United States Court of Appeals for the Federal Circuit

2007-1266

CARNEGIE MELLON UNIVERSITY
and THREE RIVERS BIOLOGICALS, INC.,

Plaintiffs-Appellants,

v.

HOFFMANN-LA ROCHE INC.,
ROCHE MOLECULAR SYSTEMS, INC.,
ROCHE DIAGNOSTIC SYSTEMS, INC.,
ROCHE BIOMEDICAL LABORATORIES, INC.,
THE PERKIN-ELMER CORPORATION,
and LABORATORY CORPORATION OF AMERICA HOLDINGS,

Defendants-Appellees.

2007-1267

CARNEGIE MELLON UNIVERSITY,

Plaintiff-Appellant,

v.

HOFFMANN-LA ROCHE INC.,
ROCHE MOLECULAR SYSTEMS, INC.,
ROCHE DIAGNOSTICS CORPORATION,
LABORATORY CORPORATION OF AMERICA,
and APPLERA CORPORATION,

Defendants-Appellees.

Frederick H. Colen, Reed Smith LLP, of Pittsburgh, Pennsylvania, argued for all plaintiffs-appellants. With him on the briefs were Charles H. Dougherty, Jr. and Mark Levin.

Stephen S. Rabinowitz, Fried, Frank, Harris, Shriver & Jacobson LLP, of New York, New York, argued for all defendants-appellees. With him on the briefs were Mitchell Epner, Randy C. Eisensmith, and Alison R. Ladd.

Appealed from: United States District Court for the Northern District of California

Judge Susan Illston

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Defendants-Appellees.

Appeal from the United States District Court for the Northern District of California in Case Nos. 95-CV-3524 and 01-CV-0415, Judge Susan Illston.

DECIDED: September 8, 2008

Before LOURIE, BRYSON, and PROST, Circuit Judges.

LOURIE, Circuit Judge.

Carnegie Mellon University ("CMU") and Three Rivers Biologicals, Inc. (collectively "appellants") appeal from the decision of the United States District Court for the Northern District of California holding that Hoffmann-La Roche, Inc., Roche Molecular Systems, Inc., Roche Diagnostic Systems, Inc., Roche Biomedical Laboratories, Inc., The Perkin Elmer Corporation, and Laboratory Corporation of America Holdings (collectively "Roche") do not infringe the patents in suit and that certain claims are invalid for lack of written description. Because we conclude that the district court did not err in holding the claims invalid for failure to meet the written description requirement, we affirm the court's judgment of invalidity. Because we conclude that the court did not err in its infringement analysis, we affirm the court's judgment of noninfringement.

BACKGROUND

Proteins, one of the most versatile biomolecules, can serve many important roles, including as signal receptors, structural elements, or enzymes. They are encoded by particular deoxyribonucleic acid ("DNA") sequences known as genes. The process by which cells use the information contained in genes to make corresponding proteins is referred to as expression. Expression involves two steps, viz., transcription and translation. During transcription, the information contained in a gene is copied into

messenger ribonucleic acid ("mRNA"). The cell then assembles amino acids in the proper sequence during translation to make the protein based on the information contained in the mRNA.

One gene in the bacterium E. coli, called the E. coli polA gene, encodes a protein known as E. coli DNA polymerase I. Since at least the 1970s, the E. coli polA gene has been the subject of scientific study. The wild-type E. coli polA gene consists of two parts—the structural gene (or gene coding region) and a promoter, which is a DNA sequence that is involved in initiating transcription. The expression of a gene can be regulated through the use of a promoter by controlling the level of transcription.

Some valuable proteins are either difficult to purify from their natural sources or occur in minute quantities in nature. Thus, methods have been developed in the field of biotechnology "to synthesize useful quantities of specific proteins by controlling the mechanism by which living cells make proteins." Carnegie Mellon Univ. v. Hoffmann-La Roche, Inc., 55 F. Supp. 2d 1024, 1027 (N.D.Cal. 1999).

One method involves introducing foreign genes into a bacterium, which can then replicate as the bacterium grows and divides. Such a method involves several steps, including isolating and cloning the gene that encodes the protein of interest and introducing the cloned gene into the host bacterium. The latter is accomplished by incorporating the gene into a cloning vector. Certain types of vectors include bacteriophages and plasmids, which are "small circular loop[s] of DNA found in bacteria, separate from the chromosome, that replicate[] like a chromosome." Id. Recombinant DNA techniques are used to modify plasmids by recombining cloned genes and other

segments of DNA that contain control sequences. The plasmid is then introduced into the host bacterium where it will replicate as the bacterium grows and divides.

The patents in suit, viz., U.S. Patents 4,767,708 ("the '708 patent"), 5,126,270 ("the '270 patent"), and 6,017,745 ("the '745 patent") relate to "novel recombinant plasmids for the enhanced expression of an enzyme, to the preparation by gene cloning of such plasmids, to bacterial strains containing said plasmids, [and] to methods for the conditional control of the expression of said enzyme."[1] '708 patent col.1 ll.7-16.

The patents teach that the enzyme of interest is DNA polymerase I (Pol I), which, as discussed above, is encoded by the structural gene known as polA. Id. col.1 ll.14-15. In the prior art, scientists encountered difficulties cloning polA into multicopy plasmids because the increase in expression of DNA polymerase I above the natural level of expression was found to be lethal to a host bacterium. Id. col.1 ll.14-18. The claimed inventions overcome that problem by constructing a novel plasmid containing "the entire and undamaged polA gene coding region enzymatically excised from a DNA molecule," which "contains essentially none of or at the most only a portion of the activity of its natural promoter." Id. col.2 ll.23-29. The patents disclose that severely damaging the natural polA promoter sequence constituted a "significant discovery of the present invention since it eliminates or greatly reduces the unregulated expression of Pol I, which would otherwise be lethal to the cell." Id. col.2 ll.43-46. By cloning the

[1] The patents in suit, which are owned by CMU, all share a common specification. The '708 patent, which was filed by Edwin G. Minkley, Jr. and William E. Brown on August 7, 1984, issued from Application No. 07/638, 638 ("the '638 application"). The '270 patent is a continuation of the application that issued as the '708 patent, and the '745 patent is a continuation of the application that issued as the '270 patent. Throughout this opinion, we will cite the '708 patent when referencing the common specification.

gene for DNA polymerase I into a vector along with a foreign promoter whose activity is conditionally controlled, one can obtain an amplified amount of DNA polymerase I. Throughout the specification, the patents teach that the host bacterial strain that is used to achieve that objective is E. coli.

The patents in suit share a common specification, and the claims are directed to recombinant plasmids that contain gene coding regions for the expression of DNA polymerase I from any bacterial source. For example, claim 1 of the '708 patent reads as follows:

> 1. A recombinant plasmid containing a cloned complete structural gene coding region isolated from a bacterial source for the expression of DNA polymerase I, under operable control of a conditionally controllable foreign promoter functionally linked to said structural gene coding region, said foreign promoter being functional to express said DNA polymerase I in a suitable bacterial or yeast host system.

'708 patent claim 1 (emphasis added). Claim 1 of the '270 patent recites:

> 1. A recombinant plasmid providing for Nick-translation activity isolated from a bacterial source, said plasmid capable of being placed in a bacterial host system such that the host system can grow and divide.

'270 patent claim 1 (emphasis added). Similarly, claim 1 of the '745 patent reads:

> 1. A recombinant plasmid containing a DNA coding sequence for the expression of DNA polymerase activity, wherein said DNA coding sequence is derived from a source that encodes a bacterial DNA Polymerase, said source not containing an amber mutation affecting expression of said DNA polymerase activity, such that when said plasmid is transformed into a bacterial host system the host system can grow and divide thereby replicating said plasmid.

'745 claim 1 (emphasis added).

Roche commercially manufactures recombinant DNA polymerases. The accused product at issue in this appeal involves a recombinant plasmid referred to as pLSG5, which causes host cells to express an enzyme known as Thermus aquaticus

("Taq") DNA polymerase. On August 30, 1994, appellants filed suit against Roche asserting that its product, pLSG5, infringes the '708 and '270 patents.[2] The district court held a claim construction hearing on January 14, 1997 and issued its claim construction ruling on March 31, 1997. The court construed the term "DNA polymerase" as requiring 3'-5' exonuclease activity. Carnegie Mellon Univ. v. Hoffmann-La Roche Inc., No. C 95-3524 SI, 1997 WL 33152823, at *8-*10 (N.D. Cal. Mar. 31, 1997). Roche filed separate motions for summary judgment seeking judgment that: 1) claims 1-19, 22-40, and 43-45 of the '708 patent were invalid for lack of written description under our holding in Regents of University of California v. Eli Lilly & Co., 119 F.3d 1559 (Fed. Cir. 1997); 2) claims 1-6, 10-19, and 22-40 of the '708 patent were not infringed; and 3) claims 1-2, 11-12, 14-15, 17-18, 20-21, 23-24, 26-27, 29-30, and 32-36 of the '270 patent were invalid for lack of written description under our holding in Gentry Gallery, Inc. v. Berkline Corp., 134 F.3d 1473 (Fed. Cir. 1998), or, in the alternative, under Eli Lilly.

On May 12, 1999, the district court granted Roche's motion for summary judgment of noninfringement. Carnegie Mellon Univ. v. Hoffmann-La Roche, Inc., 55 F. Supp. 2d 1024 (N.D.Cal. 1999). In doing so, the district court concluded that there was no genuine issue of material fact as to whether the enzyme in the accused product possessed 3'-5' exonuclease activity. Because the undisputed evidence indicated that the accused products lacked that element, the court concluded that summary judgment of noninfringement of the '708 patent was required.

[2] In its original complaint, appellants asserted that several of Roche's recombinant DNA plasmids infringe the '708 and '270 patents. On appeal, however, appellants only challenge the district court's grant of summary judgment of noninfringement with respect to the pLSG5 plasmid.

On August 19, 1999, the district court granted Roche's motion for summary judgment of invalidity as to the '270 patent. Carnegie Mellon Univ. v. Hoffmann-La Roche Inc., No. C 95-3524 SI, 1999 WL 33298545 (N.D. Cal. Aug. 19, 1999). The court determined that the specification of the '270 patent made clear that lethality was an essential feature of the invention and thus, under Gentry Gallery, the claims of the patent must contain that feature in order to comply with the written description requirement. Because the claims omit the feature of lethality, the court concluded that those claims of the '270 patent were invalid.

On June 27, 2001, relying on Eli Lilly, the district court granted Roche's motion for summary judgment of invalidity with regard to the '708 patent. Carnegie Mellon Univ. v. Hoffmann-La Roche, Inc., 148 F. Supp. 2d 1004 (N.D. Cal. 2001). The court concluded that while the claims of the '708 patent claim recombinant plasmids "containing a cloned complete structural gene coding region from [any] bacterial sources for the expression of DNA polymerase I," the '638 application only described recombinant plasmids containing the encoding gene region for E. coli DNA polymerase I and thus failed to adequately support the generic claims of the '708 patent.

On January 24, 2001, CMU initiated a second patent infringement action against Roche, alleging that Roche infringed the '745 patent. Roche moved for summary judgment that claims 1-3, 12-14, 23-28, and 30-33 were invalid under the written description requirement of 35 U.S.C. § 112. On September 29, 2003, the district court granted that motion. Carnegie Mellon Univ. v. Hoffmann-La Roche, Inc., No. C 01-0415 SI (N.D. Cal. Sept. 29, 2003). Again relying on Eli Lilly, the court determined that there was no genuine issue of material fact with regard to whether the '745 patent complies

with the written description requirement under 35 U.S.C. § 112 and granted Roche's motion. Roche also moved for summary judgment of noninfringement of claims 4-11, 15-22, and 29 of the '745 patent under the doctrine of equivalents, and on February 26, 2004, the court granted that motion. Carnegie Mellon Univ. v. Hoffmann-La Roche, Inc., No. C 01-0415 SI (N.D. Cal. Feb. 26, 2004).

Roche additionally asserted that the patents were unenforceable based on inequitable conduct committed by appellants during the prosecution of each of the asserted patents. The district court held a bench trial on that issue from August 1 to August 5, 2005. On March 22, 2007, the court issued its ruling, holding that Roche failed to present clear and convincing evidence that appellants committed inequitable conduct. Carnegie Mellon Univ. v. Hoffmann-La Roche, Inc., No. C 01-0415 SI, 2007 WL 902548 (N.D. Cal. Mar. 22, 2007). As such, the court concluded that none of the patents was unenforceable.

On May 14, 2007, the district court entered final judgment in favor of Roche. Appellants timely appealed the district court's grant of summary judgment with regard to noninfringement and invalidity. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

DISCUSSION

On appeal, appellants challenge the district court's grant of summary judgment of invalidity with regard to claims 1-19, 22-40, and 43-45 of the '708 patent, claims 1-2, 11-12, 14-15, 17-18, 20-21, 23-24, 26-27, 29-30, and 32-36 of the '270 patent, and claims 3, 14, 23-28, and 30-32 of the '745 patent. In addition, appellants challenge the court's grant of summary judgment of noninfringement of the asserted claims of the '708 patent and claims 4, 5, and 7 of the '745 patent. While the decisions of the district court

regarding the '708, '270, and '745 patents were rendered in separate opinions and judgments, the appeals were consolidated for argument in this court and we decide all of them together. We first consider appellants' arguments relating to validity.

A. Standard of Review

We review the district court's grant of summary judgment de novo, reapplying the standard applicable at the district court. See Rodime PLC v. Seagate Tech., Inc., 174 F.3d 1294, 1301 (Fed. Cir. 1999). Summary judgment is appropriate "if the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any material fact and that the moving party is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(c). In addition, in deciding a motion for summary judgment, "[t]he evidence of the nonmovant is to be believed, and all justifiable inferences are to be drawn in his favor." Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 255 (1986).

B. Written Description

Section 112, paragraph 1 of the Patent Act sets forth the written description requirement as follows:

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

35 U.S.C. § 112, ¶ 1 (emphasis added). Thus, paragraph 1 of § 112 requires a written description of the invention—a requirement separate and distinct from the enablement requirement. Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563 (Fed. Cir. 1991); see Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd., 535 U.S. 722, 736 (2002)

(noting that "a number of statutory requirements must be satisfied before a patent can issue" including that the patent application "describe, enable, and set forth the best mode of carrying out the invention") (emphasis added); see also In re Curtis, 354 F.3d 1347, 1357 (Fed. Cir. 2004) ("We interpret 35 U.S.C. § 112, ¶ 1 to require a written description requirement separate and apart from the enablement requirement."); In re Ruschig, 379 F.2d 990 (C.C.P.A. 1967) (holding that the written description requirement is a requirement separate from enablement under 35 U.S.C. § 112, paragraph 1).

The basic function of a patent specification is to disclose an invention. It has long been the case that a patentee "can lawfully claim only what he has invented and described, and if he claims more his patent is void." O'Reilly v. Morse, 56 U.S. (15 How.) 62, 121 (1853). The written description serves a quid pro quo function "in which the public is given 'meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time.'" Univ. of Rochester v. G.D. Searle & Co., Inc., 358 F.3d 916, 922 (Fed. Cir. 2004) (quoting Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 970 (Fed. Cir. 2002)). To satisfy the written description requirement, "the applicant does not have to utilize any particular form of disclosure to describe the subject matter claimed, but the description must clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." In re Alton, 76 F.3d 1168, 1172 (Fed. Cir. 1996) (citing In re Gosteli, 872 F.2d 1008, 1012 (Fed. Cir. 1989)) (quotations omitted). In other words, the applicant must "convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention," Vas-Cath Inc., 935 F.2d at 1563-64, and demonstrate that by disclosure in the specification of the patent. Whether the written

description requirement is satisfied is a fact-based inquiry that will depend on the nature of the claimed invention, Enzo, 323 F.3d at 963, and the knowledge of one skilled in the art at the time an invention is made and a patent application is filed. Such knowledge may change as time progresses. See In re Wallach, 378 F.3d 1330, 1334 (Fed. Cir. 2004) (discussing how it is now a "routine matter" to convert between an amino acid sequence and the DNA sequences that can encode it such that an applicant need not specify each possible permutation of nucleic acid sequences for a particular protein).

Our case law has examined compliance with the written description requirement in the context of biotechnological inventions in the past. In Regents of University of California v. Eli Lilly & Co., 119 F.3d 1559 (Fed. Cir. 1997), we held, inter alia, that generic claims directed to recombinant prokaryotic microorganisms comprising any vertebrate and mammalian cDNA were not adequately supported by the specification that only disclosed rat insulin cDNA. Id. at 1568. We stated that "[a]n adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the claimed invention, 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." Id. at 1566 (internal quotations omitted). We further held that "[a] description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, 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." Id. at 1569.

1. The '708 and '745 Patents

Appellants challenge the district court's conclusion that certain claims of the '708 and '745 patents are invalid under § 112 in light of our holding in Eli Lilly. According to appellants, Eli Lilly is distinguishable from the present case because the invention in Eli Lilly was tied to a specific cDNA sequence, whereas the invention here involves a combination of well known elements that create a generic biotechnological tool. Appellants further argue that the court erred by failing to conduct a factual inquiry as required by Capon v. Eshhar, 418 F.3d 1349, 1358 (Fed. Cir. 2005). Appellants contend that at the time of the invention, both DNA polymerase I and the polA gene were well known in the art. In addition, appellants assert that the court improperly made factual determinations, improperly relied on the declaration of Roche's expert while dismissing the declarations of its own experts, and failed to draw inferences in appellants' favor.

In response, Roche argues that the district court correctly determined that the claims of the '708 patent encompass more than the subject matter described in the specification and thus correctly found them invalid. Roche asserts that Eli Lilly applies to the present case as there was nothing in the Eli Lilly decision to suggest that that holding was limited to inventions involving novel DNA sequences. Roche further asserts that the court considered appellants' evidence and correctly concluded that they failed to raise a genuine issue of material fact.

We agree with Roche that there is no genuine issue of material fact regarding whether the written descriptions of the '708 and '745 patents fail to adequately describe the claimed invention. We first consider the claims at issue. Claim 1 of the '708 patent, a representative claim, recites:

> 1. A recombinant plasmid containing a cloned complete structural gene coding region isolated from a bacterial source for the expression of DNA polymerase I, under operable control of a conditionally controllable foreign promoter functionally linked to said structural gene coding region, said foreign promoter being functional to express said DNA polymerase I in a suitable bacterial or yeast host system.

'708 patent claim 1 (emphases added). Similarly, claims 1-3, and 23 of the '745 patent, also representative claims, read as follows:

> 1. A recombinant plasmid containing a DNA coding sequence for the expression of DNA polymerase activity, wherein said DNA coding sequence is derived from a source that encodes a bacterial DNA Polymerase, said source not containing an amber mutation affecting expression of said DNA polymerase activity, such that when said plasmid is transformed into a bacterial host system the host system can grow and divide thereby replicating said plasmid.
>
> 2. The recombinant plasmid of claim 1 wherein said DNA polymerase activity includes Nick-translation activity.
>
> 3. The plasmid of claim 2 wherein said Nick-translation activity is under operable control of a conditionally controllable foreign promoter, said foreign promoter being functional to express said Nick-translation activity in said host system.
>
> 23. A method of producing an enzyme possessing DNA polymerase activity comprising the steps of:
>
> transforming a recombinant plasmid having a DNA coding sequence for the expression of DNA polymerase activity that is under operable control of a conditionally controllable foreign promoter into a bacterial host system, said DNA polymerase coding sequence derived from a source that encodes a bacterial DNA polymerase, said source not containing an amber mutation affecting expression of said, DNA polymerase activity; and
>
> allowing the host system to grow and divide for at least twenty generations thereby replicating said plasmid.

'745 claim 1-3, 23 (emphases added).

The appealed claims of the '708 patent are directed to recombinant plasmids that contain a DNA coding sequence that is broadly defined, and only by its function, viz.,

encoding DNA polymerase I. Moreover, the generic claims are not limited to a single bacterial species, but broadly encompass coding sequences originating from any bacterial species. Similarly, the appealed claims of the '745 patent are broadly directed to recombinant plasmids that contain a DNA coding sequence, again, only defined by function, viz., encoding an enzyme with either DNA polymerase or nick-translation activity. Those claims are also not limited to a single bacterial species, but cover all bacterial species.

As a preliminary matter, we reject appellants' assertion that this case is distinguishable from Eli Lilly. Contrary to appellants' assertion, nothing in Eli Lilly indicates that that holding was limited to inventions involving novel DNA sequences. Indeed, in University of Rochester, we rejected a similar argument. See Rochester, 358 F.3d at 925.

In Eli Lilly, we held that "the claimed genera of vertebrate and mammal cDNA [were] not described by the general language of [a] patent's written description supported only by the specific nucleotide sequence of rat insulin." 119 F.3d at 1569. That holding was premised on the basic principle that a person of skill in the art must be able to "visualize or recognize the identity of the members of the genus." Id. Thus, to satisfy the written description requirement for a claimed genus, a specification must describe the claimed invention in such a way that a person of skill in the art would understand that the genus that is being claimed has been invented, not just a species of the genus.

The Guidelines for Examination of Patent Applications under the 35 U.S.C. § 112, ¶ 1, "Written Description" Requirement, 66 Fed. Reg. 10-99 (Jan. 5, 2001)

("Guidelines"), which we find to be an accurate description of the law by the agency responsible for examining patent applications, and thus persuasive authority, provide further guidance for determining whether the written description requirement is met for claims drawn to a genus. The Guidelines state:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species . . . by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.
>
> * * *
>
> Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.

Guidelines, 66 Fed. Reg. at 1106 (emphases added).

Here, while the claims of the '708 and '745 patents encompass a genus of recombinant plasmids that contain coding sequences for DNA polymerase or nick-translation activity from any bacterial source, in contrast, the narrow specifications of the '708 and '745 patents only disclose the polA gene coding sequence from one bacterial source, viz., E. coli. Significantly, the specification fails to disclose or describe the polA gene coding sequence for any other bacterial species.

The district court concluded that the disclosure of the E. coli polA gene was not representative of and failed to adequately support the entire claimed genus. Based on the record evidence indicating a lack of a genuine issue of material fact on the issue, we agree. Notably, the record indicates that at the time of the invention, only three bacterial polA genes, viz., E. coli, K. aerogenes, and K. pneumoniae, out of thousands of bacterial species had been cloned, and only E. coli was described in the patents. According to Roche's expert, Dr. Bambara, bacteria constitute a large class of organisms that include thousands, and potentially millions, of unidentified species. In addition, at the time of the invention, persons of ordinary skill in the art knew that DNA polymerase I was not a single enzyme, but a family of enzymes encoded by a family of genes that varied from one bacterial species to another. Dr. Bambara stated that those enzymes were encoded by genes that were distinct from the E. coli polA gene.

Significantly, the written descriptions of the '708 and '745 patents clearly indicate that the polA gene is critical to the claimed invention. Indeed, the patents disclose that a "significant discovery of the present invention" involved the need to severely damage the polA promoter sequence when constructing the recombinant plasmid in order to avoid the unregulated expression of DNA polymerase I, which otherwise would be lethal to the cell. '708 patent col.2 ll.40-46. The specifications disclose that "[t]he novel plasmid of the present invention contains the entire and undamaged polA gene coding region enzymatically excised from a DNA molecule" and emphasize that "it is an important feature of this invention that the cloned polA gene fragment contains essentially none of or at the most only a portion of the activity of its natural promoter." Id. col.2 ll.23-29.

However, although the written descriptions of the patents emphasize that the recombinant plasmids must be carefully constructed in order to overcome the lethality problem, particularly with regard to the promoter, the patents fail to disclose the nucleotide sequence or other descriptive features for a polA gene (including the promoter sequence) from any bacterial source other than E. coli. Indeed, in the Description of the Preferred Embodiments, the patents disclose only one embodiment which uses the plasmid referred to as pMP5. The patents teach that pMP5 was constructed by taking the E. coli polA gene from phage NM825, cutting the polA gene specifically at the BglII restriction site, and splicing the polA gene into a plasmid pHUB2.[3] Id. col.5 ll.49-65, Fig. 1. The specification teaches that cutting the polA gene at the BglII restriction site was a significant discovery:

> We have discovered that the restriction enzyme BglII will cut within the polA promoter sequence and severely damage it. This is a significant discovery of the present invention, since it eliminates or greatly reduces the unregulated expression of Pol I, which would otherwise be lethal to the cell.

Id. col.2 ll.40-46. As such, the patents teach that the specific gene sequence for the expression of DNA polymerase I or nick-translation activity is a critical aspect of the invention.

We agree with the district court that the narrow disclosure of the E. coli polA gene is not representative of and fails to adequately support the entire claimed genus under Eli Lilly. To satisfy the written description requirement in the case of a chemical or biotechnological genus, more than a statement of the genus is normally required.

[3] The pMP5 plasmid was transformed into E. coli strain N4830, which resulted in strain ATL100. The written description of the patent discloses that ATL100 was deposited in the American Type Culture Collection Depository on June 29, 1984, under Accession number 39753. '708 patent col.1 ll.36-41.

One must show that one has possession, as described in the application, of sufficient species to show that he or she invented and disclosed the totality of the genus. In light of the specifications' disclosure concerning the careful construction of the claimed recombinant plasmids, such that the natural promoter of the polA gene is severely damaged or eliminated, and given the record evidence that the polA gene varied among the numerous bacterial species, as well as the absence of any polA gene sequence for any bacteria other than E. coli, we conclude that that requirement was not met here.

We are unpersuaded by appellants' assertion that a different result is warranted in light of our holding in Capon v. Eshhar, 418 F.3d 1349, 1358 (Fed. Cir. 2005). The inventions in Capon involved "chimeric DNA that encodes single-chain chimeric proteins for expression on the surface of cells of the immune system, plus expression vectors and cells transformed by the chimeric DNA." Id. at 1352. We held that the Board of Patent Appeals and Interferences erred in holding that the written description requirement was not met because the disclosures failed to "reiterate the structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes." Id. at 1358. We explained that our holding in Eli Lilly did not impose "a per se rule requiring recitation in the specification of the nucleotide sequence of claimed DNA, when that sequence is already known in the field." Id. at 1360-61. Moreover, we stated that "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." Id.

Unlike the situation in Capon, however, where the prior art contained "extensive knowledge of the nucleotide structure of the various immune-related segments of DNA," including "over 785 mouse antibody DNA light chains and 1,327 mouse antibody DNA heavy chains," id. at 1355, the record here shows that only three bacterial polA genes out of thousands of genes had been cloned. As such, Capon does not aid appellants. Moreover, we disagree with appellants' assertion that the court failed to properly consider the Capon factors in its analysis. The court clearly considered the record evidence and properly determined the knowledge of one skilled in the field with respect to bacterial polA genes.

We are further unpersuaded by appellants' argument that the district court erred by failing to consider the declarations of their experts, which, according to appellants, create genuine issues of material fact. Appellants primarily point to the declarations of Drs. Benkovic, Low, Hatfull, and Davis. Having reviewed that evidence, we agree with the district court that they fail to create genuine issues of material fact. Appellants' experts did not dispute the statements made by Dr. Bambara that were material to the court's invalidity holding under Eli Lilly. Indeed, it was undisputed that by 1984, only three bacterial polA genes had been cloned. Moreover, Dr. Davis agreed with Dr. Bambara's statement that the polA gene "has different sequences for probably all the different bacterial species." Carnegie Mellon Univ. v. Hoffmann-La Roche, Inc., No. C 01-0415 SI, slip op. at 10 (N.D. Cal. Sept. 29, 2003). In addition, Dr. Benkovic agreed with Dr. Bambara's assertion that the '745 patent did not describe polA genes other than E. coli. Id. at 11. The additional expert statements relied upon by appellants, including statements concerning cloning techniques for purifying polA genes and

experiments involving E. coli, were immaterial to the relevant inquiry and thus do not raise genuine issues of material fact.

We have considered all of the remaining arguments appellants have raised in their briefs and found none that justify a reversal. Accordingly, because no genuine issues of material fact exist with regard to whether the written descriptions of the '708 and '745 patents adequately support the appealed claims, we affirm the district court's grant of summary judgment of invalidity with respect to those claims.

2. The '270 Patent

Appellants argue that the district court erred in concluding that the claims of the '270 patent are invalid under our holding in Gentry Gallery. According to appellants, the court improperly invalidated the claims for lack of written description after concluding that they do not recite the problem the invention was intended to solve. Because lethality was the key problem solved by the claimed invention, appellants argue that it cannot be an "element" of the invention. In response, Roche argues that the court correctly concluded that the claims are invalid under Gentry Gallery because they were broadened during prosecution to encompass more than the subject matter described in the application. In the alternative, Roche asserts that even if the court erred in its analysis under Gentry Gallery, the claims are still invalid under Eli Lilly.

We agree with appellants that the district court erroneously found the claims invalid under Gentry Gallery. In reaching its decision, the court found clear and convincing evidence that "lethality was an essential feature of the invention claimed in the '270 patent." Carnegie Mellon, 1999 WL 3329545 at *7. The court concluded that

under Gentry Gallery, the claims were invalid because the appealed claims did not contain that feature. In essence, the court applied an essential element test.

As we said in Cooper Cameron Corp. v. Kvaerner Oilfield Products, Inc., 291 F.3d 1317 (Fed. Cir. 2002), in Gentry Gallery "we did not announce a new 'essential element' test mandating an inquiry into what an inventor considers to be essential to his invention and requiring that the claims incorporate those elements." Id. at 1323. Rather, "we applied and merely expounded upon the unremarkable proposition that a broad claim is invalid when the entirety of the specification clearly indicates that the invention is of a much narrower scope." Id. We thus agree with appellants that the district court erred by invalidating the claims of the '270 patent by applying the essential element test. We further note that even if such a test existed, lethality was only a reason for the claimed invention, and not an element of it that needed to be defined in the claims.

However, while the court erred in holding the claims of the '270 patent invalid under Gentry Gallery, we agree with Roche that the claims are nonetheless invalid under Eli Lilly under the same rationale discussed above. The claims of the '270 patent suffer the same defects as the appealed claims of the '708 and '745 patents. Indeed, the claims of the '270 patent are also generically directed to plasmids encompassing the polA gene from any bacterial source. Thus, for the reasons set forth above, we conclude that there is no genuine issue of material fact as to whether the claims of the '270 patent are invalid for lack of written description under Eli Lilly.

Accordingly, because the specifications of the '708, '745, and '270 patents fail to provide adequate written description support for the appealed claims, all of which

encompass a genus of recombinant plasmids containing gene coding sequences from any bacterial source, we affirm the district court's grant of summary judgment of invalidity.

B. Noninfringement

In view of our affirmance of the district court's invalidity decision, the issue of infringement with respect to the asserted claims of the '708 patent has become moot and will not be considered. We will, however, consider appellant's argument with regard to the district court's grant of summary judgment of noninfringement of claims 4, 5, and 7 of the '745 patent, as the validity of those claims has not been challenged and thus presumptively they remain valid.

Claims 4, 5, and 7 of the '745 patent are all dependent claims and they incorporate the claim limitations of claim 1. Those claims, however, are narrower in scope as they require E. coli as the bacterial source. Those claims read as follows:

> 1. A recombinant plasmid containing a DNA coding sequence for the expression of DNA polymerase activity, wherein said DNA coding sequence is derived from a source that encodes a bacterial DNA Polymerase, said source not containing an amber mutation affecting expression of said DNA polymerase activity, such that when said plasmid is transformed into a bacterial host system the host system can grow and divide thereby replicating said plasmid.
>
> 4. The recombinant plasmid of claim 3 wherein the bacterial host system and the bacterial source are each E. coli; and wherein the Nick-translation activity includes polymerase and 5'-3' exonuclease activities.
>
> 5. The recombinant plasmid of claim 4 wherein said foreign promoter is a negatively regulated promoter.
>
> 7. The recombinant plasmid of claim 5 wherein said negatively regulated promoter is the leftward promoter of phage lambda.

'745 patent claims 1, 4, 5, & 7 (emphases added).

On appeal, appellants argue that the district court erred in concluding that the Roche's pLSG5 product does not infringe the '745 patent under the doctrine of equivalents. According to appellants, the substitution of Taq for E. coli was an insubstantial and unimportant change that resulted in an infringing equivalent. Roche responds that the court correctly granted summary judgment of noninfringement because appellants' infringement theory would vitiate the E. coli claim limitation of the appealed claims, which is impermissible under Warner-Jenkinson Co. v. Hilton Davis Chemical Co., 520 U.S. 17 (1997). In addition, Roche contends that, contrary to appellants' assertion, the differences between Taq and E. coli are not insubstantial.

We agree with Roche that the district court properly granted summary judgment of noninfringement under the doctrine of equivalents. Under that doctrine, "a product or process that does not literally infringe upon the express terms of a patent claim may nonetheless be found to infringe if there is 'equivalence' between the elements of the accused product or process and the claimed elements of the patented invention." Id. at 21 (citation omitted). However, the "all limitations rule" restricts the doctrine of equivalents by preventing its application when doing so would vitiate a claim limitation. Id. at 29 (stating that the doctrine of equivalents cannot be applied broadly so as to "effectively eliminate that [claim] element in its entirety"). In determining whether a finding of infringement under the doctrine of equivalents would vitiate a claim limitation, we must consider "the totality of the circumstances of each case and determine whether the alleged equivalent can be fairly characterized as an insubstantial change from the claimed subject matter without rendering the pertinent limitation meaningless." Freedman Seating Co. v. Am. Seating Co., 420 F.3d 1350, 1359 (Fed. Cir. 2005).

We agree with Roche and the district court that a finding that Taq is an equivalent of E. coli would essentially render the "bacterial source [is] E. coli" claim limitation meaningless, and would thus vitiate that limitation of the claims. Indeed, in drafting the claims, the patentees specifically chose to limit claim 4 to a recombinant plasmid where the bacterial source is E. coli. Appellants cannot now argue that any bacterial source, including Taq, would infringe that claim. Accordingly, summary judgment of noninfringement was appropriate.[4]

CONCLUSION

For the foregoing reasons, we affirm the district court's grant of summary judgment of invalidity with regard to claims 1-19, 22-40, and 43-45 of the '708 patent, claims 1-2, 11-12, 14-15, 17-18, 20-21, 23-24, 26-27, 29-30, and 32-36 of the '270 patent, and claims 3, 14, 23-28, and 30-32 of the '745 patent. In addition, we affirm the court's grant of summary judgment of noninfringement with respect to claims 4, 5, and 7 of the '745 patent.

AFFIRMED

[4] We note, as Roche states in its briefs, that Taq DNA polymerase was and continues to be integral to the success of polymerase chain reaction ("PCR"), a widely used technique in molecular biology that was invented by Kary Mullis in 1983. Indeed, in 1993, Mullis won the Nobel Prize in Chemistry for his development of PCR and the journal Science named Taq DNA polymerase the "Molecule of the Year." While we reach our decision irrespective of those facts, we readily can see why appellants have attempted to broaden the scope of their claims beyond the E. coli species disclosed.