IS *LILLY* WRITTEN DESCRIPTION A PAPER TIGER?: A COMPREHENSIVE ASSESSMENT OF THE IMPACT OF *ELI LILLY* AND ITS PROGENY IN THE COURTS AND PTO

Christopher M. Holman

Abstract

In *University of California v. Eli Lilly*, decided by the Federal Circuit in 1997, the court established for the first time a new form of patent law's written description requirement, apparently targeted specifically at biotechnology. To this day, the conventional wisdom is that the so-called *Lilly* written description requirement ("LWD") exists as a biotechnology-specific "super-enablement" requirement, substantially more stringent than the enablement requirement (the conventional standard for patentability), and standing as an impediment to effective patent protection for biotechnology inventions. My objective in writing this article was to test this conventional wisdom, by conducting a comprehensive search for all LWD decisions of the federal courts and the U.S. Patent Office's Board of Patent Appeals and Interferences ("BPAI"), and collecting and individually analyzing each case. The analysis focuses on the extent to which LWD is actually functioning as a biotechnology-specific super-enablement requirement. For many, the results of this study will likely come as a surprise, because the empirical evidence demonstrates that the impact of LWD in the courts and BPAI has been minimal—for the most part, LWD does not function as a super-enablement requirement but merely as a redundant surrogate for the enablement requirement. The article ultimately concludes that LWD's main impact has been one of doctrinal confusion, rather than imposing any substantial barrier to the patenting of biotechnology inventions, and recommends that the courts effectively discard LWD as redundant and unnecessary. It suggests alternative approaches for addressing the valid policy concerns that implicitly drove the original *Lilly* decision.

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Christopher M. Holman*

"They are paper tigers, weak and indecisive" (Frederick Forsyth).[1]

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 Thanks to Rochelle Dreyfuss, George Elliot, Robin Feldman, Mark Lemley, Arti Rai, and participants at the 2005 Intellectual Property Scholars Conference at the Cardozo School of Law for comments on an earlier draft.

[1] "Paper tiger" is a literal English translation of the Chinese phrase *zhǐ lǎohǔ*, meaning something which seems as threatening as a tiger, but is really harmless. The common usage is synonymous with the adjective *toothless*, meaning ineffective. *See, e.g.*, Answers.Com, http://www.answers.com/topic/paper-tiger (last visited Aug. 31, 2006).

I. INTRODUCTION

The patent law's written description requirement has traditionally functioned as a doctrine for policing against the late claiming of new matter, *i.e.*, to prevent patent applicants from "adding new inventions to an older disclosure."[2] However, in the 1997 decision of *Regents of the University of California v. Eli Lilly*[3] the U.S. Court of Appeals for the Federal Circuit embarked upon a new course, holding that the written description requirement is also a general disclosure requirement, applicable to originally filed claims and functioning in a manner more analogous to the enablement requirement than traditional written description.[4] *Lilly* has been perceived by many as transforming written description into a "super-enablement" requirement specifically targeting biotechnology and substantially restricting the patentability of biotechnology-related inventions.[5] In particular, the decision seems to require an explicit disclosure of chemical structure to support a patent claim reciting a biomolecule,[6] such as the DNA sequences at issue in *Lilly*, with the effect of dramatically limiting the scope of available patent protection for this critically important technology. *Lilly* engendered a strong backlash on the part of the biotechnology community, legal scholars and members of the judiciary, many of whom argued vehemently that the *Lilly* written description doctrine ("LWD") would prevent

[2] Univ. of Rochester v. G.D. Searle, 375 F.3d 1303, 1307 (Fed. Cir. 2004) (Rader, R., dissenting from denial of rehearing *en banc*).
[3] 119 F.3d 1559 (Fed. Cir. 1997).
[4] *See, e.g.*, Arti K. Rai, *Intellectual Property Rights in Biotechnology: Addressing New Technology*, 34 WAKE FOREST L. REV. 827, 834-35 (1999) ("Thus in [Lilly the Federal Circuit] broke new ground by applying the written description requirement not only to later-filed claims but also to claims filed in the original patent") requirement." See *infra* Part III.
[5] *See infra* Part III.
[6] Although the term biomolecule can be used in a broader sense, in this article the term is limited to polynucleotides (*e.g.,* DNA, RNA, nucleic acids) and polypeptides (*e.g.*, proteins and peptides).

biotechnology inventors from achieving adequate patent protection for their inventions, to the substantial detriment of the industry and society as a whole.[7]

In this article, I rigorously address the following question: in the nine years since *Lilly* was decided, what has been the actual impact of LWD in the courts and the U.S. Patent and Trademark Office (the "PTO")? To that end, I have conducted a comprehensive search for all publicly accessible decisions of the federal courts and the PTO's Board of Patent Appeals and Interferences ("BPAI") that decide an issue of LWD. Each decision is individually reviewed and analyzed, with an eye toward discerning the extent to which the dire predictions concerning LWD have come to pass. The results to be gleaned from this exercise might come as a surprise to many, for they reveal that for the most part LWD has had a relatively minor impact in the courts and BPAI.

In Part II of this paper, I begin by reviewing the traditional written description and enablement requirements, with some emphasis on the application of the enablement requirement to biotechnology and chemical inventions. Part III discusses *Lilly*, the genesis of LWD, and the Federal Circuit's subsequent retreat from a strict application of LWD in *Enzo Biochem v. Gen-Probe* (*Enzo II*). The results of my summary of LWD in the courts and BPAI are presented in Part IV, and in Part V I conclude with some general observations and commentary.

II. THE TRADITIONAL WRITTEN DESCRIPTION AND ENABLEMENT REQUIREMENTS

Section 112 of the patent statute requires that a patent specification "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 …

[7] *See infra* Part III.

to make and use the same."[8] This clause is the statutory basis for two discreet patentability requirements, the enablement and written description requirements.[9]

Prior to *Lilly*, the enablement and written description requirements were generally understood to serve distinct and essentially non-overlapping purposes, and the criteria for compliance with each were likewise distinct. The written description requirement functioned as a tool for policing against attempts by patent applicants to alter their patent claims during the course of patent prosecution[10] to encompass "new matter" not adequately described in the originally filed patent application.[11] As summarized in a recent Federal Circuit decision, the "function of the [written] description requirement is to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him."[12]

Because the written description requirement traditionally functioned solely as a tool for policing priority and to prevent patent applicants from claiming "new matter," it was considered inapplicable to originally filed patent claims. An original patent claim is part of the patent specification, and since a claim inherently describes the subject matter it encompasses it must satisfy the written description requirement, or at least that was the consensus opinion prior to *Lilly*.[13]

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[8] 35 USC § 112, ¶ 1 (2004).
[9] In re Ruschig, 379 F.2d 990 (C.C.P.A. 1967) has been identified as the earliest decision wherein the written description requirement was clearly identified as a requirement of patentability distinct from enablement. Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1561 (Fed. Cir. 1991).
[10] Patent prosecution is the "process of applying for a patent through the U.S. Patent and Trademark Office and negotiating with the patent officer". BLACK'S LAW DICTIONARY [?] (8th ed. 2004).
[11] *See, e.g.*, 3-7 DONALD S. CHISUM, CHISUM ON PATENTS § 7.04 (2006). (providing a comprehensive explanation of the written description requirement).
[12] Moba, B.V. v. Diamond Automation, Inc., 325 F.3d 1306, 1319 (Fed Cir. 2003) (citing In re Wertheim, 541 F.2d 257, 262 (C.C.P.A. 1976)).
[13] *See, e.g.*, Univ. of Rochester v. G.D. Searle & Co., 375 F.3d 1303, 1308 n.2 (Fed. Cir. 2004) (Rader, R., dissenting) (citing previous decisions of the C.C.P.A.).

The enablement requirement, on the other hand, applies to both original and amended claims, and essentially requires the patent specification to enable a person having ordinary skill in the art, often referred to as the "PHOSITA," to practice the invention without engaging in "undue experimentation."[14] The Federal Circuit has established a number of criteria, commonly referred to as the "Wands factors," to be considered by the court and PTO in assessing a patent specification for compliance with the enablement requirement.[15]

The enablement requirement is also used to police claim breadth, limiting inventors to a scope of claim coverage commensurate with the scope of the actual inventive disclosure in the patent specification. An inventor is permitted to claim her invention in broad terms that encompass various embodiments not specifically described, or even enabled by the disclosure in the patent specification.[16] However, there is a limit on overly expansive claim coverage, and that limit has traditionally been determined by application of the enablement requirement. Under conventional enablement jurisprudence, the scope of a patent claim must bear some "reasonable correlation" with the scope of disclosure in the patent specification.[17]

One of the earliest decisions where the "reasonable correlation" test was applied to what might be characterized as a biotechnology invention was *In re Fisher*.[18] The invention was an improved process for purifying adrenocorticotrophic hormones

[14] In re Wands, 858 F.2d 731, 736-737 (Fed. Cir. 1988).
[15] *Id.* at 737.
[16] *See, e.g.,* Infigen, Inc. v. Advanced Cell Technology, Inc., 65 F.Supp.2d 967, 975 (W.D. Wis. 1999) ("It is black letter law that claims are not limited to the embodiment described in the patent specifications. Moreover, a patent claim may encompass uses not anticipated by the inventor and therefore not described in the patent.") (citations omitted).
[17] In re Fisher, 427 F.2d 833, 839 (C.C.P.A. 1970).
[18] 427 F.2d 833 (C.C.P.A. 1970).

(ACTH), naturally-occurring protein hormone useful in the treatment of arthritis. Fisher asserted that the prior art had failed to produce an ACTH preparation having an activity of 1 International Units per milligram (IU/mg), but that his improved process had allowed him to produce ACTH preparations having activities of between 1.11 and 2.30 IU/mg.[19] This increase in activity translated into improved purity and potency, which enhanced therapeutic efficacy, clearly a breakthrough deserving of some patent protection. However, Fisher sought to patent all ACTH preparations having an activity greater than 1 IU/mg, including preparations far exceeding the 2.30 IU/mg he had actually enabled. Clearly the scope of the patent claim extended well beyond the inventor's actual achievement; the question for the court was did the claim's scope exceed a "reasonable correlation" with the scope of disclosure?

The court began by affirming the bedrock principle that an inventor is allowed a scope of patent coverage that will "dominate the future patentable inventions of others where those inventions were based in some way on his teachings," including improvements not specifically described and that would not be obvious based on the teachings of the disclosure.[20] However, the court held that by failing to include an upper activity limit on the claim, the scope of asserted patent coverage crossed the line between a permitted "domination" of subsequent improvements and inventions, and into the forbidden realm exceeding a "reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art."[21]

[19] *Id*. at 834. The International Unit (IU) is a measure of potency, which is related to the efficacy of the purification process.
[20] *Id.* at 839.
[21] *Id.*

In *Fisher*, the court articulated four basic tenets regarding the relationship between claim scope and enablement that are still the standard today: (1) claim scope can substantially exceed the scope of disclosure to encompass patentably distinct variants and improvements;[22] (2) claim scope cannot, however, be expanded so far as to exceed a "reasonable correlation" with the scope of disclosure;[23] (3) the permitted scope of coverage is related to the predictability of the area of technology at issue;[24] and (4) biotechnology and chemical inventions are generally less predictable than mechanical and electrical inventions, and hence generally less likely to be eligible for expansive scope of coverage.[25]

Amgen Inc. v. Hoechst Marion Roussel, Inc. (*Amgen Inc. v. HMR*) provides an example of the Federal Circuit upholding the validity of broad biotechnology claims encompassing variants not specifically described or "enabled" by the patent specification.[26] Based on the disclosure of methods for expressing recombinant EPO[27] in two mammalian cell lines (COS-1 and CHO), Amgen obtained patent claims covering (i) all pharmaceutical compositions comprising a therapeutically effective amount of human EPO purified from mammalian cell culture; (ii) the production of any EPO that is either non-naturally occurring or not isolated from human urine; and (iii) all vertebrate cells that can be propagated in vitro, comprise "non-human DNA sequences that control

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[22] *Id.*
[23] *Id.*
[24] *Id.*
[25] *Id.* However, in *In re Coo*k, the court indicated that the distinction is more properly "denominated a dichotomy between predictable and unpredictable factors in any art rather than between 'mechanical cases' and 'chemical cases.'" In re Cook , 439 F.2d 730, 734 (C.C.P.A. 1971).
[26] 314 F.3d 1313 (Fed. Cir. 2003).
[27] EPO is short for erythropoietin, a hormone that stimulates the production and release of red blood cells in response to low oxygen levels. *Id.* at 1319, 1321.

transcription" and produce a recited amount of EPO.[28] The Federal Circuit found the claims to encompass and be infringed by production methods and recombinant human cells that were not described or contemplated in the patent specification.[29] Moreover, the infringing cells and processes could not have been made at the time Amgen's patents were filed, because the necessary technology was not developed until years later.[30] Nevertheless, the court upheld the validity of the claims, skirting the "reasonable correlation" test and holding that "the law makes clear that the specification need teach only one mode of making and using a claimed composition."[31] The problem with the courts analysis, as noted by a dissent to the decision,[32] is that the specification did not teach *any* mode of creating certain embodiments falling with within the scope of the claims, such as the recombinant human cells and EPO produced by HMR.[33]

On the other hand, courts have on numerous occasions invoked the "reasonable correlation" test to invalidate broad biotechnology and chemical claims.[34] For example,

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[28] *Id*. at 1322-23.
[29] *Id*. at 1334 (finding that the patentee could not have described the infringing method because it was not developed until ten years after the patent was filed).
[30] This later-developed technology was itself the subject of its own patent protection. *Infra* n.103.
[31] *Id*. at 1335.
[32] *Id*. at 1359.
[33] Other examples where courts have found broad "dominating" claims extending well beyond the disclosure of the patent specification to nevertheless comply with the enablement requirement include In re Hogan 559 F.2d 595 (C.C.P.A. 1977) (disclosure of method of producing crystalline polymer of polypropylene was sufficient to enable a claim encompassing amorphous polymer of polypropylene, even though amorphous polymer was not enabled); and Hormone Research Foundation Inc. v. Genentech, Inc., 904 F.2d 1558 (Fed. Cir. 1990) (disclosure of a method for producing human growth hormone can provide sufficient enabling disclosure to support a claim encompassing purer and more potent forms of the hormone that could not be produced using the teaching of the disclosure).
[34] *See, e.g.,* In re Vaeck, 947 F.2d 488 (Fed. Cir. 1991) (claims directed to chimeric genes comprising a Cyanobacterium promoter region operatively linked to a gene encoding a bacillus insecticidal protein were not enabled by patent specification that describes provides working examples for only a single species of Cyanobacterium and only mentions 9 out of the roughly 150 different known genera of Cyanobacterium); In re Wright, 999 F.2d 1557 (Fed. Cir. 1993) (claims directed generically to methods of producing vaccines against avian RNA viruses not enabled by a general description of the process and one working example describing the production of a vaccine effective against a single strain of avian RNA virus); In re Goodman 11 F.3d 1046 (Fed. Cir. 1993) (claims covering expression of mammalian peptides in any plant cell (monocot or dicot) not enabled because at the time the patent application was filed the technology was not

in *In re Wright*[35] an attempt was made to claim all vaccines against RNA viruses, based on the disclosure of a single working example describing the production of a vaccine effective against a single strain of avian RNA virus.[36] Other examples from the realm of biotechnology include *In re Goodman*,[37] where the applicant attempted to claim the expression of mammalian peptides in any plant based on success in a dicot, even though monocots were not enabled,[38] and *Enzo Biochem, Inc. v. Calgene, Inc*.,[39] where the applicant essentially attempted to claim the use of antisense technology[40] in any cell type based on a disclosure limited to *E. coli*, a single species of bacteria.

Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd. is a striking example of the Federal Circuit applying a particularly strict interpretation of the reasonable correlation test.[41] Amgen's patent was based on the isolation and structural characterization the

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available for inserting genes into the genome of a monocot); Genentech Inc. v. The Wellcome Foundation Ltd., 29 F.3d 1555, 1564-65 n.24 (Fed. Cir. 1994) (in construing claims, court found that applying a broad definition of the term "human tissue plasminogen activator" would render the claims overly broad and invalid for failure to comply with the enablement requirement); Enzo Biochem v. Calgene, 188 F.3d 1362 (Fed. Cir. 1999) (claims directed broadly to use of antisense technology in any cell type were not enabled by disclosure limited to E. coli, a single species of bacteria); Plant Genetic Systems, N.V. v. DeKalb Genetics Corp.315 F.3d 1335 (Fed. Cir. 2003) (claim covering any plant cell (monocot or dicot) having defined heterologous DNA sequence inserted into its genome was not enabled because at the time the patent application was filed the technology was not available for inserting genes into the genome of a monocot); Chiron v. Genentech, 363 F.3d 1247 (Fed. Cir. 2004) (disclosure of a mouse antibody capable of binding a specific human breast cancer antigen did not enable claim covering chimeric antibody capable of binding same antigen).

[35] 999 F.2d 1557 (Fed. Cir. 1993).

[36] Note that a number of important human disease are caused by RNA viruses, such as HIV, and thus the scope of coverage would encompass potential future innovations of great importance that are not enabled by the disclosure.

[37] 11 F.3d 1046 (Fed. Cir. 1993).

[38] Flowering plants fall into two classifications: monocots characterized by having only one cotyledon ("seed leaf") produced by the embryo, and the dicot having two cotyledon produced by the embryo. University of California Museum of Paleontology Glossary, *at* http://www.ucmp.berkeley.edu/glossary/gloss8/monocotdicot.html. (last visited Sept. 6, 2006).

[39] 188 F.3d 1362 (Fed. Cir. 1999).

[40] Antisense technology is the process in which the antisense strand hydrogen bonds with the targeted sense strand. When an antisense strand binds to a mRNA sense strand, a cell will recognize the double helix as foreign to the cell and proceed to degrade the faulty mRNA molecule, thus preventing the production of the undesired protein. www.bio.davidson.edu/Courses?Molbio/MolStudents/01suschultz/homepage.html, last accessed 8/30/06.

[41] 927 F.2d 1200 (Fed. Cir. 1991).

human gene encoding erythropoietin (EPO),[42] a major accomplishment, because it allowed for the large-scale manufacturing of recombinant EPO.[43] A patent claim limited to the gene encoding naturally-occurring (*i.e.*, native) human EPO might have been easily circumvented by a competitor producing a structural variant of EPO retaining the desired functional attributes of the native protein, *e.g.*, by a technique such as site-directed mutagenesis.[44] In an attempt to preclude this sort of trivial design around, Amgen obtained a patent claim encompassing any DNA sequence encoding a protein having an amino acid sequence "sufficiently duplicative" of erythropoietin (EPO) to retain the function of EPO.[45] The Federal Circuit invoked the enablement requirement to and the "reasonable correlation" test to invalidate the claim as overly broad.

Amgen v. Chugia was written by Judge Lourie, author of *Lilly*, and the leading advocate for LWD on the Federal Circuit, and clearly foreshadows the focus on chemical structure evident in *Lilly* and other related biotechnology cases.[46] In particular, the court points to the "manifold possibilities" for changes to the structure of EPO "with attendant

[42] In the language of biotechnology, the scientists cloned and sequenced the gene, which allowed for the recombinant expression of EPO.

[43] Recombinant EPO, sold under trade names such as EPOGEN by Amgen and others, is used to treat anemia, and was one of the first, and still is one of the most successful of all biotechnology products. Amgen, Inc. website, http://www.amgen.com/patients/products_epogen.html (last visited Sept. 6, 2006).

[44] Site-directed mutagenesis was well known and specifically described in the Amgen patents, along with a description of using the technique to make functionally-equivalent variants of the disclosed EPO. *See, e.g.,* U.S. Patent No. 4,703,008. The vulnerability of narrow biomolecule claims to infringement by trivial design around is described in detail in Christopher M. Holman, *Protein Similarity Score: A Simplified Version of the BLAST Score as a Superior Alternative to Percent Identity for Claiming Genuses of Related Protein Sequences*, 21 SANTA CLARA COMPUTER & HIGH TECH. L.J. 55 (2004). *See also* Enzo Biochem, Inc. v. Gen-Probe Inc. 323 F.3d 956, 966 (Fed. Cir. 2002) (expert testified that broad claim scope covering an "astronomical" number of mutated variants of a disclosed genetic sequence is necessary to protect against copyists who could otherwise make a minor change to the sequence and thereby avoid infringement while still exploiting the benefits of the invention).

[45] In particular, any EPO variants sharing native EPO's biological property of causing an increased production of red blood cells, the characteristic that made recombinant EPO an extremely useful drug for treating anemia.

[46] *See also*, Fiers v. Revel, 984 F.2d 1164 (Fed.Cir.1993) and In re Wallach, 378 F.3d 1330 (CAFC 2004). The focus on chemical structure in assessing the patentability of biomolecule is also evident in *In re Bell* and *In re Deuel, two* other decisions penned by Judge Lourie but in the context of nonobviousness. In re Bell, 991 F.2d 781 (Fed.Cir.1993); In re Deuel, 51 F.3d 1552 (1995).

uncertainty as to what utility will be possessed by these analogs," and the failure of Amgen to identify "structural requirements for producing compounds with EPO-like activity."[47] The court also faults the Amgen for claiming "an astronomical number of species" while disclosing how to make and use only a few of them, a concern which reappears in *Lilly* albeit in the context of written description.

The BPAI has also applied the enablement requirement's "reasonable correlation" test in a similar matter to broad biomolecule claims lacking structure-based limitations. For example, in *Ex parte Maizel*,[48] a patent applicant disclosed the amino acid sequence of a protein (human B-cell growth factor) and attempted to claim any DNA vector encoding that protein or a "biologically functional equivalent thereof." The Board held the claim invalid for lack of enablement, opining that the "problem with the phrase 'biologically functional equivalent thereof' is that it covers any conceivable means, *i.e.*, cell or DNA, which achieves the stated biological result while the specification discloses, at most, only a specific DNA segment known to the inventor."[49]

Thus, it is clear that prior to *Lilly* the courts and PTO already had in the enablement requirement a fairly robust doctrinal tool for limiting patent claims to a scope commensurate with the inventor's disclosure, and had on occasion applied the requirement with some rigor to biotechnology inventions, *e.g.*, *Amgen v. Chugai* and *Ex parte Maizel*. Professor Janis has noted that the courts have for the most part failed to exercise the potential power of the enablement as a tool for limiting claim scope.[50] Any

[47] 927 F.2d at 1214
[48] 27 USPQ2d 1662 (BPAI 1992). See also, Ex parte Ishizaka, 24 USPQ2d 1621 (B.P.A.I. 1992) and Fiddes v. Baird, 30 USPQ2d 1481 (B.P.A.I. 1993).
[49] *Id.* at 1665.
[50] Mark D. Janis, *Contending with the "Written Description" Requirement (and Other Unruly Patent Disclosure Doctrines)*, 2 WASH. U. J.L. & POL'Y 55, 106-108 (2000).

critical assessment of LWD as a "super-enablement" should be undertaken with this in mind.

III. THE GENESIS OF LWD

A. *Regents of the University of California v. Eli Lilly*

In 1997, *Regents of Univ. of Cal. v. Eli Lilly & Co.* substantially blurred what had been a clear delineation between the enablement and written description requirements.[51] The patent at issue arose out of the successful cloning of the rat insulin gene,[52] a technical *tour de force* achieved by scientists at the University of California at the dawn of the biotechnology era.[53] In the patent specification, the inventors provided the chemical structure of the rat gene, *i.e*., the gene's "sequence," along with a description of the specific methodology used to isolate the gene, and a prophetic description purporting to describe how one would go about isolating the gene from other mammals and vertebrates, including man.[54] UC succeeded in convincing the PTO that this limited disclosure was adequate to support a patent claim specifically covering the human insulin gene, and other claims generically encompassing all mammalian and all vertebrate insulin genes. UC then sued Eli Lilly, alleging that Lilly's production of recombinant human insulin infringed the patent. However, the district court hearing the case held that the human,

[51] 119 F.3d 1559 (Fed. Cir. 1997).
[52] In this context the term "insulin gene" is used as shorthand for what would be more accurately described as a cDNA encoding rat proinsulin.
[53] Lilly involved two patents, but the one of interest for our purposes is U.S. Patent No. 4,652,525.
[54] A gene is essentially a chemical compound, a type of DNA molecule, comprising a string of chemical building blocks referred to as "bases." Likewise, a protein is essentially a string of amino acids, another type of chemical building block. With respect to both DNA and proteins, molecular biologists commonly use the term "sequence" to refer both to the molecule itself and to the molecule's structure. In attempt to minimize confusion, in this article I generally use the word "sequence" to refer to the actual DNA or protein molecule, and the word "structure" to refer to the molecules chemical structure.

mammalian and vertebrate claims were invalid for failure to satisfy the written description requirement, and on appeal the Federal Circuit affirmed.[55]

The biotechnology and patent communities was shocked by *Lilly*, particularly because of the novel manner in which the court applied the written description requirement to originally filed claims, and the stringent disclosure requirements the decision seemed to impose on biotechnology inventors. For example, with respect to the claim specifically directed to the human insulin gene, the court held that "[a]n adequate written description of a DNA 'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention."[56] Because the specification did not provide the "relevant structural or physical characteristics" of the human gene, *i.e.*, its genetic sequence, it did not provide adequate written description, regardless of whether the specification enabled the human gene.[57]

With respect to the broader claims directed to mammalian and vertebrate insulin genes, the court held that a generic description, such as "vertebrate insulin [gene]," was insufficient absent some structural description that would allow one to distinguish genetic sequences falling within the scope of the claim from other, non-claimed genetic sequences. The court viewed the claimed genus of genetic sequences as being defined solely in terms of function, *i.e.*, the ability to encode for insulin, and held that such a purely functional description was insufficient with respect to chemical inventions in

[55] 119 F.3d at 1575.
[56] *Id.* at 1565 (citing Fiers v. Revel, 984 F.2d 1164, 1171 (Fed.Cir.1993)).
[57] Neither the Federal Circuit nor the district court decisions even speculate as to whether any of the claims at issue were enabled, and the issue was never raised by the parties in their briefs submitted to the Federal Circuit.

general, and DNA sequences in particular. The court posited that adequate written description to support a claimed genus of genes "may be achieved by means of a recitation of a representative number of [genes], defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."[58] While providing no guidance with respect to how many representative species might be required, nor what if any alternative avenues might exist for supporting a genus claim encompassing a family of related genetic sequences, the court held that the single rat sequence was insufficient to support a claim reciting all mammalian or all vertebrate species.

In *Lilly*, the court applies written description in a manner closely analogous to enablement, but the standard for compliance appears to be more stringent than the enablement requirement. In particular, while the enablement requirement mandates that the specification to teach the PHOSITA to make and use the invention without "undue experimentation," in *Lilly* the court interprets the written description requirement as requiring a "precise definition of a molecule's physical or structural characteristics." At least with respect to genetic sequences, the court appears to be requiring a precise, nucleotide-by-nucleotide recitation of chemical structure. And while enablement merely requires a "reasonable correlation" between the scope of disclosure and the scope of the claims, *Lilly* seems require some sort of structure-based definition of a claimed genus of molecules, achievable by providing a "representative number" of structurally defined

[58] *Id.*

examples, or a recitation of common structural features sufficient to distinguish the genus.

In recognition of the fundamental difference between traditional written description and written description as applied by the court in *Lilly*, subsequent courts and commentators have characterized the written description requirement as composed of two distinct prongs: (1) the traditional written description requirement that polices priority and does not apply to originally filed claims, and (2) the *Lilly* written description requirement ("LWD").[59]

In assessing the impact of LWD, it should be noted that the claims at issue in *Lilly* could have been invalidated under the enablement requirement, without needing to resort to written description. With respect to the to the human insulin gene claim, a reasonable court could concluded that the specification did not provide sufficient guidance to enable a PHOSITA to successfully isolate the gene without engaging in "undue experimentation." In this regard, it must be remembered that the patent claimed a priority date of 1977, a time when the methodology for cloning genes was just being developed and when the process was far from routine or predictable.[60] The patent specification provides a prophetic example describing a proposed method for cloning the human gene (essentially the same method used to clone the rat gene), but this methodology apparently did not work for the human gene, because the same inventors reported eventually cloning the human gene using a very different methodology.[61] In any event, although reasonable

[59] *See, e.g.,* Moba, B.V. v. Diamond Automation, Inc., 325 F.3d 1306, 1319 (Fed. Cir. 2003).
[60] *See, e.g.,* Amgen, Inc. v. Chugai Pharm. Co., 1989 WL 169006 (D.Mass. 1989), for a description of the unpredictability associated with attempting to clone a gene in the early 1980's several years after UC's filing date.
[61] In U.S. Patent No. 4,431,740, the UC inventors report isolating the human insulin gene by *in situ* hybridization screening. In U.S. Patent No. 4,652,525, the patent with respect to which written description

minds might differ with respect to application of the "undue experimentation" standard to the facts of this case, clearly a court seeking to invalidate the claim would have been able to reasonably characterize the invention as requiring undue experimentation based on the fact that the technology was nascent, and the only methodology described in the specification for cloning the human insulin gene was apparently never successfully implemented.

Turning to the claims broadly asserting patent rights in the insulin genes from any mammal, or even any vertebrate, an invocation of the "reasonable correlation" should have been sufficient to invalidate these claims. At that early stage in the study of molecular biology, when many mammals had not been the subject of any such research, a strong case could have been made that it would have required more than an undue amount of experimentation to successfully clone the genes from other mammals and vertebrates.

B. *The Backlash Against Lilly*

Lilly has proven to be a highly controversial decision. Many commentators have characterized LWD as a "super-enablement requirement" substantially limiting the ability of inventors to patent biotechnological inventions, some going so far as to suggest that the doctrine actually poses a substantial threat to the vitality of the biotechnology industry. Typical of the tone in the immediate aftermath of *Lilly* was an article, published in 1998, which lambasted *Lilly* as "an unmitigated disaster that if followed, has the

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was at issue, the prophetic example purporting to enable the isolation of the human insulin gene relies on a different methodology that does not involve in situ hybridization screening. *In situ* hybridization screening is not even mentioned in the '525 patent.

potential for causing untold havoc in the biotechnology field."[62] In the same year, another commentator wrote that "[in] *Lilly*, the Federal Circuit has fashioned a newly heightened Written Description standard unique to biotechnological inventions. . . . The *Lilly* decision may profoundly limit the scope of protection available for new gene inventions." [63] This view of *Lilly* has survived through the years. [64] For example, in 2002, another commentator wrote that, in *Lilly*, the "Federal Circuit has effectively eliminated patent protection for biotechnology inventions pertaining to proteins." [65] And in 2004, Professor Holbrook stated that "failure to have a full disclosure of examples in the biotechnology field may invite a rejection for want of 'possession' of the invention, and hence lack of a 'written description.'"[66]

Some members of the judiciary have also weighed in with their concerns regarding LWD. For example, Judge Michel of the Federal Circuit has argued that LWD, in conjunction with a restrictive interpretation of the doctrine of equivalents, will effectively preclude biotechnology inventors from achieving adequate patent protection their inventions.[67]

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[62] Harris A. Pitlick, *The Mutation of the Description Requirement Gene* 80 J. PAT. & TRADEMARK OFF. SOC'Y 209, 222 (1998).
[63] Janice M. Mueller, *The Evolving Application of the Written Description Requirement to Biotechnological Inventions*, 13 BERKELEY TECH. L. J. 615 (1998).
[64] In a dissent by Judge Rader in the Federal Circuit's decision not to rehear *Univ. of Rochester v. G.D. Searle*, he provides an appendix summarizing much of the academic commentary with respect to the Lilly Doctrine, including "31 articles criticizing the Eli Lilly doctrine, 7 articles defending the doctrine, and 16 neutrally commenting on the state of this evolving case law."373 F.3d at 1309 n.4.
[65] Sheila R. Arriola, *Biotechnology Patents after Festo: Rethinking the Heightenedd Enablement and Written Description Requirements*, 11 FED. CIRCUIT B. J. 919, 951 (2002). *See also,* Shradda A. Upadhyaya, *The Postmodern Written Description Requirement: An Analysis of the Application of the Heightened Written Description Requirement to Original Claims,* 4 MINN. INTELL. PROP. REV. 65 (2002) (Lilly has the potential to "thwart progress of biotechnology").
[66] Harold C. Wegner, *The Disclosure Requirements of the 1952 patent Act: Looking Back and a New Statute for the Next Fifty Years*, 37 AKRON L. REV. 243, 247 (2004).
[67] Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 234 F.3d 558, 617 (Fed. Cir. 2000) (Michel, P. concurring-in-part, dissenting-in-part) ("Considering the vast number of specific amino acid sequences that an applicant would be forced to disclose and claim in order to secure meaningful protection for his

Judge Rader is probably the most outspoken critic of the *Lilly* doctrine on the Federal Circuit. For example, he wrote in his dissent to the Federal Circuit's decision not to rehear *Univ. of Rochester v. Searle en banc*:[68]

> The *Eli Lilly* doctrine also seems to impose some illogical requirements on patent drafters today. Must a software patent disclose every potential coding variation that performs a claimed function? Must a biotechnological invention list every amino acid variation for a particular protein or protein function--a task conceivably as impractical as the software disclosure requirement? Must a university or small biotech company expend scarce resources to produce every potential nucleotide sequence that exhibits their inventive functions? Perhaps more important for overall patent policy, must inventors spend their valuable time and resources fleshing out all the obvious variants of their last invention instead of pursuing their next significant advance in the useful arts? Again *Eli Lilly* and *Rochester* appear to have given little thought to these unintended consequences.

The apprehension surrounding LWD focused primarily on its apparent effect of limiting patent protection to DNA and other biomolecules for which the patent applicant has disclosed "precisely defined" chemical structures. For example, Judge Rader recently interpreted *Lilly* as requiring a "nucleotide-by-nucleotide recitation of the structure of a biotechnological invention."[69] This view that LWD requires a precise structural definition engendered much of the outcry against *Lilly*.[70]

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invention, I feel the majority's rule puts an impossible burden on both the applicant and the PTO."), *vacated* 535 U.S. 722.

[68] 373 F.3d at 1313-1314.

[69] 375 F.3d at 1308 (Fed. Cir. 2004).

[70] *See, e,g.*, Elliot Marshall, *Court Takes a Narrow View of UC's Claim,* 277 SCIENCE 1029 (1997) (predicting that *Lilly* will have a broad impact on biotechnology by "compelling gene hunters to spell out the exact sequence of the DNA they hope to claim, rather than just the function of the genes"); Margaret J. Sampson, *The Evolution of the Enablement and Written Description Requirements under 35 USC 112 in the Area of Biotechnology*, 15 BERKELEY TECH. L. J. 1233, 1273 (2000) (concluding that *Lilly* requires the disclosure of exact nucleotide sequences for genetic material, which she says is a good thing (putting her in the minority of commentators)); David Kelly , *The Federal Circuit Transforms the Written Description Requirement into a Biotech-Specific Hurdle to Obtaining Patent Protection for Biotechnology Patents,* 13 ALB. L.J. SCI. & TECH. 249, 270 (2002) (concluding that *Lilly* imposes a unique biotech-specific written description standard to limit DNA claims to specific sequence disclosed); Mueller, *supra* note 63 at 631 (concluding that Lilly announced a "precise definition" test for the written description of DNA inventions); Mark A. Lemley & Dan L. Burk, *Policy Levers in Patent Law,* 89 Va. L.R. 1575, 1678-1679 (2003)

LWD has also been viewed as profoundly limiting the scope of patent protection available for biotechnological inventions, leaving inventors with very narrow claims, easily designed around by slight modification to a disclosed structure.[71] For example, Lemley and Burk recently wrote that in biotechnology LWD "has been applied as a sort of "super-enablement" requirement, forcing biotech patentees to list particular gene sequences in order to obtain a patent covering those sequences. . . . The Federal Circuit has applied the [*Lilly*] doctrine to biotechnology cases in a way that would be inconceivable in other industries, such as software. The effect is to narrow the scope of biotechnology patents – or at least DNA patents – rather dramatically."[72] Commentators have posited that LWD, in conjunction with the Federal Circuit's apparent reluctance to find a DNA sequence obvious absent explicit disclosure in the prior art, render it very easy to get a patent covering a newly disclosed DNA sequence, but that the protection will be very narrow, resulting in numerous extremely narrow DNA patents.[73]

To summarize, LWD has been characterized as problematic for the patent system, and for biotechnology inventors in particular, owing primarily to the perception that: (1) LWD requires an explicit description of chemical structure in order to support a claim to a genetic sequence or other biomolecule, *e.g.*, a "nucleotide-by-nucleotide listing"; and

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(stating essentially that one can only patent specific sequences that have actually been isolated or sequenced); Dan L. Burk & Mark A. Lemley, *Biotechnology's Uncertainty Principle*, 54 CASE W. RES. L. REV. 691, 704 (2004) ("Under the Federal Circuit's precedent, a researcher will be able to claim only sequences disclosed under the stringent written description rules--the actual sequence in hand, so to speak.").

[71] Holman, *supra* note 44.

[72] Lemley & Burk, *supra* note 70, at 1652-54. *See also*, Mueller, *supra* note 63 at 649 ("In practical terms, Lilly may profoundly limit the scope of protection available for new gene inventions."); Daniel P. Chisholm, *The Effect of the USPTO's Written Description Guidelines on Gene Patent Applications,* 35 SUFFOLK U. L. REV. 543 (concluding that narrow patents on genetic inventions, as required by *Lilly*, could provide insufficient incentives and impede genetic research).

[73] *Id.* at 1594-95.

(2) LWD functions as a super-enablement requirement substantially restricting the availability of adequate claim scope for biotech inventions.

C. *Enzo I: The Worst Fears Confirmed*

It was not until five years after *Lilly* that the Federal Circuit decided a case involving an application of LWD, but that decision seemed to confirm the worst fears of *Lilly*'s critics. In *Enzo Biochem, Inc. v. Gen-Probe Inc.* (*Enzo I*),[74] the inventors had discovered three naturally-occurring DNA sequences (derived from the genome of *N. gonorroheae*, the pathogenic bacteria that causes gonorrhea) that were useful as hybridization probes for distinguishing between *N. gonorroheae* and *N. meningitides*, a closely related but non-pathogenic bacteria. The DNA sequences served as useful tools for diagnosing patients infected with gonorrhea, while avoiding false positives associated with the use of probes that could not distinguish between the two species of bacteria, and the inventors filed a patent application claiming the three sequences.

The inventors apparently understood that a patent limited to the three sequences would afford only narrow protection, and could easily be designed around.[75] For example, each of the three sequences was relatively long, ranging from 850 to 1300 bases in length,[76] substantially longer than would be required to serve as functional probes. Given these starting sequences, one would expect a PHOSITA to be able to identify fragments of the three sequences (subsequences), or mutated variants of the three sequences, that would retain the functional utility of the full-length sequences. Furthermore, aided by the inventors' disclosure, a PHOSITA could likely identify other

[74] 285 F.3d 1013 (Fed. Cir. 2002) (*vacated* 323 F.3d 956).
[75] *See generally* Holman, *supra* note 44.
[76] 285 F.3d at 1024.

DNA sequences from the *N. gonorroheae* genome able to distinguish between the two species of bacteria, *i.e.*, structurally distinct albeit functionally equivalent substitutes for the three specifically identified DNA sequences. In an attempt to preclude these possibilities, the inventors patented their invention broadly, claiming not only the three sequences but functionally equivalent variants. In particular, the patent included a claim encompassing subsequences and "mutated" variants of the specifically disclosed sequences retaining the ability to distinguish between the two bacteria. An even broader claim recited, in purely functional terms, essentially any polynucleotide capable of distinguishing between the two bacteria, *i.e.*, without any structural limitations on the sequence.

Prior to filing the patent application, the inventors did not determine the chemical structures of the three DNA sequences. They did, however, deposit samples of the DNA sequences with the American Type Culture Collection (ATCC), a publicly accessible depository for biological samples. While this did not explicitly make the structures of the sequences public, it did in principle enable the public to determine the structures of the sequences, which could be accomplished by obtaining samples from the ATCC and using conventional molecular biotechnology techniques to determine the structures of the deposited sequences. In the patent, the applicants described and claimed the DNA sequences by reference to the deposited samples, providing no structural description of the molecules. The PTO found that the deposits were sufficient to fulfill the disclosure requirements of section 112, and granted the patent.[77]

[77]Note that Enzo's patent issued in 1990, long before *Lilly*, and at a time when the use of biological deposits to satisfy the Section 112 disclosure requirements had long been sanctioned by the courts and PTO procedure. U.S. Patent No. 4, 900, 659. The use of deposit was thought of as being necessary, and

In *Enzo I*, a divided panel of the Federal Circuit upheld a district court's determination, as a matter of law, that LWD could not be satisfied with respect to a claimed DNA sequence by a deposit that failed to explicitly disclose the sequence's chemical structure. The court summarily dismissed the patentee's argument that "possession" is the ultimate hallmark of adequate written description, and that the deposits clearly demonstrated the inventors' actual, physical possession of the claimed DNA sequences. According to the court in *Enzo I*, mere physical possession is not necessarily enough to satisfy LWD.[78]

The court went on to cite a number of policy concerns that would arise if mere deposit were sufficient to satisfy LWD. In particular, the court noted that without a "written" description of a DNA sequence a patent examiner would not be able to determine whether or not the sequence is new or nonobvious, and hence such a description was necessary in order to assure a proper examination.[79] The court also found that a mere deposit provided insufficient notice to potential infringers as to the scope of the claim - "to 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." [80]

Both of these policy concerns would seem to be legitimate. In practice, it would be impossible for a patent examiner to determine whether the deposited sequences fell within the prior art, because the examiner would have no way of knowing the identity of

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sufficient, for the enablement of inventions involving biological materials that could not be enabled by other means. *See* 37 C.F.R. § 1.801-809 (2006).
[78] 285 F.3d at 1020-21.
[79] *Id*.at 1022.
[80] *Id*.

the sequences. The PTO has no capability for sequencing deposited biological samples. And it is clearly burdensome to require members of the public to obtain and determine the structure for the deposited samples in order to figure out whether they might infringe the patent. Indeed, if determining the sequences for the deposits is truly a routine exercise, would it not make more sense to put the burden upon the patentee to determine the sequences, than to put the burden on any third party concerned with avoiding infringement?

In any event, while *Enzo I* faithfully followed *Lilly*, and did address the policy concerns expressed by the court, the decision also raised a number of troubling policy concerns of its own. Some of these were noted by Judge Dyk in his dissent to *Enzo I*. For example, he noted that many biotechnology patents had been filed, prosecuted and issued under a regime wherein it was understood that deposit of DNA sequences was sufficient to satisfy 112, and the unfairness of disrupting the settled expectations of all these inventors by essentially changing the rules late in the game and introducing a completely new disclosure requirement, effectively invalidating a host of issued biotechnology patents.[81]

4. *Enzo II and the Demise of Strict* Lilly *Written Description*

Enzo petitioned for an en banc rehearing of *Enzo I*. Perhaps to avoid *en banc* reconsideration of the LWD doctrine, the panel that decided *Enzo I* vacated its original opinion, replacing it with *Enzo Biochem, Inc. v. Gen-Probe Inc.* (E*nzo II*).[82] *Enzo II* reversed the district court's decision, and to a large extent repudiated *Enzo I* and *Lilly* itself.

[81] *Id*. at 1028-29.
[82] 323 F.3d 956 (Fed. Cir. 2002).

In particular, *Enzo II* clearly rejects the idea that LWD requires a disclosure of structure for DNA inventions, holding as a matter of law that structure is not required when a claimed DNA molecule is made publicly accessible by means of deposit.[83] In justifying its flip-flop, the court noted the long tradition of inventors using biological deposits to satisfy the enablement requirement, the practical difficulties of describing unique biological materials in words, the potential for disruption of the settled expectations of biotechnology patent owners, and that the structures for the three DNA sequences "may not have been reasonably obtainable, and in any event were not known to Enzo when it filed its application in 1986."[84] Essentially, in *Enzo II* the court finds that the technical obstacles to determining DNA structure from a deposit justify the use of deposit to satisfy LWD, while in *Enzo I* the court had pointed to those very same technical obstacles as policy justifications for finding deposit inadequate to satisfy LWD.[85] *Enzo II* holds that the necessary "possession" can be demonstrated by a showing that a PHOSITA would be able to predictably derive the DNA structures from the deposits using standard methodology, *i.e.*, the LWD inquiry is effectively collapsed into a test for enablement.[86]

The court then went even further, holding that extremely broad claims encompassing any functional substitute for the three deposited sequences, unconstrained by any structural limitations, might comply with the written description requirement if the deposits "indicate the patentee has invented species sufficient to constitute the

[83] *Id*. at 966.
[84] *Id*.
[85] 285 F.3d at 1022.
[86] *Id*. at 965-66.

genera."[87] The court also held that the claims to subsequences and mutated variants of the disclosed sequences satisfy LWD if the deposited samples "demonstrate possession" of the claimed subsequences and mutated variants.[88] As is so often the case in subsequent Federal Circuit decisions applying LWD, the court provides no guidance for the district court with respect to what criteria it should use in its assessment of "demonstrated possession" and "invention of species sufficient to constitute the genera."

Shortly after *Enzo II*, a commentator noted that *Enzo I* was decided in a manner entirely consistent with *Lilly*, and that if *Enzo I* was indeed wrongly decided, as the court implicitly acknowledged in vacating the decision, then logically *Lilly* itself must be wrong.[89] I believe that history has borne out this assessment of the import of the *Enzo* decisions. In retrospect, it is clear that since *Enzo II* the significance of LWD as a distinct doctrine of patentability has been on a steady decline, and that the courts have for the most part limited the holding in *Lilly* to the facts of that case.[90]

Although the court's effective reversal of *Enzo I* avoided exposing LWD to the scrutiny of an *en banc* Federal Circuit, three judges on the court did dissent from the decision not to rehear the case *en banc*, including Judge Rader, the court's most vocal critic of LWD.[91] These judges asserted that the development of a distinct written description requirement outside its original context of policing new matter was wrong and should be reversed.[92] A fourth member of the court, Judge Dyk, who wrote a strong dissent in *Enzo I*, also clearly opposes an interpretation of LWD that would require a

[87] *Id*. at 967
[88] At 966
[89] MARTIN J. ADELMAN, 3-2 PATENT LAW PERSPECTIVES § 2.9 (2004).
[90] *See infra* Part IV. *See also*, 314 F.3d at 1361) (Clevenger, R., dissenting) ("the majority … verges on confining *Eli Lilly* to its facts.").
[91] 323 F.3d at 976.
[92] *Id*. at 976-82.

disclosure of structure as a requirement of patentability, and questions the existence of written description as a distinct requirement of patentability applicable to original claims. However, he was of the opinion that *Enzo* was not the appropriate case to address the issue.[93]

IV. A COMPREHENSIVE REVIEW OF *LILLY* WRITTEN DESCRIPTION IN THE COURTS AND PTO

The primary objective of this article is to provide a comprehensive survey of all publicly available decisions of the Federal Courts and the PTO Board of Patent Appeal and Interferences (BPAI)[94] pertaining to LWD. In keeping with this objective, I pursued a search strategy designed to be as comprehensive as reasonably possible. Details of the search strategy are provided in the Appendix. The relatively large number of decisions considered necessitates a succinct treatment for many of the cases. The inventions involve complex technology, and the decisions are typically driven by the facts of the case; readers seeking a richer understanding of some of the complex technologies at issue in these decisions are encouraged to refer to the actual decisions and/or biotechnology texts, treatises, and primers, of which there are many.[95]

In summarizing the decisions, I focus primarily upon the following issues: (1) the extent to which the LWD is (or is not) being applied as a "super-enablement"

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[93] *Id*. at 975-76.

[94] A patent applicant may appeal an examiner's claim rejection to the PTO's Board of Patent Appeals and Interferences (BPAI). The Board may affirm or reverse the examiner's action and may enter a new ground of rejection. From an adverse ruling by the Board, the applicant may either appeal on the record to the Court of Appeals for the Federal Circuit or file a de novo civil suit to obtain a patent against the Commissioner (Director) in the District Court for the District of Columbia. CHISUM ON PATENTS *§ 11.06. See also*, In re Zurko, 142 F.3d 1447, 1456-57 (Fed. Cir. 1998) (*en banc*) (providing a good review of BPAI procedure).

[95] *See, e.g.,* Karl DRLICA, UNDERSTANDING DNA AND GENE CLONING: A GUIDE FOR THE CURIOUS (3d ed. 1997); MOLECULAR BIOLOGY AND BIOTECHNOLOGY: A COMPREHENSIVE DESK REFERENCE (Robert A. Meyers, ed., 1995); BENJAMIN LEWIN, GENES VII *(*2000); and JAMES D. WATSON ET AL., RECOMBINANT DNA (2d ed.1992).

requirement; (2) the extent to which LWD is being applied in a manner that requires a disclosure of chemical structure, either explicitly or implicitly; and (3) the extent to which LWD is being applied in a manner that limits claim scope, particularly for biotechnology and/or chemical inventions. In other words, I focus upon the primary concerns that have been expressed in connection with the effect of LWD on the ability of biotechnology inventors to achieve adequate patent protection for their inventions.[96]

In Section A, I begin by summarizing the many decisions where the courts and BPAI have rejected LWD challenges to claim validity, illustrating the extent to which LWD is not preventing inventors from claiming biotechnology inventions in broad and/or functional terms. Then, in Section B, I review the relatively infrequent decisions where claims have been invalidated under LWD, pointing out the generally expansive scope of the invalidated claims relative the scope of disclosure, and the resultant enablement issues.

A. *Decisions Rejecting Lilly Written Description Challenges to Claim Validity*

1. LWD in the Federal Circuit

Subsequent to *Lilly*, the Federal Circuit has on six occasions explicitly rejected LWD-based challenges to claims validity, with five of the six decisions involving broad biotechnology-related claims. The first of these, *Enzo II*, was discussed above, and the others are reviewed in this section.

[96] There are a number of traditional written description decisions relating to chemical and biotechnology patents which are not considered in this article, in keeping with my objective of focusing on the LWD branch of written description doctrine. *See, e.g.,* Chiron v. Genentech, 363 F.3d 1247 (Fed. Cir. 2004) and Union Oil Co. of California v. Atlantic Richfield Co., 208 F.3d 989 (Fed. Cir. 2000).

Amgen v. HMR, decided the year after *Enzo II*, involved multiple patents relating to the cloning and expression of human erythropoietin (EPO) in recombinant, cultured mammalian cells.[97] Amgen scientists accomplished this feat by attaching a viral promoter sequence[98] adjacent to the cloned human EPO gene, and then introducing the recombinant genetic construct into cultured Chinese Hamster Ovary (CHO) cells, which allowed for the large scale production of this potent human therapeutic.[99] In understanding the case, it is critical to note that Amgen's patent disclosure related to the expression of an *exogenous* gene*, i.e.*, a human gene introduced into a foreign (hamster) cell, while the claims encompassed essentially *any* vertebrate cell containing a recombinant EPO gene-promoter construct.[100]

The Federal Circuit upheld a district court's determination that the claims were not invalid under LWD.[101] Note the expansive scope of the claims, and the lack of any meaningful structural constraints. For example, the claims were found to encompass (and to be infringed by) a human recombinant cell expressing its own native EPO gene, *i.e*., an *endogenous* gene, as opposed to the *exogenous* gene described in the patent specification.[102] The recombinant expression of an endogenous human gene was not mentioned in the patent specification, nor could it have even been accomplished using the technology available at the time the patent application was filed, *i.e,* this is an "after-

[97] *See supra* note 26.
[98] A promoter is a DNA sequence that regulates the expression of an adjacent gene.
[99] Prior to this invention, EPO had to be isolated from human urine, and could not be produced in sufficient quantities to be useful as a drug.
[100] 314 F.3d at 1322-23. The claims also encompassed methods of using such cells to produce recombinant EPO, the recombinant EPO protein itself, and other facets of the invention.
[101] *Id.* at 1334. *The* majority also found these claims did not violate the enablement requirement. *See supra* note 31.
[102] *Id,* at 1351-52, 1349.

arising technology."[103] Moreover, Amgen's patent specification pointed to "freedom from association with human proteins" as a specific advantage of its invention, an advantage that could only be achieved by expression of an exogenous EPO gene.[104]

The court's LWD analysis is substantively indistinguishable from traditional enablement analysis, focusing upon how "easy" it would be for one of skill in the art to figure out how to adapt the methodology to other cell types[105] (compare with "undue experimentation" standard), and explicitly endorsing the districts court's statement that claims encompassing "future developments of [the] process that might alter or even improve how the same product is made" do not violate LWD[106] (compare with the same position taken with respect to enablement in *In re Fisher* and *Hormone Research Foundation Inc. v. Genentech, Inc.*).[107] The court also finds the precedent of *Lilly* and *Enzo II* "inapposite to this case because the claim terms at issue here are not new or unknown biological materials" or "previously unknown DNA sequences."[108] Of course, the claims are directed to novel recombinant cells, but the court seems suggests that LWD is relevant only to newly discovered, naturally-occurring genetic sequences, not to novel recombinations of genetic elements, such as the recombinant cells at issue here. As described below, other courts have generally shared this restrictive interpretation of LWD.

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[103] *Id*. at 1331-32. Transkaryotic therapies, Inc., a defendant in the case, even obtained their own patent on the technology for expressing an endogenous gene in this manner, years after Amgen filed its patent applications. Brief of Appellants Transkaryotic Therapies, Inc. and Hoechst Marion Roussel, Inc., 2001 WL 34633545, *16-17.
[104] *Id.* at 1331. Expression of endogenous EPO involves expression of human EPO in a human cell, inevitably leading to some association with human proteins.
[105] *Id.* at 1331.
[106] *Id.* at 1332.
[107] *See supra* Part II.
[108] *Id.* at 1332.

In a strongly worded dissent, Judge Clevenger took issue with the majority's interpretation of LWD, pointing out that Amgen's claims have no meaningful limitation with respect to how the recombinant EPO is expressed, or the structure of the EPO-producing cells, so long as EPO is non-naturally occurring and produced in vertebrate cells.[109] In his view, the claims are analogous to a claim reciting any "machine that makes polymer X, wherein the machine comprises means for controlling how much polymer X is made."[110] He found that the majority opinion, in dismissing LWD on the grounds that no undisclosed DNA molecule appears in the case "verges on confining *Eli Lilly* to its facts."[111]

It bears noting that there were a number of claims directed to recombinant EPO protein *per se* which were at issue in the case but for some reason failed to trigger any sort of LWD analysis, including claims to EPO "not isolated from human urine" or EPO "having glycosylation pattern that differs from EPO purified from human urine."[112] These are extremely broad claims, lacking any structural limitation other than a negative limitation, *i.e.*, the claims encompass any and all recombinant EPO proteins, excluding only the naturally-occurring form of the protein that was in the prior art. This clearly invokes LWD, but the majority fails to even acknowledge the issue, and the dissent does so only tangentially.

In *Moba B.V. v. Diamond Automation, Inc.*,[113] one of only two Federal Circuit LWD decisions not relating to biotechnology or chemistry, the court upheld a jury's

[109] *Id.* at 1359-60.
[110] *Id.* at 1360.
[111] *Id.* at 1361.
[112] *Id.* at 1322.
[113] 325 F.3d 1306 (Fed. Cir. 2003).

determination that claims directed to a machine for processing hen eggs was not invalid for failure to comply with LWD. The decision provides a good historical description of the development of the two distinct forms of the written description requirement, and defines the test for compliance with either prong as essentially being one of "possession."[114]

The court also implicitly finds that, in general, the test for possession can be shown by enablement. In particular, the court points out that in *Enzo II* and *Amgen v. HMR* possession (and hence compliance with LWD) was satisfied by a showing of enablement, and that likewise possession of the egg processing machine at issue in *Moba* was adequately disclosed by an enabling disclosure.[115] This merger of the tests for LWD and enablement is reiterated in many subsequent cases, perhaps most explicitly in *Lizardtech*.[116]

The next Federal Circuit decision rejecting a LWD challenge to claim validity, *Capon v. Eshhar*,[117] involved an appeal of the BPAI's decision in an interference contest.[118] The claims at issue recited a genus of chimeric genes[119] comprising a first segment encoding some portion of an antibody capable of binding an antigen, and a second segment encoding at least some portion of a protein that (1) is expressed on the surface of cells of the immune system and (2) triggers activation and/or proliferation of

[114] *Id*. at 1319-1320.
[115] *Id*.at 1321.
[116] See *infra* Part IV.
[117] 418 F.3d 1349 (Fed. Cir. 2005).
[118] An interference is a contest under 35 U.S.C. 135(a) between an application and either another application or a patent. An interference is declared to assist the Director of the United States Patent and Trademark Office in determining priority, that is, which party first invented the commonly claimed invention within the meaning of 35 U.S.C. 102(g)(1)." MANUAL OF PATENTING EXAMINER PROCEDURE § 2301 (2005).
[119] A chimeric gene is an artificial gene that combines segments of DNA in a way that does not occur in nature. 418 F.3d at 1351 (Fed. Cir. 2005).

the cells.[120] In its decision, the BPAI presumed the claims to be enabled, but found them to be invalid under LWD for failure of the patent specification to disclose a complete chemical structurefor any species of chimeric gene falling within the scope of the claims.[121] The board cited *Lilly* and *Enzo I* as controlling precedent, [122] and interpreted those decisions as requiring a specific disclosure of the chemical structure of at least one species falling within the scope of the claim, *i.e.*, the BPAI correctly applied LWD in precisely the strict manner *Lilly* and *Enzo I* seemed to require.

On appeal, a unanimous panel of the Federal Circuit vacated the BPAI's decision. The court, citing *Enzo II*, specifically rejected the BPAI's interpretation of LWD requiring an explicit disclosure of at least one chimeric gene sequence falling within the scope of the claim. The court found that the structures of exemplary genetic sequences that could function as the first and second segments of the chimeric gene were known at the time the patent application was filed, as were the structures of linker sequences and techniques for joining the two segments by means of the linkers, and that this disclosure was sufficient to satisfy LWD.[123] In particular, the court faulted the BPAI for interpreting LWD as requiring a "re-analysis" of known sequences, *i.e.*, the elements of the chimeric construct, since the structures of the elements of the chimera, including the linker, were disclosed in the specifications and/or known in the prior art at the time of filing.[124]

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[120] *Id.* at 1351-52.
[121] This is notable as the only instance where a court or BPAI explicitly treated LWD as a super-enablement requirement, and the decision was subsequently reversed by the Federal Circuit.
[122] For some reason, the board failed to take into account the fact that *Enzo I* had been vacated and replaced by *Enzo II*. This is somewhat strange, since the board decision is dated March 26, 2003, and Enzo II was decided July 15, 2002.
[123] *Id.* at 1357-58.
[124] *Id.*

The extent of the court's decision was fairly limited, holding that LWD did not require an explicit disclosure of structure for any species falling within the scope of the claim, but remanding the case to the BPAI to determine whether LWD had been satisfied with respect to the "full scope" of the particular claim at issue. The court provided some limited guidance to the BPAI to consider making that determination, but as was the case in *Amgen v. HMR*, the criteria do not appear to differ substantively from traditional enablement analysis. For example, the court states that, with respect to LWD, "the determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter."[125] There is no meaningful distinction between these criteria and some of the *Wands* factors, which include the state of the prior art, the relative skill of those in the art, and the predictability or unpredictability of the art.[126]

Later, the court states that "the Board's repeated observation that the full scope of all of the claims appears to be 'enabled' cannot be reconciled with the Board's objection that [the claims do not satisfy LWD]," and observes that "the legal criteria of enablement and written description are related and are often met by the same disclosure."[127] This is yet another example of the merging of court merging the tests for enablement and LWD. The claims at issue are expansive in scope, and lack any meaningful structural

[125] *Id.* at 1359.
[126] In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988). The Federal Circuit views the Wands factors as the primary test for assessing a patent claim for compliance with the enablement requirement.
[127] 418 F.3d at 1360.

limitation.[128] Clearly this panel of the Federal Circuit did not interpret LWD as imposing any strict structure-based limitations on broad, functional claiming of biomolecules.

Shortly after *Capon*, the Federal Circuit decided *Invitrogen Corp. v. Clontech Laboratories*,[129] where the patented invention at issue in involved the genetic engineering of a functionally modified form of a protein known as a reverse transcriptase (RT). RTs are naturally-occurring enzymes that possess two distinct catalytic activities, referred to as the DNA polymerase and the RNase H activities. [130] Invitrogen scientists discovered that by deleting a section of the RT protein (using a technique known as deletion mutagenesis) they could make RT*, an RT variant that retains DNA polymerase activity, albeit with substantially reduced RNase activity.[131] This variant proved superior to natural RT in a variety of molecular biology applications, *i.e.*, RT* is useful as a research tool. Based on the disclosure of a single example of an RT*,[132] derived from a specific strain of retrovirus and generated by a specific methodology, they obtained a patent covering *any* RT*, derived from any retrovirus, yeast, Neurospora, Drosophila, primate or rodent, generated by any methodology, including functionally distinct or superior variants.[133]

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[128] The first segment of the claimed genus of chimeric genes essentially encompasses any antibody or antibody fragment capable of binding an antigen. Generally any protein or relatively large molecule (and in many cases even small molecules) can function as an antigen, and generally any antigen is recognized by a host of structurally and functionally distinct antibodies, so the possibilities with regard to the first segment are truly astronomical. The second segment is a protein defined in terms of location of expression and biological function, and would likewise cover an open-ended genus of functionally related molecules, including as of yet undiscovered proteins that would satisfy the defining criteria. *Id.* at 1352.
[129] 429 F.3d 1052 (Fed. Cir 2005).
[130] An enzyme is a protein that accelerates (catalyzes) a chemical reaction without itself being consumed. DRLICA at 243.
[131]The designation "RT*" is the author's, and is used as shorthand to designate any RT variant that retains DNA polymerase activity but with substantially reduced RNase activity.
[132] U.S. Patent 6,070,499, figure 6.
[133] 429 F.3d at 1071-72.

Clontech made its own version of RT* by a different technique, known as point mutagenesis.[134] Clearly, the different techniques would lead to structurally distinct products, and perhaps to different function.[135] In particular, it might well be the case that the product of point mutagenesis might have superior function relative to the product of deletion mutagenesis. Clontech argued that the Invitrogen patent application did not disclose or enable the production of RT* by point mutagenesis, and that the claims should be interpreted as not encompassing their RT* made by point mutagenesis or, in the alternative, if interpreted broadly enough as to encompass their product, the claims are invalid for violation of LWD. In particular, Clontech argued that the claim violated LWD for describing the claimed genus of RT* molecules in essentially functional terms, with no meaningful structural limitation.[136]

The district court held on a motion for summary judgment that the claim was not invalid under LWD, and the Federal Circuit affirmed that decision. The Federal Circuit acknowledged that the claimed genus of RT* proteins was defined solely in terms of function, but held that there was a sufficient, known relationship between the structure and function of retroviral RTs to satisfy LWD.[137] However, in this regard the court's focus appears to be misdirected, for the claim do not recite naturally-occurring retroviral RTs, but non-naturally occurring RT*s from a variety of species, of which only a single embodiment was disclosed. Beyond that limited disclosure, there is no evidence in the

[134] Point mutagenesis involves changing single amino acid in the a protein sequence, in contrast with the deletion mutagenesis technique employed by Invitrogen, which entails deleting an entire stretch of amino acids from the sequence.
[135] Deletion mutagenesis is a more crude technique than point mutagenesis, since it involves excising a relatively large stretch of the protein's amino acid chain. The resulting structural difference might easily result in functional differences between RT*s derived by different methods.
[136] 429 F.3d at 1072-73.
[137] *Id.* at 1073.

record of any disclosure of a relationship between structure and function in other species of RT*, and in particular no suggestion of disclosure which would allow one to produce a RT* variant by point mutagenesis such as the one produced by Clontech. The claim literally covers improved RT* variants sharing little structural similarity with the disclosed RT* and substantially distinct and/or superior functional characteristics. In this case, LWD is simply not functioning as any meaningful limitation on claim scope.

Note also that while an enablement challenge to the claim's validity was also rejected, the court could have easily found the broad claim invalid for lack of enablement by applying that requirement in the stringent manner to be observed in cases like *Amgen v. Chugai*.[138] In fact, by comparison the claim invalidated in *Amgen v. Chugai* was actually much narrower than the claim in *Invitrogen*. The *Amgen* claim was limited to EPO variants having "duplicative" function with respect to the disclosed EPO, while the claims in *Invitrogen* literally cover functionally distinct and/or improved variations of the disclosed RT*. Likewise, the *Amgen* claim is implicitly limited to variants of a single disclosed EPO, while the claim in *Invitrogen* literally encompasses RT* variants derived from any of a wide range of organisms, including organisms for which the RT protein had yet to be characterized.

The court attempted to reconcile its decision with previous LWD decisions, noting, for example, that in *Lilly* not one single structure was provided for a sequence falling within the claims, while in this case a single structure was provided.[139] However, on this point the court misreads *Lilly*; recall that in *Lilly* a claim directed to the genus of mammalian insulin genes was found invalid under LWD even though the structure of the

[138] *See supra* Part II.
[139] 429 F.3d at 1073.

rat gene was disclosed, *i.e.*, a species falling within the scope of the claim. A more principled distinction between the two cases, which the *Invitrogen* court did not explicitly make, is that in *Lilly* the genus encompassed naturally occurring genetic sequences, while in *Invitrogen* the claim is directed to a genus of non-naturally occurring, synthetically derived biomolecules.[140]

Falko-Gunter Falkner v. Inglis involved another appeal of a BPAI interference decision.[141] Inglis's patent specification described a method of making a safer attenuated virus vaccine that involved deleting an essential gene from the viral genome, and producing the virus in a host cell expressing the essential gene (and thereby providing the function of the essential gene necessary for the viability of the modified virus). The patent specification specifically described and exemplified the invention with respect to herpes virus. However, the specification included some passing references to a variety of other types of viruses, including poxvirus,[142] and a brief statement that the disclosed methods were not limited to herpes virus vaccines, but could also be applied generally to other viruses.[143]

Subsequent to the initial filing date, Inglis filed patent claims specifically directed to poxvirus vaccines generated by the methodology, claiming priority to the originally filed patent specification. In particular, Inglis claimed any vaccine comprising a defective poxvirus whose genome had been modified by deletion of an essential gene the

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[140] This distinction between natural and synthetic biomolecules can be seen reflected in a number of other Federal Circuit decisions, particularly *Invitrogen* (broad genus of synthetic genetic sequences satisfies LWD) and *In re Wallach* (claim to naturally-occurring genetic sequences invalid under LWD), discussed *supra*.

[141] 448 F.3d 1357 (Fed. Cir. 2006).

[142] Poxvirus is a genus of related viruses, including small pox and vaccinia virus. Human Virology at Stanford, http://www.stanford.edu/group/virus/pox/2000/vaccinia_virus.html (last visited Sept. 6, 2006)

[143] 448 F.3d at 1364(Fed. Cir. 2006).

function of which could be replaced by a host cell expressing the gene.[144] The question on appeal was whether the original patent specification, with its limited disclosure with regard to poxvirus, provided adequate support for the claim to satisfy LWD. Falkner argued that it did not, pointing out that the specification provided no specific example of a poxvirus vaccine and no specific teaching with respect to how one would make a poxvirus vaccine falling within the scope of the claim, or any teaching regarding the genome of poxvirus or the identification of essential genes.[145] In fact, the specification stated that as of the date the specification was filed no poxvirus vaccine had ever been made.[146]

However, the Federal Circuit found that the claim complied with LWD, pointing out that the structures of some poxviruses and their essential regions were known to a PHOSITA, and citing *Capon* for the proposition that LWD does not require the "re-analysis" of known structures.[147] However, the claim is not limited to only known poxviruses, but literally extends to any poxvirus, including as of yet undiscovered strains of poxvirus. The specification does not provide any structural description for the massive number of unreported poxvirus, nor does it specifically identify the essential regions of the poxvirus genome whose function could be provided by growth of virus in a host cell expressing that region. Essentially, the court finds that information in the public domain at the time the application was filed would have enabled a PHOSITA to make some species falling within the scope of the claim, and this was enough to satisfy LWD. According tot the court, LWD does not require a structure for any species falling within

[144] *Id.* at 1360.
[145] *Id.* at 1365-66.
[146] *Id.* at 1367, n.10.
[147] *Id.* at 1367.

the scope of the claim, nor does it require the actual production of any species falling within the scope of the claim *i.e.,* actual reduction of practice is not required.

With regard to claim scope, the court merely points to the fact that a number of poxviruses and their essential genes were known to the PHOSITA, without ever explicitly addressing the scope of the claim relative to scope of disclosure, or the lack of meaningful structural limitation on the claim. In *Lilly*, the court seemed to require that a broad genus claim to genetic sequences be supported by a representative number of samples, or by the identification of common structural features that distinguish the claimed genus. However, in *Falkner* the court specifically rejects the notion that any specific examples are required to support a broad genus claim, and finds that the knowledge of some relationship between structure and function in species falling within the scope of the claim is sufficient to satisfy LWD, without engaging in any analysis regarding the scope of the claims relative to the limited number of species for which any relationship between structure and function was known.[148]

In view of the breadth of the claim and lack of structural limitation, the claim could have been found invalid for insufficient enablement. The poxvirus family is vast, including numerous distinct viruses capable of infecting vertebrates and invertebrates.[149] The classification poxvirus would also presumably encompass the many poxvirus species that have yet to be discovered and/or characterized,[150] hence the claims cover vaccines against viruses not even known at the time the application was filed, and vaccines with substantially superior function, none of which could have been made based on the

[148] *Id.* at 1366.
[149] Human Virology at Stanford, http://www.poxvirus.org/index.asp (last visited Sept. 6, 2006)
[150] *Id.*

original disclosure without engaging in undue experimentation. For example, in *In re Wright*, a similar broad claim directed to viral vaccines was found overly broad and hence invalid for lack of enablement.[151]

2. LWD in the District Courts

My search identified ten district court decisions, not the subject of a subsequently reported appellate decision, wherein the court rejected LWD challenges to claim validity. Each case is discussed in this section. Three of the cases involved a determination by the court after a bench trial, and seven involved a denial of a motion for summary judgment. In one of the decisions denying a defendant's motion for summary judgment of invalidity, the court also granted patentee's summary judgment motion with regard to LWD, finding the claims to satisfy LWD as a matter of law.

In *Streck v. Beckman Coulter*, the defendant argued on motion for summary judgment that a claim reciting "analogs or surrogates" for white blood cells failed to satisfy LWD.[152] The district court rejected this argument, holding that the "claim is not so devoid of clarity that there is no means by which those skilled in the art could ascertain the scope of the claim."[153] In basing its decision on the clarity of the claim, the court appears to have blurred the line between LWD and the definiteness requirement of 35 USC 112, second paragraph. The court also posited that LWD is restricted to genetic sequences and biotechnology inventions, and in not applicable to cells.[154]

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[151] *Supra* Part II.
[152] 2002 WL 1012965 (D. Neb. 2002).
[153] *Id.* at *3.
[154] *Id.* at *5, n.5.

In *Monsanto Co. v. Scruggs*,[155] the claim at issue was directed to a chimeric gene comprising two elements: (1) a promoter sequence derived from a cauliflower mosaic virus (CaMV),[156] and (2) a "structural sequence which is heterologous with respect to the promoter."[157] The CaMV promoter element was defined so as to generically encompass two classes of promoters that are associated with many of the virus's genes (in particular, the CaMV 35S and 19S promoters).[158] Thus, the definition includes a large genus of genetic sequences, unrestrained by any explicit structural limitation. The second element of the chimeric gene could essentially be any gene, from any source, that does not occur naturally in association with the CaMV promoter element. The claim scope is very broad, analogous to the chimeric gene claim at issue in *Capon*. In granting a Monsanto motion for summary judgment, the district court held that the disclosure of a few species falling within the scope of the claim satisfied LWD as a matter of law, thus anticipating the Federal Circuit's decision in *Capon*.

In *Regents of University of California v. Monsanto Co.*, the district court denied a motion for summary judgment seeking to invalidate a claim directed to a specific nucleotide sequence for failure to comply with LWD.[159] The motion was based on the defendant's assertion that the claim listed the wrong DNA sequence.[160] In denying the motion, the judge noted that the alleged error resulted in a silent mutation, so would not change the sequence of the protein encoded by the gene, and that in any event the

[155] 342 F.Supp.2d 584 (N.D.Miss.,2004).
[156] A promoter is a genetic sequence that controls the expression of a gene with which it is in close proximity.
[157] The structural sequence is essentially a gene not normally associated with the CaMV promoter. 342 F.Supp.2d at 591.
[158] *Id.*
[159] 2005 WL 3454107 (N.D. Cal. 2005).
[160] Apparently a typographical error that occurred in drafting the patent application. *Id.* at *19.

patentee had made a deposit of the claimed sequence accessible to the public, which under *Enzo II* satisfies LWD.[161]

In *Pfizer Inc. v. Ranbaxy Laboratories Ltd*.,[162] the defendant Ranbaxy argued that the patent claims, which recited a molecule defined in terms of a generic chemical formula, should be interpreted narrowly as only covering racemic mixtures of the molecule.[163] Because they proposed marketing a purified enantiomer of the molecule, under this construction they would not have infringed the patent.[164] In the alternative, they argued that if the claims were interpreted broadly so as to encompass purified enantiomers, the claim was invalid under LWD for failure to individually describe specific enantiomers of the claimed compounds, and for failure to disclose any method for making the enantiomers.[165] In a bench trial, the district court rejected this argument, pointing out that the patent specification expressly indicates that the generic formula includes all trans-enantiomers and that methods of resolving racemates into their respective enantiomers are well known to one of skill in the art.[166] Thus, the court interpreted LWD as not requiring an explicit disclosure of structure, and gave the claims a broad reading. *Pfizer v. Ranbaxy* is notable in that it is the only decision, in either the courts of BPAI, wherein the issue of LWD was even raised in connection with a product claim directed to a chemical entity other than a biomolecule.

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[161] *Id.* at *20
[162] 405 F.Supp.2d 495 (D. Del. 2005).
[163] Ranbaxy was attempting to enter the market with a generic version of the cholesterol drug Lipitor, the largest selling pharmaceutical in history, by challenging the validity of Pfizer's patent on the drug.
[164] 405 F.Supp.2d at 502(D. Del. 2005). ("Scientific Background" section explains enantiomers, racemic mixtures, and related concepts)
[165] *Id.* at 505-06.
[166] *Id.* at 505.

In *Boston Scientific Scimed, Inc. v. Cordis Corp.*, [167] the defendant moved for summary judgment that a claim directed to a method of treatment was invalid under LWD for defining a chemical therapeutic agent in purely functional terms.[168] The claim is closely analogous to the claim at issue in *Univ. of Rochester v. G.D. Searle*,[169] as are the defendant's arguments in the two cases. However, in *Boston Scientific* the patent specification discloses a number of chemical therapeutic agents possessing the claimed function, as well as an assay to identify other compounds possessing the desired function, whereas in *Rochester* the specification failed to specifically identify a single compound possessing the required function.[170] Based on this distinction, the district court denied defendant's motion, holding that the issue of LWD was one of fact that could not be decided on summary judgment.

In *Kao Corp. v. Unilever U.S., Inc.*, the court in a bench trial held that claims directed to compositions and methods for unclogging skin pores were not invalid for inadequate LWD.[171]

In *Enzo Life Sciences, Inc. v. Digene Corp.*, defendant Digene argued on a motion for summary judgment that claims directed to a diagnostic methods involving the detection of a complex of hybridized nucleic acids comprising a "signaling domain" or a

[167] 392 F.Supp.2d 676 (D.Del. 2005).
[168] The claim at issue reads: "A therapeutic method for preventing or treating a cardiovascular indication characterized by a decreased lumen diameter comprising administering to a mammal at risk of or afflicted with said cardiovascular indication, a cytostatic dose of a therapeutic agent, wherein the cytostatic dose is effective to increase the level of TGF-beta so as to inhibit smooth muscle cell proliferation, inhibit lipid accumulation, plaque stability, or any combination thereof." *Id.* at 679, n.2.
[169] See *infra* n.246.
[170] 392 F.Supp.2d at 683-84 (D.Del. 2005).
[171] 334 F.Supp.2d 527, 550 (D. Del. 2004).

"capturing domain" were invalid under LWD.[172] In particular, Digene focused on the lack of any ordinary meaning for the terms "signaling domain" and "capturing domain," the failure of the specification to provide any definition for the terms, and the fact that the nucleic acids were defined in purely functional terms.[173] Digene especially focused on the fact that the functional definition occurred at the point of novelty in the invention, *i.e.,* the use of "signaling and capturing domains."[174] The court denied the motion for summary judgment, holding that the question of compliance with LWD was one of fact inappropriate for summary determination. In support of its decision, the court pointed to a purported PHOSITA's declaration proffered by Enzo. The declaration identified various sections of the specification which indicated that one skilled in the art "would immediately recognize that the inventions claimed in [the patent] are fully described by the specification."[175] The court also rejected a motion for summary judgment on behalf of Enzo to find the patent not invalid under LWD, again finding that the determination involved a factual dispute unsuitable for summary disposition.[176]

In *Glaxo Wellcome, Inc. v. Eon Labs Mfg., Inc.*, a generic drug manufacturer moved for a summary judgment determination that claims directed to a sustained release version of the popular anti-depressant Wellbutrin were invalid under LWD[177]. The claim recited formulations comprising HPMC, which is a generic designation for a genus of related molecular polymers. The substance of the LWD challenge sounded in enablement, with the defendant essentially arguing that the specification failed to

[172] 305 F.Supp.2d 400 (D.Del. 2004).
[173] *Id.* at 403-04.
[174] *Id.*
[175] *Id.* at 404.
[176] *Id.* at 405.
[177] 2003 WL 22004874 (S.D.N.Y. 2003).

demonstrate that certain species falling within the claimed genus could actually be used to make a functional sustained release formulation.[178] The court rejected the motion, pointing to an affidavit submitted by Glaxo's expert stating that all versions of the polymer falling within the claimed genus would be capable of performing the desired function of forming a hydrogel and retarding release of the active ingredient from a sustained release matrix, which raised an issue of fact with respect to LWD compliance.[179]

In *Scanner Technologies Corp. v. Icos Vision Systems Corp., N.V.*, the court denied a LWD-based summary judgment challenge to a patent involving technology and processes to inspect electronic components, such as "ball array devices," which are used to conduct electrical impulses in electronic devices, citing the existence of a genuine issue of material fact.[180]

In *Genlyte Thomas Group LLC v. National Service Industries, Inc.*, the court denied a motion on summary judgment to invalidate claims directed to a "recessed lighting feature" for failure to comply with LWD. [181] The substance of the challenge implicates the definiteness requirement of 35 USC 112, second paragraph, rather than LWD, with the defendant alleging that the term "plastic," as used in the claims was "too general to be useful."[182]

[178] *Id.* at *1.
[179] *Id.* at *3.
[180] 253 F.Supp.2d 624 (S.D.N.Y. 2003).
[181] 262 F.Supp.2d 762 (W.D.Ky. 2003).
[182] *Id.* at 765.

Astra Aktiebolag v. Andrx Pharmaceuticals, Inc., involved generic drug companies seeking to invalidate patents claiming formulations of Prilosec,[183] alleging that the claims were invalid for failure to comply with LWD with regard to a number of terms used in the claims.[184] In a bench trial, the court rejected all LWD-based challenges to the claims.

3. LWD in the BPAI

My search identified 22 BPAI decisions, not the subject of a subsequently reported appellate decision addressing the LWD issue, wherein the board reversed an examiner's LWD rejection. Each decision is discussed in this section, with cases grouped to some extent based on similarity of the claimed subject matter and pertinent issues of patentability.

a. The Use of Open-Ended "Comprising" Language

Inventors of novel biomolecules frequently broaden the scope of patent coverage by using "comprising" language to claim the molecule.[185] For example, a claim directed to a polynucleotide "comprising" a specified DNA sequence is understood to encompass any larger DNA sequence that includes within its length the specifically disclosed sequence.[186] Such claims are very broad in the sense that there are infinite possibilities for modification at either end of the recited sequence, and all of these variants would fall

[183] A highly profitable gastric acid inhibiting drug.
[184] 222 F.Supp.2d 423 (S.D.N.Y. 2002).
[185] In the lexicon of patent law, "comprising" is a transition word that indicates that the claim is open, and hence infringement is not avoided by a product or process incorporating elements not recited in the claim. *See*, CHISUM ON PATENTS § 8.06.
[186] Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501 (Fed. Cir. 1997) ("'Comprising' is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.")

within the scope of the claim.[187] Perhaps more problematic from a policy perspective, the use of comprising language allows the discoverer of only a fragment of a naturally-occurring protein or polynucleotide to obtain a patent claim literally covering the full-length protein or polynucleotide, as well as any larger construct comprising the full-length molecule, such as a protein fusion or gene chimera.

Some patent examiners have attempted to use LWD to thwart this approach, asserting that the disclosure of a biomolecule sequence does not support a claim encompassing biomolecules having additions to one or both ends of the disclosed sequence, particularly additions that might very well confer function not possessed by the originally disclosed sequence. However, in the single BPAI decision I identified that addresses the issue, *Ex parte Fisher*, the board found that this use of comprising language generally does not raise LWD as an issue.[188]

In *Fisher*, the board reversed an examiner's LWD rejection of claims directed to any polynucleotide comprising a recited EST sequence,[189] concluding (without explanation) that the disclosure of a specified sequence was enough to satisfy LWD for any molecule comprising that sequence.[190] The board chose instead to invalidate the claims for lack of utility, a decision ultimately affirmed by the Federal Circuit.[191] Of course, a problem with reliance on utility instead of LWD (or enablement) is that in cases where an EST does have some utility, the comprising language will still be available to

[187] *Id.* Examples would include plasmids, genomes and other genetic constructs containing the specified sequence.
[188] 72 USPQ2d 1020, 1028 (BPAI 2004) (Unpublished).
[189] An "expressed sequence tag," or EST, is essentially a fragment of a full length gene.
[190] 72 at 1028 (BPAI 2004)
[191] In re Fisher, 421 F.3d 1365 (Fed. Cir. 2005).

leverage the discovery of a gene fragment into patent coverage for the full-length gene (and the vast number of other genetic variants that might also include the sequence).

b. Percent Identity Claims

Inventors of novel biomolecules typically seek patent claims encompassing not only that specific sequence, but also a broad genus of structurally and/or functionally related variants. When used in conjunction with comprising language, as is almost always the case, such claims can be truly astronomical in scope.

One of the most common approaches to achieving expansive scope of coverage around a disclosed biomolecule is to claim all molecules sharing some defined percent identity (or percent similarity) to the specific sequence actually discovered. [192] An example would be a claim reciting "a protein comprising an amino acid sequence sharing at least 90% identity with the amino acid sequence of SEQ ID NO. 1."[193]

The PTO's Synopsis of Application of Written Description Guidelines (referred to herein as the "Written Description Guidelines," or simply the "Guidelines")[194] specifically sanction the use of percent identity claims of a reasonable scope.[195] However, patent examiners routinely reject what they perceive to be overly broad percent identity claims for violation of LWD.[196] For example, in a typical scenario, a patent applicant files a patent application claiming all proteins sharing at least 70% identity to a recited amino acid sequence, the examiner rejects the claim for violation of LWD (and

[192] For a detailed discussion of the percent identity approach to claiming biomolecules, and a proposal for a superior alternative, *See* HOLMAN *supra* n. 44.
[193] This claim is somewhat over-simplified. For a more detailed explanation, *See* HOLMAN *supra* n. 44.
[194] *See Synopsis of Application of Written Description Guidelines*, *at* http://www.uspto.gov/web/menu/written.pdf (last visited Sept. 3, 2006).
[195] *See Synopsis of Application of Written Description Guidelines*, *supra* n.194 at 53, Example 14.
[196] Results of an unpublished study conducted by the author.

typically also the enablement requirement), and after some negotiation the examiner will allow a narrower claim amended to recite proteins sharing at least 90% identity to the recited sequence. There is substantial examiner-to-examiner variation with respect to the stringency with which written description is applied to percent identity claims, with some examiners essentially refusing to allow percent identity claims no matter how narrow, others allowing extremely broad claims (*e.g.,* 50% identity, or even less), and many allowing what they determine to be a reasonable scope of coverage, as illustrated by the example where a compromise was reached by the applicant amending the percent identity term to recite 90% instead of 70% identity. In many cases, the examiner will allow broader scope of coverage (a lower percent identity term) in cases where the applicant discloses some relationship between the biomolecule's structure and function.[197] Reflecting this disparate treatment, a survey of issued biomolecule patents will reveal a wide range of percent identity terms, varying from 99% to 50% or lower.[198]

In contrast, the BPAI has been very consistent when it comes to LWD rejections of percent identity claims - my research identified six decisions wherein the board reversed an examiner's LWD rejection of a percent identity claim, and not a single instance where such a rejection was affirmed.

The earliest percent identity LWD decision that I identified is *Ex parte Sun*.[199] The rejected claim recited an "isolated Wee1 nucleic acid comprising . . . a Wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO: 1." The examiner pointed out that the patent specification failed to disclose a single

[197] *See, e.g*, *Ex parte Smith*, *infra* at note 207.
[198] *Supra* note 196.
[199] Appeal No. 2003-1993, Application No.09/470,526, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd031993.pdf (last visited Sept. 7, 2006).

example of a Wee1 variant retaining the activity of Wee1 and sharing only 80% identity with the reference sequence, and argued that the "specification does not set forth what specific structural or physical features define the claimed isolated nucleic acids," and that one skilled in the art "could not predict the structure and function of isolated nucleic acids comprising a Wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1." This would seem to be a valid application of LWD as a super-enablement requirement, focusing on claim breadth, lack of structural definition and lack of representative examples. Nevertheless, the board reversed the LWD rejection, citing *Enzo II* and holding that the disclosure of the single reference sequence and methodology for screening for variants having Wee1 activity was sufficient to satisfy the LWD requirement.

Then, in *Ex parte Bandman et al.* (*Bandman I*)[200] and *Ex Parte Au-Young et al.*,[201] the board reversed LWD rejections of claims encompassing any "naturally-occurring" polynucleotide encoding an amino acid sequence sharing 90% identity to a disclosed reference sequence.[202] In both cases, the examiners' rejections were based on a determination that the disclosure provided no guidance as to how the sequences of naturally-occurring alleles could be distinguished from non-naturally occurring sequences, and no way to predict they would all have function. The Board disagreed, finding that 90% identity and naturally occurring were enough to adequately describe the genus, even without a functional limitation. Note that the examiners rejection was based

[200] Appeal No. 2003-1805, Application No. 09/079,892 *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd031805.pdf (last visited Sept. 7, 2006).
[201] Appeal No. 2003-1817, Application No. 09/501,714 *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd031817.pdf (last visited Sept. 7, 2006).
[202] *In Bandman I*, the examiner had allowed a claim to the genus of polynucleotides having at least 90% identity to a reference sequence and retaining the functional activity of the reference sequence.

on the same rationale used by the Federal Circuit in *Amgen v. Chugai* when it found a biomolecule claim invalid for lack of enablement.[203]

In *Ex parte Meyers*,[204] the board reversed the LWD rejection of a claim encompassing all nucleotide sequences having at least 70% identity with the reference sequence and encoding a polypeptide having dehydrogenase activity. Not only is the 70% identity term broad in a structural sense, the functional limitation itself is very broad. The term "dehydrogenase activity" does not refer to single, specific function, but rather is a generic term referring to the chemical reactions catalyzed by a large family of diverse proteins involved in a variety of physiological pathways.[205]

In *Ex parte Bandman et al.* (*Bandman II*),[206] the board reversed the LWD rejection of a claim encompassing any "isolated polynucleotide encoding a polypeptide . . . comprising a naturally-occurring amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:1." The Examiner supported the rejection by pointing out that the specification provided only a single representative sequence and "no disclosure of any particular structure to function/activity relationship in the single disclosed species." The Board was not convinced, faulting the examiner for failing to provide adequate explanation or evidence to support the assertion that the specification failed to disclose any structure to function/activity relationship. Upon review of the

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[203] *See supra* Part II.
[204] Appeal No. 2003-1820, Application No. 09/464,039. This decision was not available on either Westlaw or in the PTO database, but is publicly available in the file history, and a copy was kindly provided to me by an attorney who worked on the appeal.
205 *See, e.g.*, *Enzyme Nomenclature: Recommendations of the Nomenclature Committee of the International Union of Biochemistry and Molecular Biology on the Nomenclature and Classification of Enzymes by the Reactions They Catalyse*, *at* http://www.chem.qmul.ac.uk/iubmb/enzyme/ (last visited Sept. 3, 2006).
[206] Appeal No. 2004-2319, Application No. 09/915,694, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd042319.pdf (last visited Sept. 7, 2006).

specification, it appears that the examiner's assertion was correct, in that there is no specific discussion of correlation between structure and function.

Most recently, in *Ex parte Smith*[207] the board reversed the LWD rejection of a claim reciting a method that included a step of "adding isolated viral reaper protein having at least 50% sequence similarity to SEQ ID NO:2 and capable of inducing caspase activation in a vertebrate cell."[208] Note that typically protein genuses are defined in terms of percent "identity;" not "similarity." Similarity encompasses not only identical residues, but also conservative amino acid substitutions, so the genus in this case is much broader than even 50% identity. Nonetheless, even 50% identity would be quite broad, with 70% identity usually being considered a rough cut-off for detecting homology between proteins. The board seemed to be impressed by the fact that in this case the specification described 15 variants of the reference viral reaper protein, sharing between 62%-87% similarity to the reference sequence. In the view of the board, this information amounted to a description of a relationship between structure and function, which under *Enzo II* can be used to satisfy the LWD requirement in the absence of a literal disclosure of structure.

c. Hybridization Claims

Another commonly used technique for achieving broad genus coverage of a polynucleotide is by means of a "hybridization claim," *i.e.*, a claim that encompasses any polynucleotide capable of hybridizing to a reference sequence, or the reference

[207] Appeal No. 2005-0147, Application No. 10/203,081, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd050147.pdf).
[208] The examiner had already allowed a dependent claim that recited variants sharing 75% similarity, so apparently for this examiner the issue was not the use of percent similarity, but the magnitude of the percent identity term.

sequence's complement.[209] In as sense, hybridization is a proxy for percent identity, because there is a correlation between the degree of percent identity between two polynucleotide sequences and their ability to hybridize to one another.[210]

As is the case with percent identity claims, the Written Description Guidelines specifically sanction the use of percent identity claims, at least where the claim recites relatively high stringency hybridization conditions.[211] However, an examiner will often invoke the LWD requirement to reject a hybridization claim which she feels is overly broad, such as in cases where the claim recites relatively low or moderate stringency hybridization conditions.

In my review of BPAI decisions, I found two cases where the board reversed rejections of hybridization claims, and no instance where such a rejection was affirmed. In *Ex parte Herrmann et al.*,[212] the board reversed a LWD rejection of a claim that encompassed any polynucleotide capable of hybridizing to any of a large number of reference polynucleotide sequences under defined hybridization conditions.[213]

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[209] *See Synopsis of Application of Written Description Guidelines*, *supra* n.194 at 38, Example 10.
[210] However, the ability of two polynucleotides to hybridize to one another is dictated not only by the degree of percent identity, but also by the chemical nature of the sequences (GC-rich sequences tend to hybridize more readily than AT-rich sequences sharing the same percent identity) and the specific hybridization conditions (temperature and chemical environment). Hence, the correlation between percent identity and the ability to hybridize is real, but not directly proportional.
[211] *See supra* note 209. With hybridization claims, the scope of coverage depends upon the "stringency" of the experimental conditions used to determine whether two sequences hybridize. Under high stringency conditions, only polynucleotides sharing a relatively high degree of percent identity will hybridize, while under less stringent conditions less similar polynucleotides will be able to hybridize. In other words, the lower the stringency of hybridization conditions applicable to a hybridization claim, the broader the claim.
[212] Appeal No. 2002-1630, Application No. 09/175,713, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd021630.pdf (last visited Sept. 7, 2006).
[213] The claim specifically recited hybridization claims or either (i) 4xSSC at 65°C or (ii) 50% formamide and 4xSSC at 42°C.

In the other hybridization decision, *Ex parte Chung et al.*,[214] the board reversed a LWD rejection of a claim reciting a genus of isolated nucleic acids defined essentially in terms of three criteria: (1) percent identity to a disclosed reference sequence, (2) the ability to hybridize to the reference sequence, and (3) the correspondence of the nucleic acid to an mRNA differentially expressed in certain types of cancerous tissues. The claim is analogous to Example 9 in the Written Description Guidelines, the main difference being that in Example 9 the functional limitation relates to the function of a protein encoded by the nucleic acid, while in this case the functional limitation relates to differential mRNA expression in carcinoma tissue.[215] The Examiner felt that this difference brought the claim out of compliance with LWD, but the Board disagreed, noting that in both cases the "functional" limitation could be determined by testing.

In support of the LWD rejection, the examiner argued that the functional characteristic of the genus (differential expression, which is not really a function) was "uncoupled with the structure of the claimed genus." However, the Board found that examiner had not explained why that matters; *i.e.*, the board fails to even acknowledge the role of chemical structure in compliance with LWD.

d. Fragment Claims

Another claiming technique for obtaining broad genus coverage around a disclosed biomolecule is to claim any biomolecule comprising some relatively short fragment (*i.e.*, segment) of the disclosed protein or nucleic acid sequence. Because of the power of "comprising" language in patent claims, discussed above, these fragment claims

[214] Appeal No. 2004-2201, Application No. 09/788,476, at http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd042201.pdf (last visited Sept. 7, 2006).
[215] *See Synopsis of Application of Written Description Guidelines*, *supra* n.194 at 35, Example 9.

can result in extremely broad genus coverage surrounding the disclosed biomolecule. For example, a typical disclosed protein might be made up of 300 amino acids. A claim to any protein comprising any 10 contiguous amino acid sequence of the molecule would be infringed by any protein sharing at least one stretch of 10 contiguous amino acids; any and all of the remaining 290 amino acids could be altered, and amino acids could be added or deleted. The claim could cover proteins that are almost totally unrelated (other than the short 10 amino acid fragment), including as of yet undiscovered proteins never contemplated by the inventor and having vastly different functional properties than the disclosed biomolecule.

In three of the BPAI decisions that I found in my search the board considered LWD rejections of fragment claims, and in all three cases the board reversed these rejections. For example, in *Ex parte McElroy et al.*,[216] the board reversed a LWD rejection of a polynucleotide fragment claim, specifically, a claim directed to fragments of a promoter sequence. The inventors had discovered a 3536 base long stretch of genetic sequence containing somewhere within its length a promoter sequence. Recognizing that not all of the 3536 bases were required for promoter activity, they claimed any polynucleotide comprising at least 95 contiguous bases of the disclosed promoter sequence and retaining the promoter activity. The examiner's LWD rejection was based on the lack of disclosure of any structure-function correlation that would allow one to predict which 95 contiguous base fragments would retain promoter function and which would not. However, the Board held that no disclosure of structure-function correlation was required to satisfy the LWD requirement. The disclosure of the 3536

[216] Appeal No. 2003-0936 , Application No. 09/352,806, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd030936.pdf (last visited Sept. 7, 2006).

base reference sequence inherently included the disclosure of each 95 base fragment, and according to the board this was all that was required to satisfy the LWD requirement.

In *Ex parte Hermann et al.*, a claim covering any "polynucleotide encoding a protein comprising an amino-terminal fragment of [a disclosed amino acid sequence]" was rejected for violation of the LWD requirement, and the board reversed.[217]

More recently, in *Ex parte Friedberg et al.*,[218] the board reversed a LWD rejection of claims to fragments of a protein. The inventor had discovered a novel protein (hundreds of amino acids in length) and claimed any isolated polypeptide comprising at least 10 contiguous amino acids of the protein's sequence. The case tracks the facts of *Ex parte McElroy*; the examiner found the claim to violate LWD for failing to identify which of the 10 contiguous amino acid sequences were involved in the protein's function, but the board rejected this argument, finding that since the full length protein sequence was disclosed, inherently all of the 10 amino acid segments are also described. The board did not consider function at all in its LWD analysis.

Note that in sanctioning this claiming strategy, the BPAI is opening up the door to very broad claims encompassing much larger molecules that are not described by the specification, have not been actually reduced to practice, and have not been made available by deposit. The approach is clearly at odds with the policy concerns which gave raise to LWD. In fact, if the patentee in *Lilly* itself had used this approach, and claimed any polynucleotide comprising some fragment of the disclosed rat insulin gene,

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[217] *See supra* at note 212.
[218] Appeal No. 2004-2314, Application No. 09/971,101, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd042314.pdf (last visited Sept. 7, 2006).

the claim would have likely encompassed the human insulin gene, based on the high degree of homology between the two sequences.[219]

e. Genetic Constructs and Protein Fusions

One of the methodologies that define biotechnology is genetic engineering, which includes the splicing together of DNA sequences from divergent sources to form genetic constructs that do not otherwise exist in nature. For example, genetic engineering can be used to link promoter and gene sequences that that are not naturally associated with one another, thereby placing gene expression under the control of a foreign promoter. Similar technology can be used to fuse together genetic sequences coding for elements of two or more distinct protein precursors. The expression product of such a gene chimera is a protein fusion, a single protein formed from the covalent combination of elements derived from two or more distinct protein precursors.[220] I identified several BPAI decisions wherein the board reversed LWD rejections of claims directed to chimeric genes and/or fusion proteins.

In *Ex parte Fischetti*,[221]the board reversed the rejection of a claim directed to a fusion protein comprising a "carrier" protein linked to some segment of a known protein, *i.e.*, the "conserved exposed region of the M protein of group A streptococci." The "carrier" protein element of the fusion protein is defined solely in terms of function, while the protein segment element, it is defined as encompassing any segment of the protein ranging in length from 5 to 130 amino acids. The examiner pointed out that the

[219] *Cf.* Michael D. Plimier, *Genentech, Inc. v. Novo Nordisk & University of California v. Eli Lilly and Co.*, 13 BERKELEY TECH. L.J. 149 (1998).
[220] *See, e.g.*, *Capon v. Eshhar*, *supra* note 117.
[221] Appeal No. 2001-2524, Application No. 09/369,295, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd012524.pdf (last visited Sept. 7, 2006).

specification failed to provide any guidance as to how one might distinguish between functional and non-functional segments,[222] but the board found that the disclosure of structure or structure-function relationship was in this case not required to satisfy LWD.

In *Ex parte Evans et al.*,[223] the board reversed a LWD rejection of a claim reciting cells containing exogenous DNA encoding "functional steroid receptor proteins" operably linked to a control sequence (*i.e.,* a promoter). Both elements of the chimera are defined very broadly and in terms of function, without any structural description. In particular, the genus of "functional steroid receptor proteins" encompasses a large family of diverse proteins. There are many different types of steroids, many proteins which bind them, and these proteins can respond in a variety of complex ways to the binding of a steroid. Not only does the claim encompass a large number of proteins known at the time of the invention, but many that had yet to be discovered. For example, there is no limitation with respect to the source of the protein; it could be derived from any organism, or could be a synthetic protein that does not even exist in nature. The promoter element is even broader, defined as it is solely in functional terms.

In *Ex parte Griffiths et al.*,[224] a representative claim recites a method that comprises administering to a patient a bispecific (*i.e.,* chimeric) antibody and an F-18 labeled peptide. The claim specifies that the antibody comprises an arm that is specific to a target tissue of the patient and another arm that is specific to the F-18-labeled peptide. The specification and claims impose no structural restrictions on the peptides, and the

[222] The fusion protein is intended to be used as an antigen, and so would lack function if it included a segment of the M protein that was not capable of eliciting a "protective immune response."
[223] Appeal No. 2001-2584, Application No. 08/462,917, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd012584.pdf (last visited Sept. 7, 2006).
[224] Appeal No. 2004-1660, Application No. 10/071,247, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd041660.pdf (last visited Sept. 7, 2006).

chimeric antibody is defined solely in terms of function. The specification does provide the structure of three exemplary peptides that work. The examiner rejected the claim under LWD, arguing that the three peptide species were insufficient to adequately describe the entire genuses of peptides and bispecific antibodies falling within the scope of the claims, and for lack of enablement. The Board reversed both rejections.

And most recently, in *Ex parte Peoples et al.*,[225] the board reversed a LWD rejection of a claim directed to any proteins fusion made by linking two or more proteins derived from any of the following families of proteins: β-ketothiolases, acyl-CoA reductases, PHA synthases, PHB synthetases, phasins, enoyl-CoA hydratases and beta-hydroxyacyl-ACP::coenzyme-A transferases. These classifications are based solely on the physiological functions of the proteins falling within the family, and do not imply any structural limitation upon the claim. The claim is also exceedingly broad; each of these families includes a large number of distinct proteins, including proteins of diverse function and as-of-yet undiscovered proteins.

f. Functionally Claimed Proteins

In *Ex parte Tully et al.*,[226] the board reversed a LWD rejection of a claim to a method for assessing the effect of a drug on long term memory formation comprising a step of determining "functional levels" of certain "activator or repressor" proteins. The proteins are defined broadly and in functional terms. The examiner noted that the specification failed to provide structural guidance with respect to how one would distinguish between proteins falling within the claim versus those outside the claim. As

[225] Appeal No. 2005-1383, Application No. 09/364,847, *at* http://des.uspto.gov/Foia/ReterivePdf?flNm=fd2005138301-31-2006.pdf (last visited Sept. 7, 2006).
[226] Appeal No. 2003-0835, Application No. 09/149,371, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd030835.pdf) (last visited Sept. 7, 2006)

pointed out by the examiner, known proteins falling within the scope of the claim shared little structural similarity (approximately 18% "homology"), and the claim would presumably encompass as yet undiscovered proteins.

g. Functional Protein Variants

In *Invitrogen v. Clontech*, the Federal Circuit held that the disclosure of a single genetically-engineered functional variant of a known protein was sufficient to provide adequate written description to support a claim encompassing essentially any engineered variant of the protein sharing the modified function. My search identified two BPAI decisions that reach a similar conclusion.

In *Ex parte Bornscheuer et al.*,[227] the board reversed a LWD rejection of a claim directed to a method for altering the function of a protein by random mutation of the gene encoding the protein[228] and selecting for a mutation that results in a desirable alteration in the protein's function. The claim is not limited to a particular protein, but encompasses any protein falling within the scope of "lipases, amidases, nitrilases, ether hydrolases, peroxidases, glycosidases and phytases." These are all functionally defined families of enzymes;[229] not only is there no structural limitation, but the claim scope is expansive, since each family comprises a diverse collection of functionally distinct enzymes. In support of the rejection, the examiner specifically cited the huge scope of the claim (the use of "<u>any</u> enzyme and <u>any</u> substrate" to produce a new enzyme (emphasis in original))

[227] Appeal No. 2005-1745, Application No. 09/161,680, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd051745.pdf (last visited Sept. 7, 2006).
[228] The claims specifies that the mutation occurs in a specified strain of bacteria that promotes mutations.
[229] The specification cites the use of IUB Enzyme Nomenclature,which defines these classes of enzymes solely in terms of function. *See Nomenclature Committee of the International Union of Biochemistry and Molecular Biology (NC-IUBMB), at* http://www.chem.qmul.ac.uk/iubmb/enzyme/ (last visited Sept. 7, 2006).

and the failure of the specification to describe a "correlation between the structures and functions of the reagents used in the methods."

In *Ex parte Anderson et al.*,[230] the BPAI reversed a LWD rejection of a claim directed to any mutant of a specified cellulase protein having "endoglucanase activity." Naturally occurring cellulases, including the specified cellulase, do not normally have endoglucanase activity, and the invention was the successful creation of a single cellulase mutant having the desired activity. However, based on the limited disclosure of a single mutant the inventor claimed any mutant having this desired function, with the only structural limitation being that the mutant must have a histidine at a specified position in the amino acid sequence.[231] In rejecting the claim, the examiner pointed out the extreme breadth of the claim in relation to the disclosure. For example, the cellulase protein comprises 200 amino acids, and the claim only specifies the identity of one of these (the histidine). The claim encompasses "variants mutated at any of said 200 amino acid residues," and provides no guidance with respect to which of these variants would possess the desired function other than the disclosure of a single example. The board explicitly interpreted the claim as encompassing any modifications of the cellulase, "wherein the modifications may be substitutions, insertions or deletions, with the proviso that the resulting cellulose [sic] have endoglucanase activity," but nonetheless found the claim to comply with LWD.

h. DNA Sequence Coding for a Structurally Undefined Protein

[230] Appeal No. 2005-0908, Application No. 09/261,329, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd050908.pdf (last visited Sept. 7, 2006).
[231] Histidine is one of the common amino acids encoded by the genetic code and found in nearly all proteins.

In *Ex parte Knauf et al.*,[232] the board reversed a LWD rejection of a claim covering the genus of cDNA sequences encoding "the mature protein encoding portion" of a specifically recited protein. The structure of the protein is not provided, but the claim does recite an approximate molecular weight of the "mature protein." The claim is intended to encompass structural variants of the protein, including the "Type I" and "Type II" forms. The specification does appear to disclose the structure for at least one cDNA sequence falling within the scope of the claim, which would distinguish this case from the Federal Circuits decision in In re Wallach, discussed below.[233] Still, as the doctrine is interpreted by the BPAI in this decision, LWD does not seem to impose any structural limitation on claim scope, so long as at least one structure falling within the scope of the claim is disclosed.

i. Functionally-Defined Synthetic Biomolecules

In *Ex parte Usman et al.*,[234] the BPAI reversed a LWD rejection of a claim reciting a "pharmaceutical composition, comprising: at least one enzymatic nucleic acid molecule having a ribonucleotide at a catalytically critical site, at least one deoxyribonucleotide and at least one nucleic acid analog; and a pharmaceutically acceptable carrier."[235]

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[232] 1999 WL 33501543 (B.P.A.I. 1999).
[233] In *Wallach*, the Federal Circuit found a similar claim invalid under LWD, but in that case the patent applicant had failed to disclose the structure for any DNA sequence falling within the scope of the claim. *See infra* note 258.
[234] Appeal No. 2002-1251, Application No. 08/459,340, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd021251.pdf (last visited Sept. 7, 2006).
[235] Although purporting to be a written description rejection, the substance of the rejection was actually directed to the "how to use" branch of the enablement inquiry, *i.e.*, it was based on the examiner's skepticism as to whether the claimed enzymatic nucleic acids would actually perform as pharmaceuticals. The Board reversed, finding that description in words was sufficient to satisfy LWD.

The scope of this claim is particularly expansive, the range of potential enzymatic activities is virtually limitless, and the claim covers any nucleic acid molecule having any enzymatic function, so long as it contains at least one each of a ribonucleotide, a dexoyribonucleotide, and a nucleic acid analog. The specification provides no guidance with respect to correlation between structure and enzymatic function.

j. Hybrid and Recombinant Plants and Seeds

In *Ex parte Griffith*,[236] the BPAI reversed a LWD rejection of a claim directed to the genus of "any and all hybrid corn seeds, and the hybrid corn plants produced by growing said hybrid seeds, wherein the hybrid seeds are produced by crossing [a specifically disclosed, novel inbred corn line] with any second, distinct inbred corn plant." The examiner argued that since half of the genomes of the claimed hybrids are derived from a second, non-specified inbred corn plant, the specification failed to provide adequate description to support the claims.

Likewise, the examiner rejected claims directed to variants of the disclosed inbred corn line that had been transformed to include a transgene in the plants genome, again for failing to describe the nature of the transgene. This rejection was also reversed by the board.

B. *Decisions Upholding Lilly Written Description Challenges to Claim Validity*

In the preceding section, the conventional view that LWD has dramatically restricted the ability of biotechnology inventors to claim their inventions is refuted by the large number of cases where the courts and BPAI have declined to apply LWD in such as

[236] Appeal No. 2004-1968, Application No. 10/000,311, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd041968.pdf (last visited Sept. 7, 2006).

restrictive manner. In this section I will review all of the decisions I identified wherein the courts or BPAI have found claims to be invalid under LWD. In view of the outcry over *Lilly*, it might come as a surprise to some that in the nine years since the decision there have been so few reported judicial decisions where claims have actually been invalidated under LWD. In fact, there are only four Federal Circuit decisions,[237] and a single district court decision (that was not subsequently the subject of a reported appellate decision).

1. LWD in the Federal Circuit

The first post-*Lilly* Federal Circuit decision wherein a patent claim failed to satisfy LWD was *Noelle v. Lederman*, an appeal of a BPAI decision in an interference contest.[238] Noelle had successfully isolated a monoclonal antibody (mAb) capable of binding the mouse antigen CD40CR (*i.e.,* a "mouse mAb"),[239] and deposited the mAb with the ATCC, a publicly accessible depository for biological samples. Based on this disclosure of the mouse mAb, Noelle attempted to obtain a claim encompassing any mAb capable of binding the human analog of the CD40CR antigen (the "human mAb"), and another claim directed generically to any mAb capable of binding CD40CR from any species possessing the antigen. Noelle did not provide the structure for the deposited mAb, or any mAb falling within the scope of the claim, nor did he provide a structural description of the mouse CD40CR antigen, or CD40CR antigen from human or any other species.

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[237] Excluding *Enzo I*, which was vacated. *Supra* note 74.

[238] 355 F.3d 1343 (Fed. Cir. 2004). Technically, the claims were invalidated under 102(b), not LWD, but the 102(b) rejection was premised on the party's inability to claim priority to an earlier filed patent application that did not satisfy LWD. Nevertheless, even though the written description requirement was used to police priority rather than to invalidate an originally filed claim, the BPAI and court both clearly applied the LWD form of the requirement, so it is appropriate to consider the decision in this article.

[239] CD40CR is an antigen expressed on activated T cells, and is involved in the immune response.

The BPAI found that deposit of a single mouse mAb constituted sufficient disclosure to support a broad claim encompassing any mouse mAb .[240] However, it held that the human and genus claims failed to satisfy LWD because the specification failed "to describe any structural features of the human or genus antibodies or antigens.[241]

The Federal Circuit affirmed, citing the Written Description Guidelines Example 16 (*i.e.*, the antibody example) as "past precedent."[242] In Example 16, a hypothetical patent applicant reports generating a mAb and successfully purifying and determining the molecular weight for the corresponding antigen (a protein) – chemical structures are not determined for either the antigen or mAb.[243] The Guidelines conclude, in effect, that a claim reciting a genus of functionally defined mAbs complies with LWD so long as the relevant *antigen* has been "characterized," and this characterization need not include a determination of chemical structure.[244] The mAb itself does not need to be characterized except by its ability to specifically bind the antigen, *i.e.,* its function. The court seemed to agree with the board's determination that deposit of the mouse mAb provided sufficient characterization with respect to the mouse antigen to support the mouse mAb claim. Thus, in *Noelle,* the only Federal Circuit decision not authored by Judge Lourie that finds a biotechnology claim invalid under LWD, the panel apparently would have upheld the validity of a broad genus claim defined solely in terms of function, illustrating the general lack of support for LWD on the Federal Circuit.

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[240] 355 F.3d at 1346 (Fed. Cir. 2004).
[241] *Id.*
[242] *Id.* at 1349. This was probably an overstatement. The court cited *Enzo II* for the creation of this "precedent," butb recall that *Enzo II* dealt with DNA probes, not antibodies, and while the court in *Enzo II* did refer to the Guideline's antibody example with apparent approval it was not a basis for its decision.
[243] *See Synopsis of Application of Written Description Guidelines*, *supra* n.194 at 59, Example 16. An antibody is characterized and defined by its ability to bind a specific molecule called an "antigen," which is oftentimes a protein.
[244] *Id.*

Not only were the invalidated human and genus claims extremely broad, they could have been comfortably invalidated for lack of enablement. Although the issue of enablement was never explicitly addressed, the Federal Circuit's decision implicitly but persuasively supports a finding that the claims were not enabled. In affirming the BPAI's determination that there was no interference-in-fact between the parties, the court determined that one of skill in the art would have had no "reasonable expectation of success" were they to try to isolate the human mAb based on Noelle's disclosure considering the state of the art at the time.[245] Although the "reasonable expectation of success" standard is normally associated with the nonobviousness inquiry, it is reasonable to equate a lack of reasonable expectation of success with an undue amount of experimentation, which would support a conclusion that a claim encompassing human mAb was not enabled by Noelle's disclosure. Thus, in this case LWD was not functioning as a super-enablement requirement, but merely as an alternative basis for invalidating the claims.

Shortly after *Noelle* was decided, the Federal Circuit again found claims invalid under LWD in *Univ. of Rochester v. G.D. Searle*.[246] The patent was based on an important scientific discovery that eventually led to the development of so-called "COX-2 inhibitor" drugs.[247] COX-1, an enzyme, is the target of many of the traditional non-steroidal anti-inflammatory drugs (NSAIDS), such as aspirin, acetaminophen and ibuprofen.[248] Scientists at the University of Rochester discovered a second COX enzyme, COX-2, and had the insight that if one could identify a non-steroidal compound that

[245] 355 F.3d at 1347, 1352-53 (Fed. Cir. 2004).
[246] 358 F.3d 916 (Fed. Cir. 2004).
[247] The notorious family of anti-inflammatory drugs that includes Vioxx, Celebrex and Bextra.
[248] Prior to the discovery of COX-2, COX-1 was known simply as COX.

specifically targeted COX-2 without affecting COX-1, that compound might possess the anti-inflammatory properties of traditional NSAIDS while avoiding the undesirable gastrointestinal side effects associated with traditional COX-1 inhibitors. In their patent application they disclosed this insight, along with an assay that would allow one to screen for molecules capable of specifically inhibiting the COX-2 enzyme without inhibiting COX-1.[249] However, they did not disclose a single example of a molecule that would specifically inhibit COX-2, nor did they provide any guidance as to what type of molecule might have that property.[250] Nevertheless, they obtained a patent broadly claiming any method of treating a patient with a non-steroidal COX-2 inhibitor, and they asserted this patent against drug manufacturers, such as Pfizer, who eventually did succeed in identifying and ultimately marketing COX-2 inhibitors as drugs. In *Rochester*, the Federal Circuit affirmed the invalidation of the claim on summary judgment, holding that the mere disclosure of an assay for identifying a COX-2 inhibitor was insufficient to satisfy LWD with respect to a claim generically covering the use of such an inhibitor as a therapeutic.[251]

Rochester is notable in a number of regards. For one, it is the only decision, in the courts or BPAI, to find a claim invalid for failure to comply with LWD with respect to a molecule other than a biomolecule,[252] refuting the idea that LWD is specific to genetic sequences, biomolecules, or biotechnology. And until very recently, it was the

[249] 358 F.3d 927 (Fed. Cir. 2004).
[250] In essence, they had disclosed methodology that would permit one to determine whether or not a molecule was a COX-2 inhibitor, and a use for that inhibitor, but they did not disclose how to make a COX-2 inhibitor.
[251] 358 F.3d 929 (Fed. Cir. 2004).
[252] The claim purports to cover any non-steroidal molecule that can function as a COX-2-specific inhibitor, and all of the commercial and allegedly infringing COX-2 inhibitors are small molecules, not biomolecules.

only judicial decision to invalidate a process claim under LWD[253] – other cases apply it to product claims, and in *Rochester* the patentee argued that the doctrine only applied to product claims.

The court focused its LWD analysis upon the lack of structural description for any molecule that would function as a COX-2 inhibitor. However, as was the case in *Noelle*, a strong argument can be made that the claims were invalid for lack of enablement, and that LWD functioned merely as an alternative grounds for invalidating the claims, rather than as a super-enablement requirement. Although the Federal Circuit chose not to decide the question of enablement in *Rochester*, [254] the district court had invalidated the claims for failure to comply with both the enablement requirement and LWD.[255] Not only did the purported inventors fail to disclose a single compound falling within the scope of the claim, they themselves apparently never succeeded in identifying such a molecule (and hence never enabled one to actually practice the claimed invention). Rather, history shows that is was only after multiple pharmaceutical companies instituted programs to identify and develop COX-2 inhibitors that any mode of practicing the invention was enabled.[256] Not only did the patent specification fail to enable a single mode of practicing the claimed invention, but the scope of the claim was expansive, purporting to cover the use of any molecule having the desired function, and should have

[253] The other case is *Lizardtech*, which involves computer technology. *See supra* note 271.
[254] Review of the enablement decision was considered unnecessary in light of the claims being invalid under *Lilly*. 358 F.3d 930 (Fed. Cir. 2004).
[255] *Id.* at 919.
[256] Based on the author's personal knowledge obtained while working as part of a group at a major pharmaceutical company attempting to develop a COX-2 inhibitor in the early 1990s.

been invalidated for exceeding the "reasonable correlation" test for compliance with the enablement requirement.[257]

In re Wallach,[258] decided in 2004, is notable as the only post-*Lilly* judicial that to my mind actually applies LWD as a super-enablement requirement, invalidating a genetic sequence claim that very likely could have withstood an enablement challenge. Wallach's patent specification describes the successful purification of a human protein identified as "TBP-II," along with a description of about 5% of the proteins structure and some other physical characteristics of the protein, such as its size and physiological activity.[259] Standard methodology was available at the time which would generally allow one to isolate a gene for a particular protein based on the information Wallach provided with respect to TBP-II. Based on this disclosure, the PTO issued Wallach a patent claiming the TBP-II protein, but balked at allowing claims directed to any DNA molecule that would code for the protein, *i.e.,* TBP-II genes, citing LWD and Wallach's failure to provide a chemical structure for the full-length protein, or any full-length gene encoding the protein. In effect, the PTO interpreted LWD as requiring a strict disclosure of structure for DNA sequences, but not for protein sequences.

The Federal Circuit, in an opinion authored by Judge Lourie, affirmed the BPAI's decision. The court noted that a disclosure of the complete structure for the TBP-II protein that would have been enough to satisfy LWD with respect to the TBP-II gene

[257] At the time the patent specification was filed it was recognized that COX-1 and COX-2 were structurally very similar proteins, and thus it would be difficult to identify a molecule that would be able to recognize the subtle differences between the two related proteins, and thus bind to COX-2 without also binding to COX-1.
[258] 378 F.3d 1330 (Fed. Cir. 2004).
[259] The specification defined the protein in terms of its N-terminal amino acid sequence (i.e, structure for about 5% of the full-length protein), it molecular weight, its physiological activity, and by the method used to purify the protein, but did not disclose the structure for the full-length protein. *Id.* at 1331-32.

(based on the genetic code and the known relation between DNA and protein sequence).[260] However, the specification disclosed the structure of only about 5% of the TBP-II protein, and hence only about 5% of the DNA sequence encoding it. Wallach argued that "possession" is the ultimate test for compliance with LWD, and that the partial structural information provided for the protein, combined with known methodology for using such information to isolate the corresponding gene, would have been sufficient to put a PHOSITA in possession of the gene. However, at least in this specific context, the court found that an enabling disclosure that would put a PHOSITA in constructive possession of the genetic sequence was not enough to satisfy LWD. Harking back to *Lilly*, the court interpreted LWD as strictly requiring a description of the gene's structure, either explicitly or implicitly (by disclosure of the protein's structure).[261]

The court did not address the issue of enablement; however, a quite plausible argument could be made that the claim could withstand an enablement challenge. The patent application claims priority to a 1989 filing date, long after *Lilly*'s 1977 filing date and at a time when it would have been fairly routine to clone a DNA sequence based on the protein information provided by Wallach.[262] 1989 is well after the filing dates of the patent applications at issue in *In re Bell* and *In re Deuel*, and those decisions reflect the PTO's determination that at that time the state of the art would have allowed one in possession of a protein to apply standard technologies to isolate the corresponding gene without undue experimentation.[263] In any event, the court's decision in *Wallach* is clearly focused on a lack of structural description, not the amount of experimentation that

[260] *Id.* at 1333-34.
[261] *Id*. at 1334-35.
[262] *See*, *e.g.,* JOSEPH SAMBROOK ET AL., MOLECULAR CLONING : A LABORATORY MANUAL (2nd ed. 1989).
[263] In re Bell, 991 F.2d 781, 783 (Fed.Cir.1993) (citing a 1983 patent for the general methodology); In re Deuel, 51 F.3d 1552, 1556 (1995) (citing a 1982 publication for the general methodology).

would be required to isolate the gene, or constructive possession of the gene, and in this sense LWD is being applied as a super-enablement requirement.

On appeal to the Federal Circuit, Wallach argued that it was irrational and inconsistent for the PTO to require a complete structural disclosure for the TBP-II gene but not for the corresponding protein, correctly pointing out that anyone having possession of a protein would by definition be in possession of the gene encoding it, since the protein itself implicitly defines all of the genetic sequences that would encode it. The court, however, rejected this argument, holding that regardless of whether or not structure was required to satisfy LWD with respect to a protein, structure was clearly required to satisfy LWD with respect to a genetic DNA sequence.[264]

One might conjecture that Judge Lourie's acquiescence to the PTO's determination that the protein claims satisfed LWD might merely reflect judicial restraint, and a reluctance on his part to venture an opinion on a matter not explicitly before the court. However, both the PTO and applicant had briefed this issue, and in other instances he has shown no hesitancy to express his opinion with regard to issues that have not even been addressed by the parties.[265]

How can one reconcile *Wallach*'s apparent strict requirement of structural disclosure with other Federal Circuit decisions, such as *Amgen v. HMR*, *Noelle*, *Capon*, and *Falkner*, which clearly downplay the relevance of structure? Note that the claims at issue in *Wallach* are much more closely analogous to the claims at issue in *Lilly*; in both

[264] 378 F.3d 1335 (Fed. Cir. 2004).
[265] For example, in *Wallach* he pronounced that the state of technology had advanced to the point where a protein of known amino acid sequence could put on in possession of the genus of DNA encoding it, even though that question was not before the court. In *In re Deuel*, he raised potential enablement issues with regard to certain claims, even though issues of enablement had not been addressed by the parties.

cases, the applicant attempts to claim a naturally-occurring genetic sequence *per se*. Thus, the claims assert a right to exclude any use of an isolated form of a naturally-occurring biomolecule. In other cases where the court upholds claim validity in the face of an LWD challenge, the biomolecule at issue is not naturally-occurring, but rather a synthetic product of biotechnological engineering.[266]

One way of rationalizing *Wallach*, *Lilly*, and generally a LWD that requires a structural description to support claims to naturally-occurring gene sequences, is that it provides a useful symmetry with earlier Federal Circuit decisions applying the nonobviousness requirement to newly isolated genetic sequences. In *In re Bell* and *In re Deuel*, the Federal Circuit reversed BPAI decisions that had found claims to naturally-occurring gene sequences obvious in view of prior art that would have rendered the methodology for isolating and sequencing the genes obvious.[267] *Bell* and *Deuel* have been widely interpreted as establishing a special, strict nonobviousness standard for genetic sequences (or biotechnology inventions), whereby a gene sequence can essentially only be rendered obvious by a disclosure of the genes chemical structure.[268] Note that under this standard, prior art that would "enable" a PHOSITA to isolate the gene sequences "without undue experimentation" (using the terms "enable" and "without undue experimentation" in their conventional, not legal sense) would not be enough to render the gene sequence obvious.

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[266] Examples discussed herein include genetically modified cells and proteins (*Amgen v. HMR*), monoclonal antibodies (*Noelle*), genetically modified viruses (*Falkner*), functionally-modified protein variants (*Invitrogen*), and chimeric genes (*Capon*). *See supra* Part IV[A].
[267] In re Bell, 991 F.2d 781 (Fed.Cir.1993); In re Deuel, 51 F.3d 1552 (1995).
[268] Lemley & Burk, *supra* note 70, at 1596-95.

A jurisprudence under which prior art that enables an invention and provides a clear motivation to make the invention, yet does not render the invention obvious, results in a troubling asymmetry between the patentability requirements of Section 103 (nonboviousness) and Section 112, first paragraph (adequate disclosure). LWD, by requiring a disclosure of chemical structure in the case of claims directed to gene sequences that have yet to be isolated or structurally defined, restores the symmetry between 103 and 112, and in that sense achieve a desirable policy effect. Perhaps this explains the retention of a strict requirement of structural disclosure for this particular type of invention (as exemplified in *Lilly* and *Wallach*), while the courts have distanced themselves from any strict requirement of structure outside this specific context.

This symmetry could have been achieved in other, perhaps preferable ways. For example, the Federal Circuit could effectively overrule *Bell* and *Deuel*, clarify that there is no special obviousness standard for biotechnology inventions, and find that an explicit disclosure of structure is not necessary if a biotechnology invention is otherwise obvious.[269] Alternatively, if *Bell* and *Deuel* are to be retained, the desirable symmetry might have been better achieved if the Federal Circuit had created a special enablement standard for inventions directed to naturally-occurring gene sequences in a manner that mirrors *Bell* and *Deuel*. After all, if the court can create special rules of obviousness for certain biotechnology inventions, why not corresponding special rules of enablement? One advantage of using enablement rather than written description to achieve this valid policy objective would have been an avoidance of the doctrinal confusion caused by the creation of LWD as a distinct disclosure requirement.

[269] However, there are valid policy justifications for the biotechnology-specific obviousness rules established by *Bell* and *Deuel*, though a full development of those justifications goes beyond the scope of this paper.

Finally, it should be noted that if LWD is really only functioning as a super-enablement requirement in the limited context exemplified by *Lilly* and *Wallach*, *i.e.*, attempts to claim gene sequences based solely on the disclosure of a protein and general methodology for isolating a gene based on knowledge of the protein encoded by the gene, then the actual impact of LWD will be of diminishing importance. In the very early days of biotechnology, typically a protein was isolated and characterized, and then scientists used the protein as the basis for isolating the corresponding gene - this is the scenario at play in *Amgen v. Chugai*, *Fiers v. Revel*, *Lilly*, *Wallach*, *Bell* and *Deuel*. However, as biotechnology developed it became more and more typical that the genetic sequence is determined prior to identifying the protein. Indeed, since *Lilly* was decided, *Wallach* has been the only judicial decision applying LWD to this type of invention, and there are no BPAI decisions (other than *Wallach*) applying LWD in this manner.[270] Wallach's priority date of 1989 was still relatively early in the development of biotechnology. To the extent the application of LWD as a super-enablement requirement is limited to this specific category of invention, one should expect it to be of diminishing relevance.

In *Lizardtech v. Earth Resource Mapping*, decided in late 2005, the Federal Circuit for the first time appeared to find a claim invalid under LWD that was not related to biotechnology or chemistry.[271] The specification disclosed a method for compressing a large digital image for storage in a computer memory, but broadly claimed any method of achieving that desired result.[272] While the district court found the claim invalid under LWD, the claim could (and should) have been found invalid for lack of enablement, since it claimed in functional terms any method of achieving a desired result based on a limited

[270] *See infra* Section V.
[271] 424 F.3d 1336 (Fed. Cir 2005).
[272] *Id*. at 1344.

disclosure of a single method of achieving that result. The Federal Circuit affirmed, but the manner in which the district court's decision is affirmed is quite unusual and fully supports my thesis that for most practical purposes the criteria for satisfying LWD and enablement are essentially co-extensive, so that LWD does not impose any meaningful limitations beyond those already imposed by enablement.

Although the district court in *Lizardtech* invalidated the claim under LWD, the Federal Circuit did not actually affirm on the basis of LWD, but rather effectively skirts the issues by never using the term "written description requirement" in the decision. Without even acknowledging the long line of cases that have held that the enablement and written description requirements are two distinct requirements, the court merges the two doctrines into what it terms the "written description *clause*" of section 112.[273] It then explains that the *clause* "has been construed to mandate that the specification satisfy two closely related requirements." First, it must describe the manner and process of making and using the invention so as to enable a person of skill in the art to make and use the full scope of the invention without undue experimentation, *i.e*, the traditional test for enablement. Second, it must describe the invention sufficiently to convey to a PHOSITA that the patentee had possession of the claimed invention at the time of the application, *i.e.*, the traditional written description test.[274] Further, the court states that the two requirements usually "rise and fall together,"[275] echoing back to as similar sentiment expressed in decisions like *Clontech*. Expanding upon this point, the court states that "a recitation of how to make and use the invention across the full breadth of the claim is

[273] *Id.*
[274] *Id*. at 1344-45.
[275] *Id*. at 1345.

ordinarily sufficient to demonstrate that the inventor possesses the full scope of the invention, and vice verse. This case is no exception."[276]

After effectively merging the criteria for satisfying the enablement and LWD requirements, the court essentially applied traditional enablement analysis as the basis for it's affirmation of the lower court's invalidation of the claim under LWD.[277] *Lizardtech*, far from supporting the notion of LWD as a distinct super-enablement requirement, clearly supports a conclusion that the two requirements are essentially redundant, justifying their merger into a unitary "written description clause."

2. LWD in the District Courts

Turning now to reported federal district court decisions, it is perhaps telling that I was only able to identify one decision, not the subject of a subsequent reported appellate decision, wherein a LWD-based challenge to the validity of a patent claim succeeded. In *Carnegie Mellon University v. Hoffman-La Roche, Inc.*, a representative claim at issue purported to cover recombinant plasmids containing a DNA polymerase I gene, isolated from *any bacterial source*, under the control of a conditionally controllable foreign promoter.[278] The patent specification disclosed the structure for a single DNA polymerase I gene from a single species of bacteria, *E. coli*. On motion for summary judgment, the court held the claims to be invalid under LWD.

The district court based its decision on a strict application of LWD, focusing on the lack of any structural description that would distinguish genetic constructs falling

[276] *Id*.
[277] This obfuscation was later noted by Judge Rader. Lizardtech v. Earth Resource Mapping, 433 F.3d 1373, 1380 (Rader, R., dissenting from denial of rehearing *en banc*) (Fed. Cir 2006) (" [T]wo clear statements of written description law … are relegated to bookends surrounding an enablement-based application of the new written description doctrine.").
[278] 148 F.Supp.2d 1004 (N.D. Cal. 2001).

within the scope of the claim from other genetic sequences. However, it is important to keep *Carnegie-Mellon* in perspective. Not only is this the only district court decision to apply LWD to invalidate a claim, the decision has effectively been overruled by a series of subsequent Federal Circuit decisions, particularly *Enzo II*, *Capon*, *Invitrogen* and *Falkner*.

Perhaps most on point is *Capon*. In that case, the claim at issue recited any DNA construct comprising two elements: (1) some portion of an antibody (not a specific antibody, but essentially any antibody); and (2) some portion of a protein defined solely by its function and its location of expression in the body (on the surface of cells in the immune system), and the court held that such a broad, functionally defined claim could satisfy LWD. The two genetic elements are defined in much broader, generic terms than the DNA Pol I gene recited in the *Carnegie-Mellon* claim, and with much less structural constraint.[279] If the standard for compliance with LWD adopted by the court in *Capon* were applied in *Carnegie-Mellon*, the validity of the claim under LWD would have almost certainly been upheld.

It should be noted that some commentators have identified additional decision wherein biomolecule claims have been invalidated under the written description requirement and implied that the court's decision was LWD-related. However, to the best of my knowledge all of these decisions involved traditional written description, not LWD. For example, a recently published comment seems to identify *Abbot Laboratories v. Inverness Medical Technology*[280] as an example of LWD being applied to a

[279] At least implicitly, one can assume that bacterial DNA Pol I genes will share a significant degree of homology, and hence structural similarity.
[280] 2002 WL 1906533 (D. Mass. 2002).

biotechnology patent.[281] However, the case actually involved traditional written description doctrine – in its decision, the court explicitly disclaims the applicability of LWD to the facts of the case, finding the doctrine applicable only to "biological materials."[282]

3. LWD in the BPAI

I identified nine decisions where the BPAI found claims invalid for failure to comply with LWD. This occurred either when the board affirmed an examiner's LWD rejection, or sometimes when the board raised the objection *sua sponte*. Notably, all of the BPAI's LWD decisions are in the area of biotechnology, illustrating the extent to which the PTO views LWD as a biotechnology-specific doctrine.[283]

Of the nine BPAI decisions, six involved the appeal of an examiner's decision to reject a claim or claims for failure to comply with both the enablement and LWD requirements, *i.e,* examiners tend to apply LWD in a manner that is redundant with enablement rather than as a super-enablement requirement. In three out of the six, the BPAI affirmed both the enablement and the written description rejections, and in the other three the BPAI affirmed the written description rejection and chose not to decide the enablement question as moot.

In this section I succinctly summarize the nine decisions. Note that the invalidated claims are all very broad, and as a consequence are either explicitly held

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[281] Guang M. Whitley, *A Patent Doctrine Without Bounds: The "Extended" Written Description Requirement* 71 U. CHI. L. REV. 617 (2004).

[282] 2002 WL 1906533 at *1 n.1. ("*Eli Lilly* is instructive for its general discussion of the description requirement, not for its application of the principle. That case involves the field of biological materials, which presents its own complications for the description requirement.")

[283] As reflected in the Written Description Guidelines, wherein every LWD example relates to a biotechnology invention.

invalid for violation of the enablement requirement (by the BPAI and/or the patent examiner), or could have easily been found invalid under the enablement requirement if the BPAI had elected to take that approach.

As discussed earlier, on a number of occasions the courts and BPAI have rejected LWD-based challenges to claims broadly encompassing functionally defined variants of a disclosed biomolecule.[284] However, the BPAI has on two occasions found claims of this sort invalid under LWD. In *Ex parte Copeland*,[285] the earliest BPAI decision I found that decides an LWD issue, the patent applicant disclosed the amino acid sequence of a "human polymerase catalytic polypeptide," and based on this disclosure attempted to claim any isolated DNA sequence "encoding a polypeptide having an amino acid sequence sufficiently duplicative of that of the human polymerase catalytic polypeptide" to retain human polymerase function. The claim is very similar to the claim found invalid for lack of enablement in *Amgen v.Chugai*, even using the same "sufficiently duplicative" language. The board reversed the examiner's rejections of the claim based on anticipation and obviousness, but raised enablement and LWD rejections *sua sponte*, an example where LWD and enablement were explicitly applied in a redundant fashion.

Later, in *Ex parte Grotendorst*,[286] the BPAI affirmed a LWD rejection of a similar claim. The inventor had isolated a novel protein, and attempted to claim in broad terms any variant of the protein retaining the same "reactivity" (meaning function). The examiner had also rejected the claim for lack of enablement, but the board declined to

[284] *See supra* Part IV[A].
[285] 1997 WL 1909887 (B.P.A.I. 1997). The case was heard prior to Lilly (July 22, 1997), but the decision was apparently written after Lilly and the board raised the issue *sua sponte*.
[286] Appeal No. 2002-0427, Application No. 08/179,656, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd020427.pdf (last visited Sept. 7, 2006).

address the issue of enablement as moot. Nevertheless, the claim is clearly analogous to the claim at issue in *Amgen v. Chugai* and *Copeland*, and the board could have easily upheld the enablement rejection in this case as well.

In *Ex parte Reinherz et al.,*[287] the patent application claimed a genus of chimeric genes, as well as the fusion proteins encoded by the chimeras. Although the examiner did not raise enablement or written description rejections, on appeal the BPAI raised the issues *sua sponte* and rejected the chimeric gene claims for failure to comply with LWD and the enablement requirement. The application eventually did issue as a patent, with claims limited to specific, disclosed DNA sequences.[288]

The outcome in *Reinherz* is hard to reconcile with subsequent decisions by the BPAI and Federal Circuit upholding the validity of chimeric gene claims. Note in particular the close analogy to the facts in *Capon*, where the Federal Circuit reversed a BPAI decision that had found a claim to a broad genus of chimeric genes encoding fusion proteins invalid under LWD.[289] The claims at issue in *Reinherz* and *Capon* are very similar in terms of breadth and supporting disclosure – both involve chimeric genes comprising elements encoding portions of immune system proteins, both encompass a huge genus of gene chimera variants, and both are supported by disclosure of one or a few species falling within the claim. Probably the most reasonable explanation for the divergent outcomes is that the BPAI decided *Reinherz* prior to *Enzo II*, at a time when the BPAI likely felt compelled by the strong language in *Lilly* to apply a strict, structure-focused interpretation of LWD. If the BPAI were to decide the case today, subsequent to

[287] Appeal No. 94-1483, Application No. 07/695,141, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd941483.pdf (last visited Sept. 7, 2006).
[288] U.S. Patent No. 6,416,971.
[289] See Section III[A] *supra*.

decisions like *Enzo II* and *Capon*, it would likely not find the claim to violate LWD. In fact, several examples of the BPAI reversing LWD rejections of similar chimeric gene claims are described *supra* in Section IV[A][3][e].[290]

In *Ex parte Janjic*,[291] the BPAI entered a *sua sponte* LWD rejection to a claim directed to "a method for inhibiting angiogenesis comprising administering a pharmaceutically effective amount of a *nucleic acid bFGF ligand*," *i.e*., a nucleic acid molecule capable of specifically binding the protein bFGF.[292] The board pointed out that the specification provided examples of nucleic acid bFGF ligands falling into two distinct structural families, and noted that in all likelihood other, yet to be discovered, structural families existed sharing no structural similarity with either of the two disclosed families, while the claim encompasses all nucleic acids capable of binding to a specified ligand, including the yet-to-be discovered structural families. The molecule is defined exclusively in terms of function, and the specification provides no disclosure of any correlation between structure and function. The claim is also extremely broad, and could have easily been invalidated under a conventional enablement approach.[293]

In *Ex parte Weinberg,*[294] the inventors had identified a single base difference responsible for the conversion of a proto-oncogene (a ras oncogene) to the corresponding

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[290] *Ex parte Fischetti, Ex parte Evans et al., Ex parte Griffiths et al,* and *Ex parte Anderson et al.*
[291] Appeal No. 2001-0545, Application No. 08/442,423, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd010545.pdf (last visited Sept. 7, 2006).
[292] A nucleic acid ligand is basically a nucleic acid (*e.g*., DNA) that folds to form a three-dimensional conformation that recognizes and binds specifically to another molecule, very much along the lines of an antibody. Thus, the nucleic acid is functioning in a fundamentally different manner than most claimed nucleic acids, where the function is not based on its 3-dimensional folded conformation, but rather on the information contained in the sequence of the nucleotides.
[293] Interestingly, the case was remanded to the examiner, after which the claim ultimately issued in a patent. The only change to the claim was a superficial amendment that failed to address the clear issues of overbreadth and lack of structural limitation. U.S. Patent No. 6,759,392.
[294] Appeal No. 2003-0054, Application No. 08/308,193, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd030054.pdf (last visited Sept. 7, 2006).

oncogene.[295] Based on this disclosure, they attempted to claim essentially *any* nucleic acid probe capable of detecting *any* single base difference responsible for the conversion of *any* proto-oncogene to the corresponding oncogene.[296] The claim scope is extremely broad relative to the disclosure, purporting to cover any and all oncogenes, proto-oncogenes and base differences, including the many that were not yet discovered at the time the patent application was filed. Moreover, there is no structural limitation on the claimed probes. The board raised a *sua sponte* LWD rejection to the claim. Again, in view of the extreme breadth of the claims relative to the limited disclosure, this claim could have also been invalidated for under the enablement requirement.

Interestingly, a dependent claim in *Weinberg* limited to human ras oncogenes was allowed by the BPAI and ultimately issued. Subsequent research has shown that there are actually multiple ras proto-oncogenes, and numerous base differences resulting in their conversion to oncogenes.[297] The claim has no explicit structural limitations, so these later discovered variants apparently all fall within the literal scope of the claim. Thus, we have yet another example where LWD has not restricted the ability of biotechnology inventors to obtain relatively expansive scope of protection based on a quite limited disclosure.

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[295] A proto-oncogene is a gene that can be converted into an oncogene (a gene that codes for a protein which promotes the loss of cellular division control, and can lead to malignant growth, *i.e.*, cancer). *See* DRLICA at 243. The ras oncogenes was one of the first family of oncogenes to be discovered. D.S. Goodsell, *The Molecular Perspective: The ras Oncogene*, THE ONCOLOGIST, 4: 263-264 (1999).

[296] A probe is a DNA or RNA molecule that finds complementary base locations by hybridizing to the complementary DNA or RNA. DRLICA at 314. The probes covered by the claim would be useful for diagnosing a person's likelihood of developing cancer.

[297] J.L. Bos, *ras oncogenes in human cancer: a review*, CANCER RES. 49:4682-89 (1989).

In *Ex parte Granados*,[298] the BPAI upheld LWD and enablement rejections of a claim reciting a transformed plant comprising an expression vector, the expression vector comprising a gene encoding an "invertebrate intestinal mucin (IIM) protein" operably linked to an expression control sequence (*i.e.*, a promoter). The applicant had disclosed the structures for two IIM proteins derived from a single species of insect. Note the extreme breadth of the claim, encompassing as it does all invertebrates, relative to a limited disclosure of two examples of the claimed protein family, both derived from the same insect. Appropriately, the examiner and board explicitly found the overly broad claim invalid for lack of enablement, yet another example of the redundancy between LWD and enablement as applied by the PTO.[299]

In *Ex parte Drucker et al.*,[300] claims directed to mammalian homologs of a mouse promoter region were rejected under LWD, but not for lack of enablement.[301] The rejections were essentiallly based on the fact that the claims defined the homologs primarily in functional terms without adequate disclosure of a relationship between structure and function. The BPAI affirmed, noting, for example, that the specification described neither the structure of the claimed promoters, nor a functional assay to correlate structure to function. An *Amgen v. Chugai*-type interpretation of the enablement requirement could have easily served as an alternative basis for invalidating the claims.

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[298] Appeal No. 2002-2030, Application No. 09/294,663, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd022030.pdf (last visited Sept. 7, 2006).
[299] The board states that it was "well established" that a protein sequence does not provide adequate written description for a DNA encoding it, a proposition later clearly refuted in *In re Wallach* when the Federal Circuit held that a protein sequence *does* provide adequate written description for the DNA sequences encoding it. 378 F.3d att1333-35 (Fed. Cir. 2004).
[300] Appeal No. 2004-2356, Application No. 09/833,740, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd042356.pdf (last visited Sept. 7, 2006).
[301] A homolog is a genetic sequence related to a second genetic sequence by descent from a common ancestral DNA sequence – typically homologs share some degree of structural similarity.

In *Ex parte Polonsky et al.*,[302] a method of screening for a modulator of a "calpain 10" (a class of proteins) was rejected for lack of enablement under LWD. The BPAI interpreted the claim broadly as encompassing "any 'calpain 10' of any structure from any organism." The LWD rejection was affirmed because the board agreed with the examiner that the specification failed to disclose how one would even be able to distinguish between a calpain 10 and other proteins, particularly structurally similar proteins like calpain 5 and 6. This would seem to pose a problem of definiteness; the examiner did make a definiteness rejection, but for some reason the board reversed that rejection while affirming a LWD rejection essentially premised on the "indefiniteness" of the claims. The enablement rejection was considered moot, but again I would suggest that a claim encompassing "any 'calpain 10' of any structure from any organism," without providing sufficient guidance to even distinguish between a calpain 10 and other non-calpain-10 proteins, would clearly fail to satisfy the enablement requirement.

Finally, *Ex parte Rothschild*[303] involved a claim directed to a method of screening animals for litter size by looking for polymorphisms in a specified gene sequence.[304] The claim was supported by the disclosure of three such polymorphisms, all in pig. The examiner rejected the claim for inadequate enablement and LWD, noting that the claimed genus included "an enormous number" of polymorphisms, without providing any "structural limitations or limitations which provide guidance on the identification of sequences which meet these functional limitations of associating a polymorphism with litter size." The board affirmed the LWD rejection, noting that the three examples were

[302] Appeal No. 2005-0258, Application No. 09/768,877, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd050258.pdf (last visited Sept. 7, 2006).
[303] Appeal No. 2005-1169, Application No. 09/900,063, *at* http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd051169.pdf (last visited Sept. 7, 2006).
[304] A polymorphism is often defined as a genetic variant that appears in at least 1% of a population.

insufficient to support the scope of the claim, but without providing any guidance as to how one would determine how many examples would be enough. The board also found relevant the fact the disclosure identified no common structural elements (*i.e*, no correlation between structure and function), and the fact that all the examples were from pig and the claim encompasses all animals. The board did not address the enablement rejection, finding it moot in light of it's determination based on LWD, but the enablement rejection clearly should have been upheld in view of the lack of "reasonable correlation" between the expansive claim scope and limited disclosure.

Note that in these nine decisions, there is not a single example of the BPAI applying LWD in a manner that prevents an inventor of a biotechnology invention from patenting her invention for failure to provide chemical structure, a primary fear voiced by *Lilly*'s critics. Instead, in every decision the issue is one of claim breadth, with the examiner and/or BPAI applying LWD as a tool for limiting claims to a reasonable scope of coverage, a result that could have been better achieved using enablement.[305]

V. CONCLUDING OBSERVATIONS

It has been repeatedly asserted that LWD is a super-enablement requirement, *i.e*, that the test for compliance with LWD is more stringent than for compliance with the enablement requirement.[306] If this were in fact the case, one would expect to find judicial

[305] In every case, the patent applicant would be able to patent her invention in narrower terms, and in many of the cases the applicant did ultimately receive narrower patents claims. These "narrower" claims are in many cases still quite broad, *e.g*., the claims that issued from *Ex parte Janjic* in U.S. Patent No. 6,759,392.

[306] *See, e.g.,* Amgen Inc. v. Hoechst Marion Roussel, Inc. 314 F.3d at 1334 (Fed. Cir. 2003) ("The enablement requirement is often more indulgent than the written description requirement."); Sven J.R. Bostyn, *Written Description after Enzo Biochem: Can the Real Requirement Step Forward Please?*, 85 J. PAT. & TRADEMARK OFF. SOC'Y 131, 149 (2003) ("The standard as developed in Eli Lilly and repeated now in Enzo Biochem requires a more detailed disclosure than is required under the enablement requirement. That implies that parties wishing to invoke this defense, will immediately go to the written description requirement, as this implies a more detailed description, thus making the enablement requirement a

decisions where a patent claim is found to be enabled but nevertheless invalid for failure to comply with LWD.[307] In fact, I was unable to locate a single judicial decision explicitly finding a claim enabled but invalid under LWD. There is only one BPAI decision explicitly treating LWD as a super-enablement requirement, finding a claim to be "concededly enabled" but to fail LWD, but that decision was emphatically reversed by the Federal Circuit in *Capon*.[308]

Conversely, a number of BPAI decisions explicitly find a claim to satisfy LWD but nevertheless invalid for lack of enablement. For example, in *Ex parte Reinherz* the board considered the validity of a set of claims directed to a genus of protein fusions, and another set of claims directed to the genes encoding the fusion proteins. The board found the gene claims to be invalid under LWD and enablement. However, the board did not raise a LWD rejection with respect to the corresponding protein claims, only rejecting the claims for lack of enablement, *i.e.*, the board interpreted LWD as being less restrictive than enablement, the opposite of a super-enablement requirement. Likewise, in *Ex parte Herrmann* some claims were found invalid for violating the enablement requirement but not for violation of LWD.

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redundant one."). Rai,, *supra* note 4 at 834-35 ("[T]he Lilly court used the written description requirement as a type of elevated enablement requirement."); Mueller, *supra* note 63 at 617("The Lilly decision establishes uniquely rigorous rules for the description of biotechnological subject matter that significantly contort written description doctrine away from its historic origins and policy grounding. The Lilly court elevates written description to an effective 'super enablement' standard.")

[307] The relationship would be analogous to that between lack of novelty and obviousness. Lack of novelty can be thought of as "super-obviousness;" generally it follows that if an invention lacks novelty it is implicitly obvious, while it quite common for a novel invention to nevertheless be obvious.

[308] In *Ex Parte Janjic* the BPAI reversed an examiner's enablement rejection and raised a Lilly rejection sua sponte. *Supra* note 291. However, the enablement rejection was based on the examiner's skepticism as to whether the invention would perform the asserted functional utility, *i.e.*, the "how to use" prong of the enablement inquiry, not the "how to make" prong, which is the analog of LWD. In any event, the claim at issue in *Janjic* is extremely broad, and the board could have easily rejected the claim for violation of the "how to make" prong of LWD. Interestingly, despite the board's *sua sponte* rejection these extremely broad claims did ultimately issue, for reasons that are not apparent on the record.

Most BPAI decisions involve appeals where the examiner has raised parallel LWD and enablement rejections, targeting the same alleged deficiencies of disclosure and applying functionally indistinguishable LWD and enablement tests. In other words, it appears that patent examiners are not treating LWD and enablement as functionally distinct patentability requirements, but rather as interchangeable requirements to be applied in tandem to what are perceived to be overly broad biotechnology claims.

There are a number of BPAI and court decisions where claims are invalidated solely for violation of LWD, usually because the enablement issue is found to be moot in light of the LWD determination. Nevertheless, in the majority of these cases, the claims could have easily been invalidated for violation of the enablement requirement. - LWD is generally not limiting the patenting of biotechnology in a manner that could not readily be achieved via the enablement requirement.

The one scenario where LWD appears to be functioning as a distinct "super-enablement" requirement is with respect to what I will refer to as "prophetic cloning" inventions, *i.e.*, attempts to patent specific, naturally-occurring genetic sequences prior to actually isolating the sequence or determining its structure, as in *Lilly* and *Wallach*. As discussed *supra*, there might very well be valid policy reasons for restricting the patenting of this sort of invention, *e.g.*, to provide symmetry with the obviousness test applied to prophetic cloning inventions in *Bell* and *Deuel*. In view of the technological trend away from isolating and characterizing proteins prior to their corresponding genetic sequences, this limited imposition of a "super-enablement" requirement should have little impact on the patenting of biotechnology.

In light of LWD's limited impact in the courts, perhaps it should come as little surprise that in the nine years that have elapsed since *Lilly* the courts have failed to articulate a test for compliance with LWD that bears any meaningful distinction from the criteria for establishing enablement. For example, the requirements of structure and sufficient examples to support a genus apparently mandated by *Lilly* have been steadily eroded by a series of Federal Circuit decisions exemplified by *Enzo II*, *Noelle*, *Invitrogen*, *Capon*, and *Falkner*. The Federal Circuit's fundamental test for compliance with LWD, a demonstration of "possession" of the claimed invention, has been applied in a manner indistinguishable from the test for enablement. For example, in *Capon* the courts cites enablement cases and applies enablement criteria in assessing claims for compliance with LWD, and held that the BPAI's finding that the claims were invalid under LWD could not be "reconciled" with the board's determination that the claims appeared to be enabled.[309] In *Rochester*, the court stated that LWD "serves a teaching function ... in which the public is given meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time," which sounds a lot like the policy behind the enablement requirement.[310] And in *Lizardtech*, the court combined LWD and enablement into a unified "written description clause," and effectively applied an enablement standard to assess a claim for LWD compliance.[311]

In the years since *Lilly*, there has been some confusion as to whether LWD is a doctrine particularly directed towards biotechnology,[312] or a general requirement of

[309] 418 F.3d at 1360 (Fed. Cir. 2005).
[310] 358 F.3d at 922 (Fed. Cir. 2004).
[311] *Supra* note 271.
[312] *Enzo I*. 285 F.3d at 1025 (CAFC 2002) (Dyk, T., dissenting)

patentability. There are strong indications that the PTO treats LWD as biotechnology-specific, as evidenced by the Guidelines, which provide only biotechnology examples in its treatment of LWD, and the fact that all of the BPAI decisions involve biotechnology-related invention. However, in *Rochester* the court applied LWD to invalidate claims that were not limited to biomolecules (the claims covered the use of small molecule COX-2 inhibitors), and in the decision Judge Lourie expressed his view that LWD is not technology-specific. In the recent *Lizardtech* decision the Federal Circuit upheld a district court's invalidation of a software claim under LWD, although the Federal Circuit never explicitly addressed LWD, instead folding LWD into a "written description clause" that also encompasses the enablement requirement.

Another general observation is that many judicial and BPAI decisions express the opinion that LWD is only applicable in cases where the claimed invention is a naturally-occurring biomolecule, and not to synthetic biomolecules and genetic constructs, such as the gene chimeras at issue in *Capon*, the synthetically-generated protein variants at issue in *Invitrogen*, and the genetically-modified viruses claimed in *Falkner*.

Finally, it appears that in the courts LWD is being driven almost entirely by *Lilly*'s author, Judge Lourie. Of the four post-*Lilly* decisions finding claims invalid under LWD, two were authored by Judge Lourie (*Rochester* and *Wallach*), and Judge Lourie was on the panel in a third (*Lizardtech*). *Noelle* was the only decision in which he did not participate, and in that case the claims could have easily been invalidated for lack of enablement. Furthermore, the *Noelle* panel explicitly endorsed the PTO's Written

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("*Eli Lilly* imposes a "unique written description requirement in the field of biotechnology"); Dan L. Burk & Mark A. Lemley, *Is Patent Law Technology-Specific?* 17 BERKELEY TECH. L.J. 1155 (2002) (Finding a stringent application of LWD in biotechnology patents that does not appear in other disciplines).

Description Guidelines, which provide that broad, functionally defined antibody claims can comply with LWD without providing any structural description of the antibody or the antigen recognized by the antibody, a clear departure from the original spirit of *Lilly*. Judge Lourie also authored *Enzo I*, a particularly strong interpretation of LWD that he later backed away from. Aside from *Enzo II*, Judge Lourie has apparently never sat on a panel that rejected an LWD-based challenge to claim validity.[313]

It would seem that the primary impact of LWD has been to inject substantial doctrinal confusion into the patent law. The one scenario where LWD appears to be playing a substantive role, *i.e.*, the policing of attempts to claim naturally-occurring genetic sequences prior to their isolation or structural characterization, could more appropriately be accomplished by a technology-specific application of the enablement requirement, analogous to the Federal Circuit's technology-specific application of the obviousness requirement seen in *Bell* and *Deuel*. In the interest of fostering coherent rules of patentability, the court's should explicitly acknowledge the functional redundancy of LWD and enablement and restore the historical distinction between the two doctrines, employing the written description requirement to police new matter and the enablement requirement to ensure that the scope of patents claims is commensurate with the scope of the applicant's disclosure.

[313] With the exception of an early decision where he rejected an LWD-based challenge to an antibody claim because the issue had not been properly addressed at the district court level. Johns Hopkins University v. CellPro, Inc. 152 F.3d 1342, 1361-62 (Fed. Cir. 1998).

APPENDIX: SEARCH METHODOLOGY

The primary intent of this paper is to provide a comprehensive survey of all publicly available decisions of the Federal Courts and the PTO Board of Patent Appeal and Interferences (BPAI) pertaining to LWD. In keeping with this objective, I pursued a search strategy designed to be as comprehensive as reasonably possible.

To identify relevant decisions of the federal court and BPAI, I conducted a search of the Westlaw databases containing all federal court decisions and all BPAI decision.[314] These databases were searched for any decisions subsequent to 1996 (*Lilly* was decided in 1997) containing the term "written description" in the same paragraph as a reference to any of the Federal Circuit decisions applying LWD to invalidate a patent claim prior to 2006, plus *Enzo II*.[315] The same search was conducted in the corresponding Lexis databases. I reviewed each decision to the extent necessary to make a conclusive determination as to whether the case actually was what I will refer to as a "LWD decision," *i.e.*, a case where analyzing a claim for compliance with LWD, as opposed to cases involving traditional written.

To expand upon the Westlaw and Lexis searches, I also conducted a parallel search of the PTO's on-line database of "BPAI Final Decisions."[316] This database contains final decisions of the BPAI, primarily appeal decisions, but also interference decisions. I reviewed all of the BPAI decisions dated from Jan 1, 2000 to October 31, 2005, that were posted as of February 1, 2006, and all decisions between November 1,

[314] The "All Federal Cases" and BPAI databases, searches last updated July 17, 2006.
[315] The actual search terms used were: da(aft 1996) & "written description" /p ((Lilly /5 California) (enzo /5 gen-probe) (noelle /5 lederman) (Rochester /5 Searle) Wallach).
[316] *BPAI Final Decisions* was available at http://www.uspto.gov/web/offices/dcom/bpai/bpai.htm when I began this study. The page was subsequently removed and all content relocated to the *USPTO e-FOIA page at* http://des.uspto.gov/Foia/BPAIReadingRoom.jsp (last visited Sept. 7, 2006).

2005 and May 31, 2006 that were posted as of June 7, 2006. I reviewed each decision to the extent necessary to determine whether it involved LWD. By using the PTO database of BPAI decisions, I was able to identify a number of LWD decisions that for some reason do not appear in either the Lexis or Westlaw database. Thus, the results of the BPAI search are more comprehensive than could be accomplished with Lexis and Westlaw alone.

The Jan 1, 2000 cut-off at is to some extent arbitrary, but I think justified by the diminishing returns I saw in the sampling of decision I did identify dated prior to 2000. These early decisions typically do not have well-developed LWD issues, because the examiner's typically did not include LWD or *Lilly* in their appeal briefs. Normally, in these decisions where the examiner did not have an opportunity to explicitly address LWD, the board simply pointed out the issue and directed the examiner to consider it upon remand. There are a couple cases in this time period (found in the Westlaw/Lexis searches) where the board does apply LWD to reject claims *sua sponte*, and these decisions are included in my analysis.

A few caveats should be noted with regard to BPAI decisions. The PTO will presumably only post publicly available decisions, so generally only in cases where the file history is open to the public. The PTO generally seems to only post decisions where the corresponding application has published or issued as a patent. Other decisions, which are technically publicly available, might not appear in the database if the application at issue does not publish or issue. For instance, one of the BPAI decisions I identified as an example of the BPAI reversing a *Lilly* rejection does not appear in the PTO database (nor

in the Westlaw and Lexis databases), but is publicly available because a continuation application has published claiming priority to the application subject to the appeal.[317]

Because the database only contains publicly accessible decisions, there could be some bias towards cases where rejections are reversed, since these tend to result in the issuance of a patent. One would assume that in some cases the affirmation of a rejection will result in the application becoming abandoned, and hence the decision never being made available to the public. However, I don't think this is a major issue. In many cases, an affirmed rejection does not prevent a patent from issuing, because other claims in the application are allowed. I observed many examples where a rejection has been affirmed and the application went on to issue as a patent. Also, the more recent applications will in many cases publish regardless of whether any patent issues, which is an alternative mechanism for making the decision publicly available. Finally, in a personal communication with a high ranking PTO official, I was informed that to the best of his knowledge most BPAI decisions are posted on the PTO database.[318]

In short, no claim is made that the results of the searches are totally comprehensive, and relevant decisions may have been overlooked. However, to the best of my knowledge it is far more comprehensive than any previously published review of LWD cases, and is sufficiently comprehensive to draw meaningful conclusions with respect to the impact of LWD doctrine in the courts and BPAI.

[317] This particular decision was made available to me by an attorney who had worked on the case. The file history of a pending unpublished patent application is available to the public if a U.S. patent publication claims the benefit of the unpublished patent application. 37 C.F.R. § 1.14(a)(1)(v) (2006).
[318] Personal communication.