United States Court of Appeals for the Federal Circuit

2006-1507
(Serial No. 08/405,454)

IN RE JOHN B. SULLIVAN and FINDLAY E. RUSSELL

Lawrence M. Green, Wolf, Greenfield & Sacks, P.C., of Boston, Massachusetts, argued for appellants. With him on the brief were Michael T. Siekman and Charles T. Steenburg.

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

United States Court of Appeals for the Federal Circuit

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IN RE JOHN B. SULLIVAN and FINDLAY E. RUSSELL

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DECIDED: August 29, 2007

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Before NEWMAN, LOURIE, and GAJARSA, Circuit Judges.

LOURIE, Circuit Judge.

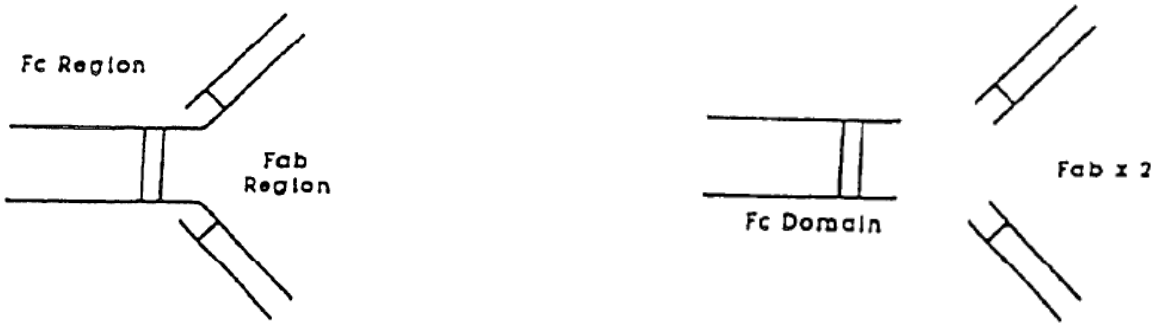
Sullivan and Russell (collectively "applicant") appeal from the decision of the United States Patent and Trademark Office ("the PTO") Board of Patent Appeals and Interferences ("the Board") affirming the examiner's final rejection of claims 40-42 and 50 of application Serial No. 08/405,454 ("the '454 application") under 35 U.S.C. § 103 as having been obvious over two prior art references. In re Sullivan, No. 2006-0220 (B.P.A.I. Mar. 30, 2006). Because the Board failed to give any weight to the rebuttal evidence of record, we vacate the Board's decision and remand for further proceedings.

BACKGROUND

The subject matter of the appeal relates to an antivenom composition used to treat venomous bites from a snake of the Crotalus genus, i.e., a rattlesnake. An

antivenom is created by injecting a small amount of the targeted venom into an animal such as a horse, sheep, goat, or rabbit. The animal will suffer an immune response to the venom, producing antibodies against the venom's active molecule. Those antibodies can then be harvested from the animal's blood and used to treat humans who have been injected with venom from a snake bite.

A whole antibody molecule, commonly referred to as an immunoglobulin, can be thought of as a Y-shaped protein comprised of three fragments. The v-shaped portion of the Y-shaped protein is called a $F(ab)_2$ fragment. When separated, each arm of the v-shaped portion is called, in turn, a Fab fragment. $F(ab)_2$ and Fab fragments recognize and bind to specific antigens, such as the toxin in rattlesnake venom. The lower stem of the Y-shaped antibody is called the Fc fragment and is not involved in antigen binding. Diagrams of an antibody and its components are provided below for reference. The diagram on the left shows a whole antibody and indicates the Fc region and the Fab region. The Fab region can be considered a $F(ab)_2$ fragment. The diagram on the right shows two Fab fragments that are separated from the Fc region.



An intact antibody, $F(ab)_2$, and Fab fragments have separate properties and utilities. Since 1969, most commercially available antivenom products have consisted of a class of whole antibodies, known as immunoglobulin G ("IgG"), but there have also

been antivenom products that comprised only $F(ab)_2$ fragments. Although antivenom products consisting of either IgG or $F(ab)_2$ fragments are effective at binding to venom toxins, they often invoke adverse immune reactions in humans. Researchers did not experiment with antivenoms containing only Fab fragments because it was believed that their unique properties would prevent them from decreasing the toxicity of snake venom. Sullivan discovered, however, that Fab fragments are effective at neutralizing the lethality of rattlesnake venom, while reducing the occurrence of adverse immune reactions in humans.

Applicant filed the '454 application with claims directed to an antivenom composition comprising Fab fragments that bind specifically to venom from snakes of the Crotalus genus and a pharmaceutical carrier.[1] Representative claim 40, as originally filed, reads as follows:

> An antivenom composition comprising Fab fragments which bind specifically to a venom of a snake of the Crotalus genus and which are essentially free from contaminating Fc as determined by immunoelectrophoresis using anti-Fc antibodies, and a pharmaceutically acceptable carrier.

The examiner rejected the claim under 35 U.S.C. § 103 as being obvious over Sullivan[2] in view of Coulter[3] and two additional references. In the first appeal to the

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[1] In the patent application as initially filed, there were also claims directed to a process for isolating the Fab fragments. The examiner required a restriction of the claims, and the inventors initially pursued the set of process claims. Those claims ultimately matured into U.S. Patent 4,849,352.

[2] J.B. Sullivan, Jr. & F.E. Russell, Isolation and Purification of Antibodies to Rattlesnake Venom by Affinity Chromatography, 25 Proc. W. Pharmacology Soc. 185, 185-92 (1982).

[3] Alan Coulter & Rodney Harris, Simplified Preparation of Rabbit Fab Fragments, 59 J. Immunological Methods 199, 199-203 (1983).

Board, the Board affirmed the rejection of claim 40 as being obvious, but only relied upon Sullivan and Coulter for its rejection. In re Sullivan, No. 2001-1255 (B.P.A.I. Jan. 29, 2003). The Board found that Sullivan teaches whole antibodies purified from horse serum for use against venom from rattlesnakes, but fails to teach the use of Fab fragments. The Board also found that Coulter discloses a method for producing Fab fragments in place of whole antibodies. The Board noted that Coulter further teaches using Fab fragments in enzyme immunoassays ("EIAs")[4] to detect textilotoxin, a kind of snake toxin from the venom of the Australian brown snake. Also, Coulter teaches that Fab fragments used in EIAs yielded results similar to those obtained with whole IgG.

Based upon those teachings, the Board agreed with the examiner that all the limitations of claim 40 were disclosed in Sullivan and Coulter. The Board concluded that a person of ordinary skill in the art would have been motivated to produce Fab fragments for use in EIAs to detect the venom from rattlesnakes because Coulter teaches that Fab fragments are able to detect textilotoxins. The Board further stated that the term "antivenom" in the preamble could not render claim 40 patentable over Sullivan and Coulter, reasoning that "the mere statement of new use, in this case 'an antivenom' for an otherwise old or obvious composition, cannot render a claim to the composition patentable." Sullivan, No. 2001-1255, slip op. at 9. The Board also held that, although it was not previously addressed, Coulter discloses collecting Fab fragments in a phosphate buffered saline ("PBS"), which is a pharmaceutically

[4] An EIA is a biochemical test that measures the level of a substance in a biological sample, such as serum or urine, using the reaction of an antibody to its antigen. Based on the amount of antibody detected, the amount of substance bound to the antibody can be determined.

acceptable carrier. The Board concluded that the asserted claims were prima facie obvious over the combination of Sullivan in view of Coulter.

The Board stated that since its decision contained a new ground of rejection, the applicant could either move for reconsideration by the Board or return to prosecution before the examiner.[5] Applicant chose to return to prosecution before the examiner. Applicant then amended claim 40 to its current form, adding language to the preamble and to the end of the claim. Amended claim 40 reads as follows, with the underlined portions identifying the portions of the claim that were added:

> An antivenom pharmaceutical composition for treating a snakebite victim, comprising Fab fragments which bind specifically to a venom of a snake of the Crotalus genus and which are essentially free from contaminating Fc as determined by immunoelectrophoresis using anti-Fc antibodies, and a pharmaceutically acceptable carrier, wherein said antivenom pharmaceutical composition neutralizes the lethality of the venom of a snake of the Crotalus genus.

The examiner rejected amended claims 40-42 and 50[6] under 35 U.S.C. § 103 as obvious over the combination of Sullivan and Coulter. The examiner found that the additional language in claim 40 did not render the claim patentable. The examiner reasoned that the originally claimed composition contained the same components as the amended claimed composition. The examiner issued a final rejection, and applicant appealed to the Board. In the second appeal to the Board, the Board noted that there

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[5] Under 37 C.F.R. § 41.50(b)(1), when the Board issues a new ground of rejection, an applicant may "[s]ubmit an appropriate amendment of the claims so rejected . . . and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner. . . . Should the examiner reject the claims, appellant may again appeal to the Board pursuant to this subpart."

[6] According to Sullivan, the claims stand or fall together. Thus, the Board limited its discussion to representative independent claim 40. Similarly, we only discuss claim 40.

were only two differences between original claim 40 and amended claim 40: (1) the recitation of intended use that states that the pharmaceutical composition is for treating a snakebite victim, and (2) the functional limitation that requires the pharmaceutical composition to neutralize the lethality of the venom of a rattlesnake. The Board addressed each amendment in turn.

With regard to the first amended portion, the Board again stated that a statement of a new use for an otherwise old or obvious composition cannot render a claim to the composition patentable. The Board noted that the phrase, "an antivenom pharmaceutical composition for treating a snakebite victim," simply states the intended use for the invention. Sullivan, No. 2006-0220, slip op. at 11. The Board also noted that "all the elements of appellants' claimed composition are accounted for in the prior art relied upon on this record." Id. at 13. Thus, the Board held that the amended preamble did not render the claim patentable.

Most relevant to the resolution of the appeal, the Board then stated in a footnote: "The remainder of appellants [sic] arguments on this record, in addition to the Declarations of record, relate to the use of the claimed composition as an antivenom. Since we have placed not [sic] weight on the intended use of appellants' composition we do not address these arguments or the Declarations." Id. at 13 n.7.

The Board then considered the second amended portion of the claim, which includes the limitation of neutralizing the lethality of the rattlesnake venom. The Board found that Coulter teaches that neutralization tests performed in mice showed that whole antibodies and Fab fragments were equivalent in their neutralizing ability. Accordingly, the Board found that the additional requirement that the composition of

claim 40 neutralize the lethality of the venom of a rattlesnake did not render the claim patentable. The Board thus held that the composition taught by the combination of Sullivan and Coulter would have been expected by a person of ordinary skill in the art at the time the invention was made to neutralize the lethality of the venom of a rattlesnake.

Applicant timely appealed, and we have jurisdiction pursuant to 28 U.S.C. § 1295(a)(4)(A).

DISCUSSION

The determination whether an invention would have been obvious under 35 U.S.C. § 103 is a legal conclusion based on underlying findings of fact. In re Kotzab, 217 F.3d 1365, 1369 (Fed. Cir. 2000). We review the Board's legal conclusion of obviousness de novo and its underlying factual determinations for substantial evidence. In re Gartside, 203 F.3d 1305, 1316 (Fed. Cir. 2000). "Substantial evidence requires the reviewing court to ask whether a reasonable person might find that the evidentiary record supports the agency's conclusion." On-Line Careline, Inc. v. Am. Online, Inc., 229 F.3d 1080, 1085 (Fed. Cir. 2000).

On appeal, applicant argues that the Board failed to establish that the claimed composition was prima facie obvious over Sullivan in view of Coulter. Applicant specifically argues that a person having ordinary skill in the art would not have been motivated to combine Sullivan and Coulter to achieve the result of "neutralizing the lethality of the rattlesnake venom." Applicant argues that Coulter teaches using Fab fragments to detect, rather than treat, venom. Applicant further argues that, even if the Board had shown that the invention was prima facie obvious, the Board erred by ignoring extensive rebuttal evidence. According to applicant, the Board failed to

consider three expert declarations on the ground that they only describe the intended use of the composition. Applicant contends that the declarations describe how the prior art taught away from using Fab fragments to neutralize rattlesnake venom, how a person having ordinary skill in the art would not have known how to use Fab fragments to neutralize rattlesnake venom, and how Fab fragment antivenom exhibits an unexpected property. Moreover, applicant contends that the rebuttal evidence relates to objective indicia of nonobviousness, and that the Board erred as a matter of law by failing to consider that evidence.

The Director of the PTO responds that the Board correctly determined that the claimed composition was prima facie obvious over Sullivan in view of Coulter. The Director asserts that all the limitations of claim 40 are taught by Sullivan and Coulter and that the motivation to combine those references is found in the references themselves and the knowledge of those skilled in the art. According to the Director, the amendments to claim 40 merely relate to the use of the claimed product and do not render the claim patentable because a new use of an obvious composition is not patentable. The Director also submits that the Board did consider the declarations and correctly gave them no weight because they only relate to the use of the claimed composition. The Director also contends that applicant's argument as to secondary considerations such as unexpected results and commercial success is being raised for the first time on appeal and should be deemed waived.

We agree with applicant that the Board improperly failed to consider the rebuttal evidence and we therefore vacate the Board's decision and remand for the Board to consider the declarations. It is well settled that the PTO "bears the initial burden of

presenting a prima facie case of unpatentability. . . . However, when a prima facie case is made, the burden shifts to the applicant to come forward with evidence and/or argument supporting patentability." In re Glaug, 283 F.3d 1335, 1338 (Fed. Cir. 2002). Rebuttal evidence is "merely a showing of facts supporting the opposite conclusion." In re Piasecki, 745 F.2d 1468, 1472 (Fed. Cir. 1984). Evidence rebutting a prima face case of obviousness can include: "evidence of unexpected results," Pfizer, Inc. v. Apotex, Inc., 480 F.3d 1348, 1369 (Fed. Cir. 2007), evidence "that the prior art teaches away from the claimed invention in any material respect," In re Peterson, 315 F.3d 1325, 1331 (Fed. Cir. 2003), and evidence of secondary considerations, such as commercial success and long-felt but unresolved needs, WMS Gaming, Inc. v. Int'l Game Tech., 184 F.3d 1339, 1359 (Fed. Cir. 1999). When a patent applicant puts forth rebuttal evidence, the Board must consider that evidence. See In re Soni, 54 F.3d 746, 750 (Fed. Cir. 1995) (stating that "all evidence of nonobviousness must be considered when assessing patentability"); In re Sernaker, 702 F.2d 989, 996 (Fed. Cir. 1983) ("If, however, a patent applicant presents evidence relating to these secondary considerations, the board must always consider such evidence in connection with the determination of obviousness.").

For purposes of this appeal, we assume that the Board established a prima facie case of unpatentability under § 103. There was no showing of unpatentability under § 102, as the subject matter of claim 40 was not described in either Sullivan or Coulter. We accept, however, that a prima facie case of obviousness was established because Sullivan teaches whole antibodies for use against rattlesnake venom and Coulter teaches using Fab fragments to detect venom of a different snake. It was not

unreasonable for one skilled in the art of snake venom to consider that a Fab fragment of a whole antibody that neutralizes one type of venom might be used to neutralize the venom of another species. See KSR Int'l Co. v. Teleflex Inc., 550 U.S. __, 2007 WL 1237837, at *13 (2007) (stating that "if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill").

Accepting that there was a prima facie obviousness case, however, there was rebuttal evidence. While the Director argues that that evidence only relates to use of an obvious composition, that is incorrect. Whether the composition would have been obvious cannot be determined without considering evidence attempting to rebut the prima facie case.

We therefore turn our attention to the Board's consideration, or lack thereof, of the rebuttal evidence submitted by applicant. Upon our review of the record, we find that there were three pieces of evidence in the record that the applicant submitted to the PTO to rebut a prima facie finding of obviousness. First, in response to the examiner's first Office Action that rejected the originally filed claims, applicant relied upon and submitted a declaration by Dr. Damon Smith, an expert involved in developing antivenoms for different snake species. That declaration discusses the state of the prior art for antivenoms and discusses why, since 1969, the only commercially available antivenom products included either intact IgG or $F(ab)_2$ fragments. The declaration further discusses why those skilled in the art would not have expected Fab fragments to

effectively neutralize venom. That declaration therefore is relevant as evidence that the prior art taught away from the claimed invention.

The second piece of rebuttal evidence submitted to the PTO is a declaration by one of the inventors, Dr. John B. Sullivan. After the claims were finally rejected, applicant filed a continuation application in March 1995 and filed the second declaration by Dr. Sullivan. That declaration also discusses why those having ordinary skill in the art would not have expected Fab fragments to be useful as antivenoms. The declaration extensively explains the unique properties of whole antibodies and $F(ab)_2$ fragments, including that the body does not clear them as quickly as it clears Fab fragments. Because venom remains in the body for an extended period of time and the body quickly clears Fab fragments, the declaration discusses why experts did not experiment with Fab fragments as an antivenom. Also, the declaration states that the success of equine-derived antivenom containing IgG results from its possessing an extra disulfide bond that allows IgG to bind to repeating protein antigens. A Fab fragment does not have such a bond, and the experts believed that Fab fragment antivenom would therefore not negate the toxic effects of venom. The declaration further explains that the inventors conducted experiments and clinical trials using Fab fragment antivenom and discovered, contrary to what the experts had believed, that it effectively neutralizes the toxicity of rattlesnake venom, while also decreasing the occurrence of adverse immune reactions in humans. This inventor's declaration thus describes an unexpected property or result from the use of Fab fragment antivenom.

The third piece of rebuttal evidence submitted by the applicant is a declaration by Dr. Russell, one of the inventors. The first version of this declaration appears to have

been submitted after the first Office Action of the continuation application. The examiner considered it but found it unpersuasive to overcome a prima facie case of unpatentability. That declaration further discusses why those having ordinary skill in the art expected antivenoms comprising Fab fragments to fail.

The Board failed to consider each of these declarations. The Board stated in a footnote that the declarations of record relate only to the use of the claimed composition as an antivenom, and thus the Board expressly declined to give any meaningful consideration to them. Sullivan, No. 2006-0220, slip op. at 13 n.7. As stated above, when an applicant puts forth relevant rebuttal evidence, as it did here, the Board must consider such evidence. The claimed composition cannot be held to have been obvious if competent evidence rebuts the prima facie case of obviousness. By failing to consider the submitted evidence, the Board thus committed error. That is not to suggest that the Board's finding of obviousness must be overturned in light of the evidence; rather, the Board must give the declarations meaningful consideration before arriving at its conclusion.

Moreover, the Board was mistaken to assert that the declarations only relate to the use of the claimed composition. The declarations do more than that; they purport to show an unexpected result from use of the claimed composition, how the prior art taught away from the composition, and how a long-felt need existed for a new antivenom composition. While a statement of intended use may not render a known composition patentable, the claimed composition was not known, and whether it would have been obvious depends upon consideration of the rebuttal evidence. Had the Board

considered or reviewed the declarations in any meaningful way, it might have arrived at a different conclusion than it did.

Furthermore, the Board's focus on the intended use of the claimed composition misses the mark. The Board cites In re Zierden, 411 F.2d 1325 (CCPA 1969), for the proposition that a statement of a new use for an otherwise old or obvious composition cannot render a claim to the composition patentable. In that case, applicant conceded that his composition was distinguished from the composition disclosed in a prior art patent only by the statement of intended use. Our predecessor court held that that intended use for the known composition could not render the claim patentable. In this case, applicant does not concede that the only distinguishing factor of its composition is the statement of intended use and, in fact, extensively argues that its claimed composition exhibits the unexpected property of neutralizing the lethality of rattlesnake venom while reducing the occurrence of adverse immune reactions in humans. Such a use and unexpected property cannot be ignored. See In re Papesch, 315 F.2d 381, 391 (CCPA 1963) ("From the standpoint of patent law, a compound and all of its properties are inseparable; they are one and the same thing. . . . There is no basis in law for ignoring any property in making such a comparison."). The issue here is not whether a claim recites a new use, but whether the subject matter of the claim possesses an unexpected use. That unexpected property is relevant, and thus the declarations describing it should have been considered by the Board.

Finally, we reject the Director's argument that the applicant for the first time on appeal argues secondary considerations, such as unexpected results, and therefore that the argument should be considered waived. As discussed above, the applicant

submitted the declarations to the examiner during prosecution, and the declarations extensively describe the unexpected property of Fab fragments neutralizing the lethality of rattlesnake venom and how this was not known in the prior art. Thus, we do not consider that argument to have been waived.

CONCLUSION

For the foregoing reasons, we vacate the Board's decision and remand for the Board to consider the declarations of record.

VACATED and REMANDED