United States District Court,
C.D. California.

SCANTIBODIES LABORATORY, INC,
Plaintiff.
v.
IMMUTOPICS, INC., and Immutopics International, LLC,
Defendants/Counterclaimants.

No. CV 04-8871 MRP (MANx)

Feb. 9, 2009.

Background: Holder of patent for method of treatment for hyperparathyroidism brought action against competitor, alleging infringement.

Holding: The District Court, Mariana R. Pfaelzer, J., held that claim terms pertaining to antibodies that bind parathyroid hormone (PTH) would be construed.

So ordered.

6,689,566. Construed.

Brian W. Kasell, Marc Marmaro, Rod S. Berman, Jeffer Mangels Butler and Marmaro, Los Angeles, CA, for Plaintiff.

Matthew A. Newboles, William J. Brucker, Stetina Brunda Garred & Brucker, Aliso Viejo, CA, Ronald S. Hodges, Shulman Hodges & Bastian, Foothill Ranch, CA, for Defendants/Counterclaimants.

SECOND AMENDED CLAIM CONSTRUCTION ORDER

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

In this patent infringement action, the Court issued a Claim Construction Order for four terms of U.S. Patent No. 6,689,566 on May 1, 2008, followed shortly by an Order granting summary judgment of noninfringement and denying summary judgment of invalidity on May 16, 2008. The Court declined to address the counterclaims for declaratory judgment of invalidity.

Plaintiff Scantibodies Laboratory, Inc. ("Scantibodies") and Defendants Immutopics, Inc. and Immutopics Int'l, LLC (collectively, "Immutopics") requested that this Court amend its Order *nunc pro tunc* to state that

there is "no just reason for delay" such that they may appeal the judgment. The Court found that there was just reason for delay and decided, *sua sponte,* to revisit claim construction and provided an Amended Claim Construction Order on November 26, 2008. FN1 The parties were invited to comment on the Amended Order, which they did on January 16, 2009. The Court has considered the parties' comments and provides this Second Amended Claim Construction Order.

I. BACKGROUND

A. Technology

Scantibodies' U.S. Patent No. 6,689,566 [FN2] ("the '566 Patent") claims antibodies that bind a protein hormone called parathyroid hormone (PTH), methods of measuring PTH, kits for measuring PTH, and methods for diagnosis of hyperparathyroidism.

The four claim terms in dispute each relate to antibodies that bind PTH and are:

-> specific for

-> specifically binds to whole parathyroid hormone

-> does not specifically bind to an interfering non-(1-84) parathyroid hormone fragment, and

-> not detecting an interfering non-(1-84) parathyroid hormone fragment.

Because of the technical nature of these claim terms, the Order presents a background of PTH and the state of the art of PTH measurements at the time the invention was made, the invention of the '566 Patent, and the procedural history of the '566 Patent before construing the claims.

a. Parathyroid hormone

PTH is a naturally occurring hormone in humans and other animals that regulates the concentration of calcium ions in the blood. *See* '566 Patent at 1:19-21. Calcium plays a key role in a variety of biological functions, including cell permeability, blood coagulation, transmission of nerve impulses, and normal muscle contraction. *Id.* at 1:16-19. As a result of PTH's role in blood calcium levels, accurate PTH measurement can be used to diagnose and monitor a number of diseases. *Id.* (noting that "[s]erum PTH level is one of the most important index[es]" for a long list of diseases that include Paget's bone disease, primary hyperparathyroidism, and renal failure).

PTH, like all proteins, is made up of a linear sequence of amino acids. It is a relatively small protein, or peptide, having only 84 amino acids. The amino acids of a whole PTH peptide are numbered starting from 1 at the N-terminus, and ending with 84, at the C-terminus, or end, of the protein. *See* the '566 Patent, Fig. 1 (illustrating whole PTH (1-84), numbered).

However, whole PTH gets broken down into smaller pieces, or fragments. The active form of the hormone contains all 84 amino acids, but in the bloodstream there are also biologically inactive fragments. PTH missing the first amino acid is less active, and PTH missing the first two amino acids is wholly inactive. *See* U.S. Pat. No. 6,030,790 at 1:10-20 ("However, upon the loss of the first amino acid, serine, the activity significantly decreases and is lost completely without the first two amino acids, serine and valine."),

invalidated in Nichols Inst. Diag., Inc. v. Scantibodies Clinical Labs., No. 06-1087, 195 Fed. Appx. 947 (Fed.Cir. Sept.20, 2006). Whole PTH may be cleaved *in vivo* between amino acids 34 and 35, 36 and 37, and 37 and 38, so inactive PTH fragments 1-34, 35-84, 1-35, 36-84, 1-37, and 38 to 84 circulate in the bloodstream as well. *See* the '566 Patent, 1:37-48. Some of these fragments are active as well, for example, the PTH (1-34) fragment stimulates bone resorption. Takeyuki Kohno et al. *Development of a highly sensitive and specific two-site* enzyme immunoassay *for parathyroid hormone (1-34): Application to* pharmacokinetic study *on intranasal parathyroid hormone (1-34) in human,* 12 J. Clin. Lab. Anal., 268 (1998). Blood also contains fragments of PTH fragments close to whole PTH in size, yet biologically inactive, meaning the fragments are incapable of regulating blood calcium levels, such as the "interfering" 7-84 fragment. *See e.g.,* the '566 Patent at 2:28-30 ("hyperparathyroid patients and renal failure patients ... have significant endogenous concentrations of large, non-whole PTH fragments"); *id*. at 2:20-27, 1:43-48 (noting the discovery of "a large PTH fragment referred to as a 'non-(1-84) PTH' ... which is clipped closer to the N-terminal end of PTH") 3:31-34 (citations omitted).

When measuring blood PTH levels for a diagnosis relating to a patient's calcium levels, it is important to measure active PTH and not the inactive forms. This can be difficult, since the fragments are just pieces of whole PTH, and of course are very similar to whole PTH, especially in the case of large fragments.

Adding to this difficulty in active biological PTH measurement is the fact that the hormone is found at extremely low concentration in the bloodstream, normally 10 pg/mL to 40 pg/mL, and therefore requires highly sensitive methods for detection. FN3 *Id*. at 1:60. Thus, methods of measuring PTH must be able to detect very low concentrations of PTH, in the presence of very similar peptides and in the presence of other molecules in serum.

b. Assays for PTH

To study and measure PTH, scientists utilize antibodies that recognize PTH. To make these antibodies, scientists have injected PTH into animals, generated an immune response, and harvested the antibodies that the animal produced. After isolating the antibodies that recognize PTH, the antibodies are used in assays, or tests (more specifically, immunoassays, since they use antibodies, *immune* system molecules), developed to recognize and quantify PTH in serum (blood free of red blood cells and blood clotting-factors). One example is an immunoradiometric assay ("IRMA," or "sandwich assay") that is disclosed as a preferred embodiment in the '566 Patent. Id. 3:44-59. While the details of the types of assays used are not at issue in the claim construction, the Court notes that the key to achieving accurate results in an assay for a biologically active PTH immunoassay is the antibody's *specificity* for whole PTH and not inactive PTH fragments.

Assays to quantify PTH were well known in the art, even before the discovery of inactive fragments of PTH. Before the application that matured into the '566 Patent was filed, inventor Gao and others described one such immunoassay for PTH measurement that purported to recognize and quantify only the initial sequence of PTH, and therefore quantify whole PTH, PTH 1-34, and PTH 1-38 but not PTH fragments having amino acids 28-48, 4-16, 39-84, 53-84, or 44-28, or even PTH-related protein. Ping Gao et al. Immunochemiluminometric Assay *with Two Monocolonal Antibodies against the N-terminal Sequence of Parathyroid Hormone,* 245 Clin. C him. Acta, 39 (1996). In addition, a commercially available test kit, the Nichols Allegro Intact PTH assay, purported to measure active "intact PTH," or "I-PTH" in blood serum. *Id*. at 2:12-15.

However, the Nichols kit in fact reported active PTH levels that were erroneously *higher* than the true patient levels because the antibody in the Nichols kit would bind to not only whole PTH, but also to a 7-84 fragment of PTH and other large, inactive PTH fragments present in the blood. *See id.* at 2:25-30. The existence of such fragments was not discovered until after the Nichols assay had been developed. *See, e.g., id.* at 2:43-45. The Gao assay was concerned with discriminating between the N-terminal fragments and C-terminal fragments, also being seemingly unaware of the existence of a 7-84 fragment. *See* Gao *supra*. As a result, the term "I-PTH," used in connection with the Nichols assay, was abandoned in favor of new terminology. The '566 patent at 2:25-27. Unfragmented, active PTH is now referred to as "whole PTH," "(1-84) PTH," "PTH (1-84)" and "wPTH." *See* id. 1:6-8, 3:26-27. Likewise, biologically inactive PTH fragments that had been measured by I-PTH assays are now termed "interfering non-(1-84) PTH fragments."

B. The invention

The '566 Patent is directed to antibodies specific for whole PTH, kits and methods for detecting whole PTH that utilize antibodies specific for PTH, as well as methods for diagnosis of hyperparathyroidism. Through the invention claimed by the '566 Patent, Scantibodies sought to create a test which would succeed where the Nichols I-PTH kit failed by "detecting wPTH in a biological sample without detecting the non-(1-84) large PTH fragment component of I-PTH." Id. at 2:43-45.

Scantibodies' solution was to generate and isolate an antibody "specific for the initial sequence for wPTH ... VAL-SER-GLU-ILE-GLN-LEU-MET (SEQ ID NO: 3) [amino acids 2-8 of PTH] ... wherein at least four amino acids are part of the antibody reactive portion of the peptide." Id. at 2:47-52. Because the antibody recognizes at least four of the amino acids in the PTH (2-8) region of whole PTH, the antibody of the '566 Patent will not bind to PTH (7-84) or similar fragments that are missing at least four of the amino acids in the 2-8 region of PTH. FN4 *See* id. at 1:23-25 (noting the fragments in I-PTH are known to include the N-terminal fragments "cleaved about amino acids 5 to 8").

The '566 Patent teaches a two-step process for generating the claimed antibody. First, an animal such as a goat is injected with an "immunogen," or antigen, which contains the initial peptide sequence, such as whole PTH or a fragment of PTH. FN5 The '566 Patent at 5:27-50. In response, the animal produces antibodies that are specific for this antigen. Some time after this immunization, blood is removed from the animals, and the blood serum is extracted by removing the red blood cells. *Id.* This serum contains all the antibodies that have been generated by the animal, including all the antibodies that have been generated in response to the injected PTH immunogen, and is therefore called antiserum. The desired antibodies, those that bind to at least four amino acids in PTH (2-8), are a subset of the anti-PTH antibodies.

The second step of the process involves isolating the desired antibodies from the antiserum through "affinity purification." *See id.* at 5:52-67. In the purification step, a short peptide having the same amino acids as an initial peptide sequence of whole PTH, is affixed to cross-linked agarose beads. FN6 *See id.* at 4:50-55. The peptide-laden beads are then packed into a separation column. *See id.* at 5:16-21, 5:52-55. Next, the animal antiserum from the previous step is poured into the column. Those antibodies in the antiserum that happen to be specific for the initial peptide sequence bind to the beads having a peptide with the initial peptide sequence attached. *See id. at* 5:52-57. Antibodies that do not recognize PTH at all, as well as those that recognize other parts of PTH than the initial peptide sequence will not bind to the beads and flow past the beads as the serum flows through the column. At the end of this step, the beads have only desired antibodies attached. *See id.*

After the serum has all flowed through the column, the beads are washed with a pH 2.5 elution buffer. Because antibodies cannot bind at such a low pH, the desired antibodies stop binding to the initial peptide sequence and flow out with the buffer. *Id*. at 5:59-63. The acidic buffer is collected and neutralized, for example, with a pH 7.5 buffer. *Id*. at 5:63-66. Thus, at the end of the process, antibodies specific for the initial peptide sequence in a neutral buffer are obtained.FN7

Purified in this manner, the claimed antibodies can then be used in immunoassays to quantify the concentration of whole PTH in the bloodstream and in methods to diagnose hyperparathyroidism.

C. Procedural history

Scantibodies filed its Complaint on October 26, 2004, alleging that Immutopics' antibody kits infringed U.S. Patent No. 6,689,566. During the course of discovery, Immutopics identified a prior art reference, known as the Colford Abstract FN8, which allegedly showed that the ' 566 Patent was invalid. Immutopics notified Scantibodies of the existence of the Colford Abstract in an August 5, 2005 letter. *See* Sept. 20, 2005 Order Granting Plaintiff's Mot. to Stay Proceedings at 2. Subsequently, Scantibodies and Immutopics filed separate requests for ex parte reexamination of the ' 566 Patent before the U.S. Patent and Trademark Office (hereinafter, "The Patent Office"), which were consolidated into a single proceeding on February 16, 2006. *See* 5/24/2006 Office Action, Newboles Cl. Constr. Decl., Ex. B. at 2. Over Immutopics' objection, Judge George P. Schiavelli granted Scantibodies' motion to stay the proceeding pending the outcome of ex parte reexamination. *See* Sept. 20, 2005 Order.

The Patent Office has indicated that the '566 Patent will survive reexamination, albeit with some claims in an amended form. *See* Notice of Intent to Issue *Ex Parte* Reexamination Certificate, January 8, 2007, Newboles Cl. Constr. Decl., Ex. F. To overcome the Colford reference and other relevant prior art, Scantibodies amended independent claims 1, 20, and 22 (the kit and antibody claims-but not the method claims) to add two key limitations. The claims as amended require that the antibody "specifically binds to whole parathyroid hormone but does not specifically bind to an interfering non-(1-84) parathyroid hormone fragment." *See* Claims As Allowed After Re-Examination, Kasell Decl. Supp. Pl.'s Mot. P. Summ. J. on Defs.' Counterclaim of Patent Invalidity, Ex. B ("Reexamination Claims"). Scantibodies also added limitations to the kit and antibody claims that require that the claimed antibodies be generated by the two-step process described in the previous section: "by immunizing a mammal with whole parathyroid hormone," collecting antiserum, and subsequently isolating the desired antibodies in the affinity purification step by "binding said antibody to at least four amino acids in the common sequence of human and rat PTH (1-8) sequence [i.e., PTH (2-8)]." *See* Reexamination Claims 1, 20, 22. Though the Patent Office still has not issued the Reexamination Certificate itself, the patentability of the claims is no longer at issue in the reexamination proceeding.FN9

On March 5, 2007, the case was transferred to this Court for further proceedings. Subsequently, on November 13, 2007, Immutopics filed summary judgment motions on five grounds: (1) invalidity based on failure to disclose the best mode known to the inventor, (2) invalidity based on lack of enablement, (3) invalidity based on obviousness, (4) invalidity based on the on-sale bar, and (5) non-infringement. The Court concluded that evaluation of Defendants' motions for summary judgment, and particularly the motions for non-infringement and enablement, required construction of the claims (as amended during reexamination). *See, e.g.,* Pl.'s Opp'n to Summ. J. of Non-Infringement, at 13 (suggesting the need for a *Markman* hearing). After a January 29, 2008 hearing on Immutopics' summary judgment motions, the Court

issued a Claim Construction Order for four terms of U.S. Patent No. 6,689,566 on May 1, 2008. The Court later decided *sua sponte,* to reconsider claim construction.

II. LEGAL STANDARD

"[T]he construction of a patent, including terms of art within its claim, is exclusively within the province of the court." Markman v. Westview Instruments, Inc., 517 U.S. 370, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996) at 372. During claim construction, the "words of a [patent] claim are generally given their ordinary and customary meaning," that is, "the meaning that the term would have to a person of ordinary skill in the art in question ... as of the [patent's] effective filing date." Phillips v. AWH Corp., 415 F.3d 1303, 1312-13 (Fed.Cir.2005) (*en banc*). Furthermore, the specification is "always highly relevant" in construing a claim. Id. at 1315. Where a claim term is disputed, the specification is "the single best guide to the meaning of a disputed term" and will usually be dispositive as to its meaning. *Id*.

In addition to the specification, a court is also to consider "intrinsic evidence, [which] consists of the complete record of the proceedings before the PTO and includes the prior art cited during examination of the patent." *Id*. at 1317 (internal quotations omitted).

Extrinsic evidence in the form of expert testimony can also help educate the court concerning the invention and the knowledge of persons of skill in the art. *Id* at 1319. However, the Federal Circuit has cautioned against undue reliance on extrinsic evidence, which is "in general ... less reliable than the patent and its prosecution history." *Id*. at 1318. Indeed, the use of extrinsic evidence is "unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence." *Id*. at 1319. Expert testimony must also be disregarded where it is at odds with the intrinsic evidence, or where an expert's conclusory assertions as to the definition of a claim term are not supported by independent sources such as industry publications. Network Commerce, Inc. v. Microsoft Corp., 422 F.3d 1353, 1361 (Fed.Cir.2005) (citing Phillips, 415 F.3d at 1318). Ultimately, decisions as to the need for and use of experts is within the sound discretion of the district court. InPro II Licensing, S.A.R.L. v. T-Mobile USA, Inc., 450 F.3d 1350, 1357 (Fed.Cir.2006).

III. CLAIM CONSTRUCTION

The following four claim terms were disputed by the parties and construed in the previous Order of this Court:

-> specific for

-> specifically binds to whole parathyroid hormone

-> does not specifically bind to an interfering non-(1-84) parathyroid hormone fragment, and

-> not detecting an interfering non-(1-84) parathyroid hormone fragment.

Claim 1 to an antibody is exemplary, having the first three of the four disputed terms:

1. A substantially pure antibody or antibody fragment *specific for* an initial peptide sequence of whole parathyroid hormone wherein

said initial peptide sequence consists of VAL-SER-GLU-ILE-GLN-LEU-MET (SEQ ID NO: 3), and

wherein at least four amino acids in said initial peptide sequence are part of a reactive portion with said antibody, and

wherein said antibody or antibody fragment is produced by immunizing a mammal with whole parathyroid hormone, collecting said antibody from said mammal and isolating said antibody by binding said antibody to at least four amino acids in the common sequence of human and rat PTH (1-8) sequence, and

said antibody or antibody fragment *specifically binds to whole parathyroid hormone* but *does not specifically bind to an interfering non-(1-84) parathyroid hormone fragment*.

Method claim 5 has the first and fourth disputed terms:

5. A method for measuring an amount of whole parathyroid hormone in a sample comprising:

a) adding to the sample a labeled antibody or antibody fragment *specific for* an initial peptide sequence of whole parathyroid hormone wherein

said initial peptide sequence consists of VAL-SER-GLU-ILE-GLN-LEU-MET (SEQ ID NO: 3), and

wherein at least four amino acids in said initial peptide sequence are part of a reactive portion to said labeled antibody;

b) allowing said labeled antibody to bind to whole parathyroid hormone present, thereby forming a complex; and

c) measuring the amount of said labeled complex to measure the amount of whole parathyroid hormone in said sample

while *not detecting an interfering non-(1-84) parathyroid hormone fragment*.

Claims as Allowed after Reexam of Patent No. 6,689,566 B1, Kasell Decl. Supp. Pl.'s Br. Supp. Construction of Terms in Reexamination Claims of U.S. Pat. No. 6,689,566, Ex. B ["Reexamination Claims"] (emphasis added).

Scantibodies and Immutopics agree that antibody specificity, binding, and detection are not defined in the '566 Patent. However, their competing claim definitions, detailed below, utilize different approaches to resolving their meaning. Scantibodies suggests that the intrinsic evidence lacks guidance simply because the concepts of antibody binding and specificity are already so well-known to persons having skill in the art that definitions of those terms are unnecessary. Pl.'s Br. Supp. Construction of Terms in Reexamination Claims ("Pl.'s Claim Constr. Br.") at 4 ("Indeed ... the only surprise would be if a definition *was* found in the record.") Dr. Monica Ranes-Goldberg, Scantibodies' expert, emphasizes that binding and specificity are relative concepts that are well understood in the art.

In contrast, Immutopics declines to offer a competing expert opinion because it believes that the intrinsic record, and in particular certain representations made during the reexamination, provide sufficient guidance

as to the claim terms at issue to overcome the seeming ambiguity inherent in the ' 566 Patent. The intrinsic record, it asserts, require that binding specificity be construed in absolute terms.

A. The parties' proposed constructions

The parties have proposed the following claim constructions.FN10

Claim Term	Scantibodies' Construction	Immutopics' Construction
specific for	The claimed antibody exhibits binding in the specified region (i.e., 2-8 PTH) *in whole PTH*[FN11] that is statistically significantly greater than the binding exhibited by the claimed antibody to any fragment of PTH not having at least four amino acids from the common sequence of human and rat PTH.	The binding of antibodies to PTH (2-8) with higher or increased affinity, as compared to the binding of the antibodies to whole PTH with weak binding or low affinity binding. The prosecution history, however, does not explain what the term "higher or increased affinity" means or what the term "weak binding or low-affinity binding" means.
specifically binds to whole parathyroid hormone	The claimed antibody exhibits binding to whole PTH in a biological sample that is statistically significantly greater than the binding exhibited by the claimed antibody with any fragment of PTH in the sample not having at least four amino acids from the common sequence of human and rat PTH.	The antibody binds only to whole PTH and does not cross-react with non-whole PTH, even at extremely high concentrations of PTH fragments. For example, such an antibody must bind to whole PTH but not cross react with a PTH (7-84) fragment when such fragment is present at a concentration of 10,000 pg/ml. Further, the antibody that "specifically binds the whole parathyroid hormone" must be raised exclusively from the use of whole PTH (1-84) as an immunogen.
does not specifically bind to an interfering non-(1-84) parathyroid hormone fragment	The claimed antibody exhibits binding to one or more interfering non-(1-84) parathyroid hormone fragment(s) in a biological sample that is statistically significantly less than the binding exhibited by the claimed antibody to whole PTH in the sample .	The antibody cannot bind to anything other than whole PTH even at extremely high concentrations of fragments, such as concentrations of 10,000 pg/ml for PTH (7-84). Further, the antibody that "does not specifically bind to an interfering non-(1-84) parathyroid hormone fragment" cannot be produced by any immunogen other than whole PTH (1-84), including but not limited to PTH (1-5), PTH (1-6), PTH (1-7), PTH (1-8), PTH (1-9), PTH (1-10), PTH (1-34), or PTH (1-38) as immunogens.
not detecting an interfering non-(1-84) parathyroid hormone fragment	The claimed antibody exhibits binding to one or more interfering non-(1-84) parathyroid hormone fragment(s) in a biological sample that is statistically significantly less than the binding exhibited by the claimed antibody to whole PTH in the sample .	The antibody must not bind to anything other than whole PTH (1-84). It must not bind to PTH fragments, including PTH (1-34), even at extremely high concentrations of the specified fragments, such as concentrations of 10,000 pg/ml for PTH (7-84).

B. The Court's constructions

The disputed claim terms encompass the concepts of antibody binding and specificity, terms of art which are left undefined in the intrinsic record. The Court agrees with Scantibodies' assertion that these concepts are well-known in the art and therefore starts with an "inquiry into how a person of ordinary skill in the art understands a claim term [which] provides an objective baseline from which to begin claim interpretation." Phillips, 415 F.3d at 1313 (citing Innova/Pure Water, Inc. v. Safari Water Filtration Systems, Inc., 381 F.3d 1111 (Fed.Cir.1996). The Court therefore begins with a discussion of antibody binding to describe certain terms often used to describe antibody binding-"antigen," "epitope," "binding affinity," and "specificity"-before construing the claims.FN12

Antibodies recognize other molecules (such as other proteins), called antigens. Ed Harlow & David Lane, Using Antibodies: A Laboratory Manual 24-25 (1999). "Antibody specificity" is a term widely used with respect to antibody-antigen binding, but is surprisingly not well defined in the art. *See, e.g.,* Lars-Inge Larsson, Immunocytochemistry: Theory and Practice 19 (1988) ("[T]he words specific and nonspecific (unspecific) are often used without a clear definition" before describing biochemical specificity, anatomical specificity, diagnostic specificity, and induced specificity).

Specificity can also be viewed as a relative concept; Scantibodies' expert, Dr. Monica Ranes-Goldberg defined the term "specific for" in her declaration as a measure of an antibody's relatively greater binding affinity for one antigen versus another antigen. Ranes-Goldberg Decl. para. 9. A technical dictionary relied upon during the prosecution of the '566 Patent defines antibody specificity as "A property of antibodies determined by their relative binding affinities, the intrinsic capacity of each antibody combining site, expressed as equilibrium dissociation (K_d) or association (K_a) for their interactions with different antigens." Julius M. Cruise & Robert E. Lewis, Illustrated Dictionary of Immunology 39 (2d 2003).

An antibody binding to an antigen is represented in the equation below:

Ab + ag ~ Ab-ag

where Ab is the antibody and ag is the antigen. The binding of an antibody to an antigen is reversible, indicated by the double arrows. The "binding affinity" of an antibody can be described by an affinity constant, K_A. The affinity constant, also referred to as the association constant, relates the amounts of the concentration of unbound antibody (denoted [Ab]), the concentration of unbound antigen (denoted [ag]) and the concentration of bound antibody-antigen complex (denoted [Ab-ag]), at equilibrium, using thermodynamic principles as follows:

K_A = [Ab-Ag]/[Ab][ag]

Id. at 28. Similarly, a dissociation constant for the reverse reaction, K_D, is the inverse of K_A. Affinity constants, or association constants, for antibodies to antigens can be measured using a range of assay techniques and have been found to range from below 10^5 liter/mole to greater than 10^{14} liter/mole. Typical association constants for antigen-antibody binding range from 10^5 to 10^{10} liter/mole, and association constants lower than 10^5 liter/mole are indicative of nonspecific binding and "difficult to measure and probably of little biological importance." *See* James W. Goding, Monoclonal Antibodies: Principles and Practice 77 (3d ed.1996) (describing antibody binding in terms of dissociation constants, which are the inverse of affinity constants).

Specificity can thus be defined as an absolute, rather than relative, property of an antibody, and antibodies "specific for" a particular antigen can be identified. Drawing on this definition, if an antibody has a sufficiently greater tendency to bind a first antigen over a second antigen, it may be said to have specificity or be "specific for" the first antigen. For an antibody to have specificity for a first antigen at all, it of course must bind to that antigen, and thus, will have detectable binding and a determinable association constant. Therefore, the only reasonable definition of an antibody "specific for" a particular antigen is an antibody that binds the antigen with an association constant of at least 10^5 liter/mole.

Rather than recognize the entirety of another protein, an antibody will recognize a particular "epitope," or antigenic region of the molecule. An epitope is not an intrinsic part of an antigen per se, but rather, is a region described only with respect to where a particular antibody binds. Harlow & Lane, supra, at 25. Protein epitopes may be made up of linear, contiguous stretches of amino acids (residues), or by noncontiguous amino acids brought into proximity when the protein folds into a three-dimensional conformation. Id. at 25-26. Protein antigens are often made up of three to eight amino acids. As with antigen specificity which is discussed above, antibody specificity of two epitopes of the same antigen can also be compared. Here too, for an antibody to be said to have specificity for an epitope of a first antigen, it must, as a threshold matter, bind to that particular epitope.

Despite the fact that antibody specificity can be determined and expressed with association and dissociation constants, it is not necessary to determine the binding constant for an antibody to be useful. In immunoassays, for example, the amount of the bound antibody detected can be correlated to known concentrations of the antigen to develop a standard curve without knowing the exact antibody specificity. See, e.g., Gao, *supra,* at 44.

The '566 Patent also describes one such method, an immunoradiometric assay, which requires two different antibodies. The '566 Patent at 3:48-4:48. In this, one antibody, the "capture antibody," is specific for the C-terminal end of PTH, (a sequence common to whole PTH as well as fragments thereof), and is attached to a solid support, such as a test tube. The other antibody, the "signal antibody," has a radioactive label and is specific for the initial peptide sequence, and therefore will only bind whole PTH. The radioactive element iodine-125 allows for easy detection of the radioactivity emitted.

To run the assay and detect whole PTH, a patient serum sample is added to the tube having immobilized capture antibodies. *Id*. All PTH molecules, biologically active and not, will bind to the capture antibodies lining the walls of the tube. A solution containing the signal antibody specific for the initial peptide sequence is then added, which binds only those captured PTH molecules having the initial peptide sequence. The excess, unbound signal antibodies are washed away from the tube, leaving only the signal antibodies bound to PTH having the initial peptide sequence, i.e., whole PTH.

The radioactivity of the signal antibody is then measured using a gamma counter. *Id*. From the data collected, the amount of signal antibody, and therefore the amount of whole PTH can be calculated using standards, and a control.

Alternatively, the antibodies may be given reverse roles, where the signal antibody is specific for the C-terminal region of PTH, and the capture antibody is specific for the initial peptide sequence epitope of PTH.

Therefore, if an antibody exhibits detectable binding to an antigen, one of skill in the art can infer that the antibody does indeed bind to the antigen. Further, one of skill in the art can infer that the binding is with a

K_A of at least 10^5 liter/mol, the association constant at the lower limit of useful antibody specificity. Therefore, the Court understands "specificity" in the context of antibody binding to mean antibody binding to a particular antigen or particular epitope of an antigen with a K_A of at least 10^5 liter/mol, which may be evidenced by the ability of antibody binding to be detected. An antibody may have a higher specificity for one antigen than another, and even for one epitope than another on the same antigen.FN13

a. "Specific for"

[1] "Specific for" appears in every independent claim in the patent, thus its construction affects every claim. *See* Reexamination Claims (independent antibody claim 1; independent kit claims 20, 22; independent method claims 5, 13, 18, 25, 27). In the claims, the term appears in the following phrase: "[an] antibody or antibody fragment *specific for* an initial peptide sequence of whole parathyroid hormone wherein said initial peptide sequence consists of VAL-SER-GLU-ILE-GLN-LEU-MET (SEQ ID NO:3) [FN14] ... wherein at least four amino acids in said initial peptide sequence are part of a reactive portion with said antibody".FN15 *See* Reexamination Claim 1 (emphasis added). Thus, the construction of "specific for" is in the context of this phrase.

In Scantibodies' proposed definition of "specific for," binding between a claimed antibody and the 2-8 PTH region "in whole PTH" FN16 must be at a level "statistically significantly greater" than the binding between that antibody and "any fragment of PTH not having at least four amino acids from the common sequence of human and rat PTH." FN17 In other words, the epitope must be comprised of at least four amino acids of the 2-8 PTH region.

In contrast, Immutopics prefers the relative definition of "specific for" put forth by the patent Examiner in the September 21, 2006 Office action: that an antibody binds PTH (2-8) with "higher or increased affinity," as compared to the strength with which the antibody binds to whole PTH. However, Immutopics does not place much faith its own construction, concluding in its brief that "specific for" is ultimately "indefinite and incapable of being construed" and that "the claim must be declared invalid rather than ascribed a speculative function." Immutopics, Inc. and Immutopics Int'l, LLC's Cl. Constr. Br. ("Defs.' Cl. Constr. Br.") at 6-7.FN18

The Court begins with its own analysis of this term in light of the role it plays in the claims of the '566 Patent.

i. "Specific for" defined as antibody with specificity for the PTH (2-8) epitope

As an initial matter, "specific for" means "has specificity for," and "specificity" is described above. What is important in the construction here are the words following "specific for," not the words "specific for" themselves. The independent claims require an antibody that is "specific for an *initial peptide sequence* of whole parathyroid hormone wherein said initial peptide sequence consists of VAL-SER-GLU-ILE-GLN-LEU-MET (SEQ ID NO: 3) [amino acids 2-8 of PTH]." *See, e.g.,* Reexamination Claim 1 (emphasis added). Furthermore, it requires that "at least four amino acids in said *initial peptide sequence* " are part of the "reactive portion" that binds with the antibody. Id. In other words, the antibody is be "specific for an epitope comprising at least four amino acids in SEQ ID NO: 3 [PTH (2-8)]."

For the antibody to be specific for an epitope having four or more amino acids of SEQ ID NO: 3, it obviously must first bind to four or more amino acids of SEQ ID NO: 3. The minimum affinity constant of

an antibody to be said to bind specifically rather than non-specifically,-as a practical matter, as would be understood by one of skill in the art, is approximately 10^5 liter/mole, the lower limit of antibody binding. Antibody binding at lower levels is difficult to detect, and such an antibody would have little utility, particularly in a clinical PTH assay, where useful antibodies are likely to have affinity constants several orders of magnitude higher.

Although the written description does not recite an association or dissociation constant for such binding, it is clear from the context of the specification, the prosecution history and prior art-all part of the intrinsic evidence-that the antibody must bind with sufficient affinity to have been purified based on its ability to bind the initial peptide sequence and to exhibit detectable binding.

One of skill in the art would have known how to determine if an antibody to a particular epitope of PTH had useful, detectable binding at the time the invention was made. Such methods are well-known; an immunoassay is described in the specification of the '566 Patent, as described above. In addition, one inventor co-authored a paper (cited in the specification and incorporated by reference) describing a sandwich assay using monoclonal antibodies specific to PTH, methods of determining the assay's detection limit, and methods of determining where the epitope specificity to whole PTH and various PTH fragments. Gao et al. *supra*. Additionally, a "highly sensitive and specific" PTH assay is described in the intrinsic record, in the cited art. Kohno, *supra* (describing antibodies "specific for" PTH (1-34), not specific for PTH (1-84), and calculating antibody assay detection limits).

This construction comports with the intrinsic and extrinsic evidence. First, the claimed antibodies (or fragments) are produced by immunization of an animal with whole PTH. Then, the antibodies that bind an epitope in the initial peptide sequence of PTH are purified from those that bind to PTH elsewhere by their affinity for an isolated peptide which has the initial peptide sequence. The '566 Patent, col. 5: 52-66, col. 4: 50-55. As a result, the antibodies claimed in the '566 Patent should bind the PTH (2-8) region *in whole PTH,* since they bind to PTH (2-8) as a standalone, affinity purification peptide. Because affinity for the initial peptide sequence is in fact the only criterion for selecting the claimed antibodies, the presence of additional amino acids (i.e., 1, 9-84) in whole PTH are unlikely to make up any part of the antibody's epitope.

Although an antibody "specific for" the initial peptide sequence required by the claims is likely to bind with substantially greater affinity to amino acids 2-8 than to amino acids 9-84, this fact is not important for the claims. FN19 Each claim requires that the antibody does not bind to an fragment made up of amino acids 7-84 of PTH, discussed below with respect to claim terms "does not specifically bind to an interfering non-(1-84) parathyroid hormone fragment" or "not detecting an interfering non-(1-84) parathyroid hormone fragment." Thus, the antibodies may not bind to an epitope outside of the initial peptide sequence, and the relative specificity for an epitope in the initial peptide sequence versus not in the initial peptide sequence is moot.

Also consistent with this construction of "specific for" is the fact that the independent kit and antibody claims were amended during reexamination to require *explicitly* that the claimed antibodies be affinity purified with the PTH (2-8) peptide. *See* Reexamination Claims 1, 20, 22 ("and wherein said antibody ... is produced by immunizing a mammal with whole parathyroid hormone, collecting said antibody ... *and isolating said antibody by binding said antibody to at least four amino acids in the common sequence of human and rat PTH (1-8) sequence* ") (emphasis added).FN20 Just as the antibody must bind to at least four amino acids of the PTH (2-8) initial peptide sequence *in whole PTH,* the amended language here also

requires that the antibody bind to the PTH (2-8) initial peptide during affinity purification ("isolating said antibody"). In addition, if an antibody specific for the initial peptide sequence also was specific for another epitope of PTH and detectably bound, it would defeat the intended purpose of the invention the inventors sought to claim, since it would not be able to "differentiate between the complete 1 to 84 amino acid sequence form of PTH and a large but incomplete 7 to 84 amino acid sequence form of PTH." The ' 566 Patent, Abstract.

Thus, an antibody specific for the PTH (2-8) initial sequence has a measurable affinity for and detectable binding to an epitope having at least four amino acids of the seven in SEQ ID NO: 3. And, that affinity is higher than the affinity for any other epitope of the whole PTH sequence.

ii. Scantibodies' definition provides no guidance as to the degree of specificity for whole PTH and is too broad

Scantibodies' amended construction is flawed for two reasons. First, it does not provide an absolute definition. Second, the "statistically significantly greater" metric is too broad.

Scantibodies' definition compares binding in the 2-8 PTH *region* (epitope) of whole PTH with binding to PTH *fragments* (molecules) missing at least four of the N-terminal amino acids between 2-8. This construction is incorrect in the context of binding specificity at issue here. In this context, an antibody's affinity for a certain epitope on the *whole PTH molecule* (2-8) with its affinity for other epitopes of the *whole PTH molecule* are compared, not the antibody affinity for a PTH epitope with *fragments* (which do not even contain that epitope).

For instance, Scantibodies' construction could be interpreted as a comparison of antibody affinity for the 2-8 *region* of whole PTH versus affinity for the *corresponding region* of a PTH fragment "not having at least four amino acids from the common [2-8] sequence of human and rat PTH." FN21 As the Court's construction demonstrates, this is not an appropriate comparison for specificity. Scantibodies' definition compares antibody binding affinity for the amino acids of the N-terminal region of PTH across molecules which do and do not have those amino acids, but "specific for" here must compare affinity for one epitope within a single molecule (whole PTH) with another epitope in that molecule (whole PTH). In addition, this construction is relative, providing no absolute definition.

Scantibodies' use of the term "statistically significantly greater" in its construction of "specific for" only further clouds the issue. This term is not supported by the patent specification and was not adequately explained at the *Markman* hearing on this issue. Dr. Ranes-Goldberg suggests that the term "statistically significantly" simply reflects the "concept that in a clinical context it is important that the antibody sufficiently discriminate between whole PTH and PTH fragments in a manner that provides a consistently reliable measurement based on a comparison with the appropriate positive and negative controls that are provided with the test kit." Ranes-Goldberg Decl. para. 12. FN22

But this description, purportedly relating to detectability in an assay, again confuses specificity for an epitope of whole PTH with specificity to PTH fragments not having that epitope, when a more correct comparison is the specificity to an epitope of whole PTH in the initial peptide sequence with another epitope on whole PTH. In addition, the need to sufficiently discriminate between whole PTH and PTH fragments is already addressed by other claim limitations-the three remaining terms at issue in this *Markman* order.

In addition, the "statistically significantly greater" construction is too vague. For example, in the case of a cross reacting antibody, such as the antibody Scantibodies describes that recognizes both whole PTH and the 7-84 fragment, the construction of "specific for" as a relative concept provides no guidance. Pl.'s Comments at 7. For example, when such an antibody is in the presence of whole PTH, it would recognize an epitope comprising at least four amino acids in the initial peptide sequence 2-8 about two orders of magnitude better than an epitope in the 7-84 amino acid sequence. Thus, urges Scantibodies, this antibody is specific for whole PTH. *Id*. However, if the same antibody were in the presence of just the 7-84 fragment, it would recognize the epitope on the fragment and be said to be specific for the fragment. Thus, there is no real definition of "specific for" in this construction.

Scantibodies' construction does not flow either from the nature of antibody specificity, or from the requirement that "at least four amino acids in said initial peptide sequence" are "part of a reactive portion with said antibody"-a separate claim limitation that *follows* "specific for." FN23 Likewise, it finds no support in the specification. Furthermore, its construction does not even appear to be consistent with the understanding that Dr. Cantor, one of the named inventors of the ' 566 Patent and the founder of Scantibodies, demonstrated in this litigation only months earlier. *See* Thomas Cantor Decl. para. 7 (Dec. 18, 2007) ("So, for illustration only, if a peptide (e.g., whole PTH) has a chain of 84 amino acids (from 1-84) and the antibody binds with amino acids 1-8 *more than it binds to 9-84,* we say that the antibody is *specific for* 1-8 ....") (emphasis added).

Scantibodies only provides the support of Dr. Ranes-Goldberg, who agrees that "[t]he critical comparison for the relevant specificity is to compare binding to the initial peptide sequence of whole PTH relative to a fragment that is missing some or all of this sequence." Ranes-Goldberg Decl. at para.para. 11, 13. But she provides no further justification for a position that contradicts the intrinsic record of the '566 Patent. In addition, Dr. Ranes-Goldberg fails to support her definition of "specific for" with sources outside of her declaration. *See* Network Commerce, Inc. v. Microsoft Corp., 422 F.3d 1353, 1361 (Fed.Cir.2005) (rejecting conclusory assertions by expert as to meaning of a claim term, where unsupported by independent evidence such as industry publications). Her definition in fact appears to be nothing more than a neat paraphrase of the proposed construction submitted by Scantibodies. *See id*. para. 11, 12.FN24 For these reasons, the Court gives no weight to her opinion on this claim term.

In short, no matter which way it is interpreted, Scantibodies' construction of "specific for" cannot be reconciled with the intrinsic evidence and the weight of the extrinsic evidence. Scantibodies repeatedly emphasizes that specificity is a relative concept, but such an argument does not transform it into one that escapes definition entirely.FN25 In offering a proposed construction that addresses the wrong issues, Scantibodies provides no guidance at all.

The Court does note, however, that while the construction of "specific for" as "statistically significantly greater" may not impart any discemable bounds to the claim rendering it indefinite, this construction, according to Scantibodies, does conveniently encompass the accused infringing product. Pl.'s Comments at 7.

iii. The Examiner's definition of specificity, as interpreted by Immutopics, does not provide a coherent construction of "specific for"

In contrast to Scantibodies' expert-based approach, Immutopics' definition of "specific for" arises from the

reexamination history, which is part of the intrinsic record. *See* Phillips v. AWH Corp., 415 F.3d at 1314 (prosecution history is part of intrinsic record); 35 U.S.C. s. 305 (stating that "reexamination will be conducted according to the procedures established for initial examination" after initial statutory period under s. 304).

The statement at issue arose during the September 21, 2006 Final Office Action, in which the patent Examiner observed that the patent specification was "silent regarding the difference between the terms 'specific for' and 'binds to.' " *See* 9/21/2006 Final Office Action, Newboles Decl. Supp. Immutopics Cl. Constr. Br. Ex. D at 4-5. She then noted that it was also "silent regarding the relative affinities of the claimed antibodies." *Id*. On this latter point, the Examiner then suggested a "default" definition for these relative affinities, stating, "in the absence of specification disclosure it is considered that the antibodies bind to the initial peptide sequence of PTH (SEQ ID NO:3) with higher or increased affinity as compared to the whole PTH, and the binding of the claimed antibodies to the whole PTH sequence is interpreted as weak binding (or low affinity binding)." Immutopics derives its proposed construction almost verbatim: "the binding of antibodies to PTH(2-8) with higher or increased affinity, as compared to the binding of the antibodies to whole PTH with weak binding or low affinity binding."

The Examiner's definition is confusing because it compares affinity for the "initial peptide sequence" of PTH (2-8) with the affinity for "the whole PTH sequence," and Immutopics does not attempt to clarify it. *See* Defs.' Claim Constr. Br. at 4 (stating without elaboration that " '[s]pecific for' means just what the Patent Examiner said it means"). Yet the Court's construction establishes that "specific[ity] for" the PTH (2-8) region requires a comparison of an antibody's affinity for that region with its affinity for the rest of whole PTH *not including that region*. The Examiner's statement is especially puzzling given that the record shows that she did in fact understand the significance of an "initial peptide sequence." In the paragraph following her statement on relative binding affinities, the Examiner stated that "[i]t is interpreted that the claimed antibodies specific to the initial peptide sequence of PTH ... would bind to the whole PTH ... since the wPTH comprises the initial peptide sequence." 9/21/2006 Office Action at 5. In this light, the Examiner's wording was merely imprecise: what she really meant was that the binding of the claimed antibodies to the whole PTH sequence *excluding the initial peptide sequence* is interpreted as weak binding.

Unlike the Examiner, Immutopics fails to recognize the dual usage of an "initial peptide sequence" in the context of the '566 Patent, that is, it may refer to as a standalone peptide fragment, as well as a region within whole PTH, and insists that it must be a fragment.FN26 Interpreting the Examiner's definition in this way renders it incoherent, however. The Court thus rejects Immutopics' construction of "specific for." Furthermore, because the claim language and specification adequately inform the meaning of "specific for," the Court does not need to consider Immutopics' argument that this term is, in fact, indefinite.FN27

While it is tempting (as the Examiner suggested) to define "specific for" as requiring an antibody with "higher or increased affinity" for PTH (2-8), but "weak" or "low affinity binding" to PTH (9-84), it would not bring additional clarity as to the degree of specificity here, since such antibodies fall outside the scope of the claims due to other claim limitations, discussed below. But, the Court's construction does indicate that an antibody's affinity to amino acids 2-8 must be higher than its affinity to the other amino acids in whole PTH.

Finally, Scantibodies raises a number of further objections to the Examiner's statement, alternately characterizing it as an irrelevant discussion regarding the distinction between two similar terms, "specific for" and "binds to," *see* 3/24/2008 Hrg. Tr. at 3:6-9, 19-25, 4:1-6, 38:6-13; arguing that it is "directed to a

form of the claims that no longer exists," Pl.'s Cl. Constr. Br. at 6 (emphasis omitted); and suggesting that the Examiner did not understand the difference between the concepts of binding affinity and specificity. *See* Ranes-Goldberg Decl. para. 9. The Court need not consider these misguided objections in further detail because it declines to adopt the Examiner's statement in its construction of "specific for." FN28

In conclusion, the Court rejects both parties' proposed constructions, and arrives at its own definition of "specific for," as used in the claims, as having a measurable affinity for and detectable binding to an epitope having at least four amino acids of the seven in SEQ ID NO: 3, the PTH (2-8) initial sequence. Further, that affinity is higher than the affinity for any other epitope of the whole PTH sequence.

b. "Specifically binds to whole parathyroid hormone" and "does not specifically bind to an interfering non-(1-84) parathyroid hormone fragment"

[2] [3] The second and third claim terms are two parts of a single phrase added to independent Claims 1, 20, and 22 during reexamination: "and said antibody or antibody fragment specifically binds to whole parathyroid hormone but does not specifically bind to an interfering non-(1-84) parathyroid hormone fragment." *See* Reexamination Claim 1, 20, 22 (kit and antibody claims). Though presented as two separate terms, they are related and treated as such by the parties.

The Court's view of these two terms is not purely advisory, although the antibody and kit claims may ultimately be outside the scope of the parties' infringement dispute.FN29 However, the analysis of specificity is consistent throughout this Order and in the same context for these two terms. Thus, "specifically binds to whole parathyroid hormone" means having a measurable affinity for and detectable binding to whole parathyroid hormone, and "does not specifically bind to an interfering non-(1-84) parathyroid hormone fragment" means having no measurable affinity for and no detectable binding to an interfering non-(1-84) parathyroid hormone fragment. No measurable affinity is indicative of an association constant of less than 10^{5} liter/mole.

i. The level of specificity for the two claim terms at issue cannot be characterized by either of the extremes proposed by the parties

For "specifically binds," Scantibodies proposes that the claimed antibody must bind to whole PTH "in a biological sample" with an affinity that is "statistically significantly greater" than the affinity between the antibody and "any fragment of PTH in the sample not having at least four amino acids from the common sequence of human and rat PTH." It construes "does not specifically bind" as requiring the claimed antibody to bind to "one or more interfering non-(1-84) parathyroid hormone fragment(s) in a biological sample" with an affinity that is "statistically significantly less" than the affinity to whole PTH in the sample.

Immutopics, on the other hand, proffers essentially the same definition for both claim terms: that "[t]he antibody binds only to whole PTH and does not cross-react with non-whole PTH, even at extremely high concentrations of PTH fragments." It also provides a quantitative threshold, drawn from the prosecution history: that an antibody must not specifically bind to the PTH (7-84) fragment even at "concentrations of 10,000 pg/mL." Immutopics further insists, as part of its proposed constructions for both claim terms, that PTH (1-84) is the only acceptable immunogen for generating the claimed antibodies.

As an initial matter, the Court will not consider Immutopics' argument that both "specifically binds to" and "not specifically bind" require the antibody to be "raised exclusively from the use of whole PTH (1-84) as

an immunogen." FN30 All the claims that employ the two terms at issue *already* include an *explicit limitation* requiring the use of PTH (1-84) as the immunogen. *See* Reexamination Claims 1, 20, 22 (independent kit and antibody claims requiring that "said antibody ... is produced by immunizing a mammal with whole parathyroid hormone").FN31

Scantibodies defines "specifically binds" for the first term at issue in terms of "any fragment of PTH not having at least four amino acids," but it defines "not specifically bind" in terms of "an interfering non-(1-84) [PTH] fragment." As noted earlier, the two terms are not identical, and the use of "any fragment of PTH ..." presents various logistical problems, such as the need to calculate binding affinities for a whole class of hypothetical PTH peptides. Because of this potential for inconsistency, the Court rejects Scantibodies' construction of "specifically binds" (which employs this anomalous definition of a PTH fragment) and considers only its construction of "not specifically bind."

What constitutes specificity for whole PTH is the heart of the disagreement between Scantibodies and Immutopics with respect to the two claim terms at issuer-as well as for the fourth claim term, "not detecting an interfering non(1-84) [PTH] fragment." The Court finds that neither party's definitions are satisfactory and uses the definition set forth above.

1. Arguments

As with "specific for," Scantibodies proposes that the proper benchmark for specificity is statistical significance. Its definition of "not specifically bind," for example, is satisfied when an antibody's binding to interfering fragments is of "statistically significantly less" strength than the binding exhibited to whole PTH "in [a biological] sample." Dr. Ranes-Goldberg explains that statistical significance, which does not appear in the patent itself, refers "to a concept of how the antibodies would be used in a clinical setting." 3/24/2008 Hrg. Tr. at 19:25-20:1-2. Viewed from the perspective of a clinician who is measuring the level of whole PTH in a biological sample, an antibody is sufficiently specific if it is able to discriminate between whole PTH and any PTH fragments in the sample "in a way to provide measurement that is consistently reliable that would be meaningful to the clinician who was doing the test." Id. at 20:8-12. Scantibodies suggests that this extrinsic standard is well-known in the art.

In stark contrast, Immutopics proposes an absolute, all-or-nothing definition of specificity for whole PTH. Under its definition, a claimed antibody must not bind to "anything other than whole PTH even at extremely high concentrations of [PTH] fragments." As its primary support, Immutopics points to published results by Dr. Gao that were cited by Scantibodies during reexamination.FN32 The Gao article reported that an antibody developed under Scantibodies' method (and presumably in accordance with the ' 566 Patent) displayed no cross reactivity with PTH (7-84) at concentrations of 10,000 pg/mL of the PTH (7-84) fragment.FN33 Immutopics now argues that, at the very least, Scantibodies is bound to this "10,000 pg/mL" standard in defining specificity for whole PTH.

2. Analysis

a. The Court declines to adopt Scantibodies' definition because it imposes essentially no restrictions on specificity

Scantibodies' focus on the "clinical" context, and in particular, the need to accurately measure whole PTH in a biological sample, finds ample support in the '566 Patent. *See* '566 Patent at 1:6-9 ("The present invention relates to ... detecting [whole PTH] in a biological sample."); 2:27-30 (noting that one problem presented by

the prior art is that "hyperparathyroid patients and renal failure patients ... have significant endogenous concentrations of large, non-whole PTH fragments" which interfered with previous anti-PTH antibody testing kits). Providing "consistently reliable measurement based on a comparison with the appropriate positive and negative controls that are provided with the test kit," *see* Ranes-Goldberg Decl. para. 12, is certainly not inconsistent with the specification. *See also* Pl.'s Cl. Constr. Br. at 13 (echoing Dr. Ranes-Goldberg's emphasis on "consistently reliable" results). As Dr. Ranes-Goldberg explains, specificity values "only take on meaning in the context of the type of testing for which the antibody is being used." Ranes-Goldberg Decl. para. 7. However, by focusing exclusively on the clinical context, Scantibodies and Dr. Ranes-Goldberg effectively propose a definition that places virtually no lower limit on the specificity for whole PTH. In addition, not all of the claims are limited to a clinical context; claims 1 to 4 are directed to antibodies and antibody fragments, with no limitations on the context of their use.

Though experiment and protocol design as well as the reliability of results are preconditions for obtaining accurate measurements of whole PTH levels, they do not address the actual issue-an antibody's *inherent* specificity for whole PTH, The Nichols Allegro kit provides a good example: as a commercially available kit for detecting levels of intact PTH in biological samples, it would obviously include well-designed instructions and protocols regarding proper use, and would provide "consistent," "reliable," and "statistically significant" results (in the ordinary meaning of that term) purportedly measuring concentrations of unfragmented PTH Yet the Nichols antibody fails to distinguish the 7-84 PTH fragment from whole PTH, and hence, does not specifically bind to whole PTH because it binds as strongly to whole PTH as to that particular interfering non-(1-84) fragment. *See* '566 Patent at 2:1-40 (describing the shortcoming of the Nichols Allegro kit). In that situation, reproducibility, consistency, or the presence of positive or negative controls simply are not at issue. They are external factors that have nothing to do with the inherent binding propensities of a given antibody.

By failing to define specificity for whole PTH over fragments, Scantibodies has chosen a definition that imposes an incredibly low threshold on the two claim terms at issue, where the definition requires only that an antibody bind to an interfering PTH fragment with " *statistically significantly less* " strength than the strength with which it binds whole PTH. This definition would encompass, for example, a slightly improved version of the Nichols antibody with an affinity for PTH (7-84) that is weakened by a small, but consistently measurable amount, yet whose affinity for whole PTH remains the same. This improved antibody would exhibit "statistically significantly less" binding to PTH (7-84) than it would to whole PTH, and thus under Scantibodies' definition would "not specifically bind to an interfering non-(1-84) [PTH] fragment." FN34 Yet it would not be useful in an assay for whole PTH.

Scantibodies objects to the Court's constructions, arguing that they "make it virtually impossible, based on current antibody technology, for *any* antibody to fall within the scope of the claims of the '566 patent, including the preferred embodiment of the invention." Pl.'s Comments at 1. This statement it false. First, the antibody employed in the IRMA Assay discussed in Gao 2001, *supra,* appears to specifically bind whole PTH while not specifically binding the interfering PTH (7-84) fragment, illustrating that it is possible that antibodies can meet these limitations using current antibody technology. FN35 Second, while the preferred embodiment described in the patent likely does not fall within the scope of certain claims, it may be because the Applicants mistakenly filed the application believing that the peptide used for affinity purification was (1-8) PTH, when it was in fact, (1-9) PTH. *See* Proposed Statement of Uncontroversial Facts Supp. Defs.'s Mot. Summ. J. Failing to Disclose Best Mode No. 23.

Additionally, Scantibodies asserts that "nothing in the claims or the specification supports the conclusion

that the antibody of the claims can exhibit no measurable binding, i.e., no cross-reactivity, to amino acids outside of the initial peptide sequence." Pl.'s Comments at 9-10. This statement, as well as Scantibodies' definition ignores the "not" in "does *not* specifically bind to an interfering non-(1-84) parathyroid hormone fragment" limitation of the third claim term. Clearly, this is not an acceptable definition of specificity.

b. Immutopics' definition of specificity for whole PTH is unreasonably restrictive and not supported by the prosecution history

Immunotopics, on the other hand, defines specificity as not binding at very high concentrations. The reexamination prosecution history does not support Immutopics' construction because nothing in the record "expressly says that ... binding to the undesirable PTH (7-84) fragment cannot occur even at concentrations of 10,000 pg/mL." *See* Defs.' Cl. Constr. Br. at 9.

In both its July 24, 2006 and November 10, 2006 Amendments, Scantibodies cited the 10,000 pg/mL figure from Gao in making an argument designed to overcome a rejection based on the Colford reference. *See* 7/24/2006 Scantibodies Amendment, Newboles Cl. Constr. Decl., Ex. C at 29; 11/10/2006 Amendment, Newboles Cl. Constr. Decl., Ex. E at 16-17. However, Scantibodies employed the Gao reference, in *both* the July and November filings, primarily to demonstrate that the " *Nichols* intact PTH IRMA" displayed "nearly 100% cross-reaction" with the 7-84 fragment. *See* 7/24/2006 Scantibodies Amendment at 29; 11/10/2006 Amendment at 16-17. While the quote from Gao also contrasted Nichols' high cross-reactivity with the lack of cross-reaction in Scantibodies' own assay "even at a PTH (7-84) concentration of 10,000 pg/mL," the mention of that figure was incidental to Scantibodies' actual point, which was an awkward attempt to distinguish the Colford reference by way of the Nichols reference. FN36

Prosecution history disclaimer requires a clear and unambiguous disavowal of claim scope during prosecution in order to obtain claim allowance. Salazar v. Procter & Gamble Co., 414 F.3d 1342, 1344 (Fed.Cir.2005). Here, the intrinsic record demonstrates that this was neither a clear and unambiguous disclaimer, nor a statement made in order to obtain claim allowance. Scantibodies simply did not make a clear and unambiguous statement committing the 10,000 pg/mL limit as a claim limitation. Additionally, the Examiner did not rely on it in allowing the claims over Colford; it was merely a characterization of the prior art. Rather, the evidence suggests that the Examiner ultimately allowed the claims over Colford after Scantibodies amended the kit and antibody claims to require an antibody that *is generated by immunization with whole PTH*.FN37 *See* 11/10/2006 Amendment at 2 (amending claims); *id*. at 15 (noting that Colford does not explain what immunogen it used to generate its PTH (1-7) antibody).

Thus, Scantibodies' usage of the Gao reference in the reexamination record does not suggest that 10,000 pg/mL provides an appropriate metric for specificity. Because it is incapable of supporting even that specific limitation on the claims, Immutopics may not use it for the even more stringent proposition that a claimed antibody may not bind to interfering fragments to any degree whatsoever.

In conclusion, the specification and prosecution history do not support either party's construction as to the level of required specificity. Using the definition of specificity set forth earlier, the Court construes the claim term "specifically binds to whole parathyroid hormone" as having a measurable affinity for and detectable binding to whole parathyroid hormone. Similarly, the Court construes the claim term "does not specifically bind to an interfering non-(1-84) parathyroid hormone fragment" as having no measurable affinity for and no detectable binding to an interfering non-(1-84) parathyroid hormone fragment. No measurable affinity means having an association constant of less than 10^5 liter/mole.

c. "Not detecting an interfering non-(1-84) parathyroid hormone fragment"

[4] The claim term "not detecting an interfering non-(1-84) [PTH] fragment" appears in every method claim and was not amended during reexamination. *See* /C566 Patent, Claims 5, 13, 18, 25, 27 (independent method claims). The parties propose virtually the same definition for this term as for their proposed constructions of "does not specifically bind"; indeed, they agree that "binding" and "detection" are related terms. *See, e.g.*, Mem. P. & A. Supp. Pl.'s Opp'n to Defs.' Mot. for Summ. J. of Non-Infringement at 9 (stating that "detection is directly associated with 'binding' " and that an antibody's ability to detect a particular antigen "proportional to the antibody's affinity for binding to" that antigen).

Similar to its construction of "does not specifically bind to an interfering non-(1-84) parathyroid hormone fragment," the Court construes "not detecting an interfering non-(1-84) parathyroid hormone fragment" as having no detectable binding to an interfering non-(1-84) parathyroid hormone fragment.FN38

IV. CONCLUSION

The Court vacates the previous claim construction order and reaches the following constructions of the terms:

-> "Specific for" is defined as having a measurable affinity for and detectable binding to an epitope having at least four amino acids of the seven in SEQ ID NO: 3. In addition, the affinity is higher than the affinity for any other epitope of the whole PTH sequence.

-> "Specifically binds to whole parathyroid hormone" means having a measurable affinity for and detectable binding to whole parathyroid hormone.

-> "Does not specifically bind to an interfering non-(1-84) parathyroid hormone fragment" means having no measurable affinity for and no detectable binding to an interfering non-(1-84) parathyroid hormone fragment.

-> "Not detecting an interfering non-(1-84) parathyroid hormone fragment" is construed to mean having no detectable binding to an interfering non-(1-84) parathyroid hormone fragment.

IT IS SO ORDERED.

FN1. The parties' comments on the Amended Claim Construction Order pointed out a typographical error but otherwise added little beyond their previous positions. As a result, the Court has changed nothing of substance in this Order while recognizing that "[d]istrict courts may engage in a rolling claim construction, in which the court revisits and alters its interpretation of the claim terms as its understanding of the technology evolves. This is particularly true where [the] issues involved are complex, either due to the nature of the technology or because the meaning of the claims is unclear from the intrinsic evidence." Guttman v. Kopykake Enters. Inc., 302 F.3d 1352, 1361 (Fed.Cir.2002) (citing Sofamor Danek Group, Inc. v. DePuy-Motech, Inc., 74 F.3d 1216, 1221 (Fed.Cir.1996) (internal citation omitted).

FN2. The 6,689,566 Patent is still the subject of pending reexamination proceedings. Thus, the claims referred to in this Order are the claims listed in the Second Supplemental Response to Final Office Action

(dated December 1, 2006), which the U.S. Patent and Trademark Office indicated were allowed in a Notice of Intent to Issue Ex Parte Reexamination Certificate (December 6, 2006).

FN3. A picogram (pg) is 1 x 10^{-12} gram, or one-millionth of one-millionth of a gram. Thus, a serum concentration of 10-40 pg per milliliter (mL) is quite small, especially in contrast to other proteins and molecules in the blood. For example, blood cholesterol levels may be 10^{8}, or one hundred million times higher.

FN4. This approach does not appear to preclude binding to *any* biologically inactive N-terminal fragment, such as PTH (3-84), which is only missing the first two amino acids. An antibody that binds to PTH amino acids 3, 4, 5 and 6, for example, would bind to at least four amino acids in the PTH (2-8) common sequence, but it would not be able to distinguish whole PTH from the PTH (3-84) fragment. Indeed, distinguishing all N-terminal PTH fragments from whole PTH does not appear to be the goal of the '566 Patent, which is apparently content to solve the problem presented by the Nichols Allegro kit: avoiding to the PTH (7-84) fragment. Yet even if PTH (7-84) is in fact the most common N-terminal PTH fragment present in the blood, it was already known at the time of filing of the ' 566 Patent that inactive fragments as large as (3-84) could interfere with a PTH assay, because loss of the first two amino acids would abolish biological activity.

FN5. Because the goal is to generate antibodies that are specific for the N-terminal region of whole PTH, the immunogen that is injected into the animal should at the very least include the initial peptide sequence.

FN6. This initial sequence is PTH (2-8), an initial peptide sequence common to both rats and humans, an express limitation of the antibody and kit claims. The method claims are silent as to the method by which the antibodies are produced.

FN7. These antibodies are called "polyclonal" antibodies. Each antibody obtained by this process recognizes the initial peptide sequence; however, each antibody is not necessarily the same as the others.

FN8. J.W. Colford, M. Salvati, et al., Isolation and Characterization of Large Molecular Weight Fragments of PTH, Newboles Claim Construction Decl., Ex. G (abstract and presentation materials presented at 79th Annual Meeting of the Endocrine Society, June 11-14, 1997).

FN9. *See* Dec. 28, 2007 Order Denying Scantibodies' Motion for Partial Summ. J. on Defendants' Counterclaim of Patent Invalidity.

FN10. *See* Joint Statement of Contentions Re: Meaning of Terms in Reexamination Claims of U.S. Pat. No. 6,689,566.

FN11. The phrase "in whole PTH" was not present in the parties Joint Statement of Contentions. However, Scantibodies proposed this amendment during its presentation at the March 24, 2008 claim construction hearing, which had been recommended by their expert, Dr. Ranes-Goldberg.

FN12. While the Court would have appreciated more complete briefing and more reasonable interpretations of the disputed claim terms, it has applied no more than routine skill in the art in its analysis, and certainly has not gone "to great lengths to supplement the deficiencies of the specification of the '566 Patent," as Immutopics states. Immutopics' Comments to Amended Claim Construction Order ("Defs.' Comments") at 7.

FN13. The Court notes that there are several ways to determine antibody specificity and detectability. As a practical matter, any method should be acceptable, as any accused infringing product would be well above the threshold limit for both specificity and detectability, or the assay would not work well enough to be a viable product. For example, useful antibodies would likely bind with association constants of at least 10^{12} liter/mole, a million times higher than the threshold level. For the sake of definiteness, detectability may be interpreted in light of the immunoradiometric assay described in the '566 Patent.

FN14. This sequence is amino acids 2-8 of the sequence of whole PTH.

FN15. Method claims 5, 13, and 18 involve some minor variations in wording, but employ "specific for" in the exact same manner as in every other independent claim.

FN16. Immutopics vigorously objected to Scantibodies' three-word amendment, "in whole PTH," following "the specified region (i.e. 2-8 PTH)" as a radical alteration of Scantibodies' proposed construction. *See* Transcript of March, 24, 2008 Claim Construction Hearing ("3/24/2008 Hrg. Tr.") at 10:8-14.

FN17. The phrase, "common sequence of human and rat PTH" is defined in the patent specification as the PTH (2-8) sequence (identified above as SEQ ID NO. 3), which is the same in both rat and human. *See* '566 Patent at 4:50-55. It does not refer to any other parts that the human and rat PTH sequences may have in common.

FN18. Because "specific for" is present in every independent claim of the '566 Patent, a finding of indefiniteness would result in every claim being declared invalid.

FN19. Scantibodies, in its comments on the Amended Claim Construction Order, objects to the "10^{5} liter/mole metric" that the Court has used. Plaintiff's Memorandum on its Positions Concerning the November 26, 2008 Amended Claim Construction Order ("Pl.'s Comments") at 1. The court emphasizes, as a clarification, that the construction of "specific for" as having a measurable affinity for and detectable

binding to has a minimum association constant of 10^5 liter/mole, a threshold value for specific binding. Thus, the construction of this term with a threshold value does not preclude an antibody that specifically binds to an antigen in more than one place, for example, an antibody that binds to PTH at the initial peptide sequence and another epitope, e.g., an epitope that does not contain at least four amino acids of SEQ ID NO: 3. Such an antibody could bind to each epitope with a different affinity. However, other claim terms recite negative limitations that further limit the claims.

FN20. This additional claim limitation is not present in the method claims because the Examiner allowed those claims without amendment. *See* 9/21/2006 Office Action at 40-41 (accepting Scantibodies' arguments that method claims were not obvious over Kohno in light of Bouillion); *see also* 7/24/2008 Scantibodies amendment at 39-48 (arguments overcoming rejections over Bouillion). The Court's analysis of "specific for," however, remains relevant to all the claims, including the method claims.

FN21. As noted earlier, human and rat PTH (1-8) have in common their PTH (2-8) sequence (also identified by the claims as "SEQ ID NO: 3"). Thus, "the common sequence of human and rat PTH (1-8)" refers to PTH (2-8) and SEQ ID NO: 3.

FN22. Dr. Ranes-Goldberg reiterated this testimony at the *Markman* hearing. *See* 3/24/2008 Hrg. Tr. at 30:18-25, 31:1-23.

FN23. Scantibodies does not explain why it is necessary to compare an antibody's binding affinity to PTH (2-8) in whole PTH to its affinity for a fragment in which that separate and independent claim term has been negated.

FN24. Dr. Ranes-Goldberg states that ' "specific for' means this antibody has a greater tendency to bind an initial peptide sequence of whole PTH relative to a fragment of PTH that is missing all or some of this initial peptide sequence." *Id*. para. 11. She then explains that by "greater tendency," she means the same thing as Scantibodies' "statistically significantly greater." *Id*. para. 12.

FN25. To support her construction of Dr. Ranes-Goldberg protests that it is "not possible to assign absolute numbers to these relative descriptions of 'greater' or 'lesser' [binding] because they only take on meaning in the context of the type of testing for which the antibody is being used." *Id*. para. 12. Yet specificity is "determined by [an antibody's] relative binding affinities," which are "quantitative measurement[s]." Ranes-Goldberg Decl. para.para. 8, 9. This supports the Court's construction-it is entirely possible to arrive at a concrete value for antibody specificity for one antigen over another.

FN26. *See* 3/24/2008 Hrg. Tr. at 10:16-25 (objection by Immutopics' counsel that Scantibodies' amendment, which added "in whole PTH" after "binding in the specified region (i.e., 2-8 PTH)," would "radically" alter Scantibodies' proposed construction) ("[with the amendment,] you would have differences between binding the whole versus fragments [instead of just] *these fragments* versus fragments") (emphasis added).

FN27. The thrust of Immutopics' claim construction brief suggests that Immutopics chose a confusing interpretation of the Examiner's statement precisely in order to drive home its argument on indefiniteness. The Court notes, however, that invalidity based on s. 112, para. 2 indefiniteness was not among the five grounds for summary judgment that Immutopics brought before this court.

FN28. The Court does note the following. First, the Examiner *was,* in fact, speaking to the concept of specificity and not to any supposed distinction between "specific for" and "binds to." Her statement mentions neither of those phrases. Rather, it speaks of "the relative affinities of the claimed antibodies," *see* 9/21/2006 Office Action at 5, which Dr. Ranes-Goldberg recognizes as a textbook definition of "specificity." *See* Ranes-Goldberg Decl. at para. 9. Second, it is clear that the Examiner understood the distinction between binding affinity and specificity. *See* 9/21/2006 Office Action at 6 ("Examiner agrees with the Patentee's assertions, that the antibody specificity is based on the binding affinities.") Lastly, Scantibodies did not, in fact, address the Examiner's concerns through by amending the claims. Scantibodies subsequently added the word "specifically" in front of "binds to," but left the term "specific for" alone. *See* 11/10/2006 Scantibodies Amendment at 2,

FN29. The antibody and kit claims contain the claim limitation, added during reexamination, that the antibody must be produced by immunizing with (1-84) PTH and affinity purified with (2-8) PTH. *See* Reexamination Claims 1, 20, 22. Yet Immutopics contends that its antibodies are generated by (i) immunizing with (1-34) PTH and (ii) affinity purifying with a peptide similar to (1-13) PTH, i.e., (1-12) PTH. *See* Transcript of January 29, 2008 Hearing ("1/29/2008 Hrg. Tr.") at 54:17-18; Defs.' Comments at 3. If true, then Immutopics is incapable of infringing either the antibody or kit claims of the '566 Patent. Scantibodies stated at the January 29 hearing that it had no independent evidence that Immutopics immunized with whole PTH (1-84) instead of PTH (1-34). 1/29/2008 Hrg. Tr. at 32:17-34:9, 62:14-63:4. *See also* 3/24/08 Hrg. Tr. at 36:21-25 ("we've already admitted in open court that if an antibody is produced and it's not produced in immunization by 1 to 84, it's not going to infringe any of the antibody or kit claims ... that's not true of the method claims").

FN30. Immutopics contends that Scantibodies disclaimed the use of other immunogens by arguing during reexamination that certain prior art antibodies did not "specifically bind to" whole PTH because they were not raised with whole PTH. In response to rejections over Magerlein, Tampe, and Adermann, Scantibodies had argued that it is "there is a strong probability, or at least possibility" that antibodies raised by immunization with antigens other than whole PTH would not be specific for whole PTH. Other than the posture in which this supposed disclaimer was made, the choice of immunogen appears to have no direct relevance to antibody specificity for whole PTH over PTH fragments. *See* 11/10/2006 Amendment at 22, 24, 26-27.

FN31. Notably, Immutopics does not argue that this limitation should be imposed upon the method claims, which, unlike the kit and antibody claims, do not expressly require that an antibody be raised by immunization with whole PTH. Immutopics' proposed construction for the fourth claim term, "not detecting an interfering ... fragment", a term which is found only in the method claims, does not include the limitation

here.

FN32. Gao et al., *J. Bone Miner. Res., 16(4):* 605-14 (2001).

FN33. This is a high concentration of fragment; for reference, normal levels of *whole* PTH in the blood serum in humans range from 10 pg/mL to 40 pg/mL. *See* '566 Patent at 1:60.

FN34. To provide a numerical example, consider an antibody whose affinity for PTH (7-84) is 30% as strong as its affinity for whole PTH. This antibody would be 30% as likely to bind to PTH (7-84) as to whole PTH; and in a sample containing equimolar amounts of whole PTH and PTH (7-84), the antibody would have a 30% error rate in measuring the concentration of whole PTH. No one would describe this antibody as having specificity for whole PTH or as useful in the clinical context. Yet as long as the binding it exhibits to PTH (7-84) is "statistically significantly less" than the binding exhibited to the whole PTH in the sample, and the experiment is conducted with appropriate positive and negative controls so as to achieve "consistently reliable" measurements, Scantibodies' definition of the term "does not specifically bind to an interfering non-(1-84) parathyroid hormone fragment" would be satisfied.

FN35. The Court offers no opinion regarding whether or not the Gao 2001 IRMA antibody meets the "specific for ... SEQ ID NO:3" or any other limitation of claim 1.

FN36. Scantibodies distinguishes Colford as follows: (1) Jensen, who was apparently linked to the authors of the 1997 Colford reference, presented a poster at a conference in 1996. Jensen is not listed as an author on the 1997 Colford reference. (2) In the poster, Jensen suggested that the results achieved by his research group's anti-PTH antibody were "higher or comparable" to Nichols' results. (3) Because Nichols does not distinguish an interfering fragment, and because Colford gives results that are "higher or comparable" to the Nichols results, it follows that Colford, like Nichols, also does not distinguish an interfering fragment and does not anticipate the claims examined during the prosecution of the '566 Patent. The flaws in this logic are staggering. The data in the Colford reference itself clearly demonstrate that the authors had generated an antibody capable of distinguishing a PTH fragment, called PTH, from whole PTH (labeled PTH a). *See* Colford Abstract, Newboles Cl. Constr. Decl., Ex. G. Yet rather than address the prior art on its own terms, Scantibodies' argument is based on an isolated, ambiguous phrase taken out of context from a different piece of prior art.

FN37. The Court notes that this limitation of the process used to generate the antibody itself cannot have imparted patentability to claims that would otherwise be anticipated or obvious by antibodies in the prior art produced in a different way. *See* In re Thorpe, 777 F.2d 695, 697 (Fed.Cir.1985) ("The patentability of a product does not depend on its method of production....If the product in a product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." (internal citations omitted)). In addition, the process of immunizing mammals with (1-84) PTH was known as early as 1990, well before the filing date of the '566 Patent. Pl.'s Statement of Genuine Issues of Material Fact in Support of its Opp'n to Defs.' Mot. for Summary J.

(admitting that Scantibodies from 1990-95 provided to third parties anti-serum derived from goats that were immunized with 1-84 PTH).

FN38. Immutopics has requested clarification of the phrase "an interfering non-(1-84) parathyroid hormone fragment." The Court has declined to do so at this time.

C.D.Cal.,2009.
Scantibodies Laboratory, Inc. v. Immutopics, Inc.