner’s rejection under Section 112, first paragraph, but stated that a rejection under Section 101 would likewise have been proper.\(^{119}\)

Regarding the examiner’s first ground for rejection, the Federal Circuit noted that the applicants had tested the claimed compounds on tumor cell lines derived from animals suffering from lymphocytic leukemias.\(^{120}\) The court thus concluded that the disclosed ameliorative activity of the claimed compounds on tumor cells constituted a proper allegation of sufficiently specific use.\(^{121}\) As for the second ground for rejection, the Federal Circuit held that the patent examiner failed to

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113. *See* id. at 1170.
115. 51 F.3d 1560 (Fed. Cir. 1995).
116. *Id.* at 1569.
117. *See* id. at 1562 (reporting the U.S. patent application at issue as Serial No. 533,944).
118. *See* id. at 1563-64.
119. *See* id. at 1564.
120. *See* id. at 1565.
121. *See In re Brana*, 51 F.3d at 1565.
satisfy the initial burden of challenging a presumptively correct assertion of utility in the disclosure. The court noted that the prior art references upon which the Board relied did not question the usefulness of any related compound as an anti-tumor agent. 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. The Federal Circuit held that even had the USPTO satisfied its initial burden, the applicants provided evidence of statistically significant animal tests sufficient to convince one skilled in the art of the invention’s asserted utility. 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 compliance, under the first paragraph of Section 112, on applicants seeking patent protection for pharmaceuticals for humans.

In In re Alton, 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. The Federal Circuit did not decide whether or not the specification contained an adequate written description. However, the court held that the patent examiner and the Board erred in dismissing a declaration submitted by the applicants concerning what one skilled in the art would have known when the patent application was filed.

The claimed technology related to an analog of human gamma interferon (“IFN-γ”). The patent specification contained twelve examples of IFN-γ analogs, but none was identical to the claimed IFN-γ analog. The closest example, Example 5, 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. The patent examiner noted this difference, stating that despite its similarity to the claimed analog, Example 5 did not constitute a description of the claimed analog.

In response, the applicants offered the declaration of Randolph Wall as evidence of what one of ordinary skill in the art would have

122. See id. at 1566.
123. See id.
124. See id.
125. See id. at 1567.
126. See id.
127. 76 F.3d 1168 (Fed. Cir. 1996).
128. Id. at 1170.
129. See id. at 1174 (“We express no opinion on the factual question of whether the specification adequately describes the subject matter of claim 70.”).
130. See id. at 1176.
131. See id. at 1170 (describing the claimed subject matter of U.S. patent application Serial No. 06/483,451).
132. See id. at 1171.
133. See In re Alton, 76 F.3d at 1171.
134. See id.
known in 1983.\textsuperscript{135} 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-\(\gamma\) to achieve the claimed analog.\textsuperscript{136} In other words, according to Dr. Wall, the skilled artisan would have interpreted Example 5 to describe the claimed analog as well, given the irrelevance of the asparagine-lysine difference.\textsuperscript{137} The patent examiner dismissed this declaration as merely an opinion stating a legal conclusion.\textsuperscript{138}

The Federal Circuit did not address whether or not Dr. Wall was correct.\textsuperscript{139} 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.\textsuperscript{140} The Federal Circuit held that the declaration, although couched in opinion terms, provided factual bases attempting to explain why one of ordinary skill in the art would construe Example 5 to cover the claimed IFN-\(\gamma\) also.\textsuperscript{141}

In \textit{Regents of the University of California v. Eli Lilly & Co.},\textsuperscript{142} 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.\textsuperscript{143} The patented technology involved human insulin produced by recombinant DNA methods.\textsuperscript{144}

The patent claims were directed to the use of human insulin cDNA, but the specification provided a written description only regarding rat insulin cDNA.\textsuperscript{145} 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.\textsuperscript{146} This disclosure provided no structural information or physical characteristics, such as a nucleotide sequence, of any of the human cDNAs in the claimed genus.\textsuperscript{147}

Absent such identification, the generic references to vertebrate or mammalian insulin cDNA were inadequate written descriptions that could not distinguish the claimed genus from others, except by function.\textsuperscript{148} The Federal Circuit stated that a proper written description of a cDNA genus, for example, might be the nucleotide sequences of a

\textsuperscript{135} See id. at 1172.
\textsuperscript{136} See id. at 1172-73.
\textsuperscript{137} See id. at 1173.
\textsuperscript{138} See id. at 1173-74.
\textsuperscript{139} See In re Alton, 76 F.3d at 1174.
\textsuperscript{140} See id. at 1176.
\textsuperscript{141} See id. at 1174-75.
\textsuperscript{142} 119 F.3d 1559, 1562 (Fed. Cir. 1997), cert. denied, 118 S. Ct. 1548 (1998).
\textsuperscript{143} Id.
\textsuperscript{144} See id. (identifying the patents-in-suit as U.S. Patents No. 4,652,525 and No. 4,431,740).
\textsuperscript{145} See id. at 1562-63.
\textsuperscript{146} See id. at 1567.
\textsuperscript{147} See id. at 1567-68.
\textsuperscript{148} See Regents, 119 F.3d at 1567-68.
representative number of cDNAs, or the recitation of structural features common to the members of the genus.\textsuperscript{149} Without more, generic references indicate only what one might achieve and provide no information about the resulting claimed material.\textsuperscript{150}

In \textit{Johns Hopkins University v. CellPro, Inc.},\textsuperscript{151} the Federal Circuit considered a case presenting a written description question but did not decide the issue of compliance.\textsuperscript{152} The claims of U.S. Patent No. 4,965,204 ("'204 patent") encompassed a broad genus of monoclonal antibodies that could bind specifically to antigens expressed on the surface of immature stem cells but not on the surface of mature cells.\textsuperscript{153} The patent disclosed only one monoclonal antibody, anti-My-10, as an embodiment of the claimed invention.\textsuperscript{154}

On appeal, CellPro contended that an application of the Federal Circuit's holding in \textit{Eli Lilly} required the conclusion that the '204 patent lacked adequate written description to support its claims.\textsuperscript{155} In \textit{Eli 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.\textsuperscript{156} 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.\textsuperscript{157} The Federal Circuit, however, never reached the merits of CellPro's \textit{Eli Lilly} argument, which the court admonished as having been raised seriously for the first time only on appeal.\textsuperscript{158}

Arguably, with no other statutory compliance issue has the Federal Circuit garnered such criticism in recent days as with its pronouncements on written description. With biotechnology subject matter involving molecular genetic information, the Federal Circuit has clearly taken an extreme position in requiring the disclosure of actual nucleotide sequences as claim support. The ideological controversy about the origins and justifications of the written description requirement aside, the Federal Circuit's holding in \textit{Eli Lilly} creates a serious question as to the continuing vitality of prophetic patent claims, certainly with respect to biotechnology inventions, if not others.

Since \textit{Eli Lilly}, the Federal Circuit seems to have opened the door to a more liberal interpretation of the written description requirement.

\textsuperscript{149} See \textit{id.} at 1568.
\textsuperscript{150} See \textit{id.}
\textsuperscript{151} 152 F.3d 1342 (Fed. Cir. 1998).
\textsuperscript{152} \textit{Id.} at 1361-62.
\textsuperscript{153} See \textit{id.} at 1347.
\textsuperscript{154} See \textit{id.}
\textsuperscript{155} See \textit{id.} at 1361.
\textsuperscript{156} See \textit{id.} (citing Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 1568 (Fed. Cir. 1997), \textit{cert. denied}, 118 S. Ct. 1548 (1998)).
\textsuperscript{157} See \textit{Johns Hopkins}, 152 F.3d at 1361.
\textsuperscript{158} See \textit{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)).
vis-à-vis the state of the relevant technology. In *Union Oil Co. of California v. Atlantic Richfield Co.*, the Federal Circuit arguably refines the written description inquiry to shift the focus of the determination away from the isolated disclosure and closer to what those skilled in the art could understand from that disclosure. Accordingly, even if the Federal Circuit were to stand firmly behind its earlier pronouncements on written description in other respects, the rapidly changing state of biotechnology should eventually alleviate the seemingly harsh results possible from the *Eli Lilly* standard alone. Following the reasoning of *Union Oil*, the disclosure of actual nucleotide sequences should not be required as claim support once the state of biotechnology advances to the point at which those skilled in the art could understand the inventor was in possession of the claimed invention at the time of the application filing, in the absence of such disclosure.

**E. Enablement**

To obtain a patent, the applicant must provide a sufficient disclosure to enable any person skilled in the art to practice the invention. 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. A party seeking to invalidate a patent based on a lack of enablement must prove such by clear and convincing evidence. Enablement is a question of law that the Federal Circuit reviews de novo. The Federal Circuit reviews the underlying facts found by a lower tribunal for clear error.

In *Enzo Biochem, Inc. v. Calgene, Inc.* the Federal Circuit considered whether broadly constructed patent claims covering the use of antisense nucleic acids to regulate gene expression in prokaryotic and

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159. Appellant refiners assert that the specification does not describe the exact chemical component of each combination that falls within the range claims of the '393 patent. However, neither the Patent Act nor the case law of this court requires such detailed disclosure. Rather, the Patent Act and this court's case law require only sufficient description to show one of skill in the refining art that the inventor possessed the claimed invention at the time of filing. *See Union Oil Co. of Cal. v. Atlantic Richfield Co.*, 208 F.3d 989, 997 (Fed. Cir. 2000) (citations omitted).

160. *Id.* "The written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." *Id.* (alterations in original) (citation omitted).


162. *See* 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).


164. *See* PPG Indus., Inc. v. Guardian Indus., Corp., 75 F.3d 1558, 1564 (Fed. Cir. 1996) (providing the court's standard of review on the enablement issue); *In re Wands*, 858 F.2d 731, 735-37 (Fed. Cir. 1988) (same); Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 1268 (Fed. Cir. 1986) (same).


166. 188 F.3d 1362 (Fed. Cir. 1999).
eukaryotic cells were invalid. The patents provided working examples limited to only one prokaryote, *Escherichia coli* ("E. coli"). The Federal Circuit affirmed the judgment of the district court that the patent claims were invalid for failure to satisfy the enablement requirement of 35 U.S.C. § 112, ¶ 1.

The patented technology related to regulation of gene expression through antisense nucleic acid. The incorporation of antisense technology in the accused Calgene FLAVR SAVR tomato permitted better control of when the fruit ripens. 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.

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. With respect to the invalidity determination, the district court held that undue experimentation would have been necessary to practice antisense technology in cells other than *E. coli*. The Federal Circuit concluded that the district court did not clearly err in its findings on this issue.

The Federal Circuit agreed with the district court's assessment that antisense was a highly unpredictable technology in 1983. In addition, the Federal Circuit recognized that the amount of experimentation required to adapt antisense technology to cells other than *E. coli* would have been quite high. 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. 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.

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167. *Id.* at 1371 (noting 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).
168. *See 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*).
169. *See id.* at 1377.
170. *See 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).
171. *See Enzo,* 188 F.3d at 1368.
172. *See id.* at 1368.
173. *See id.* at 1365 (identifying the patents-in-suit as U.S. Patents No. 5,190,931, and No. 5,208,149).
174. *See id.* at 1369.
175. *See id.* at 1372.
176. *See id.*
177. *See Enzo,* 188 F.3d at 1372.
178. *See id.* at 1372-73.
179. *See id.* at 1373.
In view of the absence of guidance, direction, or 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. Such minimal disclosure was insufficient to support the broad scope of the patent claims.

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. Genentech had sued Novo for patent infringement. The district court ruled that Genentech would likely overcome Novo's defense that Genentech's patent was invalid for lack of enablement. The Federal Circuit held that the district court erred in reaching this conclusion, and thus abused its discretion in granting Genentech's preliminary injunction motion.

The patent claims were directed to a process for cleavable fusion expression. 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. Novo argued that Genentech's patent was invalid because it failed to provide a disclosure commensurate with the scope of its claims. 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.

The Federal Circuit agreed with Novo. 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. The patent merely described several applications for which cleavable fusion expression is generally well suited, and identified trypsin and its cleavage sites. 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 the patent application.

180. See id. at 1374-75.
181. See id.
182. 108 F.3d 1361 (Fed. Cir. 1997).
183. Id. at 1362-63.
184. See id. at 1363.
185. See id.
186. See id. at 1362-63.
187. See id. at 1363 (indicating the patent-in-suit as U.S. Patent No. 5,424,199).
188. See Genentech, 108 F.3d at 1363.
189. See id. at 1365.
190. See id.
191. See id.
192. See id.
193. See id. at 1366-67.
filing to use cleavable fusion expression to make hGH without undue experimentation.\textsuperscript{194}

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.\textsuperscript{195} The court arguably viewed the evidence as irrelevant.\textsuperscript{196} 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."\textsuperscript{197}

Furthermore, the Federal Circuit embraced the fact 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.\textsuperscript{198} From this consideration, the Federal Circuit reasoned that the claimed invention was "an application of an unpredictable technology in the early stages of development."\textsuperscript{199} In such circumstances, "an enabling description in the specification must provide those skilled in the art with specific and useful teaching."\textsuperscript{200}

In \textit{Johns Hopkins University v. CellPro, Inc.},\textsuperscript{201} 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.\textsuperscript{202} 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.\textsuperscript{203} 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.\textsuperscript{204} The absence of mature cells would help minimize the risk during bone marrow transplantation of the onset of a potentially fatal condition known as Graft Versus Host Disease.\textsuperscript{205}

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 deposited under ATCC Accession No. HB-8483."\textsuperscript{206} The recited antigen would be

\begin{itemize}
  \item \textsuperscript{194} See Genentech, 108 F.3d at 1366.
  \item \textsuperscript{195} See id.
  \item \textsuperscript{196} See id. at 1366-67.
  \item \textsuperscript{197} See id. at 1367.
  \item \textsuperscript{198} See id.
  \item \textsuperscript{199} See Genentech, 108 F.3d at 1367-68.
  \item \textsuperscript{200} See id. at 1368.
  \item \textsuperscript{201} 152 F.3d 1342 (Fed. Cir. 1998).
  \item \textsuperscript{202} Id. at 1361.
  \item \textsuperscript{203} See id. at 1347.
  \item \textsuperscript{204} See id. at 1347 & n.4 (describing fluorescence-activated cell, or coating, separation).
  \item \textsuperscript{205} See id. at 1346.
  \item \textsuperscript{206} See id. at 1347 (reciting claim 1 of the '204 patent).
\end{itemize}
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.207 The '204 patent disclosed one monoclonal antibody, anti-My-10, as an embodiment of the claimed invention.208 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.209

CellPro charged that the '204 patent violated 35 U.S.C. § 112, ¶ 1 (1994), 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.210 To establish lack of enablement, CellPro carried the burden of proof at trial by clear and convincing evidence.211 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.212 The Federal Circuit agreed even when the court properly viewed the evidence in the light most favorable to CellPro, as the nonmoving party.213

The record showed that the method disclosed in the '204 patent had been used by others to produce over forty additional CD34 antibodies.214 Moreover, the preferred immunogen, namely the KG-1a cell line, described in the patent for producing the claimed monoclonal antibodies, was the same used by CellPro to make its accused 12.8 antibody.215 This notwithstanding, CellPro pointed to instances of alleged failures to obtain an anti-CD34 antibody after following the disclosed method.216

Upon scrutiny of CellPro's evidence in this regard, 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.217 In particular, the Federal Circuit noted that these specific laboratory personnel were undergraduate students with no previous experience in monoclonal antibody production.218 The Federal Circuit held that CellPro failed to establish that anyone deemed of ordinary skill in the art had encountered unsuccessful attempts in creating an anti-CD34 antibody in the described fashion.219

207. See Johns Hopkins, 152 F.3d at 1350-51.
208. See id. at 1347.
209. See id. at 1350-51 & n.13.
210. See id. at 1351-52.
211. See id. at 1359.
212. See id. at 1361.
213. See Johns Hopkins, 152 F.3d at 1359-60.
214. See id. at 1359.
215. See id.
216. See id. at 1360.
217. See id.
218. See id.
219. See Johns Hopkins, 152 F.3d at 1360.
Perhaps most importantly, the Federal Circuit discounted the testimony of CellPro's experts, which the court found lacked the required nexus between failure or difficulty in achieving the claimed antibodies and the method described in the '204 patent. One expert indicated that he did not use the screening technique disclosed in the patent specification. 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. On this point, the Federal Circuit reiterated that if it is merely routine, even a considerable amount of experimentation is not undue.

The Federal Circuit cases that focus on the enablement issue demonstrate that the court will likely conduct a closed review of the evidence presented by the parties. As such, 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 are as key in a biotechnology patent case as in any other lawsuit. Indeed, the significance to the litigation of 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, cannot be overstated.

II

The legal status of inventorship rests upon the core tenet that conception is the touchstone of invention. From the earliest cases, courts have uniformly held that an inventor is a person who conceived the patented invention. However, the relatively static nature of the patent law principles underlying inventorship belies the long-standing discontent with their practical application.

220. See id.
221. See id.
222. See id.
223. See id.
224. See Burroughs Wellcome Co. v. Barr Labs., Inc., 40 F.3d 1223, 1227-28 (Fed. Cir. 1994); Sewall v. Walters, 21 F.3d 411, 415 (Fed. Cir. 1994).
225. 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 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)).
The legal standard of conception can be considered the "formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention."

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." Of the positive indicia of inventorship, the ability to articulate the inventive concept is an important starting point. The aspects of invention and inventorship are often at the heart of patent interference proceedings before the USPTO 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. The USPTO declared an interference between the Barton patent application, the Fischoff patent application, and the Adang issued patent, the respective assignees of which were Agracetus, Monsanto, and Mycogen Plant Science, Inc. The patent applications and patent claimed methods were for expression in plants of *Bacillus thuringiensis* genes encoding insecticidal proteins.

Shortly after the declaration of the interference, Monsanto bought Agracetus, which eliminated the adversity between the Barton and Fischoff patent applications. When it notified the UPSTO of this ownership change, Monsanto asserted that good cause existed for the continuation of the interference because the content of the count was not yet firmly established. 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.

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227. See *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1376 (Fed. Cir. 1986) (quoting 1 ROBINSON ON PATENTS 532 (1890)).

228. See id. at 1378.

229. 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. 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." (internal citations omitted)).

230. 162 F.3d 1140 (Fed. Cir. 1998).

231. Id. at 1141.

232. See 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)).

233. See id.

234. See id. at 1142.

235. See id. (noting that the precise content of the count in an interference is subject to change following preliminary motions).

236. See *Barton*, 162 F.3d at 1142.
The Board issued a show cause order why judgment should not be entered against Monsanto given the commonly-owned applications.237 Monsanto responded that the indefiniteness of the count precluded a rational election between the applications.238 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 against the Barton application immediately.239 The Board granted this motion, and Monsanto appealed.240

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.241 If the final interference count were to exclude subject matter disclosed in the Barton application but not the Fischoff application, Monsanto would have lost patentable subject matter by the early dismissal of the Barton application.242 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 completion of discovery occurred.243

In Schendel v. Curtis,244 the Federal Circuit reviewed the Board's summary judgment awarding priority of invention to Curtis in a patent interference proceeding.245 The subject matter of the interference count related to a fusion protein of interleukin-3 ("IL-3") and a hematopoietin that could be granulocyte colony stimulating factor ("G-CSF") or granulocyte-macrophage colony stimulating factor ("GM-CSF").246 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.247

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.248 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.249 In particular, the absence of any

237. See id.
238. See id.
239. See id. at 1143.
240. See id.
241. See id. at 1146.
242. See Barton, 162 F.3d at 1146.
243. See id.
244. 83 F.3d 1399 (Fed. Cir. 1996).
245. Id. at 1400-01 (reporting the interference declared between U.S. patent application Serial No. 08/057,198 and U.S. Patent No. 5,073,627).
246. See id. at 1400 & n.3.
247. See id. at 1401.
248. See id. at 1404.
249. See id.
chemical composition or structural data, such as a relatively simple molecular weight determination, appeared significant to the ultimate resolution of this case.\footnote{250. See Schendel, 83 F.3d at 1404 ("[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.").}

In a patent infringement suit, the aspects of invention and inventorship can arise in an invalidity challenge or as the underlying basis to an inequitable conduct charge. In *PerSeptive Biosystems, Inc. v. Pharmacia Biotech, Inc.*,\footnote{251. No. 98-1325 (Fed. Cir. Aug. 29, 2000).} the Federal Circuit affirmed the district court's finding that the patents-in-suit were unenforceable for inequitable conduct.\footnote{252. *PerSeptive Biosystems*, No. 98-1325, slip op. at 1-2.} The patented technology related to high-speed chromatography, or separation of biological materials, of a type described by the patents as "perfusive" chromatography.\footnote{253. *Id.* at 2.}

The district court found that the named inventors were not the sole inventors of the patented subject matter.\footnote{254. *Id.* at 6-7.} The district court also concluded that they had intentionally misrepresented to the USPTO their relationship to a British company, with which they collaborated, for the purpose of concealing the issue of inventorship.\footnote{255. *Id.* at 7 (noting that PerSeptive's failure to disclose the information of its relationship with the British company could support an inequitable conduct finding, irrespective of whether the British scientists were co-inventors in fact).} The Federal Circuit agreed, holding that a full and accurate disclosure of the true nature of the relationship between PerSeptive and the British company and its scientists would have been important to a reasonable examiner's consideration of the inventorship question.\footnote{256. *Id.* at 11.}

Although the issue of inequitable conduct might be distinct in the abstract from the underlying inventorship inquiry, the considerations of materiality and intent rest on the ambiguous standards of joint inventorship. Through its holdings in cases like *PerSeptive*, the Federal Circuit arguably forces applicants into a Hobson's choice—whether to err on the side of caution by disclosing to the USPTO co-inventorship concerns to avoid inequitable conduct liability, or to follow the letter of the law and reserve such information for correction of inventorship later only if necessary. The dissent in *PerSeptive*, characterizing the majority opinion as "censorious," demonstrates the inherent susceptibility to criticism of a finding of inequitable conduct based upon questions of proper inventorship.\footnote{257. *Id.* at 14 (Newman, J., dissenting).}

As with enablement, inventorship and its related considerations require the Federal Circuit to rely heavily on the evidence presented by the parties as opposed to what the true state of the art might be from an objective perspective. Once again, documentary evidence and witness
testimony often provide the factual basis upon which the case turns. The length of time to judgment in a biotechnology patent case can begin to test the deterioration in reliability of such evidentiary materials as time marches on.

III

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

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. 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.

A literal infringement results when every limitation recited in a patent claim is present exactly in an accused product or process. A finding of infringement does not, however, require that the accused product or process embody every limitation of the claim literally. Even when a patent holder cannot prove literal infringement, a finding of infringement may be appropriate under the doctrine of equivalents.


259. 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).


261. 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) (stating that "the patentee must prove that the accused device embodies every limitation in the claim, either literally or by a substantial equivalent").

262. 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.").


265. See id.
In *Regents of the University of California v. Eli Lilly & Co.*,266 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.267 The patented technology involved recombinant genetic constructs and microorganisms that express human proinsulin.268 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.269

The applicants surrendered coverage of human proinsulin production using a fusion protein.270 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.271 The applicants amended their claims to distinguish over this prior art.272 This same action resulted in a claim interpretation that precluded a finding of literal infringement and in a prosecution history estoppel that precluded a finding of infringement under the doctrine of equivalents.273

In its nonprecedential274 disposition in *Evans Medical Ltd. v. American Cyanamid Co.*,275 the Federal Circuit affirmed the district court’s summary judgment of noninfringement.276 The patented technology involved purified *Bordetella pertussis* antigen and its use as a vaccine.277 The crux of the infringement analysis was the proper construction of the claim term, "purified."278

The Federal Circuit noted that the claim term "purified" inherently required a characterization of degree in order to be defined precisely.279 The court acknowledged that "no consensus ha[d] emerged on the plain meaning of the term to one of ordinary skill in the art."280 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.281

267. Id. at 1574.
268. See id. at 1562 (discussing U.S. Patent No. 4,431,740).
269. See id. at 1572.
270. See id. at 1573.
271. See id. at 1572-73.
272. See *Regents*, 119 F.3d at 1573.
273. See id. at 1573-74.
274. See supra note 1.
276. Id. at *1-2.
277. See id. at *2 (identifying the patents-in-suit as U.S. Patents No. 5,237,052, No. 5,438,120, and No. 5,648,080).
278. See id. at *6-7.
279. See id.
280. See id.
281. See *Evans Medical*, 1999 U.S. App. LEXIS 18436, at *14 & 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).
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 court reasoned that “other components” could not comprise more than fifty percent of the contemplated 69kD antigenic preparation as used in a vaccine.282 However, these same statements did not necessarily set a higher, upper bound on the degree of purity required.283 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 could exist.284

Patent litigation regarding biotechnology inventions can also arise in the context of interference proceedings before the USPTO.285 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.286 Even if a party chooses the district court route, the Federal Circuit is the exclusive appellate forum for any appeal in such an action.287

In Genentech, Inc. v. Chiron Corp.,288 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.289 The USPTO declared an interference between two patent applications, one assigned to Genentech and the other to Chiron.290 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.291

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.292 The Board rejected Chiron’s argument that this subject matter fell outside the scope of the interference count.293 Nevertheless, the Board

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282. See id. at *14.
283. See id.
284. See id. at *17.
286. See id. at § 146.
288. 112 F.3d 495 (Fed. Cir. 1997).
289. Id. at 496-97.
290. See id. at 497 (indicating the interference between U.S. patent applications Serial No. 06/506,078 and No. 06/922,199).
291. See 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”).
292. See id. at 497-98.
293. See id. at 498.
awarded priority of invention to Chiron based on its determination that Genentech failed to prove any practical, therapeutic utility of its fusion protein.294

Genentech appealed the Board’s decision by filing a civil action in district court.295 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.296 The district court granted this motion and, thus, affirmed the Board’s award of priority on different grounds.297

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.298 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.299 Furthermore, the district court applied a common dictionary definition of the count term “joined” instead of one tailored to the biotechnical discipline.300

The Federal Circuit noted that the interference count specifically defined a DNA construct, not the protein that is produced by expression from the construct.301 The count specified that the recited DNA construct included a DNA sequence coding for the secretory leader, a processing signal sequence, and hIGF-I.302 No dispute existed that the Genentech DNA construct contained the complete DNA sequences for these three proteins.303 The issue, therefore, was whether the addition of nine additional 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 count.304 The Federal Circuit reasoned that this depended upon the interpretation of the count phrase “joined in proper reading frame.”305

The Federal Circuit concluded that a proper construction of the phrase “in proper reading frame” meant that the nucleotides must be

294. See Genentech, 112 F.3d at 498.
295. See id.
296. See id.
297. See id. at 498-99.
298. See id. at 499.
299. See id. at 499-500.
300. See Genentech, 112 F.3d at 499-500.
301. See id. at 501 (“Although a close relationship exists between a DNA construct and the protein it encodes, the two are not equal.”).
302. See id.
303. See id.
304. See id.
305. See id.
read in such a way that the seventy amino acids of hIGF-I are incorporated in the proper sequence in the expressed protein. 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. The Federal Circuit further noted that such an interpretation of the count was consistent with the open-ended term “comprising.”

In addition, the Federal Circuit determined that the 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. 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. The Federal Circuit held that when viewed properly through the broadest, reasonable interpretation, the count did not necessitate a direct joining or connection.

In another appeal from the same case, the Federal Circuit in Genentech, Inc. v. Chiron Corp., reversed the district court’s judgment following a bench trial that awarded priority of invention to Genentech. The district court action followed the award of priority of invention to Chiron in an interference relating to recombinant production of hIGF-I. The Federal Circuit held that Genentech failed to establish that the inventors on its application reduced their invention to practice prior to the earlier effective filing date of the Chiron application, based on the conclusion that a non-inventor’s recognition of the utility of the invention of the Genentech application did not inure to the benefit of the inventors.

The district court determined that the Genentech inventors did not understand the positive radioreceptor assay (“RRA”) test results to demonstrate the practical utility of the fusion protein. The Federal Circuit held that the district court’s conclusion was not clearly erroneous. In addition, the Federal Circuit concluded that the

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306. See Genentech, 112 F.3d at 499-500.
307. See id.
308. See id. (“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.).
309. See id.
310. See id.
311. See id.
313. Genentech, No. 99-1506, slip op. at 1-2.
314. See id. at 2.
315. See id.
316. See id. at 15 (“In order to establish an actual reduction to practice, the inventor must prove that: (1) he constructed an embodiment . . . that met all the limitations of the interference count, and (2) he determined that the invention would work for its intended purpose. When testing is necessary to establish utility, there must be recognition and appreciation that the tests were successful for reduction to practice to occur.”) (internal citations omitted)).
317. See id. at 15-16.
uncommunicated recognition of the growth-promoting activity of the fusion protein by the non-inventor scientist who performed the RRA tests did not inure to Genentech's benefit.318

In contrast to those involving other technologies, biotechnology patent cases appear relatively fewer in number, perhaps indicative at least in part, of the otherwise successful navigation of patented waters by biotechnology industry members without resort to costly litigation. In any event, the stare decisis effect of such cases, notwithstanding the limited database of biotechnology patent decisions, makes it difficult to extrapolate meaningful trends with respect to the Federal Circuit's treatment of litigants in this field of technological endeavor. Indeed, the relative infrequency of such cases, coupled with the rapidly changing state of the biotechnology arts, leaves little by way of comfort from predictability. The factual predicates of these decisions arguably vary too dramatically to facilitate reliable prognostication about the application of existing patent law to the circumstances of a particular biotechnology patent case.

If anything can be said confidently of past Federal Circuit cases dealing with biotechnology inventions, it is the importance of the factual records developed with each particular case. To the extent it recognizes the existence of a gap between the evidentiary foundation and the true state of the art from a scientific perspective, the Federal Circuit has appeared content limiting itself to record considerations.

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 the patent application filing, the technical underpinnings of a Federal Circuit decision on 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

318. See id. at 18 ("[A]t least three requirements... must be met before a non-inventor's recognition of the utility of an invention can inure to the benefit of the inventor. First, the inventor must have conceived of the invention. Second, the inventor must have had an expectation that the embodiment tested would work for the intended purpose of the invention. Third, the inventor must have submitted the embodiment for testing for the intended purpose of the invention.")
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.

Lastly, 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.