United States District Court,
C.D. California.

CENTOCOR, INC,
Plaintiff.
v.
GENENTECH, INC., and City of Hope National Medical Center,
Defendants.

No. 08-CV-03573 MRP (CTx)

June 8, 2009.

Aleksander J. Goranin, Amanda M. Kessel, Barbara L. Mullin, Dianne B. Elderkin, Matthew A. Pearson, Steven D. Maslowski, Woodcock Washburn LLP, Philadelphia, PA, Bruce G. Chapman, Keith Douglas Fraser, Connolly Bove Lodge and Hutz LLP, Los Angeles, CA, for Plaintiff.

Brian G. Arnold, Thomas Whitelaw and Tyler LLP, Irvine, CA, Daralyn J. Durie, Durie Tangri Lemley Roberts and Kent LLP, David J. Silbert, John W. Keker, Keker and Van Nest, San Francisco, CA, Marcus E. Sernel, Mark A. Pals, Kirkland and Ellis LLP, Chicago, IL, for Genentech Inc.

David I. Gindler, Joseph M. Lipner, Irell and Manella, Los Angeles, CA, for City of Hope National Medical Center.

CLAIM CONSTRUCTION ORDER

MARIANA R. PFAELZER**, District Judge.**

Plaintiff Centocor, Inc. markets the monoclonal antibody drug infliximab as Remicade(R) for the treatment of certain autoimmune diseases. Centocor also manufactures abciximab (ReoPro(R)) for the prevention of certain cardiac complications. In addition, Centocor has antibody drugs ustekinumab (CNTO 1275) and golimumab (CNTO 148) in development.

Defendant Genentech, Inc. also markets monoclonal antibody drugs. Defendant City of Hope National Medical Center is a research hospital. Jointly, they developed antibody expression technology that is the subject of U.S. Patent No. 6,331,415 (the "Cabilly II patent"). Genentech is the sole assignee of the other patents in suit.

Centocor holds a license to the Cabilly II patent for infliximab and abciximab from Celltech Therapeutics, Ltd. and Genentech, respectively. First Am. Compl. at 8-9. Defendants Genentech and City of Hope allege that Centocor infringes the Cabilly II patent with three of its products. Defs.' First Am. Counterclaims at 5, Joint Rule 26(f) Report at 4-5. In addition, Defendant Genentech has alleged that Centocor infringes U.S. Patent Nos. 6,333,398; 6,870,034; 6,417,335; and 6,171,586 with two to four of its products. Defs.' First

Am. Counterclaims at 6-9. Genentech now indicates it intends to drop three of these patents from this suit, leaving only U.S. Patent No. 6,171,586 (the "Basey patent"). Joint Rule 26(f) Report at 3.

I. BACKGROUND

A. The Cabilly II patent

The Cabilly II patent is a broad patent, encompassing methods of producing humanized monoclonal antibodies, which are useful as therapeutics. Claims 18, 20, and 33, the asserted claims, cover methods of producing immunoglobulin molecules and fragments in cells, as well as the cells themselves.

The Cabilly II patent has an unusual, but not unprecedented, history. *See, e.g.,* In re Basell Poliolefine Italia S.P.A., 547 F.3d 1371 (Fed.Cir.2008) (discussing the history of U.S. Patent No. 6,365,687). The parent patent, U.S. Patent No. 4,816,567 (the "Cabilly I patent") dates back to 1983. The Cabilly I patent issued six years later on the same day as U.S. Patent No. 4,816,397 (the "Boss patent") to Celltech, also first filed in 1983. The claims of the Cabilly I patent were directed to methods of expressing either heavy chains or light chains in cells, chimeric antibodies, and expression vectors. The Boss patent claims were directed to methods of expressing both heavy and light chains in cells, vectors, and host cells.

In 1991, believing that the disclosure of the Cabilly I patent encompassed the invention of the Boss patent and that Cabilly, et al. were the first inventors, Defendants copied the Boss claims into the Cabilly II continuation application to provoke an interference under 35 U.S.C. s. 135. After seven and a half years, the U.S. Patent and Trademark Office (the "Patent Office") determined that Boss, et al. had priority of invention. Cabilly v. Boss, 55 U.S.P.Q.2d 1238 (Bd. Pat.App. & Int.1998). Genentech sought to overturn the decision by filing a civil action under 35 U.S.C. s. 146, "a hybrid of an appeal and a trial de novo," in the Northern District of California. FN1 Estee Lauder v. L'Oreal, S.A., 129 F.3d 588, 592 (Fed.Cir.1997). A settlement of this action was ultimately reached, wherein the parties agreed that the Cabilly II patent was entitled to priority based on new evidence that was not presented in the interference. *Genentech, Inc. v. Celltech Therapeutics, Ltd.,* 2001 U.S. Dist. LEXIS 3489 (N.D.Cal. Mar. 16, 2001). FN2 Upon judgment, the district court ordered the Patent Office to vacate its decision in the interference, revoke the Boss patent, and issue the Cabilly II patent in 2001. *Id.*

FN1. A s. 146 action is a means by which "[a]ny party to an interference dissatisfied with the decision of the Board of Patent Appeals and Interferences may have remedy" if it has not appealed to the Court of Appeals for the Federal Circuit. 35 U.S.C. s. 146.

FN2. The parties also entered into several other agreements.

The parties filed the Judgment with the Patent Office. The Board of Patent Appeals and Interferences vacated its decision, cancelled the claims of the Boss patent, and gave priority to Cabilly, et al. *Cabilly v. Boss,* Interference No. 102,572, Final Order after District Court Judgment (July 25, 2001). However, noting that the examiner may not have considered prior art cited after the interference was declared, the Board did not immediately issue the Cabilly II patent. *Id.* at 4. Prosecution of the Cabilly II application continued, with the patent issuing in December 2001.

In 2005, prosecution of the Cabilly II patent was re-opened by two requests for reexamination, which were

later merged into one proceeding. The patentees were able to confirm patentability of the claims by overcoming obviousness-type double patenting rejections over the Cabilly I patent and other art. The Patent Office issued the Reexamination Certificate on May 19, 2009, with amendments to three claims, and confirmation of the patentability of the other claims.

If Celltech had prevailed in obtaining priority of invention, the interfering subject matter would have been patented in the Boss patent. The Boss patent would have expired in 2006, seventeen years after its 1989 issue date. Instead, the claims have a patent term expiring in 2018, since the Cabilly II patent did not issue until 2001.

B. The Basey patent

The Basey patent, assigned to Genentech, is a relatively narrow patent directed to methods of purifying antibodies. Specifically, the Basey patent claims purification methods with an optimized range of antibody to cation exchange resin. The patent was first filed in 1998 and will expire in 2019. Genentech asserts infringement of claims 1, 2, 3, and 7 of the Basey patent.

C. Claim construction

At this stage, the parties dispute the meaning of several terms in the Cabilly II and Basey patents. The Court held a *Markman* hearing on May 12, 2009 and sets forth the necessary claim constructions here. Markman v. Westview Instruments, Inc., 517 U.S. 370 (1996).

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, 1313 (Fed.Cir .2005). 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*. The claim term is read in the context of the claim in which it appears, as well as in the context of the specification. *Id*.

In some cases, claim interpretation may "involve[ ] little more than the application of the widely accepted meaning of commonly understood words." *Id*. at 1314. However, the meaning of a claim term to those of ordinary skill in the art "is often not immediately apparent." *Id*. "In many cases that give rise to litigation," terms have "a particular meaning in a field of art." *Id*. In addition, patentees use terms "idiosyncratically." *Id*. In these instances, "the court looks to 'those sources available to the public that show what a person of skill in the art would have understood disputed claim language to mean.' " *Id*. (quoting Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc., 381 F.3d 1111, 1116 (Fed.Cir.2004)). *Phillips* outlines a general hierarchy of sources to consult during claim construction: the context in which the term is used in the claim, the other claims (both asserted and unasserted), the specification, the prosecution history (and other intrinsic evidence), and extrinsic evidence (such as dictionaries and expert testimony). *Id*. at 1314-18.

Construction of a claim term ultimately requires "a full understanding of what the inventors actually invented and intended to envelop with the claim." *Id*. at 1316 (quoting Renishaw PLC v. Marposs Societ a per Azioni, 158 F.3d 1243, 1250 (Fed.Cir.1998). Claims should be construed to be consistent with the specification, keeping in mind that patentees sometimes use a "special definition" for a term in the specification that "differs from the meaning it would otherwise possess." *Id*. at 1316. "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*. (quoting Renishaw 158 F.3d at 1250).

III. CLAIM CONSTRUCTION

A. Disputed claim terms in the Cabilly II patent

Claims 18, 20, and 33 are the asserted claims:

18. A transformed host cell comprising at least two vectors, at least one of said vectors comprising a DNA sequence encoding at least a variable domain of an immunoglobulin heavy chain and at least another one of said vectors comprising a DNA sequence encoding at least the variable domain of an immunoglobulin light chain.

20. The transformed host cell of claim 18 wherein the host cell is a mammalian cell.

33. A process for producing an immunoglobulin molecule or an immunologically functional immunoglobulin fragment comprising at least the variable domains of the immunoglobulin heavy and light chains, in a single host cell, comprising:

independently expressing a first DNA sequence encoding at least the variable domain of the immunoglobulin heavy chain and a second DNA sequence encoding at least the variable domain of the immunoglobulin light chain so that said immunoglobulin heavy and light chains are produced as separate molecules in said single host cell transformed with said first and second DNA sequences.

The patentability of each of these claims was confirmed in the reexamination, without any amendments.

Centocor has asked the Court to construe the following claim terms in the asserted claims:

-> immunologically functional immunoglobulin fragment

-> immunoglobulin

-> immunoglobulin molecule

-> produced as separate molecules in a single host cell

-> transformed host cell

-> transformed host cell comprising at least two vectors

-> variable domain

-> vector

Centocor, Inc.'s Opening Brief on Claim Construction ("Pl.'s Br.) at 3-4. Genentech and City of Hope ("Defendants") have asked the Court only to construe the term:

-> transformed host cell comprising at least two vectors

Genentech, Inc.'s and City of Hope's Corrected Opening Brief on Claim Construction ("Defs.' Br.") at 1.

Not all of the proposed claim terms require construction. Although initially in dispute, the parties now agree on the meaning of "immunologically functional immunoglobulin fragment." *See Id* . at 20, Pl.'s Br. at 20. Defendants do not wish to have the term "variable domain" construed, but would accept Centocor's construction were it to be construed. Defs.' Br. at 1.

The Court also does not find it necessary to construe the term "immunoglobulin" separately from the term "immunoglobulin molecule" because the parties' dispute is the same for each term. Similarly, it is unnecessary to construe the term "transformed host cell" outside the context of the term "transformed host cell comprising at least two vectors." Construction of these terms does not appear to affect the outcome of this case.

Although the term "vector" appears in the term "transformed host cell comprising at least two vectors," the Court will construe the term separately because it has reconsidered the construction of "vector" entered in MedImmune. MedImmune v. Genentech et al., No. CV 03-02567, 2007 WL 5760839 (CD.Cal. Aug. 16, 2007).

The Court will therefore consider the following disputed claim terms in the Cabilly II patent:

-> immunoglobulin molecule

-> produced as separate molecules in a single host cell

-> vector

-> transformed host cell comprising at least two vectors

B. Construction of claim terms in the Cabilly II patent

1. **"*Immunoglobulin molecule* "**

Defendants do not believe the term "immunoglobulin molecule" requires construction. Defs.' Br. at 17. However, if the term is to be construed, then they agree to Centocor's construction, with an additional phrase. *Id*. The parties propose to construe "immunoglobulin molecule" as follows, with the difference between the two constructions underlined:

Genentech and City of Hope	**Centocor**
Tetrameric molecule consisting of two longer polypeptide chains called heavy chains and two shorter polypeptide chains called light chains, or aggregates of such tetrameric molecules, *capable of binding to a known antigen,* whether or not specific immunoreactive activity is a property	A tetrameric molecule consisting of two longer 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

PL's Br. at 12-13; Defs.' Br. at 17. The parties agree on the structural features of the term, but not whether the term should be construed to require "capable of binding to a known antigen." FN3

FN3. Centocor also asks the Court to construe the term "immunoglobulin" but the term "immunoglobulin" does not appear in the asserted claims as a claim element. "Immunoglobulin" is a modifier to "heavy chain," "light chain," and "molecule" in the asserted claims. Centocor's proposed construction both construes immunoglobulin as a claim element on its own and is the same as its proposed construction of "immunoglobulin molecule," illustrating that the issue involved in the construction of these terms is the same. *See* Pl.'s Br. at 12-13. Thus, the statements herein discussed with respect to "immunoglobulin molecule" are also generally applicable to the claim term "immunoglobulin."

a. Specification

Centocor relies on the specification, which describes immunoglobulins, antibodies, and their binding properties, to define the term "immunoglobulin molecule." Pl.'s Br. at 13-14. The Summary of the Invention begins: "The invention relates to antibodies and to non-specific immunoglobulins (NSIs) formed by recombinant techniques using suitable host cell cultures." Cabilly II at 4:53-55. The specification describes immunoglobulins as including "both antibodies ... and analogous protein substances which lack antigen specificity." *Id*. at 1:38-40. The specification notes that "immunoglobulins which lack the specificity of antibodies are useful." *Id*. at 3:3-5. It states that non-specific immunoglobulins are "helpful in proteins replacement therapy for globulin related anemia," in which context, "an inability to bind to antigen is in fact, helpful, as the therapeutic value of these proteins would be impaired by such functionality." *Id*. at 3:5-10. Thus, Centocor reasons, the specification clearly indicates that the term "immunoglobulin molecule" must include molecules both with antigen specificity (such as antibodies) and molecules without antigen specificity (i.e., non-specific immunoglobulins). Centocor concludes that limiting "immunoglobulin molecule" to exclude non-specific immunoglobulins "directly contradicts the express definition of 'immunoglobulin' given in the specification and should be rejected." PL's Br. at 14.FN4

FN4. Immunoglobulins which are not "capable of binding to a known antigen" are not coextensive with "nonspecific immunoglobulins." Some immunoglobulins not capable of binding to a *known* antigen are capable of binding to *some* antigen. However, a nonspecific immunoglobulin is not capable of specifically binding to *any* antigen. *See, e.g.,* Sernel Decl., Ex. M, May 26, 1987 Amendment at 13.

Defendants do not rely on the specification for their proposed construction and give no reason why a person of ordinary skill in the art would not have read the specification as providing a plain and ordinary meaning for the term. Defs.' Br. at 20. Instead, they use what they call the "PTO's definition." *Id*.

b. Prosecution history

The prosecution history is an "official record that is created in the knowledge that its audience is not only the patent examining officials and the applicant, but the interested public." Biogen, Inc. v. Berlex Labs., Inc., 318 F.3d 1132, 1139 (Fed.Cir.2003). *See also* Hockerson-Halberstadt, Inc. v. Avia Group Intern., Inc., 222 F.3d 951, 957 (Fed.Cir.2000) (discussing the "public notice function provided by the prosecution history"). The prosecution history includes the patent application as well as any parent and grandparent applications. Mark I Marketing Corp. v. R.R. Donnelley & Sons Co., 66 F.3d 285, 291 (Fed.Cir.1995). Thus, relevant statements made during prosecution of the Cabilly I and II patents as well as during the

reexamination of the Cabilly II patent must be considered when construing the claim terms of the Cabilly II patent.

Defendants cite statements made during prosecution of the parent patent and during reexamination to support inserting the phrase "capable of binding to a known antigen" in Centocor's proposed construction. Defs.' Br. at 17-20.

During prosecution of the parent patent, the patentees distinguished the Cabilly I invention from the prior art by stating that it was not obvious to obtain DNA encoding an antigen with specificity for a known antigen:

It is true that the [prior art] immunoglobulins bind to *some* antigen, but the antigen is unknown.... [I]t would not have been reasonably predictable that DNA encoding a *known* antigen-specific immunoglobulin could be obtained No art of record discloses cloning an immunoglobulin having specificity for a *known* antigen.

Sernel Decl., Ex. M, May 26, 1987 Amendment at 13 (emphasis added). In a subsequent Amendment, the patentees similarly characterized the Cabilly I invention:

The art of record fails to disclose an immunoglobulin gene which could be expressed to produce an immunoglobulin chain capable of binding to a predetermined, known antigen. The claims call for a known antigen, but the references do not disclose immunoglobulins having known antigen-binding capability. Even if the prior art immunoglobulins bound to *some* antigen, the references themselves do not make it known Whether [the myeloma immunoglobulins] in fact bind any antigen is speculative. That they do not bind to a known antigen is certain.

Sernel Deck, Ex. N, May 9, 1988 Response at 4-5.

However, each claim of the Cabilly I patent explicitly requires that the chimeric immunoglobulin heavy or light chain is limited to "having specificity for a particular known antigen." In contrast, the asserted claims of the Cabilly II patent do not contain any "known antigen" limitation. Therefore, the statements made during the prosecution of the parent that Defendants cite are not useful to determine if "immunoglobulin molecule" in the claims of the Cabilly II patent should be limited to molecules which bind to a known antigen. FN5

FN5. The statements in the Cabilly I prosecution history may be useful to interpret what "immunoglobulin" means in claim 21 because claim 21 contains the limitation "said immunoglobulin being capable of binding to a known antigen." Cabilly II Reexam Cert. 2:16-17. However, claims 21, and claims 22 to 31, which depend therefrom and also contain this limitation, are not asserted in this case.

c. Reexamination

In the Notice of Intent to Issue Ex Parte Reexamination Certificate ("NIRC"), the patent examiner stated that claims 1,21, and 33 are representative of the invention. Sernel Deck, Ex. L, Feb. 23, 2009 NIRC at 3. She characterized the term "immunoglobulin molecule" in claims 1 and 33 as an "immunologically functional molecule and capable of binding to a known antigen." *Id*. Defendants state that courts give "significant weight" to statements by the Patent Office confirming patentability in support of its proposed construction.

Defs.' Br. at 19.

While Courts have used statements made by the Patent Office to determine the meaning of ambiguous claim terms, or to limit the application of the doctrine of equivalents for amended claim terms, Defendants have not pointed to any case where a statement in a NIRC was used to limit an unambiguous definition of a term in the specification where the claim was not so amended. In contrast, in *SRAM Corp. v. AD-II Eng'g, Inc.,* the Federal Circuit emphasized that a patent examiner's claim interpretation does not bind the courts-even after three reexamination proceedings. 465 F.3d 1351, 1359 (Fed.Cir.2006). The Federal Circuit criticized the Patent Office and the district court for construing a claim narrowly by reading in a limitation that was relied on for patentability. *Id.* The patent examiner's interpretation of the claim terms should be considered, but does not bind this Court.

d. Construction after interference

Defendants also cite the proposed construction for the phrase "Ig molecule or immunologically functional Ig fragment" in the s. 146 action for their argument that the term should be limited to molecules capable of binding to a known antigen. Defs.' Br. at 18. However, this reliance on statements made in the s. 146 action is misplaced for several reasons.

First, the proposed construction was not for a claim, but a count. A count is "merely the vehicle for contesting the priority of invention and determining what evidence is relevant to the issue of priority." In re Van Geuns, 988 F.2d 1181, 1184 (Fed.Cir.1993) ("Although claims of one or more of the parties may be identical to the count of an interference, the count is not a claim to an invention.").FN6 Genentech's proposed construction for the count in the interference context was based on "what Celltech said it meant in its British application and its U.S. patent" because "[t]he count's meaning has to be determined by looking to the patent from which the interference arose-here, Celltech Therapeutics, Ltd.'s United States application and patent, and the British patent application from which Celltech claims a priority date." Sernel Decl. at Ex. O, *Genentech, Inc. v. Celltech Therapeutics, Ltd.,* Case No. C98-3926 MMC, Genentech's Motion to Construe the Count at 9, 1.

FN6. Put plainly, a count is the overlapping subject matter in an interference that each party seeks to establish it invented first.

Although it is well-established that "claims must be read in view of the specification, of which they are a part," the Cabilly II patent presents the unusual situation where the claims were not a part of the specification. Phillips 415 F.3d at 1315 (*quoting* Markman v. Westview Instruments, Inc., 52 F.3d 967, 979 (Fed.Cir.1995)) (internal quotations omitted). To construe the claim terms of the Cabilly II patent, the Court must still look to the specification of the Cabilly II patent, not the Boss patent, "as if the application stood alone." *See* Rowe v. Dror, 112 F.3d 473, 479 (Fed.Cir.1997) (To assess patentability of a claim that was copied from another patent in an interference, "the PTO and this court must interpret the claim in light of the specification in which it appears."). Even when a count has identical words as the claims, the claims of each patent could have different meaning in light of each patent's specification. *See also Agilent Tech., Inc. v. Affymetrix, Inc.,* No.2008-1466, slip op. at 10 (Fed. Cir. June 4, 2009).

Second, although the term "Ig molecule or immunologically functional Ig fragment" appears in the count of the s. 146 action, the discussion that Genentech cites is actually with respect to "[t]he meaning of the phrase

'immunologically functional' Ig molecule or fragment," in particular, the term "immunologically functional," and not the broader term "Ig molecule." Sernel Decl. at Ex. O, *Genentech, Inc. v. Celltech Therapeutics, Ltd.,* Case No. C98-3926 MMC, Genentech's Motion to Construe the Count at 6, 9-10. It is not surprising that the "dispute between the parties was only as to what level of binding specificity the count required" because the scope of an "Ig molecule" that was not "immunologically functional" was not included in the discussion. Defs.' Br. at 19.

The arguments made for the construction of the *count* in the s. 146 action were in light of the *Boss patent* and file history. The construction of the *claims* in this action must be in light of the *Cabilly II patent* and file history. In addition, the term construed in the s. 146 action is narrower than the term to be construed here. Thus, statements Defendants point to in the s. 146 action are not useful to construe "immunoglobulin molecule."

Because the statements Genentech made in the s. 146 action were for terms of the count of the interference, and not for the claims of the Cabilly II patent, and because they were for a narrower claim term than "immunoglobulin molecule," they may illustrate Genentech has maintained a consistent position in different contexts, but do not shed light on the proper meaning of "immunoglobulin molecule." A consistent position is not necessarily a correct position.

e. Claim differentiation

Claim 21 explicitly recites the limitation "said immunoglobulin being capable of binding to a known antigen." Cabilly II 30:2-3. Centocor uses the doctrine of claim differentiation to argue "If 'immunoglobulin' were invariably required to be 'capable of binding to a known antigen,' then the quoted language in Claim 21 would be superfluous." Pl.'s Br. at 14. Defendants do not agree that the additional limitation in claim 21 aids the construction of "immunoglobulin molecule," essentially arguing that the examiner's statements in the NIRC trump the specification. Defs.' Br. at 19-20.

The Cabilly II patent includes claims written by different attorneys at different times for different applicants, possibly also for different purposes. Claim 21 was added during the prosecution of the Cabilly II patent, after the claims from the Boss patent were copied. It contained the language "said immunoglobulin being capable of binding to a known antigen" as originally written and the prosecution history does not shed any more light on why claim 21, but not the other independent claims, contains this limitation.FN7 Neither Genentech nor City of Hope provided any explanation when asked at the hearing. Hr'g Tr. at 41-44, 57-59.

FN7. The Court notes that issued claim 21 has a complicated technical history but a rather simple substantive history. The Cabilly II patent, a continuation of the Cabilly I patent, had the original claims of the Cabilly I application and did not contain this claim. Cabilly II File History, June 10, 1988 Application Filing.
Issued claim 21 first appeared in the Cabilly II application as claim 53, added in an amendment filed with the application. *Id.* at June 10, 1988 Preliminary Amendment at 1. The claim included the limitations "said immunoglobulin having specificity for a particular known antigen" and "said immunoglobulin being capable of binding to a known antigen" as originally filed. *Id.* Claim 53 was cancelled when the Boss claims were copied to provoke an interference. *Id.* at March 12, 1990 Amendment at 1. Defendants attempted to reinstate claim 53, but had to refile the claim as new claim 87, and later as claim 121, due to procedural errors. *Id.* at May 29, 1990 Response at 1, July 23, 1990 Supp'l Amendment at 1-2, Aug, 29, 1990 Supp'l Amendment at 1, Sept. 5, 1990 Second Supp'l Amendment at 4.

Claim 121 remained the same as first-filed claim 53 through the interference proceedings and s. 146 action. It was amended afterwards, but the "known antigen" limitations were left unchanged. *Id*. at Oct. 4, 2001 Amendment after Interference at 4, Attachment at 4. Claim 121 issued in the Cabilly II patent as claim 21, with the two "known antigen" limitations.
During reexamination, claim 21 was amended, deleting the first "known antigen" limitation and adding unrelated limitations to "confirm that the heavy and light chain polypeptides of the immunoglobulin are produced as separate molecules in the host cell." Cabilly II Reexam., Feb. 12, 2009 Proposed Amendment at 3. The limitation "said immunoglobulin being capable of binding to a known antigen" remained in the claim. Cabilly II Reexam, Feb. 13, 2009 SuppT Amendment at 2, Cabilly II Reexam Cert. 2:16-17.
The claim differentiation doctrine works best with claims with an independent and dependent relationship. Curtiss-Wright Flow Control Corp. v. Velan, Inc., 438 F.3d 1374, 1380 (Fed.Cir.2006). The doctrine has been applied more generally as well, although the Federal Circuit has cautioned that the tool of claim differentiation is to be "a guide, not a rigid rule," and "two claims with different terminology can define the exact same subject matter." Id. at 1381, 1380 (quotations and citation omitted). The Federal Circuit has outlined how to apply the doctrine to two independent claims in *Curtiss-Wright,* but in the context of resolving an ambiguity, not differentiating between a term modified by the language of a limitation present in one independent claim but not the other. *Id*. at 1381.

Here, Centocor wishes to apply the doctrine to different independent claims claiming different aspects of the invention, including a claim to a process and a claim to a cell. In addition, it is difficult to tell if the patentees meant for the term "immunoglobulin" in claim 21 (which they wrote themselves) to have a different scope than "immunoglobulin molecule" in claim 1, for example (which was copied from the Boss patent). It could have been a deliberate choice of language, or it could have been an artifact due to the fact that different attorneys wrote the claims, just as claim 1 recites steps "(i)" and "(ii)" and claim 21 recites steps "a)," "b)," ... "e)." The doctrine of claim differentiation is not clearly applicable to the claims at issue.

f. Conclusion

The Court, having asked the parties to explain the significance of the two proposed constructions at the hearing, has determined that the issue of infringement appears to be resolvable without construing the term "immunoglobulin molecule." It does not appear that the question of whether an "immunoglobulin molecule" is "capable of binding to a known molecule" is material to infringement. If at some later stage of the proceedings, construction of "immunoglobulin" or "immunoglobulin molecule" becomes material, the Court will construe the terms necessary to resolve the issue at that time.

2. "Produced as separate molecules in a single host cell "

The term "produced as separate molecules in a single host cell" appears in claim 33 in the context "said immunoglobulin heavy and light chains are produced as separate molecules in said single host cell." Cabilly II 30:39-41. Defendants do not believe this term requires construction. Defs.' Br. at 20. Centocor proposes to construe the claim term as follows:

Genentech and City of Hope	**Centocor**
No construction needed	The heavy and light chains of the immunoglobulin molecule are produced as separate molecules while in the single host cell

PL's Br. at 15, Defs.' Br. at 20.

Defendants observe that Centocor's construction simply adds "while" to the existing claim terms. Defs.' Br. at 21. By adding "while," Centocor's construction requires separate production of the light chain and heavy chain *inside* of the host cell, and assembly of the light chain and heavy chain into an immunoglobulin tetramer *outside* of the host cell.FN8 Pl.'s Br. at 17-18. Indeed, the examples and the majority of the description in the specification describe *in vivo* production of heavy chains and light chains separately, followed by *in vitro* assembly.

FN8. In addition, Centocor argues that the preamble of claim 33, which requires production of "an immunoglobulin molecule or an immunologically functional immunoglobulin fragment," means that the claim "requires more than just the expression of heavy and light chains in a host cell," but fails to explain why this distinction is a "key consideration in construing the disputed term." Pl.'s Br. at 16-17.

Genentech and the City of Hope, on the other hand, take the position that claim 33 is broad enough to encompass assembly of an immunoglobulin both *inside* the host cell and *outside* the host cell. Defs.' Br. at 22. Defendants rely on a claim differentiation argument, comparing claims 1, 9, and 10. *Id*. at 21-22. Claim 1 contains an analogous term to the term in dispute: "produced as separate molecules in said transformed single host cell." Cabilly II 28:48-49. Claim 9, which depends from claim 1, further limits the term 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," i.e., claim 9 requires assembly *inside* the host cell. *Id*. at 28:64-67. Claim 10, which also depends from claim 1, recites "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," i.e., claim 10 requires assembly *outside* the host cell. *Id*. at 29:1-5.

In this context, the doctrine of claim differentiation creates a "presumption that an independent claim should not be construed as requiring a limitation added by a dependent claim." Curtiss-Wright, 438 F.3d at 1380. The patent laws require that dependent claims refer to a previous claim and further limit the subject matter. 35 U.S.C. s. 112 para. 4. A limitation from a dependent claim should not be read into the independent claim, because it would make the dependent claim superfluous, and possibly render the claim invalid. Curtiss-Wright 438 F.3d at 1380.

Although claims 1, 9, and 10 are not at issue in this case, the interpretation of these claims is helpful to construe terms in the asserted claims because "claim terms are presumed to be used consistently throughout the patent, such that the usage of a term in one claim can often illuminate the meaning of the same term in other claims." Research Plastics, Inc. v. Federal Packaging Corp., 421 F.3d 1290, 1295 (Fed.Cir.2005) (citing Phillips, 415 F.3d at 1313-14).

Using the tool of claim differentiation, it is clear that the term "produced as separate molecules in said transformed single host cell" of claim 1 is broad enough to encompass the limitation of claim 9 (i.e., assembly *inside* the host cell) as well as the limitation of claim 10 (i.e., assembly *outside* the host cell). Similarly, Defendants reason, the analogous term "produced as separate molecules in a single host cell" in claim 33 is broad enough to encompass immunoglobulin assembly both *inside* and *outside* the host cell. The Court agrees.

By arguing that the claim term is limited to production of heavy and light chains while *inside* the host cell, Centocor's real dispute appears to be with the scope of the invention of the Cabilly II patent. PL's Br. at 15.

As discussed in Section I(A) *supra,* the claims of the Cabilly II patent were copied from the Boss patent to provoke an interference. As a result, the claims of the Cabilly II patent are somewhat discordant with the specification, since they were not written together. Because the majority of the specification describes immunoglobulin assembly outside of a host cell, Centocor asserts "Cabilly did not invent, disclose or describe an invention in which heavy and light chains expressed within a cell are combined in the cell, and is not entitled to a claim construction which is broader than his invention." *Id*. at 18. In fact, the only support in the specification for immunoglobulin assembly inside the host cell is the statement:

When heavy and light chain are coexpressed in the same host, the isolation procedure is designed so as to recover reconstituted antibody. This can be accomplished in vitro as described below, *or might be possible in vivo in a microorganism which secretes the IgG chains out of the reducing environment of the cytoplasm*.

which is followed by a detailed example of *in vitro* immunoglobulin assembly. Cabilly II 12:50-55 (emphasis added).

Centocor relies on *Biogen* to support the position that term "produced as separate molecules in a single host cell" should be limited to only the method of immunoglobulin assembly described in the specification, i.e., assembly *outside* of the host cell. 318 F.3d 1132.

In *Biogen,* the claims at issue were directed to methods of producing interferon in certain mammalian cells with an expressible gene encoding interferon as well as claims directed to such cells. *Id*. at 1134-35. Some of the claims further require the cells to have a gene for a selectable marker. The description in the specification was limited to methods and cells transformed with linked interferon and marker genes in single constructs, and did not describe cells with interferon genes without marker genes. *Id*. at 1135. In addition, a review of the prosecution history revealed that the "examiner recognized that the only supportable scope of the claims was for the linked construct." *Id*. at 1139. The district court therefore construed all of the method and cell claims to require a single linked DNA construct, including those that did not expressly recite the marker gene. *Id*. The Federal Circuit affirmed, stating "that the specification defines the invention as the use of a single DNA construct to introduce the linked human interferon gene and selectable marker gene into the host ... cell, and that the method and cell claims ... are so limited." *Id*. at 1140.

Citing *Biogen,* Centocor argues that the Cabilly II claims should similarly be limited to the methods described in the specification, i.e., *in vitro* immunoglobulin assembly.FN9 However, Centocor is not correct that "the *only* method disclosed in the Cabilly II specification for the assembly of the heavy and light chains is one that occurs *outside of the host cell* ." Pl.'s Br. at 17. The specification describes obtaining assembled antibodies secreted by a host cell. Cabilly II 12:50-55. In *Biogen,* "the district court construed the claims to conform with the basis on which the invention was presented in the specification." 318 F.3d at 1140. In contrast to the defendant in *Biogen,* Centocor has not pointed to any part of the voluminous prosecution history where the examiner or patentees made such a limiting characterization. Therefore, *Biogen* does not mandate limiting the claim to immunoglobulin assembly outside of the host cell.

FN9. Centocor has also raised the question of whether the patentees are now seeking to claim subject matter that is broader than their actual invention. Pl.'s Br. at 18.

The Court concludes that the term "produced as separate molecules in said transformed single host cell" is clear on its face and its construction is unnecessary.

3. "Vector "

The term "vector" appears in claim 18 in the context of "a transformed host cell comprising at least two vectors." The two vectors are further limited in the claim as comprising particular DNA sequences. Defendants do not wish to construe the term "vector" alone; Centocor urges the Court to adopt a similar construction to that in the *MedImmune* case:

Genentech and City of Hope	**Centocor**
No construction needed	A separate DNA molecule that is capable of transporting a DNA segment into another cell

Pl.'s Br. at 6-7.

The parties dispute the "functional essence" of the term-whether a vector remains a vector when it has become integrated into the chromosomal DNA of the transformed host cell. *Id*. at 7-8. Defendants take the position that integrated vectors meet the claim limitation, and Centocor disagrees, arguing that once a vector has lost its functional ability to transfer DNA, it is no longer a vector. Defs.' Br. at 10; Pl.'s Br. at 7-8.

To determine how one of skill in the art would have understood the term "vector" at the time of invention, Centocor looks to the specification for a definition; finding none, it then turns to extrinsic evidence. *Id*. at 7. The term "vector" is generally understood to encompass DNA molecules that transfer a DNA segment into a host cell, and Centocor provides such a definition from a technical dictionary. *Id*.

To define the term, Centocor's analysis moves away from the specification too hastily. Claim terms must be read "in the context of the entire patent, including the specification," where the patentee may give a claim term a "special definition ... that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." Phillips, 415 F.3d at 1313, 1316.

Centocor and the prior claim construction order in *MedImmune* are correct in characterizing the term "vector" as having a functional definition. PL's Br. at 7, Op. at 19. However, the Court now reconsiders its previous statement that "the utility of the patent's definition of 'expression vector' for the Court's construction of 'vector' is limited." Op. at 16.

While it is true that the claim term "vector" is not defined in the specification, the specification offers a definition, description, and examples of "expression vectors." Reading the Cabilly II patent, one of skill in the art would have understood "expression vector" to be a type of "vector."

The specification defines "expression vector" as including:

vectors which are capable of expressing DNA sequences contained therein.... It is implied, although not always explicitly stated, that these *expression vectors must be replicable in the host organisms either as*

episomes or as an integral part of the chromosomal DNA. Clearly a lack of replicability would render them effectively inoperable.... *In sum, "expression vector" is given afunctional 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. As at present, such vectors are frequently in the form of plasmids, thus "plasmid" and "expression vector" are often used interchangeably.

Cabilly II 8:3-22 (emphasis added).

It is clear from the specification that the term "expression vector"

encompasses any DNA sequence capable of effecting expression of a specified DNA sequence. This includes replicable sequences of DNA that are episomal (i.e., not integrated) as well as replicable sequences of DNA that are integrated into the host cell's chromosomal DNA. Thus, Centocor's argument that a vector does not remain a vector once it is "integrated and has lost its 'functional essence' " fails in the context of the Cabilly II patent. Pl.'s Br. at 9 (citing *MedImmune* Op. at 17).

Although Centocor is likely correct when it argues that it may have been more common in the art at the time the invention was made to refer to a vector as a separate DNA molecule capable of transferring a DNA segment into a host cell, it is clear using the inventors' lexicography, "expression vector" was given the meaning of a vector "capable of effecting expression of a specified contained DNA code" and expression vectors could be "integrated into the host cell chromosome." *Id*. at 8:16-19, 10:24-25. Once integrated, some vectors may not retain the ability to transfer DNA into another host cell, but that does not mean that one of skill of the art would not have understood the meaning of "expression vector" set forth in the specification.FN10

FN10. Genentech and Centocor present evidence to show that "the 'separateness' of a vector in a host cell can change over time and be influenced by [external] factors" citing bacteriophage lambda vectors to support their contention that vectors remain vectors when integrated. Defs.' Br. at 13. The Court does not find it necessary to delve into this argument, since the issue can be resolved on other bases.

The only type of vector described in the specification of the Cabilly II patent is an expression vector. Expression vector was explicitly defined in the specification. Cabilly II 8:3-25. Each of the particular vectors described in the specification were designed to effect expression of specified DNA sequences contained therein. *See, e.g.,* Cabilly II, Figs. 6, 7, 11, 12, and 13; 4:17-29; 8:3-25; 9:53-55; 27:42-28:28. Even the expansive language in the specification, which is meant to broaden the invention to include after-arising technologies, is limited to expression vectors. Cabilly II 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 *Biogen* pan el recognized that "the specification is the basic presentation by the applicant, and claims represent the final product of a sometimes imperfect process." 318 F.3d at 1140. The fact that the claims recite the term "vector," and not "expression vector," is likely an artifact from the interference between the Boss patent and the Cabilly II application. The claims were copied from another patent and do not comport with the specification verbatim, consistent with interference practice.FN11 The claims written by patentees were not restricted to the language used by the drafters of the Boss patent, and recite the term "expression vector," rather than "vector." FN12 Here, as in *Biogen,* the claim term should be limited by how the

specification defines the invention.

FN11. Copying another's claims in a patent or application into a pending application to provoke an interference has been standard practice. *See e.g.,* Vas-Cath, Inc. v. Curators of Univ. of Missouri, 473 F.3d 1376, 1379 (Fed.Cir.2007) ("The University invoked the procedures to institute an interference between the University's pending application and Vas-Cath's issued patent; the University amended its application by copying into the application all nineteen claims from the Vas-Cath patent, as the practice permits."). *See also Agilent,* No.2008-1466, slip op. at 2.
Because it was standard practice to copy the claims of another patent to attempt to provoke an interference, it would be unfair not to acknowledge the practice.
FN12. Claim 21, written by patentees, recited "expression vector," rather than "vector," since its inception. (The history of claim 21 is set forth in footnote 7.) The claims of the Cabilly I patent, written by patentees, also recite "expression vector."

Thus, the Court construes the term "vector" as limited to "expression vector" in the Cabilly II patent. Although this analysis may seemingly conflict with the Court's analysis of the term "immunoglobulin molecule," where the Court has not adopted the patentees' own language, there are two distinctions. First, this construction of the term "vector" embraces, rather than contradicts, a definition found in the specification. Second, the interpretation of "vector" as limited to "expression vector" was never relied on as a point of patentability during prosecution of the Cabilly II patent, where the patentees had ample opportunity and reason to limit the term by amendment.

4. "Transformed host cell comprising at least two vectors "

The term "transformed host cell comprising at least two vectors" appears in claim 18, and is limited to a mammalian cell in claim 20. The parties dispute the meaning of this term and propose the following constructions:

Genentech and City of Hope	**Centocor**
Host cell whose heritable DNA has been altered to include foreign DNA from at least two DNA constructs	A cell into which foreign DNA has been introduced comprising at least two separate DNA molecules that are capable of transporting a DNA segment into another cell

Defs.'Br. at 10, PL's Br. at 6.

The parties' dispute centers on whether or not a stable cell line with integrated vectors falls within the claims. Defs.' Br. at 10. A stable cell line has heritable DNA, that is, the DNA in each cell passes down into progeny cells when the cell divides.

The Court has rejected the idea that a vector must be capable of transporting a DNA molecule into another cell. *See supra* s. III(B)(3). In addition, the specification makes it clear that vectors may be integrated or not, and integrated vectors are usually incapable of transporting a DNA segment into another cell. Thus Centocor's proposed construction can not be correct. The remaining issue is whether or not the term "transformed host cell comprising at least two vectors" refers to host cells whose *heritable* DNA has been altered.

To support the word "heritable" in its proposed construction for host cell, Genentech points to examples of usage of the term "transformation" by those of skill in the art at the time the invention was made. Defs.' Br. at 15 ("Transformation is the heritable modification of the properties of one strain of microorganism (acceptor) by deoxyribonucleic acid (DNA) extracted from the cells of another strain of microorganism (donor)." (quoting U.S. Patent No. 3,930,956)).

While not dispositive, the description of the prior art in the specification of the Cabilly II patent sheds light on "what the inventors actually invented and intended to envelop with the claim[s]" and to determine the construction which "most naturally aligns with the patent's description of the invention." Phillips 415 F.3d at 1316. The specification of the Cabilly II patent distinguishes the invention from the prior art, stating hybridoma antibody production "suffer[s] from certain disadvantages ." Cabilly II 2:41-43. The specification explains "hybridoma lines producing monoclonal antibodies tend to be unstable and may alter the structure of antibody produced or stop producing antibody altogether." *Id*. at 2:49-51. The patentees sought to overcome these drawbacks of the prior art, including unstable cell lines, in which the ability to express protein from the introduced DNA sequences has been lost. Introduction of heritable DNA, which is passed down to progeny cells, would avoid this problem.

Centocor takes the position that "heritable DNA" in Genentech's proposed construction "cannot be correct as it would exclude the only example provided in the Cabilly II specification- *i.e.*, the use of a plasmid which generally does not become integrated and is not necessarily passed on to progeny." PL's Br. at 12. Even if a plasmid "is not necessarily" heritable, this fact alone would not be enough to exclude host cells with altered heritable DNA from the claim term. Centocor's proposed definition contradicts the specification, particularly the description relating to replicable expression vectors.

The specification explains that the vector DNA must be able to be passed on to progeny cells: "It is implied, although not always explicitly stated, that these expression vectors *must be replicable* in the host organisms.... Clearly *a lack of replicability would render them effectively inoperable*." Cabilly II at 8:6-11 (emphasis added). Therefore, the specification contemplates heritable vector DNA.

Further, the Summary of the Invention describes isolating immunoglobulins from "host cell cultures" and the specification states "the terms 'cell' and 'cell culture' are used interchangeably." *Id*. at Cabilly II 4:53-55, 8:33-36. Stable transformation of host cells, i.e., alteration of a host cell's heritable DNA with replicable vectors to produce a cell culture, is the meaning that most naturally aligns with the patent's description of the invention.

At the time of the invention, transformation of cells was known to be a heritable modification of cells and patentees sought to make stable cell lines with replicable vectors. Centocor's argument that not all cells having plasmids introduced have altered heritable DNA is not enough to overcome the ordinary and customary meaning of the claim term. Limiting "transformed host cell" to only that particular cell into which the vectors were introduced is contrary to the discussion of cell culture in the specification. Limiting "transformed host cell" to exclude such cells would also contradict the description.

Thus, the Court construes the term "transformed host cell comprising at least two vectors" to mean "a host cell into which two or more vectors have been introduced, including a host cell whose heritable DNA has been altered by the integration of two or more vectors." It is clear from the description in the specification and the purpose of the invention that the vector DNA is heritable. Similarly, it is clear from the specification that the vectors may be episomal or integrated into the cell's chromosomal DNA.

C. Disputed claim term in the Basey patent

Centocor has asked the Court to construe the claim term "about" in claim 1 of the Basey patent. Genentech does not wish to construe the term; Centocor proposes to construe the claim term as follows:

Genentech	Centocor
No construction needed	Within the range of experimental error that occurs in any experiment

Pl.'s Br. at 21, Defs.' Br. at 23.

Courts are not required to construe a claim term when the meaning of the term "does not appear to have required % 7Fconstruction,' or to depart from its ordinary meaning." Biotec Biologische Naturverpackungen GmbH & Co. KG v. Biocorp, Inc., 249 F.3d 1341, 1349 (Fed.Cir.2001). *See also* U.S. Surgical Corp v. Ethicon, Inc., 103 F.3d 1554, 1568 (Fed.Cir.1997) ("The *Markman* decisions do not hold that the trial judge must repeat or restate every claim term in order to comply with the ruling that claim construction is for the court.").

Centocor has not presented any reason why the term "about" in the Basey patent is unclear, should not be given its ordinary meaning, or needs to be construed at all. The Court notes that the prosecution history of the Basey patent is straightforward.

Thus, the Court declines to construe the term "about" at this time.

IV. CONCLUSION

The Court reaches the following conclusions:

In the Cabilly II patent:

-> The term "immunoglobulin molecule" does not require construction at this time.

-> The term "produced as separate molecules in a single host cell" is clear on its face and does not require construction.

-> The term "vector" means "expression vector."

-> The term "transformed host cell comprising at least two vectors" means "a host cell into which two or more vectors have been introduced, including a host cell whose heritable DNA has been altered by the integration of two or more vectors."

In the Basey patent:

-> The term "about" does not require construction at this time.

IT IS SO ORDERED.

C.D.Cal.,2009.
Centocor, Inc. v. Genentech, Inc.