United States District Court,
E.D. California.

**CHIRON CORPORATION,**
Plaintiff.
v.
**GENENTECH, INC,**
Defendant.

No. CIV.S-00-1252 WBS GG

**April 22, 2002.**

Owner of patent for monoclonal antibodies capable of binding to specific human breast cancer antigens sued competitor for infringement. Construing claims, the District Court, Shubb, J., held that antibody called for in patent meant homogeneous population of antibodies from any source or species, including humanized antibodies.

Claims construed.

Court-Filed Expert Resumes

6,054,561. Construed.

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***MEMORANDUM AND ORDER***

SHUBB**, District Judge.**

In this lawsuit, Chiron alleges that Genentech's product, Herceptin, infringes Chiron's United States Patent No. 6,054,561 (" '561 patent"). The court is now called upon to construe the terms of '561 patent. *See* Markman v. Westview Instruments, Inc., 52 F.3d 967, 968 (Fed.Cir.1995) (en banc), *aff'd,* 517 U.S. 370, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996).

## I. *Factual and Procedural Background*

The '561 patent issued on April 25, 2000 from a long line of patents and patent applications dating back to February 8, 1984 and January 11, 1985. Generally, the patent claims monoclonal antibodies capable of binding to specific human breast cancer antigens.

Antibodies, also known as "immunoglobulins," are produced by the immune system in response to the presence of an antigen, or foreign substance, in the body. Antibodies recognize and bind to specific receptor sites, or "epitopes," on the antigen. Because antibodies are capable of homing in on specific antigens, they are useful for identifying and destroying harmful agents in the body, such as bacteria, viruses, and cancer cells. For example, a toxin may be attached to an antibody so that it will kill the antigen to which it binds.

Structurally, an antibody is a "Y" shaped molecule composed of four "chains" of amino acids: two identical heavy chains, and two identical light chains. The two arms of the "Y" are collectively referred to as the "variable region," while the tail end is called the "constant region." It is the variable region of the antibody that does the important work of recognizing and binding to the antigen. More specifically, "complimentary determining regions" ("CDRs") and "framework regions" ("FRs") within the variable region form a three-dimensional structure that fits in lock-and-key fashion to a particular receptor site on the antigen. The portion of the antibody that binds to the antigen is sometimes referred to as "the antigen binding site."

When responding to the presence of an antigen, the body may produce many different antibodies that bind to different receptor sites on the antigen. Antibodies that have identical antigen binding sites, however, will attach to the same receptor site on the same antigen.

Homogenous preparations of identical antibodies, all of which have a high affinity for binding to cancerous antigens and can distinguish cancer antigens from normal tissue, are useful in the treatment and diagnosis of cancer. In the 1980s, scientists at Cetus (Chiron's predecessor) attempted to create antibodies having these characteristics. To do so, they utilized the "hybridoma method," FN1 which is described at length in the '561 patent, as well as in the 1984 and 1985 priority applications. Briefly put, it involves taking a human cancer cell and injecting it into a mouse, which produces antibodies in response. The murine (mouse) B-cells that produce the antibodies are then isolated. Because each B-cell is unique and produces only one kind of antibody, a B-cell with an extended life span can produce numerous, identical antibodies. Accordingly, once the B-cell is isolated, it is fused with an immortal myeloma tumor cell. The resulting hybrid cell, or "hybridoma," is an immortal cell line that is capable of producing an unlimited supply of identical antibodies. The parties agree that antibodies produced by these methods are "monoclonal antibodies" (i.e. coming from "one cloned" cell).

FN1. This method was developed by Drs. Georges Kohler and Cesar Milstein in 1975, and is sometimes referred to as the "Kohler-Milstein method".

Cetus scientists tested hundreds of these monoclonal antibodies until they isolated ones capable of recognizing human breast cancer antigens, and binding strongly to them but not to normal cells and tissues. Specifically, they found that antibodies 454 C11 and 520 C9 bound to an antigen that occurred with great frequency in breast cancers, but with little frequency in normal tissue.

Scientists soon discovered that the murine monoclonal antibodies produced by the hybridoma method described above could be problematic for treatment. The murine origin of the antibodies provoked a HAMA ("Human Anti-Mouse Antibody") response in patients, as the human body rejected the murine antibodies as foreign matter. Scientists therefore began investigating other methods for producing antibodies that would retain the antigen binding sites of the murine monoclonal antibodies, but would not produce an immunogenic response.

One such development was a "chimeric antibody," created by attaching mouse-derived variable regions to human constant regions.FN2 Subsequently, scientists developed a more sophisticated "humanized antibody," in which only the antigen binding sites were murine in origin. Scientists were able to identify the amino acid sequences in the murine antibody that code for the cancer-specific antigen binding sites. They then used recombinant DNA technology to combine these murine amino acid sequences with human amino acid sequences. Thus, the resulting humanized antibody retained the beneficial binding properties of the murine antibody while minimizing the potential for an adverse immune response. The accused product, Herceptin, is precisely this kind of humanized antibody.

FN2. The literature also refers to "hybrid," "altered" and "recombinant" antibodies.

The central dispute in this case is whether the term "monoclonal antibody" as used in the '561 patent encompasses humanized antibodies. The parties also dispute the meaning of the claim terms "binds," "antigen," "strong staining," "immunoassay," "extracellular domain," and "human c-erbB-2 antigen."

A *Markman* hearing was held on March 5-7, 2002 before Magistrate Judge Hollows. On March 25, 2002, Magistrate Judge Hollows filed findings and recommendations regarding the construction of the above terms. ( *See* Mar. 25, 2002, Findings and Recommendations) (hereinafter "F & R's"). Both Chiron and Genentech filed objections to the findings and recommendations, which the court now reviews de novo. *See* 28 U.S.C. s. 636(b)(1)(C); Local Rule 72-304.

**II.** ***Discussion***

[1] [2] Claim construction is a matter of law for the court to decide. Phonometrics v. Northern Telecom Inc., 133 F.3d 1459, 1463 (Fed.Cir.1998). The purpose of claim construction is to "elaborat[e] the normally terse claim language in order to understand and explain, but not to change, the scope of the claims." Gart v. Logitech, 254 F.3d 1334 (Fed.Cir.2001) (quoting Embrex, Inc. v. Service Eng'g Corp., 216 F.3d 1343, 1347 (Fed.Cir.2000)) (internal quotations and citation omitted). In construing claim terms, "the focus is on the objective test of what one of ordinary skill in the art at the time of the invention would have understood the term to mean." Markman, 52 F.3d at 968; Kopykake Enterprises, Inc. v. Lucks Co., 264 F.3d 1377, 1383 (Fed.Cir.2001) (construing the patent "as of the date the invention was constructively reduced to practice-the date the patent application was filed").

[3] [4] In this case, the '561 patent claims priority based on the 1984 and 1985 applications. For the invention claimed in the '561 patent to get the benefit of the 1984/1985 filing dates, it must have been reduced to practice in 1984/1985. *See* Transco Products, Inc. v. Performance Contracting, Inc., 38 F.3d 551 (Fed.Cir.1994) (holding that an invention is entitled to the filing date of parent applications if it is supported by the disclosure in the parent applications). Accordingly, the court construes the disputed terms as they would have been understood by one skilled in the art in 1984 and 1985.

[5] The objective meaning of the claims can ordinarily be ascertained from three pieces of "intrinsic evidence": the claim language, the patent specification, and the prosecution history. Level One Communications, Inc. v. Seeq Technology, Inc., 987 F.Supp. 1191 (N.D.Cal.1997) (citing Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed.Cir.1996)). "[T]he actual words of the claim are the controlling focus," and the starting point for claim construction. Digital Biometrics, Inc. v. Identix, Inc., 149 F.3d 1335, 1344 (Fed.Cir.1998) (discussing the "hierarchy of analytical tools"). The specification (also called the written description) aids in defining the terms used in the claims, particularly if the patentee has elected to define the terms himself. *See* Vitronics, 90 F.3d at 1582, York Prods. Inc. v. Central Tractor Farm and Family Ctr., 99 F.3d 1568, 1572 (Fed.Cir.1996). Finally, the prosecution history is relevant "because it may contain contemporaneous exchanges between the patent applicant and the PTO about what the claims mean." Digital Biometrics, 149 F.3d at 1344. The intrinsic evidence is "the most significant source of the legally operative meaning of disputed claim language." Vitronics, 90 F.3d at 1582.

[6] [7] If the intrinsic evidence is insufficient for determining the scope of the disputed claims, the court may then rely on extrinsic evidence, such as dictionaries and expert testimony, in "coming to the proper understanding of the claims." Id. at 1583. In addition, extrinsic evidence "may be accepted by the court to enhance its understanding of the technology." Gart, 254 F.3d at 1340; *see also* Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1308 (Fed.Cir.1999) ("It is entirely appropriate, perhaps even preferable for a court to consult trustworthy extrinsic evidence to ensure that the claim construction ... is not inconsistent with clearly expressed, plainly, apposite and widely held understandings in the pertinent technical field"). In referring to these additional sources, the focus, of course, "remains on the meaning of claim language." Gart, 254 F.3d at 1340.

**A. "*Monoclonal Antibody*"**

[8] The term "monoclonal antibody" appears in all of the patent claims. Claim 1 is representative:

A monoclonal antibody that binds to a human breast cancer antigen that is also bound by monoclonal antibody 454 Cll which is produced by the hybridoma deposited with the American Type Culture Collection having Accession No. HB 8484.FN3

FN3. The American Type Culture Collection ("ATCC") is a bank of tissues and cell lines. Thus, persons skilled in the art can obtain hybridoma No. HB 8484 on file with the ATCC and make the 454 C11 monoclonal antibody referred to in the claim. Using that antibody, the person can identify the breast cancer antigen described in the claim.

'561 Patent, Claim 1.
Chiron and Genentech vigorously dispute the meaning of the term "monoclonal antibody." Genentech argues that "monoclonal antibody" refers to a homogenous population of antibodies having a structure that can be made by a murine hybridoma.FN4 Chiron agrees that the term refers to a homogeneous population of antibodies, but contends that the term is not limited in any way by the type of antibodies making up the population.

FN4. Genentech's proposed construction of this term has changed over the course of this litigation. Initially, Genentech proposed that a monoclonal antibody referred to "a uniform population of antibodies produced

from a hybridoma." (Genentech Claim Construction Statement, at 2:5-6.) Magistrate Judge Hollows rejected this construction because, among other things, it improperly attempted to limit a product by the process in which it was made. ( *See* F & R's at 24-27) ("It is well established that if the 'patent is upon a product, and if the product complained of is the patented article substantially as described, it makes no difference by what path or process, new or old, inferior or improved, the infringing product is manufactured.' ") (quoting Amgen Inc. v. Chugai Pharm. Co., 706 F.Supp. 94, 103-104 (D.Mass.1989)). Genentech's new proposed construction of "monoclonal antibody" defines the antibody in terms of its structural characteristics, rather than as a product of a particular process. Genentech has also shifted its focus away from the patent itself toward the prosecution history of the patent. Because Genentech has refocused its arguments, the court's analysis will not track the analysis set forth in Magistrate Judge Hollows' findings and recommendations. However, many of the substantive issues remain the same.

**1.** ***Claim Language*** FN5

FN5. Genentech's objections to the findings and recommendations do not discuss the term "monoclonal antibody" as it is used in the '561 patent. Rather, Genentech refers to the prosecution history, and argues that it is dispositive of the meaning of "monoclonal antibody." Although the prosecution history is relevant to claim construction, it is never the starting point of the analysis. The court looks first to the patent itself.

Looking at the claim language itself, only one structural limitation can be inferred from the way "monoclonal antibody" is used: the antibody must have a structure that enables it to bind to the referenced human breast cancer antigen. The language of the claims, standing alone, does not support Genentech's more limited construction.

**2.** ***Specification***

The specification also supports a broad construction of the term. The specification expressly defines "monoclonal antibody" as follows:

As used herein, the term "monoclonal antibody" refers to an antibody composition having a homogeneous antibody population. *The term is not limited regarding the species or source of the antibody, nor is it intended to be limited by the manner in which is is made*. The term encompasses whole immunoglobulins.

'561 Patent, 8 :40-45 (emphasis added).

[9] It is a well established rule of claim construction that "an inventor may be his own lexicographer." Kopykake, 264 F.3d, at 1383. Thus "[w]hen the meaning of a term is sufficiently clear in the patent specification, that meaning shall apply," even if common understandings of the term are different. Multiform Desiccants, Inc. v. Medzam, Ltd., 133 F.3d 1473, 1477-78 (Fed.Cir.1998).

In light of the above quoted definition, one skilled in the field of microbiology and immunology in 1984 and 1985 would interpret the term "monoclonal antibody" to encompass any antibody, from any source or species (murine or otherwise), produced by any method (known at the time or not), so long as the population of antibodies is homogenous. Therefore, the term "monoclonal antibody" as defined in the specification is broad enough to include homogenous populations of humanized antibodies. Genentech's more limited construction is inconsistent with this definition.

Genentech argues that other language in the specification suggests that the term "monoclonal antibody" does not include chimeric, hybrid, or humanized antibodies. First, Genentech points to the definition of "antibody":

The term "antibody" encompasses polyclonal [non-homogeneous] and monoclonal antibody preparations, as well as preparations including hybrid antibodies, altered antibodies, chimeric antibodies and, humanized antibodies. FN6

FN6. In discussing this language, Magistrate Judge Hollows referred to chimeric, hybrid, and humanized antibodies as "distinct" subsets of antibodies. ( *See* F & R's at 23:6-7.) Chiron objects to the characterization of these subsets of antibodies as "distinct," and argues that they are overlapping. (Chiron Objections at 7.) How these subsets are characterized, however, is irrelevant to the construction of the term "monoclonal antibody." Accordingly, the court will not decide this issue at this time.

'561 Patent, 8 :36-39.
Genentech contends that the use of "as well as" indicates that monoclonal antibody preparations are separate and distinct from preparations including hybrid, chimeric, and humanized antibodies. As Genentech puts it, "saying that 'a balanced diet consists of meats, fruits and vegetables, *as well as* bread and dairy products' does not connote that bread and dairy products are subsets of meats or fruits or vegetables." (Genentech Objections to F & R's, at 5.)
However, "as well as" does not always differentiate between mutually exclusive categories. *See* In re Hyatt, 708 F.2d 712, 714 (Fed.Cir.1983) (stating that patent claims "must be read in accordance with precepts of English grammar.") For example, one might say, "Our city is very diverse. It has a large African American and Asian population, *as well as* people from many different religious backgrounds, such as Muslims, Buddhists, and Jews." No one would interpret this phrase to mean that African Americans cannot also be Muslims. Likewise, it is not necessary to interpret monoclonal and humanized antibodies to be mutually exclusive. An equally plausible interpretation of the quoted language from the patent is that it describes two separate attributes of antibodies: their composition (monoclonal or polyclonal), and their structure (hybrid, chimeric, and humanized). Under this interpretation, an antibody can be both monoclonal and humanized.

The specification supports the latter interpretation. For example, it discusses humanized antibodies, and refers to non-hybridoma derived molecules as embodiments of the claimed monoclonal antibodies. *See* '561 Patent, 11:12-12:26 (discussing humanized antibodies); 5:40-46 ("In various related embodiments, nucleic acid molecules are provided including ... molecules which combine murine CDRs with supporting human FRs ...."); *see* Bell Atlantic Network Services v. Covad Communications Group, Inc., 262 F.3d 1258, 1269 (Fed.Cir.2001) ("The written description of the preferred embodiments ... guides our interpretation of the claim language, as claims must be read in light of the specification.") FN7

FN7. Genentech argues that this interpretation renders the categories of antibodies discussed in the patent "demonstrably incomplete" because the mentioned structures do not include the hybridoma-derived antibodies that are referenced throughout the patent. (Genentech Objections to F & R's at 7.) The definition of "antibody," however does not purport to be all-inclusive.

Next, Genentech contends that language in the "background" section of the specification "makes ... clear"

that homogeneity is merely one of several attributes of a monoclonal antibody. Specifically, Genentech points to the following sentence:

A monoclonal antibody belongs to a group of antibodies whose population is substantially homogeneous, i.e. the individual molecules of the antibody population are identical except for naturally occurring mutations.

'561 Patent, 1: 50-54

This sentence certainly suggests that homogeneity is an attribute of a monoclonal antibody, but it has nothing to say one way or another about whether homogeneity is one of many relevant attributes, or the only relevant attribute of a monoclonal antibody. The definition in the specification does; it makes clear that a monoclonal antibody is an antibody that comes from a homogeneous antibody population, without any other limitations.

Finally, Genentech argues that because the humanized antibodies described in the patent are not referred to as "monoclonal antibodies," the patentees must have intended to carve out humanized antibodies from the classification of monoclonal antibodies. Given the express definition of the patent, this interpretation is implausible. The extrinsic evidence helps to clarify this point. At the Markman Hearing, experts for both parties testified that humanized antibodies would not be useful if they were not homogeneous. (Mar. 7 Markman Tr. at 57:6-15) (testimony of Genentech expert Dr. Unkeless that those in the field understand that a humanized antibody is homogeneous "otherwise, why would you have it.") Thus, one skilled in the art would have understood humanized antibodies as that term is used in the '561 patent to refer to homogeneous populations of antibodies. Because homogeneity would have been assumed, using the term "monoclonal antibody" when referring to humanized antibodies would have been unnecessary.

Therefore, looking at the claim language and the specification, one skilled in the art in 1984 and 1985 would broadly construe the term "monoclonal antibody" to mean any homogeneous antibody population. There is no support in the issued patent for reading an additional structural limitation into the claims.

**3. *Prosecution History***

[10] The analysis does not end, however, with a review of the claims and the specification. The prosecution history, or the back-and-forth between the patentee and the Patent and Trademark Office ("PTO") prior to the issuance of the patent, can shed light on the meaning of terms in the claims, and even limit claim terms. *See* Biovail Corp. Int'l v. Andrx Pharmaceuticals, Inc., 239 F.3d 1297, 1301 (Fed.Cir.2001) ("Claim language ... must be read consistently with the totality of the patent's applicable prosecution history."). For example, "the prosecution history limits the interpretation of claim terms so as to exclude any interpretation that was disclaimed during the prosecution." Southwall Techs., Inc. v. Cardinal IG Co., 54 F.3d 1570, 1576 (Fed.Cir.1995). The prosecution history may also "show a particular meaning attached to the terms, or a position taken by the applicant to ensure that the patent would issue." Markman, 52 F.3d at 991. "Although the prosecution history can and should be used to understand the language used in the claims, it ... cannot 'enlarge, diminish, or vary the limitations in the claims.' " Markman, 52 F.3d at 979 (quoting Goodyear Dental Vulcanite Co. v. Davis, 102 U.S. 222, 227, 12 Otto 222, 26 L.Ed. 149 (1880)).

The prosecution history of the '561 patent is long and complicated. In February of 1984, Chiron's predecessor, Cetus, filed an application for a patent for monoclonal antibodies. In 1985, and then again in 1995, Chiron filed continuation applications.FN8

FN8. A "continuation" of an earlier parent application claims the same invention as the parent application, with some variation in scope. For example, a continuation might add new claims, or it might disclose newly discovered embodiments of the existing claims. To the extent that continuations add "new matter" that is not supported by the disclosures in the earlier applications, they are not entitled to the filing dates of the earlier applications; otherwise, continuations date back to the parent application. *See* Transco Products, Inc. v. Performance Contracting, Inc., 38 F.3d 551 (Fed.Cir.1994). Thus, "[p]atent claims may ... be amended to cover a competitor's product discovered subsequent to the filing of the original application, so long as the amendments are supported by the disclosure in the original application." Laitram Corp. v. Morehouse Indus., Inc., No. Civ. S-94-0452 WBS/GGH, 1997 WL 33320572, at *37-38 (E.D.Cal. Apr. 24, 1997).

The 1985 application, though similar in many relevant respects to the 1984 application, offered an explicit definition of "monoclonal antibody" that did not appear in the 1984 application. That definition is almost identical to the definition found in the '561 patent. The 1985 application eventually became U.S. Patent No. 4,753,894 (the '894 patent), which is the subject of related litigation between Chiron and Genentech. *See Chiron v. Genentech,* CIV-S-01-503 WBS/GGH.

The 1995 application was much longer than the 1984 and 1985 applications, and is the first application in the chain to discuss recombinant and humanized antibodies. The 1995 application initially contained claims to nucleic acid molecules encoding single chain polypeptides capable of binding to human breast cancer antigens. These claims were rejected by the PTO on the basis that they were not supported by the priority applications, and were obvious in light of intervening prior art. Chiron then withdrew the rejected claims and added claims to "monoclonal antibodies," which the PTO allowed.

After the claims were allowed, but before the patent was issued, Chiron sought two "post allowance" amendments pursuant to 37 C.F.R. s. 1.312(a). The first amendment revised the definition of monoclonal antibody to "encompass[ ] only subject matter that was encompassed by the term 'monoclonal antibody' in the priority applications." (Chiron Markman Exhibit 175, Tab 156). The second amendment sought to add claims to (1) monoclonal antibodies prepared by a hybridoma process; (2) a hybridoma capable of producing monoclonal antibodies; (3) monoclonal antibodies prepared by a cell line process; (4) a cell line capable of producing monoclonal antibodies. (Chiron Markman Exhibit 175, Tab 157). The patent examiner allowed only the hybridoma claims, finding that the cell line claims did not find support in the priority applications. On April 25, 2000, the '561 patent issued.

**a.** ***The 1984 and 1985 Priority Applications***

Genentech argues that given the prosecution history of the patent, the meaning of the term "monoclonal antibody" as used in the 1984 and 1985 priority applications controls the construction of the term as it is used in the '561 patent. Further, Genentech argues that the 1984 and 1985 applications use the term "monoclonal antibody" in the limited sense of an antibody having a structure derived from a murine hybridoma.

The court accepts Genentech's argument that the meaning of "monoclonal antibody" in the '561 patent must be consistent with the way the term was used in the priority applications. During prosecution of the '561 patent, Chiron disclaimed an interpretation of "monoclonal antibody" broader than the 1984 and 1985 applications. To escape the examiner's prior art rejection of the 1995 patent, Chiron withdrew the originally

submitted claims and added claims to monoclonal antibodies, stating that "no new matter has been added by way of these amendments, and the entry thereof is respectfully requested." (Chiron Markman Ex. 175, Tab 146.) Thus, Chiron represented to the PTO that the monoclonal antibody claims were equivalent in scope to the parent applications. *See* York Products, Inc. v. Central Tractor Farm & Family Center, 99 F.3d 1568, 1575 (Fed.Cir.1996) (holding that an applicant can limit claims during prosecution by altering claim language to escape an examiner rejection or by clearly disavowing claim coverage). In addition, in its first post-allowance amendment, Chiron amended its definition of "monoclonal antibody" to "encompass[ ] only subject matter that was encompassed by the term 'monoclonal antibody' in the priority applications." (Chiron Markman Exhibit 175, Tab 156).FN9 Accordingly, the court turns to the 1984 and 1985 applications.FN10

FN9. Genentech offers a number of other reasons why the court should look to the priority applications. For example, Genentech points out that the priority applications are incorporated by reference into the '561 patent, and that Chiron submitted a terminal disclaimer during the prosecution of the '561 patent. Because Chiron's statements during the prosecution history regarding the meaning of "monoclonal antibody" are sufficient to disclaim a meaning of the term broader than the 1984 and 1985 applications, the court expresses no opinion regarding the merits of these additional arguments.

FN10. Chiron argues that interpreting the '561 patent in light of the priority applications impermissibly blurs issues of validity and priority with the question of claim construction. *See* Vandor Corp. v. Wilson, No. IP 99-0946 CMS, 2001 WL 747281 (S.D.Ind. July 3, 2001) (holding that a partially formed validity argument cannot force a claim construction that is contrary to the plain meaning of the claim language read in light of the specification). It is not clear to the court, however, that these issues can be separated. Whether or not there was new matter added to the '561 patent, and regardless of the possibility that new matter in the '561 patent might have been invalidated by intervening prior art, Chiron represented to the PTO that the term "monoclonal antibody" was no broader than the scope of the 1984/1985 applications. *See* Bai v. L & L Wings, Inc., 160 F.3d 1350, 1356 (Fed.Cir.1998) (a patentee can disclaim a particular interpretation even if the examiner was incorrect in making the rejection). As a matter of claim construction (not validity or priority), the court is compelled to consider those applications.

### i. *The 1984 Application*

Like the '561 patent, the 1984 application concerns monoclonal antibodies capable of binding to human breast cancer antigens. Although the application discusses primarily murine monoclonal antibodies, it is not necessarily so limited. For example, while Claim 1 of the 1984 application claims "a murine monoclonal antibody that ... binds selectively to human breast cancer cells," Claim 2 is not expressly limited to murine monoclonal antibodies. ( *See* 1984 Application, at 28:1-18.) Rather, it is directed toward "a monoclonal antibody selected from the group consisting of [various antibodies including] 454 C 11 and monoclonal antibodies that are functionally equivalent to a member of said group." (1984 Application, at 28:7-18.)

A more difficult question is how the term "monoclonal antibody" should be construed in light of the 1984 specification. The 1984 application lacks the expansive definition of "monoclonal antibody" found in the '561 patent; indeed, the term is not defined at all in the 1984 application.

In some respects, the 1984 specification supports a narrow construction of the term. For example, the specification repeatedly refers to the invention as a " *murine* monoclonal antibody," *see* 1984 Application,

1:5-9 ("This invention ... concerns murine monoclonal anti-human breast cancer antibodies, [and] hybridomas that produce those antibodies ....."); *id*. at 2: 7-17 (describing the 454 Cll antibody and its functional equivalents as preferred embodiments of murine monoclonal antibodies that bind selectively to human breast cancer cells), and the only preferred embodiment disclosed in the specification is a murine, hybridoma-derived monoclonal antibody.

On the other hand, in describing the "important characteristics" of the invention, the 1984 specification does not refer to its murine hybridoma-derived structure:

The important characteristics of the monoclonal antibodies are (1) their immunoglobulin class, (2) their selectivity for human breast cancer cells and the range of human breast cancer cells to which they bind and (3) their usefulness in making effective anti-human breast cancer immunotoxins.

1984 Application, at 5: 1-7.

In fact, it is evident from the application's discussion of prior art that murine monoclonal antibodies derived from hybridomas had already been discovered, and that the novel aspect of the invention concerned monoclonal antibodies capable of binding to specific breast cancer antigens. *See* 1984 Application at 1:11-2:5 (describing "background art" regarding murine monoclonal antibodies); *id*. at 10:24-11 (describing how, in order to make the invention, the inventors prepared somatic cell hybrids using existing hybridoma methods). Moreover, before setting forth the best mode for making the invention, the 1984 specification emphasizes that the monoclonal antibodies are not intended to be limited by the manner in which they are made:

The following *examples* provide a detailed description of the preparation, characterization, and use of *representative* monoclonal antibodies of this invention. *These examples are not intended to limit the invention in any manner*.

*Id*. at 10: 1-5 (emphasis added).

Nevertheless, Genentech argues that because only one preferred embodiment is described in the specification, the invention claim in the 1984 application is limited to that embodiment.

**ii. *1985 Application***

Genentech makes the same argument with respect to the 1985 application. Like the 1984 application, the only preferred embodiment disclosed in the 1985 specification is a monoclonal antibody derived from a hybridoma. However, the 1985 application expressly defines "monoclonal antibody" for the first time:

As used herein, the term "monoclonal antibody" means an antibody composition having a homogeneous antibody population. It is not intended to be limited as regards the source of the antibody or the manner in which it is made.

1985 Application, at 3:19-23.

This definition is virtually identical to the broad definition of "monoclonal antibody" found in the '561 patent.FN11

FN11. The definition in the '561 patent adds that the invention is not limited regarding the *species* from which the antibody is derived. Genentech argues that the addition of the word "species" means that "monoclonal antibody" has a broader meaning in the '561 patent. However, the PTO allowed the definition in the '561 patent with the reference to "species" on the understanding that it had the same scope as the definition in the 1985 application. In addition, both the issued patent and the 1985 application define "monoclonal antibody" as a homogeneous population of antibodies, with no other structural limitations. Given ordinary understandings of the phrase "not limited by the manner in which it is made," it would not matter for either the 1985 application or the '561 patent whether hybridoma or recombinant techniques were used. The court, like Magistrate Judge Hollows, rejects Genentech's "strained conjecture" that the "manner" in which the monoclonal antibody was created refers to in vivo or in vitro creation and the "source" of the antibody refers to culture media or body fluids. ( *See* F & R's at 22.) The only support for this argument comes from a phrase that is in a completely different part of the application from the definition, and makes no reference to the terms used in the definition. *See* 1985 Application, 5:7-13.

The question for the court is whether, under these circumstances, the monoclonal antibodies claimed in the priority applications are limited to the preferred embodiment described therein.

**iii. *Preferred Embodiment As Limitation***

[11] The Patent Act, 35 U.S.C. s. 112, requires the patent to include a written description of the invention, including the manner and method of its making and the best mode (or preferred embodiment) for carrying it out, so that others skilled in the art can use it. *See* Brookhill-Wilk 1, L.L.C. v. Intuitive Surgical, Inc., 178 F.Supp.2d 356, 363 (S.D.N.Y.2001) (citing Wang, 197 F.3d at 1383). A claim is ordinarily not limited to the preferred embodiment described in the specification. *See* Ethicon Endo-Surgery, Inc. v. United States Surgical Corp., 93 F.3d 1572, 1582 n. 7 (Fed.Cir.1996). "However, in a given case, the scope of the right to exclude may be limited by a narrow disclosure." Gentry Gallery, Inc. v. Berkline Corp., 134 F.3d 1473 (Fed.Cir.1998). For example, "[t]here are times when an enumerated 'best mode' or 'preferred embodiment' of an invention is, in fact, nothing more than the invention itself." Brookhill-Wilk 1, L.L.C. v. Intuitive Surgical, Inc., 178 F.Supp.2d 356, 363 (S.D.N.Y.2001) (citing Wang Labs. Inc. v. America Online, Inc., 197 F.3d 1377, 1383 (Fed.Cir.1999)).

As the Federal Circuit has recognized, there is sometimes a "fine line" between reading a claim in light of the specification, which is permissible, and reading a limitation into the claims from the specification, which is not. *See* Comark Communications v. Harris Corp., 156 F.3d 1182, 1186 (Fed.Cir.1998). Although no hard and fast rules exist for drawing this "fine line," some general principles can be gleaned from the case law. Courts have limited the claims to the preferred embodiments disclosed in the specification in certain narrow circumstances where (1) it is clear from the specification that the embodiment is essential to the invention, or (2) the disclosure expressly distinguishes other embodiments that the patentee later argues are encompassed by the invention.FN12

FN12. Genentech appears to advocate a bright-line rule that would limit an invention to the preferred embodiment if only one embodiment is disclosed in the specification. Such a categorical rule is contrary to the principle that "an applicant is not required to describe in the specification every conceivable and possible future embodiment of his invention." *Rexnord,* 274 F.3d at 1344. The case law suggests that a more nuanced approach is required. *See* Gentry Gallery, 134 F.3d 1473 (patent for L shaped sofas with side-by-side

recliner seats did not encompass sofas with controls for the recliners located on arms of sofa, where the embodiment described the invention as having a console between the seats, and the only discernable purpose for the console was to house the controls); Brookhill-Wilk, 178 F.Supp.2d 356 (patent for surgery system that permits a surgeon to operate from "a remote location beyond a range of direct manual control" did not encompass virtual surgery systems used within the operating room, given distinctions over prior art on the basis that the invention allowed surgeons to operate from outside the hospital, as well as repeated emphasis in specification that the patent would facilitate surgery around the world and reduce the cost of surgery by eliminating the need to travel to a qualified surgeon); Modine, 75 F.3d 1545 (patent limited to particular embodiment because of an unambiguous amendment that narrowed the range of the claim term); Bell Atlantic, 262 F.3d 1258 (Fed.Cir.2001) (rate of data transfer was not included in the "plurality of different modes" claimed in the invention, because the specification repeatedly referred to "rate" and "mode" as distinct concepts); Laitram Corp. v. Morehouse Industries, Inc., 143 F.3d 1456 (Fed.Cir.1998) (limited because patentee argued the embodiment distinguished over prior art).

For example, in Watts v. XL Systems, Inc., 232 F.3d 877 (Fed.Cir.2000), the Federal Circuit held that a patent for joints and couplings in oil well pipes was limited to the preferred embodiment disclosed in the specification, which was a pipe joint having a varying tapered angle feature. The specification expressly stated that "the present invention utilizes" a varying tapered angle feature, thereby equating the invention with the preferred embodiment. In addition, the patentee had referred to the tapered angle feature in distinguishing prior art.

Similarly, in Wang Labs., 197 F.3d at 1383-84, a patent claiming a system providing computer users with "frames" of textual and graphic information via a telephone network was limited to the character-based "frames" disclosed in the patent. The patent described only a character-based system, and language describing the embodiment as a "preferred" embodiment that those skilled in the art "may" make was insufficient to suggest that other systems were contemplated. In addition, the inventors had distinguished over prior art by focusing on the character-based aspect of the invention.

This case bears some similarity to *Watts* and *Wang Labs* in that the invention is described in the priority applications as if it were the preferred embodiment. *See* 1984 Application ( *see* 1984 Application, 1:5-9) ("This invention ... concerns murine monoclonal anti-human breast cancer antibodies, [and] hybridomas that produce those antibodies ....."). However, unlike the inventors in *Watts* and *Wang Labs,* the inventors here did not focus on the murine-hybridoma structure to distinguish prior art. More importantly, unlike the patents at issue in *Watts* and *Wang Labs,* the 1984 and 1985 applications expressly contemplate other embodiments of the claimed invention. Both the 1984 and 1985 applications refer to the preferred embodiment as an "example" of the invention, and emphasize that "these examples are not intended to limit the invention in any manner." *Id*. at 10: 1-5. The 1985 application, which contains the broad definition of "monoclonal antibody" adopted by the '561 patent, is even more explicit on this point. FN13

FN13. Genentech argues that the definition in the 1985 application expands the scope of "monoclonal antibody" beyond the meaning of the term as it was used in the 1984 application. However, the prosecution history reveals that both Chiron and the PTO understood the definition in the 1985 application to be consistent with the scope of the 1984 application. When Chiron proposed to define "monoclonal antibody" in the '561 patent to encompass the same subject matter as encompassed in the priority applications, it specifically cited the examiner to the 1985 application. ( *See* Chiron Markman Ex. 175 at tab 156.) Thus, Chiron represented to the PTO that all priority applications, including the 1984 application, fell within the

definition of "monoclonal antibody" in the 1985 application. As Magistrate Judge Hollows correctly concluded, this "renders the statement to the Examiner less than and 'clear disavowal' of its presently asserted interpretation." (F & R's at 28.)

In Rexnord Corp. v. Laitram Corp., 274 F.3d 1336 (Fed.Cir.2001), the Federal Circuit refused to limit the invention to the preferred embodiment where the patent contained similar non-limiting language:

The written description explicitly states that aside from the preferred embodiment, "[t]he invention is capable of other embodiments and of being practiced and carried out in different ways." .... These phrases reflect the inventor's teaching that his invention could be embodied "in various ways." Finally, the inventor explicitly qualified his detailed "Description of a Preferred Embodiment" by stating that "it is to be understood that the invention is not limited in its application to the details of construction and the arrangements of components or illustrated drawings." Id. at 1345 (internal citations to patent omitted).

Similarly, the text of the 1984 and 1985 applications teaches that the claimed antibodies are not limited to the disclosed embodiment. *Contrast* North American Vaccine, Inc. v. American Cyanamid Co., 7 F.3d 1571, 1576 (Fed.Cir.1993) (limiting the invention to one type of linkage because the specification taught that other linkages were "unlikely" or "not significant"); O.I. Corp. v. Tekmar Co., 115 F.3d 1576 (Fed.Cir.1997) (finding that the term "passage" in a patent for an apparatus for removing water vapor from a sample did not include smooth-walled passages, where the specification stated "although a threaded configuration is shown, other non-smooth geometries may be used to remove water vapor," and therefore only contemplated non-smooth geometries); Tronzo v. Biomet, Inc., 156 F.3d 1154, 1158 (Fed.Cir.1998) (holding that the invention was limited to the conical prosthetic hip sockets described in the specification, where the specification "[did] not attempt to identify other, equally functional shapes or talk in terms of a range of shapes.").

Moreover, it is clear from those applications that the importance of the invention is not its murine hybridoma-derived structure, but its ability to selectively bind to human breast cancer cells, and its usefulness as an effective therapeutic against cancer. *See* 1984 Application, at 5: 1-7 (listing the "important characteristics of the monoclonal antibodies," without any mention of their hybridoma-derived structure).

Genentech therefore cannot successfully argue that the murine hydridoma-derived structure was essential to the invention. The priority applications do not support reading such a limitation into the broad language of the claims in the issued patent.

**b. *Rejections by the PTO***

Genentech argues that not to limit the definition of "monoclonal antibody" gives Chiron a claim scope that was repeatedly rejected by the PTO during the application process. This argument misrepresents much of what occurred during the prosecution history, and fails to acknowledge Chiron's non-acquiescence with these rejections.

**i. *Functional Equivalent Claims***

The 1984 and 1985 applications, as well as a subsequent continuation in part application filed in 1986, attempted to claim monoclonal antibodies and their "functional equivalents." The "functional equivalent" claims were rejected each time by the PTO on the grounds that the term was indefinite and not enabled by

the disclosure in the specification. According to Genentech, this history indicates that the PTO believed the claims were limited in scope to murine hybridoma derived monoclonal antibodies. However, in setting forth the reasons for the rejection, the Examiner never explained why the functional equivalent claims were not enabled, and never stated that the priority applications were limited to antibodies with murine hydbridoma derived structures. *See* Rexnord, 274 F.3d at 1345 ("It is significant that the examiner made no explicit reference to [the disputed claim scope] in rejecting the claim.") Rather, the Examiner focused on the indefinite nature of the claims:

Claim 2 is indefinite as to the scope of the term "functionally equivalent." Which function(s) need to be equivalent to be included in this claim. [sic.] For example, which of the following are functionally equivalent: monoclonal/antibody able to (1) fix compliment, (2) bind to a human cell, (3) specifically bind to any human carcinoma, (4) binds only to breast carcinoma, (5) binds to the same antigen on or in the cell, (6) binds to the same site on the same antigen, or (7) the same isotype binding to the same eptiope? (Chiron Markman Ex. 175 tabs 7, 26.)

Thus, contrary to Genentech's assertions, the Examiner's rejection of the functionally equivalent claims tells us little about the proper scope of the priority applications and the issued patent. Moreover, Chiron never acquiesced in the rejection or "clearly disavowed" a claim scope that would cover functional equivalents. *See* York Products, 99 F.3d at 1575. In fact, Chiron withdrew the claims to functional equivalents stating that it was doing so "without prejudicing applicant's rights to antibodies having equivalent properties." (Chiron Markman Ex. 175, at Tab 55.) Ultimately, Chiron was issued both the '774 patent and '561 patent without the adjective "murine" in claims to monoclonal antibodies. ( *See* Chiron Markman Ex., at Tab 101.)

**ii.** ***Single Chain Antibody Claims***

Genentech next points out that during the prosecution of the 1995 application, the PTO rejected claims to nucleic acid molecules "encoding a humanized, single chain antibody" on the basis that they were preempted by prior art. (Chiron Markman Ex. 175 at Tab 140, p. 4.) The patent examiner explained that these claims "only have a priority date, 06/07/1995 because the claimed invention is not disclosed in the parent cases." ( Id. at p. 6.)

The examiner obviously did not believe that *single chain* humanized antibodies were supported by the priority applications. The examiner was silent, however, about whether humanized antibodies having the usual four-chain antibody structure were encompassed by the priority applications.FN14 "Drawing inferences of the meaning of claim terms from an examiner's silence is not a proper basis on which to construe a patent claim." DeMarini Sports, Inc. v. Worth, Inc., 239 F.3d 1314, 1326 (Fed.Cir.2001). Therefore, the rejection of claims to single chain humanized antibodies does not justify limiting the term "monoclonal antibody" to exclude four-chain humanized antibodies.

FN14. The prior art cited by the patent examiner discusses single chain humanized antibodies as distinct from humanized antibodies with four chains. ( *See* Chiron Markman Ex. 175 at Tab 140) (citing Ladner, et. al., U.S. Patent No. 4,946,778, August 7, 1990). The Ladner patent, for example, describes the advantages of single chain antibodies over recombinantly manufactured multiple chain antibodies: "[A]ntibodies are three-dimensional aggregates of two heavy and two light chains.... In order to produce such complex materials by recombinant DNA technology ..., it becomes necessary to clone and express a gene coding for each one of the different kinds of polypeptide chains.... The approach ... necessitates expression of multiple genes, and as indicated, in some cases, multiple and different hosts. These approaches have proven to be

inefficient.... [Therefore], it would indeed be greatly advantageous to be able to produce, by genetic engineering, single polypeptide chain binding proteins having the characteristics and binding ability of multi-chain variable regions of antibody molecules."

### iii. *Cell Line Claims*

Finally, Genentech relies on Chiron's failed attempt to add claims to cell lines. After the monoclonal antibody claims had been allowed, but before the patent issued, Chiron sought to add new claims for hybridoma processes, as well as a claim for a monoclonal antibody "prepared by a process [involving] a cell line capable of producing the monoclonal antibody" and a claim for the cell line itself. ( *See* Chiron Markman Ex. 175, Tab 157.) The patent examiner rejected the cell line claims on the basis that they did "not find support in the specification as well as in the priority specification," and asked Chiron to "resubmit ... with claims only to the hybridomas and the antibodies produced by hybridomas."( Id., Tab 162.) Chiron resubmitted the proposed amendment with only claims to hybridomas, which were allowed. ( Id., Tab 159.)

The term "cell line" is broader than "hybridoma" and could include recombinant, genetically engineered cell lines such as those used to produce a humanized antibody. Accordingly, Genentech argues that the rejection of the cell-line claims indicates that the patent examiner did not consider humanized antibodies to be within the scope of the patent.

Genentech's argument would have more force if it were not for the timing of the rejection. Before rejecting the cell line claims, the examiner had already allowed the claims to monoclonal antibodies on the understanding that they had the same scope as the priority applications, and without taking any limiting action with respect to the broad definition of monoclonal antibody found in the 1995 application. As discussed above, both this definition and the priority applications suggest that a monoclonal antibody is nothing more or less than a homogeneous population of antibodies.

[12] [13] The proposed claims to cell lines were narrower, dependent claims containing additional "process" limitations on the product (monoclonal antibody) that had already been accepted by the PTO.FN15 Because the proposed cell line claims imposed additional "process" limitations on the invention, any rejection of those claims has little bearing on the scope of the broader, allowed claims. It would be improper for the court to read a limitation into the broad monoclonal antibody claims because narrower claims to cell lines were rejected. *See* Ethicon Endo-Surgery v. United States Surgical Corp., 93 F.3d 1572, 1582 n. 7 (Fed.Cir.1996) (finding that the examiner's rejection of a narrow claim because it was not supported by the disclosure could not be used to limit a broad claim to the disclosed embodiment.); FN16 Markman, 52 F.3d at 979 ("Although the prosecution history can and should be used to understand the language used in the claims, it ... cannot 'enlarge, diminish, or vary the limitations in the claims.' ") (quoting Goodyear Dental Vulcanite Co. v. Davis, 102 U.S. 222, 227, 12 Otto 222, 26 L.Ed. 149 (1880)).

FN15. There are three ways an inventor may seek protection for his invention under the patent laws: product claims, process claims, and product by process claims. A "product" claim is defined in terms of its physical and structural characteristics, and is not limited by the process in which it is made. A "process" claim is directed toward the method of manufacture used to make a given product. The hybrid "product by process" claim is one in which a product is claimed in terms of the process by which it is made. *See* Amgen Inc. v. Chugai Pharm. Co., 706 F.Supp. 94, 103-104 (D.Mass.1989) *aff'd in part and rev'd in part on other grounds,* 927 F.2d 1200 (Fed.Cir.1991) (describing the difference between product and process claims). These three

types of claims are not mutually exclusive, and it is not uncommon for a patentee to seek all three types of claims to maximize protection for his invention.

FN16. "[T]he district court confused a claim supported by the specification, which is not allowable, with a broad claim, which is. Claim 1 was properly rejected because it *recited* an element not supported by [the] disclosure, i.e. a lockout 'on the stapler.' It does not follow, however, that [the] disclosure could not support claims sufficiently broad to read on a lockout off of the cartridge.... If Fox did not consider the precise location of the lockout to be an element of his invention, he was free to draft claim 24 broadly (within the limits imposed by the prior art) to exclude the lockout's exact location as a limitation of the claimed invention ... Such a claim would not be unsupported by the specification even though it would be literally infringed by undisclosed embodiments. *The district court should not have imposed on claim 24 an additional limitation which it does not contain*." Ethicon, 93 F.3d at 1582 n. 7 (internal citations omitted) (emphasis added). Though somewhat counter-intuitive, the Federal Circuit's reasoning is that a broad claim encompasses even subject matter that cannot be specifically claimed. Thus, a rejection of a narrow claim because it is not supported by the disclosure cannot be used to limit issued claims that are written broadly.

Plant Genetic Systems, N.V. & Biogen, Inc. v. DeKalb Genetics Corp., 175 F.Supp.2d 246 (D.Conn.2001), cited by Genentech, is inapposite. In that case, the court held that "plant" was limited to dicotyledonous plants, because during prosecution the examiner expressed his view that the specification did not enable the invention as to monocotyledonous plants. Id. at 268. Not only did this happen *before* the patent examiner allowed the claims to "plants," the discussion that took place directly referenced the claims in dispute. *Id.* ("there can be little question from the exchanges between the examiner and the applicants that the issue of whether the plant ... claims would cover both dicots and monocots arose on several occasions").

Here, the exchange between the patent examiner and Chiron took place *after* the claims to monoclonal antibodies had been allowed, and without reference to the meaning or scope of "monoclonal antibody." The relevance of the examiner's rejection to the already allowed monoclonal antibody claims is ambiguous at best. Absent a more detailed explanation of the reasons for rejection, the court will not guess at what was in the mind of the patent examiner. *See* Rexnord, 274 F.3d at 1348 (refusing to deviate from broad interpretation of claim terms where prosecution history was "inconclusive"); Markman v. Westview Instruments, Inc., 52 F.3d 967, 985 ("Of course the views of the [PTO] are generally not obtainable, except as reflected in the prosecution history.")

Moreover, nothing about Chiron's response to the rejection of the second proposed amendment can be considered a "clear disavowal" or "disclaimer" of claim scope by Chiron. Entry of a post-allowance amendment is completely discretionary. If the amendment is rejected, the applicant has no right to appeal and is not entitled to a detailed explanation of the reasons for the rejection. *See Ex parte Stone,* 1902 C.D. 434 (Comm'r Pat.1902); *Ex parte* Labore, 1965 WL 7402, 145 U.S.P.Q. 494 (Pat. & Tr. Office Bd.App.1964); 3 Lester Horowitz, *Patent Office Rules and Practice* s. 312a[4] at 31-8 (2001). Because Chiron could not appeal the rejection of the proposed amendments, it cannot be said to have acquiesced in the patent examiner's rejection.

Therefore, the court adopts Magistrate Judge Hollows' finding that rejected amendments went to 'process' and 'product by process' claims "that did not affect the pure 'product' claims at issue in this litigation." (F & Rs at 29). The court agrees with Magistrate Judge Hollows' conclusion that the patent examiner thus "left

intact the product claims ... as well as the examiner's prior analysis for allowance which did not limit the claims to hybridoma (murine) based antibodies." ( *Id*. at 29-30). Thus, both the '561 patent and the priority applications define "monoclonal antibody" broadly to encompass non-hybridoma derived, non-murine antibody structures.

**c. *Schering/Kopykake***

Genentech contends that if the court interprets the 1984 and 1985 applications to encompass humanized antibodies, it will in effect allow Chiron to claim an invention it did not make. Citing two recent federal circuit decisions, Schering Corp. v. Amgen, Inc., 222 F.3d 1347 (Fed.Cir.2000), and Kopykake Enterprises, Inc. v. The Lucks Co., 264 F.3d 1377, 1383 (Fed.Cir.2001), Genentech argues that the phrase "monoclonal antibody" cannot encompass humanized antibodies because humanized antibodies had not been discovered in 1984.FN17 However, neither case cited by Genentech is on point.

FN17. Antibodies produced through recombinant technology were first discussed in 1984. A humanized antibody was developed in the late 1980s.

*Schering* involved a patent for recombinant DNA molecules encoding what was originally described in the patent application as a "leucocyte interferon." A leucocyte is a white blood cell. Leucocytes produce interferons, which are molecules that help the body fight viral infections and tumors by immunizing healthy cells. At the time of the invention, scientists thought that leukocytes produced only one interferon having a specific amino-acid sequence. That interferon, along with its amino-acid sequence, was the subject of the claims in the initial application. Subsequently, it was discovered that leucocytes produce numerous interferons. Scientists therefore revised the nomenclature so that "leucocyte interferon" referred to the source of the interferon, while "IFN-alpha" was used to refer to a category of interferons produced by leucocytes. Due to these changes, the inventor amended the patent to substitute the term "leucocyte interferons" with the term "polypeptide of the IFN-alpha type."

Later, the owner of the patent tried to argue that the patent claimed all interferons falling within the IFN-alpha category. The court rejected this contention because "the patentee expressly limited the term 'IFN-alpha' to define the leucocyte interferon described in the initial application." *Id*. at 1353. The interferon described in the initial application was a single, specific polypeptide; therefore, the court reasoned, persons skilled in the art would not interpret the invention to claim the later-discovered interferons, which had different amino-acid sequences. "Because, at the time of the '901 application neither [the inventor] nor others skilled in the art knew of the existence of, let alone the identity of, the specific polypeptides now identified as subtypes of IFN-alpha, those subtypes cannot be within the scope of the claims." *Id*. at 1353. Thus, the term "did not and could not enlarge the scope of the patent to embrace technology arising after its filing." *Id*. The court concluded that "to grant broader coverage would reward [the inventor] for inventions he did not make." *Id*. at 1354.

The similarities between this case and *Schering* are superficial. Like the inventor in *Schering,* Chiron defined the disputed term with reference to the way that term was initially used. However, as discussed at length above, in this case, neither the priority applications nor the PTO placed any express limitations on the meaning of the term. Unlike the claims in *Schering,* the claimed monoclonal antibodies of the priority applications are not directed toward molecules described by specific amino acid sequences. Rather, they are expressly defined by (1) their homogeneity, and (2) their ability to bind to specific human breast cancer

antigens. These characteristics do not depend on whether the antibody is humanized or murine in structure (although at a molecular level murine and humanized antibodies are undoubtedly different in structure to a degree). Whereas the inventors in *Schering* were attempting to claim a completely different invention than what was claimed in the initial application, Chiron is claiming the same invention described in the priority applications: a homogenous preparation of antibodies capable of binding to human breast cancer antigens.

The full relevance of *Schering* to this case cannot be appreciated without reference to the extrinsic evidence in the record. This evidence reveals that, unlike the meaning of "leucocyte interferon," the meaning of "monoclonal antibody" has not changed since 1984/1985. Chiron's expert, Dr. Lanier, testified that the understandingof "monoclonal antibody" to those skilled in the art is consistent with the definition in the '561 patent, and has been so since 1984/1985. Genentech's expert, Dr. Unkeless, agreed that the meaning of "monoclonal antibody" had not changed, but testified at the hearing that humanized and chimeric antibodies are not understood to be the same thing as monoclonal antibodies. This testimony was substantially impeached on cross examination by numerous references in the literature (including some of Genentech's own publications) in which humanized and chimeric antibodies were referred to as monoclonal antibodies.FN18 In light of these references, Dr. Unkeless began to refer to his conclusions as his "personal view," rather than the objective understanding of one skilled in the art. Like Magistrate Judge Hollows, this court is persuaded by Dr. Lanier's testimony that one skilled in the art would consider any homogeneous population of antibodies to be monoclonal. ( *See* F & R's at 35.) Thus, Chiron is not claiming a different invention than that disclosed in the priority applications; Chiron is merely claiming a later-developed embodiment of the same invention.FN19 *See* Amgen Inc. v. Chugai Pharm. Co., 706 F.Supp. 94, 103-104 ("Although the development of recombinant technology provides the scientific and commercial communities with innovative techniques for manufacturing certain products and compositions, the patent protection of product claims has not changed."); Scripps Clinic & Research Found. v. Genentech, Inc., 927 F.2d 1565 (Fed.Cir.1991) (upholding district court's finding that claims to purified blood clotting factor, Factor VIII:C, encompassed "any Factor VIII:C preparation, regardless of how produced, having the same material and functional characteristics as the plasma-derived preparation.").

FN18. Patents and publications referring to genetically engineered humanized antibodies as "monoclonal" date from the 1990s. Genentech suggests that therefore these publications have no bearing on the meaning of "monoclonal antibody" to one skilled on the art in 1984 and 1985. To the contrary, given the testimony of both experts that the meaning of "monoclonal antibody" has not changed, its use in 1990 must be consistent with its use in 1984 and 1985. Therefore, the term must have been understood broadly in 1984 and 1985 to mean nothing less than a homogeneous population of antibodies. Moreover, in 1984 and 1985, methods other than hybridoma methods were being used to produce monoclonal antibodies. ( *See* Markman Tr. at 31:20-32:3, testimony of Dr. Lanier regarding four ways of making monoclonal antibodies known in the art in 1984). By November of 1984, scientists had published articles about chimeric antibodies. ( *See* Chiron Markman Ex. 5, Morrison article discussing chimeric antibodies). Thus, one skilled in the art in 1984 and 1985 would have understood a "homogenous population of antibodies" to include not just murine, hybridoma derived antibodies.

FN19. It is true, as Genentech points out, that Dr. Lanier testified at the Markman hearing that the named inventors of the '561 patent did not invent humanized antibodies. ( *See* Mar. 6, 2002 Markman Tr., at 77:3-10.) However, Dr. Lanier was not testifying as an expert in patent law, and the court will not impute a legal conclusion into his testimony.

[14] As Chiron points out, the *Schering* court did not state that it overruled a long history of Federal Circuit decisions holding that an applicant is not required to do the impossible and "describe in the specification every conceivable and possible future embodiment of his invention." *See* Rexnord, 274 F.3d at 1344; SRI Int'l v. Matsushita Elec. Corp., 775 F.2d 1107, 1121 (Fed.Cir.1985). Rather, *Schering* appears to carve out an exception to this rule in cases where the inventor has expressly limited the claims to particular embodiments known at the time of the invention.

For similar reasons, Kopykake, 264 F.3d 1377, is also inapposite. *Kopykake* involveda patent that claimed a method for "screen printing" decorations onto food stuffs. At issue was whether the term "screen printing" was broad enough to include ink jet printing. The court began its analysis by looking to the specification, which defined "screen printing" to include "any other conventional methods" of printing pictorial images onto food. Because it was not "conventional" at the time of the invention to use ink jet printing to print images on food, the court held that "screen printing" did not encompass ink jet printing. *Id*. at 1383-84. Thus, the court stated that "when a claim term understood to have a narrow meaning when the application is filed later acquires a broader definition, the literal scope of the term is limited to what it was understood to mean at the time of filing." *Id*.

In *Kopykake,* the fact that the specification was expressly limited by its terms to "conventional printing processes" carried dispositive weight. Because what is "conventional" necessarily changes over time, and because patents must be construed at the time of their filing, the *Kopykake* patent could only be understood by reference to conventional methods at the time of the patent's filing. In contrast, the priority applications in this case have no similar teaching that their claims are limited to what was "conventional" at the time. Moreover, as discussed above, the meaning of "monoclonal antibody" has not changed since those applications were filed.FN20 Therefore, the 1984 and 1985 applications do not limit the broad definition of monoclonal antibody found in the '561 patent to homogeneous populations of antibodies having structures that can be made by murine hybridomas.

FN20. Magistrate Judge Hollows distinguished *Kopykake* on the grounds that it involved a process patent, while this case involves a product patent. The court is not convinced that *Kopykake* is distinguishable on these grounds, since its sister case, *Schering,* was a product case.

Accordingly, the court adopts the definition of monoclonal antibody proposed by Magistrate Judge Hollows:

**The term "monoclonal antibody" means an antibody composition having a homogeneous (essentially identical) antibody population. The term is not limited regarding the species or source of the antibody, nor is it limited by the manner in which it is made. For example, the term includes monoclonal antibodies produced by a methodology other than hybridoma which results in monoclonal antibodies no matter how subcategorized, e.g., hybrid, altered, chimeric, or humanized. The term includes variants that naturally arise during the production of monoclonal antibodies. The term includes whole immunoglobulins.**

**B. "*Binds*"**

The parties also dispute the meaning of the term "binds" as it is used in the patent claims. *See e.g*. '561 Patent, Claims 1, 9("A monoclonal antibody that *binds* to a human breast cancer antigen ..."); '561 Patent,

Claim 19("A monoclonal antibody that *binds* to human c-erbB-2 antigen") (emphasis added).

[15] The term "bind" has a specific meaning to those skilled in the art of immunology. As previously discussed, the antigen binding sites on an antibody are custom-tailored to attach or "bind" to a specific receptor site on the antigen, much the way a lock and key fit together. However, sometimes an antibody will randomly and weakly attach at a site other than the specific one recognized. Both parties agree that the term "binds" as used in the patent does not refer to this random, backgroundbinding; it would make little sense for Chiron to patent an antibody that bound at random to human breast cancer cells. Thus, the parties agree that one skilled in the art in 1984 and 1985 would interpret the term "bind" to mean the attachment between an antibody and antigen that occurs at the specific antigen-binding site.

The parties' agreement ends there. Genentech contends that the term should be construed to mean a degree of attachment greater than background levels, while Chiron argues that the term should be construed more narrowly to refer to a degree of attachment that is immunologically significant given the purposes of the invention.

The specification does not define the term "binds," but "immunological binding" is defined as "the non-covalent interactions of the type which occur between an immunoglobulin molecule and an antigen for which the immunoglobulin is specific." This definition suggests that specificity is an important aspect of binding, but nothing more. Thus, on its face, it is consistent with Genentech's interpretation of the term binds.

[16] [17] However, a reading of the patent as a whole reveals that the term "binds" as used in the claims has a more precise meaning. Claim terms should be construed in accordance with the purposes of the claimed invention. *See* Renishaw PLC v. Marposs Societa' per Azioni, 158 F.3d 1243, 1251 (Fed.Cir.1998); CVI/Beta Ventures, Inc. v. Tura LP, 112 F.3d 1146, 1160 (Fed.Cir.1997). In addition, where alternative interpretations exist, the court should not construe the patent in a way that would render it useless. Process Control Corp. v. Hydreclaim Corp., 190 F.3d 1350, 1356 (Fed.Cir.1999).

In this case, the invention claimed in the '561 patent relates to antibodies that are "useful in specific binding assays, affinity purification schemes, drug or toxin targeting, imaging, and genetic or immunological therapeutics for various cancers ...." '561 Patent, 1:27-31. For these uses, it is important that the antibody does more than just specifically bind to the antigen of interest. Sometimes, antigens that are present in high numbers on cancer cells are also present in lower numbers on normal, healthy cells. Thus, if an antibody used for cancer diagnosis attaches to normal tissue in addition to cancer cells, it will give false positives. Similarly, an antibody used for therapy that is incapable of distinguishing between normal and cancerous tissue can have fatal effects. In cancer treatment, toxins are attached to the antibodies so that when the antibodies bind with cancer cells, the toxin kills that cell. If the antibodies also attaches to healthy cells, it can kill the healthy cells.

Accordingly, the patent states that "it is desirable to target malignant lesions while avoiding normal tissue." *Id*. 1: 67-4. The ability of an antibody to target a specific type of cell or tissue to the exclusion of others is called "selectivity." As is evident from the stated purposes of the invention, selectivity in binding is an important aspect of the claimed invention.

"Affinity," or strength of binding, is also an important aspect of the invention. An antibody that binds weakly to an antigen will not be particularly useful in therapy or diagnosis. Thus, the specification begins by

stating that "[i]t is an object of the invention to provide novel compositions that are derived from the antigen-biding sites of immunoglobulins *having affinity for* cancer *antigens*." ('561 Patent Col 3:30-33) (emphasis added).

The methods described in the specification for making the invention confirm that the inventors were concerned with isolating antibodies with specificity, affinity, and selectivity for breast cancer antigens. *See* '561 Patent, 15:34-45 ("monoclonal antibodies capable of binding specifically to a human tumor antigen ... were produced ...."); id. at 16:43-45 ("Wells that gave a reaction on the breast cancer membrane extract of greater than 0.7 O.D. were saved."); *id*. at 16:63 ("Hybridoma wells showing strong fluorescent binding to breast cancer cells but no fluorescent binding to fibroblasts were saved."); *id*. at 17:38-42 ("Antibodies were deemed to bind selectively to breast cancer if they bound strongly to less than about 1/3 of the normal tissues and blood cell types"); *id*. at 18:31 (describing how the inventors ran the isolated antibodies through a series of immunoassays FN21 to "evaluate their selectivity for breast cancer"); *id*. at 25:35-45 (describing tests to termine the "affinity constant," which measures the affinity of binding). Reading the patent as a whole, one skilled in the art would understand the term "binds" to mean a degree of attachment that is immunologically significant in the context of the uses for the monoclonal antibody described in the patent.FN22

FN21. The term "immunoassay" as used in the patent is construed below.

FN22. Genentech argues that the court should construe the term to mean binding that is greater than background binding because Chiron's expert, Dr. Lanier, testified that "immunologically relevant" binding refers to binding that is "greater than background binding." First, it is unnecessary for the court to rely on extrinsic evidence in the form of expert testimony to construe the term. Second, Genentech ignores other statements by Dr. Lanier that indicate more than mere specificity is required for immunologically relevant binding. *See* Transcript of Proceedings, Vol. 2, at 17 ("Q: is a certain level of affinity required for what you referred to earlier as immunologically relevant binding? A: Yeah. In fact .. you want something which binds much stronger in order to have good resolution powers for selectivity and specificity.") Third, the term "specificity" as used by Dr. Lanier incorporates the idea of affinity: ("Q: Could you explain what [specificity] means? A: [S]pecificity comes back to this lock and key idea where ... the antibody specifically *binds quite firmly* and specifically to its particular antigen.") (emphasis added).

Therefore, the court adopts the following construction of "binds":

**The term "binds" refers to a degree of attachment that is immunologically significant, i.e. a degree of attachment that is (1) above background levels; (2) specific; (3) selective for** cancer **as opposed to normal cells and/or tissues; and (4) has a useful degree of affinity.**

This definition departs slightly from the construction recommended by Magistrate Judge Hollows. He proposed that "except where the context of binding expressly indicates a phenomenon of isolated, random attachment, "binds" refers to a degree of attachment that is immunologically significant in the context of the uses for the monoclonal antibodies described in the patent." (F & R's at 39-40.) In an effort to promote clarity, the court's construction defines what is meant by "immunologically significant," something that the proposed construction does not do. In addition, the court's construction omits the first phrase of the proposed definition, which is unnecessary and may be confusing. The question is not how the term is used elsewhere

in the patent *specification,* but how it is used in the terms of the *claims*. Although the specification sometimes uses "binds" to refer to background binding, the claims universally use "binds" in the sense of immunologically significant binding. *See* Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1311 (Fed.Cir.1999) ("In circumstances such as this, where the language of the written description is sufficient to put a reader on notice of the different uses of a term... it is appropriate to depart from the normal rule of construing seemingly identical terms in the same manner. This entirely accords with the public notice function of claims.").

**C. "*Human* Breast Cancer *Antigen That is Also Bound by Monoclonal Antibody 454 C11*"**

[18] The court has also been asked to construe the term "antigen" as it is used in Claim 1 of the patent.FN23 The antigen of Claim 1 is described by reference to the monoclonal antibody 454 C11:

FN23. The parties agree that generally, an antigen refers to any substance that may be specifically bound by an antibody.

A monoclonal antibody that binds to a human breast cancer antigen that is also bound by monoclonal antibody 454 C11 which is produced by the hybridoma deposited with the American Type Culture Collection having Accession No. HB 8484.
'561 Patent, Claim 1.

Chiron contends that the referenced antigen is human c-erbB-2, which is sometimes referred to as HER2. This argument is based on the text of the patent specification, which describes laboratory tests showing that antibody 454 C11 bound to c-erb-B2:

Immunoprecipation tests on the antibodies indicated that seven of them (454 C11 ... 520 C9 ...) bind a common monomeric c.a. 210,000 dalton protein found in cancerous breast tissue.... The 520 C9 antibody binds an approximately 200 kD protein found in cancerous breast tissue which has been identified as c-erbB-2 .... The 200kD proteinaceous antigen bound by monoclonal antibody 520 C9 is identical to the 210 kD antigen mentioned herein above .... The 200,000 dalton protein bound by 520 C9 and 454 C11 was designated as the 210,00 dalton protein in U.S. Pat. No. 4,753, 894.

'561 Patent at 27:1-17.

Thus, the patent states that 454 Cll binds to a 210kD antigen that is identical to the 200kD antigen that has been identified as c-erbB-2. All parties agree that c-erbB-2 is synonymous with HER2. Therefore, when claim 1 refers to the antibody bound by 454 C11, it is referring to the antibody known as c-erbB-2 or HER2.

Genentech argues that whether the referenced antigen is actually human c-erbB-2 is a factual question that the court should not resolve at this time. The court does not purport to resolve this question as a factual matter, however. The court is simply relying on the express language in the specification equating the antigen bound by 454C 11 with human c-erbB-2. Even if it were necessary to resort to extrinsic evidence, experts for both parties appear to agree that the antigen referred to in claim 1 is, in fact, c-erbB-2. ( *See* 3/7 Markman Tr. at 28:17-25). Therefore the court adopts Magistrate Judge Hollows' recommended construction of the phrase containing the referenced antigen:

**The claimed monoclonal antibodies bind to the same** breast cancer **antigen as the identified reference antibody produced by the identified hybridoma. The 454 C11 monoclonal antibody binds to the human** breast cancer **antigen now referred to as "c-erB-2," sometimes referred to as "HER2."**

**D. "*Strong Staining*"**

[19] The term "strong staining" appears in several dependent claims. Claim 2 is representative:

The monoclonal antibody of claim 1, wherein the monoclonal antibody exhibits strong staining intensity as determined an immunoassay with three or less of the normal tissues and blood cells selected from the group consisting of pancreas, esophagus, lung, kidney, colon, stomach, brain, tonsil, liver, heart, ovary, skin, breast, platelets, red cells, lymphocytes, monocytes and granulocytes.

'561 Patent, Claim 2.

Genentech's initial claim construction brief proposed that "strong staining" means staining that is more than weak. (Genentech Claim Construction Brief at 33). In light of Magistrate Judge Hollows' findings and recommendations, Genentech now argues that the court should construe "strong staining" to refer to a "clear, definite, readily detectable signal." (Genentech Opp'n to F & R's at 18.) Chiron, on the other hand, construes "strong staining" to mean "a clear and definite, intense readily detectable signal resulting directly or indirectly from an interaction between an antibody and antigen, for example a color change as determined by light microscopy or a change in fluorescence determined by FACS. 'Strong staining' does not encompass staining that is less than strong, such as weak or moderate staining." (Chiron Opp'n to F & R's at 5.)

Staining is used by those skilled in the art to determine how many antibodies are interacting with antigens on a particular tissue or cell.FN24 Staining involves tagging antibodies with a stain so that they "signal" their attachment to an antigen on a cell or tissue by staining that cell or tissue. This can be accomplished either directly (by attaching the tag to the antibody of interest) or indirectly (by attaching the tag to another antibody that will bind to the antibody of interest). Stronger staining occurs when many antibodies attach to the surface of a cell or tissue. Given the common understanding of how staining works, the construction proposed by Genentech is incomplete in that it does not convey that the signal results from an interaction between an antibody and an antigen.

FN24. The degree of staining is important in ascertaining the selectivity of a particular monoclonal antibody (i.e. the degree to which the antibody binds to the cancer antigen of interest but not to normal tissues). The more antibodies that attach to normal tissue, and the more normal tissues to which they attach, the less value the antibodies will have for diagnosis and treatment. Thus, the patent claims monoclonal antibodies that exhibit strong staining with only a small percentage of normal tissues and cells. *See* '561 Patent, Claim 2 (claiming antibodies that exhibit strong staining with no more than three of eighteen specified normal tissues or cells); id. Claim 4 (claiming antibodies that exhibit strong staining with no more than one of eighteen specified normal tissues or cells).

Genentech's proposed construction also fails to clarify the important question of whether "strong staining" includes moderate staining, an issue which the parties debated at length during the Markman Hearing. The '561 patent specification contains a series of tables that grade staining intensity on a 0-1-2 scale, 0 being "negative," or no staining, 1 being "weak" staining, and 2 being "strong" staining. Genentech has taken the

position that the grading system described in the patent indicates that "strong" means "not weak," while Chiron has argued that "strong" means "strong." Because "strong staining" is not defined in the specification, and because its meaning is ambiguous from the tables depicted in the '561 patent, it is appropriate to resort to extrinsic evidence. *See* Vitronics, 90 F.3d at 1583.

Experts for Chiron and Genentech agree that "strong staining" is a term of art that is commonly used and understood by pathologists. (Parslow Reply Decl. para. 11; Cote Decl. para. 6). However, they disagree as to whether "strong staining" can encompass moderate staining when the 0-1-2 scale described in the '561 patent is employed.

This disagreement arises from the fact that scientists have not used uniform scales for grading staining intensity. Some use the 0-1-2 criteria described in the '561 patent, while others use a four-point scale, with "0" indicating no staining, "1" barely perceptible staining, "2" weak to moderate staining, and "3" strong staining. ( *See* F & R's at 44; Yu Decl. Ex. 6.) At the Markman Hearing, Genentech's expert, Dr. Cote, testified that a grade of strong staining on a three point scale encompassed both the strong staining grade and the moderate staining grade on the four point scale. Chiron's expert, Dr. Parslow, disagreed, testifying that strong staining was the same no matter what scale was used.

Magistrate Judge Hollows found Dr. Parslow's testimony to be more persuasive, and after a review of the record, this court agrees with that finding. The "virtually universal" use of the term "strong staining" among pathologists, ( *see* Parslow Reply Decl. para. 11), indicates that those skilled in the art share a common understanding of the term that does not change depending on what scale is used to grade the staining intensity. Dr. Cote's testimony on cross examination supports this observation. As Magistrate Judge Hollows notes:

[O]n cross examination Dr. Cote could not point to one exhibit where "strong staining" was ever defined in other than the last category no matter what scale was used, or one exhibit where moderate staining was included within a "strong" score. His opinion was impeached significantly by Exhibit 125-the staining done by his own company. In fact, the "moderate" staining found in Exhibit 125 was segregated from the strong staining description. The testimony indicated that for most immunoassay purposes, the categories between negative staining and strong staining ran a rather large area because the most significant categories for staining purposes, negative and strong, were much more precise, objective, and consistent in their definitions.

(F & R's at 45.)

Thus, the court adopts the following construction of the term "strong staining":

**The term "strong staining" refers to a clear and definite readily detectable signal resulting directly or indirectly from an interaction between an antibody and antigen, for example a color change as determined by light microscopy or a change in fluorescence determined by FACS. "Strong staining" does not encompass staining that is less than strong, such as weak or moderate staining.**FN25

FN25. This construction is identical to the one recommended by Magistrate Judge Hollows, except that it adds the sentence " 'Strong staining' does not encompass staining that is less than strong, such as weak or moderate staining." These changes simply make explicit that which was implicit in the definition recommended by Magistrate Judge Hollows. Chiron argues that the adjective "intense" should be added so

that the first sentence refers to "a clear and definite, *intense* readily detectable signal." However, adding the adjective "intense" unnecessarily clutters the sentence without conveying much useful additional information.

Genentech objects that the references to the light microscopy and FACS immunoassay procedures are superfluous. Although these examples are not necessary to define the term, they may assist the jury in understanding the meaning of "strong staining." Therefore, the court sees no reason to exclude them from the definition of "strong staining."

**E.** Immunoassay

[20] The term "immunoassay" is used in claims 2, 4, 10, 12, 20, and 22 to describe the procedure used to determine strong staining. Magistrate Judge Hollows adopted Chiron's proposed construction of the term:

**The term "**immunoassay**" refers to a laboratory technique that makes use of the binding between an antigen and an antibody in order to identify or quantify the specific antigen, and more particularly, to a protocol which uses the minimal concentration of the antibody which provides strong staining of the positive control.**

Genentech first argues that this construction is too narrow, because an immunoassay measures interactions between antibodies and a sample of cells or tissue, which include but are not limited to antibody-antigen binding. Although immunoassays can be used to measure things other than antibody-antigen binding, the '561 patent is exclusively concerned with antibody-antigen binding. This fact is apparent from the claims themselves, which describe the immunoassay technique in connection with strong staining, the purpose of which is to measure antigen-antibody interactions.

Genentech next argues that the construction recommended by Magistrate Judge Hollows improperly limits the term "immunoassay" to a protocol using minimal concentrations of the relevant antibody. This protocol is set forth in the specification. *See* '561 Patent, at 18:31-40 (describing an immunoperoxidase staining procedure in which "pure antibodies were first titrated to find the minimal concentration giving strong immunoperoxidase staining on breast cancer sections"). Although limitations from the specification may not be read into the claims, the claims must be read in light of the specification. Bell Atlantic, 262 F.3d at 1269. Given the purposes of the patent and the uses toward which the immunoassays of the patent claims are directed, it would be important to use a minimal concentration of the antibody of interest. Use of a high concentration of the antibody may flood the tissue and give strong staining everywhere, thus making it impossible to determine the extent of actual binding.FN26 Therefore, the court adopts the recommended construction in full.

FN26. Genentech states that Chiron's expert, Dr. Parslow, "conceded that an immunoassay can be performed using either a minimal concentration or a higher concentration." (Genentech Opp'n to F & R's, at 19.) Because the specification and the purposes of the patent support Magistrate Judge Hollows' interpretation, the court need not consider this extrinsic evidence. In any case, the fact that an immunoassay can be performed using a higher than minimal concentration of antibodies does not make it useful for purposes of the patent. Dr. Parslow never testified that effective staining results could be achieved by using higher than minimal concentrations. ( *See* Transcript, Vol II, at 206:23-207:12) ("Q: [I]n fact, when IMPATH did its tests, it used the maximum concentration of the antibody that did not give unduly high background staining;

right? A: I believe Dr. Cote testified in the deposition that *the two concentrations would be effectively the same* in his view, that *there wouldn't be very much difference in the concentration* that you arrived at by those two methods.") (emphasis added).

**F. "*Extracellular Domain*"**

[21] A number of dependent claims in the patent are directed toward monoclonal antibodies that "bind[ ] to the extracellular domain of the human breast cancer antigen." '561 Patent, Claims 7, 11, 15, 21, 25. The parties agree that one skilled in the art would interpret "extracellular" to mean "outside the cell." The meaning of "domain" is the focus of the parties' dispute.

"Domain" is ordinarily understood to refer to "region" or "area." Thus, Chiron posits that "extracellular domain" means "the portion of the human breast cancer antigen that is external to the cell." Genentech would have the court ignore the plain meaning of the term because the specification states: "The term 'domain,' or 'polypeptide domain' refers to that sequence of a polypeptide that folds into a single globular region in its native conformation, and that may exhibit discrete binding or functional properties." *Id*. at 12:38-42. Read in context, however, it is clear that the quoted text refers to antibodies, not antigens. The specification states that the invention relates to "novel polypeptides having structure and function substantially homologous to native antibody-antigen binding sites." *Id*. at 1:31-33. The specification further describes polypeptides as embodiments of the invention (i.e. monoclonal antibodies). *See id*. 4:1 ("in various related embodiments, monomeric polypeptides are provided ..."). Thus, by polypeptides, the specification is clearly referring only to antibodies. Therefore, the definition of "domain" in the specification has no bearing on what is meant by the "extracellular domain" of the human breast cancer antigen. Accordingly, the court adopts the following construction:

**The term "extracellular domain" means the portion of the human** breast cancer **antigen that is external to the cell.**

**G. "*Human c-erB-2 antigen*"**

[22] Magistrate Judge Hollows recommends the following construction for the claim term "Human c-erbB-2 antigen":

**"Human c-erbB-2 antigen" means the approximately 200kD protein associated with human** breast cancer**.**

Although Genentech originally proposed a different construction, it does not object to Magistrate Judge Hollows' interpretation of this term. Having reviewed the record, the court finds that the recommended construction is accurate and therefore adopts it.

IT IS THEREFORE ORDERED that the disputed claims be construed as set forth above in boldface.