IN THE UNITED STATES DISTRICT COURT FOR THE
EASTERN DISTRICT OF VIRGINIA
Alexandria Division

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| UCB, INC., | ) | |
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| Plaintiff / Counterclaim-Defendant, | ) | |
| | ) | |
| v. | ) | 1:14cv1038 (LMB/TCB) |
| | ) | |
| YEDA RESEARCH AND DEVELOPMENT CO. LTD., | ) | |
| | ) | |
| Defendant / Counterclaim-Plaintiff. | ) | |

MEMORANDUM OPINION

Plaintiff / Counterclaim-Defendant UCB, Inc. ("UCB") brought this declaratory judgment action seeking a declaration that its Cimzia® product, a humanized monoclonal antibody approved by the Food and Drug Administration ("FDA") for the treatment of rheumatoid arthritis, psoriatic arthritis, active ankylosing spondylitis, and Crohn's disease, does not infringe defendant's patent and that the patent is invalid. Specifically, UCB argues that the defendant's patent does not cover humanized monoclonal antibodies like Cimzia®. Defendant / Counterclaim-Plaintiff Yeda Research and Development Co. Ltd. ("Yeda") owns United States Patent No. 6,090,923, titled "Murine Monoclonal Antibody Binding TNFα" (the "'923 Patent"). In its answer and counterclaim, Yeda alleges that the '923 Patent is valid and that UCB infringes claims 1, 5, and 9 of the '923 Patent by producing Cimzia®.

Before the Court are Yeda's Motion for Partial Summary Judgment, [Dkt. No. 83],[1] and UCB's Motion for Summary Judgment of Non-Infringement and Invalidity, [Dkt. No. 80], which focuses on the meaning of "monoclonal antibody" in the '923 Patent. UCB argues that the term

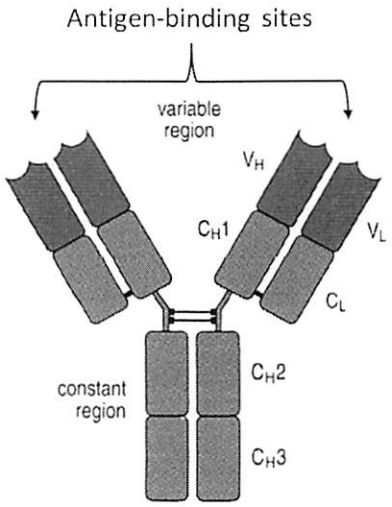
[1] Yeda's Motion for Partial Summary judgment addresses whether a laches defense is available to UCB.

"monoclonal antibody," used in claims 1, 5, and 9 of the '923 Patent, does not include humanized antibodies like Cimzia® because the technology to make humanized antibodies did not exist when the '923 Patent was filed in December of 1984. Yeda responds that the plain meaning of "monoclonal antibody" is broad enough to include humanized antibodies. Although the parties raise numerous other arguments, deciding the meaning of "monoclonal antibody" resolves this action. For the reasons that follow, UCB's Motion for Summary Judgment will be granted in part and Yeda's Motion for Partial Summary Judgment will be denied as moot.

## I. BACKGROUND

### A. Monoclonal Antibodies

Humans and animals have immune systems which produce specialized cells called "antibodies" to attack viruses, bacteria, and other foreign invaders (also referred to as "antigens"). Plaintiff's Opening Brief in Support of Summary Judgment [Dkt. No. 81] ("UCB's MSJ Br.") at 3; Defendant Yeda's Opening Claim Construction Brief [Dkt. No. 88] ("Yeda's CC Br.") at 9. An antibody contains a "constant region" and a "variable region," also referred to as a "variable domain." Yeda's CC Br. at 9. An antibody genus consists of all antibodies with the same constant region. Id. Species within that genus have identical constant regions, but different variable regions. Id. The antibody genus relevant to the present civil action is the immunoglobulin G ("IgG") antibody, as shown below:




Yeda's CC Br. Ex. 4 at 4. All antibodies in a given species have identical constant and variable regions. In addition, each antibody species is produced by a specialized immune cell called a "B-cell." Declaration of Dr. Scott A. Siegel [Dkt. No. 166] Ex. 1 ("Siegel Opening Report") ¶ 16. Each B-cell is only capable of making a single antibody species. Id.

An antibody attacks an antigen by binding its variable region to the antigen. Yeda's CC Br. at 3. Multiple species of antibodies can bind to the same antigen, but each antibody will bind to the antigen in a different way. Id. at 8. For example, different species of antibodies may bind to different parts of the same antigen, to the same part of the antigen but in a different orientation, or bind more or less strongly to the antigen. Id. Binding location, binding orientation, and binding strength all contribute to how successfully an antibody can neutralize an antigen. Id. The variable region not only determines which antigen the antibody attacks, but also how effectively the antibody attacks that antigen. Id.

To develop antibodies useful for treating human illnesses, scientists had to be able to produce large quantities of the particular antibody they sought to study. In 1975, two scientists developed a method which allowed researchers to study populations of homogenous antibodies.

By fusing the B-cell for a particular antibody with benign tumor cells, researchers could create a single, hybrid cell, referred to as a "hybridoma,"[2] which would continuously produce clones of the antibody produced by the B-cell. Id.; Yeda's CC Br. Ex. 5 at 3-4; Yeda's CC Br. Ex. 6 at 3. The resulting homogenous antibody population is referred to as "monoclonal." Yeda's CC Br. Ex. 4 at 9. The B-cell provides the "blueprint" for the antibody to be created, while the tumor cell provides the ability for the hybridoma cells "to grow rapidly and continuously in the research laboratory, in a process development lab, or therapeutic manufacturing facility." Id. By December of 1984, the method of making monoclonal antibodies using hybridomas was well known. Yeda's CC Br. Ex. 5 at 4.

Initially, the cells used to make the hybridoma which created monoclonal antibodies came from mice.[3] Using antibodies derived from non-human animals to treat humans presents complicated problems because these foreign substances often cause the human immune system to reject the substance, harming the patient and reducing the efficacy of the treatment. Declaration of Dr. James S. Huston [Dkt. No. 167] Ex. 1 ("Huston Opening Report") ¶ 51. To avoid rejection, it is desirable for the antibody to resemble a human antibody as closely as possible. Id.

During the 1980s, researchers began to use genetic engineering to create antibodies less likely to induce immune responses. Instead of being produced by a hybridoma, genetic engineering involved isolating the gene responsible for producing the antibody, altering the gene,

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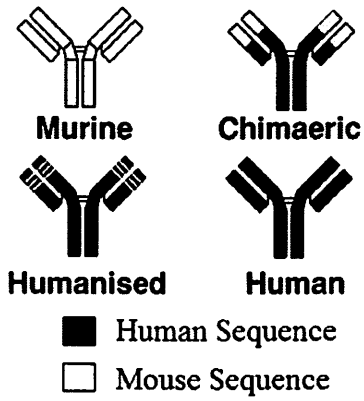
[2] "Hybridoma" comes from "hybrid," meaning "an animal or plant produced from parents different in kind, such as parents belonging to two different strains, varieties, or species," and "-oma," meaning "tumor or neoplasm." See Dorland's Illustrated Medical Dictionary 620, 920 (W.B. Saunders Co., 26th ed. 1981).

[3] For example, the '923 Patent is titled "Murine Monoclonal Antibody Binding TNFα." "Murine" means "pertaining to or affecting mice or rats." Dorland's Illustrated Medical Dictionary, supra n.2, at 843.

and introducing that gene into a host cell capable of producing large amounts of the antibody. Id. ¶ 26. "Chimeric"[4] monoclonal antibodies had a variable region from a mouse and a constant region from a human. Yeda's CC Br. Ex. 4 at 9. Because a chimeric antibody has a large human region, it is less likely to cause an immune response. See Huston Opening Report ¶ 51. Later, scientists developed "humanized" monoclonal antibodies, which are primarily human with only small portions of nonhuman material. Id. Because humanized monoclonal antibodies are closer to pure human antibodies than chimeric antibodies, there is an even further decreased chance that the human immune system will reject the antibody. Id. The image below shows the relative differences between mouse (murine), chimeric, humanized, and human antibodies:




Yeda's Supplemental Brief [Dkt. No. 217] ("Yeda's Supp. Br.") at 29.

**B. Tumor Necrosis Factor**

In 1975, scientists discovered that some animals, including humans, produced a substance that killed tumor cells. Yeda's CC Br. Ex. 3 at 6. That substance is now called "tumor necrosis factor" ("TNF"). Id. TNF became the target of intense research during the early 1980s as a possible cancer treatment due to its ability to destroy tumor cells. Id. at 6, 9; Declaration of Dr.

[4] "Chimeric" is derived from "chimera," which is an organism or cell "in which tissues or cells of another organism have been introduced." Dorland's Illustrated Medical Dictionary, supra n.2, at 254.

Wayne A. Marasco [Dkt. No. 165] Ex. 1 ("Marasco Report") ¶ 65. To study TNF, researchers needed a method to purify it and to obtain enough of it to use in experiments. Yeda's CC Br. Ex. 5 at 4. The "most efficient and effective method" of purifying TNF was to use monoclonal antibodies. Id. There was considerable difficulty in purifying human TNF, however, because it only naturally occurred in the human body in very small amounts. Yeda's CC Br. Ex. 3 at 9.

High levels of TNF were also found to lead to serious medical conditions such as "sepsis, rheumatoid arthritis, and Crohn's disease." Marasco Report ¶ 64. As research continued into the late 1980s, scientists discovered that in addition to being used to purify TNF, "the antibodies themselves could serve as therapeutic agents." Yeda's CC Br. Ex. 5 at 4. Specifically, the antibodies could be used to reduce the levels of TNF in a person's body, thereby reducing the debilitating effects of those disorders. This realization, and subsequent research, eventually led to the development of Cimzia®, a humanized monoclonal antibody that functions by binding (and therefore neutralizing) TNF.[5] UCB's MSJ Br. at 1.

### C. The Claimed Invention

The application which would become the '923 Patent was filed on December 12, 1985, claiming priority to an Israeli patent application filed on December 20, 1984. The '923 Patent did not issue until July 18, 2000. The nearly fifteen-year pendency of that application led Yeda's own attorney to describe the '923 Patent as a "'submarine' patent"[6] and used the "exceedingly

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[5] Cimzia® had sales of $818 million in 2013. Declaration of Ashley J. Stevens [Dkt. No. 164] Ex. 1 ("Stevens Report") ¶ 35. The three products which compete with Cimzia® are Remicade®, Humira®, and Simponi®. Id. ¶¶ 36, 37, 39, 42. Yeda does not sell any of those products. See id. ¶¶ 37, 39, 42. Remicade®, Humira®, and Simponi® had combined sales of over $18 billion in 2013. Id. ¶¶ 38, 41, 43.

[6] Until 1994, a patent application was not publicly available until it issued as a patent. A "submarine" patent is a patent that remains "submerged" from the public view during a long examination process and then "surfaces" after the patent issues, to the surprise of the relevant industry. Reiffen v. Microsoft Corp., 104 F. Supp. 2d 48, 49 n.3 (D.D.C. 2000). The length of the

long pendency" to seek expedited patent issuance. Yeda's CC Br. Ex. 2 (the "Prosecution History") at YEDA_00000573.[7]

The claims of the '923 Patent are directed to a monoclonal antibody which binds to a cytotoxin[8] that Yeda now claims to be TNF. See Claim 1. Rather than outright claim a monoclonal antibody which binds TNF, however, claim 1 of the patent describes the attributes of the toxin to which the monoclonal antibody binds as:

> A monoclonal antibody which specifically binds a human cytotoxin having a molecular weight of about 17,500 as determined by polyacrylamide gel electrophoresis, said cytotoxin being obtainable from stimulated human monocytes, said cytotoxin being further characterized by exhibiting a cytotoxic effect on cycloheximide-sensitized SV-80 cells and by being obtainable in a state of enhanced purity by adsorption of the cytotoxin from an impure preparation onto controlled pore glass beads, and subsequent desorption of the cytotoxin in a state of enhanced purity.

Independent claims 5[9] and 9[10] recite similar limitations. Yeda argues that the cytotoxin described by claims 1, 5, and 9 (and referred to in the written description of the '923 Patent as "CT") is TNF.[11]

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examination period allows the applicant to adopt a "wait and see" approach to a developing field of technology. The applicant can use that time to craft claims to ensnare the most valuable innovations in a particular field, thereby maximizing potential damages in ensuing infringement litigation. Mohsenzadeh v. Lee, 5 F. Supp. 3d 791, 795 n.2 (E.D. Va. 2014).

Under the 1994 Uruguay Round Agreements Act, Pub. L. No. 103-465, 108 Stat. 4809 (Dec. 8, 1994) the secrecy of the patent application process ceased. With rare exceptions, applications are now public; however, because that change did not affect pending applications, the application which became the '923 Patent was not known to the public until it issued on July 18, 2000.

[7] The Prosecution History is Bates-stamped with "YEDA_00000XXX" numeration. For ease of reference, future citations will use only the three terminal digits of the relevant page (for example, "573" rather than "YEDA_00000573").

[8] A cytotoxin is a type of cell "that has a specific toxic action upon cells of special organs." Dorland's Illustrated Medical Dictionary, supra n.2, at 344.

[9] Claim 5 is directed to "[a] monoclonal antibody which specifically recognizes and binds a human cytotoxin having a molecular weight of 17,000±500 D as determined by polyacrylamide gel electrophoresis, said human cytotoxin being obtainable from stimulated human monocytes, said cytotoxin being further characterized by exhibiting a cytotoxic effect on cycloheximide-sensitized SV-80 cells."

Although claim 1 is directed to a monoclonal antibody, much of the patent's written description addresses a process to purify the cytotoxin to which the monoclonal antibody binds. For example, the "Background of the Invention" is directed to describing "[p]roteins which exert a toxic effect on cells," and the history of "cytotoxic proteins." '923 Patent Col. 1 lines 24-56. The "Summary of the Invention" describes a "purified cytotoxic protein referred to as cytotoxin (CT)," "a procedure for effectively inducing this protein," and "a process for preparing . . . purified, essentially homogeneous CT." Id. col. 1 lines 59-65. The summary also describes CT in more detail, and provides a method to deliver CT in "a pharmaceutically acceptable carrier" to treat "virus infected cells and tumor target cells." Id. Col. 2 lines 10-17. Monoclonal antibodies are discussed as a method for isolating and purifying CT. Of significance to this litigation, the monoclonal antibodies are described as being produced by hybridoma, see id. at col. 1 line 66 – col. 2 line 52, and consistent with the title of the patent, "Murine Monoclonal Antibody Binding TNFα," the hybridomas are described as being "derived from . . . mice." Id. col. 2 lines 63-65.

The preferred embodiment of the invention is also focused on purification of CT. The major steps of the preferred embodiment are "Induction of CT," "Quantitation of CT," and "Chromatographic Enrichment of CT." Id. col. 3 line 52 – col. 4 line 49. Monoclonal antibodies are only referenced for their ability to screen for and purify CT, and those antibodies again are

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[10] Claim 9 is directed to "[a] monoclonal antibody which specifically recognizes and binds a human cytotoxin having a molecular weight of 17,000±500 D as determined by polyacrylamide gel electrophoresis, said human cytotoxin being obtainable from stimulated human monocytes, said cytotoxin being further characterized by being obtainable in a state of enhanced purity by adsorption of the cytotoxin from an impure preparation onto controlled pore glass beads, and subsequent desorption of the cytotoxin in a state of enhanced purity."

[11] According to Yeda, research into TNF was sufficiently nascent when the '923 Patent was filed that scientists could only describe the material that they were attempting to purify, and could not specifically identify it.

consistently described as being produced by a mouse-derived hybridoma. Id. col. 5 lines 22-30, 63-64; Id. col. 6 lines 13-22.

## II. DISCUSSION

Regarding claim construction, UCB argues that the term "monoclonal antibody" in claims 1, 5, and 9 only includes antibodies made via mouse-derived hybridoma because the technology at the relevant period had not reached the point where the term "monoclonal antibody" included chimeric or humanized antibodies. UCB's Opening Claim Construction Brief [Dkt. No. 86] ("UCB's CC Br.") at 6-9. Yeda responds that the ordinary meaning of "monoclonal antibody" does not encompass the method through which the antibody was made. Yeda's Responsive Claim Construction Brief [Dkt. No. 161] ("Yeda's CC Opp'n") at 3-13.

Regarding infringement, UCB argues that under its claim construction Cimzia® does not literally infringe the '923 Patent because Cimzia® is a humanized antibody. UCB's MSJ Br. at 20. UCB further argues that Yeda is estopped from arguing that Cimzia® infringes under the doctrine of equivalents because Yeda cancelled claims to chimeric and humanized antibodies during prosecution of the '923 Patent. Id. at 9-14; UCB's Responsive Supplemental Brief [Dkt. No. 218] ("UCB's Supp. Br.") at 8-17. Yeda responds that Cimzia® does literally infringe, given the broad scope of the ordinary meaning of the term "monoclonal antibody," Yeda's Memorandum of Law in Opposition to UCB's Motion for Summary Judgment [Dkt. No. 162] ("Yeda's MSJ Opp'n") at 20-27, and even if Cimzia® does not literally infringe, Yeda is not estopped from asserting a doctrine of equivalents argument that a humanized antibody like Cimzia® is equivalent to an antibody made via hybridoma.

### A. Standard of Review

Summary judgment is appropriate where the record demonstrates "that there is no genuine issue as to any material fact and that the moving party is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(c). A genuine issue of material fact exists "if the evidence is such that a reasonable jury could return a verdict for the nonmoving party." Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 247-48 (1986).

The Court must view the record in the light most favorable to the nonmoving party, see Bryant v. Bell Atl. Md., Inc., 288 F.3d 124, 132 (4th Cir. 2002); however, the "mere existence of a scintilla of evidence in support of the [nonmovant's] position will be insufficient; there must be evidence on which the jury could reasonably find for the [nonmovant]." Anderson, 477 U.S. at 252; see also Othentec Ltd. v. Phelan, 526 F.3d 135, 140 (4th Cir. 2008); TecSec, Inc. v. Int'l Bus. Machines Corp., 763 F. Supp. 2d 800, 804-05 (E.D. Va. 2011) aff'd, 466 F. App'x 882 (Fed. Cir. 2012). When relying on expert testimony, "[a] party does not manufacture more than a merely colorable dispute by submitting an expert declaration that something is black when the moving party's expert says it is white; there must be some foundation or basis for the opinion." Invitrogen Corp. v. Clontech Labs., 429 F.3d 1052, 1080 (Fed. Cir. 2005).

### B. Claim Construction

"The first step of the infringement analysis is claim construction," Nazomi Comm'ns, Inc. v. Nokia Corp., 739 F.3d 1339, 1343 (Fed. Cir. 2014), an issue of law for determination by the Court. Markman v. Westview Instruments, Inc., 517 U.S. 370, 387 (1996). In claim construction, the words of the claim are "given their ordinary and customary meaning as understood by a person of ordinary skill in the art when read in the context of the specification and prosecution history." Thorner v. Sony Computer Entm't, 669 F.3d 1362, 1365 (Fed. Cir.

2012). The "primary focus in determining the ordinary and customary meaning of a claim limitation is to consider the intrinsic evidence of record, viz., the patent itself, including the claims, the specification and, if in evidence, the prosecution history, from the perspective of one of ordinary skill in the art." Atofina v. Great Lakes Chem. Corp., 441 F.3d 991, 996 (Fed. Cir. 2006) (citing Phillips v. AWH Corp., 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (en banc)).

Because the meaning of words may change over time, it is important that claim construction be tied to the appropriate timeframe. "[T]he ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." Phillips, 415 F.3d at 1312-13. That means that when "a claim term understood to have a narrow meaning when the application is filed later acquires a broader definition, the literal scope of the term is limited to what it was understood to mean at the time of filing." Mass. Inst. of Tech. and Elecs. For Imaging, Inc. v. Abacus Software, 462 F.3d 1344, 1353 n.3 (Fed. Cir. 2006) (quoting Kopykake Enters., Inc. v. Lucks Co., 264 F.3d 1377 (Fed. Cir. 2001)).

In construing a claim term, the Court begins with the language of the claims themselves. Philips, 415 F.3d at 1314. "[T]he context in which a term is used in the asserted claim can be highly instructive," and "claim terms are normally used consistently throughout the patent." Id. Specifically, under the doctrine of claim differentiation there is a presumption "that an independent claim should not be construed as requiring a limitation added by a dependent claim " Curtiss-Wright Flow Control Corp. v. Velan, Inc., 438 F.3d 1374, 1380 (Fed. Cir. 2006); however, claim differentiation is merely a presumption, "not a rigid rule and it cannot overcome a construction required by the prosecution history." TecSec, Inc. v. Intern. Bus. Mach. Corp., 731 F.3d 1336, 1345 (Fed. Cir. 2013) (citing Regents of Univ. of Cal. v. Dakocytomation Cal.,

Inc., 517 F.3d 1364, 1375 (Fed. Cir. 2008)). In particular, claim differentiation "cannot enlarge the meaning of a claim beyond that which is supported by the patent documents, or relieve any claim of limitations imposed by the prosecution history." Fenner Investments, Ltd. v. Cellco P'ship, 778 F.3d 1320, 1327 (Fed. Cir. 2015). Claim differentiation also may not "serve to broaden claims beyond their meaning in light of the specification." Id. (quoting Toro Co. v. White Consol. Indus., Inc., 199 F.3d 1295, 1302 (Fed. Cir. 1999)).

In addition to the language of the claim, the specification must also be considered. Indeed, "claims must be read in view of the specification, of which they are a part." Phillips, 415 F.3d at 1315 (internal quotations marks and citation omitted). "[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.'" Phillips, 415 F.3d at 1315 (quoting Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996)). Although claims are generally not limited to the preferred embodiment disclosed in the specification, id. at 1323, "[t]he written description and other parts of the specification . . . may shed contextual light on the plain and ordinary meaning [of a claim term.]" Aventis Pharms. Inc. v. Amino Chems. Ltd., 715 F.3d 1363, 1373 (Fed. Cir. 2013).

The history of prosecution before the United States Patent and Trademark Office ("USPTO") must also be considered. "Any explanation, elaboration, or qualification presented by the inventor during patent examination is relevant, for the role of claim construction is to capture the scope of the actual invention that is disclosed, described, and patented." Fenner Investments, 778 F.3d at 1323 (internal quotation marks omitted). The relevant determination is how "persons in the field of the invention" would have understood the prosecution history. Id. Accordingly, the inventor's subjective intent to claim certain subject matter "is of little or no

probative weight in determining the scope of a claim." Howmedica Osteonics Corp. v. Wright Medical Tech., Inc., 540 F.3d 1337, 1346 (Fed. Cir. 2008).

Evidence extrinsic to the patent, including "expert and inventor testimony, dictionaries, and learned treatises" may also be considered, Phillips, 415 F.3d at 1317; however, the Federal Circuit has expressed a preference for intrinsic evidence over extrinsic evidence. "Intrinsic evidence . . . is a more reliable guide to the meaning of a claim term than are extrinsic sources like technical dictionaries, treatises, and expert testimony." Chamberlain Grp., Inc. v. Lear Corp., 516 F.3d 1331, 1335 (Fed. Cir. 2008). "Although definitions based on dictionaries, treatises, industry practice, and the like are often important aids in interpreting claims, they may not be 'used to contradict claim meaning that is unambiguous in light of the intrinsic evidence.'" ArcelorMittal France v. AK Steel Corp., 700 F.3d 1314, 1320 (Fed. Cir. 2012) (quoting Phillips, 415 F.3d at 1312-17).

One of "only two exceptions" to the general rule that the meaning of the words in a claim should be based on what one of ordinary skill in the art when the patent application was effectively filed would have understood the term to mean, is "when a patentee sets out a definition and acts as his own lexicographer." Thorner, 669 F.3d at 1365. "To act as its own lexicographer, a patentee must 'clearly set forth a definition of the disputed claim term' other than its plain and ordinary meaning." Id. (quoting CCS Fitness, Inc. v. Brunswick Corp., 288 F.3d 1359, 1366 (Fed. Cir. 2002)).

The second exception to the general rule is "when a patentee disavows the full scope of a claim term either in the specification or during prosecution." Thorner, 669 F.3d at 1365. Accordingly, "when a patentee unequivocally and unambiguously disavows a certain meaning to obtain a patent, the doctrine of prosecution history disclaimer narrows the meaning of the claim

consistent with the claim scope surrendered." Biogen Idec, Inc. v. GlaxoSmithKline LLC, 713 F.3d 1090, 1095 (Fed. Cir. 2013).

1. "Monoclonal antibody"

The parties dispute the meaning of several claim terms; however, because the construction of "monoclonal antibody" leads to resolution of the present action, only that term will be construed.[12] Yeda argues that "monoclonal antibody" should be construed to mean "a homogenous (essentially identical) population of a single species of an immunoglobulin protein capable of specifically binding to an antigen," while UCB urges that the term should be construed to mean "an antibody that binds to a single antigen and that is produced by a hybridoma and not a genetically-engineered cell." Yeda's CC Br. at 14. UCB argues that its definition is correct because as of December 20, 1984 (the effective filing date of the '923 Patent), a person of ordinary skill in the art would have understood the term "monoclonal antibody" to mean a monoclonal antibody made via hybridoma and not as including chimeric or humanized monoclonal antibodies. Yeda responds that the plain language of the claims is not so narrow.

a. Claim Language

Claims 1, 5, and 9 do not provide any detail regarding the meaning of "monoclonal antibody," instead defining the claimed antibody through the specific, single human cytotoxin to which the antibody binds. Therefore, the asserted claims themselves are not helpful in

[12] The parties also offer competing definitions of "specifically binds," "specifically recognizes and binds," "in a state of enhanced purity," and "a human cytotoxin having a molecular weight of about 17,500 as determined by polyacrylamide gel electrophoresis, said cytotoxin being obtainable from stimulated human monocytes, said cytotoxin being further characterized by exhibiting a cytotoxic effect on cycloheximide-sensitized SV-80 cells and by being obtainable in a state of enhanced purity by adsorption of the cytotoxin from an impure preparation onto controlled pore glass beads, and subsequent desorption of the cytotoxin in a state of enhanced purity."

determining what "monoclonal antibody" would have meant to a person of ordinary skill in the art in 1984.[13]

Unasserted claims may also be relevant to claim interpretation. Curtiss-Wright, 438 F.3d at 1380. Each of claims 1, 5, and 9 have associated dependent claims (claims 3, 7, and 11) which add, among other things, that the monoclonal antibody of the independent claim "is produced by a hybridoma formed by a fusion of myeloma cells with spleen cells from a mammal previously immunized with a pure or impure preparation of said cytotoxin." Yeda argues that because dependent claims must be narrower than the independent claims on which they depend, the presence of "produced by a hybridoma" in dependent claims 3, 7, and 11 means that independent claims 1, 5, and 9 are not so limited. Yeda's CC Br. at 15. Because claims 3, 7, and 11 were filed more than 14 years after the effective filing date of the '973 Patent, that argument has less force. Moreover, the remainder of the intrinsic evidence defeats Yeda's argument by showing that when the '923 Patent was filed, the term "monoclonal antibodies" was not understood to include chimeric or humanized antibodies.

b. Specification

The specification, which went unchanged through the course of prosecution, provides better evidence of how a person of ordinary skill in the art would have understood the term "monoclonal antibody" in 1984. The way that the written description and other parts of the specification use the term "monoclonal antibody" may be considered in determining the plain

[13] Although construction begins with the language of the claims, that language is not very helpful in the present case because of the number of years between when the patent application was filed and when the relevant claims were added. In an ordinary patent action, the claims which issued with the patent are filed at or around the time of application. That is not the case here. Claim 41, which became claim 1, was added on June 30, 1998, nearly 14 years after the effective filing date of the application. Prosecution History at 488. The claims which became claims 2 through 9 were added on October 28, 1999. Id. at 537-39. The claims which became claims 10 through 12 were added on January 10, 2000. Id. at 556-57.

and ordinary meaning of the term, Aventis Pharms. Inc., 715 F.3d at 1373, and that use supports the conclusion that "monoclonal antibody" only included antibodies produced via hybridoma. For example, the "Field of the Invention" states that the written description provides a method "for screening of hybridoma cultures in order to locate cultures producing antibodies capable of binding CT." '923 Patent col. 1 lines 13-15. The written description also states that lines of "anti-CT antibodies" are established "by screening a plurality of hybridomas." Id. col. 2 lines 3-5. The written description specifies that "[s]uch monoclonal antibody is produced by such hybridoma cell lines and is used for isolating CT in substantially homogeneous purified form." Id. col. 2 lines 7-9 (emphasis added). Each time the written description describes production of anti-CT antibodies, it describes those antibodies as being produced through hybridoma.[14] Indeed, Yeda described "screening a large number of hybridoma cultures for detecting a few producing antibodies against CT" as "[t]he critical step" in the invention. Id. col. 3 lines 5-7. Additionally, as evidence of the claimed capability to produce anti-CT antibodies, Yeda made available for the USPTO's inspection "[h]ybridoma cells producing the antibodies." Id. col 2 lines 48-52.

There is no description of chimeric or humanized monoclonal antibodies anywhere in the '923 Patent. The drawings and written description do not contain the terms "chimera," "chimeric," "humanized," or any derivatives of those words. There is also no description of an antibody with a human constant region and a mouse variable region (a chimeric monoclonal antibody), or an antibody with a chimeric variable region (a humanized monoclonal antibody). Indeed, the words "constant," "variable," "domain," and "region" are also completely absent from the patent. The '923 Patent does not even address the possibility that monoclonal antibodies would be made through genetic engineering in general, and the words "genetic" and

[14] Id. col. 2 lines 48-51, 64-76; col. 3 lines 5-10; col 5 lines 23-26, 60-67.

"engineering" do not appear. By contrast, the word "hybridoma" appears in the specification sixteen times.[15] Accordingly, the specification supplies strong evidence that, in 1984, the term "monoclonal antibody" only included antibodies made using hybridoma.

In response, Yeda does not argue that the specification of the '923 Patent describes monoclonal antibodies produced by genetic engineering. See Yeda's CC Opp'n at 4-5. Instead, Yeda cites the patent law truism that "the fact that the specification describes only a single embodiment, standing alone, is insufficient to limit otherwise broad claim language." Id. at 4 (quoting Howmedica, 540 F.3d at 1345). Because the claims appear to sweep broadly enough to include more than just monoclonal antibodies made via hybridoma, Yeda asserts that the scope of "monoclonal antibody" should not be limited to the only described embodiment.

Yeda's argument misses the mark. UCB's argument is that there were no other methods for making monoclonal antibodies in December of 1984 at all. If the embodiment disclosed in the specification is the only embodiment which could have been understood to fall within the claim terms at the time of filing, then interpreting the claims to be coextensive with that single embodiment is simply giving the claims their correct meaning. In other words, Yeda's argument that the claims cannot be limited only to disclosed embodiments fails when no other embodiments existed at the time of filing.

Accordingly, the use of the term "monoclonal antibody" in the written description and other parts of the specification of the '923 Patent supports the conclusion that the term is limited to an antibody made through hybridoma and did not extend to chimeric or humanized monoclonal antibodies.

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[15] '923 Patent Abstract line 5; Figs. 1 and 3; col. 1 line 14; col 2 lines 5, 8, 48, 63, and 65; col. 3 lines 6 and 10; col. 5 lines 25, 26, 33, 63, and 67.

c. Prosecution History

The prosecution history of the '923 Patent, as part of the intrinsic evidence, must also be considered in determining the meaning of claim terms. The evidence in the prosecution history supports the conclusion that "monoclonal antibody" in 1984 only meant an antibody made through hybridoma.

As they were filed closest to the effective filing date of the '923 Patent, the original claims provide additional evidence regarding the meaning of "monoclonal antibody" during the relevant period. Those original claims only describe production of monoclonal antibodies through hybridoma. For example, original claim 11 was directed to a method "by which multiple hybridoma cultures can be screened for the production of antibodies." Prosecution History at 13. Similarly, original claim 16 was directed to "a process for preparing monoclonal antibodies" including "detecting hybridomas which produce such antibodies." Id. The originally-filed drawings, consistent with the final drawings, also only describe production of monoclonal antibodies through hybridoma. Id. at 161, 163.

On July 21, 1988, Yeda added claim 31 which described a monoclonal antibody secreted by a hybridoma "or a hybridoma derived therefrom."[16] Id. at 184. The examiner rejected that claim for lack of written description[17] and lack of enablement.[18] Id. at 362-63. The enablement

[16] Claim 31 was directed to "[A monoclonal antibody which specifically recognizes and binds the 17KD species of tumor necrosis factor], wherein said antibody is secreted by hybridoma CNCM I-472 or a hybridoma derived therefrom." Id. at 184.

[17] To be eligible for a patent, the inventor must provide "a written description of the invention, and of the manner and process of making and using it." 35 U.S.C. 112 ¶ 1 (1982). "A specification adequately describes an invention when it 'reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." Boston Scientific Corp. v. Johnson & Johnson, 647 F.3d 1353, 1362 (Fed. Cir. 2011) (quoting Ariad Pharm., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc)). "[T]he hallmark of written description is disclosure." Ariad Pharm., 598 F.3d at 1351.

rejection was maintained through numerous responses. On November 26, 1996, Yeda attempted to overcome the rejection by arguing that new hybridomas could be "derived from . . . spontaneous mutation, deliberate mutation and selection, and genetic engineering." Id. at 424. That response, made almost twelve years after the effective filing date of the application, is the first time that the words "genetic engineering" appear in the prosecution history. Yeda argues that because it argued before the USPTO on November 26, 1996 that the claims included genetic engineering, genetic engineering was a part of the claim scope at least as early as the July 21, 1988 amendment.

That argument fails. Yeda's argument to the examiner in 1996, which was rejected by the examiner and was made regarding language that was eventually removed,[19] cannot inform the meaning of the claim term when that term was introduced in 1988. After Yeda asserted to the examiner that genetic engineering was within the scope of claim 31, the examiner rejected the claim and did not withdraw the rejection until Yeda removed the "or hybridoma derived therefrom" language from claim 31. Id. at 475.

Yeda also argues that the prosecution history supports a construction including chimeric and humanized antibodies because at various times beginning on March 10, 1999, Yeda attempted to define "monoclonal antibody" as including chimeric and humanized antibodies. Specifically, Yeda refers to its March 20, 1999 response to an office action in which Yeda

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[18] To be eligible for a patent, the inventor must also "enable any person skilled in the art to which [the invention] pertains, or with which it is most nearly connected, to make and use" the claimed invention. 35 U.S.C. § 112 ¶ 1 (1982). The Federal Circuit has interpreted this requirement to mean that "[t]he specification must 'enable one of ordinary skill in the art to practice the claimed invention without undue experimentation.'" Transocean Offshore Deepwater Drilling, Inc. v. Maersk Contractors USA, Inc., 617 F.3d 1296, 1305 (Fed. Cir. 2010) (quoting Nat'l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc., 166 F.3d 1190, 1196 (Fed. Cir. 1999)).

[19] Id. at 431,437, 444, 465, 474-75.

quoted a 1992 "Dictionary of Biochemistry" for a broader definition of "monoclonal antibody." Yeda's CC Br. at 16-17; Prosecution History at 509, 511.

Although providing a broad definition of monoclonal antibody in 1999 might be evidence of a subjective intent to claim chimeric and humanized antibodies, the subjective intent to claim certain subject matter "is of little or no probative weight in determining the scope of a claim." Howmedica, 540 F.3d at 1346. The focus in claim construction is on "the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." Phillips, 415 F.3d at 1312-13. The expanded scope of protection that Yeda sought in 1999 or even a definition given in a technical dictionary in 1992 is of little weight when determining the meaning of that claim term in 1984.

On June 2, 1999, Yeda also submitted the Declaration of Hartmut Engelmann, an assistant professor at the Munich University Institute of Immunology. Prosecution History at 527-31. Dr. Engelmann claimed that the first description of the generation of mouse-human antibody chimeras was published in an article by S.L. Morrison et al. in November of 1984 ("Morrison Article"), and therefore that a person of ordinary skill in the art could make mouse-human chimeras in December 1984 without undue experimentation. Id. at 529-30. Dr. Engelmann did not make any conclusions regarding what the term "monoclonal antibody" meant or whether the term "monoclonal antibody" would have been understood in 1984 to include chimeric antibodies. See id.

Examination of the prosecution history reveals that for the first ten years of prosecution, neither Yeda nor the examiner understood the term "monoclonal antibodies" to include chimeric or humanized antibodies. Like the evidence in the specification, the prosecution history weighs towards a construction of "monoclonal antibodies" which does not include chimeric or

humanized antibodies. As the specification was created at the time of filing, and the prosecution history developed beginning at that time, those pieces of intrinsic evidence are given great weight.

d. Extrinsic Evidence

To the extent that it does not conflict with the intrinsic evidence, extrinsic evidence may also be relevant to claim construction. Phillips, 415 F.3d at 1318. The Federal Circuit has cautioned, however, that expert reports are "generated at the time of and for the purpose of litigation and thus can suffer from bias that is not present in intrinsic evidence." Id. That bias can be particularly problematic "if the expert's opinion is offered in a form that is not subject to cross-examination." Id. Expert reports regarding the meaning of a claim term must therefore be viewed with skepticism, as "undue reliance on extrinsic evidence poses the risk that it will be used to change the meaning of claims in derogation of the indisputable public records consisting of the claims, the specification and the prosecution history, thereby undermining the public notice function of patents." Id. Accordingly, "extrinsic evidence may be useful to the court, but it is unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence." Id. at 1319.

Yeda produces several pieces of extrinsic evidence which it claims establish that a person of ordinary skill in the art in 1984 would have understood "monoclonal antibody" to include chimeric and humanized antibodies. For the reasons that follow, the extrinsic evidence does not establish that the term "monoclonal antibody" included chimeric or humanized antibodies in 1984.

Yeda first argues that because UCB scientists referred to Cimzia® as a "monoclonal antibody," the term "monoclonal antibody" should be construed to include chimeric and

humanized antibodies. Yeda's CC Br. at 17. The statements at issue do not help Yeda because they were published in 2006 and 2010, more than twenty years after the relevant period. The statements of UCB's scientists only provide evidence of what the term "monoclonal antibody" meant in the mid-to-late 2000s, but have no relevance to what the term meant in 1984.

Yeda also cites to United States Patent No. 4,816,567 (the "'567 Patent"), which is assigned to Genentech, Inc. The application for that patent was filed in 1983, and the patent issued in 1989. Yeda argues that the '567 Patent is evidence that the term "monoclonal antibody" included chimeric antibodies. Specifically, Yeda points to the patent's statement that chimeric antibodies "can be readily prepared in pure 'monoclonal' form. They can be manipulated at the genomic level to produce chimeras of variants . . . from species which differ from each other." '567 Patent col. 4 lines 59-63.

This argument fails because each time that the '567 Patent uses the term "monoclonal antibodies," it explicitly uses the term to refer to antibodies made via hybridoma.[20] The '567 Patent actually draws a distinction between monoclonal antibodies and the antibodies being claimed in the '567 Patent by stating that "monoclonal[] antibodies have a variety of useful properties similar to those of the present invention." Id. col. 2 lines 17-19. When the '567 Patent discusses "chimeric antibodies," it refers to antibodies made through genetic engineering, separate from antibodies made via hybridoma. Id. col. 6 lines 48-59; col. 15 lines 58-68.[21] This language establishes that the inventors of the '567 Patent viewed monoclonal antibodies as differing from chimeric antibodies.

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[20] '567 Patent col. 1 lines 60-68; col. 2 lines 3-20, 40-50.

[21] The '567 Patent specifically states that the chimeric antibodies may be "derived from" hybridoma.

Even if Yeda were right about the meaning of "monoclonal antibody" in the '567 Patent, that understanding of "monoclonal antibody" would not help Yeda because when the '567 Patent was pending, patent applications were kept secret until they issued.[22] The '567 Patent could not have had any impact on how those of ordinary skill in the art understood the term "monoclonal antibody" until the patent was published on March 28, 1989. Accordingly, the '567 Patent is of no help to Yeda.[23]

Yeda also provides a number of expert declarations claiming that, in December 1984, the term "monoclonal antibody" included chimeric and humanized antibodies. Huston Opening Report ¶¶ 26, 28, 29, 31-33, 36, 46; Siegel Opening Report ¶¶ 20, 52-53. These declarations have limited value because they are not adequately supported. For example, none of Yeda's experts address the specification of the '923 Patent in the context of claim construction, and none address whether and how the patent's description of only the hybridoma method of production affects their conclusions. See Huston Opening Report ¶¶ 28-37; Siegel Opening Report ¶¶52-53. Instead, Yeda's experts skip straight to extrinsic evidence to reach their claim construction. Even then, across Yeda's expert reports, only two pieces of objective evidence are offered to support the conclusion that in December 1984 the term "monoclonal antibody" was understood by those of ordinary skill in the art to include chimeric and humanized antibodies. The two references are the November 1984 Morrison Article, see Siegel Opening Report ¶¶ 20, 52; Huston Opening

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[22] Reikp Watase, Note, The American Inventors Protection Act of 1999: An Analysis of the New Eighteen-Month Publication Provision, 20 Cardozo Arts & Ent. L.J. 649, 650 (2002).

[23] Yeda also asserts that the '567 Patent establishes that in 1983 the term "monoclonal" included chimeric and humanized antibodies; however, none of Yeda's experts rely on the '567 Patent in reaching their claim construction conclusions and therefore not even Yeda's experts appear to agree with their argument.

Report ¶¶ 26, 32, and a December 8, 1984 Nobel Prize speech by Cesar Milsten, see Huston Opening Report ¶ 33 ("Milsten Speech").

At best, these references establish that scientists knew of chimeric antibodies in November 1984. Establishing that chimeric antibodies existed in 1984, however, is different from establishing that a person of ordinary skill in the art would have understood chimeric antibodies to be monoclonal antibodies in 1984. See Abacus Software, 462 F.3d at 1353 n.3 (citing Kopykake Enters., Inc. v. Lucks Co., 264 F.3d 1377 (Fed. Cir. 2001)). For example, although the title of the Morrison Article uses the phrase "[c]himeric human antibody molecules," it does not use the term "monoclonal" or "monoclonal antibodies." Huston Opening Report ¶ 26 n.5. Moreover, the cited excerpt of the Milsten Speech, although it does appear to describe what is now known to be chimeric antibodies, does not use the terms "chimeric" or "monoclonal." Accordingly, the extrinsic evidence relied upon by Yeda's experts does not support the conclusion that the understanding of "monoclonal antibodies" in 1984 included either chimeric or humanized antibodies.

Moreover, the expert opinions regarding "monoclonal antibody" are artfully worded to create the impression that the experts concluded that humanized antibodies were within the literal meaning of "monoclonal antibodies" in 1984. See Huston Opening Report ¶ 46 ("[I]t is my opinion that in 1984, a person of ordinary skill in the art would have understood the term 'monoclonal antibody' to include antibodies produced by a genetically engineered cell"); Siegel Opening Report ¶ 53 ("[T]he term 'monoclonal antibody' as used in the Wallach patent encompasses genetically engineered antibodies"). Yet, Yeda does not dispute that the first paper to disclose a humanized antibody was published in May of 1986. UCB's MSJ Br. at 6 (Undisputed Material Fact ¶ 19); Yeda's MSJ Opp'n at 9-10 (omitting Undisputed Material Fact

¶ 19 from those disputed by Yeda). One of Yeda's experts even characterizes humanized antibodies as "later-arising." Marasco Report ¶ 177. Accordingly, the expert opinions attempt to reach further than even Yeda is willing to argue, and so appear to contain bias that decreases any weight they should be given.

Yeda's admission that humanized antibodies were not developed until 1986 is independently dispositive of the issue of whether in December 1984 the term "monoclonal antibody" was understood to include humanized antibodies. If humanized antibodies were not recognized until May of 1986, there is clearly no way that a person of ordinary skill in the art would have understood them to be included in the term "monoclonal antibody" in December of 1984.[24] Phillips, 415 F.3d at 1312-13.

Lastly, Federal Circuit precedent confirms the conclusion that in 1984 the understanding of "monoclonal antibody" did not include chimeric and humanized antibodies. In Chiron Corp. v. Genentech, Inc., the Federal Circuit was also confronted with construing the term "monoclonal antibody." 363 F.3d 1247, 1250 (Fed. Cir. 2004). In that case, the Federal Circuit found that "the first publication to disclose humanized antibodies appeared in May 1986," id. at 1251, and that "the term 'monoclonal antibody' in 1984 apparently referred to antibodies made with hybridoma and was not broad enough to encompass chimeric antibodies." Id. at 1257. In that opinion, the

[24] In its supplemental briefing, Yeda argues that the Federal Circuit has stated that "after-arising technology [can] be captured within the literal scope of valid claims that are drafted broadly enough." Yeda's Supp. Br. at 3 n.1 (quoting Innogenetics, N.V. v Abbott Labs., 512 F3d 1363, 1371-72 (Fed. Cir. 2008)). In Phillips, the en banc Federal Circuit ruled that "the ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." 415 F.3d at 1312-13. The intrinsic and, to the extent that it is relevant, extrinsic evidence makes clear that as of the effective filing date of the '923 Patent, the term "monoclonal antibody" did not include chimeric or humanized antibodies. Assuming that the apparent tension between Innogenetics and Phillips can be resolved, the claims of the '923 Patent were not drafted broadly enough to reach chimeric and humanized antibodies.

Federal Circuit also referred to a 1983 treatise which defined "monoclonal antibody" as only including hybridoma, and another 1984 article which differentiated monoclonal antibodies from chimeric antibodies. Id.

Although the parties center their dispute on whether "monoclonal antibody" would have only included the hybridoma method of production, there are other differences between the parties' proposed definitions. Specifically, Yeda's proposed definition includes "a homogenous (essentially identical) population of a single species of an immunoglobulin protein capable of specifically binding to an antigen," while UCB's proposed definition includes "an antibody that binds to a single antigen." Yeda's CC Br. at 14. Yeda observes that the experts in the present action appear to agree that "monoclonal antibody" descriptively refers, and referred in December 1984, to "a homogenous population of a single type of antibody." See Yeda's CC Br. at 14. Accordingly, that aspect of Yeda's proposed construction will be included. The proposed definitions also appear to incorporate the dispute over "specifically binds," which, as explained previously, need not be addressed to resolve this action and so will not be included.

Accordingly, in December 1984 the term "monoclonal antibody" would not have included chimeric or humanized antibodies. Therefore, the term "monoclonal antibody" in claims 1, 5, and 9 is construed to mean "a homogenous population of a single type of antibody produced via hybridoma and not including chimeric or humanized antibodies."[25]

### C. Literal Infringement

"To establish literal infringement, all of the elements of the claim, as correctly construed, must be present in the accused [product]." TechSearch, L.L.C. v. Intel Corp., 286 F.3d 1360,

[25] Because the intrinsic and extrinsic evidence is sufficiently clear, the parties' arguments regarding prosecution history disclaimer and the statements that Yeda's licensee made during arbitration need not, and will not, be addressed.

1371 (Fed. Cir. 2002). Under the Court's construction of "monoclonal antibody" as "a homogenous population of a single type of antibody produced via hybridoma and not including chimeric or humanized antibodies," Cimzia®, which is a humanized antibody, cannot literally infringe claims 1, 5, and 9 of the '923 Patent. See, e.g., Yeda's Supp. Br. at 27; UCB's MSJ Br. at 10. For this reason, UCB's Motion for Summary Judgment will be granted as to its claim that Cimzia® does not literally infringe the '923 Patent.

**D. Doctrine of Equivalents**

Yeda argues that even if Cimzia® does not literally infringe claims 1, 5, and 9 of the '923 Patent, Cimzia® infringes under the doctrine of equivalents because a humanized antibody is equivalent to an antibody made via hybridoma. "Even without literal infringement of a certain claim limitation, a patentee may establish infringement under the doctrine of equivalents if an element of the accused device 'performs substantially the same function in substantially the same way to obtain the same result as the claim limitation.'" EMD Millipore Corp. v. AllPure Techs., Inc., 768 F.3d 1196, 1202 (Fed. Cir. 2014) (quoting AquaTex Indus., Inc. v. Techniche Solutions, 419 F.3d 1374, 1382 (Fed. Cir. 2005)). The purpose of the doctrine of equivalents is to "allow[] the patentee to claim those insubstantial alterations that were not captured in drafting the original patent claim but which could be created through trivial changes." Festo Corp v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd., 535 U.S. 722, 733 (2002) ("Festo I"). "Thus the doctrine of equivalents is invoked to prevent a 'fraud on the patent,' when an accused infringer is 'stealing the benefit of the invention' by making insubstantial changes that avoid the literal scope of the claims." EMI Grp. North America, Inc. v. Intel Corp., 157 F.3d 887, 898 (Fed. Cir. 1998).

UCB responds that Yeda is estopped from asserting that humanized or chimeric antibodies are equivalent to antibodies made via hybridoma by its actions during prosecution of

the '923 Patent. The doctrine of prosecution history estoppel is a "legal limitation" on the range of equivalents available to a patentee, Warner-Jenkinson Co., Inc. v. Hilton Davis Chem. Co., 520 U.S. 17, 30 (1997), which "requires that the claims of a patent be interpreted in light of the proceedings in the PTO during the application process." Festo I, 535 U.S. at 733. Prosecution history estoppel ensures that a patentee does not use the doctrine of equivalents to reach subject matter covered in claims "that have been cancelled or rejected." Id. (quoting Schriber-Schroth Co. v. Cleveland Trust Co., 311 U.S. 211, 220-21 (1940)). "When . . . the patentee originally claimed the subject matter alleged to infringe but then narrowed the claim in response to a rejection, he many not argue that the surrendered territory comprised unforeseen subject matter that should be deemed equivalent to the literal claims of the issued patent." Festo I, 535 U.S. at 733-34. "A rejection indicates that the patent examiner does not believe that the original claim could be patented. While the patentee has the right to appeal, his decision to forgo an appeal and submit an amended claim is taken as a concession that the invention as patented does not reach as far as the original claim." Id. at 734. "Were it otherwise, the inventor might avoid the PTO's gatekeeping role and seek to recapture in an infringement action the very subject matter surrendered as a condition of receiving the patent." Id.

Prosecution history estoppel analysis proceeds in four steps. First, the accused infringer must establish that an amendment filed before the USPTO narrowed the literal scope of a claim. Festo Corp v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd., 344 F.3d 1359, 1366 (Fed. Cir. 2003) (en banc) ("Festo II"). Although prosecution history estoppel arises most often when a claim is narrowed to avoid the prior art, "a narrowing amendment made to satisfy any requirement of the Patent Act may give rise to an estoppel." Festo I, 535 U.S. at 736.

If the accused infringer establishes a narrowing amendment, then the reason for the amendment must be assessed. If the prosecution history does not reveal the reason for the amendment, then the amendment is presumed to be substantially related to patentability and a presumption of prosecution history estoppel arises. Festo II, 344 F.3d at 1366-67. The patentee may then attempt to rebut the presumption that the amendment was related to patentability. Id. at 1367.

At the third step, the scope of the surrendered subject matter must be determined. The presumption is that the patentee surrendered all subject matter between the original claim and the narrowed claim. Id. The scope of surrender is evaluated through reference to the intrinsic evidence in the patent. See Abbott Labs. v. Novopharm Ltd., 323 F.3d 1324, 1331 (Fed. Cir. 2003).

Finally, "the patentee may rebut the presumption of total surrender by demonstrating that it did not surrender the particular equivalent in question." Festo II, 344 F.3d at 1368. The patentee may rebut the presumption of total surrender by showing that "an alleged equivalent would have been 'unforeseeable at the time of the amendment and thus beyond a fair interpretation of what was surrendered," id. at 1369 (quoting Festo I, 535 U.S. at 738), that "the rationale underlying the narrowing amendment [bore] no more than a tangential relation to the equivalent in question," id. (quoting Festo I, 535 U.S. at 740), or that there was "some other reason suggesting that the patentee could not reasonably be expected to have described the insubstantial substitute in question." Id. at 1370 (quoting Festo I, 535 U.S. at 741). If the patentee fails to rebut the presumption of total surrender, prosecution history estoppel bars the patentee from relying on the doctrine of equivalents. Id. at 1367.

The application and scope of prosecution history estoppel is an issue of law. Biagro Western Sales, Inc. v. Grow More, Inc., 423 F.3d 1296, 1301-02 (Fed. Cir. 2005). Although rebuttal of the surrender presumption may rely on factual determinations, those factual issues may be decided by the Court. Id. at 1302.

1. Narrowing Amendment

The prosecution history of the '923 Patent establishes that Yeda attempted to claim chimeric and humanized antibodies, that the attempt was rebuffed by the USPTO, and that Yeda then cancelled any claim to that subject matter rather than appealing the examiner's rejection.[26] The '923 Patent issued almost immediately following Yeda's last cancellation of a claim to chimeric and humanized antibodies.

Specifically, the prosecution history shows that Yeda added claim 41, the claim which would become claim 1 of the '923 Patent, on June 30, 1998.[27] Prosecution History at 488. After claim 41 was rejected for lack of written description and lack of enablement, id. at 499-500, Yeda added a series of claims specifically directed to chimeras of antibodies from several species and to monoclonal antibodies bearing different "hypervariable regions." Id. at 507-09. Yeda specifically indicated that it intended the term "chimeric" to encompass both chimeric and humanized antibodies. Id. at 509 n.1. Yeda emphasized its desire to claim chimeric and

[26] UCB presents arguments regarding both claim 31 and 41. As UCB's arguments regarding claim 41 are sufficient to find Yeda estopped from asserting chimeric and humanized antibodies and equivalents, the parties' arguments regarding claim 31 need not, and will not, be addressed.

[27] At that time, claim 41 was directed to "[a] monoclonal antibody which specifically binds a human cytotoxin having a molecular weight of about 17,000 as determined by polyacrylamide gel electrophoresis, said cytotoxin being obtainable from stimulated monocytes or monocyte-like cultured cells, the binding of said antibody to said human cytotoxin being inhibited by the reference monoclonal antibody (CT-1) produced by the hybridoma cell line deposited with the Institut Pasteur under accession number CNCM I-472." This claim was added six months after the first humanized antibody therapy was approved by the FDA and introduced to the market. Declaration of John P. Padro [Dkt. No. 87] ("Padro Dec.") Ex. 11.

humanized antibodies, and even asked for the examiner's help in crafting claims with that scope. Id. at 511-512. Rather than provide that help, the examiner rejected the claims to chimeric antibodies and antibodies with "hypervariable regions" for lacking written description.[28] Id. at 524. In response to that rejection, Yeda cancelled those claims, id. at 537, and less than three months after that cancellation the patent went to allowance without any similar additions. Id. at 557. Yeda's cancellation of the claim language is "taken as a concession that the invention as patented does not reach as far as the original claim." Festo I at 734. By removing language claiming chimeric and humanized antibodies, Yeda narrowed the scope of its claims.

Yeda argues that its cancellations did not narrow the scope of the claims for several reasons. First, Yeda argues that the cancellation of dependent claims does not narrow the scope of a broader independent claim that was not amended. Yeda's Supp. Br. at 16. As authority, Yeda cites Smith v. Snow, in which the Supreme Court stated that "[i]t is of no moment that in the course of the proceedings in the Patent Office the rejection of narrow claims was followed by the allowance of the broader claim 1." 294 U.S. 1, 16 (1935).

In Smith, "[f]our groups of method claims were successively presented to the Patent Office, and three were successively rejected." Id. at 15. The final group of method claims ultimately matured into the asserted claims of the patent. Id. The accused infringer argued that a

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[28] Specifically, the examiner maintained the rejection of claim 41 "under 35 U.S.C. 112, first paragraph, as containing new matter." Id. at 524. The prohibition against introducing new matter into the disclosure of a patent application does not stem from 35 U.S.C. § 112 ¶ 1; instead, the prohibition is found in 35 U.S.C. § 132 ("No amendment shall introduce new matter into the disclosure of the invention."). The Manual of Patent Examining Procedure ("MPEP") at the relevant time period, however, instructed that "[i]f new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph – written description requirement." MPEP Seventh Edition (July 1998) § 2163.06 (citing In re Rasmussen, 650 F.2d 1212 (C.C.P.A. 1981)). Although his explanation was not precise, the examiner did articulate a written description rejection under the USPTO guidelines at the time.

limitation introduced in one of the previous three groups of method claims should be read into issued claim 1. Id. at 8-9. In that context, the quotation simply means that limitations introduced when attempting to claim one embodiment of the invention do not cause prosecution history estoppel if that embodiment is not encompassed by the claims which ultimately issue. By contrast, the cancelled claims at issue in the present action are directed to Yeda's attempts to claim humanized and chimeric antibodies, the specific subject matter that Yeda is now seeking as equivalent. Accordingly, Smith does not apply.

Moreover, the Supreme Court has held that narrower claims cancelled during prosecution may limit the scope of the independent claims on which they were intended to depend. In Schriber-Schroth Co. v. Cleveland Trust Co., the Supreme Court stated that "[i]t is a rule of patent construction consistently observed that a claim in a patent as allowed must be read and interpreted with reference to claims that have been cancelled or rejected and the claims allowed cannot by construction be read to cover what was thus eliminated from the patent." 311 U.S. 211, 220-21 (1940). Accordingly, "[t]he patentee may not, by resort to the doctrine of equivalents, give to an allowed claim a scope which it might have had without the amendments, the cancellation of which amounts to a disclaimer." Id. at 221. Although the Supreme Court recognized that "the rule is most frequently invoked when the original and cancelled claim is broader than that allowed," it also found that "the rule and the reason for it are the same if the cancelled or rejected claim be narrower." Id. Using that rationale, the Supreme Court found that by "having acquiesced" to the rejection of the narrow claims, the patentee was "no longer free to gain the supposed advantage of the rejected claims by a construction of the allowed claims as equivalent to them." Id. at 221-22. Schriber-Schroth was cited with approval by the Supreme Court in Festo I for the proposition that "claims are interpreted by reference to 'those that have

been cancelled or rejected.'" Festo I, 535 U.S. at 733 (quoting Schriber-Schroth, 311 U.S. at 220-21). Yeda does not address, or even cite, Schriber-Schroth in its briefing. Given this line of cases, it is clear that cancelled claims can operate to narrow the issued claims.

Yeda further argues that cancelling the dependent claims did not narrow the scope of claim 41 because claim 41 independently covered chimeric and humanized antibodies, again invoking the presumption of claim differentiation. Yeda's Supp. Br. at 15, 20. That argument is beside the point. The issue is not what the scope of claim 41 would have been if the dependent claims had not been introduced or had not been cancelled. The issue is how the cancellation of the dependent claims in response to the examiner's rejection affected the scope of the independent claim. The examiner's rejection was, in effect, a statement that Yeda could not properly claim chimeric or humanized antibodies, and Yeda's cancellation in response "is taken as a concession that the invention as patented does not reach as far as the original claim." Festo I, 535 U.S. at 734. Accordingly, the cancellation of the claims operated to narrow the patent's scope.[29]

2. Reason for Amendment

Yeda argues that when it agreed to cancel the dependent claims, it did not have the purpose of renouncing coverage of chimeric and humanized antibodies, but instead was merely acknowledging that it was not entitled to dependent claims directed to those types of antibodies. Yeda's Supp. Br. at 17. Under Festo I, however, the analysis is not whether the patentee intended to renounce claim scope through its actions, but instead whether the narrowing amendment was

[29] Yeda also argues that it only needed to disclose a genus of monoclonal antibodies to meet the written description requirement, and did not need to disclose all species within that genus. Yeda's Supp. Br. at 18. That argument is similarly beside the point. The propriety of the examiner's rejection is irrelevant to determining whether prosecution history estoppel applies. Warner-Jenkinson Co., 520 U.S. at 33 n.7.

made "for a 'substantial reason related to patentability.'" Festo II, 344 F.3d at 1366 (quoting Warner-Jenkinson, 520 U.S. at 33). Yeda's admission that the claims were cancelled because they did not meet the written description requirement of 35 U.S.C. § 112 ¶ 1 establishes that the dependent claims were cancelled for reasons substantially related to patentability, and the allowance of the '923 Patent shortly after that cancellation, without Yeda adding claims of scope similar to the cancelled claims, is compelling further evidence that the cancellation of the claims was substantially related to patentability.

3. Scope of Surrender

Because the dependent claims to chimeric and humanized antibodies were cancelled for reasons substantially related to patentability, the "presumption that the patentee has surrendered all territory between the original claim limitation and the amended claim limitation" applies. Festo II, 344 F.3d at 1367. Yeda argues that the scope of surrender does not extend to humanized antibodies because the word "humanized" does not specifically appear in the cancelled claims. Yeda's Supp. Br. at 25.

The evidence does not support Yeda's argument. When Yeda introduced claim 41, it defined the term "chimeric" as being "intended to encompass both mouse variable/human constant chimeras, and those with chimeric variable domains (mouse hypervariable/human framework) and human constant domains." Prosecution History at 509 n.1. Yeda therefore specifically defined "chimeric" as including humanized antibodies, and later introduced claims to chimeras. Id. at 507-09. By later cancelling those claims, Yeda surrendered both chimeric and humanized antibodies.[30]

[30] Yeda argues that its later use of the phrase "humanized or chimeric derivative of a mouse monoclonal antibody" indicates that humanized antibodies were not subsumed within the "chimeric" term, and that the phrase creates a factual issue which prevents summary judgment.

In a footnote, Yeda also argues that Cimzia® is different from "traditional" humanized antibodies because it "required further engineering beyond a traditional humanized antibody." Yeda's Supp. Br. at 27 n.21. Therefore, according to Yeda Cimzia® is not within the scope of the surrender, and Yeda can assert that Cimzia® is an equivalent. There is no evidence in the record supporting this argument. Yeda's experts do not draw a distinction between "traditional" and "non-traditional" antibodies; instead they clearly describe Cimzia® as a humanized antibody. Siegel Opening Report ¶¶ 53-55; Huston Opening Report ¶¶ 37, 42. Accordingly, both chimeric and humanized antibodies are within the scope of surrender.

4. Rebuttal of Presumption

The presumption of prosecution history estoppel may be rebutted if the patentee can demonstrate that the alleged equivalent was not foreseeable at the time that the narrowing amendment was made. Festo II, 344 F.3d at 1365 n.2. Yeda argues that allowing prosecution history estoppel here would strip the doctrine of equivalents of its ability to claim after-arising technology because humanized antibodies are an after-arising technology that Yeda could not have foreseen at the time of invention. Yeda's Supp. Br. at 23-24, 26. This argument fails because "the time when the narrowing amendment was made, and not when the application was filed, is the relevant time for evaluating unforeseeability." Festo II, 344 F.3d at 1365 n.2. When the dependent claims were cancelled in 1999, chimeric and humanized antibodies were not unforeseeable. To the contrary, Yeda was specifically attempting to claim chimeric and humanized antibodies when it introduced the relevant dependent claims. Accordingly, Yeda has

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Yeda is wrong. "Issues relating to the . . . scope of prosecution history estoppel . . . are questions of law to be decided by the court." Biagro Western Sales, Inc., 523 F.3d at 1301-02. Yeda's explicit definition of the term "chimeric" to include humanized antibodies indicates that humanized antibodies are within the scope of the surrender.

not overcome the estoppel presumption, and Yeda cannot now assert Cimzia®, a humanized antibody, infringes under the doctrine of equivalents.

When the USPTO rejected Yeda's efforts to claim chimeric and humanized antibodies and Yeda acquiesced to those rejections, Yeda's competitors and interested members of the public were entitled to rely on Yeda's actions. Having conceded the correctness of the rejections made by the USPTO, Yeda cannot now complain that it is estopped from re-capturing that subject matter as an equivalent. Accordingly, UCB's motion for summary judgment of no infringement under the doctrine of equivalents will be granted.

## III. CONCLUSION

Because Cimzia® does not infringe the '923 Patent either literally or under the doctrine of equivalents, the issues of the validity of the '923 Patent[31] and whether laches is available to UCB as a defense need not, and will not, be addressed. Accordingly, the remaining issues in UCB's motion for summary judgment, and the entirety of Yeda's motion for partial summary judgment, as well as Yeda's Motions to Realign the Order of Proof [Dkt. No. 191] and to Strike UCB's Untimely Discovery Responses, [Dkt. No. 194], will be denied as moot by an appropriate Order to be issued with this Memorandum Opinion.

Entered this 30th day of July, 2015.

Alexandria, Virginia

/s/
Leonie M. Brinkema
United States District Judge

[31] Although neither party moved for summary judgment regarding prosecution laches, Complaint ¶¶ 27-30, the non-infringement decision renders that issue moot.