United States District Court,
D. Delaware.

GLAXO WELLCOME INC,
Plaintiff.
v.
GENENTECH, INC,
Defendant.

No. CIV.A.99-335-RRM

July 28, 2000.

Owner of patent for method of stabilizing antibodies against degradation sued competitor for infringement. On defendant's motion for summary judgment on issue of infringement, the District Court, McKelvie, J., construed claims and held that fact issue existed as to whether competitor's products were infringing.

Motion denied.

5,545,403, 5,545,405, 5,654,403, 5,792,838. Cited.

James M. Mulligan, Jr., Connolly Bove Lodge & Hutz, LLP, Wilmington, DE, Stephen B. Judlowe, Brian P. Murphy,Robert G. Gibbons, Jason A. Lief, Richard J. McCormick, Hopgood, Calimafde, Kalil & Judlowe, LLP, New York City, for plaintiff.

Philip A. Rovner, Potter Anderson & Corroon LLP, Wilmington, DE, Leora Ben-Ami, Jason E. Kidd, Patricia A. Carson, Kurt M. Rogers, Clifford, Chance, Rogers & Wells LLP, New York City, for defendant.

OPINION

McKELVIE**, District Judge.**

This is a patent case. Plaintiff Glaxo Wellcome Inc. ("Glaxo") is a North Carolina corporation with its principal place of business in Research Triangle Park, North Carolina. Glaxo is a subsidiary of Glaxo Wellcome plc, a company based in the United Kingdom. Glaxo owns U.S. Patent Nos. 5,654,403 and 5,792,838 (collectively, the "Smith patents") and U.S. Patent Nos. 5,545,403 and 5,545,405 (collectively, the "Page patents"). Defendant Genentech, Inc. is a Delaware corporation with its principal place of business in San Francisco, California.

On May 28, 1999, Glaxo filed a complaint alleging that Genentech infringes one or more claims of the Smith and Page patents. Genentech answered the complaint on July 19, 1999, denying Glaxo's allegation of infringement, asserting affirmative defenses of invalidity and unenforceability, and seeking a declaratory

judgment of noninfringement, invalidity and unenforceability. On March 16, 2000, the court granted Genentech's motion to amend its pleading to assert additional counterclaims for invalidity and unenforceability of the Smith patents.

On March 31, 2000, Genentech moved for a partial summary judgment that it does not infringe the claims of the Smith patents. In response, Glaxo moved for a continuance pursuant to Fed.R.Civ.P. 56(f), arguing that it needed additional discovery to respond to Genentech's motion. During a teleconference on April 24, 2000, the court directed Glaxo to file an answering brief and stated that it would consider Glaxo's discovery request in the context of arguments made in opposition to the motion for summary judgment. The parties have completed briefing on the motion and the court heard oral argument on May 8, 2000. This is the court's decision on the motion for summary judgment.

I. *FACTUAL AND PROCEDURAL BACKGROUND*

The court draws the following facts from the affidavits and documents submitted by the parties and from the prosecution histories of the patents at issue.

A. *General Description of the Technology*

The patents at issue relate to technology for stabilizing antibodies against degradation. Antibodies or immunoglobulins are proteins made by the human body's immune cells to defend against disease. The body makes specific antibodies in response to different disease-causing agents called antigens. The body produces specialized antibodies to defend against particular antigens. The antibodies bind to their complementary antigens and initiate immune attacks that destroy the antigens.

Antibodies have a shape that is typically depicted graphically as a "Y." Four protein chains combine to create a single antibody. Two long chains called "heavy chains" correspond to the entire length of the "Y," while two shorter chains called "light chains" correspond to the arms of the "Y." The tips of the "Y," called complementarity-determining regions ("CDR"), are responsible for binding to the antigen.

Humans and other living organisms store information needed to produce proteins such as antibodies in their molecules of deoxyribonucleic acid ("DNA"). Using genetic engineering and recombinant DNA technology, scientists are able to create identical copies of specific antibodies that react with particular antigens. Antibodies created this way are referred to as "monoclonal antibodies."

Scientists identify the strands of DNA containing the code for particular antibodies and introduce these DNA strands into living cells called "host cells." Commonly used host cells include bacterial or mammalian cells which can be reproduced in the laboratory. The host cells are reproduced in a nutrient medium which generally contains an energy source and the vitamins and minerals needed to support the cells' metabolic process. Metal ions are often added to the cell culture medium because metal ions improve the growth of the host cells.

As the host cells containing the artificially-introduced DNA grow and replicate in the culture medium, the cells produce the desired antibody along with other proteins normally made by the cells. The desired antibody is then extracted from the host cells and purified through a series of steps which enrich the antibody by selectively removing undesired material. Scientists have found that the metal ions which promote cell growth in the host cells have the detrimental effect of degrading the antibodies when they are removed from the host cells. To improve the stability of monoclonal antibodies, scientists attempt to remove

the metal ions during antibody purification.

B. ***The Smith Patents***

Marjorie Smith and Valentina Riveros-Roja are two scientists at Glaxo who set out to improve the stability of monoclonal antibodies. Smith and Riveros-Roja discovered a process for stabilizing an immunoglobulin composition containing copper ions by adding a chelator of copper ions. In 1994 and 1995, Smith and Riveros-Roja submitted applications to the U.S. Patent and Trademark Office ("PTO") for two patents based on their invention. In the first application for U.S. Patent No. 5,654,403 (the '403 patent), the inventors claim a stabilized immunoglobulin composition containing copper ions and an amount of a chelator of copper ions sufficient to bind the copper ions present in the composition. In the second application for U.S. Patent No. 5,792,838 (the '838 patent), the inventors claim the method for stabilizing an immunoglobulin composition containing copper ions by adding a chelator of copper ions.

C. ***Prosecution History of*** the '403 Patent

1. ***Application of April 28, 1994***

On April 28, 1994, inventors Smith and Riveros-Rojas applied for a patent for a stabilized immunoglobulin composition containing copper ions and a chelator of copper ions. As it was originally submitted, the application for the '403 patent contains 21 claims. The application includes claims for the process that were later withdrawn and re-submitted in a separate application for the '838 patent.

In the patent specification, the applicants explain that their invention is based on the "surprising discovery that trace amounts of copper ($Cu^{//}$) have a destabilizing effect on immunoglobulin molecules on storage and that this effect can be eliminated by formulating the immunoglobulin with a suitable chelator of copper ions." The specification further provides:

It has also surprisingly been found that a presence of a chelator of copper ions may have a stabilizing effect on the immunoglobulin molecule even when the immunoglobulin does not contain amounts of copper which are detectable by conventional techniques such as atomic absorption spectroscopy. Whilst not wishing to be bound by any particular theory, it may be that the presence of copper ions in amounts below the detectable limits of techniques such as atomic absorption spectroscopy still has a destabilizing effect on the immunoglobulin molecule which can be eliminated by the addition of a suitable chelating agent.

According to the applicants, a "stabilizing amount of a chelator of copper ions such as EDTA or citrate" is added to the immunoglobulin to ensure that any copper present is bound by the chelating agent and thus rendered ineffective in destabilizing the immunoglobulin. The specification further provides that a "particularly preferred metal ion chelating agent" is ethylenediamine tetraacetic acid ("EDTA").

In the original application, Claim 1 reads as follows:

1. A stabilized immunoglobulin composition comprising at least one immunoglobulin together with a stabilizing amount of a chelator of copper ions.

2. ***Office Action of October 5, 1994***

On October 5, 1994, the examiner issued a restriction requirement because the claims were directed to more

than one invention. According to the examiner, Claims 1-15 were drawn to a stabilized immunoglobulin composition, while Claims 16-21 were drawn to a process for enhancing the stability of an immunoglobulin. The examiner stated that the stabilized immunoglobulin composition in the first invention would not suggest the stabilizing process in the second invention. Therefore, the examiner directed the applicants to elect a single invention.

The examiner further stated that regardless of which invention the applicants elected to pursue, they were required under 35 U.S.C. s. 121 to elect a single disclosed species to which their claims would be restricted if no generic claim was finally held allowable. FN1 According to the examiner, if the applicants pursued Claims 1-15, they were required to elect a specific antibody stabilized by a specific chelator of copper ions. If the applicants pursued Claims 16-21, they were required to elect a specific purified immunoglobulin.

FN1. 35 U.S.C. s. 121 provides in pertinent part:
If two or more independent and distinct inventions are claimed in one application, the Director may require the application to be restricted to one of the inventions.

3. ***Response of November 8, 1994***

On November 8, 1994, the applicants submitted a response to the PTO's restriction requirement. The applicants elected to prosecute Claims 1-15 and they elected anti-CD4 as the specific antibody for those claims.

4. ***Rejection of January 26, 1995***

On January 26, 1995, the examiner rejected Claims 1-15 and withdrew Claims 16-21 from further consideration. The examiner stated that the claimed "chelator of copper ions" was not properly enabled under 35 U.S.C. s. 112, para. 1. FN2 According to the examiner, "[b]esides EDTA and sodium citrate, the specification does not provide any guidance as to what other chelator of copper ions can be used to stabilize an immunoglobulin ...." The examiner also objected to the claimed "chelator of copper ions" under 35 U.S.C. s. 112, para. 2 as indefinite and ambiguous.FN3

FN2. 35 U.S.C. s. 112, para. 1 provides:
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.

FN3. 35 U.S.C. s. 112, para. 2 provides:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The examiner further rejected the claims as obvious under 35 U.S.C. s. 103 in light of a number of prior art

references including U.S. Patent No. 5,367,060 (the '060 patent). FN4 The '060 patent issued to Genentech as assignee of inventors Richard L. Vandlen and William E. Holmes on November 22, 1994. According to the examiner, the '060 patent teaches that therapeutic formulations of antibodies can be prepared for storage by mixing the antibodies with stabilizers such as EDTA or citrate in the form of lyophilized cake or aqueous solutions. Therefore, the examiner wrote that "it would have been obvious to one of ordinary skill in the art at the time the [Glaxo] invention was made to mix the chelator of copper ions with the antibody with the expectation that the copper ions attached to the antibody would be removed by the chelator and that the antibody would be stabilized."

FN4. 35 U.S.C. s. 103(a) provides:
A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

5. ***Amendment of April 26, 1995***

On April 26, 1995, the applicants submitted an amendment to the PTO. The applicants canceled Claims 1-21 from the original application and substituted 17 new claims numbered 22-38. In Claim 22, which later issued as Claim 1 of the '403 patent, the applicants claim a composition comprising immunoglobulin and an amount of a chelator of copper ions sufficient to bind to copper ions present in the composition. Claim 22 reads as follows:

22. A stabilized immunoglobulin composition comprising an IgG_1 immunoglobulin together with an amount of a chelator of copper ions sufficient to bind copper ions present in the solution and protect the immunoglobulin from degradation by the copper ions.

In response to the examiner's objection that the claimed "chelator of copper ions" was not enabled, the applicants stated that no objective evidence was presented to show that it would require more than routine experimentation for one of ordinary skill in the art to determine which chelators are best suited for use in the invention. The applicants argued that "chelator of copper ions" was enabled because the specification provides specific examples of embodiments within the class.

The applicants also disagreed with the examiner's decision that the claimed "chelator of copper ions" was indefinite and ambiguous. According to the applicants, "[c]opper chelators have been known in the prior art for many years and one of ordinary skill in the art would have no difficulty selecting a compound to add to an antibody composition to chelate copper ions present in the composition."

In response to the examiner's rejection of the claims for obviousness in light of the '060 patent and other prior art references, the applicants suggested that their invention was distinguishable from the prior art in part based on the presence of copper ions in the immunoglobulin composition. The applicants wrote:

There is no suggestion in the '060 patent that [chelators] be used in compositions of HRG or HRG antibodies to bind copper ions present in the compositions. More specifically, there is no discussion at all in the patent that copper ions may be present in the antibody compositions, that the presence of even minute

amounts of copper in an antibody composition can cause the degradation of the antibody during storage or that this degradation can be avoided by adding to such compositions a chelator of copper ions in an amount sufficient to bind the copper ions present in the composition.

According to the applicants, none of the prior art references, taken alone or in combination, suggested that copper ions could degrade immunoglobulins, or that immunoglobulins could be stabilized with a chelator of copper ions. The applicants stated that "[t]he examiner's statement that the present invention differs from the primary reference 'only' by the use of the chelator of copper ions to stabilize the antibody is hardly a trivial distinction, as this was the very focus of the present invention." Therefore, the applicants argued that the prior art references cited by the examiner did not render their invention obvious under 35 U.S.C. s. 103.

6. ***Final Rejection of July 10, 1995***

On July 10, 1995, the examiner sent the inventors a final action letter canceling Claims 1-21 and rejecting Claims 22-36.FN5 The examiner rejected Claims 22-36 for the same reasons that she had previously rejected the corresponding Claims 1-15.

FN5. The examiner also withdrew Claims 37 and 38. The examiner stated that the Claims 37 and 38 were distinct from the invention because the claims were equivalent to cancelled, non-elected Claims 18 and 19.

The examiner maintained her objection to the claimed "chelator of copper ions" in Claims 22 and 28 (previously Claims 1 and 11), for lack of enablement. After considering the applicants' arguments the examiner wrote, "the fact remains that only EDTA and citrate ion are disclosed in the specification as the chelator of copper ions." According to the examiner, it would take undue experimentation to determine which chelators of copper ions could be used in the invention. The examiner also maintained the objection to "chelator of copper ions" as indefinite under 35 U.S.C. s. 112, para. 2.

Furthermore, the examiner rejected Claims 22-36 as obvious in light of the '060 patent and other prior art references. The examiner stated that the '060 patent teaches that a therapeutic formulation of HRG antibody can be prepared for storage by mixing the antibody with stabilizers such as EDTA and citrate. Among the stabilizers listed in the '060 patent, the examiner stated that only citrate and EDTA are chelating agents. The examiner wrote, "[s]ince citrate and EDTA are chelating agents, it is obvious to one skilled in this art to use said chelating agents as stabilizers to remove any metals that are bound by said chelating agents including copper ions present in the immunoglobulin composition."

7. ***Interview Summary Record of November 9, 1995***

On November 9, 1995, the examiner issued an Interview Summary Record from her interview with the applicants on that day. The Interview Summary Record states: "We agreed that the s. 112, para. 1 enablement & scope will be withdrawn. We agreed that an amendment regarding the level of copper and stabilizer in the solution would probably overcome the s. 103 objections."

8. ***Response of January 11, 1996***

On January 11, 1996, the applicants submitted an amendment to the PTO. The applicants amended Claim 22 "to make explicit that which was implicit in the claim before, namely, that the composition of IgG_1 immunoglobulin also contains copper ions." Claim 22, as submitted in the proposed amendment, reads as

follows, with the underlining and brackets indicating added and retracted language, respectively:

22. *In an* [A stabilized] immunoglobulin composition *of* [comprising] IgG_1 immunoglobulin *containing copper ions in an amount sufficient to degrade the immunoglobulin, wherein the improvement comprises the addition of* [together with] an amount of a chelator of copper ions sufficient to bind *the* copper ions present in the [solution] *composition* and protect the immunoglobulin from degradation by the copper ions *and thus stabilize the* IgG_1 *composition*.

The applicants also added a new Claim 39, which later issued as Claim 16 of the '403 patent. As it was submitted in the amendment, Claim 39 reads as follows:

39. A stabilized immunoglobulin composition comprising an IgG_1 immunoglobulin and copper ions, wherein the copper is present in an amount sufficient to degrade the immunoglobulin, together with an amount of chelator of copper ions sufficient to bind the copper ions present in the composition and protect the immunoglobulin from degradation by the copper ions.

The applicants stated that the claimed composition had sufficient amounts of chelator to bind "trace amounts of copper" to prevent the degradation of the immunoglobulin that the copper would otherwise cause. According to the applicants, such compositions are not rendered obvious by the teachings of the '060 patent or the other prior art references cited by the examiner.

9. ***Notice of Allowability***

On March 19, 1996, the examiner allowed Claims 22-36 and Claim 39 of the application as amended. The claims were re-numbered 1-16.

10. ***Issuance of*** the '403 Patent

On August 5, 1997, the PTO issued the 403 patent to Glaxo as assignee of the inventors, Marjorie Smith and Valentina Riveros-Roja.FN6 The '403 patent is entitled "Immunoglobulins Stabilized with a Chelator of Copper Ions."

FN6. The '403 patent lists Burroughs Wellcome Co. as assignee. Burroughs Wellcome merged with Glaxo Inc. in 1995 to form Glaxo Wellcome Inc.

D. ***Prosecution History of*** the '838 Patent

1. ***Application of June 5, 1995***

On June 5, 1995, Smith and Riveros-Rojas applied for a patent for a method for stabilizing an immunoglobulin composition containing copper ions by adding a chelator of copper ions. As noted above, certain claims of this application were included together with the composition claims in the application for the '403 patent. As a result, the original application for the '838 patent is virtually identical to the application for the '403 patent. Because the application for the '838 patent is a continuation of the application for the '403 patent, the patents share a common specification.

In the original application, Claim 11 reads as follows:

11. Use of a chelator of copper ions to stabilize an immunoglobulin against degradation on storage.

2. ***Preliminary Amendment of July 22, 1995***

On July 22, 1995, the applicants submitted a preliminary amendment to the PTO. The applicants modified several claims in the original application to change them from a "use" claim format to a "method" claim format. For example, Claim 11 was amended as follows, with the underlining and brackets indicating added and retracted language, respectively:

11. (amended) [Use of a chelator of copper ions to stabilize] *A method for stabilizing* an immunoglobulin against degradation on storage *which comprises adding to said immunoglobulin a chelator of copper ions in an amount sufficient to stabilize said immunoglobulin*.

3. ***Preliminary Amendment of June 20, 1996***

On June 20, 1996, before the examiner considered the application for the '838 patent, the applicants filed a second preliminary amendment. The applicants canceled Claims 1-10 and amended Claim 11 to state that the immunoglobulin composition contains "copper ions in an amount sufficient to degrade the immunoglobulin." Claim 11, as amended, reads as follows, with the underlining and brackets indicating added and retracted language, respectively:

11. (twice amended) A method for stabilizing *against degradation on storage* an immunoglobulin *composition of IgG_1 which contains copper ions in an amount sufficient to degrade the immunoglobulin* [against degradation on storage] which comprises adding to said immunoglobulin a chelator of copper ions in an amount sufficient to stabilize said immunoglobulin.

4. ***Office Action of October 2, 1996***

On October 2, 1996, the examiner canceled Claims 1-10 and issued a restriction requirement for Claims 11-21. According to the examiner, Claims 11-21 were directed to more than one invention. Claims 11-15 and 18-21 were drawn to a method of stabilizing immunoglobulin solutions against copper ion degradation and a composition of immunoglobulins substantially free of copper ions. Claims 16-17 were drawn to a second method for stabilizing a immunoglobulin. The examiner directed the applicants to elect a single invention.

5. ***Response of December 2, 1996***

On December 2, 1996, the applicants submitted a response to the examiner's restriction requirement. The applicants elected to pursue Claims 11-15 and 18-21, and stated that the non-elected matter would be deleted.

6. ***Preliminary Amendment of December 13, 1996***

On December 13, 1996, the applicants submitted a third preliminary amendment to add new Claims 22 and 23.

7. ***Preliminary Amendment of April 9, 1997***

On April 9, 1997, the applicants submitted a fourth preliminary amendment to the PTO. The applicants canceled Claim 11 and added a new Claim 24. In the amendment, Claim 24, which later issued as Claim 1 of the '838 patent, reads as follows:

24. A method of making a stabilized IgG_1 composition comprising adding to a starting composition comprising:

i) IgG_1 and

ii) copper ions in an amount sufficient to degrade said IgG_1, an amount of a chelator of copper ions sufficient to stabilize said IgG_1 against copper ion-mediated degradation, so that said stabilization IgG_1 composition is made.

8. ***Interview Summary of May 27, 1997***

On May 27, 1997, the examiner issued a Interview Summary of his May 21, 1997 interview with the applicants. The Interview Summary states: "Applicant consults regarding claim language. Examiner indicated a statement would be made in reasons for allowance regarding starting composition. Applicant agreed with proposed statement regarding starting composition."

9. ***Notice of Allowability***

On May 27, 1997, the examiner allowed Claims 24 and 12-15 of the application, as amended. The claims were re-numbered 1-5. In a statement of reasons for allowance, the examiner stated that "the method claims of this application are allowable given the allowance of the ['403 patent] claiming the compounds. The starting composition of Claim 1 is considered to comprise IgG_1 class antibodies and an amount of copper sufficient to degrade the IgG_1 antibodies."

10. ***Issuance of*** the '838 Patent

On August 11, 1998, the PTO issued the '838 patent to Glaxo as assignee of the inventors Smith and Riveros-Rojas. The '838 patent is entitled "Method for Stabilizing Immunoglobulin Compositions."

E. ***The Lawsuit***

On May 28, 1999, Glaxo filed a complaint in this court alleging that Genentech's cancer drugs, Herceptin and Rituxan, infringe one or more claims of the '403 and '838 patents.FN7 Genentech answered the complaint on July 19, 1999, denying Glaxo's allegation of infringement, asserting affirmative defenses of invalidity and unenforceability, and seeking a declaratory judgment of noninfringement, invalidity and unenforceability. On January 31, 2000, Genentech moved to amend its pleading to assert additional counterclaims for invalidity and unenforceability of the '403 and '838 patents. On March 16, 2000, the court granted Genentech's motion.

FN7. As noted above, Glaxo's complaint also alleges that Genentech infringes one or more claims of the Page patents. The present motion for summary judgment, however, is limited to the Smith patents.

On March 31, 2000, Genentech moved for a partial summary judgment that it does not infringe the claims of the '403 and '838 patents. According to Genentech, the claims of the '403 and '838 patents require an immunoglobulin composition containing (1) copper ions in an amount sufficient to degrade the immunoglobulin; and (2) a chelator of copper ions. Genentech contends that summary judgment is appropriate in this case because Glaxo has not proved that Herceptin and Rituxan contain either of these two limitations. In support of its motion for summary judgment, Genentech submitted the affidavit of Dr. Ronald T. Borchardt in which he states that the use of histidine and citrate buffers in the accused products does not prove that copper ions are present. In addition, Borchardt states that histidine does not act as a chelator of copper ions in Herceptin.

In response to Genentech's motion for summary judgment, Glaxo moved for a continuance pursuant to Fed.R.Civ.P. 56(f), arguing that it needed additional discovery to respond to Genentech's motion.FN8 During a teleconference on April 24, 2000, the court directed Glaxo to submit its answering brief in opposition to the motion for summary judgment. The court stated that it would consider Glaxo's discovery request in the context of arguments made in opposition to the motion for summary judgment.

FN8. Fed.R.Civ.P. 56(f) provides:
Should it appear from the affidavits of a party opposing the motion that the party cannot for reasons stated present by affidavit facts essential to justify the party's opposition, the court may refuse the application for judgment or may order a continuance to permit affidavits to be obtained or depositions to be taken or discovery to be had or may make such other order as is just.

On April 21, 2000, Glaxo submitted its answering brief in opposition to Genentech's motion for summary judgment. Glaxo contends that Herceptin and Rituxan infringe the '403 and '838 patents because both accused products contain all of the claim limitations of the patents. Glaxo also argues that summary judgment is not appropriate because there are genuine issues of material fact concerning infringement. Glaxo submitted the affidavit of Professor Ralph A. Bradshaw in which he states that Herceptin and Rituxan "almost certainly contain copper ions in amounts sufficient to degrade the IgG_1 antibodies ...." Bradshaw also states that citrate and histidine, which are found in Rituxan and Herceptin respectively, are chelators of copper ions.

On May 5, 2000, Glaxo filed a supplementary opposition to the motion for summary judgment in which it submitted the results of laboratory tests of Herceptin and Rituxan. The affidavit of Dr. Robert Samuel Houk states that samples of Rituxan and Herceptin contained at least 10 parts per billion of copper. On the same day, Genentech submitted a letter to the court arguing that Glaxo's test results should not be considered for purposes of the motion for summary judgment because they were not included in Glaxo's answering brief.

II. ***DISCUSSION***

[1] [2] To determine whether Genentech is entitled to a summary judgment that its accused products do not infringe the '403 and '838 patents, the court performs a two-step analysis. Markman v. Westview Instruments, Inc., 52 F.3d 967, 976 (Fed.Cir.1995). First, the court construes the claims of the patents. Id. at 976. Second, the court compares the properly construed claims of the patents to the accused products to determine whether all of the limitations of the claims are present. *Id*. Where the parties do not dispute relevant facts regarding the accused products, but disagree over which of two possible meanings of a claim

is the proper one, the question of patent infringement collapses to one of claim construction and is thus amenable to summary judgment. Athletic Alternatives, Inc. v. Prince Mfg., Inc., 73 F.3d 1573, 1578 (Fed.Cir.1996).

A. *Claim Construction of the Smith Patents*

[3] Claims are construed from the vantage point of a person of ordinary skill in the art at the time of the invention. Markman, 52 F.3d at 986. In construing a claim, a court looks to the intrinsic evidence of record, namely, the claims, the specification and the prosecution history. Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1309 (Fed.Cir.1999).

[4] [5] The starting point in claim construction is the words of the claims themselves. *Id*. Words in the claims are generally given their ordinary and customary meaning unless a patentee clearly sets forth a different definition in the specification or file history. Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed.Cir.1996). Thus, the claims must also be read in view of the specification, of which they are a part. Markman, 52 F.3d at 979. As the Federal Circuit has stated:

The specification contains a written description of the invention which must be clear and complete enough to enable those of ordinary skill in the art to make and use it. Thus, the specification is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term.

Vitronics, 90 F.3d at 1582. In addition, the prosecution history is often of critical significance in determining the meaning of the claims. *See* Markman, 52 F.3d at 980 ("The prosecution history limits the interpretation of claim terms so as to exclude any interpretation that was disclaimed during prosecution.").

Although the Federal Circuit has held that claims should be read in view of the specification and the prosecution history, the court has repeatedly cautioned against limiting the scope of a claim to the preferred embodiment or specific examples disclosed in the specification. *See, e.g.,* Ekchian v. Home Depot, Inc., 104 F.3d 1299, 1303 (Fed.Cir.1997); Intervet America, Inc. v. Kee-Vet Laboratories, Inc., 887 F.2d 1050, 1053 (Fed.Cir., 1989) ("[L]imitations appearing in the specification will not be read into claims, and ... interpreting what is meant by a word in a claim 'is not to be confused with adding an extraneous limitation appearing in the specification, which is improper.' ") (citation omitted).

In this case, Glaxo and Genentech disagree over the proper construction of two phrases that are used in the claims of the '403 and '838 patents. First, the parties disagree over the construction of "copper ions in an amount sufficient to degrade." Second, the parties disagree over the meaning of "chelator of copper ions."

1. "*copper ions in an amount sufficient to degrade*"

[6] Genentech contends that the phrase "copper ions in an amount sufficient to degrade" requires a specific numerical amount of copper ions. Genentech argues that Glaxo added this language to overcome the examiner's rejections for obviousness in light of Genentech's own patent, the '060 patent. Genentech cites the Interview Summary Record of November 9, 1995 in which the examiner wrote, "[w]e agreed that an amendment regarding the level of copper and stabilizer in the solution would probably overcome the s. 103 objections." During oral argument, counsel for Genentech argued that the claims require a specific level of copper ions based on the prosecution history.

Glaxo counters that the phrase "copper ions in an amount sufficient to degrade" should be construed according to its plain meaning. According to Glaxo, the specification and the prosecution history contain numerous references to the "trace" or "minute" amounts of copper ions that have a destabilizing effect on immunoglobulins. Therefore, Glaxo argues that the court should construe "copper ions in an amount sufficient to degrade" to mean enough copper to degrade whether or not the copper is detectable.

The specification of the '403 and '838 patents does not define "copper ions in an amount sufficient to degrade" as a numerical amount or a level of copper ions. Rather, the specification states that "it may be that the presence of copper ions in amounts below the detection limits of techniques such as atomic absorption spectroscopy still has a destabilizing effect on the immunoglobulin which can be eliminated by the addition of a suitable chelating agent." Glaxo correctly notes that the specification and the prosecution history contain a number of references to "trace" or "minute" amounts of copper ions.

The phrase at issue was apparently added to the claims after the applicants and the examiner agreed during an interview that an "amendment regarding the level of copper" would probably overcome the obviousness rejection. In the amendment that followed, the applicants stated that the phrase, copper ions in an amount sufficient to degrade, "makes explicit that which was implicit in the claim before, namely, that the composition of IgG1 immunoglobulin also contains copper ions." The applicants also stated that the claimed compositions comprise sufficient amounts of copper ion chelator to bind to the "trace amounts of copper" and thus prevent degradation.

After reviewing the specification and the prosecution history, the court finds that the phrase, "copper ions in an amount sufficient to degrade," should be construed according to its plain meaning. *See* Vitronics, 90 F.3d at 1582 (holding that words in the claims are generally given their ordinary and customary meaning unless a patentee clearly sets forth a different definition in the specification or file history). The inventors did not set forth an alternative definition of the phrase in the specification or in the prosecution history. Moreover, both the specification and the prosecution history provide support for Glaxo's argument that even small amounts of copper ions are sufficient to degrade. Therefore, the court finds that the phrase "copper ions in an amount sufficient to degrade" requires enough copper ions to degrade.

2. "*chelator of copper ions*"

[7] Genentech argues that the phrase "chelator of copper ions" does not encompass the amino acid histidine. According to Genentech, Glaxo conceded during prosecution that amino acids are not "chelator[s] of copper ions." Genentech points to the examiner's rejection of the claims as obvious in light of the '060 patent. The examiner stated that "[a]mong the various additives listed under column 38 [of the '060 patent], only citrate and EDTA belong to the chelating agents." According to Genentech, the list of additives in the '060 patent includes amino acids. Therefore, if Glaxo believed that amino acids were "chelators of copper ions," Genentech argues that Glaxo had an affirmative duty to bring that to the examiner's attention. Having failed to do so, Genentechargues that "chelator of copper ions" must be construed to exclude amino acids.

Glaxo counters that "chelator of copper ions" should be construed to include histidine. Glaxo argues that it is not estopped from claiming histidine as a "chelator of copper ions" because there were no amendments or arguments made during the patent prosecution regarding the meaning of the phrase. During oral argument, counsel for Glaxo stated that the debate between the applicants and the examiner had nothing to do with whether amino acids were chelators. Rather, counsel argued that the debate had to do with the examiner's rejection for obviousness. Therefore, Glaxo contends that "chelator of copper ions" includes histidine.

The specification of the '403 and '838 patents provides that the immunoglobulin composition contains "a stabilizing amount of a chelator of copper ions such as EDTA or citrate." The specification also states that EDTA is a "particularly preferred metal ion chelating agent." Therefore, it appears that the inventors did not limit the phrase, "chelator of copper ions," to EDTA or citrate.

Furthermore, the prosecution history does not support Genentech's argument that histidine is not "chelator of copper ions." Originally, the examiner objected to the phrase, "chelator of copper ions," for lack of enablement. The inventors never responded to the examiner's statement that the only chelators listed in the '060 patent are citrate and EDTA because the examiner agreed to withdraw her objection to "chelator of copper ions" following the interview with the applicants on November 9, 1995. As a result, the court finds that the phrase, "chelator of copper ions," does not exclude histidine.

B. ***Motion for Summary Judgment***

[8] Genentech argues that the court should grant its motion for a summary judgment of noninfringement of the '403 and '838 patents because Glaxo has failed to show that the Herceptin and Rituxan contain "copper ions in an amount sufficient to degrade." Genentech relies on Borchardt's affidavit in which he states that the presence of histidine and citrate in the accused products does not prove that copper ions are present. In addition, Genentech contends that Herceptin does not contain a "chelator of copper ions," because histidine does not act as a chelator of copper ions in the accused product.

Glaxo contends that Herceptin and Rituxan infringe the '403 and '838 patents because the products contain "copper ions in an amount sufficient to degrade" and "a chelator of copper ions." Glaxo relies on Houk's affidavit which states that Herceptin and Rituxan contain 10 parts per billion of copper, and Bradshaw's affidavit which states that Herceptin and Rituxan "almost certainly contain copper ions in amounts sufficient to degrade the IgG_1 antibodies ...." Glaxo also point to Bradshaw's statement that citrate and histidine are chelators of copper ions.

Summary judgment is appropriate when 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 the moving party is entitled to judgment as a matter of law." Fed.R.Civ.P. 56.

[T]he plain language of Rule 56(c) mandates the entry of summary judgment, after adequate time for discovery and upon motion, against a party who fails to make a showing sufficient to establish the existence of an element essential to that party's case, and on which that party will bear the burden of proof at trial.

Celotex Corp. v. Catrett, 477 U.S. 317, 322, 106 S.Ct. 2548, 91 L.Ed.2d 265 (1986). The moving party bears the initial burden of demonstrating the absence of material issues of fact. Id. at 323, 106 S.Ct. 2548. When deciding a motion for summary judgment, the court views the facts, and all permissible inferences from those facts, in the light most favorable to the non-moving party. Matsushita Elec. Indus. Co. v. Zenith Radio Corp., 475 U.S. 574, 587-88, 106 S.Ct. 1348, 89 L.Ed.2d 538 (1986).

To establish that it is entitled to a summary judgment of noninfringement, Genentech has the burden of demonstrating that the accused products do not contain all of the limitations of the claims either exactly or by substantial equivalent. *See* Glaxo, Inc. v. Novopharm, Ltd., 110 F.3d 1562, 1566 (Fed.Cir.1997). If any of the claim limitations is absent from Genentech's products, there can be no infringement, either literally or

under the doctrine of equivalents. Dolly, Inc. v. Spalding & Evenflo Cos., 16 F.3d 394, 397 (Fed.Cir.1994).

In this case, Glaxo's laboratory test results show that Herceptin and Rituxan contain 10 parts per billion of copper. The parties dispute whether this amount of copper constitutes "copper ions in an amount sufficient to degrade," as required by the '403 and '838 patents. The parties also disagree whether histidine is a "chelator of copper ions." Bradshaw states that histidine is a chelator. Borchardt counters that histidine does not act as a chelator in Herceptin. Because there are genuine issues of material fact, the court will deny Genentech's motion for a summary judgment of noninfringement.

The court will enter an order in accordance with this opinion.

D.Del.,2000.
Glaxo Wellcome Inc. v. Genentech, Inc.

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