NUCLEOTIDE SEQUENCES AND RECOMBINANT TECHNOLOGIES: TRENDS IN THE APPLICATION OF THE WRITTEN DESCRIPTION REQUIREMENT TO INVENTIONS FROM THE BIOTECHNOLOGY INDUSTRY

Scott D. Locke[*]

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[*] Scott D. Locke (A.B., biology, Brown University; J.D., University of Pennsylvania) is a partner at the law firm of Kalow & Springut LLP. Mr. Locke is a registered patent attorney whose practice includes patent prosecution, licensing and litigation, as well as client counseling on the protection, licensing and enforcement of other intellectual property rights.

I. INTRODUCTION

As the biotechnology industry moves from its golden age to its platinum era, members of the public will increasingly look to that industry for revolutionary improvements to their lives. In response, hopefully the best and the brightest of our researchers will continue to probe the genome; study cells; fold, unfold and refold proteins; apply bioinformatics techniques; and advance recombinant technologies. However, in order for society to continue to attract a critical mass of the highest caliber innovators, it must provide incentives. In today's world, among the greatest incentives is the possibility to obtain strong patent rights.

The use of patents to incentivize development is nothing new, and recognizing its importance to a growing nation, the Founding Fathers placed in the U.S. Constitution, among the enumerated powers of Congress, that of creating a patent system.[1] Unique among the powers that the Constitution grants to Congress, this power not only provides Congress with the authority to create the patent system, but it also explicitly gives Congress the authority to use a specific type of incentive, an exclusive right.[2]

In the implementation of the patent system, Congress has required a *quid pro quo*: an inventor may obtain patent rights only if the inventor sufficiently discloses his or her invention to the public.[3] These exclusive rights exist for only a limited time,[4]

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[1] U.S. CONST. art. I, § 8, cl. 8 ("To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries . . . .").

[2] *Id.*; *see* Edward C. Walterscheid, *To Promote the Progress of Science and Useful Arts: The Anatomy of a Congressional Power*, 43 IDEA 1, 7 (2002) (quoting U.S. CONST. art. I, § 8, cl. 8) ("[T]here is a tendency to forget that this power is unique among the congressional powers set forth in the Constitution in that it alone specifies a particular mode for exercising the general power, i.e., 'by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries.'").

[3] 35 U.S.C. § 112 (2006), *amended by* Leahy-Smith America Invents Act, Pub. L. No. 112-29, § 4(c), (e), 125 Stat. 284, 296–97 (2011); Capon v. Eshhar, 418 F.3d 1349, 1357 (Fed. Cir. 2005) ("The written description requirement thus satisfies the policy premises of the law, whereby the inventor's technical/scientific advance is added to the body of knowledge, as consideration for the grant of patent exclusivity."); *see also* Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, 1, "Written Description" Requirement, 66 Fed. Reg. 1,099, 1,104 (Jan. 5, 2001) ("The written description requirement of the Patent Act promotes the progress of the useful arts by ensuring that patentees adequately describe their inventions in their patent

and during that time of exclusivity, the public benefits from the patent disclosure's contribution to the world's collective knowledge, upon which new ideas can grow.[5] Moreover, during the life of the patent, anyone can develop improvements to the invention, so long as he or she compensates the patent owner for any activity that is within the patent claims, and anyone can use the ideas disclosed in the patent as suggestions for how to design around what is claimed.[6] After expiration of the patent, the public is free to make and to use the claimed invention (provided that the user of these rights does not infringe anyone else's patent rights or other intellectual property rights).[7]

specifications in exchange for the right to exclude others from practicing the invention for the duration of the patent's term."). The invention itself must also be patentable, that is, new, not obvious, useful, and directed to statutory subject matter. 35 U.S.C. § 101 (2006); 35 U.S.C. §§ 102–03 (2006), *amended by* America Invents Act § 3(b)(1), (c), (n). However, the present article focuses only on the written description requirement for obtaining a patent, and not the patentability of the underlying invention.

[4] 35 U.S.C.A. § 154(a)(2) (West, Westlaw through P.L. 112-54 (excluding P.L. 112-40) approved 11/12/11) (stating that for utility patents, the period is defined as expiring twenty years from the earliest effective filing date). This term may be adjusted due to Patent Office delays, but it is offset by any applicant delay. *Id.* § 154(b)(1)(A), (2)(C). Additionally, for patents that issue off of applications that were filed before June 8, 1995, the term may be measured by a seventeen year period that starts on the day of issuance, if that period is longer than the period that would be measured as twenty years from the earliest effective filing date. *Id.* § 154(c)(1); Changes to Implement 20-Year Patent Term and Provisional Applications, 60 Fed. Reg. 20,195 (Apr. 25, 1995).

[5] State Indus., Inc. v. A.O. Smith Corp., 751 F.2d 1226, 1235–36 (Fed. Cir. 1985) (illustrating how the patent system encourages innovation and competition by forcing inventors to "'design around'" patented inventions); Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, 1, "Written Description" Requirement, 66 Fed. Reg. 1,099, 1,104 (Jan. 5, 2001); *see* Walterscheid, *supra* note 2, at 42–43; Brent Rabowsky, Note, *Recovery of Lost Profits on Unpatented Products in Patent Infringement Cases*, 70 S. CAL. L. REV. 281, 311–12 (1996) ("[T]he ultimate goal of the patent system is to encourage the introduction of new products and manufacturing processes into the economy—in other words, the commercialization of inventions.").

[6] I A.O. Smith Corp., 751 F.2d 1336 (describing the "design around" feature of patent law as one that encourages innovation); Rabowsky, *supra* note 5, at 317 (noting that the potential liability for damages may thwart competitors from designing improvements).

[7] Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225, 230–31 (1964) ("[W]hen the patent expires the monopoly created by it expires, too, and the right to make the article—including the right to make it in precisely the shape it carried when patented—passes to the public."); *see* David Silverstein, *Will Pre-Grant Patent Publication Undermine United States Trade Secret Law?*, 23 AIPLA Q.J. 695, 707 (1995) (examining the Federal preemption of State laws that have attempted to extend the life of patents and trade secrets).

The tradeoff is sound in concept. Unfortunately, determining the level of detail of disclosure necessary to entitle one to a requested scope of a patent right, and the appropriate scope of that right, is not an exact science. One of the ways in which the sufficiency of a disclosure is measured is compliance with the written description requirement, which mandates that in order to obtain patent rights, an inventor must adequately disclose his or her invention.[8]

In theory this requirement should not vary by technology area. However, practitioners who prosecute patent applications across many different areas, as well as commentators, have been heard to complain of a heightened written description requirement (as well as a heightened enablement requirement) for inventions that arise out of the biotechnology industry.[9] This perceived heightened standard, if it is indeed heightened, may have been created by courts' perceptions of the level "of ordinary skill in the art," and the degree of unpredictability of biotechnology during the early years in which the patents were litigated.[10] Regardless of whether there is a heightened standard or merely the perception of a heightened standard, the overeager patent applicant who does not appreciate the level of detail necessary to comply with his or her end of the bargain for patent rights may be surprised to find himself or herself on the receiving end of rejections from the Patent Office that are difficult to overcome or find himself or herself defending invalidity challenges in court. This article presents a survey of the written description requirement as applied to the biotechnology industry over the past two decades.

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[8] *See* 35 U.S.C. § 112 (2006), *amended by* America Invents Act § 4(c), (e), 125 Stat. 284; Manual of Patent Examining Procedure § 2163[I] at 2100-172 (8th ed. Rev. 6, Sept. 2007) ("'[T]he 'essential goal' of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed.' Another objective is to put the public in possession of what the applicant claims as the invention.") [hereinafter MPEP]; *Written Description—Little Used Perhaps, but Extremely Useful to Ensure Claims are Appropriately Scoped*, USPTO (May 5, 2010), http:/www.uspto.gov/blog/director/entry/written_description_little_used_perhaps. ("[T]he written description requirement is an essential 'backstop' against overclaiming.").

[9] Jeffie A. Kopczynski, *A New Era for § 112? Exploring Recent Developments in the Written Description Requirement as Applied to Biotechnology Inventions*, 16 HARV. J.L. & TECH. 229, 262 (2002) (examining the history of the more stringent written description requirements for biotechnology).

[10] *See id.* at 240–41.

II. DISCUSSION

Section 112, paragraph one, of title 35 of the U.S. Code provides that in a patent application:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.[11]

Out of this language arises the written description requirement, as well as the enablement requirement.[12] The written description requirement dictates that an applicant for a patent shall reasonably convey to the artisan that at the time of filing the patent application the inventor had possession of the claimed subject matter.[13] The requirement is intended to prevent an applicant from obtaining a patent before he or she has invented what he or she claims, thereby precluding the award of patents based on wish lists, and to prevent an applicant from receiving a broader patent claim than to which the inventor should be entitled, that is, obtaining a patent on what the inventor did not invent.[14]

Whether a patent applicant has complied with the written description requirement is determined by comparing the claims

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[11] 35 U.S.C. § 112 (2006), *amended by* America Invents Act § 4(c), (e).

[12] *See* Ariad Pharm., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1351 (Fed. Cir. 2010) ("Since its inception this court has consistently held that § 112, first paragraph, contains a written description requirement separate from enablement . . . ."); Kopczynski, *supra* note 9, at 232–35.

[13] Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, 1, "Written Description" Requirement, 66 Fed. Reg. 1,099, 1,104 (Jan. 5, 2001); Capon v. Eshhar, 418 F.3d 1349, 1357 (Fed. Cir. 2005); Regents of the Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1566 (Fed. Cir. 1997) (quoting Lockwood v. Am. Airlines, Inc., 107 F.3d 1565, 1572 (Fed. Cir. 1997)) ("To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that 'the inventor invented the claimed invention.'").

[14] *See In re* Katz Interactive Call Processing Patent Litig., 639 F.3d 1303, 1319 (quoting Reiffin v. Microsoft Corp., 214 F.3d 1342, 1345 (Fed. Cir. 2000)) ("The purpose of the written description requirement 'is to ensure that the scope of the right to exclude, as set forth in the claims, does not overreach the scope of the inventor's contribution to the field of art as described in the patent specification.'"); *In re* Skvorecz, 580 F.3d 1262, 1269 (Fed. Cir. 2009) ("A purpose of the written description requirement is to provide the public with knowledge of the patented technology, thereby to advance the useful arts.").

to the patent application as originally filed.[15] The specification need not "recite the claimed invention *ín haec verba,*" but if the written description requirement is going to be deemed satisfied, then the specification must not "merely render[] the invention obvious."[16] Unfortunately, the recognition of the scope of what the inventor actually invented, and the determination of when the inventor has sufficiently gone down the road of invention, is not always easy to ascertain. Although one could imagine a standard by which, in order to obtain a patent, the written description requirement demands that there be working examples commensurate in scope with the claimed subject matter, or that there be actual reduction to practice, or in the case of biological macromolecules, that there be a recitation of a structure—none of these are the case under U.S. patent law.[17]

With respect to the application of the written description requirement to biotechnology inventions that are directed to genetic sequences and recombinant technologies, the courts and the U.S. Patent and Trademark Office (PTO) have confronted two primary issues: (i) filings before the complete sequences of proteins, RNA or DNA, have been determined, instead claiming compounds by reference to other identifying characteristics; and (ii) claims to genuses of sequences or recombinant molecules or constructs when fewer than all of the members of the genus have been disclosed.[18] Each of these issues is described below.

A. Filings Before a Molecule is Sequenced

Today, sequencing an oligonucleotide is common and, in large

[15] Janice M. Mueller, *The Evolving Application of the Written Description Requirement to Biotechnological Inventions*, 13 BERKELEY TECH. L.J. 615, 621 (1998).

[16] *Ariad*, 598 F.3d at 1352. The asymmetry between the non-obviousness requirement and the written description requirement underscores that the primary purpose of the patent system is to benefit the public and not to reward the inventor. *See id.* at 1353.

[17] Falko-Gunter Falkner v. Inglis, 448 F.3d 1357, 1366–67 (Fed. Cir. 2006) ("[W]e hold, in accordance with our prior case law, that (1) examples are not necessary to support the adequacy of a written description (2) the written description standard may be met (as it is here) even where actual reduction to practice of an invention is absent; and (3) there is no *per se* rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure.").

[18] *See* Kopczynski, *supra* note 9, at 242–51.

part, automated.[19] Therefore, to include one or more sequences in a patent application typically is not difficult if an inventor can isolate it.[20] However, before the sequencing of polynucleotides became fully automated, the Court of Appeals for the Federal Circuit (CAFC) confronted the issue of what level of detail was needed to entitle an applicant to patent rights that are directed to proteins, oligonucleotides, or polynucleotides.[21] In these cases, the claims were often drafted with reference to one or more other characteristics of a molecule rather than to a sequence itself.[22]

The issue of how to apply the written description requirement to a patent claim directed to a protein or an oligonucleotide when an amino acid or nucleotide sequence is not disclosed in a patent application became of the utmost concern to the biotechnology industry in the 1980s and 1990s.[23] During this period, a number of applicants, many of whom might have been competitors of one another, raced to the PTO before fully sequencing their molecules.[24] As one can imagine, there were numerous possible

[19] *See* Andrew Chin, *Artful Prior Art and the Quality of DNA Patents*, 57 ALA. L. REV. 975, 983 (2006).

[20] *See id.* at 1036–38 (showing that automation is the commonly used process for the sequencing of molecules and it has become efficient enough not to require purification for relatively long strands); Arti K. Rai, *Engaging Facts and Policy: A Multi-Institutional Approach to Patent System Reform*, 103 COLUM. L. REV. 1035, 1070–72 (2003) (illustrating the ease by which molecules can be sequenced when using an automated system).

[21] *See* Invitrogen Corp. v. Clontech Labs., Inc., 429 F.3d 1052, 1071–74 (Fed. Cir. 2005); Regents of the Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1566–69 (Fed. Cir. 1997); Fiers v. Revel, 984 F.2d 1164, 1170–71 (Fed. Cir. 1993).

[22] *See Invitrogen*, 429 F.3d at 1071–74; *Regents*, 119 F.3d at 1562–63, 1566–69; *Fiers*, 984 F.2d at 1167–71.

[23] *See Invitrogen*, 429 F.3d at 1057–60, 1071–74; *Regents*, 119 F.3d at 1562–63, 1566–69; *Fiers*, 984 F.2d at 1166–71; U.S. Dep't of Energy Genome Programs, *Genetics and Patenting,* HUMAN GENOME PROJECT INFORMATION, http://www.ornl.gov/sci/techresources/Human_Genome/elsi/patents.shtml (last modified July 7, 2010) (main site: http://genomics.energy.gov) [hereinafter *Genetics and Patenting*].

[24] *Genetics and Patenting, supra* note 23. Although under the U.S. patent system, currently rights are awarded to the inventor who is "first to invent," most of the world relies on a "first to file" principle, that is, when two inventors file patent applications for the same invention, if the invention is otherwise patentable, the inventor who filed first will be the party to receive patent rights, regardless of who invented it first. *See* Paul M. Schoenhard, *Reconceptualizing Inventive Conception: Strengthening, Not Abandoning the First-To-Invent System*, 17 FED. CIR. B.J. 567, 572–73 (2008). Therefore, if an inventor wishes to obtain patent rights outside of the United States, winning the race to the PTO can be important. *See id.* Moreover, during certain time periods, reduction to practice prior to filing of an application could only be shown in reference to

filing strategies that might have been considered by early applicants, including filing wish lists with no sequences but describing other unifying features, filing an application with only portions of sequences, or waiting to file until complete sequences were known.[25] More than a decade after applicants in the biotechnology field started to file these types of patent applications, the CAFC set a standard that prevented many filers from obtaining broad patents and permitted the invalidation of patents that had issued with claims to sequences when the respective specification did not show that at the time of invention the inventors had the claimed molecules sufficiently within their possession.[26]

In 1993, in *Fiers v. Revel*, the CAFC confronted the issue of how to apply the written description requirement to polynucleotides when no sequences were disclosed.[27] In that case, the court held, "[a]n adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself."[28] Thus, the CAFC was explicit that wish lists of sequences could not be patented.

The court also cautioned: "Claiming all DNA's that achieve a result without defining what means will do so is not in compliance with the description requirement; it is an attempt to preempt the future before it has arrived."[29] Thus, although the CAFC did not mandate disclosure of a claimed oligonucleotide sequence, as a practical matter, it warned inventors not to file too soon: the inventors must have invented and not merely identified what they wanted to invent.[30]

Conversely, the CAFC has also consistently held that there is

activity in the United States. *See id.* at 573. Additionally, beginning with patent applications that have an effective date of March 16, 2013 or later, the PTO will apply a first to file standard. America Invents Act § 3(n)(1).

[25] *See Invitrogen*, 429 F.3d at 1057–60, 1071–74*; Regents of the Univ. of Cal.*, 119 F.3d at 1562–63, 1566–69; *Fiers*, 984 F.2d at 1166–71.12

[26] *See Fiers*, 984 F.2d at 1170–71; William C. Mull, Note, *Using the Written Description Requirement to Limit Broad Patent Scope, Allow Competition, and Encourage Innovation in Biotechnology*, 14 HEALTH MATRIX 393, 394–97, 403–06, 415–16 (2004).

[27] *Fiers*, 984 F.2d at 1170–71.

[28] *Id.* at 1170.

[29] *Id.* at 1171.

[30] *See id.* at 1169, 1171–72.

an avenue for identifying a nucleotide sequence without setting forth the sequence itself:

> To satisfy the written description requirement of 35 U.S.C. § 112 for inventions pertaining to DNA, a patent must provide "sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, *functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics*."[31]

Between the guideposts of precluding patent claims based on wish lists and allowing claims defined by properties of a sequence, the CAFC has set the stage for highly technical and case-specific factual issues to be addressed by the PTO and the lower courts.

Further complicating matters, one must be mindful that the written description requirement is to be considered in the context of the relevant state of the art.[32] For example, although at one time the disclosure of an amino acid sequence was held not to satisfy the written description requirement for a DNA sequence,[33] the CAFC has more recently—and correctly—taken the position that "the state of the art has developed such that the complete amino acid sequence of a protein may put one in possession of the

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[31] Monsanto Co. v. Scruggs, 459 F.3d 1328, 1336 (Fed. Cir. 2006) (emphasis in original) (quoting Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 964 (Fed. Cir. 2002)). The CAFC has also elaborated and recognized that:

> Given the sequence of a single strand of DNA or RNA, it may therefore have become a routine matter to envision the precise sequence of a "complementary" strand that will bind to it. Therefore, disclosure of a DNA sequence might support a claim to the complementary molecules that can hybridize to it.

Univ. of Rochester v. G.D. Searle & Co., Inc., 358 F.3d 916, 925 (Fed. Cir. 2004). The MPEP also states that:

> [I]f an applicant disclosed an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid sequences that encoded the amino acid sequence. Since the genetic code is widely known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence, but not necessarily any particular species.

MPEP, *supra* note 8, § 2163 at 2100-183.

[32] 35 U.S.C. § 112 (2006), *amended by* America Invents Act § 4(c), (e); *see* Patrick Brian Giles, *How to Claim a Gene: Application of the Patent Disclosure Requirements to Genetic Sequences*, 27 GA. ST. U. L. REV. 695, 710–12 (2011).

[33] *See in re* Deuel, 51 F.3d 1552, 1558–59 (Fed. Cir. 1995).

genus of DNA sequences encoding it."[34]

Below is a review of both the early application of the written description requirement to inventions arising out of the biotechnology industry and the evolution of the doctrine. Then discussion turns to the application of the written description requirement in specific circumstances, including: to specific issues in tissue culture cases, in cases with methods for using oligonucleotides, as related to antibody inventions, and in cases related to chimeric genes and mutant viruses.

1. The Early Standard and Its Evolution

The filing of a patent application directed to nucleotide sequences dates at least as far back as the late 1970s. *Fiers v. Revel*, which is one of the earliest appellate cases to apply the written description requirement to claims directed to nucleotide sequences, arose in the context of a three-way interference in which the parties filed priority applications in 1979 and 1980.[35] The interference involved the following lone count: "A DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide."[36]

One of the parties, Sugano, in his priority application disclosed both the "complete nucleotide sequence of a DNA" that coded for beta-interferon and a method for isolating it.[37] A second party, Revel, in his priority application disclosed a method for isolating a fragment of DNA coding for beta-interferon and a method for isolating mRNA coding for beta-interferon but not the complete DNA sequence.[38] The third party, Fiers, also included the complete DNA sequence in his priority application.[39] Fiers asserted that he was entitled to priority of an even earlier date because two American scientists to whom Fiers had disclosed his ideas outside of the U.S., disclosed them in the U.S.[40] Applying the written description requirement to Revel's priority document,

[34] *In re* Wallach, 378 F.3d 1330, 1333 (Fed. Cir. 2004).
[35] *Fiers*, 984 F.2d at 1166–67, 1170.
[36] *Id.* at 1166.
[37] *Id.* at 1166–67 & n.4.
[38] *Id.* at 1170–71.
[39] *Id.* at 1168.
[40] *Id.* at 1167. At the time, evidence of conception and reduction could only be submitted if the evidence reflected activity that occurred in the United States. *See id.* at 1167–68 ("The Board held that Fiers failed to establish conception in the United States prior to his April 3, 1980 British filing date.").

the CAFC deemed Revel's disclosure inadequate, emphasizing, "A bare reference to a DNA with a statement that it can be obtained by reverse transcription is not a description; it does not indicate that Revel was in possession of the DNA."[41] Thus, the CAFC held that Revel had not sufficiently described that molecule to demonstrate that it was within his possession.[42]

Fiers is important for its place in the history of patent jurisprudence, because it set the written description bar relatively high and presented a hurdle for early patent applicants to overcome when seeking patent protection. But one should note that the actual inventions that were the subject of *Fiers* were invented over thirty years ago, and from a technical perspective, this hurdle has become easier to overcome.

In re Wallach,[43] which was decided more than ten years after *Fiers,* presents a more recent example of how the CAFC looks at claims to nucleotides in the absence of full disclosure of them.[44] In that case, the inventors had claimed a DNA sequence by reference to a partial amino acid sequence of a protein and the function of that protein.[45] In a family member application, the PTO had allowed claims to the protein, though those claims were the subject of an interference proceeding.[46] Those claims were

[41] *Id.* at 1170–71. It is also worth contrasting *Fiers* with the more recent case *Scripps Research Institute v. Genentech, Inc.*, which is another interference case. In *Scripps*, the count at issue was "[a] composition comprising an aqueous solution of human tissue factor heavy chain protein wherein said protein is soluble and has an amino acid residue sequence represented by FIG. 1 [a sequence 295 amino acids long] from position 1 to position 219." Scripps Research Inst. v. Genentech, Inc., No. 150, 135, 2005 Pat. App. LEXIS 19, *3 (B.P.A.I., Feb. 28, 2005). In *Scripps*, Genentech had disclosed residues 1 through 263 in the application and "identifie[d] one aspect of the invention as directed to hTF derivatives, in particular derivatives lacking the signal sequence and the hydrophobic or transmembrane portion of the protein near the C-terminal of the protein." *Id.* at *14. During the interference, Genentech presented a declaration that asserted that a person of ordinary skill "would have understood the descriptions of deletion of the transmembrane region . . . to include tissue factor proteins [in] which the entire C-terminal region . . . had been deleted." *Id.* at *16. Accordingly, although the specification did not explicitly recite residues 1 to 219, the specification was deemed to provide an adequate written description for that fragment. *See id.* at *19.

[42] *Fiers*, 984 F.2d at 1170–71.

[43] 378 F.3d 1330 (Fed. Cir. 2004).

[44] *Id.* at 1334–35. The fact pattern of *In re Wallach* is now part of the PTO's Written Description Training Materials. USPTO, WRITTEN DESCRIPTION TRAINING MATERIALS 17 (2008).

[45] *In re Wallach*, 378 F.3d. at 1331–32.

[46] *Id.* at 1332.

defined by a partial amino acid sequence and the function of the protein.[47]

In the case at issue, the applicants made a two-part argument before the CAFC to demonstrate that they had complied with the written description requirement. First, the applicants argued that the disclosure of the partial amino acid sequence and of the function provided an adequate written description for the protein. Second, they argued that the protein provided the adequate written description for the DNA.[48] The CAFC agreed with the second point, stating that "the state of the art has developed such that the complete amino acid sequence of a protein may put one in possession of the genus of DNA sequences encoding it,"[49] but glossed over the first point ~~one~~, holding: "Until Appellants obtained the complete amino acid sequence of TBP-II, they had no more than a wish to know the identity of the DNA encoding it."[50] Thus, the applicants had filed their patent application too soon.

In re Wallach is significant because it recognized the changing level of skill in the art, while still requiring a disclosure of an amino acid sequence from which to extrapolate a nucleotide sequence.[51] It reemphasizes the implicit recommendation of *Fiers,* if one can provide a sequence then she should do so.

2. Tissue Culture Cases

In addition to recommending, though not mandating, the disclosure of sequences, the CAFC has addressed other ways to satisfy the written description requirement. One important line of cases involves tissue cultures. In *Enzo Biochem Inc. v. Gen-Probe Inc.,*[52] the patent at issue was directed to "nucleic acid probes that selectively hybridize[d] to the genetic material of the bacteria that cause gonorrhea, *Neisseria gonorrhoeae*."[53] Enzo had derived "three . . . sequences that preferentially hybridized to six common strains of *N. gonorrhoeae* over six common strains of

[47] *Id.* at 1332–33.

[48] *Id.*

[49] *Id.* at 1333.

[50] *Id.* at 1335. The CAFC takes an artificial position when it argues "possession of the protein says nothing about whether they were in possession of the protein's amino acid sequence." *Id.* at 1334.

[51] *Id.* at 1335.

[52] 323 F.3d 956 (Fed. Cir. 2002).

[53] *Id.* at 960.

N. meningitidis. . . . Enzo deposited those [strains] in the form of a recombinant DNA molecule within an *E. coli* bacterial host at the American Type Culture Collection."[54] The broadest claim was directed to a composition of matter that was defined by its differential hybridization to chromosomal DNA of *Neisseria gonorrhoeae* as compared to chromosomal DNA of *Neisseria meningitis* as measured by a specific protocol.[55]

In analyzing the issue of whether the claims complied with the written description requirement, the CAFC took judicial notice of the PTO guidelines "that the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . *i.e.*, complete or partial structure, other physical and/or chemical properties, *functional characteristics when coupled with a known or disclosed correlation between function and structure*, or some combination of such characteristics.'" [56] The CAFC then tackled the issue of whether reference in a specification to a deposit in a public depository that makes its contents accessible to the public constitutes an adequate written description requirement, and the CAFC answered in the affirmative.[57] In response to what it characterized as a question of first impression, the CAFC held that "reference in the specification to a deposit in a public depository, [that] makes its contents accessible to the public when it is not otherwise available [satisfies] . . . the written description requirement."[58]

3. Method Cases

Although the human genome has been sequenced, and obtaining and including a sequence in a specification is common, a number of cases may still be pending in the PTO or the courts

[54] *Id.* at 961.

[55] *Id.* at 961–62, 974.

[56] *Id.* at 964 (alteration in original) (emphasis in original) (quoting Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, 1, "Written Description" Requirement, 66 Fed. Reg. 1,099, 1,106 (Jan. 5, 2001)).

[57] *Id.* at 964–65. However, the claims at issue were also directed to mutated versions of those sequences. Accordingly, the CAFC remanded the case on the issue of whether the particular claims satisfied the written description requirement. *Id.* at 966. *See* Monsanto Co. v. Scruggs, 459 F.3d 1328, 1337 (Fed. Cir. 2006) (reaffirming the recognized law that where a patent incorporates by reference deposits with the American Type Culture Center, the written description requirement will be satisfied).

[58] *Enzo*, 323 F.3d at 964–65.

in which there are no complete nucleotide sequences disclosed. Recently, the CAFC has confronted this issuee when the subject patents have method claims.

In *Ariad Pharmaceuticals, Inc. v. Eli Lilly & Co.,*[59] the CAFC addressed the written description requirement in the context of a challenge to patent claims that were directed to gene regulation through the control of the transcription factor NF-kB.[60] The challenged claims were directed to methods that comprised the step of reducing NF-kB activity.[61]

In response to a charge of patent infringement, Lilly alleged that the claimed methods were not supported by the specification and did not comply with the written description requirement because the specification did not "adequately disclose how the claimed reduction of NF-kB [was] achieved."[62] The specification "hypothesiz[ed] three classes of molecules [that were] potentially capable of reducing NF-kB activity:" decoy, dominantly interfering, and specific inhibitor molecules.[63] Lilly asserted that this "amount[ed] to little more than a research plan."[64] In response, Ariad argued that because the claim did not contain terms that recited specific molecules, it was entitled to patent rights directed to the claimed methods.[65]

The CAFC sided with Lilly, emphasizing that in order to comply with the written description requirement, the specification needed to "demonstrate that Ariad possessed the claimed [molecules] by sufficiently disclosing molecules capable of reducing NF-kB activity."[66] There was only one example of a specific inhibitor, and it merely held NF-kB in an inactive state until certain external influences were received.[67] Additionally, there were no examples of dominantly interfering molecules,[68] and although decoy molecules were disclosed, there was no description of a link between the decoy molecules and reducing the NF-kB activity.[69] Thus, because "the specification at best

[59] 598 F.3d 1336 (Fed. Cir. 2010).
[60] *Id.* at 1340.
[61] *Id.* at 1340–41.
[62] *Id.* at 1354.
[63] *Id.*
[64] *Id.*
[65] *Id.*
[66] *Id.* at 1354–55.
[67] *Id.* at 1356.
[68] *Id.* at 1356–57.
[69] *Id.*

described decoy molecule structures and a hypothesis with no accompanying description that they could be used to reduce NF-KB activity" the CAFC held the claims invalid for failing to comply with the written description requirement.[70] The absence of disclosure of any molecules for use in connection with the claimed invention meant that the application did not show that the inventors were in possession of what was claimed.[71]

In a second recent case, the CAFC relied heavily on *Fiers* when upholding a finding of invalidity of patent claims directed to methods of identifying humans predisposed to a genetic disorder by detecting a mutation of a gene. In *Billups-Rothenberg, Inc. v. Associated Regional and University Pathologists, Inc.*,[72] the patentee's claimed methods were directed to detecting a predisposition to hemochromatosis.[73] The claims recited detection of a mutation and the result of the mutation.[74] However, the specification failed to disclose the sequence of the gene or any specific mutations that would result in the disorder.[75] The specification did disclose "a [three-hundred] base pair region of a defined exon," and the patent holder took the position that given the state of the knowledge in the art, by defining the range there was sufficient description in the specification.[76] However, the CAFC disagreed, emphasizing the "immaturity and unpredictability of the science" during the relevant timeframe.[77]

4. Antibody Inventions

In addition to cases in which inventions are directed to oligonucleotides, an area of particular interest to the biotechnology community is how to obtain patent rights for antibodies. Assisting applicants to understand the written description standard as applied to antibody claims, the PTO published guidelines that indicate the acceptability of a functional claim that recites "'an isolated antibody capable of binding to [protein] X' is adequately described[,] where the

[70] *Id.* at 1358.
[71] *Id.* at 1357–58.
[72] 642 F.3d 1031 (Fed. Cir. 2011).
[73] *Id.* at 1033 (quoting U.S. Patent No. 5,674,681 (filed Dec. 6, 1994)).
[74] *Id.*
[75] *Id.* at 1036.
[76] *Id.* at 1036–37.
[77] *Id.* at 1037.

specification fully characterizes protein X[,] even if there are no working or detailed prophetic examples. . . ."[78] However, those guidelines are only appropriate if the protein is new and the production of the antibody is routine.[79] The CAFC, in applying the guidelines has held, "an applicant can claim an antibody to novel protein X without describing the antibody when (1) the applicant fully discloses the novel protein and (2) generating the claimed antibody is so routine that possessing the protein places the applicant in possession of an antibody."[80]

In *Centocur v. Abbott*,[81] the claims at issue were directed to antibodies that had high affinity human variable regions.[82] The relevant priority application did not disclose any fully human high affinity antibodies for the target with human variable regions.[83] The specification did disclose a mouse variable region and a wish plan.[84] Because "the patent broadly claimed a class of antibodies that contain[ed] human variable regions, [but] the specification d[id] not describe a single antibody that satisfie[d] the claim limitations . . . [or] relevant identifying characteristics," and the ability to obtain such a high affinity antibody was not routine during the relevant time period, the CAFC held that there was a failure to comply with the written description requirement.[85]

5. Chimeric Genes and Mutant Viruses Inventions

Chimeric genes are combinations of nucleotide sequences that do not exist in nature and typically have components from two or more species.[86] Each of the components may already be known, and when claiming them, there is no *per se* rule that requires the nucleotide sequence to be fully recited in a specification.[87] Mutant viruses can similarly have sequences that do not exist in

[78] Centocor Ortho Biotech, Inc. v. Abbott Labs., 636 F.3d 1341, 1351 (Fed. Cir. 2011) (quoting USPTO, *supra* note 45, at 45–46).

[79] *Id.* at 1351–52.

[80] *Id.*

[81] 636 F.3d 1341 (Fed. Cir. 2011).

[82] *Id.* at 1348.

[83] *Id.* at 1349, 1351.

[84] *Id.*

[85] *Id.* at 1350–53.

[86] *See* Capon v. Eshhar, 418 F.3d 1349, 1351, 1355 (Fed. Cir. 2005).

[87] *See id.* at 1360–61 ("[T]he Board erred in ruling that § 112 imposes a *per se* rule requiring recitation in the specification of the nucleotide sequence of claimed DNA, when that sequence is already known in the field.").

nature,[88] and thus can implicate similar issues.

For example, in *Falko-Gunter Faulkner v. Ingles*,[89] the parties to an Interference proceeding had claimed vaccines directed to mutant poxviruses.[90] One of the parties described the poxvirus in detail, while the other party focused on a different subgenus of vaccine vectors, providing three passages that describe the poxvirus.[91] The CAFC held that because the essential genes for the poxvirus were well known, there was no need to provide working examples, to have reduced the invention to practice or to have recited a structure.[92]

Capon v. Eshhar[93] provides an example of when a specification for a claimed invention directed to a chimeric gene might comply with the written description requirement even in the absence of disclosure of numerous species.[94] This case arose out of an appeal by both parties to an interference proceeding.[95]

The chimeric gene contained "DNA segments that [were] both endogenous and nonendogenous to a cell. . . . Both parties explain[ed] that [the] genes [were] produced by selecting and combining known heavy- and light-chain immune-related DNA segments, using known DNA-linking [mechanisms]."[96] One of the applicant's specifications contained nucleotide sequences from which the chimeric genes encoding it could be obtained, and the other applicant's specification cited literature sources that contained the information.[97]

The Board of Patent Appeals and Interferences deemed these disclosures inadequate because they did not include the complete

[88] *See* Falko-Gunter Falkner v. Inglis, 448 F.3d 1357, 1360 (Fed. Cir. 2006) (discussing inventors deactivating an essential gene from a virus genome to create a safer vaccine).

[89] 448 F.3d 1357, 1360 (Fed. Cir. 2006).

[90] *Id.* at 1364.

[91] *Id.*

[92] *Id.* at 1366; *C.f.* Monsanto Co. v. Scruggs, 459 F.3d 1328, 1337 (Fed. Cir. 2006) ("Given the knowledge in the art, it was unnecessary for the '605 patent to include specific gene sequences when referring to the CaMV 35S promoter to meet the written description requirement."). *But see* Goeddel v. Sugano, 617 F.3d 1350, 1356 (Fed. Cir. 2010) (explaining that envisioning an invention not yet made does not constitute a reduction to practice).

[93] 418 F.3d 1349 (Fed. Cir. 2005).

[94] *Capon*, 418 F.3d at 1359–61.

[95] *Id.* at 1350, 1352.

[96] *Id.* at 1352, 1355.

[97] *Id.* at 1356.

nucleotide sequences "of 'at least one' chimeric gene."[98] The CAFC disagreed and reversed, holding: "When the prior art includes the nucleotide information, precedent does not [create] a *per se* rule that the information must be determined afresh."[99] Consequently, the CAFC remanded for the Board of Patent Appeals and Interferences to "explore the support for each of the claims."[100]

Thus, although the combination of two or more known sequences may be non-obvious, the explicit recitation of each sequence is not always necessary for claims directed to the recombined sequences.[101]

B. Genuses When Fewer Than All Species Are Disclosed

A second written description issue that arises in the context of inventions directed to biotechnology is the issue of claims to large numbers of sequences but disclosure of relatively few of the claimed sequence.[102] The CAFC has held that in order to evaluate the generic claims to biological subject matter, one may examine: "'[i] the existing knowledge in the particular field, [ii] the extent and content of the prior art, [iii] the maturity of the science or technology, [and] [iv] the predictability of the aspect at issue.'"[103]

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[98] *Id.* (quoting Capon v. Eshhar, No. 103,887, 2003 WL 25748145 (B.P.A.I. Mar. 26, 2003)).

[99] *Id.* at 1358.

[100] *Id.* at 1360–61.

[101] *See id.* at 1356–58 (explaining that the requirements of written descriptions vary based on the characteristics of the invention, and the inclusion of a complete nucleotide sequence is not automatically required).

[102] The issue of whether a claim to a genus complies with the written description requirement is similar to the issue of whether a claim to a genus complies with the enablement requirement. *See* Regents of the Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1569 (Fed. Cir. 1997) (explaining that the genus-species issue under written description requirement is similar to genus-species issue under enablement requirement). One should note that Congress or the courts could have limited patent rights only to those species whose entire sequences are actually disclosed. *C.f.* Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement, 60 Fed. Reg. 1099, 1101 (Jan. 5, 2001) (rejecting a comment "that the written description of a claimed DNA should be required to include the complete sequence of the DNA and claims should be limited" to those species). However, this standard was not adopted. *See Capon*, 418 F.3d at 1360–61 (holding that there is no "*per se* rule requiring recitation in the specification of the nucleotide sequence of claimed DNA, when that sequence is already known in the field.").

[103] Ariad Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1351 (Fed. Cir. 2010) (fourth alteration in original) (quoting *Capon*, 418 F.3d at 1359). In the *en*

The PTO has also provided guidelines for analyzing genus-species issues with respect to the written description requirement and has noted that the written description requirement may be satisfied by a disclosure of a

> sufficient description of a representative number of species by actual reduction to practice . . . reduction to drawings . . . or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.[104]

Unfortunately for applicants who like clarity, there are no hard and fast rules as to what number is representative. Instead, the PTO has taken the position that "[a] 'representative number of species' means that the species [that] are [in fact] adequately described are representative of the entire genus."[105]

The seminal case for this issue is *Regents of the University of California v. Eli Lilly*.[106] At issue were two patents that were directed "to recombinant plasmids and microorganisms that produce human insulin."[107] The CAFC applied the written description requirement with respect to a few different types of claims.[108] Among the types of claims were claims that were directed generically to "cDNA encoding vertebrate insulin," and "cDNA encoding mammalian insulin."[109] During the litigation, when faced with an invalidity challenge, the patentee argued that a description of rat insulin cDNA is a description of the

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banc hearing the panel adapted the application of the written description requirement to the facts. *Id.* at 1358–59 (Newman, J., additional views).

[104] MPEP, *supra* note 8, § 2163(II)(A)(3)(a)(ii), at 2100-182 (citation omitted).

[105] *Id.* The MPEP elaborates:

> Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicate[s] that the patentee has invented species sufficient to constitute the gen[us]."

Id. (second alteration in original) (quoting Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 967 (Fed. Cir. 2002)).

[106] 119 F.3d 1559 (Fed. Cir. 1997).

[107] *Regents of the Univ. of Cal.*, 119 F.3d at 1562.

[108] *Id.* at 1566–67.

[109] *Id.* at 1567.

broad classes of vertebrate and mammalian insulin cDNA.[110] The CAFC disagreed and held: "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials."[111]

The CAFC elaborated that "[i]n claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. . . . Accordingly, such a formula is normally an adequate description of the claim genus. . . . [H]owever, . . . generic statement[s] such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more," were deemed inadequate because although the genus was defined by function, it would not provide "any structural features commonly possessed by members of the genus that distinguish[es] them from other[] [genuses]."[112]

In a more recent case, the CAFC summarized the two ways by which to disclose a genus, and noted that an applicant may disclose: "(1) a representative number of species in [a] genus; or (2) its 'relevant identifying characteristics,' such as 'complete or partial structure, other physical and/or chemical properties, functional characteristics when [compounds] with a known or disclosed correlation between function and structure, or some combination of such characteristics.'"[113] The latter way is consistent with the description by characterization cases described above in section A. However, the former leaves open the issue of how many species are representative.[114] This issue is discussed further below, as are the genus species issues as applied to antibody cases, expressed sequence tag inventions, and claims that recite a homology or complementarity percentage.

1. The Magic Number

At the heart of the *Regents of the University of California* case

[110] *Id.* at 1567–68.

[111] *Id.* at 1568 (alteration in original) (quoting Fiers v. Revel, 984 F.2d 1164, 1171 (Fed. Cir. 1993)).

[112] *Id.*

[113] *In re* Alonso, 545 F.3d 1015, 1019 (Fed. Cir. 2008) (quoting Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 964 (Fed. Cir. 2002)).

[114] *See id.* at 1021–23 (the court explains that one species is not enough to describe a class or genus but does not establish a hard line rule of how many would be enough).

was the question of how many species must be disclosed before a genus could be claimed.[115] In that case, only one cDNA was recited.[116] Accordingly, it was easy for the court to hold that the patent did not satisfy the written description requirement.[117] However, the CAFC left open the issue of the scope of disclosure necessary to entitle one to a claim directed to a genus.[118] Instead, it provided only guideposts requiring "a recitation of a representative number of cDNAs, defined by nucleotide sequence[s], falling within the scope of [a] genus or . . . a recitation of structural features common to the members of the genus."[119]

The written description standard as set out in *Regents of the University of California* is not limited to cases in which new genes have been discovered. In *Carnegie Mellon University v. Hoffman-La Roche Inc.*,[120] "[t]he patents-in-suit [were] directed to . . . recombinant plasmids . . . [,] processes related to the construction of [those] plasmids, and . . . cells containing [those] plasmids."[121]

In that case, on appeal, the CAFC described the claims as defining a genus by its function—its function of encoding DNA polymerase I or nick translation without any limit on the bacterial species.[122] The defendants argued that the patents did not satisfy the written description requirement because the claims were directed to plasmids that coded for the expression of

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115 *See Regents of the Univ. of Cal.*, 119 F.3d at 1566–67.

116 *Id.* at 1567.

117 *Id.* at 1569.

118 *Id.*

119 *Id.* One must also be careful to consider and to calculate correctly, the number of species in a genus. *See* Singh v. Brake, 317 F.3d 1334, 1343–44 (Fed. Cir. 2002) (rejecting the challenging party's overestimation of the size of the genus).

120 148 F. Supp. 2d 1004 (N.D. Cal. 2001), *aff'd*, 541 F.3d 1115 (Fed. Cir. 2008).

121 *Id.* at 1007. By way of example, claim 1 of one of the patents in suit provided

A recombinant plasmid containing a cloned complete structural gene coding region isolated from a bacterial source for the expression of DNA polymerase I, under operable control of a conditionally controllable foreign promoter functionally linked to said structural gene coding region, said foreign promoter being functional to express said DNA polymerase I in a suitable bacterial or yeast host system.

Id. at 1007 n. 2.

122 Carnegie Mellon Univ. v. Hoffman-La Roche, 541 F.3d 1115, 1123–24 (Fed. Cir. 2008).

a DNA polymerase, but were not limited to any particular bacterial source, while the specification described only recombinant plasmids from one type of bacteria, *E. coli*.[123] The plaintiff unsuccessfully tried to distinguish *Regents of the University of California* by arguing that in the patent at issue, the claims were not directed to novel sequences.[124]

The limited disclosure of only the *E. Coli polA*, warranted an affirming of the claims of invalidity.[125] Of particular interest to the CAFC was the fact that at the time of invention, only two other bacterial *polA* genes had been sequenced.[126]

Ex parte Gleave[127] provides a contrasting example of when a genus may be adequately described by a representative number of species. In *ex parte Gleave* the Board of Appeals and Patent Interferences applied the written description issue to two types of claims: "[(1) M]ethod[s] for delaying progression of hormone-regulated mammalian tumor[s] . . . comprising treating . . . with . . . antisense oligonucleotide[s]"; and (2) "method[s] for treating a hormone-responsive cancer . . . [comprising] administering . . . a composition effective [at] inhibit[ion]."[128]

"[T]he specification [disclosed] . . . the sequences of DNA molecules encoding the mouse and human IGFBP-5s" and what the Board referred to "as a number of antisense sequences [that] target[] specific regions of the mouse and human IGFBP-5 DNAs."[129] With respect to the claims directed to methods that use antisense technology, the Board reversed the rejection, noting that it was incumbent upon the examiner to present evidence or reasons why the applicants had not complied with the written description requirement.[130] By contrast, the Board sustained rejections on the claims in which the methods were not limited to the use of antisense compositions because the specification provided no examples of these types of compounds.[131]

There is no absolute number of species that must be disclosed,

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123 *Id.* at 1123–25.

124 *Id.* at 1124.

125 *Id.* at 1125–26.

126 *Id.* at 1125.

127 *Ex parte* Gleave, No. 2005-2447, 2006 Pat. App. LEXIS 45, (B.P.A.I. Jan. 31, 2006).

128 *Id.* at *4.

129 *Id.* at *19.

130 *Id.* at *17, *20. The Board similarly reversed a rejection based on alleged lack of enablement. *Id.* at *26–28.

131 *Id.* at *20, *24.

and the MPEP has summarized:

> [W]hen there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. . . .
>
> . . .
>
> What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. . . . For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.[132]

Because of the courts' tendency to treat biotechnology inventions as unpredictable, preferably an applicant will disclose a plurality of sequences from within a genus, and more preferably a super plurality that represents the genus as well as common features of species within the genus.[133]

2. Antibody Cases

As noted above, antibody cases have been addressed by the PTO guidelines, and it is not always necessary to recite any complete structures. But there have been claimed inventions directed to antibodies in which the genus-species issue arises.

For example, in *Noelle v. Lederman*[134] one claim at issue focused on antibodies that bind to CD40CR from any species, while a second claim was directed to antibodies that bind to human CD40CR.[135] The specification only disclosed the mouse CD40CR and an antibody to it.[136] Because the specification did not disclose any antibodies to human CD40CR, and the specification did not disclose CD40CR from any species except mouse, the CAFC held that there was not an adequate written description for the broad claims.[137]

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132 MPEP, *supra* note 8, § 2163(II)(A)(3)(a)(ii), at 2100-182 to 2100-183.

133 *See id.*

134 355 F.3d 1343 (Fed. Cir. 2004).

135 *Id.* at 1346.

136 *Id.* at 1349.

137 *Id.* at 1349–50. *See also In re* Alonso, 545 F.3d 1015, 1019–21 (Fed. Cir. 2008) (stating that a claim to a method for treating cancer by administering a monoclonal antibody that binds to a neurofibrosarcoma cell, where only one monoclonal antibody was disclosed, was found invalid because "the scope of the genus [was found] to vary substantially" (there was shown to be "considerable antigenic 'heterogeneity of tumors both between patients and metastatic sites within a single patient'") and "the single antibody [disclosed was found to be] insufficiently representative to provide adequate written descripti[on] support").

3. ESTs

A similar issue can arise in expressed sequence tag (EST) cases. At one time, prior to the development of rapid sequencing devices, there was a fear that inventors would rush to the PTO and file patent applications directed to expressed sequence tags,[138] which are "small pieces of DNA . . . (usually 200 to 500 nucleotides long) that are generated by sequencing either one or both ends of an expressed gene."[139] They "correspond[] to only part of a protein-encoding open reading frame (ORF)" and one can readily surmise that patent practitioners were tempted to file claims phrased as "[a]n isolated DNA comprising SEQ ID NO: [XXX]."[140]

Because of the open-ended language "comprising" such a claim would include sequences attached to either end of XXX.[141] The PTO, in its Written Description Training Materials correctly noted that "[t]here may be substantial variability among the species of DNAs [that are] encompassed by the scope of the claim."[142] However, under the PTO guidelines, the specification satisfies the written description requirement because the sequence is a structural feature common to all members of the genus.[143]

However, one should note that *Noelle* was decided by CAFC in response to an appeal from a decision of the Board of Patent Appeals and Interferences. *Noelle*, 355 F.3d at 1344. At least one court has declined to interpret *Noelle* as holding that as a matter of black letter law a description of a mouse protein is not a description of a human protein and declined to issue summary judgment that two patents were invalid. Rockefeller Univ. v. Centocor, Inc., 2006 U.S. Dist. LEXIS 43143, at *4–5 (E.D. Tex. June 13, 2006).

138 Andrew T. Knight, Note, *Pregnant with Ambiguity: Credibility and the PTO Utility Guidelines in Light of Brenner*, 73 IND. L.J. 997, 997–98 (1998).

139 USPTO, *supra* note 45, at 13 (practice note).

140 *See id.* (speculating as to the way that patent applicants would phrase ORFs).

141 *Id.* (explaining that the term "comprising" in the name of a phrase means that it will include additional adjacent sequences).

142 *Id.*

143 *Id.* at 13–14. Patent applications directed to ESTs might comply with the written description requirement, but they also may raise issues with respect to enablement and whether they read on the prior art. *Id.* at 14 (practice note). Only one reported decision addresses expressed sequence tags and the claims at issue were deemed unpatentable for lack of utility and failure to comply with the enablement requirement. *See In re* Fisher, 421 F.3d 1365, 1379 (Fed. Cir. 2005) (holding that five ESTs lacked utility and were not enabled and, thus, the patent was correctly rejected).

4. Percentage Homology or Complementarity

The issue of a representative number of species has also been addressed in the context of claims that recite at least 95 percent complementarity to a recited sequence or that code for a protein that is "at least 95 percent identical" to a recited protein.[144] These types of claims have been deemed patentable even when only the referenced sequence has been disclosed.[145]

III. CONCLUSION

Biotechnology has the potential to revolutionize society, particularly with respect to complex problems that traditional small molecule strategies have not been able to solve. In order to continue to entice the most creative and smartest men and women to work in this field, now more than ever they will need to be given the proper incentives, which means the opportunity to pursue patent rights. For the practitioner who counsels the inventor and the investor who funds the inventor, there must be an appreciation of the nuances of the written description requirement as applied under the patent law.

Particularly in view of the completion of the sequencing of the human genome project a decade ago and the ease with which nucleotides can now be sequenced, the next generation of inventions will likely include an increasing number of recombinant oligonucleotides and proteins and methods for using them. To the extent that an inventor will be able to obtain broad rights to these new compounds and their uses, he or she will need to be cognizant of the hurdles that the PTO may present, and practitioners should try to position their clients in the best position possible to satisfy the written description requirement.

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144 *Ex parte* Bandman, No. 2004-2319, 2005 Pat. App. LEXIS 33, *1–*2,*6 (B.P.A.I. June 14, 2005).

145 *See id.* at *6 (holding that claims "at least 95% identical" to recited sequence were adequately described). The claims were also deemed enabled by the same disclosure. *See id.* at *8–9. *See also* Novozymes A/S v. Genencor Int'l, Inc., 446 F. Supp. 2d 297, 329–30 (D. Del. 2006) (holding that enablement requires at least 95 perecent homology). *But see Ex parte* Kubin, No. 2007-0819, 83 U.S.P.Q.2d 1410, 1416–17 (B.P.A.I. May 31, 2007) (holding that a claim of at least 80 percent identity was inadequately supported when the specification disclosed two working examples within the claim and three fusion proteins within the claim, but no variants in which amino acids 22 through 221 of the sequence were varied), *aff'd sub nom. In re* Kubin, 561 F.3d 1351 (Fed. Cir. 2009).