United States Court of Appeals for the Federal Circuit

01-1399
(Interference no. 104,021)

JOHN H. GRIFFIN and JUDITH GREENGARD,

Appellants,

v.

ROGIER M. BERTINA and PIETER H. REITSMA,

Appellees.

Talivaldis Cepuritis, Olson & Hierl, Ltd., of Chicago, Illinois, argued for appellants. With him on the brief was Steven D. Weseman.

Ronald J. Kubovcik, Kubovcik & Kubovcik, of Washington, DC, argued for appellees.

Appealed from: United States Patent and Trademark Office
Board of Patent Appeals and Interferences.

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DECIDED: April 2, 2002

Before MICHEL, LOURIE, and DYK, Circuit Judges. LOURIE, Circuit Judge.

John H. Griffin and Judith Greengard (collectively, "Griffin") appeal from the decision of the United States Patent and Trademark Office Board of Patent Appeals and Interferences awarding judgment in an interference to the senior party, Rogier M. Bertina and Pieter H. Reitsma (collectively, "Bertina"). Griffin v. Bertina, Inter. No. 104,021 (Bd. Pat. App. & Inter. Feb. 21, 2001). Because the Board's decision was supported by substantial evidence and was not contrary to law, we affirm.

BACKGROUND

Griffin filed U.S. Patent Application 07/410,488 on March 24, 1995, claiming an invention directed to diagnosing thrombosis, a disease characterized by excessive blood clotting. Griffin, slip op. at 4. Bertina filed U.S. Patent Application 08/454,353 on June 6, 1995, claiming a similar invention. Id. The Board then declared an interference between the two applications and designated the following count:

A method according to claim 62 of the Bertina application

OR

A kit according to claim 81 of the Bertina application.[1]

Id. at 2. Claim 62 of the Bertina application is as follows:

> A method for diagnosing an increased risk for thrombosis or a genetic defect causing thrombosis comprising the steps of:
> (A) obtaining, from a test subject, test nucleic acid comprising codon 506 within EXON 10 of the human Factor V gene; and
> (B) assaying for the presence of a point mutation in the nucleotides of codon 506 within EXON 10 of the human Factor V gene, wherein said point mutation correlates to a decrease in the degree of inactivation of human Factor V and/or human Factor Va by activated protein C,
> wherein the presence of said point mutation in said test nucleic acid indicates an increased risk for thrombosis or a genetic defect causing thrombosis.

Id. (emphases added). Bertina's application was accorded the benefit of the filing dates of Patent Cooperation Treaty Application PCT/EP95/00553, filed February 14, 1995, and European Patent Application 94-200377.3, filed February 14, 1994. Griffin, slip op. at 4. Bertina elected to rely on his accorded benefit date of February 14, 1994, rather than attempt to establish an earlier priority date. Id. at 3. Griffin, on the other hand, took testimony in order to establish an actual reduction to practice prior to Bertina's accorded date. Griffin alleged in his preliminary statement that he and his co-inventor had reduced to practice the invention set forth in Bertina's claim 62 no later than December 2, 1993. Id. at 4. If proved, such activity would enable Griffin to prevail in the interference. Griffin did not allege that he and Dr. Greengard conceived the invention earlier than Bertina and then exercised reasonable diligence in reducing it to practice. Id. at 9 n.12.

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[1] Reduction to practice of Bertina's claim 81 is not at issue in this appeal.

Drs. Griffin and Greengard testified that in the summer of 1993, they were trying to find mutations in the Factor V protein that might cause activated protein C ("APC") resistance, which is an indication of excessive blood clotting. Id. They ordered primers for the purpose of amplifying the DNA of known cleavage sites in the Factor V gene in July 1993. Id. In August of 1993, Dr. Griffin received a shipment of blood samples from the "S" family.[2] Id. A colleague, not named as an inventor, determined that "LS" of that family exhibited APC resistance, whereas "AS" did not. Id. at 6. In an effort to correlate that resistance with a mutation in the gene, another colleague prepared sequencing gels of the "S" family Factor V gene samples on October 18 and 25, 1993. Id. Those samples indicated that only AS had a band in the G column for nucleotide 1691, corresponding to codon 506 of EXON 10 as set forth in the count. Id. The inventors maintained that those findings constituted a reduction to practice of their invention.

The Board concluded otherwise, finding that there was no indication in the sequencing gels that the inventors recognized that there was any particular difference between LS and AS's gene sequences. Id. Dr. Griffin had testified that he had noted the mutation and discussed it with Dr. Greengard before a weekly laboratory meeting on December 2, 1993, id. at 7, and a colleague testified that he had heard of the point mutation from Dr. Greengard before attending a meeting held December 3-7, 1993, id. Dr. Greengard also identified several other point mutations of interest in a handout distributed at a laboratory meeting on December 2, 1993. Id. at 10. The handout, however, did not identify the point mutation at issue.

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[2] The initial "S" is used here to maintain the privacy of the individuals involved.

The Board construed the count as requiring "an appreciation of the significance of a mutation at codon 506 within exon 10 of the human Factor V gene to the diagnosis of an increased risk of thrombosis due to a genetic defect." Id. at 3. It then determined that, at best, Griffin's evidence "indicates that the Griffin inventors had, by 2 December 1993, identified a mutation of interest at an interesting place in a gene of interest in one affected patient." Id. at 9. The Board concluded that the inventors did not recognize the significance of the discovery by December 2, 1993, and thus did not have a reduction to practice of an invention defined by all the limitations of the count by that date. Id. at 10. The Board therefore awarded priority to Bertina.

Griffin requested reconsideration of the Board's decision, which was denied. Griffin v. Bertina, Inter. No. 104,021 (Bd. Pat. App. & Inter. Mar. 27, 2001). The Board clarified Griffin's burden to establish reduction to practice as follows: "Griffin had to establish that it had actually made the invention described in the count, recognized it for what it was, and knew it would work for some practical purpose." Slip op. at 2. Because the count did not require recognition that the point mutation was the "sole, causative mutation" for APC resistance, it would have sufficed for Griffin "to show appreciation of a mutation that reliably correlated with APC resistance." Id. (emphasis added). Nevertheless, because it determined that Griffin's evidence failed to show that the Griffin inventors recognized a correlation between the point mutation and APC resistance, the Board concluded that Griffin did not show that it had reduced the invention to practice before Bertina and accordingly confirmed its award of priority to Bertina. Griffin timely appealed to this court; we have jurisdiction pursuant to 28 U.S.C. § 1295(a)(4)(A).

DISCUSSION

We review the Board's legal conclusion determining priority of invention de novo, Kridl v. McCormick, 105 F.3d 1446, 1449, 41 USPQ2d 1686, 1688 (Fed. Cir. 1997), and the factual underpinnings of its decision for substantial evidence, In re Gartside, 203 F.3d 1305, 1315, 53 USPQ2d 1769, 1774 (Fed. Cir. 2000). In particular, we review the Board's construction of the count, a legal determination, de novo. Davis v. Loesch, 998 F.2d 963, 967, 27 USPQ2d 1440, 1444 (Fed. Cir. 1993). A junior party seeking a determination of priority must demonstrate by a preponderance of the evidence reduction to practice before the senior party's priority date, or prior conception coupled with reasonable diligence in reducing the invention to practice from a time just before the senior party entered the field to the junior party's own reduction to practice. 35 U.S.C. § 102(g) (1994); Mahurkar v. C.R. Bard, Inc., 79 F.3d 1572, 1577, 38 USPQ2d 1288, 1290 (Fed. Cir. 1996).

Griffin argues that the count should be construed as limited only to its manipulative steps, i.e., obtaining test nucleic acid and identifying a point mutation in codon 506 within EXON 10 of the Factor V gene. Griffin asserts that he and his co-inventor performed those steps before December 2, 1993, and that they therefore reduced the count to practice prior to Bertina's priority date. Griffin argues that the count is not limited by the preamble "for diagnosing an increased risk of thrombosis or a genetic defect causing thrombosis" or by the "wherein" clauses directed to a correlation between the point mutation and decreased inactivation of Factor V by APC (i.e., increased APC resistance) because those clauses merely state the inherent result of performing the manipulative steps. Griffin argues, relying on Reese v. Hurst, 661 F.2d 1222, 1228, 211 USPQ 936, 942 (CCPA 1981), that the sequencing gels themselves demonstrate that the inventors knew that the invention would work for its intended purpose, i.e., to identify a point mutation at an enzyme cleavage site in human Factor V protein, and that the Board erred in requiring more explicit recognition of

the success of the invention as held in Estee Lauder Inc. v. L'Oreal S.A., 129 F.3d 588, 594-95, 44 USPQ2d 1610, 1615 (Fed. Cir. 1997).

Bertina responds that the preamble and "wherein" clauses limit the count and require recognition of the correlation between the specific point mutation and the decrease in inactivation of Factor V by APC. Bertina also argues that Griffin did not perform the manipulative steps because it did not use a "test subject" and because the "assaying" step requires prior knowledge of the point mutation. Bertina asserts that the Board correctly determined that Griffin did not show that the inventors appreciated that the invention worked for its intended purpose, viz., to diagnose an increased risk of thrombosis. Finally, Bertina argues that Griffin's evidence does not establish that the inventors identified the point mutation because the evidence was not independently corroborated.

We conclude that the Board did not err in construing the count to be limited by the preamble. A preamble to a claim "has the import that the claim as a whole suggests for it." Bell Communications Research, Inc. v. Vitalink Communications Corp., 55 F.3d 615, 620, 34 USPQ2d 1816, 1820 (Fed. Cir. 1995). The preamble language in this case is directed to "diagnosing an increased risk for thrombosis of a genetic defect causing thrombosis." That aspect of the invention is again stated in the body of the count: "wherein the presence of said point mutation in said test nucleic acid indicates an increased risk for thrombosis or a genetic defect causing thrombosis." Diagnosis is thus the essence of this invention; its appearance in the count gives "life and meaning" to the manipulative steps. See Kropa v. Robie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951) (stating that a preamble is limiting when it is "necessary to give life, meaning and vitality to the claims or counts"). Consideration of the preamble gives meaning and purpose to the manipulative steps in this case. The first step recites that the test nucleic acid should be obtained from a "test subject." In the absence of the preamble's stated objective to diagnose thrombosis, the

term “test subject” is empty language. What is one testing for, and who is a suitable subject? Similarly, without the preamble, “assaying for the presence of a point mutation” has no purpose. Obtaining nucleic acid and assaying for a point mutation alone are merely academic exercises. The preamble is thus a necessary limitation.

Furthermore, the Board did not err in giving limiting effect to the “wherein” clauses because they relate back to and clarify what is required by the count. Each “wherein” clause refers to the point mutation, giving meaning and purpose to the manipulative steps. The first “wherein” clause expresses the inventive discovery of the correlation between the point mutation and APC resistance, i.e., that the presence of the point mutation causes an increased risk of thrombosis. The second “wherein” clause elaborates the meaning of the preamble, indicating that the point mutation correlates with a decrease in the degree of inactivation of human Factor V and/or human Factor Va by APC (i.e., increased APC resistance), and hence an increased risk of thrombosis. The manipulative steps set forth in the count have little meaning or utility unless they are placed within the context of the diagnosis of an increased risk of developing thrombosis, recited in the preamble and “wherein” clauses. Griffin cites other cases in which the court determined that “whereby” clauses were nonlimiting. Aside from the fact that “wherein” is an adverb and “whereby” is a conjunction, those cases are all fact-specific, and what is clear here is that the “wherein” clauses are a necessary part of this count.

We are not persuaded by Griffin’s arguments that the “wherein” clauses merely state the inherent result of performing the manipulative steps. A party seeking to show that it need not establish reduction to practice of every feature recited in the count based on the alleged inherency of some of those features must show that the “inherent” properties add nothing to the count beyond the other recited limitations and are not material to the patentability of the invention. Hitzeman v. Rutter, 243 F.3d 1345, 1354-55, 58 USPQ2d

1161, 1167 (Fed. Cir. 2001). In this case, as discussed above, the allegedly inherent properties of the "wherein" clauses provide the necessary purpose to the steps of obtaining test nucleic acid from a "test subject" and "assaying" that material. Moreover, the correlation between the point mutation and an increased risk of thrombosis appears to be material to the patentability of the count, as that correlation, rather than mere knowledge of the point mutation, indicates the purpose of the method. As Bertina points out, the point mutation that Griffin allegedly identified could have been a polymorphism or the result of a sequencing error, in which case it would not have been useful for much of anything, let alone for indicating an increased risk of thrombosis. Griffin did not offer any evidence that prior to December 2, 1993, the inventors appreciated that the identified point mutation actually correlated with an increased risk of thrombosis. In fact, in the handout distributed at a laboratory meeting on that date, Dr. Greengard identified point mutations other than the one in the count as likely candidates for Factor V defects correlating with APC resistance.

We are also not persuaded by Griffin's argument that the Board erred in requiring the inventors to show appreciation of the significance of the point mutation because the test results (sequencing gels) themselves demonstrated the success of the invention, citing Reese, 661 F.2d at 1228, 211 USPQ at 942. That argument is premised on Griffin's limited view of the meaning of the count as merely the identification of a point mutation at an enzyme cleavage site in human Factor V protein. Griffin failed to demonstrate successful reduction to practice because it had not appreciated the utility of the point mutation as actually correlating with an increased risk of thrombosis. See Estee Lauder, 129 F.3d at 593, 44 USPQ2d at 1614 ("[A] reduction to practice does not occur until the inventor has determined that the invention will work for its intended purpose."). Griffin only offered evidence concerning performance of the manipulative steps in which it was

discovered that LS possessed the point mutation of the count. He did not demonstrate that the inventors diagnosed that LS had an increased risk of thrombosis based on their prior knowledge of a correlation between the point mutation and APC resistance. Rather, Griffin's evidence shows only that the inventors may have unearthed one data point in their pursuit to identify a genetic mutation that might correlate with an increased risk of thrombosis. The Board's factual determination that Griffin's activities did not meet the count was therefore supported by substantial evidence.

At oral argument, Griffin's counsel commendably conceded that it could not demonstrate an earlier reduction to practice if we construed the count as limited by the preamble and "wherein" clauses. In light of our affirmance of the Board's construction, Griffin must therefore lose. That construction also necessarily forecloses Griffin's arguments, relying on this court's decision in Mycogen Plant Science, Inc. v. Monsanto Co., 243 F.3d 1316, 58 USPQ2d 1030 (Fed. Cir. 2001), that Griffin reduced the invention to practice by merely identifying the point mutation because its inventors allegedly understood that mutations in the preselected regions would be associated with APC resistance and an increased risk of thrombosis. In Mycogen, we upheld a jury's determination that a patent was invalid under 35 U.S.C. § 102(g) for prior invention. Id. at 1336, 58 USPQ2d at 1047. Although the prior inventors there did not have an appreciation of each of the limitations of the claim in haec verba, the evidence showed that those inventors appreciated the subject matter of the claims and the utility of that subject matter because its work leading to its reduction to practice was part of a research program specifically directed toward the purpose of the claim. Id. at 1335-36, 58 USPQ2d at 1046. In this case, however, the Board's determination that Griffin's evidence does not indicate that it appreciated the actual correlation of the point mutation in the count with APC resistance and thus an increased risk of thrombosis was not lacking in substantial evidence. In any event, proof of

a correlation sufficient to constitute a reduction to practice of a diagnostic test would normally require more than one data point, which was not shown here. In light of our conclusion, we need not reach Bertina's argument that Griffin's evidence lacked sufficient corroboration, because that evidence, even if corroborated, would not have demonstrated Griffin's reduction to practice. The Board's decision was supported by substantial evidence and contained no errors of law.

CONCLUSION

Because the Board properly construed the count as including the preamble and the "wherein" clauses, and thus required Griffin to show appreciation of a correlation between the point mutation and APC resistance, it did not err in concluding that Griffin failed to show that it reduced the invention to practice before Bertina's priority date. The Board's decision to award judgment to Bertina is therefore

AFFIRMED.