United States District Court,
N.D. California.

The REGENTS OF the UNIVERSITY OF CALIFORNIA, Abbott Molecular Inc., and Abbott Laboratories Inc,
Plaintiffs.
v.
DAKO NORTH AMERICA, INC. and Dako A/S,
Defendants.

No. C 05-03955 MHP

Aug. 1, 2006.

Background: State university and research laboratories brought action against biotechnology company, alleging infringement of patents for in situ DNA hybridization. Company moved for summary judgment.

Holdings: The District Court, Patel, J., held that:
(1) phrase "heterogeneous mixture of labeled unique sequence nucleic acid fragments" meant "heterogeneous mixture of labeled nucleic acid fragments that includes only unique sequence fragments";
(2) patent was not infringed under doctrine of equivalents;
(3) fact issues existed whether patent was literally infringed; and
(4) narrowing amendment of claim was applicable.

Motion granted in part and denied in part.

5,447,841, 6,596,479. Construed.

Carolyn Chang, Chien-Ju Alice Chen, Lynn H. Pasahow, Michael J. Shuster, Virginia K. Demarchi, Wendy Lynn Bjerknes, Fenwick & West LLP, Mountain View, CA, for Plaintiffs.

Richard J. Smith, Finnegan, Hederson, Farabow, et al., Palo Alto, CA, for Defendants.

MEMORANDUM & ORDER

Re: Motion for Summary Judgment

PATEL**, District Judge.**

Plaintiffs The Regents of the University of California ("UC Regents"), Abbott Molecular Inc., and Abbott

Laboratories Inc. (collectively, "Abbott") brought this patent infringement action against defendants Dako North America, Inc. and Dako A/S (collectively, "Dako"), alleging infringement of two United States patents related to in situ DNA hybridization. Now before the court is Dako's motion for summary judgment of noninfringement. Having considered the parties' arguments and submissions, and for the reasons set forth below, the court enters the following memorandum and order.

BACKGROUND

The history of this litigation and the nature of the technology at issue are already discussed in some detail in the court's previous orders and need not be repeated in full here. The following summary is sufficient for purposes of resolving Dako's motion.

Abbott holds the two patents at issue in this lawsuit, U.S. Patent No. 5,447,841 (the "'841 patent") and U.S. Patent No. 6,596,479 (the "'479 patent"). The two asserted patents have substantially identical specifications but were issued almost eight years apart and have different claims. Both patents relate to the identification and analysis of target genes in a tissue sample through DNA hybridization. In DNA hybridization, sections of nucleic acid that are labeled, usually with a fluorescent dye ("hybridization probes"), are bonded to complementary "target" regions of chromosomal DNA-typically, sections which encode a protein of interest. *See, e.g.,* '841 patent at cols. 2-3. The fluorescent label provides visual confirmation of the presence of the target gene. Id.

Dako manufactures diagnostic kits which make use of DNA hybridization to determine the presence and frequency of certain genes of interest, as well as information about whether genes of interest have undergone translocation. The accused products differ in some respects, but share two relevant characteristics. First, the parties do not dispute that each accused product employs a mixture of labeled probes which includes both unique sequence and repetitive sequence fragments, as construed by this court. Second, the parties agree that each accused product uses a synthetic compound called "PNA" to block the binding of repeat sequence fragments to the target chromosomal DNA.

Abbott filed this lawsuit on September 29, 2005 and moved for a preliminary injunction on October 17. In connection with the motion for a preliminary injunction, the parties proposed definitions for certain critical terms in the patent. The court construed the phrase "morphologically identifiable cell nucleus" (in the '479 patent) and "morphologically identifiable ... cell nucleus" (in the '841 patent) to mean "a single cell nucleus that contains the full complement of chromosomal DNA." The court also considered the meaning of the phrase "heterogeneous mixture of labeled unique sequence nucleic acid fragments," found in claim 1 of the'479 patent. On the incomplete record available at the time of resolving the motion for a preliminary injunction, the court concluded that the recited "heterogeneous mixture" could not include repeat sequence fragments. In light of the court's preliminary claim construction, questions regarding the validity and enforceability of the asserted patents, and the apparent adequacy of monetary damages, the court denied Abbott's motion for a preliminary injunction. Abbott's interlocutory appeal of the denial, including the proposed constructions of "morphologically identifiable cell nucleus" and "heterogeneous mixture of labeled unique sequence nucleic acid fragments," is currently pending before the Federal Circuit.

The parties subsequently submitted proposed constructions for the remaining disputed claim terms, which this court construed in a recently issued order. Relevant to the instant motion, the court revised its construction of the phrase "heterogeneous mixture of labeled unique sequence nucleic acid fragments" to mean "a heterogeneous mixture of labeled nucleic acid fragments that includes unique sequence fragments."

The parties have also stipulated that the phrase "nucleic acid" does not literally encompass the synthetic PNA which the accused products employ to block the binding of repeat labeled fragments.

Simultaneously with the claim construction briefing, Dako filed the instant motion for summary judgment. Dako based its motion on the court's preliminary constructions of "morphologically identifiable cell nucleus" and "heterogeneous mixture of labeled unique sequence nucleic acid fragments," as well as the stipulation that "nucleic acid" does not literally encompass PNA. Abbott opposes the motion on the merits, and further moves for postponement of the motion and additional discovery under Federal Rule of Civil Procedure 56(f).

LEGAL STANDARD

I. ***Summary Judgment***

Summary judgment is proper when the pleadings, discovery and affidavits show 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). Material facts are those which may affect the outcome of the case. Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 248, 106 S.Ct. 2505, 91 L.Ed.2d 202 (1986). A dispute as to a material fact is genuine if there is sufficient evidence for a reasonable jury to return a verdict for the nonmoving party. Id. The party moving for summary judgment bears the burden of identifying those portions of the pleadings, discovery, and affidavits that demonstrate the absence of a genuine issue of material fact. Celotex Corp. v. Catrett, 477 U.S. 317, 323, 106 S.Ct. 2548, 91 L.Ed.2d 265 (1986). On an issue for which the opposing party will have the burden of proof at trial, the moving party need only point out "that there is an absence of evidence to support the nonmoving party's case." Id.

Once the moving party meets its initial burden, the nonmoving party must go beyond the pleadings and, by its own affidavits or discovery, "set forth specific facts showing that there is a genuine issue for trial." Fed.R.Civ.P. 56(e). Mere allegations or denials do not defeat a moving party's allegations. Id.; Gasaway v. Northwestern Mut. Life Ins. Co., 26 F.3d 957, 960 (9th Cir.1994). The court may not make credibility determinations, and inferencesto be drawn from the facts must be viewed in the light most favorable to the party opposing the motion. Masson v. New Yorker Magazine, 501 U.S. 496, 520, 111 S.Ct. 2419, 115 L.Ed.2d 447 (1991); Anderson, 477 U.S. at 249, 106 S.Ct. 2505.

The moving party may "move with or without supporting affidavits for a summary judgment in the party's favor upon all or any part thereof." Fed.R.Civ.P. 56(a). "Supporting and opposing affidavits shall be made on personal knowledge, shall set forth such facts as would be admissible in evidence, and shall show affirmatively that the affiant is competent to testify to the matters stated therein." Fed.R.Civ.P. 56(e).

II. ***Patent Infringement***

[1] [2] Determination of infringement is a two-step process. First, the court must determine the meaning of the language of the claims, a question of law. Markman v. Westview Instruments, Inc., 517 U.S. 370, 384, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996). Second, the finder of fact must compare the construed claims to the accused product, to determine if each claim element is present, either literally or under the doctrine of equivalents. Irdeto Access, Inc. v. Echostar Satellite Corp., 383 F.3d 1295, 1299 (Fed.Cir.2004).

DISCUSSION

I. '479 Patent

A. ***Construction of "heterogeneous mixture of labeled unique sequence nucleic acid fragments"***

Dako filed its summary judgment motion based on the court's observations in the preliminary injunction as to the likely construction of "heterogeneous mixture of labeled unique sequence nucleic acid fragments." The court revised its interpretation of this phrase in light of the more thorough claim construction briefing submitted by the parties, ultimately accepting Abbott's argument that the word "of," read in the context of the dependent claims of the '479 patent, should be construed to mean "comprising." Although the court expressed concerns about adopting the broad construction proposed by Abbott-particularly in light of the inoperative subject matter encompassed in Abbott's interpretation of the claim-the court found that the relationship among the independent and dependent claims provided clear evidence that the patentee intended to allow the heterogeneous mixture recited in claim 1 to include repetitive as well as unique fragments.

In the briefs accompanying the instant motion, however, Dako has discussed additional excerpts from the prosecution history which call the court's previous construction into question. The excerpts were included in the declarations accompanying the parties' Markman submissions but were not cited in the accompanying briefs or highlighted at argument. FN1 The cited excerpts follow the development of the claims of the ' 479 patent in some detail, and bear careful review.

FN1. The court points out that it is not the court's responsibility to comb the record in search of evidence or arguments not raised in the parties' briefing. That is the lawyers' job. Had this been done in the claim construction phase this issue would have been resolved at that time-the proper time-and would not need to be revisited here.

Originally filed application claim 17, which is the predecessor to claim 1 of the '479 patent, read as follows:

17. A method of staining chromosomal DNA of a particular chromosome type or portion thereof, or a particular group of chromosome types, the method comprising the steps of:

providing a heterogeneous mixture of labeled nucleic acid fragments, substantial portions of each labeled nucleicacid fragment in the heterogeneous mixture having base sequences substantially complementary to base sequences of the chromosomal DNA; and

reacting the heterogeneous mixture with the chromosomal DNA by in situ hybridization.

Hoffman Dec., Exh. N at 47. Of particular note is that claim 17 recited a "heterogeneous mixture of labeled nucleic acid fragments," without the "unique sequence" modifier. *See* id. The examiner rejected the claim under 35 U.S.C. section 112 for lack of enablement, noting that

the disclosure is enabling only for claims limited to reacting practice (last 2 lines of claim 17) which promotes at least some specificity of hybridization so as to stain only the desired target chromosome or portion thereof. As worded there is no specificity practice in the actual claim steps *that would result in staining of the target only without so much background that the desired target nucleic acid would be obscured*.

Id., Exh. O at 2 (emphasis added). In other words, claim 17 as drafted contained no provision for reducing nonspecific binding. This court noted precisely the same concern in its Markman order. Slip op. at 8-9.

In response to the rejection, the applicants cancelled the pending claims and submitted amended claims. Amended application claim 18, which is also the predecessor to claim 1 in the final patent, read as follows:

18. A method of staining target interphase chromosomal DNA to detect amplifications, deletions, and rearrangements comprising:

(a) providing a heterogeneous mixture of labeled unique sequence nucleic acid fragments which are substantially complementary to nucleic acid segments within the interphase chromosomal DNA for which detection is desired; and

(b) employing the heterogeneous mixture and interphase chromosomal DNA in in situ hybridization to permit detection of labeled nucleic acid fragments which are hybridized to interphase chromosomal DNA, wherein the chromosomal DNA is present in a morphologically identifiable cell nucleus during the in situ hybridization.

Hoffman Dec., Exh. P at 2. Although the claim language changed in several ways in the progression from claim 17 to claim 18-such as adding the types of conditions to be detected, the requirement that the process be performed on interphase DNA, and the "morphologically identifiable cell nucleus" limitation-the only changes to address the examiner's concern regarding nonspecific binding were the addition of the phrase "unique sequence" and the clarification that the recited fragments are "substantially complementary to nucleic acid segments within the interphase chromosomal DNA for which detection is desired."

The applicants did not provide a detailed explanation of the significance of their changes, but argued that the previous rejection under section 112 was moot in light of the newly drafted claims. The examiner accepted the applicants' argument that the change adequately addressed the enablement concern. *Id.,* Exh. Q at 3-4. It is also apparent that the examiner recognized that the fragments in the heterogeneous mixture were intended to bond only to the target region, as demonstrated by the examiner's question as to whether use of the word "unique" was appropriate to cover "detecting apparently non-unique 'extra' chromosomes"-i.e., targets which occurred more than once per haploid. *Id.,* Exh. Q at 4.

The dependent claims added as part of the same amendment are also revealing, as they do not include the later-added dependent claims which this court found to support Abbott's proposed construction. *See id.,* Exh. P at 1-4. Dependent claim 12, which recites the inclusion of repetitive sequence fragments in the heterogeneous mixture, was not added until March 1999, almost two-and-one-half years after the applicants added the "unique sequence" limitation. *Id.,* Exh. V at 2.

The cited excerpts are significant because they evince a disclaimer of methods employing labeled repeat sequence fragments, the inclusion of which in the probe mixture would result in "so much background that the desired target nucleic acid would be obscured." *Cf. id.,* Exh. O at 2. Based on the approaches to reducing nonspecific binding set forth in the specification, the applicant could have chosen to address the examiner's section 112 rejection in two ways: the addition of blocking nucleic acid to prevent the repeat sequence fragments from hybridizing to the target, or the elimination of repeat sequence probes from the heterogeneous mixture. By representing to the examiner that the amended claim, which did not include any

limitation requiring blocking, addressed the problem of nonspecific binding, the applicants represented that the claimed heterogeneous mixture would not bind to undesirable locations-in other words, that the claimed mixture was free of repeat sequence fragments.

In addition, as the court observed in the claim construction order, the applicants argued to the examiner that " '[u]nique sequence nucleic acid fragments are in contrast with, and free of, 'repetitive sequence' nucleic acid.' " Slip op. at 10. The court previously noted in its Markman order that this definition for "unique" is compatible with Abbott's proposed construction, which depends on the word "of" for inclusion of repetitive sequence fragments in addition to the unique sequence fragments which are expressly recited in the claim. *Id*. Viewed in the broader context of the purpose for adding the "unique sequence" modifier, however-overcoming the examiner's rejection for inoperability-the applicant's definition of the word "unique" provides further evidence that the applicant disclaimed embodiments using repeat sequence fragments and blocking as part of the amendment.

[3] [4] A patent applicant may relinquish subject matter through claim cancellation or amendment during prosecution. "The doctrine of prosecution disclaimer is well established in Supreme Court precedent, precluding patentees from recapturing through claim interpretation specific meanings disclaimed during prosecution." Omega Eng'g, Inc. v. Raytek Corp., 334 F.3d 1314, 1323 (Fed.Cir.2003). Under the doctrine of prosecution disclaimer, which is distinct from prosecution history estoppel, the literal scope of claim terms is limited as a result of disclaimers made during prosecution: "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." Id. (citing Schriber-Schroth Co. v. Cleveland Trust Co., 311 U.S. 211, 312 U.S. 654, 220-21, 61 S.Ct. 235, 85 L.Ed. 132 (1940)).

[5] Here, it is clear from the file history that the "unique sequence" limitation was added to address the examiner's concern about the lack of any claim element which would reduce nonspecific binding. Abbott's proposed construction in this case-that the heterogeneous mixture might include repeat sequence fragments-is equivalent in scope to the broader claim limitation rejected by the examiner. Abbott cannot reclaim what it relinquished.

Abbott argues that the words "unique sequence" were added only to clarify that the heterogeneous mixture must contain *some* unique sequence fragments, in addition to whatever repeat sequence fragments might be present. In support of this argument, Abbott notes that as part of the same office action in which the examiner rejected claim 17 under section 112, the examiner also rejected claim 17 under section 102(b) as anticipated by three pieces of prior art. Two of the references described the use of heterogeneous mixtures of labeled repeat sequence DNA; the third reference described the use of labeled unique sequence DNA. Hoffman Dec., Exh. O at 3-4. Abbott notes that none of the cited references used a mixture of unique and repeat sequence fragments and argues that the modified version of claim 17 is distinct because it includes both.

Abbott's alternate explanation is not plausible because the applicant did not distinguish the amended claim 17 from the cited prior art on the basis of the "unique sequence" limitation. Instead, the applicant distinguished the prior art by limiting the use of the claimed method to interphase DNA and by requiring that the method detect amplifications, deletions and rearrangements: "The prior art fails to disclose or even suggest the methods of staining target interface [sic: interphase] chromosomal DNA to detect amplifications, deletions and rearrangements, as now claimed." *Id*., Exh. P at 5. Also, as Dako correctly points out, the phrase "heterogeneous mixture" as defined generally in the specification for the '479 patent clearly includes

unique sequence fragments: "In particular, chromosome specific staining reagents are provided which comprise heterogeneous mixtures of labeled nucleic acid fragments having substantial portions of substantially complementary base sequences to the chromosomal DNA for which specific staining is desired." ' 479 patent at 3:51-56. Thus it was not necessary to add the "unique sequence" modifier to suggest that the heterogeneous mixture included some unique sequences.

Abbott also argues, as it did at the claim construction hearing, that the examiner must have understood the claim to include repeat sequence fragments when she allowed dependent claims 12 through 14 to be added without objection. Abbott, however, does not cite any portion of the file history suggesting that the examiner considered the tension between her previous rejection under section 112 and her subsequent allowance of claim 12. Absent some explanation for or qualification of the otherwise clear disclaimer, Abbott is not entitled to recover the disclaimed scope. The court therefore modifies its construction of the phrase "heterogeneous mixture of labeled unique sequence nucleic acid fragments" to mean "a heterogeneous mixture of labeled nucleic acid fragments that includes only unique sequence fragments."

B. ***Literal Infringement of the*** '479 Patent

The parties do not dispute that each of Dako's accused kits employs a mixture of nucleic acid fragments which includes repeat sequence fragments. Thus there is no dispute, given the revised claim construction, that Dako's kits do not literally infringe the '479 patent.

C. ***Infringement of the*** '479 Patent ***Under the Doctrine of Equivalents***

[6] [7] The prosecution history discussed *supra* is equally applicable in evaluating infringement under the Doctrine of Equivalents. *See* Terlep v. Brinkmann Corp., 418 F.3d 1379, 1385-86 (Fed.Cir.2005) (relying on an amendment during prosecution both in determining the literal scope of a claim and in assessing infringement under the Doctrine of Equivalents). Determining whether prosecution history estoppel applies is a two-step process. First, if there was a narrowing amendment made during prosecution, a presumption arises that the applicant "surrendered the territory between the original claims and the amended claims." Id. at 1385. The patentee may overcome the presumption by showing that "the alleged equivalent was unforeseeable at the time the amendment was made, that the alleged equivalent was tangential to the purpose of that amendment, 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. (citing Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 535 U.S. 722, 740-41, 122 S.Ct. 1831, 152 L.Ed.2d 944 (2002)).

[8] Here, the addition of "unique sequence" to the claims was clearly narrowing, as it limited the claimed process to the use of unique sequence fragments in hybridization. Abbott does not attempt to argue that the use of blocking agents was unforeseeable (as it is discussed at length in the specification for the '479 patent) or that the abandoned equivalent was tangential to the purpose of the amendment. The court therefore concludes that none of the accused products infringes the '479 patent under the Doctrine of Equivalents. Dako's motion for summary judgment with respect to the '479 patent is therefore granted.

II. '841 Patent

A. ***Construction of "blocking nucleic acid"***

The parties have stipulated that the phrase "blocking nucleic acid" in claim 1 of the '841 patent means "fragments of repetitive-sequence-enriched DNA or RNA." Hoffman Dec., Exh. Y at 2. The court will

therefore consider whether the phrase as the parties have defined it covers the accused products.

B. ***Literal Infringement of the*** '841 Patent

Abbott argues that most of the accused Dako kits, which indisputably employ PNA to block the binding of repeat sequence labeled fragments, also make use of DNA to perform a blocking function. With two exceptions, each accused product includes unlabeled "total human DNA" as well as unlabeled PNA. Chang Dec., Exh. I at 180:25-182:20. Abbott argues that total human DNA is rich in repeat sequences and serves a blocking function, therefore falling within the literal scope of the "blocking nucleic acid" recited in claim 1 of the '841 patent. Dako argues that total human DNA does not satisfy the claim limitation because it is not artificially "enriched" with additional repeat sequence fragments.

The parties' dispute has two separate components. First, although the parties purported to stipulate to a definition for "blocking nucleic acid," they apparently disagree as to the meaning of the word "enriched" in the stipulated construction. Abbott interprets "enriched" as meaning that the DNA must have a high ratio of repeat to unique sequences. Dako argues that "enriched" means that the ratio of repeat to unique sequences must be above that found in naturally occurring DNA. Although neither party addressed the proper claim construction in their briefs, both offered various citations to the intrinsic record at oral argument.

Assuming for the sake of argument that Dako's proposed interpretation is correct, Abbott also claims that the total human DNA used in Dako's kits may have a higher proportion of repeat sequences than naturally occurring DNA. At oral argument, Abbott claimed that total human DNA is generally manufactured by subjecting a single set of DNA to amplification. During the amplification process repeat sequence fragments are duplicated at a higher rate than unique sequence fragments. Thus the resulting DNA contains a higher proportion of repeat sequence fragments than normal human DNA.

[9] The court finds that the record submitted in connection with Dako's motion is not developed enough to permit construction of "blocking nucleic acid" or application of the properly construed phrase to Dako's kits. The parties were unable to address the issue in detail in their briefs because Abbott did not disclose its literal infringement contention based on the total human DNA as part of its preliminary infringement contentions. *See* Hoffman Dec., Exh. BB. The court also notes that Abbott's representations at oral argument about the effect of creating large quantities of total human DNA through amplification appear to lack support in the current factual record. Abbott submitted a supplemental declaration from Professor David Pinkel in support of its contention that total human DNA can be an effective blocking agent, but the article attached to the declaration does not appear to describe the process by which total human DNA is manufactured. The only relevant passage the court has discovered describes the total human DNA as follows: "Placental DNA (Sigma) was treated with proteinase K, extracted with phenol, and sonicated to a size range of 200-600 base pairs (bp)." Supp. Pinkel Dec., Exh. A at 9139. This passage appears to describe the preparation of total human DNA without the use of amplification.

Without a clear record, the court must deny Dako's motion under Rule 56(f), subject to renewal at the point when a fully developed record as to the proper construction of "blocking nucleic acid" and the use of total human DNA in Dako's accused kits becomes available.

Two of Dako's products, however-the HER2 kit and the TOP2A kit-do not make use of total human DNA at all and therefore do not literally infringe the claims of the '841 patent. The court will therefore consider infringement under the Doctrine of Equivalents for those two products.

C. *Infringement of the* '841 Patent *Under the Doctrine of Equivalents*

The "blocking nucleic acid" limitation was not present in the original claims of the '841 patent, but was added during prosecution. The earliest claims of the '841 patent purported to cover "the generic invention where the repetitive sequences are disabled by any means." Chang Dec., Exh. D at A-351. The claims ultimately pursued in connection with the '841 patent, however, were limited by the applicant to methods in which "disabling is performed by selective blocking of the repetitive sequences." Id. The broader claims were pursued in connection with a divisional application. Dako contends that the limitation of the claims to the use of blocking was a narrowing amendment for a substantial reason related to patentability, giving rise to a presumption of prosecution history estoppel.

Prior to the amendment in question, application claim 28 read as follows:

28. (Twice amended) A method of staining chromosomal DNA that can be used to stain a particular chromosome type or portion thereof, or a particular group of chromosome types or portions thereof, whether the targeted chromosomal sequences are present at normal copy numbers for diploid or haploid cells or at higher copy numbers, the method comprising the steps of:

providing a heterogeneous mixture that contains labeled nucleic acid fragments that are substantially complementary to unique sequence regions of complexity of at least 35 kilobases (kb) in the targeted chromosomal DNA[;]

disabling the hybridization capacity of repetitive sequences within said heterogeneous mixture;

reacting the heterogeneous mixture with the target chromosomal DNA by in situ hybridization; and

rendering visible the hybridized, labeled fragments.

Id. at A-221-22 (editorial notations omitted and emphasis added). Dependent application claim 99, prior to the amendment in question, recited

[t]he method of staining chromosomal DNA according to Claim 28 wherein said disabling step includes substantially blocking the labeled repetitive nucleic acid fragments in the heterogeneous mixture by hybridization with unlabeled repetitive nucleic acid fragments that are complementary to those in the heterogeneous mixture.

Id. at A-238.

The examiner rejected application claim 28 as anticipated by or obvious in light of a prior art reference ("Weissman") which disclosed the use of "single-copy" probes in hybridization. Id. at A-318-21. In Weissman, repeat sequence probes were eliminated from the probe mixture "by preassociation with total human DNA." Id. at A-320. In response to the rejection, the applicants cancelled their existing claims and added application claim 132:

A method of staining chromosomal DNA comprising:

(a) providing 1) labeled nucleic acid that comprises fragments which are substantially complementary to nucleic acid sequences within the chromosomal DNA for which staining is desired, and 2) blocking nucleic acid that comprises fragments which are substantially complementary to repetitive sequences in the labeled nucleic acid;

(b) employing said labeled nucleic acid, blocking nucleic acid, and chromosomal DNA in in situ hybridization so that labeled repetitive sequences are substantially blocked from binding to the chromosomal DNA, while allowing substantial hybridization of unique sequences within the labeled nucleic acid to the chromosomal DNA.

Id. at A-348.

[10] Dako argues that claim 132 is a narrowing amendment because it incorporates the limitations of formerly dependent claim 99 into the previous independent claim 28. Incorporating the limitations of a dependent claim into an independent claim is a narrowing amendment when it is done to avoid a rejection:

Thus, the fact that the scope of the rewritten claim has remained unchanged will not preclude the application of prosecution history estoppel if, by canceling the original independent claim and rewriting the dependent claims into independent form, the scope of subject matter claimed in the independent claim has been narrowed to secure the patent.

Honeywell Int'l Inc. v. Hamilton Sundstrand Corp., 370 F.3d 1131, 1142 (Fed.Cir.2004) (en banc).

Abbott argues that the amendment is not narrowing under Honeywell because although claim 132 requires the use of "blocking nucleic acid" to disable the hybridization capacity of the repetitive sequence labeled probes, it is broader than claims 28 and 99 in other respects. For example, claim 132 omits any requirement as to the length of the unique sequence regions and does not require "rendering visible the hybridized fragments." The fact that the new claim may have broadened in other, unrelated respects is not relevant to determining whether prosecution history estoppel applies to the disputed element, as prosecution history estoppel is evaluated on an element-by-element basis. Id. at 1144 ("The scope of the patentee's concession is determined on a limitation-by-limitation basis."); *see also* Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 344 F.3d 1359, 1367 (Fed.Cir.2003) (en banc) (" Festo VIII imposes the presumption that the patentee has surrendered all territory between the original claim limitation and the amended claim limitation."). Here, limiting the methods of "disabling the hybridization capacity of repetitive sequences" to the use of blocking nucleic acid provided a basis for distinguishing Weissman, which used preassociation with total human DNA to remove repeat sequence probes prior to hybridization. *See* Chang Dec., Exh. D at A-351 ("Previously, the broadest claims had been directed to the generic invention where the repetitive sequences are disabled by any means, *the other major embodiment being by removal of the repetitive sequences. Claims to that subject matter ... will be pursued in a separate application*.")(emphasis added); *id.* at A-355-56 (distinguishing Weissman on the basis that "prior to the filing of the grandparent to the present application in January 1986, the direction of the art for unique sequence in situ hybridization involved careful selection of probes that did not contain repetitive sequences" and that "until the grandparent to the present application was filed in January 1986, the use of blocking copies of a sequence in in situ hybridization had been limited to testing whether a hybridization signal was due to repeat sequences.").

Abbott also argues that claim 132 should not be viewed as a narrowing amendment because the applicant continued to pursue the broader claim in a divisional application. This argument is not persuasive because

the fact that Abbott pursued the disclaimed subject matter in prosecuting another patent has no bearing on the proper range of equivalents for the claims of the '841 patent. As noted *supra,* the applicant disavowed the subject pursued in the divisional application, in the context of the '841 patent, by adding the blocking limitation. Id., Exh. D at A-351 ("Claims to that subject matter ... will be pursued in a separate application.").

Abbott also argues that the amendment is not narrowing because the applicant separately disagreed with the merits of the examiner's rejection. *See* Chang Dec., Exh. D at A-353-59. As already noted, the applicant distinguished Weissman on the grounds that it suggests removing repeat sequence probes from the mixture prior to hybridization, rather than using blocking DNA during hybridization. *See* id. at A-355 ("prior to the filing of the grandparent to the present application in January 1986, the direction of the art for unique sequence in situ hybridization involved careful selection of probes that did not contain repetitive sequences."). The flaw in Abbott's argument is that the cited passage attempts to distinguish Weissman from *the revised claim,* 132, and not from the previous claim 28. *See id*. at A-353 ("the following remarks will address only those rejections which pertain to the new claims."). In other words, the applicant felt it was necessary to distinguish the prior art cited by the examiner even after filing revised claims. The applicant's arguments are not an attempt to preserve some of the scope of the previously rejected claims; thus the cancellation of claim 28 and the submission of claim 132 constitutes a narrowing amendment. Specifically, the submission of claim 132 presumptively narrowed the scope of the invention from "disabling the hybridization capacity of repetitive sequences" using any means (as recited in claim 28) to using "blocking nucleic acid" to accomplish the same function.

Having concluded that a narrowing amendment took place, the court must next consider whether "the alleged equivalent was unforeseeable at the time the amendment was made, that the alleged equivalent was tangential to the purpose of that amendment, or that there was some other reason suggesting that the patentee could not reasonably be expected to have described the insubstantial substitute in question." *See* Terlep, 418 F.3d at 1385. Abbott argues that the purpose of the amendment was "to pursue in separate applications claims involving other embodiments of the invention that do not involve blocking." Brief in Opposition at 23. While Abbott's characterization of the purpose may be valid when considered from the perspective of the applicant's attempts to pursue multiple patents on the same parent application, from the narrower vantage point of the prosecution of the '841 patent, the purpose of the amendment was to overcome the examiner's rejections under sections 102 and 103. This purpose-to narrow the methods of eliminating repeat sequences in order to avoid prior art-is directly related to the "blocking nucleic acid" limitation.

Abbott also argues that the critical distinction over the prior art was the use of "blocking" generally rather than some other method of disabling hybridization, and did not depend on the particular type of blocking used. Abbott argues that Insituform Technologies, Inc. v. CAT Contracting, Inc., 385 F.3d 1360 (Fed.Cir.2004) found an alleged equivalent to be only tangentially related to the purposes of amendment under similar circumstances. In Insituform, the patent covered a method of repairing underground pipes by installing a liner inside the pipes. Id. at 1362-63. Prior to installing the liner, the liner had to be filled with resin, which the claimed invention accomplished through the use of a vacuum pump. Id. During prosecution of the patent, the claims were amended to avoid prior art which located the vacuum pump at the end of the liner, but required the use of a large vacuum pump as a result. Id. at 1370. The patentee added the requirement that the vacuum pump use a single cup attached at the middle of the liner, rather than at the end. Id. The accused product employed multiple cups, and the alleged infringer argued that the use of multiple cups was disclaimed as a result of the narrowing amendment. Id. The Federal Circuit disagreed, holding that the location of the vacuum pump at the center of the liner, rather than the number of vacuum

cups, provided the critical distinction over the prior art: "[t]here is no indication in the prosecution history of any relationship between the narrowing amendment and a multiple cup process, which is the alleged equivalent in this case." Id. Thus the use of multiple cups was not disclaimed as part of the narrowing amendment. Id.

Here, according to Abbott's characterization, the focus of the narrowing amendment was on the use of blocking. Blocking using unlabeled nucleic acid is a subspecies of blocking in general; thus the specific choice of blocking agent is not unrelated to the use of blocking in the same way that the number of vacuum cups is unrelated to the location of the vacuum. The exception applied in Insituform Technologies is narrow, as the Supreme Court noted in Festo. A narrowing amendment raises a presumption that the resulting element is confined to its literal scope. The presumption can only be overcome by a showing that "at the time of the amendment one skilled in the art could not reasonably be expected to have drafted a claim that would have literally encompassed the alleged equivalent." Festo, 535 U.S. at 741, 122 S.Ct. 1831. Abbott has not demonstrated that it would have been unreasonable or even difficult to claim the use of blocking generally, if, as Abbott claims, the use of blocking provided the relevant distinction over the prior art. Blocking using PNA is thus excluded from the scope of equivalents covered by the amended claim.

Dako's motion for summary judgment of noninfringement of the '841 patent as to the HER2 and TOP2A products is therefore granted.

III. ***Contributory and Induced Infringement***

Abbott further alleges that Dako is secondarily liable for infringement of the patents under principles of contributory and induced infringement. No contributory or induced infringement exists, however, absent direct infringement by a third party. Here, with the exception noted above for certain products under the '841 patent, use of the accused kits does not directly infringe either asserted patent. Thus Abbott's secondary liability arguments are unavailing.

CONCLUSION

For the foregoing reasons, the court GRANTS IN PART Dako's motion for summary judgment of noninfringement. As to the '479 patent, Dako's motion is GRANTED in its entirety. As to the '841 patent, Dako's motion is GRANTED for the HER2 and TOP2A products and DENIED without prejudice for the remaining accused products.

IT IS SO ORDERED.

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