UNITED STATES DISTRICT COURT

CENTRAL DISTRICT OF CALIFORNIA

GLAXO GROUP LIMITED, ET AL., Plaintiffs, v. **GENENTECH, INC., ET AL.,** Defendants.	Case No. 2:10-CV-02764-MRP (FMOx) **CLAIM CONSTRUCTION ORDER**

I. INTRODUCTION

Plaintiffs Glaxo Group Limited and GlaxoSmithKline LLC (collectively, "GSK") seek a declaration that U.S. Patent No. 6,331,415 titled "Methods of Producing Immunoglobulins, Vectors and Transformed Host Cells for Use Therein" (the "Cabilly II patent") is invalid, unenforceable, and not infringed by the manufacture, use, sale, offer to sell, or importation of GSK's ofatumumab (Arzerra™) antibody product. Complaint (Docket No. 1). Defendants Genentech, Inc. and City of Hope (collectively, "Defendants") are co-assignees of the Cabilly II patent. Arzerra™ is marketed and sold in the United States for the treatment of chronic lymphocytic leukemia that is refractory to previous therapies. Complaint at ¶ 2. Arzerra™ competes with Defendants' monocolonal antibody product, Rituxan®. Defendants' Opening Brief on Claim Construction ("Defendants' Opening Brief") at 4. The parties dispute the meaning of, and ask for constructions from this Court for seven (7) claim terms contained in the

Cabilly II patent. Defendants preliminarily assert claims 1, 3, 11, 12, 14, 15, 17, 19, and 33 of the Cabilly II patent against GSK's Arzerra™ product. Disclosure of Asserted Claims and Infringement Contentions to GSK (Docket No. 79).

The Cabilly II patent has been the subject of two previous lawsuits before this Court in which the Court issued claim construction orders. *See Centocor, Inc. v. Genentech, Inc.*, No. 08-cv-03573 (C.D. Cal. June 8, 2009) Claim Construction Order (Docket No. 93) ("Centocor Claim Construction Order"); *MedImmune Inc. v. Genentech, Inc.*, No. 03-cv-02567 (C.D. Cal. Aug. 16, 2007) Claim Construction Order (Docket No. 243) ("MedImmune Claim Construction Order"). The Court's Centocor Claim Construction Order details the unusual history of the Cabilly II patent.[1] *See* Centocor Claim Construction Order at 2-4.

II. LEGAL STANDARD

Patent claims are generally given their "ordinary and customary meaning," which 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." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (citation omitted). How a person of ordinary skill in the art would have understood a claim term at the time of the invention (i.e., the effective filing date) serves as the "objective baseline" from which to begin claim construction. *Id.* at 1313. "A determination that a claim term 'needs no construction' or has the 'plain and ordinary meaning' may be inadequate when a term has more than one 'ordinary' meaning or when reliance on a term's 'ordinary' meaning does not resolve the parties' dispute." *O2 Micro Intern. Ltd. v. Beyond Innovation Tech. Co., Ltd.*, 521 F.3d 1351, 1361 (Fed. Cir. 2008). The court may be required to construe the ordinary words of a claim term if it is necessary to resolve the parties' dispute. *Id.*

The claim term is read in the context of the claim in which it appears, as well as in the context of the specification. *Phillips*, 415 F.3d at 1314-15; *see ACTV, Inc. v. Walt*

[1] U.S. Patent No. 4,816,397 owned by Celltech R&D, Ltd. that was the subject of an interference proceeding with the Cabilly II application will be referred to as the "Boss patent" in this Order.

Disney Co., 346 F.3d 1082, 1088 (Fed. Cir. 2003) ("While certain terms may be at the center of the claim construction debate, the context of the surrounding words of the claim also must be considered in determining the ordinary and customary meaning of those terms."); *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995) ("Claims must be read in view of the specification, of which they are a part."). The specification derives its importance from the written description requirement that requires the patentee to describe the claimed invention. *Phillips*, 415 F.3d at 1316. The specification gives the patentee the opportunity to give claim terms a special definition that differs from its ordinary meaning, acting as his own lexicographer. *Id.* The prosecution history is useful to show the inventor's understanding of the invention and how the inventor limited the invention in the course of prosecution. *Id.* at 1317. However, "[a]bsent contravening evidence from the specification or prosecution history, plain and unambiguous patent claim language controls the construction analysis." *DSW, Inc. v. Shoe Pavilion, Inc.*, 537 F.3d 1342, 1347 (Fed. Cir. 2008). Extrinsic evidence, although viewed as less reliable, may be relied upon where the court deems it helpful in determining the meaning of the claim terms. *Phillips*, 415 F.3d at 1317-19. Extrinsic evidence is best used in combination with intrinsic evidence. *Id.* at 1319. In some cases, claim interpretation may "involve[] little more than the application of the widely accepted meaning of commonly understood words." *Id.* at 1314.

Phillips outlines a general hierarchy of sources to consult during claim construction: (1) intrinsic evidence such as the context in which the term is used in the claim, the other claims (both asserted and unasserted), the specification, and the prosecution history, and (2) extrinsic evidence such as dictionaries, treatises, and expert testimony. *Id*. at 1314-18. "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." *Id*. at 1316 (quoting *Renishaw PLC v. Marposs Societá per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998)).

III. DISCUSSION

A. Background

During the process of briefing the claim construction issues, the parties have narrowed the number of claims to be construed. The parties have come to an agreement on the construction of (1) "host cell transformed" / "transformed host cell" and (2) "different insertion sites." *See* GSK's Responsive Brief on Claim Constructions of U.S. Patent No. 6,331,415 ("GSK's Responsive Brief") at 8. GSK has also withdrawn its proposed constructions of (1) "first DNA sequence" and "second DNA sequence" as limited to "cDNA sequences" and (2) "the constant domain is derived from the same source as the variable domain." *Id.* This leaves seven (7) terms remaining for construction by the Court.

B. "vector"

The parties propose to construe this term of the Cabilly II patent as follows:

Term	GSK's Proposed Construction	Defendants' Proposed Construction
"vector"	"a DNA molecule that transfers a DNA segment into a host cell"	"a DNA construct comprising DNA foreign to the DNA host cell, which DNA construct is capable of effecting the expression of the foreign DNA"

GSK's Responsive Brief at 9.

The parties dispute whether "vector" should be construed as limited to expression vectors. GSK advocates the adoption of the construction in the MedImmune Claim Construction Order that construes "vector" as "a separate DNA molecule that transfers a DNA segment into a host cell." MedImmune Claim Construction Order at 19. Defendants argue that the Court should adopt a construction similar to that in the Centocor case that incorporated the functional requirement of being capable of effecting the expression of foreign DNA. *See* Centocor Claim Construction Order at 24 ("[T]he Court construes the term "vector" as limited to "expression vector" in the Cabilly II patent.").

GSK argues that vector cannot be limited to mean only expression vectors because (1) an expression vector is not the only type of vector disclosed in the Cabilly II patent and (2) the patentees were not legally obliged to copy the Boss patent claims to provoke the interference. First, GSK points to the specification of the Cabilly II patent to show that cloning vectors were disclosed in addition to expression vectors. *See* Cabilly II patent, 11:48-51 ("Alternative means of forming cloning vectors containing the cDNA using other tails and other cloning vector remainder may, of course, also be used but the foregoing is a standard and preferable choice."); 4:7-9 ("Recombinant DNA technology has reached sufficient sophistication that it includes a repertoire of techniques for cloning and expression of gene sequences."). Second, GSK explains that in an interference the statute requires only that the subject matter of one claim interfere with another by being "the same or substantially the same subject matter . . . ." 35 U.S.C. § 135. Neither did the Cabilly II patentees copy the claims of the Boss patent in every case.[2]

The context of the specification and interference procedure, however, support a construction that vector should be limited to expression vectors. The Court must consider the context of the entire intrinsic record for interpretation of disputed claim terms. *See, e.g., V-Formation, Inc. v. Benetton Group SpA*, 401 F.3d 1307, 1310 (Fed. Cir. 2005). Although there are a few mentions of cloning vectors, the specification describes expression vectors at length. The specification states:

> "Expression vector" includes vectors which are capable of expressing DNA sequences contained therein, i.e., the coding sequences are operably linked to other sequences capable of effecting their expression. It is implied, although not always explicitly stated, that these expression vectors must be replicable in the host organism either as episomes or as an integral part of

[2] The Boss patent in claim 13 included a limitation "wherein the constant domain is derived from a source different from that from which the variable domain to which it is attached is derived." Boss patent, 24:34-36. The Cabilly II applicants copied the claim into their then-pending application as claim 79 as "wherein the constant domain is derived from a species or class different from that from which the variable domain to which it is attached is derived." McCormick Decl., Ex. H [3/12/90 Amendment] at 263.

> the chromosomal DNA. Clearly a lack of replicability would render them effectively inoperable. . . . In sum, "expression vector" is given a functional definition, and any DNA sequence which is capable of effecting expression of a specified contained DNA code is included in this term, as it is applied to the specified sequence.

Cabilly II patent, 8:3-19. No definition of "vector" is given in the specification. Indeed, the original claims of the Cabilly patent were all directed to expression vectors. *See* Durie Decl., Ex. B [U.S. Patent Appl. No. 07/205/419 file history (the "'419 file history"), Continuation Appl. at 56-61 (filed June 10, 1988) (containing the only originally filed claims that recite a "vector" (29, 30, 32, 34, 36-40, 42-44, 47-52), all of which recite a "replicable expression vector")] at 79-84. The issued claims referring to "vector" were copied from the Boss patent for the interference. *See* Durie Decl., Ex. C [Suppl. Prelim. Amendment and Req. for Interference at 2-3 (filed Mar. 9, 1990) (adding Cabilly Application claims 68-70 and 81-84, imported from the Boss patent verbatim, save claim 70, which corrects a grammatical error in the corresponding Boss patent claim] at 87-88. Because such copying of claims in an interference is standard practice, the Court does not give significant weight to GSK's argument that the claims could have been adapted to be substantially the same although not identical. GSK has not presented supporting evidence in the file history to suggest that the patentees intended for there to be a meaningful distinction between the vector in the Boss claims and the expression vector of the Cabilly claims.

Even the expansive language in the specification that is meant to broaden the invention to include after-arising technologies is limited to expression vectors. *See* Cabilly II patent, 8:22-25 ("However, the invention is intended to include such other forms of expression vectors which serve equivalent functions and which may, from time to time become known in the art."). The bulk of the intrinsic evidence suggests that vector was meant to be limited to expression vectors.

Furthermore, the parties have stipulated to the meaning of "different insertion sites" to mean that "in the vector, the DNA sequence encoding for at least the variable domain of the heavy chain is not contiguous to the DNA sequence encoding for at least the variable domain of the light chain, the former being separated from the latter by sufficient DNA sequence to ensure independent expression." *See* GSK Responsive Brief at 8. Understanding vector to mean only expression vectors is consistent with the use of vector in claim 15 and the parties' construction of "different insertion sites."

The Court therefore construes "vector" to mean "a DNA construct comprising DNA foreign to the DNA host cell, which DNA construct is capable of effecting the expression of the foreign DNA."

C. "said immunoglobulin heavy and light chains are produced as separate molecules in said [transformed] single host cell"

The parties propose to construe this term of the Cabilly II patent as follows:

Term	GSK's Proposed Construction	Defendants' Proposed Construction
"said immunoglobulin heavy and light chains are produced as separate molecules in said [transformed] single host cell"	"the heavy and light chains are produced and remain as separate molecules while in the transformed single host cell"	"heavy and light chain are translated separately"

GSK's Responsive Brief at 13.

The parties dispute whether this claim limitation covers *in vivo* assembly of an immunoglobulin molecule in a host cell. GSK seeks to limit the claim limitation to covering *in vitro* assembly of the immunoglobulin molecule outside of the transformed host cell by requiring that the heavy and light chains "remain as separate molecules while in the transformed single host cell." Defendants argue that claim differentiation dictates that the claim limitation includes heavy and light chains that are translated separately and assembled *in vivo*.

GSK argues that there is no support in the specification for *in vivo* assembly and thus the claims should be construed to exclude that possibility. GSK relies heavily on the

statement in the specification that assembly "can be accomplished *in vitro* as described below, or might be possible *in vivo* in a microorganism . . . ." Cabilly II patent, 12:52-54. GSK further argues that claim 9 which recites *in vivo* assembly was copied from the Boss patent during the interference. The Boss patent disclosed a working example of an *in vivo* assembly, but the Cabilly II patent did not.

GSK argues that the aspirational language of "might be possible" is not sufficient to place the *in vivo* subject matter within the scope of the claims. GSK cites numerous cases standing for the proposition that an unfulfilled wish for a desired outcome or a mere research plan without results are not sufficient to place the subject matter within the scope of the claims. The Court, however, notes that these arguments regarding whether the requirements of 35 U.S.C. § 112 have been met are more appropriate for a summary judgment motion supported by expert testimony, particularly considering there is other evidence supporting a construction that includes *in vivo* assembly.

Defendants rely on claim 9 from the Boss patent to argue that the claims themselves suggest that either *in vivo* or *in vitro* assembly was contemplated by the patentees. Claim 9 further limits claim 1 by stating "wherein the immunoglobulin heavy and light chains are expressed in the host cell and secreted therefrom as an immunologically functional immunoglobulin molecule or immunoglobulin fragment." Cabilly II patent, 28:64-67. Claim 9 requires *in vivo* assembly. Claim 10 further limits claim 1 by stating "wherein the immunoglobulin heavy and light chains are produced in insoluble form and are solubilized and allowed to refold in solution to form an immunologically functional immunoglobulin molecule or immunoglobulin fragment." *Id.* at 29:1-5. Claim 10 requires *in vitro* assembly. Because there is a "presumption in claim differentiation that an independent claim should not be construed as requiring a limitation added by a dependent claim," Defendants argue that the claim limitation in claim 1 of "produced as separate molecules in said transformed single host cell" must be broad enough to encompass *in vivo* assembly from claim 9 and *in vitro* assembly in claim

10. *Curtiss-Wright Flow Control Corp. v. Velan, Inc.*, 438 F.3d 1374, 1380 (Fed. Cir. 2006).

The Court finds that claims 1 and 33 are broad enough to encompass *in vivo* and *in vitro* assembly. The Court recognizes that some of the claims of the Cabilly II patent were copied from the Boss patent to provoke an interference and that as a result, the claims and specification are not perfectly aligned. There is, however, support in the Cabilly II patent specification for *in vivo* assembly. The specification discloses obtaining antibodies that have been assembled *in vivo* and secreted by a host cell. Cabilly II patent, 12:50-55. In addition, the original claim 1 was never limited to *in vitro* assembly. *See* Durie Decl., Ex. B ['419 file history, Continuation Appl. at 54] at 77. The specification further describes the recovery of immunoglobulins that have naturally assembled *in vivo*. Cabilly II patent, 8:36-39 ("In other words, recovery of antibody from the 'cells' may mean either from spun down whole cells, or from the cell culture containing both the medium and the suspended cells."). Although the Cabilly II patent contains only one embodiment, that for *in vitro* assembly, the claims cannot necessarily be limited to that preferred embodiment. *See Phillips*, 415 F.3d at 1323 ("In particular, we have expressly rejected the contention that if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment."). Patentees are not required to describe every possible embodiment, in part, so that broad patents are allowed.

The Court finds that the claim limitation need not be construed as only including *in vitro* assembly of heavy and light chains. The Court therefore concludes that the term "said immunoglobulin heavy and light chains are produced as separate molecules in said [transformed] single host cell" has its plain and ordinary meaning and construction is unnecessary.

D. "immunoglobulin molecule"

The parties propose to construe this term of the Cabilly II patent as follows:

Term	GSK's Proposed Construction	Defendants' Proposed Construction
"immunoglobulin molecule"	"A tetrameric molecule consisting of two relatively long polypeptide chains called heavy chains and two shorter polypeptide chains called light chains, or aggregates of such tetrameric molecules, whether or not specific immunoreactive activity is a property, and in which the immunoglobulin molecule does not contain human heavy chain and human light chain variable domains"	No construction necessary

GSK's Responsive Brief at 19.

The parties dispute whether "immunoglobulin molecule" should be construed to exclude human variable domains such that the patent would not encompass fully human antibodies. GSK argues that human variable regions are not disclosed in the Cabilly II patent and the patentees did not invent fully human antibodies. Defendants argue that there is no evidence in the specification and claims to justify the exclusion of human immunoglobulin molecules.

GSK argues that the specification does not describe or reference a fully human immunoglobulin molecule created by the Cabilly II method, or isolated human DNA sequences for variable regions of an immunoglobulin. GSK explains that it was not until the 1990s with the development of phage display technology that the ability to select antigen-specific cells and isolate DNA encoding for the human variable and constant domains of heavy and light chains became possible.

Defendants argue that immunoglobulin molecule is not given a narrow scope in the specification or prosecution history. "Absent a clear disavowal or contrary definition in the specification or the prosecution history, the patentee is entitled to the full scope of the claim language." *Home Diagnostics, Inc. v. LifeScan, Inc.*, 381 F.3d 1352, 1358

(Fed. Cir. 2004). The Court agrees. There is no evidence to suggest that the patentees intended to exclude human immunoglobulin molecule from the patent. GSK's argument is that the source of DNA encoding for at least the variable domain of the heavy and light chains of an antibody was not available. However, the specification did disclose human/human hybridomas. *See* Cabilly II patent, 2:11-17. The patent also teaches the use of "mammalian" DNA sequences. *See id.* at 6:12-18. The intrinsic evidence does not support the limitation of "immunoglobulin molecule" to exclude human variable domains. Therefore, the Court declines to construe "immunoglobulin molecule."

E. "immunologically functional immunoglobulin fragment"

The parties propose to construe this term of the Cabilly II patent as follows:

Term	GSK's Proposed Construction	Defendants' Proposed Construction
"immunologically functional immunoglobulin fragment"	"a fragment of an immunologlobulin molecule that is capable of binding to antigen"	No construction necessary

GSK's Responsive Brief at 23.

GSK argues that the Court should adopt its construction of "immunologically functional immunoglobulin fragment" as a clarification to prior constructions in the MedImmune and Centocor cases. Although Defendants do not believe the term must be construed because there is no dispute about the meaning and scope of the claim term, they do not object to the construction proposed by GSK. The Court has construed this term in the MedImmune case as "a portion of an immunoglobulin that is capable of selectively binding to a particular antigen or antigen family." MedImmune Claim Construction Order at 7. The Court has also construed this term in the Centocor case as "a portion of an immunoglobulin that is capable of binding to a known antigen." Centocor Claim Construction Order at 7. Although the Court is under no obligation to construe the term, the Court construes "immunologically functional immunoglobulin fragment" to mean "a fragment of an immunoglobulin molecule that is capable of binding to antigen."

F. "immunoglobulin heavy chain" and "immunoglobulin light chain"

The parties propose to construe this term of the Cabilly II patent as follows:

Term	GSK's Proposed Construction	Defendants' Proposed Construction
"immunoglobulin heavy chain" and "immunoglobulin light chain"	"the heavy chain of an immunoglobulin molecule" and "the light chain of an immunoglobulin molecule," respectively, in which the term "immunoglobulin molecule" is construed the same as in claims 1 and 33	No construction necessary

GSK's Responsive Brief at 24.

GSK argues that the Court should adopt its construction of "immunoglobulin heavy chain" and "immunoglobulin light chain" because it would ensure consistency. There is, however, no clear dispute about the meaning and scope of these claim terms. "A determination that a claim term 'needs no construction' or has the 'plain and ordinary meaning' may be inadequate when a term has more than one 'ordinary' meaning or when reliance on a term's 'ordinary' meaning does not resolve the parties' dispute." *O2 Micro Intern. Ltd. v. Beyond Innovation Tech. Co., Ltd.*, 521 F.3d 1351, 1361 (Fed. Cir. 2008). In this case, the Court is not required to construe the terms because there is no dispute over the meaning of the terms. The Court declines to construe "immunoglobulin heavy chain" and "immunoglobulin light chain."

G. "host cell"

The parties propose to construe this term of the Cabilly II patent as follows:

Term	GSK's Proposed Construction	Defendants' Proposed Construction
"host cell"	"a cell into which DNA will be introduced"	No reason to construe "host cell" separately from "transformed host cell," "host cell transformed" and "transforming said single host cell"

GSK's Responsive Brief at 18.

GSK does not provide a reason to construe "host cell" other than it is a stand-alone term. Because there is no dispute over the meaning of "host cell", the Court does not find

it necessary to construe the term "host cell." The parties have already stipulated to the meaning of "transformed host cell" and "host cell transformed." The Court declines to construe "host cell."

H. "transforming said single host cell"

The parties propose to construe this term of the Cabilly II patent as follows:

Term	GSK's Proposed Construction	Defendants' Proposed Construction
"transforming said single host cell"	"altering the DNA of a host cell by the inclusion of foreign DNA"	"altering the cell's heritable DNA by the inclusion of foreign DNA; the term includes the progeny of the originally transformed cell"

GSK's Responsive Brief at 17.

GSK does not provide a reason to construe "transforming said single host cell" other than to distinguish a single act of transformation. Because it is not clear to the Court why the construction of this term is necessary at all, the Court declines to construe it at this time. The parties are free to raise the construction of this term in conjunction with summary judgment motions if the parties deem it appropriate.

IV. CONCLUSION

The Court adopts the constructions set forth in this opinion for the disputed terms of the Cabilly II patent. The constructions shall govern all proceedings in this case.

IT IS SO ORDERED.

DATED: February 23, 2011

Mariana R. Pfaelzer

Hon. Mariana R. Pfaelzer
United States District Judge