QUESTIONING THE REQUIREMENT FOR WRITTEN DESCRIPTION: *ENZO BIOCHEM V. GEN-PROBE* AND OVERLY BROAD PATENT CASES

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INTRODUCTION

Imagine the following patent claim: "An isolated protein capable of inhibiting beta-amyloid." Assume that the patent explains that beta-amyloid is the protein responsible for plaques in the brain associated with Alzheimer's disease and that inhibition of beta-amyloid may be therapeutically useful to treat, cure, or prevent Alzheimer's disease. The patent relates that the physical and chemical structures of beta-amyloid are well known, and it explicitly describes the beta-amyloid molecule and a method for identifying inhibitors of the molecule. Additionally, the patent explains that proteins in general have been extensively studied such that it is an advanced field of biochemistry. Accordingly, proteins can be characterized by numerous methodologies in the art, and the basic structure of proteins—the primary, secondary, tertiary, and in some cases, quaternary structure—can be readily determined by the skilled artisan. Given that disclosure, a person of ordinary skill might hypothesize generally about the types of proteins that would inhibit beta-amyloid, but the full scope of which proteins are encompassed by this claim would be difficult, if not impossible, to comprehend. The scope could encompass literally billions of proteins. Should the inventor on this patent, who discovered the method of identifying inhibitors of beta-amyloid *but did not disclose any proteins that inhibit beta-amyloid*, be granted exclusive rights to all proteins discovered to have this property?

To allow a patent claim of such broad scope would be inconsistent with the goals of patent law. The scope of the claim is not commensurate with the inventor's contribution to the field of Alzheimer's research. He discovered how to identify proteins that inhibit beta-amyloid; claims to his method may be patentable by him. Additionally, any proteins that he can characterize by structure or partial structure correlated with function may be patentable by him. Nonetheless, this inventor has not conceived of all possible proteins that may inhibit beta-amyloid. Because the patent system provides exclusivity to inventors for a specific period, allowing him such a broad scope would exclude other researchers who are investigating potential treatments, cures, and preventive methods for Alzheimer's disease using proteins to inhibit beta-amyloid. Exclusivity would limit research to this inventor, his licensees, and parties willing to risk an infringement suit later. This limitation could be disastrous for Alzheimer's research.

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Despite the possible ruinous results, claims that are nearly as broad, such as "[a]n isolated antibody capable of binding to Antigen X,"[1] are being advocated by the United States Patent and Trademark Office (USPTO), and more recently by the U.S. Court of Appeals for the Federal Circuit, as complying with current patent law.[2] Lawsuits are being litigated over patents in which the inventor was granted a claim with very broad scope, but the inventor did not produce even a single composition. For example, in *University of Rochester v. G.D. Searle & Co.*,[3] the U.S. District Court for the Western District of New York granted a motion for summary judgment of patent invalidity for failure to meet the written description requirement of 35 U.S.C. § 112, first paragraph.[4] The invalid patent claimed "a pharmaceutical 'method for selectively inhibiting PGHS-2 activity in a human host' in which 'the activity of PGHS-1 is not inhibited,'" but the inventors produced no compositions.[5] The court held that the patent could not be practiced until a composition was invented for use in the method.[6] Thus, the inventors did not possess the complete invention, and the patent failed to meet the written description requirement. Permitting such a broad claim is not in accordance with public policy relating to patent exclusivity. Instead, it frustrates the practice of patent law by confusing inventors and practitioners regarding the requirements for obtaining a patent, particularly the written description requirement.

This Note discusses recent cases dealing with written description law, particularly with respect to biotechnology,[7] and the associated rise of discord among judges in the U.S. Court of Appeals for the Federal Circuit. Recent questions concerning changes in written description law are addressed by

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1. *See Synopsis of Application of Written Description Guidelines*, at 59-60, *available at* http://www.uspto.gov/web/menu/written.pdf (last visited Oct. 22, 2003) [hereinafter *Synopsis of Application*].

2. *See* Enzo Biochem, Inc. v. Gen-Probe, Inc., 323 F.3d 956, 964 (Fed. Cir. 2002).

3. 249 F. Supp. 2d 216 (W.D.N.Y. 2003).

4. 35 U.S.C. § 112 para. 1 (2000). Citations to the written description requirement vary widely. For consistency, all references to the statute in the text of this Note are stated as "§ 112, first paragraph," and in the footnotes as "35 U.S.C. § 112, para. 1" or in short form as "§ 112, para. 1." The abbreviation "para. 1" is used rather than "¶ 1" or "(1)" because the "authority is organized in part by indented paragraphs not introduced by paragraph symbols . . ." or by numbered paragraphs. THE BLUEBOOK: A UNIFORM SYSTEM OF CITATION 37 (Columbia Law Review Ass'n et al. eds., 17th ed. 2000). Exceptions to these citations in this Note occur when the statute is cited otherwise in a quote or in a title; in those situations, the citation is not revised.

5. *Univ. of Rochester*, 249 F. Supp. 2d at 219-20. *Cf. Ariad Announces Filing of Lawsuit Against Eli Lilly Alleging Infringement of Pioneering NF-KB Treatment-Method Patent*, *at* http://media.corporate-ir.net/media_files/nsd/aria/releases/062502-2.pdf. This case was filed in the U.S. District Court for the District of Massachusetts on June 25, 2002 and is awaiting trial at the date of this Note.

6. *Univ. of Rochester*, 249 F. Supp. 2d at 218.

7. "Biotechnology," "biotechnical," and "biotechnological" are commonly abbreviated as "biotech" and will hereinafter be referred to as such.

analyzing *Enzo Biochem, Inc. v. Gen-Probe, Inc.*,[8] a series of cases from 2002. The second decision in the *Enzo* series, *Enzo* II, signifies an inflection point in the court's concurrence on the use of a discrete written description requirement, separate from enablement. Suddenly, patent practitioners are uncertain how to meet the written description requirement.[9] Furthermore, this question is not likely to be resolved in the near future. The court denied *en banc* review,[10] and Enzo Biochem and Gen-Probe settled the remanded case out of court, providing no resolution to the outstanding questions in the case. In the meantime, attorneys and agents continue to file patent applications, merely guessing at what the written description requirements will be and hoping to meet the standard to protect their clients' rights. This Note addresses the far-reaching implications that these changes will have on patent practice and the biotech industry in general.

I. BRIEF INTRODUCTION TO BIOTECHNOLOGY AND BIOTECH PATENTS

A. The Importance of Biotech Patents

The biotech field is a rapidly growing area of the pharmaceutical industry, the fruits of which may cure some of today's worst diseases. Yet, drug development costs money. It is estimated that the average cost to develop a drug is near $900 million.[11] Thus, biotech drugs share one common need—the need for economic protection in the form of patent rights. Patent protection provides exclusive rights, thereby enticing investors by assuring legal protection for their investment. The prospects of legal protection and possible profit stimulates investment in the industry, leading to industrial growth, which in turn yields larger quantities and improved quality of biotech drugs. Better drugs improve the quality of life for people who take them, which is the ultimate goal of every pharmaceutical company.

Patent protection in biotechnology has been controversial. Critics believe that no one should have exclusive rights to the essential proteins needed for life,

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8. References to the *Enzo Biochem, Inc. v. Gen-Probe, Inc.* line of cases and the related court decisions will hereinafter be referred to generically as *Enzo*, or specifically as *Enzo* I or *Enzo* II for the April 2, 2002 case (opinion at 285 F.3d 1013 (Fed. Cir. 2002)) and the July 15, 2002 case (opinion at 323 F.3d 956 (Fed. Cir. 2002)), respectively. The company, Enzo Biochem, Inc., will hereinafter be referred to as Enzo Biochem.

9. *See, e.g.*, Edward R. Ergenzinger Jr. & W. Murray Spruill, *First Get the Patent: Quirks of Biotech Innovation and Innovators Complicate Securing of Rights*, LEGAL TIMES, Nov. 4, 2002; Robert C. Scheinfeld & Parker H. Bagley, Enzo Biochem*: What Direction is Written Description Taking?* N.Y. L.J., Sept. 25, 2002.

10. Enzo Biochem, Inc. v. Gen-Probe, Inc., 63 U.S.P.Q.2d 1618, 1618 (Fed. Cir. 2002).

11. *Price Tag for New Drugs Almost $900 Million*, AM. ASS'N OF PHARMACEUTICAL SCIENTISTS NEWSMAGAZINE, July 2003, at 8, *available at* http://www.aaps.org/publications/newsmagazine/2003/jul03/08.pdf.

such as insulin or human growth hormone.[12] However, biotech patent protection has been quite beneficial for the field and for society in general. It has led to tremendous growth and scientific breakthroughs over the past two decades, yielding life-saving drugs like Humulin® (human insulin) and Epogen® (erythropoietin). This growth arises from public disclosure of the invention. Patent exclusivity is a quid pro quo; the patent owner must disclose his invention to the public so that others may build upon the technology, modify it, or use the invention once the patent has expired. Over time, the technology advances to higher levels.

Nevertheless, one cannot obtain a patent for something he merely wishes to invent. Specific criteria must be met to demonstrate that the inventor has conceived of the invention and has, at least conceptually, reduced it to practice. Namely, the inventor must possess, or at least be able to describe, a working embodiment of his invention, proving that his "invention" is not just a research plan. Title 35 of the United States Code governs the patentability of inventions. Specifically, § 112, first paragraph, states, in relevant part, that "[t]he specification shall contain a written description of the invention . . . ."[13] Yet, controversy arises over how to meet the written description requirement,[14] especially in the biotech area.

Written description in the biotech area has developed through a relatively small number of cases. Over time, the Federal Circuit has attempted to progressively define the requirement such that patent protection is neither too narrow nor overly broad. Narrow protection diminishes incentives for investment by allowing potential infringers to easily modify the invention by designing around the claims to obtain their own patents, thereby diminishing the value of a patent. On the other hand, overly broad patent protection retards the development of new technology by granting protection to future developments of existing technology. This would give the owner exclusivity over too much property, arguably more than he has actually conceived.[15] This would hinder growth in the industry as the patent owner could "hold out" for excessive licensing fees and cut off entire areas of research.

Consider the beta-amyloid claim previously discussed.[16] That inventor will effectively be the only scientist researching proteins that inhibit beta-amyloid. Other possible researchers would avoid the field for fear of a future infringement suit; the large investment required for drug discovery would make the risk of a lawsuit too costly. Nonetheless, the patent owner may not have the resources to perform extensive research. In essence, he has narrowly limited the field of

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12. *See generally* James Bradshaw, *Gene Patent Policy: Does Issuing Gene Patents Accord with the Purposes of the U.S. Patent System?*, 37 WILLAMETTE L. REV. 637, 646-53 (2001) (describing various theories for precluding genetic information from patentability).

13. 35 U.S.C. § 112 para. 1 (2000).

14. *Conflicts in Federal Circuit Patent Law Decisions*, 11 FED. CIR. B.J. 723, 734 (Pasquale A. Razzano ed.) (2002) [hereinafter *Conflicts*].

15. *See, e.g.*, Gentry Gallery, Inc. v. Berkline Corp., 134 F.3d 1473 (Fed. Cir. 1998).

16. *See* introductory discussion *supra*.

Alzheimer's research, perhaps without even producing a therapeutic product to help patients with the disease. This example illustrates the importance of allowing claims that are commensurate with the scope of the invention, rather than overly broad claims. By construing the written description requirement to provide a moderate scope of protection, the court is serving the goal of § 112, first paragraph, and promoting advancement in the technology as well as growth in the biotech industry.

B. Biotech Terminology

As a scientific discipline, biotechnology and discussions thereof require understanding of key concepts relating to the field, such as complementarity and hybridization.[17] DNA typically occurs as a double-stranded molecule, meaning that one strand of DNA binds to another strand. DNA consists of combinations of four nucleotides: adenine (A), cytosine (C), guanine (G), and thymine (T). Binding occurs between the nucleotides of the two strands. In order to bind, a nucleotide in one strand must be "complementary" to a nucleotide in the other strand.[18] Adenine and thymine are complementary (*viz.*, A binds T); cytosine and guanine are complementary (*viz.*, C binds G).[19]

The process of joining two complementary single strands of DNA is known as "hybridization."[20] Hybridization will occur if the DNA strands are complementary.[21] As DNA are often large molecules, some portions of the two strands may not be complementary, while other portions are. For example, assume that two strands of DNA have twenty contiguous nucleotides of the following complementarity: the first ten nucleotides are complementary, the next five nucleotides are not complementary, and the last five nucleotides are complementary. In that case, the strands may bind together loosely, but small environmental changes may break the strands apart. Fundamentally, the more complementary the strands are, the more stringent the hybridization will be, and the more difficult it will be to break the strands apart.[22] Thus, if the sequence of a strand of DNA is known, and stringent hybridization occurs with another strand, one can infer that the two strands are complementary to some degree. Nonetheless, it may be difficult to determine the exact degree of complementarity and precisely which nucleotides in the strands are not complementary, unless one knows the sequence of the second strand.

To search for DNA strands that contain a certain sequence or function, scientists often use nucleotide probes that will hybridize stringently to the

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17. For a primer in basic principles of molecular biology and biotechnology, *see generally* BRUCE ALBERTS ET AL., MOLECULAR BIOLOGY OF THE CELL (3d ed. 1994) and JAMES DARNELL ET AL., MOLECULAR CELL BIOLOGY (2d ed. 1990).

18. DARNELL ET AL., *supra* note 17, at 88-89.

19. *Id*.

20. ALBERTS ET AL., *supra* note 17, at G-12.

21. *Id*. at 300.

22. *Id*. at 306.

DNA.[23] The probes are designed to be complementary to a portion of the desired DNA. For example, assume that a scientist knows the sequence of a small portion (fragment) of a certain DNA of interest to him. Further, assume that the fragment consists of the sequence "ATGCAG," but the entire DNA is much larger and has not yet been sequenced. The scientist can prepare a fully complementary probe with the sequence "TACGTC" and add it to a cell suspected to contain the DNA of interest. The probe will search for the DNA with the complementary portion and hybridize to it. A dye or other identifying label added to the probe will enable the scientist to readily identify it after it hybridizes to the desired DNA. He can then recover both the probe and the DNA hybridized to it.[24] Next, the scientist can break the bonds between the probe and the retrieved strand, and sequence the entire DNA strand obtained. Note, however, that even though the probe hybridizes to the DNA strand, probes are usually small sequences of DNA that only bind a portion of the large DNA strand retrieved.[25] Stringent hybridization to this small portion of the retrieved DNA tells the scientist nothing about the remaining portion of the DNA sequence.

Another key area of importance to biotech deals with antibodies. An increasing number of antibodies are being developed and used as therapeutic drugs to treat disorders such as colorectal cancer, breast cancer, and organ transplant rejection.[26] An antibody is a protein produced naturally by white blood cells in response to a foreign molecule or invading organism, such as a bacterium, that could harm the invaded cell. To protect the cell from harm, the antibody tightly binds to the invading organism or molecule, known as an antigen, and either inactivates it or causes it to be destroyed.[27] To avoid destroying or inactivating the wrong thing, antibodies can distinguish between similarly structured molecules.[28] The antigen specifically binds to a small region of the antibody. The remainder of the antibody is not involved in antigen binding.[29]

The structure of antibodies has been studied extensively.[30] As a protein, an antibody consists of a contiguous sequence of amino acids. This sequence is composed of two regions: a constant region and a variable region. The constant region occurs in one of only a few different biochemical forms, but the variable region may occur in a virtually infinite number of forms. This variability provides an array of antibodies that can bind to an equally large number of

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23. *Id*. at G-19.

24. *Id*. at 300.

25. *Id*.

26. Rathin C. Das, *Proteins and Antibodies Make Advances as Therapeutic Products*, AM. CLINICAL LABORATORY, June 2001, at 12-14.

27. ALBERTS ET AL., *supra* note 17, at G-2.

28. DARNELL ET AL., *supra* note 17, at 65.

29. *Id*. at 1004-06.

30. CHARLES A. JANEWAY, JR. ET AL., IMMUNOBIOLOGY 16 (Sarah Gibbs et al. eds., 5th ed. 2001).

antigens.[31] Thus, the sequence of the variable region of any particular antibody differs from the variable region of any other antibody.[32]

The variable region of the antibody is the portion that binds to the antigen. However, unlike complementarity in DNA in which A binds to T and C binds to G, this level of complementarity does not exist between specific amino acids. Generally, antibodies and antigens bind together based on their shapes and attractions between the chemical structures.[33] This results in unpredictability of the antibody sequence. One cannot know the exact sequence of the variable region of an antibody simply by identifying the antigen that it binds.

Moreover, different antibodies bind to different locations on an antigen.[34] For example, assume the antigen is a protein that consists of twenty amino acids. One antibody may bind to the first ten amino acids of the antigen sequence, and a completely different antibody may bind to the next ten. Additionally, antibodies may exist that bind to amino acids number two through eleven, number three through twelve, and so on. Even more, some antibodies may bind to ten amino acids of the antigen, while others only bind to five amino acids of the antigen. The variability, and hence the unpredictability, is immense.[35]

II. DEVELOPMENT OF THE WRITTEN DESCRIPTION REQUIREMENT

The written description requirement is one of several requirements that a patent disclosure must include to be valid. This requirement, along with two others, the enablement and best mode requirements, is specifically stated in 35 U.S.C. § 112, first paragraph:

> 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.[36]

Because this area of patent law has changed little from the Patent Act of 1793,[37] the annals are devoid of legislative history on the topic. Sufficient

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31. *Id*.

32. *Id*. at 100.

33. Such attractions include electrostatic forces, hydrogen bonding, Van der Waals forces, and hydrophobic forces. *Id*. at 101-04.

34. *Id*. at 100-01.

35. *Id*. at 124.

36. 35 U.S.C. § 112 para. 1 (2000).

37. Act of Feb. 21, 1793, ch. 11, § 3, 1 Stat. 318, 321. Subsequent Patent Acts include: Act of July 4, 1836, ch. 357, § 6, 5 Stat. 117, Act of July 8, 1870, ch. 230, § 26, 16 Stat. 198, 201, and Act of July 19, 1952, ch. 950, § 1, 66 Stat. 792 (codified as amended at 35 U.S.C. §§ 1-376 (2000)). *See* Mark J. Stewart, *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, 538

written description of an invention has been required in case law from at least the early nineteenth century.[38] Nonetheless, many commentators have associated modern jurisprudence on the subject with the 1967 case *In re Ruschig*,[39] which explicated that the written description is a distinct requirement for patentability.[40] Since then, this statute has been construed repeatedly in the case law from the U.S. Court of Appeals for the Federal Circuit, yet it remains an unsettled area of law, especially in the context of biotech inventions.[41]

Methods used for determining whether a patent application complies with the written description requirement vary in the case law. Opinions differ with respect to the degree to which an invention must be described. The two extremes of the description continuum can be illustrated by the cases *Lockwood v. American Airlines, Inc.*[42] and *Hyatt v. Boone*.[43] *Lockwood* represents a rigid test for compliance with the written description requirement, requiring express disclosure of all claim elements by explicit description in the patent application.[44] On the other end of the spectrum, *Hyatt* represents a relaxed written description requirement, allowing the requirement to be met by less than express disclosure if the applicant can show that a skilled artisan reading the application would have necessarily comprehended and understood the missing description.[45]

Biotech cases fall between the two extremes. As a result of the degeneracy of the genetic code,[46] a narrow claim to DNA may be easily "designed around." If the patent were restricted to the exact DNA actually reduced to practice, a subsequent inventor could change a small portion of the biomolecule and still achieve the same biological activity without infringing the patent. To protect biotech inventors from this occurrence, claimed biomolecules may be generically described, providing a group or "genus" of biomolecules which fall within the scope of the patent. In this situation, requiring a rigid description of all elements of the claimed biomolecules would not provide adequate protection to the patentee, without listing thousands or perhaps millions of possible variations. In consideration of this, the USPTO and courts may allow patentees to claim

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(1999).

38. *See, e.g.*, Evans v. Eaton, 20 U.S. 356 (1822).

39. *See, e.g.*, Moba, B.V. v. Diamond Automation, Inc., 325 F.3d 1306, 1319 (Fed. Cir. 2003); Enzo Biochem, Inc. v. Gen-Probe Inc., 63 U.S.P.Q.2d 1618, 1623-24 (Fed. Cir. 2002); Mark. D. Janis, *On Courts Herding Cats: Contending with the "Written Description" Requirement*, 2 WASH. U. J.L. & POL'Y 55, 59 (2000); Janice M. Mueller, *The Evolving Application of the Written Description Requirement to Biotechnological Inventions*, 13 BERKELEY TECH. L.J. 615, 616-17 (1998).

40. 379 F.2d 990, 995 (C.C.P.A. 1967).

41. *Conflicts*, *supra* note 14, at 734.

42. 107 F.3d 1565 (Fed. Cir. 1997).

43. 146 F.3d 1348 (Fed. Cir. 1998).

44. 107 F.3d at 1572.

45. 146 F.3d at 1354-55.

46. The exact sequence of a biomolecule may vary from species to species, or even among the same species, yet provide the same biological activity.

sequences within a specific homology, variants, mutants, fragments, subsequences, and the like, if enough examples are provided to sufficiently describe the genus being claimed.[47]

The liberal "skill of the art" written description requirement of *Hyatt* is not typically allowed in biotech patents. The patentee cannot presume that the skilled artisan would necessarily know that fragments or conservative substitutions are allowed. Instead, he must describe the claimed genus with some specificity.[48] For example, the application should define how many amino acids are required to constitute a "fragment." Assume a protein has fifty amino acids. Will a fragment of ten amino acids function the same way? Will five contiguous amino acids suffice? The application should describe what length of fragment retains functionality. Moreover, which nucleotides can be substituted at specific positions in the generic sequence to qualify as a "variant"? The application should list the possible amino acids that can be substituted and still achieve the same biological activity. Such a description is a compromise between *Lockwood* and *Hyatt*: the scope of the claims may be so large that it is not feasible to explicitly describe all possible biomolecules that fall within the scope, but by specifying which substitutions or fragments are allowed, the skilled artisan can envision the scope of the claimed invention.

Another conflict regarding the written description requirement is whether the enablement requirement and the written description requirement, both from § 112, first paragraph, are separate requirements that must be fulfilled by the patentee. In the 1991 case *Vas-Cath, Inc. v. Mahurkar*,[49] the court clarified this unresolved question by asserting:

> 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*.[50]

Clearly and succinctly, the *Vas-Cath* court established the distinction between the two requirements, seeming to resolve the issue.[51]

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47. *See, e.g.*, *Synopsis of Application*, *supra* note 1, at 20-35, 41-47.

48. Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1568 (Fed. Cir. 1997).

49. 935 F.2d 1555 (Fed. Cir. 1991).

50. *Id*. at 1563-64.

51. Debate still remains over this issue. *See, e.g*., Enzo Biochem, Inc. v. Gen-Probe, Inc., 63 U.S.P.Q.2d 1618, 1622-33 (Fed. Cir. 2002). Many commentators feel that the written description requirement, especially in the field of biotechnology, is merely a heightened form of the enablement requirement—"super-enablement." Moba, B.V. v. Diamond Automation, Inc., 325 F.3d, 1306, 1325 (Fed. Cir. 2003) (quoting Arti Rai, *Intellectual Property Rights in Biotechnology: Addressing New Technology*, 34 WAKE FOREST L. REV. 827, 834-35 (1999) and Mueller, *supra* note 39, at 617).

Moreover, *Vas-Cath* explained that although an *exact* description of the claimed subject matter is not required for compliance, "the description must clearly allow persons of ordinary skill in the art to recognize that [the applicant] invented what is claimed"[52] and that "compliance with the 'written description' requirement of § 112 is a question of fact, to be reviewed under the clearly erroneous standard."[53] Although *Vas-Cath* did not involve biotechnology, the *Vas-Cath* court set a clear standard to be relied upon and expounded upon in future written description requirement cases.

Prior to *Enzo*, three landmark biotechnology cases shaped written description law: *Amgen, Inc. v. Chugai Pharmaceutical Co.*,[54] *Fiers v. Revel*,[55] and *Regents of the University of California v. Eli Lilly & Co.*[56] The first of these three cases, *Amgen, Inc. v. Chugai*, was a patent infringement case.[57] Amgen, Inc. sued Chugai Pharmaceutical Co. and Genetics Institute, Inc. (GI) for infringement of Amgen's patent claiming the DNA sequence encoding human erythropoietin (EPO), a therapeutic protein used to treat anemia. GI asserted an affirmative defense of patent invalidity under 35 U.S.C. § 102(g),[58] alleging that it conceived the DNA sequence prior to Amgen's conception. By 1981, GI had isolated and purified the protein EPO and conceived a "probing strategy" to isolate the gene, which it successfully reduced to practice in 1984.[59] In 1983, Amgen cloned the gene encoding EPO, thereby obtaining the structure.

The *Amgen* court held that conception was not achieved until reduction to practice occurred. "Conception is the 'formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention, as it is hereafter to be applied in practice.'"[60] "Conception requires both the idea of the invention's structure and possession of an operative method of making it."[61] Although GI alleged to have conceived in 1981, the inventor could not define the

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52. *Vas-Cath, Inc.*, 935 F.2d at 1563 (quoting *In re* Gosteli, 872 F.2d 1008, 1012 (Fed. Cir. 1989)).

53. *Id*.

54. 927 F.2d 1200 (Fed. Cir. 1991).

55. 984 F.2d 1164 (Fed. Cir. 1993).

56. 119 F.3d 1559 (Fed. Cir. 1997).

57. 927 F.2d at 1202.

58. 35 U.S.C. § 102(g) (2000). Section 102(g) provides in relevant part that:

> A person shall be entitled to a patent unless—
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> (g) before the applicant's invention thereof the invention was made . . . by another who had not abandoned, suppressed, or concealed it. In determining priority of invention there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to the conception by the other.

Id.

59. *Amgen*, 927 F.2d at 1205-06.

60. *Id*. at 1206 (quoting Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1376 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987)).

61. *Id*. at 1206.

DNA "so as to distinguish it from other materials" until 1984.[62] In 1981, GI could only describe the DNA by its principal biological property, i.e., encoding human EPO, which was "simply a wish to know the identity of any material with that biological property."[63] Description merely by biological property was not sufficient to meet the requirement for conception.[64] Conception is closely related to written description because, to prove conception, an inventor has to prove by contemporaneous documentation that he had "a mental picture of the structure" or could define it by its distinguishing characteristics, but not solely by function.[65]

The second landmark biotech case of the trilogy, *Fiers v. Revel*, was a three-way interference proceeding—three separate inventors filed patent applications on the same DNA, the DNA encoding human fibroblast beta-interferon (β-IF).[66] As the patent system of the United States is a "first to invent" system,[67] the *Fiers* court had to determine which of the three inventors was first to invent β-IF—that is, which inventor had "priority."[68] One criterion used by the court was conception.

The *Fiers* court stressed that "conception of a DNA . . . requires a definition of that substance other than by its functional utility."[69] The court related conception to written description, stating, "If a conception of a DNA requires a precise definition, such as by structure, formula, chemical name, or physical properties, as we have held, then a description also requires that degree of specificity. To paraphrase the Board, one cannot describe what one has not conceived."[70]

Looking at the descriptions of β-IF in the three patent applications of *Fiers*, the court found that only one application contained a description of the DNA itself.[71] That application set forth the "complete and correct nucleotide sequence," thereby demonstrating that the inventor was in possession of the DNA as of the application filing date.[72] Consequently, only the application with the complete DNA sequence met the written description requirement and was patentable.

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62. *Id*.

63. *Id*.

64. *Id*.

65. *Id.*

66. 984 F.2d 1164, 1166 (Fed. Cir. 1993).

67. 35 U.S.C. § 102(g) (2000).

68. To establish priority in an interference, Inventor A must show that he was first to conceive of the invention and reduce it to practice by actual or constructive reduction to practice (e.g., filing a patent application). Alternatively, if he were first to conceive but last to reduce to practice, he must show that he was diligent from a time just prior to the time that Inventor B conceived of the invention until the time that Inventor A reduced it to practice. *See id*.

69. *Fiers*, 984 F.2d at 1169.

70. *Id*. at 1171.

71. *Id*. at 1172.

72. *Id*.

The third landmark biotech case, *Regents of the University of California v. Eli Lilly & Co.*, was a patent infringement case.[73] The University of California (UC) obtained a patent claiming cDNA[74] encoding vertebrate insulin. To describe vertebrate insulin, the patent contained the amino acid sequence of human insulin, already known in the art, and a constructive example of a method that could be used to obtain human cDNA. Unlike the inventors in *Amgen* and *Fiers*, UC had actually isolated, cloned, and characterized the rat insulin cDNA. However, the patent contained no sequence or structural information regarding which nucleotides constitute human insulin cDNA.[75]

UC sued Eli Lilly and Company (Lilly), alleging that Lilly infringed its patent by manufacturing and selling human insulin. Lilly responded that it did not infringe the patent, and that the patent was invalid for failure to meet the written description requirement of § 112, first paragraph.[76] Judge Lourie, writing for the majority, agreed with Lilly. Reiterating the essence of *Fiers*, he explained that providing an enabling disclosure of how one could obtain a biomolecule does not necessarily provide a written description of that biomolecule.[77] Judge Lourie then elaborated on the use of generic statements to describe a genus:

> In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function . . . does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. It is only a definition of a useful result rather than a definition of what achieves that result.[78]

Thus, describing only the rat gene did not adequately describe a genus that encompassed the human gene.

Furthermore, the court used an obviousness analysis to show UC's lack of written description for the human cDNA. The mere fact that a description makes a claimed invention obvious does not necessarily mean that the same description satisfies the written description requirement.[79] In the cases *In re Deuel* and *In re Bell*, the court held that a claim to a specific DNA was not obvious merely

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73. 119 F.3d 1559, 1559 (Fed. Cir. 1997).
74. "cDNA" is a form of DNA.
75. *Lilly*, 119 F.3d at 1566-67.
76. *Id*. at 1562.
77. *Id*. at 1567.
78. *Id*. at 1568 (citations omitted).
79. *Id*. at 1567.

because the sequence of the encoded protein and a method for generating the DNA were known.[80] Accordingly, knowledge of the human insulin protein sequence and a method for generating the cDNA did not make human insulin cDNA obvious. Moreover, a description that did not render the human cDNA obvious also did not adequately describe the human cDNA under § 112, first paragraph.[81]

UC's "description" of human insulin added nothing new to the art: (1) the human insulin protein sequence was known;[82] (2) the method for generating the cDNA was known; and (3) the mere words "human insulin cDNA" were known. The sequence of human insulin cDNA was unknown and remained unknown after UC filed its patent application. Hence, the court held that UC did not satisfy the written description requirement for human insulin cDNA and was indeed invalid.[83]

After *Lilly*, the USPTO promulgated "Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1, 'Written Description' Requirement."[84] The Guidelines are intended to assist USPTO personnel in the examination of patent applications for compliance with the written description requirement.[85] Along with the Guidelines, the USPTO published training materials for patent examiners that include biotech examples such as antibody and hybridization disclosures.[86] Each example provides a fact pattern, at least one putative claim, an analysis describing how to determine whether each claim meets the written description requirement, and a conclusion explaining whether the claim is adequately described.[87] Application of the training materials will be discussed in more detail in Part IV of this Note.

III. THE *ENZO* CASES

A. Background and Procedural History

Enzo Biochem is the assignee of U.S. Patent 4,900,659 (the '659 patent).[88] The purpose of the invention is to find compositions of matter that are useful in screening for the bacteria causing the disease gonorrhea, *Neisseria gonorrhoeae* (*N. gonorrhoeae*). Prior to this invention, the bacteria that causes meningitis, *Neisseria meningitidis* (*N. meningitidis*), interfered with the gonorrhea screening

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80. *In re* Deuel, 51 F.3d 1552, 1558 (Fed. Cir. 1995); *In re* Bell, 991 F.2d 781, 785 (Fed. Cir. 1993).

81. *Lilly*, 119 F.3d at 1567.

82. Stewart, *supra* note 37, at 553.

83. *Lilly*, 119 F.3d at 1575.

84. Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1, "Written Description" Requirement, 66 Fed. Reg. 1099 (Jan. 5, 2001).

85. *Id*. at 1104.

86. *Synopsis of Application*, *supra* note 1.

87. *Id*.

88. U.S. Patent No. 4,900,659 (issued Feb. 13, 1990).

process, yielding false positives. Enzo Biochem's patent resolved this interference problem.[89]

The '659 patent claims compositions of matter comprising nucleotide sequences which preferentially hybridize to *N. gonorrhoeae* over *N. meningitidis* at a ratio of greater than five to one.[90] Another claim specifically lists the American Type Culture Collection (ATCC)[91] accession numbers of three specific probes[92] that yield a ratio greater than about fifty.[93] It further claims "discrete nucleotide subsequences"[94] of the deposited probes, mutations of the probes and subsequences of the mutations, and mixtures thereof.[95]

Enzo Biochem sued Gen-Probe and several other defendants for infringement of the '659 patent.[96] The defendants moved for summary judgment, alleging that the claims were invalid for failure to meet the written description requirement of § 112, first paragraph. The district court granted the defendants' motion, stating that the claimed compositions of matter were defined only by biological activity or function (*viz.*, hybridization).[97] Enzo Biochem appealed.[98]

B. Enzo *I*

The Court of Appeals for the Federal Circuit heard the appeal. Judge Lourie, the author of numerous other cases involved in the evolution of the written description requirement,[99] authored the opinion, decided on April 2, 2002. In

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89. *Id*. at cols. 2-3.

90. *Id*. at Claims 1-3, col. 27, l. 29 to col. 28, l. 30.

91. ATCC is a public depository commonly used for long-term storage of biological samples. The depository effectively serves as a public biotech "bank." It is recognized by most patent offices worldwide as an approved facility for the deposit of biological samples claimed in patents. A patentee deposits a sample of an invention in a depository so that the sample is obtainable by the public. Each sample is given its own unique identifier, known as an accession number, used to reference the stored material. *See generally Patent Depository*, ATCC Services, *at* http://www.atcc.org/Services/PatentDep.cfm (last visited Oct. 22, 2003)(describing features, fees, and means for depositing biological materials).

92. U.S. Patent No. 4,900,659 (issued Feb. 13, 1990), Claim 4, col. 28, ll. 31-49.

93. *Id*. at col. 13, ll. 9-13.

94. The '659 patent does not define subsequences, but it does define "discrete nucleotide sequences" as "a nucleotide sequence greater than about 12 nucleotides" in length. *Id*. at col. 3, ll. 26-29.

95. *Id*. at Claim 4, col. 28, ll. 31-49.

96. Enzo Biochem, Inc. v. Gen-Probe, Inc., 285 F.3d 1013, 1016 (Fed. Cir.), *vacated*, 323 F.3d 956 (Fed. Cir. 2002).

97. *Id*. at 1016.

98. *Id.* (describing Enzo Biochem, Inc. v. Gen-Probe Inc., No. 99-CV-4548, transcript of hearing at 28, 42 (S.D.N.Y. Jan. 24, 2001)).

99. *E.g.*, Judge Lourie also authored the following: Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559 (Fed. Cir. 1997); Lockwood v. Am. Airlines, 107 F.3d 1565 (Fed. Cir. 1997); *In re* Deuel, 51 F.3d 1552 (Fed. Cir. 1995); *In re* Bell, 991 F.2d 781 (Fed. Cir. 1993); Fiers v.

accordance with other written description cases of recent years, the *Enzo* I opinion continued to require a stringent written description, rejecting biological function *alone* as adequate written description. The court affirmed the summary judgment motion granted by the district court in favor of the defendants, holding:

> [T]he claimed nucleotide sequence is described only by its binding to *N. gonorrhoeae* in a preferential ratio of "greater than about five" with respect to *N. meningitidis*. While that description of the ability of the claimed probe to bind to *N. gonorrhoeae* may describe the probe's function, it does not describe the probe itself.[100]

The court rejected Enzo Biochem's argument that hybridization is a chemical property, which *Fiers* lists as a "precise definition" that meets the written description requirement.[101] When Enzo Biochem argued that binding affinity satisfies the requirements of the Written Description Guidelines,[102] the court responded that: 1) the Guidelines are not binding on the court, and 2) the Guidelines do not "set[] forth a rule that a description of a compound by its binding affinity is sufficient to satisfy § 112, ¶ 1."[103] Instead, functional characteristics, such as binding affinity, meet the Guidelines' requirements "when coupled with a known or disclosed correlation between function and structure."[104] Enzo Biochem did not assert such a correlation.[105]

Furthermore, the court rejected Enzo Biochem's argument that reducing the invention to practice and depositing the nucleotide sequences met the "possession" test of *Vas-Cath*, clarifying that possession alone does not always meet the written description requirement.[106] Reemphasizing the statutory written description requirement, the court stated that if the specification does not contain a written description, "despite a showing of possession, the specification does not adequately describe the claimed invention."[107] The claimed nucleotide sequences of the '659 patent were not so unusual that the inventors could not have described them. Consequently, the deposit did not meet the written description requirement.[108]

Revel, 984 F.2d 1164 (Fed. Cir. 1993); Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200 (Fed. Cir. 1991).

100. *Enzo*, 285 F.3d at 1018.

101. *Id.*

102. Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1, "Written Description" Requirement, 66 Fed. Reg. 1099, 1099-1111 (Jan. 5, 2001).

103. *Enzo*, 285 F.3d at 1018-19.

104. *Id*. at 1019 (citing Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001)).

105. *Id*.

106. *Id*. at 1020.

107. *Id*. at 1021.

108. *Id*. at 1022-23.

C. Rehearing and Vacating of Enzo *I:* Enzo *II*

Enzo Biochem petitioned for rehearing of the case *en banc*.[109] The court denied the *en banc* request[110] but granted a rehearing of the case by the original three-judge panel.[111] Again, Judge Lourie wrote the opinion, which vacated the earlier holding and remanded the case to the district court for factual determination of whether compositions, which were not specifically deposited, satisfy the written description requirement.[112]

The court's analysis began by stressing that not all functional descriptions fail to meet the written description requirement.[113] Referencing the USPTO Guidelines[114] and the Synopsis of Application[115] of the Guidelines, the court indicated that they "are not binding on [the] court, but may be given judicial notice to the extent they do not conflict with the statute."[116] According to the USPTO, the written description requirement is 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."[117] The court was "persuaded by the Guidelines on this point and adopt[ed] the PTO's applicable standard" for analysis of the issues.[118]

The *Enzo* II court defined the issues as two-fold: 1) whether the deposits of the claimed DNA sequences may constitute an adequate written description of those sequences, and 2) whether the description requirement is met for all claims based on functional ability of the claimed DNA sequences to hybridize to strains of *N. gonorrhoeae* that are accessible by deposit.[119] Addressing the first issue, the court reiterated that deposits are typically used to satisfy the enablement requirement, not the written description requirement.[120] Yet, in a complete reversal, the court stated that its "prior decision that a deposit may not satisfy the written description requirement was incorrect," vacating the *Enzo* I holding.[121]

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109. Enzo Biochem, Inc. v. Gen-Probe, Inc., 63 U.S.P.Q.2d 1618, 1618 (Fed. Cir. 2002).

110. *Id*.

111. Enzo Biochem, Inc. v. Gen-Probe, Inc., 323 F.3d 956, 960 (Fed. Cir. 2002).

112. *Id*.

113. *Id.* at 964.

114. Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1, "Written Description" Requirement, 66 Fed. Reg. 1099 (Jan. 5, 2001).

115. *Synopsis of Application*, *supra* note 1.

116. *Enzo*, 323 F.3d at 964.

117. *Id.* (quoting Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001)) (emphasis added by the court).

118. *Id.*

119. *Id*.

120. *Id*. at 965.

121. *Id*. at 960.

The court's rationale provided that Enzo Biochem's deposits were incorporated by reference into the patent, and a skilled artisan could obtain the sequences from the depository, if desired.[122] Moreover, the exact sequences may not have been "reasonably obtainable" at the time of filing due to "severe time constraints in sequencing DNA," and even if they were obtainable, the sequences were not known to Enzo Biochem at the time of filing the application.[123] The court held that compliance with the written description requirement was "grounded on the fact of the deposit and the accession number" in the body of the patent.[124]

However, Enzo Biochem deposited only three sequences.[125] The defendants argued that the breadth of the claims, which included subsequences, mutants of sequences and subsequences, and mixtures thereof, was overly broad. Even Enzo Biochem's own expert testified that the claims covered an "astronomical" number of variations.[126] Nevertheless, the court felt that it is conceivable a skilled person may readily understand whether any variations are viable. Because the level of skill is a question of fact, the court remanded the issue to the lower court for evaluation of "whether a person of skill in the art would glean from the written description, including information obtainable from the deposits of the claimed sequences, subsequences, mutated variants, and mixtures sufficient to demonstrate possession of the generic scope of the claims."[127]

With respect to the second issue, the *Enzo* II court briefly compared this case to *Lilly*, as both involved broad claims to a genus.[128] Looking at the USPTO's Synopsis of Application of the Guidelines, which includes a hypothetical example similar to the *Lilly* case,[129] the court described a contrasting example involving the use of hybridization properties to satisfy the written description requirement.[130] Enzo Biochem argued that the functional description of hybridization coupled with the deposit met the written description requirement.[131] Relying on the USPTO's analysis of hybridization claims in the Synopsis of Application example, the court held that there was a genuine issue of material fact regarding whether Enzo Biochem's claims met the written description requirement, thereby reversing the district court's grant of summary judgment for

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122. *Id*. at 965-66.

123. *Id*. at 966 (referring to U.S. Patent No. 4,900,659 (issued Feb. 13, 1990), col. 3, ll. 40-46).

124. *Id.* at 970.

125. *Id*. at 961.

126. *Id*. at 966.

127. *Id*.

128. *Id*. at 967 (citing Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559 (Fed. Cir. 1997)).

129. Example 17: Genus-species with widely varying species. *Synopsis of Application*, *supra* note 1, at 61-64.

130. *Enzo*, 323 F.3d at 967 (citing Example 9: Hybridization, *Synopsis of Application*, at 35-37).

131. *Id.* at 967-68.

the defendants.[132] The court remanded the issue to the lower court to "consider whether one of skill in the art would find the generically claimed sequences described on the basis of Enzo[Biochem]'s disclosure of the hybridization function and an accessible structure, consistent with the PTO Guidelines. If so, the written description requirement would be met."[133]

To conclude, the court discussed the relationship among possession, reduction to practice, and the written description requirement. Stressing that a difference exists, the court emphasized that the written description requirement "is not subsumed by the 'possession' inquiry. A showing of 'possession' is ancillary to the *statutory* mandate . . . and that requirement is not met if, despite a showing of possession, the specification does not adequately describe the claimed invention."[134] Nor does reduction to practice, without an adequate description of the invention that was reduced to practice, suffice to describe or identify the invention under the written description requirement.[135] Noting that possession and reduction to practice are particularly useful when claiming priority to an earlier date of filing or invention, the court emphatically pointed out that an adequate written description is still required. "Such description 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."[136]

On the same day, the court published the order denying rehearing of the case *en banc*.[137] Several of the judges attached statements to the order explaining why they voted either for or against *en banc* rehearing.[138] Strangely, the commentary focused largely on the difference, or lack thereof, between the written description requirement and the enablement requirement of § 112, first paragraph.[139]

The dissent voted to rehear the case *en banc*.[140] Writing for the dissent, Judge Rader argued that the case should not be remanded to determine whether the patentee met the written description requirement.[141] According to Rader, the patentee met the *Vas-Cath* "possession" test for the written description requirement by depositing the DNA sequences.[142] Judge Rader expounded upon his understanding that the written description requirement is not separate from the enablement requirement by providing a history of written description case law and describing the factual scenarios under which the court has addressed the

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132. *Id*. at 968.
133. *Id*.
134. *Id.* at 969.
135. *Id*.
136. *Id*. at 970.
137. Enzo Biochem, Inc. v. Gen-Probe, Inc., 63 U.S.P.Q.2d 1618, 1618 (Fed. Cir. 2002).
138. *Id*. at 1618-33.
139. *Id*.
140. *Id*. at 1622-23 (Rader, J., dissenting).
141. *Id*. (Rader, J., dissenting).
142. *Id*. (Rader, J., dissenting).

written description requirement.[143] Contrasting *Enzo* to prior cases, he noted that *Enzo* did not involve new matter or priority issues—the types of issues that had previously been addressed in written description requirement cases.[144] He warned that both *Lilly* and *Enzo*, by supplanting the enablement requirement with a more arduous written description requirement that is not required by the statute, threaten to disrupt settled expectations in the inventing community by "up[ping] the ante" required to comply with patentability requirements.[145]

Disagreeing with the dissent, Judge Lourie argued that the case should not be heard *en banc* merely for the purpose of revising written description law because "[t]hat law is sound."[146] Reiterating the essence of *Vas-Cath*, he emphasized that enablement and written description are separate and distinct, pointing out the United States Supreme Court's substantiation of a distinct written description requirement in a recent case.[147] Although the written description requirement has been "applied rigorously" in recent cases, Judge Lourie expressed his belief that these cases have not been decided wrongly because they further the goal of requiring claims to be "commensurate in scope with what has been disclosed to the public,"[148] thereby avoiding overly broad claims.

In response to Judge Rader's averment that the written description requirement "operated solely to police priority,"[149] Judge Lourie explained that, when trying cases, the court merely addresses the issues raised before them. That the written description requirement arose in *Enzo* under different facts than previous cases was mere evolution of the case law.[150] Nothing existed in the law prior to *Enzo* to preclude written description cases from arising under situations other than priority contests.[151]

Furthermore, Judge Lourie countered the argument that recent written description law "elevate[s] 'possession' to the posture of a statutory test of patentability."[152] He explicated that although possession is a relevant factor for determining whether an invention has been described, demonstrating possession is not necessarily the same as providing a written description.[153] Just as written description law has its critics, it also has advocates who support a robust requirement[154] and the benefits it provides to the public.[155] According to Lourie,

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143. *Id.* (Rader, J., dissenting).

144. *Id*. (Rader, J., dissenting).

145. *Id*. (Rader, J., dissenting).

146. *Id*. at 1619.

147. *Id*. (citing Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 535 U.S. 722, 736-37 (2002)).

148. *Id*. at 1620.

149. *Id.* at 1626.

150. *Id*. at 1619.

151. *Id*.

152. *Id*. at 1620.

153. *Id*.

154. For critical evaluations of written description law, see, for example, Janis, *supra* note 39,

the court has "evolved a consistent body of [written description] law over a number of years, based on the statute and basic principles of patent law."[156] Thus, there is no reason to rehear *Enzo en banc* and "rewrite the statute."[157] To do so would simply delay and frustrate the remand.[158]

IV. THE ERRORS OF *ENZO* II

A. Dealing with Deposits

Enzo II does not comport with the written description requirement. Over at least the past twenty years, as technology has advanced, the law has been evolving toward more stringent criteria for satisfying the written description requirement. Federal Circuit cases such as *Vas-Cath*, *Fiers*, and *Lilly* have more sharply defined what is required to comply with the statute: a separate and distinct description of the invention that indicates to a skilled artisan that the inventor was in possession of the invention at the time of filing,[159] described by more than just function of the invention or the method of making and using it,[160] and that endows the skilled artisan with the ability to visualize the identity of the invention.[161] By holding that the deposit of molecules into a public depository meets the written description requirement, *Enzo* II deviates from the requirement that a written description of the invention appear in the patent disclosure.

The only "descriptions" of the DNA sequences claimed in the '659 patent were the ATCC accession numbers and the function of the sequences. Although the accession number is a unique identifier for a sample, it does not correlate to the structure, function, or any other characteristic specific to that sample; it is merely an ordinal number assigned to the sample for tracking it. The Court of Appeals for the Federal Circuit recognized this in the 1985 case *In re Lundak*, where the court found, "An accession number and deposit date add nothing to the written description of the invention. They do not enlarge or limit the disclosure."[162] Yet, in *Enzo* II, the court justified the variance from *Lundak* by

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at 59; Mueller, *supra* note 39; Rai, *supra* note 51; and Harold D. Wegner, *An* Enzo *White Paper: A New Judicial Standard for a Biotechnology "Written Description" Under 35 U.S.C. § 112, ¶ 1*, 1 J. MARSHALL REV. INTELL. PROP. L. 254 (2002). *But see* Margaret Sampson, *The Evolution of the Enablement and Written Description Requirements Under 35 U.S.C. § 112 in the Area of Biotechnology*, 15 BERKELEY TECH. L.J. 1233 (2000); Stewart, *supra* note 37, at 542-46; Scott A. Chambers, *"Written Description" and Patent Examination Under the U.S. Patent and Trademark Office Guidelines*, IP LITIGATOR, Sept.-Oct. 2000, at 9-10.

155. *Enzo*, 63 U.S.P.Q.2d at 1620-21.

156. *Id*. at 1622.

157. *Id*.

158. *Id*. at 1618.

159. Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563 (Fed. Cir. 1991).

160. Fiers v. Revel, 984 F.2d 1164, 1171-72 (Fed. Cir. 1993).

161. Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1568 (Fed. Cir. 1997).

162. 773 F.2d 1216, 1223 (Fed. Cir. 1985).

noting that deposits are often used to meet the enablement requirement "[w]here the invention involves a biological material and words alone cannot sufficiently describe how to make and use the invention in a reproducible manner"[163] and stating that the '659 patent sequences "may not have been reasonably obtainable and in any event were not known to Enzo when it filed its application."[164] The court references a statement in the '659 patent which describes the time-intensive procedure required to sequence the genome of *Neisseria gonorrhoeae* and *Neisseria meningitidis*.[165]

However, the '659 patent does not claim DNA of either *Neisseria gonorrhoeae* or *Neisseria meningitidis*. Instead, it claims the DNA of probes that hybridize to those bacteria.[166] Probes are typically much smaller than the DNA with which they seek to hybridize. Accepting Enzo Biochem's statements that sequencing large DNA is labor- and time-intensive, the smaller probes should require much less time to sequence. Furthermore, most probes are synthetic constructs that are synthesized to have a specific sequence. This suggests that Enzo Biochem should have known the sequences of the probes they generated to selectively hybridize to the bacteria, especially since the sequences of the bacteria were at least partially known.[167] Accordingly, the DNA sequences of at least the three deposited probes should have been "reasonably obtainable" to Enzo Biochem, even at the time of filing the patent application. In that case, allowing the deposits to comply with the written description requirement rather than requiring that the probes be sequenced is not in accordance with patent law or the public policy behind it.

Moreover, the court could have simply clarified the meaning of possession. *Vas-Cath* established that the inventor must convey, to those skilled in the art, that he was in possession of the invention when the patent application was filed.[168] Yet, the application may include a *constructive* reduction to practice, meaning that the inventor has not yet made the invention but has disclosed how it will be made and used. In light of this, it is evident that possession does not necessarily imply tangible possession. Instead, it is related to conception; possession means that, in the least, the inventor possesses knowledge and understanding of his final and complete invention. Note that intangible possession must be differentiated from a mere wish or research plan; the inventor does not have possession until he knows the precise composition that he will eventually reduce to practice.

Enzo Biochem could not have met the possession test under these criteria.

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163. Enzo Biochem, Inc. v. Gen-Probe, Inc., 323 F.3d 956, 965 (Fed. Cir. 2002) (quoting U.S. DEP'T OF COMMERCE, MANUAL OF PATENT EXAMINING PROCEDURE § 2402 (Magdalen Y.C. Greenlief ed., 8th ed. 2001)).

164. *Id*. at 966.

165. U.S. Patent No. 4,900,659 (issued Feb. 13, 1990), col. 3, ll. 40-46.

166. *Id*. at col. 27, l. 29 to col. 28, l. 56.

167. Enzo Biochem, Inc. v. Gen-Probe, Inc., 285 F.3d 1013, 1026 (Fed. Cir. 2000) (Dyk, J., dissenting), *vacated*, 323 F.3d 956 (Fed. Cir. 2002).

168. 935 F.2d 1555, 1563-64 (Fed. Cir. 1991).

It is true that the patentee had physical possession of the materials that it deposited. Nevertheless, it did not have mental possession of its invention. Enzo Biochem was not able to describe the invention that it deposited and claimed it was because it had not sequenced the invention. In effect, the inventors had actually reduced the invention to practice without having conceived what the invention truly was. Until conception was achieved, Enzo Biochem's invention was not complete or patentable.

By reversing the holding of *Enzo* I and allowing the deposit to meet the written description requirement, the court disregarded the public policy behind the possession test. Possession is required to ensure that the inventor actually invented what he claims to have invented. If he does not possess the invention, then he cannot describe the invention. Accordingly, written description is one measure of possession. When the court allowed Enzo Biochem to use its deposit to meet the written description requirement, it did not ensure that the inventor was in mental possession of the invention. There was no measure of whether the inventor knew what he had invented or not. The court simply knew that Enzo Biochem reduced the invention to practice, with or without conception. Permitting this type of "unknown invention" does not provide the public with the *quid* that it must get in return for giving patent term exclusivity to Enzo Biochem.

The "unknown invention" may be harmful to the public in several ways. First, the public will be unaware of the metes and bounds of the invention. A prospective inventor, searching the patent literature, may not find the '659 patent unless he is looking for the same function as claimed by that patent (*viz.*, selective hybridization to *N. gonorrhoeae*). Without finding the '659 patent, he could invent another use for the claimed sequences, thereby unintentionally infringing the patent claiming the sequences. Yet, if the sequences were available in the patent literature, the prospective inventor could search sequence databases, find the '659 patent, and avoid infringement.

Second, if the prospective inventor does find the '659 patent, he will not be able to determine the scope of the claims unless he orders the deposits and analyzes the DNA sequences. Even Judge Lourie felt that this would not accord with public policy, as evidenced by his statement in *Enzo* I, "[T]o require the public to go to a public depository and perform experiments to identify an invention is not consistent with the statutory requirement to describe one's invention in the specification."[169] Just over four months later, Judge Lourie reversed that holding,[170] but he still indicated that "claims [were] being asserted to cover what was not reasonably described in the patent."[171] Although one commentator suggests that the "panel had no choice . . .,"[172] the sudden change

169. *Enzo*, 285 F.3d at 1021.

170. Enzo Biochem, Inc. v. Gen-Probe, Inc., 323 F.3d 956, 966 (Fed. Cir. 2002).

171. Enzo Biochem, Inc. v. Gen-Probe, Inc., 63 U.S.P.Q.2d 1618, 1619 (Fed. Cir. 2002).

172. Harold C. Wegner, *When a Written Description Is Not a "Written Description": When* Enzo *Says It's Not*, 12 FED. CIR. B.J. 271, 273 (2002). Wegner suggests that the Supreme Court's holding in *J.E.M. AG Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc.*, 534 U.S. 124 (2001) set precedent with respect to deposits and the written description requirement. In *J.E.M.*, the Court held that

of opinion regarding deposits is most likely indicative of conflict among the Court of Appeals for the Federal Circuit with respect to the written description requirement. Whatever the reasoning for the reversal, in a situation like *Enzo*, description by deposit does not meet the intended requirement for public disclosure and merely frustrates the public policy behind granting a patent in the first place.

Third, the unknown invention does not provide the USPTO with the necessary information to perform patentability searches. Like a prospective inventor, the USPTO must obtain a sample and sequence it. Without sequence information, the USPTO cannot adequately determine whether the invention is novel and non-obvious. Experimentation would add cost and delay, especially considering that the USPTO does not have testing facilities to analyze samples. Consequently, the patentability search cannot be performed effectively, further harming the public.

B. Adoption of the USPTO's Standard

The *Enzo* II court took judicial notice of the USPTO's Written Description Guidelines.[173] However, the court erred by implying, in dicta, that it also deferred to the Synopsis of Application[174] of the Guidelines because the examples therein are substantively flawed. Recall that the USPTO promulgated the Guidelines and the Synopsis of Application after *Lilly* to assist USPTO personnel in determining patent applicants' compliance with the written description requirement.[175] Noting that the Guidelines are not binding as law, the *Enzo* II court "adopt[s] the PTO's applicable standard for determining compliance with the written description requirement."[176] Specifically, the court refers to three examples from the Guidelines: hybridization, genus-species with widely varying species, and antibodies.[177]

1. Analysis of the Hybridization Example.—The hybridization example[178]

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seeds, which were deposited in a public depository, were patentable. *Id*. at 124. Wegner fails to consider that a seed is much more complex than a simple nucleic acid sequence such as those in *Enzo*. Case law has long held that complex structures may be enabled by deposit. *Enzo*, 323 F.3d at 965. Perhaps, for complex structures, deposition should also satisfy the written description requirement. Nonetheless, a per se rule that any deposit satisfies the written description requirement, no matter how simple the molecule is, does not protect public interest in disclosure of inventions. Instead, such a rule would discourage sequencing any biomolecules.

173. Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1, "Written Description" Requirement, 66 Fed. Reg. 1099 (Jan. 5, 2001).

174. *Synopsis of Application*, *supra* note 1.

175. *See* discussion *supra* Part II.

176. *Enzo*, 323 F.3d at 964.

177. Examples 9, 17, and 16, respectively. *Synopsis of Application*, *supra* note 1, at 35-37, 59-64.

178. Example 9: Hybridization. *Id.* at 35-37.

describes a patent specification that discloses a single cDNA (SEQ ID NO:1).[179] The cDNA encodes a protein that binds a specific receptor and stimulates a certain activity.[180] The specification exemplifies the use of a complementary[181] strand to SEQ ID NO:1 under highly stringent conditions to isolate nucleic acids which encode proteins that bind the same receptor and stimulate the same activity as above. The isolated nucleic acids are not sequenced, but their activity is demonstrated.[182]

The claim in the example is directed to "[a]n isolated nucleic acid that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO:1, wherein said nucleic acid encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity."[183] The USPTO's analysis indicates that SEQ ID NO:1 is novel and unobvious, and it is the only sequence disclosed within the scope of the claimed genus—nucleic acids which hybridize to the complement of SEQ ID NO:1 and encode a protein with the specified activity. Yet, the USPTO asserts that because the hybridization conditions are highly stringent, a skilled person would not expect substantial variation among species within the scope of the genus.[184] "Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention."[185] According to the Synopsis of Application, the invention in the hybridization example is adequately described.[186]

This analysis is incorrect for several reasons. First, a complementary strand to SEQ ID NO:1 is used as a probe. More likely than not, the target DNA will not be the same length as the probe. The skilled artisan has no means of determining, solely from hybridization, which strand is longer, the probe or the target. If the probe is longer, which nucleic acids on the probe bind with nucleic acids on the target? If the target is longer, at what location on the target does the probe hybridize? One simply has no measure for length or binding location on the target DNA by the mere fact that a probe hybridizes, even if it occurs under highly stringent conditions.

Second, highly stringent conditions do not guarantee full complementarity. One would have no means to determine which nucleic acids hybridize and which ones do not. Moreover, for the nucleic acids that do not hybridize, there is no

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179. The sequence identity number (SEQ ID NO) is the label by which DNA or protein sequences listed in a patent application are identified. Each sequence is given an ordinal number.

180. *Synopsis of Application*, *supra* note 1, at 35.

181. For every "T" in SEQ ID NO:1, the complement contains an "A" and vice versa; for every "C" in SEQ ID NO:1, the complement contains a "G" and vice versa.

182. *Synopsis of Application*, *supra* note 1, at 35.

183. *Id*. at 35-36.

184. *Id*. at 36.

185. *Id.* at 36-37.

186. *Id*.

way to know which nucleic acid is actually present in the sequence. Considering the first and second points, the applicant has not described the structure of the invention. He has no "mental picture of the structure" and thus has not yet conceived of the invention as claimed.[187]

Third, the specification contains no structure-function relationship, as recommended by the Guidelines where minimal structure is disclosed.[188] Because only one structure was described, the skilled artisan probably would not know which amino acids correlate to the activity. Accordingly, one would not know which nucleic acids must be present to encode the functional protein and which could be varied or deleted.

Fourth, a representative number of species is not disclosed.[189] Only one is disclosed: SEQ ID NO:1. Other species are mere speculation because one cannot know whether modifications of the disclosed specie will lead to the desired activity. If not, then these species do not belong to the genus.

In light of these considerations, the hybridization example does not comport with written description law. Instead, hybridization claims merely define a genus by what the DNA does, not what it is. The claims are not limited to specific metes and bounds but instead describe an unknown but potentially astronomical number of compounds of unknown sequences and structures, yielding overly broad claims.

Enzo Biochem deposited only three DNA sequences.[190] It did not sequence those DNA,[191] and thus could not describe any characteristic feature of the sequence. It could only describe the DNA by its function, the ability to hybridize preferentially to *N. gonorrhoeae* over *N. meningitidis*. Yet, in the '659 patent Enzo Biochem claimed all DNA that preferentially hybridizes in that manner, including the three deposited sequences, subsequences, mutations of those sequences and subsequences, and mixtures thereof.[192]

Applying the USPTO's analysis of the hybridization example to *Enzo*, one might conclude that any sequences, subsequences, or mutations that hybridize *N. gonorrhoeae* preferentially under highly stringent conditions would be adequately described. However, as explicated earlier, this analysis would provide no means for the skilled artisan to envision the length of the subsequences or mutations that will remain functional. Moreover, only three representative species were deposited.[193] These species were obtained using DNA that had not been sequenced; thus, SEQ ID NOs:1 and 2 (*N. gonorrhoeae* and *N. meningitidis*) were not known. Allowing this type of claim to satisfy the written description requirement would yield extremely broad scope: billions of

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187. *See* Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1206 (Fed. Cir. 1991).

188. Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001).

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

190. Enzo Biochem, Inc. v. Gen-Probe, Inc., 323 F.3d 956, 961 (Fed. Cir. 2002).

191. *Id*. at 966.

192. *Id*. at 961-62.

193. *Id*. at 961.

DNA could be encompassed. Yet, coverage of that scope would be achieved *without requiring Enzo Biochem to sequence even one DNA*! That scope would allow the inventor to claim more than he has actually invented, directly contradicting the public policy of providing the inventor with patent scope that is commensurate with his contribution to the art.

2. Analysis of the Antibody Example.—The antibody example[194] describes a patent specification teaching that antigen X has been isolated and is useful for detecting HIV. The specification teaches the method of isolation and purification of antigen X and provides a characterization of the antigen in the form of molecular weight.[195] An example in the specification "contemplates but does not teach" antibodies which specifically bind to antigen X and asserts that the contemplated antibodies can be used in immunoassays to detect HIV.[196] The skill of the art is that antibodies are structurally well characterized, and the constant and variable regions from a variety of species have been published in the art.[197]

A claim is made to "[a]n isolated antibody capable of binding to antigen X."[198] The claim is directed to *any* antibody capable of binding the antigen. The USPTO's analysis indicates that antibody-antigen binding technology is mature, and the level of skill is high and advanced. Antigen X is novel and unobvious.[199] According to the USPTO, the skilled person considering all this would recognize that the "spectrum of antibodies which bind to antigen X were implicitly disclosed as a result of the isolation of antigen X."[200] Therefore, the Synopsis of Application asserts that the written description requirement is satisfied by this disclosure in the specification.[201]

The USPTO's analysis of the antibody example, like that for the hybridization example, allows an overly broad claim to stand. Consequently, it, too, is incorrect. Although the general structure of antibodies is well understood in the skill of the art, it does not follow that the antibody sequence is adequately described. The antibody is divided into regions of alternating constant and variable domains. The variable domains vary not only from species to species, but also from member to member. In other words, one human might not produce the exact same antibody against a given antigen as the next human would.[202] One antigen introduced into 100 different humans may produce 100 different antibodies, all of which bind the same antigen and fall within the scope of the claim.

One cannot readily hypothesize which amino acids will constitute the variable region. The sequence of the antibody's variable region will depend

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194. Example 16: Antibodies. *Synopsis of Application*, *supra* note 1, at 59-60.

195. *Id*. at 59.

196. *Id*.

197. *Id*.

198. *Id*.

199. *Id*. at 60.

200. *Synopsis of Application*, *supra* note 1, at 60.

201. *Id*.

202. JANEWAY ET AL., *supra* note 30, at 124.

upon the location on the antigen to which it binds. Considering that proteins, which can be conservatively substituted for one another, comprise an antibody, the number of possible sequences that would bind to the antigen is astronomical. Consequently, the structure or sequence of the antibody cannot be described simply by knowing the antigen's sequence.

Applying written description case law to this example, the claim cannot stand. First, the possession test cannot be met. The applicant did not make any antibodies, nor did he conceive of any antibodies that could be described by a method other than "any antibody, having a general antibody structure, which functions in this way." One cannot merely claim to possess anything and everything that works without being able to describe at least one structure or sequence. With a claim of this scope, the applicant does not have a mental picture of the structure and has not yet conceived the full invention covered by the claims.[203]

Second, no structure-function relationship is established.[204] The applicant has not described any amino acids in the antibody that are complementary to and that are responsible for the binding function of the antigen, assuming that the antigen is a protein. Even if the antigen is not a protein, no structural information can be surmised other than general concepts regarding polar attractions between the antibody and antigen. In either case, no specific structure has been described. Nor has any function been linked to any structure.

Considering the failure to meet the possession test and the lack of a structure-function relationship, such a broad antibody claim should not be permitted. It simply does not describe the antibody with any particularity such that a skilled person could visualize the invention. The claim is overly broad; any antibody subsequently developed would be covered by the scope of this claim. Thus, it does not preserve the public policy of allowing claims that are commensurate with the scope of the invention. The applicant averring this claim is asserting rights to any antibody that he may have discovered as well as any that will be developed in the future. This type of protection is not in accordance with the goals of the patent system.

C. Minimizing the Error of Enzo *II*

In *Enzo* II, the Court of Appeals for the Federal Circuit remanded the case to the lower court to answer the questions of fact: whether the hybridization claims and the claims to non-deposited sequences of the '659 patent comply with the written description requirement. To ensure an appropriate outcome, the lower

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203. *See* Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1206 (Fed. Cir. 1991).

204. *See* Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001) ("A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.").

court needed to consider the technology associated with the *Enzo* case. Unfortunately, "*Enzo* III" will not resolve these issues because the parties settled the case out of court.

One major difference between *Enzo* and prior cases like *Amgen*, *Fiers*, and *Lilly* is the technology. The prior cases involved relatively simple biotech issues concerning descriptions of DNA or proteins within the scope of the claims. Conversely, *Enzo* involved technology that is more complex. Enzo Biochem's invention claimed DNA that hybridize to specific other DNA.[205] Determining whether that claim complies with the written description requirement demands full understanding of the implications of hybridization—what structural information can be inferred from hybridization under stringent conditions. The science associated with hybridization is more technologically advanced than merely determining whether the words "human insulin" adequately describe a DNA sequence.[206]

Referring to the *USPTO Guidelines* and the *Synopsis of Application of the Guidelines*, the *Enzo* court also discussed antibody technology.[207] Like hybridization, the antibody field is more complex than the technology of previous cases. In what may be regarded as dicta, the court addressed hybridization and antibody technologies and then stated that it adopts the standards of the *Guidelines* for determining compliance with the written description requirement.[208]

The complexity of hybridization and antibody technologies has not been fully considered and analyzed by the court. To ensure appropriate outcomes in future cases with such complex technologies, the science relating to those technologies should be thoroughly addressed. The court should consider factual assessments controverting the examples in the *Synopsis of Application*,[209] and contrast assessments in support thereof. Only then can the court accurately decide whether deference to the *Synopsis of Application* is appropriate.

V. THE EFFECT OF *ENZO* II ON PATENT PRACTICE AND BIOTECHNOLOGY

*A. A Post-*Enzo *Biotech Written Description Case: The* TKT *Case*

Since *Enzo*, the Court of Appeals for the Federal Circuit has decided another biotech written description case, *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*[210]

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205. U.S. Patent No. 4,900,659 (issued Feb. 13, 1990), Claims 1-3, at col. 27, l. 29 to col. 28, l. 30.

206. Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1568 (Fed. Cir. 1997).

207. Enzo Biochem, Inc. v. Gen-Probe, Inc., 323 F.3d 956, 964 (Fed. Cir. 2002).

208. *Id.*

209. *See* discussion *supra* Part IV.B.

210. 314 F.3d 1313 (Fed. Cir. 2003). To distinguish this case from *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200 (Fed. Cir. 1991), the short citation for this case will be "*TKT*." TKT is used rather than Hoechst because most of the arguments revolve around Transkaryotic Therapies, Inc.'s technology.

This was a patent infringement case involving five patents, each being a continuation[211] of the Amgen patent litigated in the 1991 case of *Amgen, Inc. v. Chugai Pharmaceutical Co.*[212] These patents broadly claimed compositions, processes, or uses related to Amgen's pioneering erythropoietin (EPO) product, Epogen®. Epogen® was launched in 1989,[213] and since that time, the product has become a huge success, earning billions of dollars in sales.[214] When Hoechst Marion Roussel and Transkaryotic Therapies (collectively "TKT") collaborated to launch a competing product, HMR4396,[215] Amgen filed a declaratory judgment action against them,[216] alleging that HMR4396 infringed Amgen's patents.[217]

The main difference between Epogen® and HMR4396 is the production technology. TKT's EPO product is produced through an innovative process referred to as "endogenous" expression.[218] This process inserts a non-native "promoter" upstream from the native EPO gene in human cells. This promoter activates the gene to produce high amounts of EPO.[219] Endogenous expression was discovered approximately ten years after Amgen's patent priority date.[220]

Amgen's product is produced using "exogenous" expression.[221] Amgen introduces the EPO gene into Chinese hamster ovary (CHO) cells, a type of mammalian cell, which use their own native processes to produce the human EPO protein. Exogenously expressed EPO differs from native human EPO only by the glycosylation pattern.[222]

Amgen's patent claims did not specify endogenous or exogenous production, but their patents exemplified only exogenous production.[223] TKT argued that the Amgen patents did not meet the written description requirement because they

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211. A "continuation" is a subsequently filed application having the same disclosure as the previous application but introducing a new claim set or further right to prosecution. *See* U.S. DEP'T OF COMMERCE, MANUAL OF PATENT EXAMINING PROCEDURE § 201.07 (Magdalen Y.C. Greenlief ed., 8th ed. 2001). The continuations involved in the *TKT* litigation included U.S. Patent Nos. 5,955,422 (issued Sept. 21, 1999) (the '422 patent); 5,756,349 (issued May 26, 1998) (the '349 patent); 5,621,080 (issued Apr. 15, 1997) (the '080 patent); 5,618,698 (issued Apr. 8, 1997) (the '698 patent); and 5,547,933 (issued Aug. 20, 1996) (the '933 patent). *TKT*, 314 F.3d at 1319-23.

212. 927 F.2d 1200 (Fed. Cir. 1991).

213. Epogen® Backgrounder, *at* http://www.amgen.com/product/epogen/epogenBackgrounder.html (last visited Oct. 22, 2003).

214. Amgen, Inc. v. Hoechst Marion Roussel, Inc., 126 F. Supp. 2d 69, 77 (D. Mass. 2001).

215. *Id*. at 94.

216. *TKT*, 314 F.3d at 1319.

217. *Id*. at 1324-25.

218. *Id*.

219. *Id*. at 1325.

220. *Id*. at 1334.

221. *Id*. at 1321.

222. Glycosylation is the pattern of branched carbohydrate chains that bind to the protein structure. *Id.* at 1321-22.

223. *Id*.

failed to "sufficiently describe the use of all vertebrate and mammalian cells," and they excluded endogenous EPO DNA, both expressly and implicitly.[224]

As written description is a question of fact, the Court of Appeals for the Federal Circuit examined the district court's finding for clear error.[225] The District Court of Massachusetts rejected TKT's written description argument, holding that TKT had proven Amgen's failure to meet the written description requirement only by a preponderance of the evidence rather than by clear and convincing evidence.[226] On appeal, TKT argued that it had indeed "clearly and convincingly proven invalidity" under *Lilly*, *Enzo* II, and *Gentry Gallery*.[227] Judge Michel, writing for the majority, did not agree.[228]

The *TKT* case provided the Court of Appeals for the Federal Circuit a means to discuss recent written description requirement cases. The court explained:

> We held in *Eli Lilly* that the adequate written description of claimed DNA requires a precise definition of the DNA sequence itself—not merely a recitation of its function or a reference to a potential method for isolating it. . . . More recently, in *Enzo Biochem*, we clarified that *Eli Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.[229]

The majority distinguished *Lilly* and *Enzo* II from *TKT* by explaining that "the claim terms at issue here are not new or unknown biological materials that ordinarily skilled artisans would easily miscomprehend."[230] Here, the terms "vertebrate" and "mammalian" simply designate the types of cells used to produce the EPO protein. In contrast, these terms in *Lilly* modified the invention itself—the protein—an "undescribed, previously unknown DNA sequence. . . ."[231] The *TKT* majority agreed with the district court's holding that the specification's description, which included two examples of vertebrate and mammalian cells used, adequately supported claims to EPO produced by "the genus vertebrate or mammalian cells."[232]

Moreover, the majority rejected TKT's argument that *Gentry Gallery*[233] requires essential elements of an invention to be incorporated into patent claims.

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224. *Id*. at 1331.

225. *Id*. at 1330.

226. Amgen, Inc. v. Hoechst Marion Roussel, Inc., 126 F. Supp. 2d 69, 101 (D. Mass. 2001).

227. *TKT*, 314 F.3d at 1331.

228. *Id*.

229. *Id*. at 1332 (citations omitted).

230. *Id*.

231. *Id*.

232. *Id*.

233. Gentry Gallery, Inc. v. Berkline Corp., 134 F.3d 1473 (Fed. Cir. 1998).

TKT argued that Amgen's use of certain terms[234] in the specification as well as representations made during patent prosecution limited the scope of Amgen's claims to exogenously produced EPO.[235] TKT alleged that exogenous expression was an essential element of Amgen's invention and thus should be required to limit the claims.[236]

The majority disagreed. It stressed that, despite popular opinion, *Gentry Gallery* did not introduce an "essential elements" test but instead applied "the settled principle that a broadly drafted claim must be fully supported by the written description and drawings."[237] According to the court, Amgen's statements, unlike *Gentry*'s, did not indicate "that exogenous expression is the *only* possible mode of the invention or that other methods were outside the stated purpose of the invention."[238] Furthermore, the court "cannot invalidate a patent for failure to describe a method of producing the claimed compositions that is not itself claimed," especially considering that the other method was not developed until ten years after the patent application was filed.[239] Thus, the majority held the district court was not clearly erroneous in its finding that Amgen's patents satisfied the written description requirement.[240]

The dissent, written by Judge Clevenger, strongly disagreed with the majority's written description decision. Judge Clevenger asserted that the issue is "whether Amgen's disclosure of *one* means of producing synthetic EPO in mammalian cells, namely exogenous DNA expression, entitles it to claim *all* EPO produced by mammalian cells in culture, or *all* cultured vertebrate cells that produce EPO."[241] Yet, the district court and the majority refused to consider this issue because the asserted claims were directed to compositions, not processes.[242]

Judge Clevenger emphasized that claim limitations that are essential to patentability must comply with the written description requirement of § 112, first paragraph.[243] Here, the majority allowed composition claims to stand with modifiers such as "non-naturally occurring" and "purified from mammalian cells grown in culture" without requiring compliance. According to Judge Clevenger:

> The majority holds that patentees are free to decorate their composition claims with source and process limitations without any concern for whether the full scope of those limitations is enabled or described, and

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234. Terms included statements such as the following: the advantage of Amgen's invention was "freedom from association with human proteins" and the invention was "uniquely characterized" by exogenous expression. *TKT*, 314 F.3d at 1331.

235. *Id*. at 1331.

236. *Id*.

237. *Id*. at 1333.

238. *Id*.

239. *Id*. at 1334.

240. *Id.*

241. *Id*. at 1359 (Clevenger, J., dissenting).

242. *Id*. (Clevenger, J., dissenting).

243. *Id*. (Clevenger, J., dissenting).

> that these requirements of section 112 are waived so long as the patentee succeeds in characterizing its claims as "product" claims. Competent patent attorneys should be quick to take advantage of the majority's broad exemption from the disclosure requirements by the appropriate phraseology. Rather than endorse the district court's elevation of form over substance, I would vacate its decision . . . and remand for further consideration in light of the vast scope of the claims in suit for which there appears to be insufficient . . . written description.[244]

Furthermore, Judge Clevenger disagreed with the majority's opinion that *Lilly* and *Gentry Gallery* did not apply to this case.[245] He asserted that by dismissing *Lilly*, the majority "verges on confining [Eli] Lilly to its facts."[246] *Gentry Gallery*, he argued, is inescapably parallel: the claims recite elements readily found in the specification but did not include limitations on the "arrangement" of the elements. The Amgen patents did not include the arrangement of "the non-human control sequences and coding DNA . . . on an exogenous expression vector in the cell."[247] According to Judge Clevenger, the majority's holding allows claims to "become more resistant to written description challenges the more broadly drafted they are."[248]

B. Analysis of TKT *and the Effect of* Enzo *on Written Description Law*

The inflection point where the robust requirement for written descriptions changed direction appears to be the reversal of *Enzo* I. Up to that point, much dissension was noted among patent practitioners with respect to case law, especially after the *Lilly* case.[249] Yet, the strong conflict of opinions in the Court of Appeals for the Federal Circuit concerning written description law did not become apparent until the denial of the *en banc* hearing for *Enzo* I.[250] At that time, written description law seems to have changed. The balance between public disclosure and exclusivity for the inventor shifted from a position emphasizing public disclosure to a position emphasizing inventors' needs.

From *Vas-Cath* through *Lilly*, the court stressed the importance of describing the full scope of the claims. This precedent required that the description be sufficient to allow the ordinarily skilled artisan to recognize that the applicant invented what was claimed.[251] Evidence of conception—a mental picture of the invention—must be present.[252] The invention must be described by more than

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244. *Id*. at 1359-60 (Clevenger, J., dissenting).
245. *Id*. at 1360-61 (Clevenger, J., dissenting).
246. *Id.* at 1361 (Clevenger, J., dissenting).
247. *Id*. (Clevenger, J., dissenting).
248. *Id*. (Clevenger, J., dissenting).
249. *See supra* note 154.
250. *See* discussion *supra* Part III.C.
251. Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563 (Fed. Cir. 1991).
252. *See* Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1206 (Fed. Cir. 1991).

mere function.[253] The description cannot be a simple wish or research plan, but instead must be a description that has definite boundaries, such that the members of the genus can be visualized or recognized.[254] By requiring that the specification include a written description of the sequences deposited to comply with the requirement,[255] *Enzo* I followed this line of precedent.

With the reversal of *Enzo* I, written description law appears to have veered away from precedent. *Enzo* II allowed incorporation by reference of three deposited sequences to serve as written description of those species.[256] This does not follow precedent because, without physically obtaining samples from the depository and sequencing them, the skilled artisan would have no way to visualize the boundaries. Enzo Biochem or the USPTO could not visualize the boundaries either. The court's comment that the sequences were not obtainable to Enzo Biochem is no justification for this exception to precedent. These molecules were small enough that they could have been readily sequenced.[257] It appears that the court made a decision to relax the written description requirement. Then, by adopting the USPTO's standard for determining compliance with the written description requirement in the *Synopsis of Application*, the *Enzo* II court suggested that it may allow extremely broad claims to stand—claims to compositions whose structures are not described anywhere in the patent.[258] This is certainly not in accordance with precedent.

The Court of Appeals for the Federal Circuit confirmed this change in philosophy toward the written description requirement in the *TKT* case. Although the court stated, "A broadly drafted claim must be fully supported by the written description and drawings," it allowed Amgen to have very broad scope of its patent claims.[259] Despite limitations in the claims, the court granted interpretations of the limitations that went beyond descriptions in the specification itself. TKT challenged the court to apply precedent to Amgen's patents, precedent that would require a robust description of the entire claimed invention, limitations included. Yet, the court refused to apply the precedent. By doing so, the court effectively limited the precedent to its facts, thereby allowing broad scope of the claimed invention and contradicting the written description requirement of cases like *Fiers* and *Lilly*.

TKT demonstrates the derogation of public policy associated with permitting broad patent claims. Even though the method of endogenous expression was not developed until ten years after Amgen filed its patent application, the scope of its claims were so broad that they covered all methods of expressing EPO in mammalian and vertebrate cells. TKT's advancement of the technological field,

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253. *See* Fiers v. Revel, 984 F.2d 1164, 1169 (Fed. Cir. 1993).

254. *See* Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1568 (Fed. Cir. 1997).

255. Enzo Biochem, Inc. v. Gen-Probe, Inc., 285 F.3d 1013, 1023 (Fed. Cir.), *vacated*, 323 F.3d 956 (Fed. Cir. 2002).

256. Enzo Biochem, Inc. v. Gen-Probe, Inc., 323 F.3d 956, 965-6 (Fed. Cir. 2002).

257. *See* discussion *supra* Part IV.A.

258. *Enzo*, 323 F.3d at 967.

259. Amgen, Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1333 (Fed. Cir. 2003).

through the development of the endogenous expression method, was found to infringe Amgen's patent.[260] That holding of infringement will prevent TKT's product from being marketed, resulting in a lack of competition which will likely keep Epogen®'s price at its current level. Additionally, litigation is tremendously expensive; Amgen may even have to raise its price to pay costs. Moreover, TKT may have nothing more than litigation expenses and trial experience to show for its advancement of the technology. Considering that Amgen never produced or even conceived of producing EPO using the endogenous method, the negative impact on the economic investment and subsequent fallout cannot be justified.

CONCLUSION

Patent protection of biotech inventions is essential to provide incentive for investment and development. To date, biotech inventions have proven to be extremely useful as medical diagnostics, pharmaceutical treatments and prophylaxes, and much growth of the industry is expected to continue in the future.[261]

Yet, to ensure continued growth, patent protection must be provided that is commensurate with the contribution of the invention to the art. The written description requirement is one means of assurance. By strictly requiring written description of the invention, the public is guaranteed that the inventor was in possession of the invention when the patent application was filed. In effect, the written description defines the scope of the invention—the metes and bounds that will be given exclusivity. The scope should be neither too narrow nor too broad.

The *USPTO Synopsis of Application of the Written Description Guidelines* represent very broad, relaxed interpretations of the law for biotech patent claims. They allow the inventor to satisfy the written description requirement by providing very little contribution to the skill of the art. Indeed, in the hybridization and antibody examples, the inventor need not provide any structural information for the actual invention.[262] Such broad scope is in direct conflict with the public policies of advancing science, improving healthcare, and promoting industrial growth. Enforcement of these overreaching claims would be devastating to the field of biotechnology.

Cases such as *Enzo* II, which defers to the broad claim interpretation of the *Guidelines*, and *TKT*, which seems to limit *Lilly* and *Gentry Gallery* to their facts, evidence a change in the stringent requirement for written description. Rather than allowing moderate claim scope that is proportional to contribution, the court appears to be moving toward allowing broad, overreaching claims. This change in direction will lead to even more confusion in an already unsettled area of patent law, leaving the patent practitioner to guess how to satisfy the written description requirement.

Nonetheless, litigation over the written description requirement continues.

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260. *Id.* at 1358.

261. Das, *supra* note 26, at 14.

262. *See Synopsis of Application*, *supra* note 1, at 35-37, 59-60.

Hopefully, the courts will thoroughly consider the complexity of technology in the current cases and reevaluate the *Synopsis of Application of the Written Description Guidelines*. Results at the district court level for the *Rochester* case[263] indicate a possible return to moderation of claim scope. Yet, the ultimate standard for written description remains unresolved until future cases like *Enzo* III and *Ariad Pharmaceuticals, Inc. v. Eli Lilly & Co.*[264] are decided.

263. Univ. of Rochester v. G.D. Searle & Co., Inc., 249 F. Supp. 2d 216 (W.D.N.Y. 2003). *See* introductory discussion *supra*.

264. *Ariad Announces Filing of Lawsuit Against Eli Lilly Alleging Infringement of Pioneering NF-KB Treatment-Method Patent*, at http://media.corporate-ir.net/media_files/nsd/aria/releases/062502-2.pdf.