UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

ABBOTT BIOTECHNOLOGY LTD. and ABBOTT LABORATORIES,	)	
Plaintiffs,	)	**Civil Action No. 09-40089-FDS**
v.	)	
CENTOCOR ORTHO BIOTECH, INC.,	)	
Defendant.	)	

MEMORANDUM AND ORDER ON
CLAIM CONSTRUCTION

SAYLOR, J.

This is a patent dispute involving a pharmaceutical product used to treat certain autoimmune diseases. Plaintiffs Abbott Biotechnology Ltd. and Abbott Laboratories (collectively "Abbott") seek a judgment that the drug Simponi, manufactured by defendant Centocor Ortho Biotech, Inc. infringes its patents to the extent that it is used with the drug methotrexate to treat rheumatoid arthritis. Centocor seeks declarations of non-infringement and invalidity of Abbott's patents.

The parties' allegations hinge in part on the construction of claims in Abbott's U.S. Patents No. 7,223,394 (the "'394 patent") and No. 7,541,031 (the "'031 patent"). The Court conducted a *Markman* hearing with respect to the construction of the claims on March 29, 2011.

Abbott's '394 and '031 patents claim the following: "A method for treating a subject suffering from rheumatoid arthritis, comprising administering to the subject both an antibody and methotrexate, such that the rheumatoid arthritis is treated . . ." Abbott and Centocor dispute the

construction of the term "administering to the subject both an antibody and methotrexate."

I. Background

The '394 and '031 patents are part of a family of patents owned by Abbott. The parent patent, U.S. Patent No. 6,090,382 (the "'382 patent"), was filed in 1996 and issued in 2000. It is directed to certain human antibodies designed to attach to a naturally-occurring protein in the human body called tumor necrosis factor alpha ("hTNFα").

A. Development of Anti-hTNFα Antibodies

Human TNFα is involved in regulation of the immune system, a role it performs by triggering inflammation in response to invasion by a foreign entity. Overproduction of hTNFα can lead to excessive inflammation that can result in tissue damage. This occurs in diseases such as rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, and psoriasis, which are known as autoimmune diseases because of the way the body's own immune system—in this case, through hTNFα—targets healthy human tissue instead of foreign contaminants.

Antibodies are proteins that bind with harmful foreign substances, or "antigens," such as viruses or bacteria. An antibody attaches itself to an antigen by binding with a portion of the antigen called an "epitope." By occupying the antigen's epitope, the antibody diminishes the antigen's ability to bind with other receptors in the body to harmful effect.

The human immune system rarely produces antibodies that target hTNFα, because hTNFα is a protein that the body itself produces, not a foreign contaminant. To prevent an overabundance of hTNFα from causing tissue damage, Abbott invented an antibody that binds to hTNFα. The process of binding is known as "neutralization" of hTNFα. In order for an antibody to effectively neutralize hTNFα, it must attach to it with sufficient strength. The strength of an

antibody's interaction with hTNFα is called its "affinity" for hTNFα.

Researchers have long sought to develop antibodies that neutralize hTNFα and bind to it with high affinity. An antibody that inhibits hTNFα in this manner could become a treatment for, among other things, autoimmune diseases. In the 1980s, researchers invented a high-affinity, neutralizing anti-hTNFα antibody that derived from mouse DNA. It could not effectively treat human autoimmune diseases, however, because humans often exhibit adverse reactions to non-human antibodies.

The development of chimeric antibodies, or antibodies with components that derive from both mouse and human DNA, advanced treatment options for autoimmune diseases. Centocor, together with the Kennedy Institute, obtained a patent in 2001 that disclosed a method for treating arthritis by co-administering chimeric anti-hTNFα antibodies with a pre-existing drug called methotrexate. (*See* U.S. Patent No. 6,270,766).[1] In 1999, the FDA approved Remicade, a drug manufactured by Centocor and based on chimeric antibodies, for treatment of rheumatoid arthritis.

Abbott's '382 patent, filed in 1996, for the first time disclosed a class of fully-human, high-affinity, neutralizing anti-hTNFα antibodies and certain uses of those antibodies. A subsequent application filed in 1997 under the Patent Cooperation Treaty claimed priority to the '382 patent application and disclosed substantially the same invention, but also added a description of the use of therapeutic agents with human anti-hTNFα antibodies. Another patent in

[1] Methotrexate was invented in the 1940s, initially as a chemotherapy drug. It is now categorized as a disease-modifying anti-rheumatic drug ("DMARD") and can be an effective treatment for rheumatoid arthritis. Physicians may prescribe only methotrexate or may prescribe it in combination with a drug developed from anti-hTNFα antibodies. The prescribing physician determines the frequency and dosage of methotrexate administrations.

the family, U.S. Patent No. 6,509,015, likewise claimed a "method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental," including rheumatoid arthritis, by "administer[ing the human antibody] with at least one additional therapeutic agent." (*See* U.S. Patent No. 6,509,015 claims 4, 17, 69).

B. The Asserted Patents

The '394 and '031 patents, the two patents-in-suit, are continuations of a patent in the '382 family. The '394 patent, issued in 2007, is directed to a method for treating rheumatoid arthritis by administering the human anti-hTNFα antibody with methotrexate. The '031 patent, issued in 2009, shares the same specification and claims substantially the same invention. Both patents claim priority to the 1997 Patent Cooperation Treaty application.

Based on the technology disclosed in the '382 patent and its progeny—in particular, the '394 and '031 patents—Abbott developed Humira, a drug prescribed for several autoimmune diseases. The FDA approved Humira in December 2002 to treat rheumatoid arthritis, either alone or in combination with methotrexate or other DMARDs. Rheumatoid arthritis patients typically take a combination of Humira once every two weeks and methotrexate weekly, but may take Humira weekly when it is not prescribed in combination with methotrexate.

In the past decade, Centocor researchers also developed a fully-human, high-affinity, neutralizing anti-hTNFα antibody. In 2009, Centocor obtained approval from the FDA to manufacture and sell Simponi, the drug based on Centocor's human anti-hTNFα antibody. Simponi was indicated for the treatment of moderate to severe rheumatoid arthritis, to be used in combination with methotrexate. It was also indicated for the treatment of psoriatic arthritis, either alone or in combination with methotrexate, and ankylosing spondylitis. For all three

conditions, patients are administered monthly subcutaneous injections. Abbott alleges that Centocor's manufacture, marketing, and sale of Simponi infringes its '394 and '031 patents under 35 U.S.C. § 271(a) and (b) when used in the treatment of rheumatoid arthritis.

C. The Licensing Agreement

In late 2002, Abbott and Centocor agreed to cross-license a series of patents directed to anti-hTNFα antibodies. Centocor extended to Abbott rights under its 2001 patent, which covered a method for treating arthritis by co-administering chimeric anti-hTNFα antibodies with methotrexate. In exchange, Abbott extended to Centocor rights under the '382 patent and other patents in the family, including U.S. Patent No. 6,509,015, which covered a method for treating rheumatoid arthritis (among other diseases) by co-administering human anti-hTNFα antibodies with a therapeutic agent. The license agreement contained an arbitration clause and excluded from coverage "any claim . . . directed to subject matter added" to subsequent patent applications in the '382 family.

After Abbott initiated this action against Centocor in May 2009, the parties proceeded to arbitrate whether the agreement extended to Centocor an implied license under the '394 and '031 patents. The arbitrator determined in June 2010 that the agreement did not cover the subject matter claimed in Abbott's '394 and '031 patents.

II. Legal Framework

The construction of claim terms is a question of law. *Markman v. Westview Instruments*, 517 U.S. 370, 372 (1996) ("[T]he construction of a patent, including terms of art within its claim, is exclusively within the province of the court.").

In *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (*en banc*), the Federal Circuit

clarified the proper approach to claim construction and set forth principles for determining the hierarchy and weight of the definitional sources that give the patent its meaning. The guiding principle of construction is "the meaning that the term would have to a person of ordinary skill in the art in question at the time of . . . the effective filing date of the patent application." *Id.* at 1313. Courts thus seek clarification of meaning in "the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art." *Id.* at 1314 (quoting *Innova/Pure Water, Inc. v. Safari Water Filtration Sys.*, 381 F.3d 1111, 1116 (Fed. Cir. 2004)).

A. The Words of the Claims

The claim construction analysis normally begins with the claims themselves.[2] The claims of a patent "define the invention to which the patentee is entitled the right to exclude." *Id.* at 1312 (quoting *Innova*, 381 F.3d at 1115).

In some instances, the arrangement of the disputed term within the claims is dispositive. The use of a term within the larger context of the claim can provide a firm basis for construing the term. *Id.* at 1314. For example, because claim terms are normally used consistently throughout the patent, the meaning of a term in one claim is likely the meaning of that same term in another.

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[2] In *Phillips*, the Federal Circuit discredited the practice of starting the claim construction analysis with broad definitions found in dictionaries and other extrinsic sources:

> [I]f the district court starts with the broad dictionary definition . . . and fails to fully appreciate how the specification implicitly limits that definition, the error will systematically cause the construction of the claim to be unduly expansive. The risk of systematic overbreadth is greatly reduced if the court instead focuses at the outset on how the patentee used the claim term in the claims, specification, and prosecution history, rather than starting with a broad definition and whittling it down.

Id. at 1321. Of course, if no special meaning is apparent after reviewing the intrinsic evidence, claim construction might then "involve[] little more than the application of the widely accepted meaning of commonly understood words." *Id.* at 1314.

Id. Differences among claims may furnish an additional basis for understanding the meaning of particular claim terms. *Id.*

A construction of a claim that gives effect to all terms in the claim is preferable to a construction that renders a term superfluous. See *Mangosoft, Inc. v. Oracle Corp.*, 525 F.3d 1327, 1330-31 (Fed. Cir. 2008); *Merck & Co. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1372 (Fed. Cir. 2005).

B. The Specification

"The claims, of course, do not stand alone." *Id.* at 1315. Rather, "they are part of a fully integrated written instrument, consisting principally of a specification that concludes with the claims." *Id.* (internal citations and quotations omitted). For that reason, the specification must always be consulted to determine a claim's intended meaning. "[T]he specification is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Id.* (citing *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). The importance of the specification derives from the Patent Act, which instructs that the specification shall describe the claimed invention in "full, clear, concise, and exact terms." 35 U.S.C. § 112; *Phillips*, 415 F.3d at 1316.

"In general, the scope and outer boundary of claims is set by the patentee's description of his invention." *On Demand Mach. Corp. v. Ingram Indus.*, 442 F.3d 1331, 1338 (Fed. Cir. 2006); *see also Phillips*, 415 F.3d at 1315-1317 ("[T]he interpretation to be given a term can only be determined and confirmed with a full understanding of what the inventors actually invented and intended to envelop with the claim"). The claims are to be construed in a way that makes them consistent with, and no broader than, the invention disclosed in the specification. *On Demand*,

442 F.3d at 1340 ("[C]laims cannot be of broader scope than the invention that is set forth in the specification."); *Phillips*, 415 F.3d at 1316 ("[C]laims must be construed so as to be consistent with the specification, of which they are a part.").

Courts must be careful to "us[e] the specification [only] to interpret the meaning of a claim" and not to "import[] limitations from the specification into the claim." *Phillips*, 415 F.3d at 1323; *see also Gillette Co. v. Energizer Holdings, Inc.*, 405 F.3d 1367, 1375 (Fed. Cir. 2005) (internal quotations omitted). A patent's "claims, not specification embodiments, define the scope of patent protection." *Kara Tech. Inc. v. Stamps.com Inc.*, 582 F.3d 1341, 1348 (Fed. Cir. 2009); *see also Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1381 (Fed. Cir. 2009) ("[E]mbodiments appearing in the written description will not be used to limit claim language that has broader effect."). Ultimately, "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be . . . the correct construction." *Phillips*, 415 F.3d at 1316 (citing *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998)).

C. The Prosecution History

After the specification and the claims themselves, the prosecution history is the next best indicator of term meaning. The prosecution history consists of the complete record of the proceedings before the PTO and includes the prior art cited during the examination of the patent. *Id.* at 1317. "Like the specification, the prosecution history provides evidence of how the PTO and the inventor understood the patent." *Id.* "[T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope

narrower than it would otherwise be." *Id.* (citing *Vitronics*, 90 F.3d at 1582-83).

However, "because the prosecution history represents an ongoing negotiation between the PTO and the applicant, rather than the final product of that negotiation, it often lacks the clarity of the specification and thus is less useful for claim construction purposes." *Id.* As a result, courts generally require that "a patent applicant [] clearly and unambiguously express surrender of subject matter" to disavow claim scope during prosecution. *Voda v. Cordis Corp.*, 536 F.3d 1311, 1321 (Fed. Cir. 2008) (quoting *Sorensen v. Int'l Trade Comm'n*, 427 F.3d 1375, 1378 (Fed. Cir. 2005)).

D. Extrinsic Sources

Extrinsic evidence consists of "all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." *Phillips*, 415 F.3d at 1317. It "can help educate the court regarding the field of the invention and can help the court determine what a person of ordinary skill in the art would understand claim terms to mean." *Id.* at 1319. However, extrinsic evidence suffers from a number of defects, including its independence from the patent, potential bias, and varying relevance. *Id.* at 1318-19. Such evidence is therefore "unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence," and courts may consider, or reject, such evidence at their discretion. *Id.* at 1319.

III. Analysis

A. Agreed-Upon Terms

The parties have agreed upon the construction of the following terms:

CLAIM TERM	AGREED-UPON CONSTRUCTION
"K_d"	"the dissociation constant of a particular antibody-antigen interaction"
"K_{off}"	"the off rate constant for dissociation of an antibody from the antibody/antigen complex"
"surface plasmon resonance"	"an optical phenomenon that allows for the analysis of real-time biospecific interactions by detection of alterations in protein concentrations within a biosensor matrix"
"recombinant antibody"	"antibody that is prepared, expressed, created or isolated by recombinant means"
"isolated human antibody"	"An antibody having variable and constant regions derived from human germline immunoglobulin sequences (which may include mutations introduced in vitro or in vivo) that is substantially free of other antibodies having different antigenic specificities (e.g., an isolated antibody that specifically binds hTNFα is substantially free of antibodies that specifically bind antigens other than hTNFα). An isolated human antibody is not intended to include antibodies in which CDR sequences derived from the germline of another mammalian species, such as a mouse, have been grafted onto human framework sequences. An isolated human antibody that specifically binds hTNFα may, however, have cross-reactivity to other antigens, such as TNFα molecules from other species"

The Court will adopt the parties' proposed constructions of these terms.

B. <u>Disputed Term</u>

Claim 1 of the '394 patent is representative of the asserted claims with respect to the single disputed term. It claims:

A method for treating a subject suffering from rheumatoid arthritis, comprising

> administering to the subject both an antibody and methotrexate, such that the rheumatoid arthritis is treated, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, tat dissociates from human TNFα with a K_d of $1x10^{-8}$ M or less and a K_{off} rate constant of $1x10^{-3}s^{-1}$ or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard in vitro L929 assay with an IC_{50} of $1x10^{-7}$ M or less.

The parties disagree over the proper construction of the phrase "administering to the subject both an antibody and methotrexate."

Abbott contends that the term is clear on its face and proposes that the Court adopt its plain meaning.[3] Both a skilled artisan and an ordinary citizen, Abbott maintains, would understand the phrase to refer to treating rheumatoid arthritis with the combination of an antibody and methotrexate. Centocor contends that "administering to the subject" means "introducing to the body of the subject." It also contends that "both an antibody and methotrexate" means "an antibody and methotrexate together." In its entirety, Centocor's proposed construction reads as follows: "introducing to the body of the subject an antibody and methotrexate together." The Court will construe the term's separate clauses in turn.

1. <u>"Administering to the Subject"</u>

Centocor contends that a person of ordinary skill in the art would understand "administering to the subject" to mean "introducing to the body of the subject." Centocor submits that its proposed construction is the plain meaning of the term. Abbott contends that "administering to the subject" possesses a clear meaning and therefore requires no rephrasing.[4]

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[3] In the alternative, should the Court adopt Centocor's construction, Abbott urges the Court to clarify that "introducing the drugs 'together' does not require that they be delivered simultaneously or with identical dosing frequency, but only sufficiently together that rheumatoid arthritis is treated with the combination of both drugs, and that 'introducing' is not limited to the first time the drug is administered." (Abbott Br. at 15).

[4] The Federal Circuit recently reaffirmed that a court may construe a claim term to have its plain meaning when such a construction resolves a dispute between the parties. *Finjan Inc. v. Secure Computing Corp.*, 626 F.3d

Centocor's construction, Abbott contends, injects ambiguity into the term, as "introducing" suggests that "administering" is limited to the first time a subject is treated with a drug.

Centocor contends that its rephrasing of the term is motivated by its concern that "administering" a treatment not be confused with a physician's act of "prescribing" a treatment. It cautions that "'[a]dministering to the subject' is distinct, for example, from *prescribing* a drug that is then administered by someone else." (Centocor Br. at 8). But that concern is exaggerated at best. The act of prescribing is clearly distinct from the subsequent act of administering medication, and indeed Abbott does not dispute that "administering" is an action distinct from prescribing. The Court therefore concludes that the plain meaning of the phrase "administering to the subject" does not encompass the act of prescribing, and no further construction as to that issue is required.

The remaining dispute concerns whether Centocor's proposed construction improperly reads a limitation into the claims by temporally restricting "administering" to the first act of treatment. Centocor does not identify the source of its proposal that "introducing to the body" clarifies "administering," and nothing in the claim language obviously commands its construction. The specification, however, clearly shows that "introducing" and "administering" are not interchangeable concepts.

"Introducing," or a variation on the root word "introduce," appears fifteen times in the specification. On ten occasions, it refers to the introduction of vectors into cells. ('394 patent at

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1197, 1206-07 (Fed. Cir. 2010); *see also U.S. Surgical Corp. v. Ethicon, Inc.*, 103 F.3d 1554, 1568 (Fed. Cir. 1997) ("Claim construction is a matter of resolution of disputed meanings and technical scope, to clarify and when necessary to explain what the patentee covered by the claims, . . . [but] is not an obligatory exercise in redundancy.").

col. 4, l. 53; col. 9, ll. 10-11; col. 9, l. 31; col. 14, l. 32; col. 17, l. 17; col. 17, l. 21; col. 17, ll. 52-53; col. 18, ll. 14-15; col. 19, ll. 64-65; col. 21, ll. 40-41). On four other occasions, it refers to the introduction of mutations into gene sequences. (*Id.* at col. 7, l. 42; col. 21, l. 7; col. 21, l. 25; col. 34, ll. 27-28). In these contexts, "introducing" describes the act of exposing something to a foreign substance that it did not previously contain. Used in this manner, "introducing" refers to the initial interaction or contact between a vector and cell or a mutation and sequence. It does not suggest ongoing exposure, as one might expect in the context of medical treatment for rheumatoid arthritis.

The fifteenth occasion appears in a portion of the specification that reads as follows:

> The invention provides methods for [sic] TNFα activity in a subject suffering from [a disorder in which TNFα activity is detrimental], which method comprises administering to the subject an antibody or antibody portion of the invention such that TNFα activity in the subject is inhibited. Preferably, the TNFα is human TNFα and the subject is a human subject. Alternatively, the subject can be a mammal expressing a TNFα with which an antibody of the invention cross-reacts. Still further the subject can be a mammal into which has been introduced hTNFα (e.g., by administration of hTNFα or by expression of an hTNFα transgene). An antibody of the invention can be administered to a human subject for therapeutic purposes.

(*Id.* at col. 27, ll. 50-61). In this context, "introduced" refers to the exposure of non-human mammals to human TNFα, where it would not be expected that human TNFα would exist in the body of a non-human mammal. Once again, the specification's usage of "introduced" suggests initial exposure; the phrase "has been introduced" suggests that there was one occasion on which introduction of human TNFα occurred. Indeed, it would be odd to refer to ongoing introduction of human TNFα to a non-human mammal after the mammal had already been exposed to human TNFα.

Moreover, the excerpted paragraph describes "administration of hTNFα" as a means by which introduction of human TNFα may be accomplished. "Administration," used here, is the act of injecting human TNFα into the body of the mammal, while the introduction refers to the transition of the mammal from a state without human TNFα to a state with human TNFα. In the passage, as with the other appearances of forms of "introduce" in the specification, the concept of "administration" is distinct from the concept of "introduction."

By contrast, the term "administering" or a variation on the root word "administer" pervades the specification. The following usage is typical: "The antibodies or antibody portions of the present invention can be administered by a variety of methods known in the art, although for many therapeutic applications, the preferred route/mode of administration is intravenous injection or infusion. As will be appreciated by the skilled artisan, the route and/or mode of administration will vary depending on the desired results." ('394 patent at col. 22, ll. 38-44). It is clear that the words "administered" and "administration" here denote the act of giving treatment to a patient. They do not suggest a temporal restriction; instead, they can comfortably accommodate both the initial treatment and ongoing treatments.

Centocor offers no extrinsic or intrinsic evidence to support its proposed construction, nor does it explain how its construction can be harmonized with the specification. Because Centocor's proposed construction narrows the meaning of the term and injects—one might say "introduces"—ambiguity, the Court will reject it and will adopt the plain meaning of "administering to the subject." That approach is most consistent with the claims and specifications at issue here.

2. "Administering to the Subject both an Antibody and Methotrexate"

Centocor next contends that the phrase "both an antibody and methotrexate" means "an antibody and methotrexate together." This construction, according to Centocor, gives meaning to the word "both," which otherwise would be superfluous. Abbott contends that the phrase needs no construction and urges the Court to adopt its plain meaning. According to Abbott, Centocor's proposed construction improperly constricts the scope of the claim to require simultaneous administration of the invented antibody and methotrexate. The proper function of "both," Abbott maintains, is to emphasize that the patent claims a method for treatment rheumatoid arthritis by using the invented antibody and methotrexate in combination.

The parties' dispute centers on whether, in context, the word "both" means "together," or whether it is a term of emphasis and clarification. It should be noted at the outset that Centocor's proposed construction is not entirely clear with regard to its usage of "together." A bare reading of the phrase "administering to the subject an antibody and methotrexate together" could suggest that the invention claims a method of administering an antibody and methotrexate such that they are "together" in a physical location (for example, the blood stream or human tissue). But that is not the reading Centocor advocates. Rather, Centocor's proposed construction interprets "both" to impose a time constraint on administration of the antibody and methotrexate. Centocor's briefs speak of "administ[ration] . . . together" as simultaneous administration, or administration according to identical dosing schedules. (*E.g.*, Centocor Reply Br. at 4, 8). The Court will therefore proceed on the understanding that Centocor advocates for a construction whereby the antibody and methotrexate must be administered at the same time.

The Court begins with the claim language. The word "both" appears twice in claim 1: in the disputed term, and again in the phrase "wherein the antibody . . . tat dissociates from human

TNFα with a K_d of $1x10^{-8}$ M or less and a K_{off} rate constant of $1x10^{-3}s^{-1}$ or less, both determined by surface plasmon resonance . . . ." The second phrase defines constants that characterize the invented antibody. It explains that these constants are "both" determined by surface plasmon resonance, a particular method of analyzing protein interactions. Here, the word "both" performs a clarifying function. It if were omitted, a reader might reasonably believe that the phrase "determined by surface plasmon resonance" modifies only "K_{off} rate constant of $1x10^{-3}s^{-1}$ or less" because it immediately follows that clause. On that reading, the the K_d might be determined by something other than surface plasmon resonance. Inclusion of "both" in the claim clarifies that the K_d is measured by a surface plasmon resonance analysis, as is the K_{off} rate constant.

The functional usage of "both" in the second phrase does not fit neatly with either Centocor's or Abbott's proposed construction of the disputed claim term.[5] In the second phrase, it does not obviously mean "together" or "simultaneously" such that the constants are determined at the same time, although that construction is possible. And it is not merely a word of emphasis. The term "both" thus can have different meanings and serve different functions depending on context, even in the same claim. In order to understand the usage of "both" in the term "both an antibody and methotrexate," then, consultation of other intrinsic evidence is necessary.

The specification contains five uses of the word "both" that follow the same grammatical structure of the disputed claim term—that is, with the structure "both X and Y." On three occasions, "both" is used merely for emphasis. (*See* '394 patent at col. 10, ll. 15-16; col. 27, ll. 24-25; col. 37, ll. 10-11). Used in this way, an interpretation of "both" to mean "together" or "simultaneously" may be nonsensical. For example, the patent teaches that "[t]he antibodies and

[5] Note that the word "either" in this sentence simply emphasizes the word "or."

antibody portions of the invention are capable of neutralizing hTNFα activity both in vitro and in vivo." (*Id.* at col. 27, ll. 24-25). While it might be literally possible for the antibodies to neutralize hTNFα activity in a petri dish and a live subject at the same time, that is obviously not what the sentence means.[6] In the two other occasions, "both" is used to describe two DNA sequences that are together in the same physical location. (*Id.* at col. 18, ll. 13-14 ("vector encoding both the antibody heavy chain and the antibody light chain"); col. 19, ll. 53-54 (same)). In none of these usages can the word "both" be understood to denote simultaneous action.

More significant is the specification's lengthy discussion of methods of administration and co-administration with therapeutic agents, such as methotrexate. (*See id.* at col. 23, l. 55 (identifying methotrexate as one of the therapeutic agents that can be combined with the invented antibody to treat rheumatoid arthritis)). The discussion begins by identifying preferred and permissible modes of administering the human anti-hTNF α antibodies, which include intravenous infusion, injection, and oral administration. The patent teaches that the mode of administration will "vary depending on the desired results" of the treatment, an instruction that anticipates an approach to dosing and administration that is tailored to individual patients' needs. (*Id.* at col. 22, ll. 43-44).

Shortly thereafter, the specification explains that dosage regimens may vary depending on the desired effect of the treatment. Pharmaceutical compositions may deliver to the patient a "therapeutically effective amount" or a "prophylactically effective amount." ('394 patent at col.

[6] It is easy to construct similar examples from daily life. One might eat both pizza and salad for dinner, but probably not together. A student might enroll in both science and humanities courses, but no university would permit her to take the courses at the exact same time. One might speak both English and Spanish, but not simultaneously.

25, ll.62-67, col. 26, ll.1-14). These amounts are those quantities "effective, at dosages and for periods of time necessary," to achieve the desired therapeutic or prophylactic effect. (*Id.* at col. 25, ll. 66-67; col. 26, ll. 9-10). Doses for prophylactic purposes will be smaller than doses for therapeutic purposes. (*Id.* at col. 26, ll. 11-14).

Indeed, a variety of factors justify variable dosing schedules. "Dosage regimens may be adjusted to provide the optimum desired response. . . . For example, a single bolus may be administered, several divided doses may be administered over time or the dose may be proportionally reduced or increased as indicated by the exigencies of the therapeutic situation." (*Id.* at col. 26, ll. 15-20). These teachings explain that dosage regimens can vary depending on intended outcomes. What is more, the therapeutically effective amount of the antibody "may vary according to factors such as the disease state, age, sex, and weight of the individual" and "dosage regimens should be adjusted over time according to the individual need." (*Id.* at col. 26, ll. 2-3). The specification is abundantly clear that dosage schedules of the invented antibody can and should differ in order to achieve effective treatment. Nothing indicates that the dosage schedule of the antibody must be tied to that of a therapeutic agent—in this case, methotrexate—used in combination.[7]

Centocor relies on only one passage from the specification, which in fact undermines its argument that the patent covers only simultaneous administration of the antibody and methotrexate. "In certain embodiments," the patent instructs, "an antibody or antibody portion of

[7] Centocor and Abbott agree that, during the relevant time frame, methotrexate was typically administered on a weekly basis. (Abbott Br., Ex. 11, TEXTBOOK OF RHEUMATOLOGY 773 (Kelley et al., eds. 1993); Centocor Reply Br. at 7). If methotrexate was a weekly drug and dosages for the invented antibody were expected to vary with patients' individual characteristics and the desired treatment effects, it is an obvious inference that at least some of the contemplated co-administrations of methotrexate and the invented antibody would be on different dosing regimens.

the invention is coformulated with and/or coadministered with one or more additional therapeutic agents that are useful for treating disorders in which TNFα is detrimental. . . . Such combination therapies may advantageously utilize lower dosages of the administered therapeutic agents, thus avoiding possible toxicities or complications." ('394 patent at col. 23, ll. 5-9, 21-23).

Centocor contends that the verbs "co-formulated" and "co-administered" in the passage each mean "administered together."[8] Abbott agrees that a "co-formulated" embodiment would call for simultaneous administration of methotrexate and the antibody. But co-administration, disclosed as an alternative to co-formulation, must mean something different. Indeed, in 1997, a person of ordinary skill in the art would have understood that dosage regimens varied for drugs "co-administered" in the treatment of rheumatoid arthritis. (*See* Levesque Decl. ¶¶ 21, 23 (explaining that drugs such as aspirin and ibuprofen were administered several times per day, while certain DMARDs like methotrexate were administered once a day, weekly, or biweekly)). The evidence suggests, therefore, that "co-administration" denotes administering the medications in combination, but not necessarily simultaneously. Moreover, the passage contemplates that the dosing regimens of therapeutic agents may be altered to avoid unwanted side-effects. Again, nothing suggests that these dosing regimens must be tied to the dosing schedules of the human anti-hTNFα antibodies.

An approach that requires administration of methotrexate and the antibody on the same dosing schedules might in fact undermine treatment. The specification teaches that dosing schedules should remain flexible to account for changed conditions, desired outcomes, and

[8] To reach this conclusion, Centocor relies only on general purpose online dictionaries, which in fact say nothing about administration at the same time. The Court does not credit the argument.

individual characteristics. An inflexible treatment regimen might not, therefore, achieve the therapeutically or prophylactically effective dosing amount necessary for effective treatment. But construing a claim term to undermine treatment of rheumatoid arthritis is inconsistent with the invention, which claims a method of administration "such that rheumatoid arthritis is treated." ('394 patent, claim 1). Construction of "both" as only simultaneous administration therefore risks frustrating the claim command that the method actually treat rheumatoid arthritis.

The words of the claim, context of the claim, and specification all confirm that "administering to the subject both an antibody and methotrexate" do not mean simultaneous administration of the antibody and methotrexate. Centocor's proposed construction that "both" means "an antibody and methotrexate together" is unconvincing, and the Court will not adopt it. The remaining question, then, is whether adopting the plain meaning of the term provides sufficient clarity to the parties.

Centocor contends that adopting the plain meaning of "both" fails to ascribe independent meaning to the claim term. If "both" does not mean "together," Centocor protests, the claim construction would effectively read "both" out of the claim. *See Merck*, 395 F.3d at 1372 ("A claim construction that gives meaning to all the terms of the claim is preferred over one that does not do so."). Simply adopting the plain meaning, in this view, suggests that "both" does not carry independent meaning.

Centocor points to Abbott's addition of the word "both" during the prosecution of the '394 patent as evidence that the term must be given a construction. After the examiner allowed the claim language without the word "both," Abbott amended the claim to add the term "for clarity." (*See* Verrecchio Decl. Exs. 11-13). Centocor contends that Abbott's insertion of "both"

into the claim must mean *something*, for it would not have added another word without intending to change the meaning of the claim.

The Court agrees that the term "both" should be given meaning. But Centocor's proposal that "both" means "together" or "simultaneous" ascribes too much importance to the addition of the term to the claim. As a practical matter, it defies common sense that Abbott would have voluntarily narrowed the scope of the claimed invention to only cover administration of its invented antibody and methotrexate at the same time, particularly when that narrowing might have diminished the effectiveness of treatment. As Centocor acknowledges, Abbott did not add "both" to the claim because it was required to do so by the examiner to achieve allowable claim language. Adding a term, for the stated purpose of enhancing clarity, is not the sort of clear and unmistakable departure from a claim's ordinary meaning that is required to show disclaimer of claim scope. *Voda*, 536 F.3d at 1321; *SanDisk Corp. v. Memorex Prods., Inc.*, 415 F.3d 1278, 1286-87 (Fed. Cir. 2005) ("When the patentee makes clear and unmistakable prosecution arguments limiting the meaning of a claim term in order to overcome a rejection, the courts limit the relevant claim term to exclude the disclaimed matter, . . . [but] the court will not use [an ambiguous disclaimer] to limit a claim term's ordinary meaning."); *see also Phillips*, 415 F.3d at 1317 (cautioning against overreliance on prosecution history, which lacks the clarity of the specification). If Abbott had intended to alter the claim to cover only simultaneous administration, any number of formulations would have been clearer, including "co-formulating . . . an antibody and methotrexate"; or "administering . . . an antibody and methotrexate at the same time"; or "administering . . . an antibody and methotrexate simultaneously."

In any event, the term "both" is not superfluous, for it serves an emphasizing and

clarifying function. It is commonplace in English usage to use the term "both" as a conjunction to emphasize the correlative conjunction "and," as in the phrase "both X and Y." The addition of "both" in such circumstances may be arguably superfluous, but it unquestionably performs a clarifying function.[9]

The term "both," in the context of the claims, clarifies that the invented antibody and methotrexate are to be used in combination. If the term "both" were excised, so that the claim read "administering to the subject an antibody and methotrexate," one might read the claim to permit exclusive treatment with one drug, followed by cessation of treatment with that drug and commencement of treatment with another drug. The addition of the term "both" clarifies that the patent claims a method for treating rheumatoid arthritis with the combination of the invented antibody and methotrexate, a claim that is amply supported by the specification. (*See* '394 patent at col. 23, ll. 5-9, 21-22 ("an antibody or antibody portion of the invention is coformulated with and/or coadministered with one or more additional therapeutic agents that are useful for treating disorders in which TNFα is detrimental. . . . Such combination therapies may advantageously utilize lower dosages of the administered therapeutic agents."); col. 23, ll. 25-27, 55 ("Nonlimiting examples of therapeutic agents for rheumatoid arthritis with which an antibody . . . of the invention can be combined include[s] . . . methotrexate.")).

The Court will therefore construe the phrase "both an antibody and methotrexate" to mean "an antibody and methotrexate in combination." This construction addresses Centocor's concern that the asserted patents not be misconstrued to cover treatment of rheumatoid arthritis only with methotrexate or only with the invented antibody. It also clarifies any possible ambiguity

[9] The term "either" in the conjunction pair "either . . . or" performs a similar function.

inherent in the term "both," while permitting (but not requiring) co-administration of methotrexate and the invented antibody on independent dosing schedules. Finally, the construction remains consistent with the claim language, specification, and prosecution history.

III. Conclusion

For the foregoing reasons, the following is the construction of the disputed claim term:

The term "administering to the subject both an antibody and methotrexate" means "administering to the subject an antibody and methotrexate in combination."

So Ordered.

/s/ F. Dennis Saylor
F. Dennis Saylor IV
United States District Judge

Dated: August 12, 2011