United States District Court,
E.D. Texas, Marshall Division.

The ROCKEFELLER UNIVERSITY and Chiron Corporation,
Plaintiffs.
v.
CENTOCOR, INC. and Abbott Laboratories,
Defendants.

Civil Action No. 2:04-CV-168 (TJW)

Oct. 3, 2005.

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MEMORANDUM OPINION AND ORDER

T. JOHN WARD**, District Judge.**

The court issues this memorandum opinion and order to resolve the parties' claim construction disputes.

1. Introduction

The plaintiffs, The Rockefeller University ("Rockefeller") and Chiron Corp. ("Chiron"), claim the defendants, Centocor, Inc. ("Centocor") and Abbott Laboratories ("Abbott"), infringe United States Patent Nos. 6,309,640 ("the '640 patent") and 6,419,927 ("the '927 patent") (collectively "the patents-in-suit"). The parties filed claim construction briefs and the court held a *Markman* hearing. For the reasons explained more fully below, the court construes the disputed terms in accordance with the rulings made in this opinion.

2. Description of the Technology

The present case involves technology related to pharmaceutical compositions containing antibodies and methods of treatment relating to the same. The patents-in-suit generally describe the discovery made by the patentees that a substance produced by mammals as part of the immune response system has certain negative effects associated with serious disease states, and that antibodies that counteract the effects of this substance are useful for medical treatment. The '640 patent is directed to pharmaceutical compositions

containing such antibodies. The '927 patent is directed to methods of treating humans by administering such antibodies.

The patents-in-suit share essentially the same specification. They both claim priority to a series of applications, the earliest of which was filed on September 8, 1981, application no. 06/299,932 ("the "2 application"). That application was succeeded by a continuation in part application filed on February 22, 1982, application no. 06/351,290 ("the '290 application"). Another continuation in part application was filed on September 7, 1982, application no. 06/414,098 ("the '098 application"). All of the subsequently filed applications that ultimately led to issuance of the patents-in-suit were continuation or divisional applications of the '098 application. Thus, the specifications of the patents-in-suit, with the exception of amendments made during prosecution, are the same as that of the '098 application.

The invention described in the patents-in-suit was the result of research conducted by the inventors in the late 1970s and early 1980s to determine the causes of cachexia and shock observed in mammals responding to infection-conditions that could result in death. After observing that these conditions were associated with the suppression of certain anabolic enzymes, the inventors set out to identify what agent(s) within the body mediated the suppression of those enzymes. They also sought to determine whether the same agent(s) also accounted for the anemia commonly observed in mammals afflicted with chronic infection, endotoxemia, cancer, and rheumatoid arthritis, by investigating inhibitory effects on red blood synthesis. The patents-in-suit describe an agent that the inventors identified as having these disease-associated effects.

The patents-in-suit teach that antibodies that neutralize the effects of the mediator can be used in pharmaceutical compositions and administered to patients to treat disease. It is this teaching that is the subject of the pharmaceutical composition claims of the '640 patent and the method of treatment claims of the '927 patent at issue in this case.

3. General Principles Governing Claim Construction

"A claim in a patent provides the metes and bounds of the right which the patent confers on the patentee to exclude others from making, using or selling the protected invention." Burke, Inc. v. Bruno Indep. Living Aids, Inc., 183 F.3d 1334, 1340 (Fed.Cir.1999). Claim construction is an issue of law for the court to decide. Markman v. Westview Instruments, Inc., 52 F.3d 967, 970-71 (Fed.Cir.1995) (en banc), *aff'd,* 517 U.S. 370, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996).

To ascertain the meaning of claims, the court looks to three primary sources: the claims, the specification, and the prosecution history. Markman, 52 F.3d at 979. Under patent law, the specification must contain a written description of the invention that enables one of ordinary skill in the art to make and use the invention. A patent's claims must be read in view of the specification, of which they are a part. *Id*. For claim construction purposes, the description may act as a sort of dictionary, which explains the invention and may define terms used in the claims. *Id*. "One purpose for examining the specification is to determine if the patentee has limited the scope of the claims." Watts v. XL Sys., Inc., 232 F.3d 877, 882 (Fed.Cir.2000).

Nonetheless, it is the function of the claims, not the specification, to set forth the limits of the patentee's claims. Otherwise, there would be no need for claims. SRI Int'l v. Matsushita Elec. Corp., 775 F.2d 1107, 1121 (Fed.Cir.1985) (en banc). The patentee is free to be his own lexicographer, but any special definition given to a word must be clearly set forth in the specification. Intellicall, Inc. v. Phonometrics, 952 F.2d 1384, 1388 (Fed.Cir.1992). And, although the specification may indicate that certain embodiments are preferred, particular embodiments appearing in the specification will not be read into the claims when the claim language is broader than the embodiments. Electro Med. Sys., S.A. v. Cooper Life Sciences, Inc., 34 F.3d 1048, 1054 (Fed.Cir.1994).

This court's claim construction decision must be informed by the Federal Circuit's recent decision in Phillips

v. AWH Corporation, 415 F.3d 1303, 2005 WL 1620331 (Fed.Cir. July 12, 2005) (en banc). In *Phillips,* the court set forth several guideposts that courts should follow when construing claims. In particular, the court reiterated that "the *claims* of a patent define the invention to which the patentee is entitled the right to exclude." 415 F.3d 1303, 2005 WL 1620331 at *4 (emphasis added) (*quoting* Innova/Pure Water, Inc. v. Safari Water Filtration Systems, Inc., 381 F.3d 1111, 1115 (Fed.Cir.2004)). To that end, the words used in a claim are generally given their ordinary and customary meaning. *Id*. at *5. The ordinary and customary meaning of a claim term "is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e. as of the effective filing date of the patent application." *Id*. This principle of patent law flows naturally from the recognition that inventors are usually persons who are skilled in the field of the invention. The patent is addressed to and intended to be read by others skilled in the particular art. *Id*.

The primacy of claim terms notwithstanding, *Phillips* made clear that "the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Id*. Although the claims themselves may provide guidance as to the meaning of particular terms, those terms are part of "a fully integrated written instrument." *Id*. at ----6-7 (*quoting* Markman, 52 F.3d at 978). Thus, the *Phillips* court emphasized the specification as being the primary basis for construing the claims. *Id*. at * *7-8. As the Supreme Court stated long ago, "in case of doubt or ambiguity it is proper in all cases to refer back to the descriptive portions of the specification to aid in solving the doubt or in ascertaining the true intent and meaning of the language employed in the claims." Bates v. Coe, 98 U.S. 31, 38, 25 L.Ed. 68 (1878). In addressing the role of the specification, the *Phillips* court quoted with approval its earlier observations from Renishaw PLC v. Marposs Societa' per Azioni, 158 F.3d 1243, 1250 (Fed.Cir.1998):

Ultimately, the interpretation to be given a term can only be determined and confirmed with a full understanding of what the inventors actually invented and intended to envelop with the claim. The construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction.

Consequently, *Phillips* emphasized the important role the specification plays in the claim construction process.

The prosecution history also continues to play an important role in claim interpretation. The prosecution history helps to demonstrate how the inventor and the PTO understood the patent. Phillips, 415 F.3d 1303, 2005 WL 1620331 at *9. Because the file history, however, "represents an ongoing negotiation between the PTO and the applicant," it may lack the clarity of the specification and thus be less useful in claim construction proceedings. *Id*. Nevertheless, the prosecution history is intrinsic evidence. That evidence is relevant to the determination of how the inventor understood the invention and whether the inventor limited the invention during prosecution by narrowing the scope of the claims.

Phillips rejected any claim construction approach that sacrificed the intrinsic record in favor of extrinsic evidence, such as dictionary definitions or expert testimony. The *en banc* court condemned the suggestion made by Texas Digital Systems, Inc. v. Telegenix, Inc., 308 F.3d 1193 (Fed.Cir.2002), that a court should discern the ordinary meaning of the claim terms (through dictionaries or otherwise) before resorting to the specification for certain limited purposes. *Id*. at ----13-14. The approach suggested by *Texas Digital*-the assignment of a limited role to the specification-was rejected as inconsistent with decisions holding the specification to be the best guide to the meaning of a disputed term. *Id*. According to *Phillips,* reliance on dictionary definitions at the expense of the specification had the effect of "focus[ing] the inquiry on the abstract meaning of words rather than on the meaning of the claim terms within the context of the patent." *Id*. at * 14. *Phillips* emphasized that the patent system is based on the proposition that the claims cover only the invented subject matter. *Id*. What is described in the claims flows from the statutory requirement imposed on the patentee to describe and particularly claim what he or she has invented. *Id*. The definitions

found in dictionaries, however, often flow from the editors' objective of assembling all of the possible definitions for a word. *Id*.

Phillips does not preclude all uses of dictionaries in claim construction proceedings. Instead, the court assigned dictionaries a role subordinate to the intrinsic record. In doing so, the court emphasized that claim construction issues are not resolved by any magic formula. The court did not impose any particular sequence of steps for a court to follow when it considers disputed claim language. *Id*. at * 16. Rather, *Phillips* held that a court must attach the appropriate weight to the intrinsic sources offered in support of a proposed claim construction, bearing in mind the general rule that the claims measure the scope of the patent grant. The court now turns to a discussion of the disputed claim terms.

4. The Asserted Claims

Claim 1 of the '640 patent

1. A pharmaceutical composition comprising an effective amount of a neutralizing antibody to the about 70 kDa mediator substance which results from endotoxin stimulation of macrophages and which has the biological activity of suppression of lipoprotein lipase activity and a pharmaceutically active diluent, adjuvant or carrier.

Claims 1 and 2 of the '927 patent

1. A method for treating an adverse effect in a human of the about 70 kDa mediator substance which results from endotoxin stimulation of macrophages and which has the biological activity of suppression of lipoprotein lipase activity, said method comprising administering an antibody specifically reactive with said about 70 kDa mediator in an amount effective to neutralize suppression of an anabolic enzyme selected from the group consisting of lipoprotein lipase, acetyl coA carboxylase and fatty acid synthetase, said suppression induced by said about 70 kDa mediator.

2. A method for treating an adverse effect in humans of the about 70 kDa mediator substance which results from endotoxin stimulation of macrophages and which has the biological activity of suppression of lipoprotein lipase activity, said method comprising administering an amount of an antibody capable of reducing inhibition of growth and differentiation of erythroid-committed cells wherein said inhibition is induced by said about 70 kDa mediator substance.

5. Analysis of the Disputed Terms

Now that the Court has set out the general technology of the patents-in-suit, the law regarding claim construction, and the asserted claims, the Court will now turn to the more difficult task of determining the appropriate construction for the disputed claim terms.

A. *Antibody*

"Antibody" is a hotly disputed term wherein both parties cite to a Federal Circuit opinion, Chiron Corp. v. Genentech, Inc., 363 F.3d 1247 (Fed.Cir.2004), to support their position. In that case, the Federal Circuit stated:

"[a]n antibody is a protein generated by the immune system that is capable of recognizing and binding to a specific antigen. Described in terms of its structure, an antibody is a Y-shaped protein consisting of four amino acid chains, two heavy and two light. In a simplified model sufficient for this appeal, each antibody has primarily two regions: a variable region and a constant region."

Id. at 1250. It is important to note that the Federal Circuit made clear that it was not construing "antibody" when it made those statements. Claim construction was not at issue on appeal and the "court [did] not reach the question of claim construction." *Id*. at 1257. Thus, while *Chiron v. Genentech* certainly provides some

guidance as to claim construction, the opinion does not set forth the Federal Circuit's construction of the term.

In light of *Chiron v. Genentech,* Plaintiffs' construction is a description of an antibody based on its structure and function. Thus, Plaintiffs contend that antibody is "an immunoglobulin (a Y-shaped protein comprising 2 heavy chains and 2 light chains) that binds a defined antigen at its antigen-combining site."

Defendants do not dispute, as they cannot, that an antibody is a Y-shaped protein with 2 heavy chains and 2 light chains. Further, Defendants do not dispute that the function of an antibody is to bind to an antigen at its antigen-combining site. However, Defendants assert that the term "antibody" is subject to a time limitation thereby requiring that antibody be limited by how it was made in September, 1981. FN1 Accordingly, Defendants contend that the term should be defined as "a protein generated by the immune system, or prepared by techniques known as of September 8, 1981, which is capable of recognizing and binding to a specific antigen." FN2

FN1. The Court notes that, structurally and functionally, the term antibody has not changed over time. The Federal Circuit in *Chiron v. Genentech* makes clear, however, that methods of making antibodies have changed over time.

Further, the Court notes Defendants' attempt to have the term "antibody" limited to its method of manufacture as of the September, 1981 priority date while at the same time contending that Plaintiffs are not entitled to the September, 1981 priority date.
FN2. Defendants' focus on "a protein generated by the immune system" is based on a general statement made by the Federal Circuit in *Chiron v. Genentech*. However, the Federal Circuit clearly was providing a background description in how an antibody is made as later in the same opinion the Federal Circuit goes into great detail discussing antibodies not generated by the immune system. Thus, the Court does not construe an antibody to be limited to proteins generated by the immune system.

Defendants' basis for contending that the term "antibody" is subject to a time limitation is largely based on the allegation that the specification (not the claims) requires that the antibodies be developed using "known techniques." It is this phrase in the Summary of the Invention, Defendants contend, that makes antibodies time sensitive. Defendants' position is wrong.

A review of the entire phrase reveals just how untenable Defendants' argument truly is. The actual phrase from the specification is "[t]hese antibodies ***may be*** prepared by known techniques ..." 3:56-57 (emphasis added). Thus, the phrase contemplates that the antibodies ***might be made*** by known techniques but does not exclusively limit the antibodies to the know techniques. Nor does the Court hold that this phrase acts as a definition. Instead, this phrase recites various examples of how to make antibodies-a subject relating to enablement, not claim construction. Finally, there is nothing in the claim language to suggest in any way that "antibody" is a time sensitive term. Accordingly, the Court concludes that antibody is not subject to a time limitation and should be construed according to its well-known meaning.

After a careful review of the specification and a review of the *Chiron v. Genentech* opinion, the Court finds that "antibody" is more appropriately defined by its structure and function rather than its method of manufacture. FN3 Accordingly, the Court adopts Plaintiffs' proposed construction.

FN3. Relying heavily on *Chiron v. Genentech's* analysis of "monoclonal antibodies," Defendants also assert that adoption of any construction of "antibody" not limited by time renders the patents-in-suit invalid. The Federal Circuit, however, has "not endorsed a regime in which validity analysis is a regular component of claim construction" and has deemed the doctrine of construing claims to preserve their validity "of limited utility." Phillips v. AWH Corp., 415 F.3d 1303, 1327-28 (Fed.Cir.2005). Accordingly, the Court will

construe "antibody" according to its well-known meaning and leave the issue of invalidity for another day.

B. ***the about 70 kDa mediator substance which results from endotoxin stimulation of macrophages and which has the biological activity of suppression of lipoprotein lipase activity***

This phrase appears in all asserted claims. Defendants seek to break down the phrase into various parts and construe them separately. Plaintiffs seek to have the phrase construed in its entirety to mean "biologically active TNF-(alpha)." FN4 What makes this dispute unique is that it is a clear case of role reversal. Plaintiffs wish to be limited by statements made during prosecution while Defendants want a broader construction based on statements made during prosecution and recent experimental testing that indicates that the substance described in the claims is more than just TNF.FN5

FN4. Plaintiffs' position, while slightly unorthodox, is not without precedent. *See* Johns Hopkins Univ. v. CellPro, Inc., 152 F.3d 1342 (Fed.Cir.1998).

FN5. The Court will address Defendants' assertions regarding the prosecution history. However, experimental evidence performed more than twenty years after an application is filed is entitled to little, if any, weight in claim construction analysis. This experimental evidence may, however, be highly relevant to invalidity.

Because this patent is a continuation from numerous continuations (nearly twenty years of examination before the USPTO), the complete prosecution history is lengthy and full of numerous statements from the inventors. Defendants contest Plaintiff's proposed construction because of statements made in an affidavit submitted to the PTO in the 1980's stating that the mediator substance was broader than just TNF.

However, the prosecution history is clear that the PTO was informed that the data contained in the affidavit was found to be incorrect. Moreover, the inventors made clear to the examiner that the "about 70 kDa mediator" of the claims "is now known to constitute the homotrimeric biologically active form of TNF." Prosecution of Application 08/472,753 (which issued as the '640 patent) at 8/2/99 Amendment, Paper 21, p. 2.FN6 Of particular importance is that the Examiner placed its imprimatur on this issue by stating that the applicants intended the "about 70 kDa mediator" claim language "to be limited to biologically active TNFa homotrimer." Id. at 12/8/99 Office Action, paper 26, p. 2 .FN7

FN6. There are numerous consistent statements in the prosecution histories of the patents-in-suit in this regard. *See* Prosecution of Application 08/472,753 at 8/2/99 Amendment, paper 21, p. 2-3, 9/24/99 Supplement to Amendment, paper 24, p. 1, 4/20/00 Amendment, paper 30, p. 2; *see also* Prosecution of Application 08/345,226 (which issued as the '927 patent) at 7/9/99 Amendment, paper 37, pp. 2-3, 9/24/99 Supplement to Amendment, paper 40, pp. 1-2, 4/20/00 Amendment, paper 46, p. 2.

FN7. The Examiners explicitly acknowledged that the 70 kDa mediator claim language was limited to TNF numerous times. *See* Prosecution of Application 08/472,753 at 12/8/99 Office Action, paper 26, p. 2-3; *see also* Prosecution of Application 08/345,226 at 12/8/99 Office Action, paper 42, p. 2-6, 7/7/00 Office Action, paper 47, p. 3.

Defendants do not ignore the statements made by Plaintiffs during prosecution but instead assert that Plaintiffs are estopped from using the corrected information to overcome the mistaken affidavit statements because two related applications issued as patents before the mistake was brought to the attention of the

PTO.FN8 However, the two related patents do not use the "about 70 kDa mediator" term in the claims and case law permits Plaintiffs to correct errors in related applications. *See* Biogen, Inc. v. Berlex Labs., 318 F.3d 1132, 1141 (Fed.Cir.2003) (addressing subsequently corrected mischaracterization of prior art reference and stating in context of doctrine of equivalents that "[w]hen the applicant is seeking different claims in a divisional application, estoppel generally does not arise from the prosecution of the parent").

FN8. Defendants also assert that attorney statements made during prosecution should be accorded less weight than statements made in an affidavit by an inventor. Defendants do not point to any case law supporting their proposition. Further, the Court is well aware of the duty of candor required of any attorney prosecuting an application before the PTO. The Court therefore gives no weight to Defendants' assertions on this issue. However, whether the prosecution attorneys made false statements to the PTO on this issue would relate to inequitable conduct and invalidity defenses which may well come before this Court in the not so distant future.

Further, the law is well settled that "the public has a right to rely on ... definitive statements made during prosecution." Rheox, Inc. v. Entact, Inc., 276 F.3d 1319, 1325 (Fed.Cir.2002). In this case, it could not be clearer that both the inventors and the PTO limited the "about 70 kDa mediator" term to "biologically active TNF-(alpha)." While the inventors' mistake in the earlier affidavits may have some effect on other patents issued before the mistake was corrected in the PTO, those patents are not before this Court.

Accordingly, the phrase "the about 70 kDa mediator substance which results from endotoxin stimulation of macrophages and which has the biological activity of suppression of lipoprotein lipase activity" is construed as "biologically active TNF-(alpha)." FN9

FN9. The Court would note that it allowed Defendants to file a supplemental brief addressing "new" arguments related to this contested phrase. The Court considered Defendants' supplemental brief but concludes that the arguments raised in the brief do not change this Court's ruling. Accordingly, Plaintiffs are absolved from the responsibility to file a reply to Defendants' supplemental brief.

C. "***Neutralizing antibody***"

Plaintiffs construction of "neutralizing antibody" is "an antibody that binds to the 70kDa mediator substance which results from endotoxin stimulation of macrophages and which has the biological activity of suppression of lipoprotein lipase activity in a way that counteracts and thus reduces its biological activity of suppression of lipoprotein lipase activity." Defendants' construction is somewhat similar: "an antibody that binds to the about 70 kDa mediator substance in a way that counteracts its biological activity of suppression of lipoprotein lipase activity to provide treatment. Thus, the real dispute of "neutralizing" centers around "counteracts and thus reduces" versus "counteracts ... to provide treatment."

The Court holds that "to provide treatment" is a limitation met by other language in the claim (i.e. "effective amount"). Accordingly, it is an additional and unnecessary element that should not be included in construing "neutralizing antibody." Further, the Court notes that at no time did Defendants object to Plaintiffs' assertions that antibodies regularly bind, release, and then bind again to antigens at the antigen binding site. Accordingly, the Court adopts Plaintiffs' construction of "counteracts and thus reduces." FN10

FN10. Likewise, the Court construes "neutralize suppression" in the ' 940 patent to also mean "counteracts and thus reduces."

D. ***Specifically reactive with***

At the claim construction hearing, the parties reached agreement as to the correct construction of this phrase. Accordingly, "specifically reactive with" is construed as "binding above background level to a particular antigen, through its antigen-combining site."

E. ***An amount of an antibody capable of reducing inhibition of growth and differentiation of erythroid-committed cells***

During claim construction briefing, the parties reached agreement on this phrase. Accordingly, the construction of "an amount of an antibody capable of reducing inhibition of growth and differentiation of erythroid-committed cells" is "a therapeutic amount of an antibody capable of reducing inhibition of growth and differentiation of erythroid-committed cells."

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