NOTE: This disposition is nonprecedential

United States Court of Appeals for the Federal Circuit

(Serial No. 10/667,216)

IN RE SHAKER A. MOUSA

2011-1294

Appeal from the United States Patent and Trademark Office, Board of Patent Appeals and Interferences.

Decided: April 19, 2012

JACK P. FRIEDMAN, Schmeiser, Olsen & Watts LLP, of Latham, New York, for appellant.

RAYMOND T. CHEN, Solicitor, Office of the Solicitor, United States Patent and Trademark Office, of Alexandria, Virginia, for appellee. With him on the brief were KRISTI L.R. SAWERT and LYNNE E. PETTIGREW, Associate Solicitors. Of counsel was JANET A. GONGOLA, Associate Solicitor.

Before PROST, SCHALL, and REYNA, *Circuit Judges*.

REYNA, *Circuit Judge*.

This matter comes before the court on appeal from a final decision of the United States Board of Patent Appeals and Interferences ("BPAI") sustaining the invalidity of U.S. Patent Application No. 10/667,216 ("'216 application") for anticipation and obviousness. Because substantial evidence supports the BPAI's determination, we *affirm*.

BACKGROUND

I. The Technology

Heparin is a drug that is typically used as a blood thinner, or anticoagulant, to prevent blood clots from forming. Heparin is less commonly used to prevent new blood vessel growth in cancerous tissue. Heparin controls this growth, known as angiogenesis, by blocking an enzyme, fibroblast growth factor ("FGF2"), that induces blood vessel growth in tumors. Heparin's use as a treatment for angiogenesis is limited because its anticoagulant properties cause bleeding complications.

On a molecular level, heparin is a long-chain carbohydrate molecule consisting of repeating disaccharide units with, *inter alia*, hydroxyl (-OH), carboxylated hydroxyl ($-OCOO^-$), and sulfated hydroxyl ($-OSO_3^-$) groups. This molecule can be chemically fractured into smaller segments, called heparin fractions, which retain the anticoagulant and angiogenesis properties of heparin.

II. The '216 Application

The '216 application discloses super-sulfated, oxidized heparin fractions ("'216 heparin fractions"), which are produced by oxidizing some of the hydroxyl groups on the heparin fraction and by substituting sulfate groups for the hydrogen atoms in other hydroxyl groups. The '216

application does not define the term "super-sulfated," but instead discloses that the '216 heparin fraction has a high ratio of sulfate ($-SO_3^-$) groups to carboxylate ($-COO^-$) groups, which can range from 2:1 to 5:1.

According to the '216 application, the increased oxidation of the '216 heparin fractions fully inhibits FGF2-induced angiogenesis. Additionally, the bleeding complications normally associated with heparin use can be eliminated by using these super-sulfated, oxidized heparin fractions, because they possess weaker anticoagulant properties than heparin.

III. The Prior Art

U.S. Patent No. 4,727,063 ("Naggi patent"), which issued on February 23, 1988, discloses a super-sulfated heparin fraction with weak anticoagulant properties. The Naggi patent teaches treating heparin with a mixture of sulfuric acid and chlorosulfonic acid, chemicals that are strong oxidizing agents, to produce super-sulfated heparin fractions ("Naggi heparin fractions").

IV. The Prosecution History

On September 19, 2003, Appellant Shaker A. Mousa filed the '216 application for a patent claiming "oxidized heparin fractions and their use in inhibiting angiogenesis" with the United States Patent and Trademark Office ("PTO"). In a final office action dated April 9, 2008, the Examiner rejected claims 1, 2, 5, 6, 43, and 91-94 as anticipated under 35 U.S.C. § 102(b) by the Naggi patent and claims 1, 43, 49-54, 56-59, 61, and 62 as obvious under 35 U.S.C. § 103(a) in view of the Naggi patent in combination with other prior art. The Examiner found that the Naggi heparin fractions were inherently oxidized because the Naggi patent teaches treating heparin with oxidizing agents and that the resulting structure was

identical to the '216 heparin fractions. Further, the Examiner found that the weak anticoagulant activity of the Naggi heparin fractions indicated that the Naggi heparin fractions inherently possess the anti-angiogenesis properties of the '216 heparin fractions.

Mousa filed a Request for Continued Examination ("RCE") on August 11, 2008, and amended the claims to include the limitation that the super-sulfated, oxidized heparin fraction "fully inhibit*s fibroblast growth factor (FGF2) induced* angiogenesis," where the underlined portion is germane to this appeal. Mousa argued that this limitation distinguished the Naggi patent from the '216 application because the '216 application does not claim all super-sulfated, oxidized heparin fractions that may exist - only those that fully inhibit FGF2-induced angiogenesis. Mousa further argued that the Naggi patent does not teach or suggest full inhibition of the FGF2 factor and, thus, does not anticipate the '216 application.

The Examiner issued a non-final rejection of the '216 application on October 27, 2008, which maintained the rejections of the claims at issue as made in the previous final office action of April 9, 2008, for anticipation or obviousness in light of the Naggi patent. The Examiner found that the Naggi patent discloses treating heparin with sulfuric acid and chlorosulfonic acid, a strong oxidizing agent, which would fragment the heparin molecule into fractions and would result in a super-sulfated heparin. The Examiner stated that this reaction would necessarily encompass the reaction sequence of oxidizing said heparin and then performing sulfate substitution at the oxygen bonds within the depolymerized heparin. Further, the Examiner found that the Naggi heparin fractions possess a reduced anticoagulation reduction characteristic as shown by the activated partial thromboplastin time ("APTT") and Heparin Antifactor Xa Assay ("Anti-Xa")

results are disclosed in the Naggi patent. The Examiner found that the APTT and Anti-Xa results indicated that the Naggi heparin fractions inherently possess the angiogenesis and anticoagulant characteristics claimed by Mousa in the '216 application.

Independent claim 1 is representative of the rejected claims.[1] It provides:

> 1. An oxidized heparin fraction having a molecular weight of from about 2,000 to about 4,000 daltons,
>
> wherein the oxidized heparin fraction is super-sulfated such that the super-sulfated oxidized heparin fraction comprises an anticoagulant reduction characteristic and an angiogenesis inhibition characteristic;
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> *wherein the super-sulfated oxidized heparin fraction has a chemical structure of a first oxidized heparin fraction after the first oxidized heparin fraction has been O-sulfated by sulfate substitution*

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[1] The parties also treat dependent claims 93 and 94 as representative. Claim 93 explains the anticoagulant reduction and angiogenesis inhibition characteristics recited in claim 1 and identifies specific techniques that can be used to determine these characteristics. Claim 94 is a product-by-process claim that recites a method for creating the '216 heparin fraction wherein the heparin fraction is first oxidized and then O-sulfated via sulfate substitution at the oxygen bonds. Although claims 93 and 94 are treated separately by the BPAI and the parties, Mousa's arguments and the Board's findings address the same claim language and the same portions of the Naggi patent. Because claim 1 is representative of all the rejected claims, we do not address them separately given that our review applies equally to all of the rejected claims at issue in this appeal.

> *at oxygen bonds within repeating units of the first oxidized heparin fraction*;
>
> *wherein the super-sulfated oxidized heparin fraction fully inhibits fibroblast growth factor (FGF2) induced angiogenesis.*

(emphasis added).

V. The BPAI's Decision

Mousa appealed the Examiner's non-final rejection to the BPAI on February 27, 2009, arguing that the method the Naggi patent uses to produce heparin fractions would not result in super-sulfated, oxidized heparin fractions with a chemical structure that is the same as that of the '216 heparin fractions because Naggi merely treats heparin with oxidizing agents while Mousa teaches O-sulfating a first oxidized heparin fraction. Mousa also argued that the Naggi patent does not teach a heparin fraction which *fully* inhibits FGF2 induced angiogenesis, a limitation that is required by the '216 claims. Mousa contended that without experimental proof that the Naggi heparin fraction could fully inhibit angiogenesis, the Naggi patent could not anticipate the '216 application.

On appeal, the Examiner maintained that the Naggi patent teaches a method that inherently oxidizes the Naggi heparin fractions. Further, the Examiner maintained that the results of the APTT and Anti-Xa experiments disclosed in the Naggi patent showed that the Naggi heparin fractions possess a weak anticoagulant property. The Examiner argued that this weak anticoagulant property was the same as the property claimed by Mousa and that this indicated that the Naggi heparin fractions also inherently possess the anti-angiogenesis properties claimed by the '216 application.

The BPAI affirmed the rejection of the claims. The BPAI found that the Naggi patent discloses, inherently or expressly, each and every limitation of the claims at issue in the '216 application. According to the BPAI, the Naggi patent teaches super-sulfated heparin fractions with a molecular weight between 3000 and 5000 daltons, a sulfate to carboxylate ratio of 2.5, and a weak anticoagulant reduction characteristic as compared to heparin. Further, the BPAI found that the Naggi patent inherently teaches an oxidized heparin fraction because it treats heparin with sulfuric and chlorosulfonic acids, strong oxidizing agents.

Based on these findings, the BPAI concluded that the Examiner had established that the heparin fractions taught by the Naggi patent and the '216 application were "the same or substantially the same." The BPAI held that Naggi heparin fraction inherently possesses the anti-angiogenesis characteristic required by claim 1 of the '216 application. The BPAI then found that the Examiner had properly shifted the burden of proof to Mousa to show that the Naggi heparin fraction does not inherently possess the anti-angiogenesis characteristics recited in claim 1 of the '216 application.[2] Because claim 1 is representative of all claims on appeal, Mousa bore the burden of proving that none of the characteristics claimed by the '216 application were inherent to the Naggi heparin fraction.

The BPAI went on to find claims 1, 43, 49-54, 56-59, 61, and 62 obvious under 35 U.S.C. § 103(a) in view of the Naggi patent in combination with other prior art. While the BPAI addressed each prior art reference relied upon

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[2] In addition to claims 1, 93 and 94, the BPAI addressed claims 91, 92, and 43 as representative of the anticipated claims. As these claims were not raised by the parties on appeal, we do not address them.

by the Examiner in its decision, on appeal, Mousa argues that the BPAI and Examiner failed to invoke the prior art other than the Naggi patent in making this determination and relies solely on his argument that the Naggi patent does not anticipate.

The BPAI affirmed the Examiner's rejection of all the claims at issue and denied a subsequent request for rehearing. This appeal followed. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(4)(A).

DISCUSSION

I. Standard of Review

Anticipation is a question of fact that this court reviews for substantial evidence. *See In re Aoyama*, 656 F.3d 1293, 1296 (Fed. Cir. 2011); *See Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1363 (Fed. Cir. 2006). "[T]he possibility of drawing two inconsistent conclusions from the evidence does not prevent an administrative agency's finding from being supported by substantial evidence." *Crash Dummy Movie, LLC v. Mattel, Inc.*, 601 F.3d 1387, 1390 (Fed. Cir. 2010) (quoting *Consolo v. Fed. Maritime Comm'n,* 383 U.S. 607, 620 (1966)). Obviousness is a question of law that this court reviews *de novo*. *In re Klein*, 647 F.3d 1343, 1347 (Fed. Cir. 2011). The BPAI's factual findings underlying a determination of obviousness are reviewed for substantial evidence. *Id.*

II. Anticipation of the Claims on Appeal

Anticipation of a claim under 35 U.S.C. § 102 occurs when each claimed element and the claimed arrangement or combination of those elements is disclosed, inherently or expressly, by a single prior art reference. *Therasense, Inc. v. Becton, Dickinson & Co.*, 593 F.3d 1325, 1332 (Fed. Cir. 2010). A reference inherently discloses an element of a claim "if that missing characteristic is *necessarily* pre-

sent, or inherent, in the single anticipating reference." *Schering Corp. v. Geneva Pharms.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003) (citation omitted) (emphasis added). "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *Therasense*, 593 F.3d at 1332 (citing *Cont'l Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1269 (Fed. Cir. 1991)). The Examiner has the burden of providing reasonable proof that a claim limitation is an inherent characteristic of the prior art. *In re Best*, 562 F.2d 1252, 1254-55 (C.C.P.A. 1977); *see also Crown Operations Int'l, LTD v. Solutia Inc.,* 289 F.3d 1367, 1377 (Fed. Cir. 2002). The Examiner meets this "burden of production by 'adequately explaining the shortcomings it perceives so that the applicant is properly notified and able to respond.'" *In re Jung*, 637 F.3d 1356, 1362 (Fed. Cir. 2011) (quoting *Hyatt v. Dudas*, 492 F.3d 1365, 1370 (Fed. Cir. 2007)). The burden of proof then shifts to the applicant "to prove that the subject matter shown to be in the prior art does not possess the characteristic relied on." *Best*, 562 F.2d at 1254-55; *In re Schreiber*, 128 F.3d 1473, 1478 (Fed. Cir. 1997) (holding that once the Examiner established a *prima facie* case of anticipation, the burden of proof was properly shifted to the inventor to rebut the finding of inherency).

Here, the BPAI held that the Naggi patent expressly or inherently discloses each and every limitation of claims 1, 2, 4, 5, 43, and 91-94 of the '216 application. According to the BPAI, the Naggi patent inherently discloses oxidized, super-sulfated heparin fractions that are "the same or substantially the same compound" as the '216 heparin fractions.

On appeal, Mousa argues that the Naggi patent does not disclose "a chemical structure of a first oxidized

heparin fraction" nor the claimed characteristic of a heparin fraction that "fully inhibits fibroblast growth factor (FGF2) induced angiogenesis." The PTO counters that the Examiner established that treating heparin with the strong oxidizing agents taught in the Naggi patent necessarily results in oxidized heparin and that the Examiner appropriately shifted the burden of proof to Mousa to show that those oxidizing agents did not oxidize heparin. The PTO also argues that once the Examiner demonstrated that the structures of the two heparin fractions were identical, the burden of proof shifted to Mousa to show that the Naggi heparin fractions did not possess the same FGF2-inhibiting characteristics as the '216 heparin fractions.

We agree with the BPAI. "[W]hen the PTO shows sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 708 (Fed. Cir. 1990) (citations omitted). The BPAI noted that the '216 application teaches treating heparin with oxidizing agents[3] but places no limitation on which oxidizing agents may be used. The BPAI also noted that the Naggi patent discloses treating heparin with sulfuric acid and chlorosulfonic acid, chemicals that the Examiner stated are known to be strong oxidizing agents. These findings, along with the weak anticoagulant properties of the Naggi heparin fraction, are substantial evidence that support the BPAI's finding that the Naggi patent teaches a super-sulfated, oxidized heparin fraction identical to the '216 heparin fraction.

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[3] The '216 application lists oxidizing agents as "including, but not limited to, periodic acid, metals in high valence states, halogens, halogen atoms, and compounds with O-O bonds, such as O_3, diacyl peroxides, H_2O_2, and O_2."

Having established that the two heparin fractions are "the same or substantially the same compound" and that the Naggi fractions necessarily possessed the FGF2-inhibiting characteristic recited in claim 1, the Examiner properly shifted the burden of proof to Mousa to prove that the structures were different and that the claimed properties were not inherent. The fairness of this shifting "is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products." *Best*, 562 F.2d at 1255 ("Where, as here, the claimed and prior art products are identical or substantially identical . . . the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product.").[4] Mousa failed to satisfy this burden. Although Mousa argues that oxidizing agents do not oxidize every substance and that the Examiner did not establish that these chemicals can oxidize heparin, Mousa provided no proof in support of this contention to the Examiner or to the BPAI. "Appellant's unsupported statements . . . are not sufficient evidence to rebut the examiner's contention." *In re Hoke*, 560 F.2d 436, 438 (C.C.P.A. 1977).

Furthermore, once the Examiner established that the Naggi patent read identically on the limitations of the '216 claims, Mousa bore the burden to show that the Naggi heparin fractions did not inherently possess the FGF2-inhibiting characteristics of the '216 heparin frac-

[4] Mousa contends that this court created a new and more stringent standard in *Spada*, 911 F.2d at 708, that requires the "virtual identity" of compounds to establish inherency. Mousa argues that this standard overrules the requirement of "identical or substantially identical" compounds established by *Best*. 562 F.2d at 1255. We disagree. The standard applied in *Spada* is consistent with that articulated and applied in *Best*.

tions as recited by claim 1. *Best*, 562 F.2d at 1255. Mousa again failed to satisfy his burden of proof.[5]

In affirming the rejection of the claims in the '216 application, the BPAI addressed the factual bases for the findings of inherency and anticipation based on the Naggi patent. Because we find that the BPAI's factual findings are supported by substantial evidence, we affirm the BPAI's decision.

In light of this holding, we need not analyze the issue of obviousness separately. The Examiner rejected independent claims 1 and 43 as being both anticipated under 35 U.S.C. § 102 and obvious under 35 U.S.C. § 103(a). The Examiner also rejected dependent claims 49-54, 56-59, 61 and 62 as obvious based on Naggi and certain other references. Mousa challenges the obviousness rejections of the dependent claims solely on the ground that the prior art does not disclose the limitations of claims 1 and 43 from which claims 49-54, 56-59, 61 and 62 depend. As discussed above, the BPAI's factual findings that the Naggi patent anticipates the claims at issue in this appeal are supported by substantial evidence. As we hold that the Board did not err in finding that Naggi anticipates claims 1 and 43 and thus discloses every limitation of those claims, Mousa's challenge to the obviousness rejections of claims 49-54, 56-59, 61 and 62 also fails.

CONCLUSION

For the foregoing reasons, we affirm.

AFFIRMED

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[5] Although Mousa presents other arguments related to the Examiner's review of prior art, the BPAI noted that the prior art was not properly before the Examiner and that the BPAI could therefore not consider the prior art. We agree.

COSTS

Each party shall bear its own costs.