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HOW TO CLAIM A GENE: APPLICATION OF THE PATENT DISCLOSURE REQUIREMENTS TO GENETIC SEQUENCES

Patrick Brian Giles*

INTRODUCTION

Prior to 1980, the only source of insulin for diabetics was the pancreas of animals, such as cows or pigs.[1] While supply was not a problem, this source did carry the risk of infection and allergic reaction.[2] Other therapeutic proteins, such as growth hormone, were previously only available in minuscule amounts from the pituitary glands of human cadavers.[3] However, by 1980 the emerging field of biotechnology provided methods for producing mass quantities of human proteins such as insulin and growth hormone using the science of genetic engineering.[4] These laboratory methods generally involve inserting a gene[5] that encodes the desired therapeutic protein into a deoxyribonucleic acid (DNA) vector.[6] The product of this "DNA recombination" is then introduced to appropriate cells, the cells are cultured in the laboratory, during which time the cells produce the

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1. Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1562 (Fed. Cir. 1997); *Tests Begin on Insulin Synthesized from Bacteria Through Gene-Splicing*, N.Y. TIMES, July 24, 1980, at D18; Cristine Russell, *FDA Approves Insulin Made by Splicing Genes*, WASH. POST, Oct. 30, 1982, at A6.

2. *Lilly*, 119 F.3d at 1562; *Tests Begin on Insulin Synthesized from Bacteria Through Gene-Splicing*, *supra* note 1, at D18; Russell, *supra* note 1, at A6.

3. *See, e.g.*, Sandra Blakeslee, *Supply of Growth Hormone Brings Hope for New Uses*, N.Y. TIMES, Feb. 10, 1987, at C1.

4. *See supra* notes 1–3; CYNTHIA ROBBINS-ROTH, FROM ALCHEMY TO IPO 11 (Perseus Publishing 2000).

5. Gregor Mendel was the first to appreciate that certain traits, such as flower color, do not blend in offspring, but are instead inherited based on the passage of a discrete factor, later termed a "gene," to the offspring from both the mother and the father. It is now known that these genes are discrete segments of deoxyribonucleic acid (DNA), which contain instructions for producing functional units, such as proteins. *See generally* Mark B. Gerstein et al., *What is a Gene, Post-ENCODE? History and Updated Definition*, 17 GENOME RES. 669–81 (2007).

6. See HARVEY LODISH ET AL., MOLECULAR CELL BIOLOGY 176–98 (6th ed. 2008), for a description of many of the principles involved in molecular biology and recombinant DNA technology.

recombinant protein along side their natural proteins, and the recombinant protein is then collected and purified.[7]

Not surprisingly, biotechnology companies have sought patent protection for these novel genes and their uses.[8] Of course, these efforts are futile if a competitor can circumvent the patent by making changes to the claimed DNA sequence while preserving, or possibly improving, the therapeutic efficacy of the encoded protein.[9] In fact, a competitor can routinely engineer non-naturally occurring variants using one of many recombinant techniques.[10] Notably, in some cases, 50% or more of the amino acid positions within the sequence of a protein can be substituted without substantially altering protein function.[11] Inventors of novel genes and recombinant technologies, therefore, have sought patent protection beyond the scope of the specific genetic sequence they exemplified.[12] While this can be done by specifically reciting each and every possible alternative sequence, to do so would be impractical.[13] Instead, it is far more feasible to refer to the gene generically (e.g., by name or function), thereby describing a genus of genetic sequences covered by the claim.[14] The

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7. *Id.* at 194–96.

8. Christopher M. Holman, *Learning from Litigation: What Can Lawsuits Teach Us About the Role of Human Gene Patents in Research and Innovation?*, 18 KAN. J.L. & PUB. POL'Y. 215, 221–22 (2009) [hereinafter Holman, *Learning from Litigation*] (noting the early "belief that patent protection could prove critical in providing the necessary incentive for the development of drugs based on newly identified human genes").

9. *Id.* at 226–27 ("[A] form of human insulin with a single amino acid change . . . renders the product faster acting than native insulin.").

10. Christopher M. Holman, *Protein Similarity Score: A Simplified Version of the BLAST Score as a Superior Alternative to Percent Identity for Claiming Genuses of Related Protein Sequences*, 21 SANTA CLARA COMPUTER & HIGH TECH. L.J. 55, 60 (2004) [hereinafter Holman, *Protein Similarity Score*] (noting that it is routine to make mutations in a protein and screen those mutants for one that retains the desired function).

11. *Id.* at 59.

12. *Id.* at 57.

13. A protein is a polymer of amino acids linked together in a chain. *See id.* at 72 n.70. There are twenty different amino acids to choose from for each position in that chain. *Id.* Thus, for a typical protein having three hundred amino acids residues, there are nineteen alternative amino acids at each of the three hundred positions. *Id.* Using the equation ((19 x 300) + (19 x 300)(19 x 299)), this results in over thirty-two million possible protein variants that have a single amino acid change. *See id.*

14. When an aspect of an invention includes one of multiple alternative embodiments, a generic term may be used to represent each of those alternatives. ROBERT C. FABER, FABER ON MECHANICS OF PATENT CLAIM DRAFTING § 6:9 (6th ed. 2008). For example, the term "mammal" represents a genus encompassing the species mice and humans. *See id.* Note that the genus can also cover a subgenus. *Id.* For example, "rodents" is a genus covering mice and rats, but it is also a sub-genus of mammals. *See id.*

problem, however, is that an overreaching genus claim may not satisfy the patent disclosure requirements codified in the first paragraph of 35 U.S.C. § 112,[15] which (according to the most current interpretation of the statute)[16] requires that the disclosure (1) contain an adequate written description of the invention; (2) enable one to make and use the invention; and (3) disclose the inventor's best mode for carrying out his invention.[17]

Prior to 1997, the courts relied primarily on the enablement requirement to invalidate overreaching claims.[18] However, in *Regents of the University of California v. Eli Lilly & Co.*,[19] a court, for the first time, invalidated an original—arguably overreaching—claim for lack of written description.[20] Specifically, the *Lilly* court concluded that the patentee's description of the rat insulin DNA sequence was not a sufficient disclosure to support claims to vertebrate, mammalian, or human insulin DNA.[21] As a consequence, inventors have had to find other ways to describe and claim genetic sequences in a manner that would cover predictable variants while at the same time not running afoul of the *Lilly* written description requirement.

15. 35 U.S.C. § 112 (2006) ("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.").

16. *See* discussion *infra* Part II.A.

17. Under § 112, first paragraph, as enacted as part of the Patent Act of 1952, the inventor must adequately set forth and describe three items: (1) the invention (the description requirement); (2) the manner and process of making and using the invention (the enablement requirement); and (3) the best mode contemplated by the inventor of carrying out his invention (the best mode requirement). 3 DONALD S. CHISUM, CHISUM ON PATENTS § 7.01 (2010).

18. *E.g.*, *In re* Fisher, 427 F.2d 833, 839 (C.C.P.A. 1970) (arguing that an inventor should be allowed to dominate future patentable inventions based on his teachings so long as the scope of the claims "bear a reasonable correlation to the scope of enablement provided by the specification"); *see also* Christopher M. Holman, *Is* Lilly *Written Description a Paper Tiger?: A Comprehensive Assessment of the Impact of* Eli Lilly *and Its Progeny in the Courts and PTO*, 17 ALB. L.J. SCI. & TECH. 1, 12 (2007) [hereinafter Holman, *Paper Tiger*] (noting that prior to *Lilly*, the enablement requirement was sufficiently robust to limit patent claims "to a scope commensurate with the inventor's disclosure").

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

20. Holman, *Paper Tiger*, *supra* note 18, at 4.

21. *Lilly*, 119 F.3d at 1568.

One approach taken by inventors,[22] and originally endorsed by the Patent Office,[23] was the claiming a genus of genetic sequences based on percent identity[24] to a reference sequence—generally the naturally occurring gene—that is limited by a functional limitation.[25] However, the Patent Office has recently reversed its position[26] and proposed that inclusion of a functional limitation, which narrows the genus of genetic sequences to those that produce a functional protein (e.g., "wherein the polypeptide has activity X"), actually increases the burden on the specification to satisfy the written description requirement by disclosing a correlation between structure and function.[27] This reversal in the application of the written description

22. According to a search of the USTPO Patent Full-Text and Image Database, forty-one U.S. patents filed prior to 2000 and fifty-six U.S. patents filed between the years 2000 and 2007 were issued with the phrases "percent identity" and "SEQ ID NO" in the claims. USPTO Patent Full-Text and Image Database, http://patft.uspto.gov/netahtml/PTO/search-bool.html.

23. U.S. PATENT AND TRADEMARK OFFICE, U.S. DEP'T OF COMMERCE, REVISED INTERIM WRITTEN DESCRIPTION GUIDELINES TRAINING MATERIALS, 53–55 (1999), http://web.archive.org/web/20070101024139/http://www.uspto.gov/web/offices/pac/writtendesc.pdf [hereinafter INTERIM TRAINING MATERIALS] (superseded). Example 14 of the Interim Training Materials suggested that a description of a protein isolated from liver having the sequence SEQ ID NO: 3 and shown to catalyze the reaction of A to B without exemplification of any variants with this activity nonetheless would satisfy the written description requirement for a claim reciting "[a] protein having SEQ ID NO: 3 and variants thereof that are at least 95% identical to SEQ ID NO: 3 and catalyze the reaction of A [to] B." *Id.* at 53–55.

24. Percent sequence identity refers to the percentage of nucleic acid or amino acid residues within a given DNA or protein, respectively, that are identical to the reference sequence. *See* Holman, *Protein Similarity Score*, *supra* note 10, at 69. For example, a protein is essentially a biopolymer composed of amino acids in a specific order. *Id.* at 58–59. Thus, for a protein that is one hundred amino acids in length, one can substitute amino acids at five of the positions and still be at least 95% identical to the natural protein. *See id.* at 69–73. Moreover, there are twenty different amino acids in humans, so each position on the protein chain can be substituted with one of nineteen different amino acids. *Id.* at 59. These include conservative and non-conservative substitutions, which are not reflected in the percent identity. *See id.* at 73.

25. A functional limitation limits the claimed genetic sequences to those that are able to perform a recited function, thereby excluding from the claim non-functional variants that would fail to satisfy the utility requirement. *See id.* at 70, 82.

26. *See* U.S. PATENT AND TRADEMARK OFFICE, U.S. DEP'T OF COMMERCE, WRITTEN DESCRIPTION TRAINING MATERIALS, 37–39 (2008), http://www.uspto.gov/web/menu/written.pdf [hereinafter REVISED TRAINING MATERIALS]. Dr. George Elliott, director of Technology Center 1600 responsible for examination of patent applications in the biotechnology and organic fields, acknowledged that the revision represented a reversal in the Office's position. Donald Zuhn, Kubin, *Panel Questions Motivation Behind Reversal in New Written Description Training Materials*, PATENT DOCS, Jan. 8, 2009, http://www.patentdocs.org/2009/01/kubin-panel-questions-motivation-behind-reversal-in-new-written-description-training-materials.html.

27. REVISED TRAINING MATERIALS, *supra* note 26, at 37–39 ("[I]n this example there is no general knowledge in the art about activity X to suggest that general similarity of structure confers the activity.

requirement has been upheld by the Board of Patent Appeals and Interferences (Board).[28] However, the issue has not been considered by the Court of Appeals for the Federal Circuit (Federal Circuit).

Notably, the Federal Circuit recently upheld a rejection by the Board for a percent identity claim to a genus of nucleic acid molecules encoding the protein Natural Killer Cell Activation Inducing Ligand (NAIL) wherein the protein binds CD48.[29] The Board had affirmed the Examiner's rejection of the claim as both obvious and lacking written description in the specification.[30] However, the Federal Circuit chose to affirm the decision of the Board based solely on the obviousness rejection[31] and therefore did not address the sufficiency of the disclosure under the written description requirement.[32]

This Note examines application of the Patent Act disclosure requirements to percent identity claims. Part I of this Note reviews and discusses the development of the disclosure requirements and their application to genetic sequences.[33] Part II of this Note analyzes the application of these disclosure requirements to percent identity claims.[34] This analysis first evaluates the severability of the written

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Accordingly, one of skills in the art would not accept the disclosure of SEQ ID NO: 2 as representative of other proteins having activity X.").

28. The Board reviews ex parte appeals from adverse decisions of examiners. 35 U.S.C. § 6(b) (2008). Prior to 2006, the Board had not upheld any rejections of percent identity claims based on a failure to satisfy the written description requirement. Holman, *Paper Tiger*, *supra* note 18, at 45, 83.

29. *In re* Kubin, 561 F.3d 1351, 1361 (Fed. Cir. 2009).

30. *Ex parte* Kubin, 83 U.S.P.Q.2d 1410, 1416–17 (B.P.A.I. 2007).

31. *In re* Kubin, 561 F.3d at 1361. While sidestepping the written description issue, the court nevertheless sent shockwaves with its decision. The *Kubin* court concluded that the Supreme Court had essentially overturned the obviousness standard set forth in *In re Deuel*, 34 U.S.P.Q.2d 1210, 1216 (Fed. Cir. 1995). *In re* Kubin, 561 F.3d at 1358. The *Deuel* court had determined that a protein does not always render the DNA encoding that protein obvious, even if it was obvious to try. *Deuel*, 34 U.S.P.Q.2d at 1216. The *Kubin* court held that the ruling in *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398 (2007), "cast doubt on the viability of *Deuel*" and subsequently found that claims to the cDNA encoding NAIL were obvious since the prior art disclosed the existence of the protein. *In re* Kubin, 561 F.3d at 1358, 1361.

32. This silence despite evident interest at oral argument could be considered sub silentio approval of the written description rejection and the approach taken in the Revised Training Materials. Kevin E. Noonan, *Gene Patenting and the Wisdom of Judge Lourie*, PATENT DOCS, Apr. l2, 2009, http://www.patentdocs.org/2009/04/gene-patenting-and-the-wisdom-of-judge-lourie.html; *see also* Zuhn, *supra* note 26.

33. *See* discussion *infra* Part I.

34. *See* discussion *infra* Part II.

description and enablement requirements[35] and then explores the effect of omitting the functional limitation in sequence identity claims on the enablement requirement.[36] Part III of this Note argues that identifying genetic sequences by percent identity without a functional limitation is adequate disclosure of the genus.[37]

I. BACKGROUND

In order to obtain a patent, the inventor must file with her application a specification that fully discloses the invention to assure that the public receives a quid pro quo in exchange for the limited monopoly the patent grants to the inventor.[38] This disclosure requirement of the Patent Act of 1952 is codified in the first paragraph of 35 U.S.C. § 112,[39] which, according to current interpretation of the statute,[40] requires that the disclosure (1) contain an adequate written description of the invention; (2) enable one to make and use the invention; and (3) disclose the inventor's best mode of carrying out the invention.[41] The Patent Office and courts are using the first two disclosure requirements—written description and enablement—to prevent overreaching by inventors beyond the quid pro quo the public receives for granting the limited monopoly.[42]

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35. *See* discussion *infra* Part II.A.

36. *See* discussion *infra* Part II.B.

37. *See* discussion *infra* Part III and Conclusion.

38. Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 970 (Fed. Cir. 2002) ("[D]escription [of the invention] is the *quid pro quo* of the patent system; the public must receive meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time."); 3 CHISUM, *supra* note 17, § 7.01.

39. 35 U.S.C. § 112 (2006) ("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.").

40. *See* discussion *infra* Part II.A.

41. 3 CHISUM, *supra* note 17, § 7.01 ("Under Section 112, . . . the inventor must adequately set forth and describe three items: (1) the invention (the description requirement); (2) the manner and process of making and using the invention (the enablement requirement); and (3) the best mode contemplated by the inventor of carrying out his invention . . . .").

42. *Id.*

A. Written Description Requirement

The written description requirement first appeared in the Patent Act of 1793.[43] At that time, patents did not contain claims, so the written description served to both enable the invention and provide notice to the public of what the inventor was claiming as his invention.[44] This notice function of the written description requirement put the public "in possession" of the scope of the claimed invention.[45] However, with the Patent Act of 1870, this notice function was achieved by the claims instead of the specification.[46] Thus, with the advent of claims, the "written description" language of the Patent Act was presumed for many decades to constitute superfluous words not distinct from the enablement requirement.[47]

The written description requirement was reborn in 1967 with the *In re Ruschig* decision.[48] The applicants in *Ruschig* attempted to add a new claim that was not fully supported by the specification to their application a year after it had been filed.[49] Rather than reject the claims as new matter under § 132 of the Patent Act,[50] however, the court "calved a new [written description] doctrine out of the § 112 enablement requirement."[51] The court later distinguished these two

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43. Patent Act of 1793, ch. 11, § 3, 1 Stat. 318, 321 (repealed 1836) ("[E]very inventor, before he can receive a patent, . . . shall deliver a written description of his invention . . . in such full, clear, and exact terms, as to distinguish the same from all other things before known . . . .").

44. Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 977 (Fed. Cir. 2002) (Rader, J., dissenting) (citing Evans v. Eaton, 20 U.S. (7 Wheat.) 356 (1822)); Janice M. Mueller, *The Evolving Application of the Written Description Requirement to Biotechnological Inventions*, 13 BERKELEY TECH. L.J. 615, 619–20 (1998).

45. *Enzo*, 323 F.3d at 977; *Evans*, 20 U.S. (7 Wheat.) at 434; Mueller, *supra* note 44, at 620.

46. 35 U.S.C. § 112, ¶ 2 ("The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention."); *see also Enzo*, 323 F.3d at 977; 3 CHISUM, *supra* note 17, § 8.01; Mueller, *supra* note 44, at 620.

47. *In re* Gay, 309 F.2d 769, 772 (C.C.P.A. 1962) (finding only two requirements in § 112: enablement and best mode); *see also In re* Barker, 559 F.2d 588, 594 (C.C.P.A. 1977) (Rich, J., concurring) (arguing that the words "written description" were "of ancient lineage and, in spite of the fact they are inappropriate to some situations, they were preserved, in writing the Patent Act of 1952, because they were familiar and had many times been construed"); Mueller, *supra* note 44, at 620.

48. *In re* Ruschig, 379 F.2d 990 (C.C.P.A. 1967).

49. *Id.* at 991.

50. 35 U.S.C. § 132 ("No amendment shall introduce new matter into the disclosure of the invention.").

51. *Enzo*, 323 F.3d at 978.

sections as distinct and not interchangeable.[52] Even so, the policy of this new written description requirement appeared to prevent inventors from *later* claiming more than they had invented at the time the application was filed.[53] The Federal Circuit followed this precedent and applied the judicially created written description requirement strictly to later filed or amended claims that sought the benefit of the priority date of an earlier filed specification.[54]

In 1997, however, the court in *Lilly* applied the written description requirement for the first time to original claims without any priority question.[55] The patents at issue in *Lilly* were based on the cloning of the insulin gene, which, as discussed above, was a breakthrough that opened the way to modern methods of insulin production.[56] Nevertheless, while the claims in *Lilly* recited vertebrate, mammalian, and human insulin cDNA,[57] only rat insulin cDNA was

52. *In re* Rasmussen, 650 F.2d 1212, 1214 (C.C.P.A. 1981) (arguing that § 132 "prohibits the introduction of new matter into the disclosure of an application," while § 112, "[the] first paragraph, requires that claim language be supported in the specification").

53. *See Enzo*, 323 F.3d at 979 ("[T]he § 112 doctrine, like its corollary § 132, policed priority, nothing more."); Mueller, *supra* note 44, at 621.

54. *See* Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1561 (Fed. Cir. 1991) ("Adequate description of the invention guards against the inventor's overreaching by insisting that he recount his invention in such detail that his future claims can be determined to be encompassed within his original creation." (quoting Rengo Co. v. Molins Mach. Co., 657 F.2d 535, 551 (3d Cir. 1981))); *In re* Wright, 866 F.2d 422, 424 (Fed. Cir. 1989) ("[The] essence of the so-called 'description requirement' of § 112, first paragraph" involves inquiring whether "newly claimed subject matter was *described* in the patent application when filed.").

55. Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1566–69 (Fed. Cir. 1997); *see also Enzo*, 323 F.3d at 979–80 (arguing that the court for the first time applied the written description requirement "as a general disclosure doctrine in place of enablement, rather than as a priority doctrine"); Mueller, *supra* note 44, at 633 (noting that *Lilly* was a departure from prior written description cases because the court applied the requirement to original claims rather than to claims presented or amended after the application filing date, and the court set a significantly higher standard for biotechnology inventions by requiring an express disclosure in the specification of the nucleic acid sequence for DNA claims).

56. *Lilly*, 119 F.3d at 1562; *see also supra* note 2.

57. Cells use the DNA sequence of a gene as a template to produce (transcribe) messenger ribonucleic acid (mRNA), which is complementary to the DNA sequence from which it is transcribed. HARVEY F. LODISH ET AL., MOLECULAR CELL BIOLOGY 120–22 (6th ed. 2008). Cells may then use the mRNA produced to synthesize a protein encoded by the mRNA sequence. *Id.* However, unlike DNA, RNA is unstable. AN INTRODUCTION TO MOLECULAR BIOTECHNOLOGY 305–06 (Michael Wink ed., 2006). Thus, scientists use the viral enzyme reverse transcriptase to do the reverse process—that is to produce a DNA complement from the mRNA. *Id.* This DNA is referred to as complementary DNA (cDNA). *Id.*

exemplified in the specification.[58] While the court conceded that the specification provided a process for obtaining the human insulin-encoding cDNA,[59] it nevertheless concluded that the specification did not provide a written description of human, mammalian, or vertebrate insulin cDNA.[60] The court opined that "a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself." [61] The court likewise determined that "a description of rat insulin cDNA is not a description of the broad classes of vertebrate or mammalian insulin cDNA."[62] While this case has been heavily criticized as creating an unprecedented "super-enablement" requirement for DNA-based inventions,[63] the court was in fact building on past precedent indicating a reluctance to grant broad protection to biotechnology inventions absent structural descriptions.

For example, in *Amgen, Inc. v. Chugai Pharmaceutical Co.*, the patent at issue recited claims to a DNA sequence encoding human erythropoietin (EPO).[64] It was conceded that Amgen was the first company to isolate the EPO gene and produce recombinant EPO for therapeutic use.[65] The defendants asserted, however, that Amgen's claims were invalid under § 102(g)[66] based on prior invention by one of their scientists who was allegedly first to conceive the strategy for isolating the EPO gene.[67] In response, the court opined that invention

58. *Lilly*, 119 F.3d at 1562.

59. *Id.* at 1567.

60. *Id.* (arguing that the specification provided "only a general method for obtaining the human cDNA" based on the amino acid sequences of human insulin A and B and the method used to obtain the rat cDNA; it thus did not provide a description of the cDNA encoding human insulin, whether or not the disclosure was enabling).

61. *Id.*

62. *Id.* at 1568.

63. *E.g.*, Holman, *Paper Tiger*, *supra* note 18, at 4; Mueller, *supra* note 44, at 633.

64. Amgen, Inc. v. Chugai Pharm. Co., Ltd., 927 F.2d 1200, 1203 (Fed. Cir. 1991). Erythropoietin protein stimulates the production of red blood cells and is therefore a "useful therapeutic agent in the treatment of anemias or blood disorders characterized by low or defective bone marrow production of red blood cells." *Id.* at 1203.

65. Edmund L. Andrews, *Ruling May Hurt Amgen's Rights to Drug*, N.Y. TIMES, Dec. 18, 1989, at D1.

66. 35 U.S.C. § 102(g) (2006) ("A person shall be entitled to a patent unless . . . before such person's invention thereof, the invention was made . . . by another who had not abandoned, suppressed, or concealed it.").

67. *Amgen*, 927 F.2d at 1205.

of a gene occurs when it is actually isolated in cases where "an inventor is unable to envision the detailed constitution of a gene so as to *distinguish* it from other materials."[68]

Likewise, in *Fiers v. Revel*, the court went on to hold that "[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."[69] The *Lilly* court relied on the *Fiers* holding to find that written description of a genus of genetic sequences can be achieved by "recitation of a representative number of [sequences] within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."[70] The court later confirmed that these rules apply "[r]egardless [of] whether a compound is claimed *per se* or a method is claimed that entails the use of the compound."[71]

The court has, however, made some concessions to the *Lilly* written description requirement. On rehearing, the court in *Enzo Biochem, Inc. v. Gen-Probe Inc.* reversed its prior decision and held that reference in the specification to a deposit in a public depository constitutes adequate written description of the deposited material.[72] Moreover, the *Enzo* court clarified that functional limitations can satisfy the written description requirement if they are "coupled with a known or disclosed correlation between function and structure."[73]

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68. *Id.* at 1206 ("Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.").

69. Fiers v. Revel, 984 F.2d 1164, 1170 (Fed. Cir. 1993). The court further clarified the holding in *Amgen*, finding that "conception only of a process for making a substance, without conception of a structural or equivalent definition of that substance, can at most constitute a conception of the substance claimed as a process." *Id.* at 1169.

70. Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1569 (Fed. Cir. 1997).

71. Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 926 (Fed. Cir. 2004).

72. Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 965 (Fed. Cir. 2002) (arguing that deposit makes the contents of nucleotide sequence accessible to the public when it is not otherwise available in written form).

73. *Id.* at 964 (adopting the standard described in the Written Description Guidelines for showing that an invention is complete).

The court has further held that adequate written description can occur absent working examples or actual reduction to practice.[74] Likewise, the written description requirement does not require recitation of known structures or sequences.[75]

With these guideposts in mind, the Board recently chose to uphold a rejection of a percent identity claim containing a functional limitation as lacking sufficient written description, even though the skilled artisan[76] admittedly could have made and used the full scope of the claim through routine experimentation.[77] Citing *Enzo*, the Board opined that the specification may have met the written description requirement if the functional limitation—binding to CD48—had been coupled with a disclosed or known correlation between the function and structure.[78] Interestingly, even though the genus of nucleic acids was primarily defined structurally based on sequence identity, the Board nevertheless argued that "[w]ithout a correlation between structure and function, the claim does little more than define the claimed invention by function."[79]

The Patent Office's position in the *Training Materials* suggests that a valid percent identity claim becomes invalid when further limited in scope to a subgenus of genetic sequences having a particular function.[80] Nevertheless, the Patent Office alluded in the

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74. Falko-Gunter Falkner v. Inglis, 448 F.3d 1357, 1366 (Fed. Cir. 2006).

75. *Id.* at 1366–67. "*Lilly* does *not* set forth a *per se* rule that whenever a claim limitation is directed to a macromolecular sequence, the specification must always recite the gene or sequence, regardless of whether it is known in the prior art." *Id.* at 1367; *see also* Capon v. Eshhar, 418 F.3d 1349, 1357 (Fed. Cir. 2005) (holding that prior cases do not require a re-description of what is already known).

76. The "person skilled in the art" referred to in 35 U.S.C. § 112 is a legal fiction—similar to the "reasonable person" found in the common law of torts—representing a hypothetical person having knowledge in the particular technical field (art) without being a genius. *See* 3 CHISUM, *supra* note 17, § 8.03(3); U.S. PATENT AND TRADEMARK OFFICE, U.S. DEP'T OF COMMERCE, MANUAL OF PATENT EXAMINING PROCEDURE § 2141.03 (8th ed., rev. 8 July 2010), *available at* http://www.uspto.gov/web/offices/pac/mpep/index.htm.

77. *Ex parte* Kubin, 83 U.S.P.Q.2d 1410, 1416–17 (B.P.A.I. 2007) ("[An] invention may be enabled even though it is not described." (citing Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 921 (Fed. Cir. 2004))).

78. *Id.* at 1417.

79. *Id.*

80. Compare Claim 1 *with* Claim 2 in Example 11A of REVISED TRAINING MATERIALS, *supra* note 26, at 37–39.

Training Materials to the possibility that percent identity claims could also raise enablement issues.[81]

B. Enablement Requirement

To be patentable, "the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art."[82] In order for a patent specification to enable a claimed invention, one skilled in the art must be able to make and use the full scope of the claimed invention based on the disclosures in the specification, coupled with information known in the art, without undue experimentation.[83]

Whether undue experimentation is needed to practice the claimed invention is not determined by analyzing a single factor, but rather by weighing many factual considerations.[84] For example, although the quantity of experimentation necessary is a factor to be considered by the court,[85] it is not dispositive "since a considerable amount of experimentation is permissible, if it is merely routine."[86] Similarly, the patent specification can omit what is well known in the art[87] even though the amount of direction or guidance presented is an important

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81. REVISED TRAINING MATERIALS, *supra* note 26, at 41.

82. Amgen, Inc. v. Chugai Pharm. Co., Ltd., 927 F.2d 1200, 1214 (Fed. Cir. 1991); *In re* Fisher, 427 F.2d 833, 839 (C.C.P.A. 1970).

83. *In re* Wands, 858 F.2d 731, 737 (Fed. Cir. 1988); Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384 (Fed Cir. 1986); Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1576 (Fed. Cir. 1984) ("That some experimentation is necessary does not preclude enablement; the amount of experimentation, however, must not be unduly extensive.").

84. The *Wands* court set forth the following factors for consideration: "(1) the quantity of experimentation necessary [i.e., time and expense], (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *Wands*, 858 F.2d at 737 (citing *Ex parte* Forman, 230 U.S.P.Q. 546, 547 (B.P.A.I. 1986)). However, it is not necessary that every enablement analysis consider all of these factors. *Amgen*, 927 F.2d at 1213.

85. *Amgen*, 927 F.2d at 1212.

86. *Wands*, 858 F.2d at 737 (quoting *Ex parte* Jackson, 217 U.S.P.Q. 804, 807 (B.P.A.I. 1982)).

87. *Hybritech*, 802 F.2d at 1384 ("[A] patent need not teach, and preferably omits, what is well known in the art."); Lindemann Maschinenfabrik GMBH v. Am. Hoist & Derrick Co., 730 F.2d 1452, 1463 (Fed. Cir. 1984) ("The question is whether the disclosure is sufficient to enable those skilled in the art to practice the claimed invention, hence the specification need not disclose what is well known in the art.").

consideration.[88] Moreover, whereas the presence or absence of working examples is relevant to an enablement inquiry,[89] the specification does not have to include actual embodiments or examples to be enabling.[90]

A claim can be rejected, however, under the "how-to-use" aspect of the enablement requirement if it is so broad as to cover inoperative embodiments.[91] While a claim does not have to specifically exclude all possible inoperative embodiments to be enabled,[92] the claim may be invalid if the number of inoperative embodiments forces the skilled artisan to use undue experimentation to identify those embodiments that are functional and covered by the claim in order to practice the invention.[93]

II. ANALYSIS

A. Separating the Written Description and Enablement Requirements

1. Are the Written Description and Enablement Requirements Severable?

While there is some argument whether the court in *Ruschig* in fact discerned a separate written description requirement severable from the enablement requirement,[94] a panel of the Federal Circuit in *Vas-*

88. *Wands*, 858 F.2d at 737.

89. *Id.*

90. *In re* Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993) ("Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples.").

91. 3 CHISUM, *supra* note 17, § 7.03(7)(c). As part of the quid pro quo in the form of an enabling disclosure, "an applicant must provide sufficient assurance that at least substantially all of the compounds within a generic claim are useful." *Id.* (citing *In re* Cavallito, 282 F.2d 357 (C.C.P.A. 1960)).

92. *In re* Cook, 439 F.2d 730, 735 (C.C.P.A. 1971) (arguing that there is nothing wrong with claims reading on vast numbers of inoperative embodiments so long as the skilled artisan could determine utility without unreasonable effort).

93. Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1576–77 (Fed. Cir. 1984) ("Of course, if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid.").

94. Principal Brief for Plaintiffs-Appellees on Rehearing En Banc at 24–27, Ariad Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336 (Fed. Cir. 2010) (No. 2008-1248).

Cath Inc. v. Mahurkar cited *Ruschig* for this position[95] and held that there was a distinct written description requirement that must convey that, as of the filing date, the inventor was "in possession" of the invention.[96] Nevertheless, the court applied this separate requirement only to later-filed claims that sought the benefit of the priority date of an earlier-filed specification.[97] Therefore, the court was using this judicially recognized written description requirement as an alternative to a new matter rejection[98] and not to determine the adequacy of the disclosure for original claims.[99]

As this statutory interpretation did not create any new, substantive limitations but instead applied existing new matter requirements, the validity of the *Ruschig* and *Vas-Cath* interpretations was not of critical concern. In *Lilly*, however, the Federal Circuit, for the first time, invalidated an original claim for lack of written description, thereby recognizing a new substantive requirement.[100] For that reason, the issue of whether the statute can be correctly read to contain a separate written description requirement has become critically important.

35 U.S.C. § 112 requires that "[t]he 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

95. Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1561 (Fed. Cir. 1991) ("[T]he severability of [the] 'written description' provision from its enablement ('make and use') provision was recognized . . . as early as *In re Ruschig*.").

96. *Id.* at 1563–64 ("[W]e hereby reaffirm, that 35 U.S.C. § 112, first paragraph, requires a 'written description of the invention' which is separate and distinct from the enablement requirement. The purpose of the 'written description' requirement is broader than to merely explain how to 'make and use'; the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.").

97. *Id.* at 1560 ("[T]he 'written description' requirement most often comes into play where claims not presented in the application when filed are presented thereafter. Alternatively, patent applicants often seek the benefit of the filing date of an earlier-filed . . . application . . . for claims of a later-filed application.").

98. 35 U.S.C. § 132 (2006) ("No amendment shall introduce new matter into the disclosure of the invention."); 4 CHISUM, *supra* note 17, § 11.04 ("An applicant may amend an application's specification or drawings after the application is filed," but may not insert into the application new matter that involves a departure from or an addition to the original disclosure).

99. *Vas-Cath Inc.*, 935 F.2d at 1560 ("The question raised by these situations is most often phrased as whether the application provides 'adequate support' for the claim(s) at issue; it has also been analyzed in terms of 'new matter' under 35 U.S.C. § 132.").

100. Holman, *Paper Tiger*, *supra* note 18, at 5.

enable any person skilled in the art . . . to make and use the same."[101] Judicial proponents of a separate written description requirement read the statute to require "a written description of the invention" that is separate from the requirement that the disclosure "enable any person skilled in the art . . . to make and use the same."[102] Others, however, view the "written description of the invention" as the means for enabling the skilled artisan to make and use the invention and not as a separate requirement.[103] The Federal Circuit recently agreed to finally consider this question en banc[104] where it reaffirmed that 35 U.S.C. § 112 contains a written description requirement separate from enablement.[105]

2. *What is the Difference?*

Whether the statute supports a separate, substantive written description requirement is an important question because the requirement set forth in *Lilly* and reaffirmed in *Ariad* creates a heightened disclosure standard that is more difficult to apply than enablement without providing the public additional quid pro quo benefits.[106]

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101. 35 U.S.C. § 112.

102. *E.g.*, Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 971 (Fed. Cir. 2002) (Lourie, J., concurring with denial of rehearing en banc) ("The statute states that the invention must be described . . . . [W]hen the statute began requiring claims, it was not amended to delete the requirement; note the comma between the description requirement and the enablement provision, and the 'and' that follows the comma."); *see* 35 U.S.C. § 112.

103. Univ. of Rochester v. G.D. Searle & Co., 375 F.3d 1303, 1325 (Fed. Cir. 2004) (Linn, J., dissenting from denial of rehearing en banc) ("The sufficiency of [the] written description [requirement] . . . depends solely on whether it enables any person skilled in the art to which the invention pertains to make and use the claimed invention . . . ."); *Enzo*, 323 F.3d at 976 (Fed. Cir. 2002) (Rader, J., dissenting from denial of rehearing en banc); *Enzo*, 323 F.3d at 988 (Linn, J., dissenting from denial of rehearing en banc) ("35 U.S.C. § 112 requires a written description of the invention, but the measure of the sufficiency of that written description . . . should depend solely on whether it enables any person skilled in the art to which the invention pertains to make and use the claimed invention.").

104. The Federal Circuit granted en banc rehearing to reconsider the severability, scope, and purpose of the written description requirement. Ariad Pharms., Inc. v. Eli Lilly & Co., 595 F.3d 1329, 1330 (Fed. Cir. 2009). The parties were requested to file new briefs addressing (1) "[w]hether 35 U.S.C. § 112, paragraph 1, contains a written description requirement separate from an enablement requirement" and (2) if so, "what is the scope and purpose of the requirement." *Id.*

105. Ariad Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1340, 1344 (Fed. Cir. 2010).

106. Mark D. Janis, *On Courts Herding Cats: Contending with the "Written Description" Requirement (and Other Unruly Patent Disclosure Doctrines)*, 2 WASH. U. J.L. & POL'Y 55, 69 (2000)

Critics have viewed the *Lilly* written description requirement as a "super enablement" standard for biotechnology inventions because it requires a description of the invention beyond that which is required to enable the skilled artisan to make and use the invention.[107] For example, citing *Fiers v. Revel*, the *Lilly* court stated that an adequate written description of a DNA "requires a precise definition, such as by structure, formula, chemical name, or physical properties."[108] Importantly, this bright line rule increases the disclosure requirements for DNA sequences without taking into account the quantity or quality of the experimentation necessary to obtain the sequences.[109] In contrast, such a disclosure could be sufficient to enable the invention if undue experimentation would not be required.[110]

For enablement, the finder of fact weighs several objective factors, such as the predictability of the art and the relative skill of those in the art, to determine whether practicing the claimed invention at the time the application was filed would have required undue experimentation.[111] In contrast, to determine whether the written description requirement was met, the finder of fact must determine whether the inventor was in possession of the invention at the time the application was filed based entirely on the patent specification and knowledge in the art.[112]

("Proponents of the written description requirement have yet to explain exactly what benefits the requirement provides that are not already provided by the enablement requirement.").

107. Moba, B.V. v. Diamond Automation, Inc., 325 F.3d 1306, 1325 (Rader, J., concurring) ("[T]he only way to distinguish the *Lilly* rule from enablement is to construe *Lilly* as requiring more disclosure than necessary to enable one of skill in the art to make and use the invention, a 'super-enablement' standard. Interpreting *Lilly* in those terms, however, presents severe consequences for biotechnology."); Mueller, *supra* note 44, at 617 ("The *Lilly* court's elevation of written description to an effective 'super enablement' standard of uncertain scope and applicability will likely chill development in this critically important technology field and frustrate the . . . patent system's policy goal of encouraging prompt disclosure of new inventions.").

108. Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1566 (Fed. Cir. 1997) (quoting Fiers v. Revel, 984 F.2d 1164, 1171 (Fed.Cir.1993)).

109. *See id.*

110. *In re* Wands, 858 F.2d 731, 737 (Fed. Cir. 1988); Hybritech Inc. v. Monoclonal Antibodies Inc., 802 F.2d 1367, 1384 (Fed Cir. 1986); Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1576 (Fed. Cir. 1984).

111. *See, e.g.*, *Wands*, 858 F.2d at 737.

112. Falko-Gunter Falkner v. Inglis, 448 F.3d 1357, 1366–67 (Fed. Cir. 2006); Capon v. Eshhar, 418 F.3d 1349, 1357 (Fed. Cir. 2005).

For example, if a DNA sequence was already known in the art, such evidence would be applicable to the sufficiency of both written description and enablement. However, in evaluating the written description, the finder of fact would have to ignore evidence that the skilled artisan could have determined the sequence of additional DNA variants using routine methods. Thus, even if every single variant covered by the claim could be sequenced and tested for function in a single week using routine skill, the written description requirement might not be satisfied. It is for these reasons that the *Lilly* possession test is viewed as representing a heightened disclosure standard requiring "far more specific disclosure than enablement."[113]

Nevertheless, the Federal Circuit rejected the characterization that the *Lilly* written description requirement is a "super enablement" standard.[114] Moreover, according to the Federal Circuit, the written description requirement is part of the quid pro quo of a patent in that it "allows the [Patent Office] to examine applications effectively; courts to understand the invention, determine compliance with the statute, and to construe the claims; and the public to understand and improve upon the invention and to avoid the claimed boundaries of the patentee's exclusive rights."[115]

Application of the written description requirement also has procedural disadvantages. Importantly, whereas post-filing publications may be used to show that the specification was enabling in view of the state of the art at the time the application was filed,[116] the court will not consider post-filing evidence when determining adequacy of the written description.[117] In other words, an inventor

113. Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 981–82 (Fed. Cir. 2002) (Rader, J., dissenting from denial of rehearing en banc).

114. Ariad Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1352 (Fed. Cir. 2010) (arguing that the court has always expressly permitted the disclosure of structural features common to members of the genus (citing Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1569 (Fed. Cir. 1997))).

115. *Id.* at 1345.

116. *See, e.g.*, Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1336–37 (Fed. Cir. 2003) (allowing evidence of post-filing publications that demonstrated the extent of the enabling disclosure). *But see* Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1375–76 (Fed. Cir. 1999) (indicating that courts do not have to give post-filing evidence much weight).

117. *Ariad*, 598 F.3d at 1355 ("Because written description is determined as of the filing date . . . evidence of what one of ordinary skill in the art knew [after the application was filed] cannot provide

can use data gathered after the application was filed—demonstrating that the invention works as claimed—to prove that his patent was enabling. He cannot, however, use that same evidence to show he was also in possession of the invention when the application was filed.

3. Can the Lilly *Written Description Requirement be Satisfied for Generic DNA Claims?*

An important issue to consider is whether the written description requirement can ever be satisfied when applied to generic DNA claims.[118] According to the court in *Enzo*, functional limitations can satisfy the written description requirement for claims to genetic sequences if they are "coupled with a known or disclosed correlation between function and structure."[119] This position is based on the presumption that the more that is known about the structure of a protein, the greater the ability to predict genetic variants that will retain function.[120] Nevertheless, no matter how much is known about a protein's structure, it is generally impossible to predict with certainty the effect of a change in protein sequence—and thus structure—on protein function.[121]

Since some amino acid residues within a protein are directly involved in the activity of the protein, it is predictable that substitution of these residues, especially non-conservative substitutions,[122] might affect protein function.[123] On the other hand,

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substantial evidence to the jury that the asserted claims were supported by adequate written description.").

118. *See* discussion *supra* note 14.

119. Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 964 (Fed. Cir. 2002) (adopting the standard described in the Written Description Guidelines for showing that an invention is complete).

120. REVISED TRAINING MATERIALS, *supra* note 26, at 42 ("[A]mino acid substitutions outside of the two identified functional domains are unlikely to greatly affect activity Y.").

121. Brief of Amicus Curiae Law Professor Christopher M. Holman in Support of Neither Party at 14–15, Ariad Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336 (Fed. Cir. 2010) (No. 2008-1248) ("[D]espite recent advances in the field . . . protein engineering remains as much an art as it is a science . . . because the rules defining sequence-structure-function relationships are still not well understood." (second and third alteration in original) (quoting PROTEIN ENGINEERING AND DESIGN vii (Sheldon J. Park & Jennifer R. Cochran eds., CRC Press 2010))).

122. A conservative substitution is "the replacement in a protein of one amino acid by another, chemically similar, amino acid . . . [which] is generally expected to lead to either no change or only a

the sequence of a protein also determines how the amino acid polymer folds into secondary and tertiary shapes, which in turn affects the activity and stability of the protein.[124] Therefore, substitution of amino acid residues within the polymer can affect the structure, and thus the activity or stability of the protein.[125] While experimental three-dimensional (3D) structures predicted from crystallography studies greatly improve the ability to correlate protein function and stability, these predicted structures are available for only a small percentage of proteins.[126] Moreover, efforts to predict protein function based on changes in protein stability have so far failed to provide a simple correlation between protein stability and function.[127]

In light of this uncertainly, a rational application of *Lilly*'s written description requirement to genetic sequences may require that the specification provide evidence that each and every sequence covered under the claim be functional. If invention requires actual possession by the inventor, rather than merely placing the public in possession of the invention without undue experimentation, then it stands to reason that no claim to a DNA or protein is valid if it were not first shown to possess the desired function. Of course, such an application of the *Lilly* written description standard could seem unduly strict in view of the constitutional mandate to promote scientific progress,[128] which may be why the *Enzo* court attempted to reduce the impact of the written description requirement.

Interestingly, the *Enzo* court relaxed the written description requirement based on evidence that deposit of genetic sequences in a public depository "makes its contents accessible to the public when it is not otherwise available in written form."[129] Admittedly, "[t]he practice of depositing biological material arose primarily to satisfy

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small change in the properties of the protein." DICTIONARY OF BIOCHEMISTRY AND MOLECULAR BIOLOGY 97 (John Wiley & Sons, 2d ed. 1989).

123. Yana Bromberg & Burkhard Rost, *Correlating Protein Function and Stability Through the Analysis of Single Amino Acid Substitutions*, 10 (Supp. 8) BMC BIOINFORMATICS, S8 (2009).

124. *Id.*

125. *Id.*

126. *Id.*

127. *Id.*

128. U.S. CONST. art. I, § 8, cl. 8.

129. Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 965 (Fed. Cir. 2002).

the enablement requirement," but the court extended this application to written description even though the inventors did not know the structure of the sequences.[130] The court made this concession because "[a] person of skill in the art, reading the accession numbers in the patent specification, can obtain the claimed sequences from the . . . depository by following the appropriate techniques to excise the nucleotide sequences from the deposited organisms containing those sequences."[131] Thus, while the deposit enabled the skilled artisan to determine the structure of the genetic sequences without undue experimentation, it did nothing to show that the inventors were actually in possession of this structure when the application was filed.[132] The court nevertheless concluded that the written description was satisfied.[133]

The court continued to apply enablement standards to relax the written description requirement in *Noelle v. Lederman*, holding that inventors can show possession of an antibody by disclosing the antigen to which the antibody binds.[134] The court came to this conclusion based on the "well defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature."[135]

The rulings in *Enzo* and *Noelle* have been correctly criticized as a clear departure from the *Lilly* standard of requiring sufficient structural disclosure of the claimed invention.[136] More importantly, these cases blur the distinction between these supposedly divergent requirements by applying enablement standards in *Lilly* clothing.

This blurring continued in the *Ariad* en banc decision, where the court identified a number of factors for evaluating the adequacy of disclosure for generic claims that are surprisingly similar to the *In re*

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130. *Id.* at 965–66.
131. *Id.*
132. *See id.*
133. *Id.* at 966.
134. Noelle v. Lederman, 355 F.3d 1343, 1349 (Fed. Cir. 2004).
135. *Id.* (quoting *Enzo*, 323 F.3d at 964).
136. Wenrong Huang, Enzo*'s Written Description Requirement: Can It Be an Effective Check Against Overly Broad Biotechnology Claims?*, 16 ALB. L.J. SCI. & TECH. 1, 13–14 (2006).

Wands factors used to evaluate enablement.[137] In identifying these factors, the court was recognizing that "the level of detail required to satisfy the written description requirement varies depending on the nature and scope of the claims and on the complexity and predictability of the relevant technology."[138] Therefore, the amount of detail needed to satisfy the written description requirement will depend upon similar factors to that of the enablement requirement, albeit with different goals in mind.

4. Does the Lilly *Written Description Requirement Protect the Public?*

Many commentators have defended the substantive written description requirement set forth in *Lilly* based on public policy reasons.[139] These commentators appear to be reacting to a fear that a select few will gain a monopoly over all of the valuable genes and thereby hinder research and development.[140] The economics of how patent scope affects the progress of science, however, is actually quite complicated.[141] Courts, therefore, have used the disclosure requirements to ensure that the scope of patent claims at least do not

137. Ariad Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1351 (Fed. Cir. 2010) ("For generic claims, we have set forth a number of factors for evaluating the adequacy of disclosure, including 'the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue.'" (alteration in original) (quoting Capon v. Eshhar, 418 F.3d 1349, 1359 (Fed. Cir. 2005))); *cf. supra* note 84 and accompanying text.

138. *Id.*

139. Huang, *supra* note 136, at 14 (arguing that the written description requirement prevents the granting of monopolies to inventors for something they did not invent); William C. Mull, *Using the Written Description Requirement to Limit Broad Patent Scope, Allow Competition, and Encourage Innovation in Biotechnology*, 14 HEALTH MATRIX 393, 421 (2004) (arguing that without *Lilly*, "an applicant would be able to claim more than he invented simply by including the claims in the original application"); Zhibin Ren, *Confusing Reasoning, Right Result: The Written Description Requirement and* Regents of the University of California v. Eli Lilly & Co., 1999 WIS. L. REV. 1297, 1321 (1999) (arguing that had the inventors in *Lilly* wanted to claim cDNA from other species, they could have cloned and sequenced them); Mark J. Stewart, *The Written Description Requirement of 35 U.S.C. § 112(1): The Standard After* Regents of the University of California v. Eli Lilly & Co., 32 IND. L. REV. 537, 562–63 (1999) (arguing that upholding the claims would have rendered the species obvious, effectively blocking others from obtaining patents on those molecules, which would have crippled the biotechnology industry).

140. *See supra* note 136.

141. *See* Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839, 904–09 (1990); Mull, *supra* note 139, at 426–30.

reach beyond the quid pro quo provided by the disclosure in exchange for the government granted monopoly.[142]

Prior to *Lilly*, adequacy of disclosure in satisfying the quid pro quo was evaluated in terms of enablement,[143] which requires that the inventor enable the full scope of the invention and thereby place the invention into the public's possession without undue experimentation.[144] In contrast, the written description requirement demands that disclosure demonstrate that the inventor was in possession of the invention at the time the application was filed.[145]

While there may be economic theories to support limiting the scope of biotechnology patent claims to less than what was enabled,[146] these theories are not based on the traditional quid pro quo concern.[147] Instead, the *Lilly* court defended this strict application of the disclosure requirement on the grounds that the description must further demonstrate to the skilled artisan that the inventor "invented" what is claimed.[148]

To understand how this "invention" standard benefits the public, it is necessary to consider the context of the cases in which it was first enumerated. Prior to *Lilly*, the written description requirement was used to prevent applicants from amending their applications to claim aspects of their invention that they had not originally described in the

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142. Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 970 (Fed. Cir. 2002) ("[D]escription [of the invention] is the quid pro quo of the patent system; the public must receive meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time."); 3 CHISUM, *supra* note 17, § 7.01.

143. *E.g.*, *In re* Fisher, 427 F.2d 833, 839 (C.C.P.A. 1970); *see also* Holman, *Paper Tiger*, *supra* note 18, at 6–8.

144. *In re* Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993) ("Although not explicitly stated in section 112, to be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'").

145. Falko-Gunter Falkner v. Inglis, 448 F.3d 1357, 1366–67 (Fed. Cir. 2006); Capon v. Eshhar, 418 F.3d 1349, 1357 (Fed. Cir. 2005).

146. *See* Mull, *supra* note 139, at 426–30; Merges & Nelson, *supra* note 141, at 904–09.

147. *See* Brenner v. Manson, 383 U.S. 519, 534 (U.S. 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.").

148. Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1566 (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.'" (citing Lockwood v. Am. Airlines, Inc., 107 F.3d 1565, 1572 (Fed. Cir. 1997))).

patent specification or original claims.[149] In that context, the court determined that it is not enough that a disclosure enable or make obvious the later-claimed invention; it must also disclose the invention sufficiently to support the conclusion that the inventor had actually invented it at the time the disclosure was filed.[150] For example, if someone invents a doorknob and describes how to make the doorknob out of wood, he would not be allowed a year later to amend his application to recite that the doorknob could be made of porcelain, even though a porcelain doorknob would be enabled and considered obvious in view of his patented wooden doorknob.[151]

Therefore, this use of written description to police priority and new matter amendments serves a purpose distinct from the quid pro quo requirement of enablement—it prevents an applicant from claiming improvements and specific embodiments she had not contemplated when the application was filed. Importantly, this view does not prevent an inventor from claiming a genus that covers multiple embodiments if she has enabled the full scope of the genus; it does, however, prevent her from later claiming a specific embodiment covered by her genus claim that is merely obvious in view of her disclosure of the genus.[152]

B. Claiming Genes that Do Not Work

Since it is possible that written description can be secured for sequence identity claims by excluding a functional limitation from

149. *See, e.g.*, *Lockwood*, 107 F.3d at 1571–72 (considering whether claims should receive the benefit of an earlier filed application where the invention would have been obvious in view of the disclosure of the prior application); Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1560 (Fed. Cir. 1991) (noting that the written description requirement is relevant to new claims not present in the application or in claims seeking the benefit of the filing date of an earlier-filed application); *In re* Ruschig, 379 F.2d 990, 991 (C.C.P.A. 1967) (considering the validity of a claim added to the application a year after it was filed to a specific drug that was not disclosed in the specification).

150. *Ruschig*, 379 F.2d at 995 ("While we have no doubt a person so motivated would be enabled by the specification to make [the claimed compound], this is beside the point for the question is not whether he would be so enabled but whether the specification discloses the compound to him, specifically, as something appellants actually invented.").

151. *See, e.g.*, *Hotchkiss v. Greenwood*, 52 U.S. (11 How.) 248 (1851).

152. A genus does not always anticipate or make obvious a species of that genus. Eli Lilly & Co. v. Bd. of Regents of Univ. of Wash., 334 F.3d 1264, 1269–70 (Fed. Cir. 2003); 1 CHISUM, *supra* note 17, § 3.02(2)(c).

the claim,[153] it is important to consider the impact of this claim strategy on enablement.

Notably, the Board has shown a willingness to find enablement of sequence identity claims when the functional limitation is included.[154] For example, the claims in *Ex parte Kubin* contained a functional limitation, which limited the scope of the percent identity claim to operable embodiments.[155] The Board found that the percent identity claims limited by a functional limitation lacked sufficient written description.[156] The court also concluded, however, that even though the amount of experimentation needed to practice the full scope of the invention might have been extensive, it would have been routine based, inter alia, on the state of the art and the relative skill of those in the art.[157] The Board based this opinion on evidence that methods of making the claimed nucleic acid sequences and screening for activity were known in the art and described in the specification.[158]

Therefore, for claims to a genus of genetic sequences reciting a function for the proteins encoded by the sequences, the enablement inquiry is whether the skilled artisan can make genetic sequences within the structural scope of the claim and screen them for the claimed function without undue experimentation.[159]

Since the purpose of the functional limitation is to expressly limit the scope of the claimed sequences to those that are functional and to thereby exclude inoperative embodiments, it is important to consider the impact of omitting the function from the claims on the enablement inquiry. A claim to a genus can be enabled even when it

153. Compare Claim 1 *with* Claim 2 in Example 11A of REVISED TRAINING MATERIALS, *supra* note 26, at 37.

154. *See, e.g.*, *Ex parte* Abad, 2008 WL 904456, at *8 (B.P.A.I. Apr. 3, 2008); *Ex parte* Kubin, 83 U.S.P.Q.2d 1410, 1416 (B.P.A.I. 2007).

155. Claim 73 recited: "An isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide at least 80% identical to amino acids 22–221 of SEQ ID NO:2, wherein the polypeptide binds CD48." *Ex parte* Kubin, 83 U.S.P.Q.2d 1410, 1412 (B.P.A.I. 2007).

156. *Id.* at 1416–17 ("While we conclude one skilled in the art would have been able to make and use the full scope of [the invention] through routine experimentation, we find Appellants did not describe the invention . . . sufficiently to show they had possession of the claimed genus of nucleic acids.").

157. *Id.* at 1416.

158. *Id.*

159. *Id.*

covers some inoperative embodiments.[160] If, however, the number of inoperative embodiments is so high that it forces the skilled artisan to use undue experimentation to identify functional embodiments and practice the invention, the claim will fail for lack of enablement.[161]

Therefore, for claims to a genus of genetic sequences that do *not* recite a function for the sequence, the enablement inquiry is whether the skilled artisan can make nucleic acids within the structural scope of the claim and screen them for a function identified in the specification without undue experimentation. Sound familiar? The only apparent difference in the two enablement inquiries is that in the first instance, the function is recited in the claim, and in the second instance, a function is provided in the specification.[162]

Certainly, a difference in scope exists between these two types of genus claims. A claim to a genus of genetic sequences that does not recite a function most likely reads on inoperative embodiments such that the inventor can exclude others from making and using genetic sequences that do not have a use disclosed in the patent application. For example, a claim to a genus of proteins having 95% sequence identity to insulin will inevitably cover many protein variants that would not be effective in treating diabetes.[163] Moreover, were one to later identify another novel use for one or more of those inoperative insulin variants, such as the ability to repair cartilage,[164] the genus claim would still dominate that later invention even though the inventor had not enabled a use for that insulin variant.

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160. *In re* Cook, 439 F.2d 730, 735 (C.C.P.A. 1971) (arguing that there is nothing wrong with claims reading on vast numbers of inoperative embodiments so long as the skilled artisan could determine utility without unreasonable effort).

161. Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1576–77 (Fed. Cir. 1984) ("Of course, if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid.").

162. The specification must provide a specific and substantial utility for the claimed invention. *In re* Fisher, 421 F.3d 1365, 1371 (Fed. Cir. 2005) (arguing that the claimed invention must provide a well-defined and particular benefit to the public as disclosed in its current form); 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.").

163. *See* Holman, *Protein Similarity Score*, *supra* note 10, at 72 n.70.

164. *See* Use of Insulin for the Treatment of Cartilagenous Disorders, U.S. Patent No. 6,689,747 (filed Mar. 22, 2001).

III. PROPOSAL

Inventors should consider claiming genetic inventions based on sequence identity without reciting a function for the genetic variants in the claim. While this approach will result in claims covering genetic sequences that do not function according to the invention—inoperative embodiments—the burden on the skilled artisan to practice the invention with this approach is no more onerous than when the function is recited.[165] The fact that inclusion of the functional limitation can cause otherwise patentable claims to become invalid is a testament to the problems inherent with severing enablement and written description standards.

A. Enablement is Enough

The *Lilly* written description requirement demands more than placing the public in possession of the invention—it requires that the disclosure demonstrate the inventor was in actual possession of the invention at the time the application was filed.[166] This additional check on the patent system is based on the premise that inventors should not be granted patents for things they did not invent;[167] an appealing proposition, on its face. Nevertheless, the public is equally enriched either way since the enablement standard requires that the public gain possession of the invention without undue experimentation.

Consider the following hypothetical. Andy discovers gold using his gold detector. He is able to prove that there is at least one ounce of gold buried in the ground, but only additional digging will determine the full scope of the treasure. He subsequently makes a

165. *See* discussion *supra* Part II.B.

166. Falko-Gunter Falkner v. Inglis, 448 F.3d 1357, 1366–67 (Fed. Cir. 2006); Capon v. Eshhar, 418 F.3d 1349, 1357 (Fed. Cir. 2005).

167. Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 975 (Fed. Cir. 2002) (Newman, J., concurring) ("The description of the invention . . . sets forth what has been invented, and sets boundaries of what can be claimed. . . . The dissent's citation of cases . . . reinforces . . . the role of the description of the invention in establishing what has been invented.").

contract[168] with Bob to split the treasure if Bob does the digging. Bob digs three feet down, as instructed, and finds a 100-ounce nugget of gold. Should it matter whether Andy knew the exact amount of gold beforehand? Bob is equally enriched regardless of whether Andy had foreknowledge of the full scope of the treasure. Moreover, were we to require more initial disclosure by Andy in order for him to enforce his claim, he would be less inclined to contract with other prospectors at the point when he first discovered the source of gold.

The proponents of the *Lilly* written description requirement would presumably want Andy to forfeit his claim to his share of the remaining ninety-nine ounces of gold since he only disclosed one ounce. Applying these proponents' public policy arguments, Andy should not be able to claim the full scope of the treasure until he was in "possession" of his discovery, i.e., until Andy could describe it with structural detail.[169] It would not satisfy them that Andy enabled Bob to gain possession of the gold by identifying the location of the gold and giving Bob a shovel.[170] Rather, to protect his secret, Andy should have determined how much gold was present before he started handing out shovels.[171]

Of course, *Lilly* proponents claim they are protecting the public by preventing prospectors from laying claim to all the treasure in the ground prematurely.[172] This concern, however, is unfounded, since the claim has to place the public in possession of the full scope of the treasure being claimed without undue experimentation.[173] For

168. A patent can be viewed as a contract between the inventor and the public. Pickering v. Holman, 459 F.2d 403, 407 (9th Cir. 1972) ("A patent is in the nature of a contract between the public and the inventor . . . . The publication bar goes upon the theory that the idea is already in the public domain and there can be no consideration offered in exchange for the grant of the monopoly.").

169. *See* Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1566 (Fed. Cir. 1997) ("An adequate written description of a DNA . . . 'requires a precise definition, such as by structure, formula, chemical name, or physical properties' . . . ." (quoting Fiers v. Revel, 984 F.2d 1164, 1171 (Fed. Cir. 1993))).

170. *See* Ren, *supra* note 139, at 1321 (arguing that had the inventors in *Lilly* wanted to claim cDNA from other species, they could have cloned and sequenced them).

171. *See id.*

172. *See* Huang, *supra* note 139, at 14 (arguing that the written description requirement prevents the granting of monopolies to inventors for something they did not invent); Mull, *supra* note 139, at 421 (arguing that without *Lilly*, an applicant would be able to claim more than he invented simply by including the claims in the original application).

173. *In re* Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993).

example, Andy would have a much harder time justifying his claim had he merely told Bob that there was a precious metal somewhere underground within a specified square mile and had only given Bob a spoon to dig with.

Likewise, the role of the written description requirement recognized in *Ruschig* and *Vas-Cath* provides a distinct role in protecting the public. For example, if Bob is rewarded for his digging efforts by finding diamonds in addition to gold, Andy would not be heard to say he had a claim to the diamonds as well.[174] Why can he claim the additional amounts of gold but not the diamonds? A simple answer is that he did not assert a credible claim to diamonds when handing out the shovels.[175] Someone specifically looking for diamonds would not have been any closer to finding them based on Andy's claim. Moreover, had Andy tried to claim diamonds when he only had evidence of gold, his claim would likely not have been considered credible.[176] Thus, the enablement standard is sufficient to satisfy the quid pro quo disclosure requirement; whereas the written description standard judicially recognized in *Ruschig* serves a limited purpose in policing priority claims.[177]

Unfortunately, the court did not apply the enablement standard to the claims rejected in *Lilly*.[178] It is possible that in the early days of biotechnology, finding homologous cDNAs in other mammalian species was more akin to using a spoon than a shovel to dig for treasure, and that the claims in those early cases were properly rejected.[179] Since then, however, cloning and sequencing methods

174. *See* discussion *supra* Part II.A.4.

175. The claims define "the invention for the purpose of applying the conditions of patentability" determining infringement. 3 CHISUM, *supra* note 17, § 8.01.

176. *See* Rasmusson v. SmithKline Beecham Corp., 413 F.3d 1318, 1325 (Fed. Cir. 2005) (arguing that plausibility of invention is not enough and that some data supporting the claimed invention is necessary to enable an invention).

177. *See* discussion *supra* Part II.A.4.

178. *See* Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1566 (Fed. Cir. 1997).

179. *See* Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 980, n.7 (Fed. Cir. 2002) (Rader, J., dissenting) ("In 1977, biotechnology was still in its infancy. In fact, the Maxam and Gilbert method of sequencing DNA was just published in 1977. Cloning in that era was, at a minimum, unpredictable and would have required vast amounts of experimentation to accomplish. Therefore, the patent's prophetic disclosure of human insulin cDNA hardly enabled its production as claimed. Instead of pursuing this

have become more conventional.[180] Therefore, the court should ascertain the level of experimentation required for the public to *gain* possession of the full scope of the invention since the inventor's possession at the time the application was filed does little for the public.

B. Function Recited or Implied

In view of the Written Description Training Materials published by the Patent Office[181] and the application of this view by the Board,[182] genetic sequences should be claimed based on percent identity to a reference sequence without reciting the function of the genetic sequence in the claim. Without the functional limitation, a genus of genetic sequence based on sequence identity is defined entirely by structure, which is alone sufficient to describe the invention.[183] The only problem with this approach is that the genus is likely to cover inoperative embodiments based on the substitution of amino acid residues critical for protein function or stability.[184]

However, the amount of experimentation necessary to avoid inoperative embodiments covered by the claim when function is omitted should be the same as the amount of experimentation necessary to identify sequences that have the functional limitation recited in the claim.[185] For example, if Andy's gold mine contains both gold and pyrite,[186] the amount of experimentation needed for Bob to separate the gold from the pyrite is the same no matter how it was claimed. It is therefore reasonable to conclude that sequence

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obvious avenue of rejection, the Federal Circuit reached out beyond the statute and the case law to create a new general disclosure test.").

180. *See In re* Kubin, 561 F.3d 1351, 1356 (Fed. Cir. 2009).

181. *See* REVISED TRAINING MATERIALS, *supra* note 26, at 37–42.

182. *See Ex parte* Kubin, 83 U.S.P.Q.2d 1410, 1416–17 (B.P.A.I. 2007).

183. *Lilly*, 119 F.3d at 1566 ("An adequate written description of a DNA . . . 'requires a precise definition, such as by structure, formula, chemical name, or physical properties' . . . ." (quoting Fiers v. Revel, 984 F.2d 1164, 1171 (Fed.Cir.1993))).

184. *See* discussion *supra* Part II.A.3.

185. *See* discussion *supra* Part II.B.

186. Interestingly, while the mineral pyrite is nicknamed "fool's gold" due to its resemblance to gold, iron pyrite has been found to have other—inventive—uses. *See, e.g.*, Katherine Bourzac, *Mining Fool's Gold for Solar: Cyrus Wadia is Using Abundant Materials to Grow Nanocrystals for Cheaper Photovaltaics*, 112 TECH. REV. 80 (Nov. 1, 2009); U.S. Patent No. 4,119,769 (filed Oct. 31, 1977).

identity claims that do not recite a functional limitation can likewise be enabled.

Importantly, the Board has been willing to find sequence identity claims enabled when the genus of sequences are further limited to those having a particular function.[187] This willingness is based on the understanding that undue experimentation is not required when methods of making nucleic acid sequences covered by the claim and methods of screening for those sequences having the desired activity are sufficiently known in the art and described in the specification.[188]

C. Experimentation in the Genetic Age

The primary issue with sequence identity claims is that the number of possible variants covered by the claim can be enormous.[189] Even allowing for a single amino acid change can result in millions of possible genetic sequences covered by a claim.[190] While it may be reasonable for the skilled artisan to make a few genetic variants covered by the claim and screen them for the desired function, it may not be reasonable to ask that same person to test several thousand variants. On the other hand, what was unreasonable yesterday may be reasonable tomorrow due to technological improvements and automation. That is why the court considers several factors in determining whether a disclosure would require undue experimentation.[191] In *In re Wands*, the court set forth several factors to be considered in determining whether a disclosure would require undue experimentation, including the amount of guidance in the patent application, the state of the art, the relative skill of those in the art, the predictability of the invention, and the breadth of the claims.[192]

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187. *See, e.g.*, *Ex parte* Abad, 2008 WL 904456, at *8 (B.P.A.I. Apr. 3, 2008); *Ex parte* Kubin, 83 U.S.P.Q.2d at 1416.
188. *Kubin*, 83 U.S.P.Q.2d at 1416.
189. *See supra* note 13 and accompanying text.
190. *See id.*
191. *In re* Wands, 858 F.2d 731, 737 (Fed. Cir. 1988) (citing *Ex parte* Forman, 230 U.S.P.Q. 546, 547 (B.P.A.I. 1986)).
192. *Id.*

Currently, even with the advancements made in the field of *in silico* protein structure prediction, it is still generally impossible to predict with certainty the effect that a change in protein sequence, and thus structure, will have on protein function.[193] Therefore, whether a sequence identity claim is enabled will depend inter alia upon the level of identity claimed, which determines the breadth of the claim, and the nature of the assay for testing for activity.[194] For example, if a high-throughput assay can be used to test for function of the genetic variants, a lower percent identity—a larger genus and thus more non-functional variants—can be tolerated without undue experimentation.[195] In contrast, a higher percent identity—a smaller genus—would be necessary where the invention requires *in vivo* testing to determine whether a genetic variant has the desired activity.[196]

CONCLUSION

It is reasonable for inventors of novel genes and recombinant technologies to desire patent protection beyond the scope of the specific genetic sequence they exemplify.[197] Notably, it is becoming increasingly simple for a competitor to engineer genetic variants that preserve, or in some cases improve, the therapeutic efficacy of an encoded protein in order to circumvent a patent.[198] In contrast, while simple to identify one variant, the number of such functional variants is potentially so enormous that it is impractical—if not impossible—for the inventor to recite each and every one.[199] Nevertheless, reasonable efforts by inventors to define genetic inventions in a

193. *See* discussion *supra* Part II.A.3.
194. *See Wands*, 858 F.2d at 737.
195. *See id.*
196. *Id.*
197. *See* discussion *supra* Introduction.
198. Holman, *Learning from Litigation*, *supra* note 8, at 226–27; Holman, *Protein Similarity Score*, *supra* note 10, at 57–60.
199. *See supra* note 13 and accompanying text.

manner that will prevent routine circumvention are being viewed as overreaching.[200]

The patent disclosure requirements codified in the first paragraph of 35 U.S.C. § 112[201] are intended to prevent overreaching by inventors beyond the quid pro quo the public receives for granting the limited monopoly.[202] Prior to 1997, the courts relied primarily on the enablement requirement to invalidate overreaching claims.[203] However, in *Regents of the University of California v. Eli Lilly & Co.*,[204] the court for the first time invalidated an original, arguably overreaching, claim for lack of written description.[205] In doing so, the court stated that an adequate written description of a DNA "requires a precise definition, such as by structure, formula, chemical name, or physical properties."[206] This bright line rule creates a heightened disclosure standard that is more difficult to apply than enablement without providing to the public additional quid pro quo benefits.[207]

Notably, the court has attempted to relax the stringency of this requirement.[208] These efforts have, however, involved application of enablement principles to show possession by the inventor.[209] This blurring of the distinction between these supposedly divergent requirements begs the question whether enablement and written description are properly severable in the first place.[210]

One approach originally endorsed by the Patent Office[211] to satisfy the *Lilly* written description requirement for genetic inventions was the claiming a genus of genetic sequences based on percent identity to a reference sequence that is limited by a functional limitation.[212] According to the court in *Enzo*, however, in order for functional

200. *See* discussion *supra* Part I.A.
201. 35 U.S.C. § 112 (2006).
202. 3 CHISUM, *supra* note 17, § 7.01.
203. *See* discussion *supra* Part I; *supra* note 18.
204. Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559 (Fed. Cir. 1997).
205. Holman, *Paper Tiger*, *supra* note 18, at 4.
206. *Lilly*, 119 F.3d at 1566 (quoting Fiers v. Revel, 984 F.2d 1164, 1171 (Fed. Cir. 1993)).
207. *See* discussion *supra* Part II.A.2.
208. *See* discussion *supra* Part II.A.3.
209. *See* discussion *supra* Part II.A.3.
210. *See* discussion *supra* Part II.A.1.
211. *See supra* note 23.
212. *See* discussion *supra* Part I.A.

limitations to satisfy the written description requirement, they must be "coupled with a known or disclosed correlation between function and structure."[213] Consistent with this decision, the Patent Office recently reversed its position and proposed that inclusion of a functional limitation, which narrows the genus of genetic sequences to those that produce a functional protein, actually increases the burden on the specification to satisfy the written description requirement by disclosing a correlation between structure and function.[214] This position is based on the presumption that the more you know about the structure of a protein, the greater the ability to predict genetic variants that will retain function.[215] This, however, may not be true since no matter how much is known about a protein's structure, it is generally impossible to predict with certainty the effect of a change in protein sequence, and thus structure, on protein function.[216]

Inventors should therefore consider defining genetic inventions completely by structure without reciting the function in the claims. While this approach will result in claims covering genetic sequences that do not function according to the invention—inoperative embodiments—the burden on the skilled artisan to practice the invention with this approach is no more onerous than when the function is recited.[217] That is because the amount of experimentation for the skilled artisan to avoid inoperative embodiments—when the function is omitted—is identical to the amount of experimentation necessary to identify functional variants when function is recited in the claim.[218] Either way, the skilled artisan must make variants defined structurally by the claim and then use an assay to test the variants for the desired function. The fact that the written description

213. Enzo Biochem, Inc. v. Gen-Probe Inc, 323 F.3d 956, 964 (Fed. Cir. 2002) (adopting the standard described in the Written Description Guidelines for showing that an invention is complete).

214. *See* discussion *supra* Part I.A; *see also* REVISED TRAINING MATERIALS, *supra* note 26, at 37–39.

215. REVISED TRAINING MATERIALS, *supra* note 26, at 42 ("[A]mino acid substitutions outside of the two identified functional domains are unlikely to greatly affect activity Y.").

216. *See* discussion *supra* Part II.A.3.

217. *See* discussion *supra* Part II.B.

218. *See* discussion *supra* Part II.B.

standard treats these two situations so differently is another testament to the problems inherent with severing these standards.