IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ENZO LIFE SCIENCES, INC., Plaintiff. v. HOLOGIC INC., GRIFOLS DIAGNOSTICS SOLUTIONS, INC., and GRIFOLS, S.A., Defendants.	)	C.A. No. 16-894-LPS-CJB

Brian E. Farnan, Michael J. Farnan, FARNAN LLP, Wilmington, DE

John M. Desmarais, Michael P. Stadnick, Justin P.D. Wilcox, Jordan Malz, Peter C. Magic, Kerri-Ann Limbeek, DESMARAIS LLP, New York, NY

Attorneys for Plaintiff Enzo Life Sciences, Inc.

Karen L. Pascale, Pilar G. Kraman, YOUNG CONAWAY STARGATT & TAYLOR LLP, Wilmington, DE

Matthew M. Wolf, ARNOLD & PORTER KAYE SCHOLER LLP, Washington, DC
Jennifer Skelnar, Wallace Wu, ARNOLD & PORTER KAYE SCHOLER LLP, Los Angeles, CA
Marty Koresawa, ARNOLD & PORTER KAYE SCHOLER LLP, San Francisco, CA

Attorneys for Defendants Hologic Inc., Grifols Diagnostics Solutions, Inc., and Grifols, S.A.

MEMORANDUM OPINION

October 15, 2018
Wilmington, Delaware

STARK, U.S. District Judge:

Plaintiff Enzo Life Sciences, Inc. ("Plaintiff") sued Defendants Hologic, Inc., Grifols Diagnostics Solutions, Inc., and Grifols S.A. (collectively, "Defendants"), alleging that Defendants infringe Plaintiff's U.S. Patent No. 6,221,581 ("'581 patent"). (*See generally* D.I. 28-1) The patent relates to "[n]uclei acid hybridization assays" that are "detection processes in which target polynucleotides can be detected or the presence or absence of genetic mutations or defects in genetic material can be determined" using "[d]ouble hybrid or multihybrid probes." '581 patent, Abstract; 1:26-31.

Presently before the Court are the parties' disputes over the meaning of certain claim terms in the asserted claims. The parties submitted technology tutorials (D.I. 88, 89), comments on the opposing side's technology tutorial (D.I. 96, 99), and claim construction briefs (D.I. 83, 84, 95, 97). The Court held a claim construction hearing on July 2, 2018. (*See* D.I. 115 ("Tr.")) Thereafter, on August 17, the parties provided their updated positions on one disputed term. (D.I. 127)

I. LEGAL STANDARDS

A. CLAIM CONSTRUCTION

The ultimate question of the proper construction of a patent is a question of law. *See Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 837 (2015) (citing *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 388-91 (1996)). "It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (internal quotation marks omitted).

"[T]here is no magic formula or catechism for conducting claim construction." *Id.* at

1324. Instead, the Court is free to attach the appropriate weight to appropriate sources "in light of the statutes and policies that inform patent law." *Id.*

"[T]he words of a claim are generally given their ordinary and customary meaning [which 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." *Id.* at 1312-13 (internal citations and quotation marks omitted). "[T]he ordinary meaning of a claim term is its meaning to the ordinary artisan after reading the entire patent." *Id.* at 1321 (internal quotation marks omitted). The patent 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." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996).

While "the claims themselves provide substantial guidance as to the meaning of particular claim terms," the context of the surrounding words of the claim also must be considered. *Phillips*, 415 F.3d at 1314. Furthermore, "[o]ther claims of the patent in question, both asserted and unasserted, can also be valuable sources of enlightenment . . . [b]ecause claim terms are normally used consistently throughout the patent." *Id.* (internal citation omitted).

It is likewise true that "[d]ifferences among claims can also be a useful guide. . . . For example, the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." *Id.* at 1314-15 (internal citation omitted). This "presumption is especially strong when the limitation in dispute is the only meaningful difference between an independent and dependent claim, and one party is urging that the limitation in the dependent claim should be read into the independent claim." *SunRace Roots Enter. Co., Ltd. v. SRAM Corp.*, 336 F.3d 1298, 1303 (Fed. Cir. 2003).

It is also possible that "the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Phillips*, 415 F.3d at 1316. It bears emphasis that "[e]ven when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." *Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1372 (Fed. Cir. 2014) (quoting *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004)) (internal quotation marks omitted).

In addition to the specification, a court "should also consider the patent's prosecution history, if it is in evidence." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 980 (Fed. Cir. 1995), *aff'd*, 517 U.S. 370 (1996). The prosecution history, which is "intrinsic evidence," "consists of the complete record of the proceedings before the PTO [Patent and Trademark Office] and includes the prior art cited during the examination of the patent." *Phillips*, 415 F.3d at 1317. "[T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." *Id.*

In some cases, "the district court will need to look beyond the patent's intrinsic evidence and to consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art during the relevant time period." *Teva*, 135 S. Ct. at 841. Extrinsic evidence "consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." *Markman*, 52 F.3d

at 980. For instance, technical dictionaries can assist the court in determining the meaning of a term to those of skill in the relevant art because such dictionaries "endeavor to collect the accepted meanings of terms used in various fields of science and technology." *Phillips*, 415 F.3d at 1318. In addition, expert testimony can be useful "to ensure that the court's understanding of the technical aspects of the patent is consistent with that of a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field." *Id.* Nonetheless, courts must not lose sight of the fact that "expert reports and testimony [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.* Overall, while extrinsic evidence "may be useful" to the court, it is "less reliable" than intrinsic evidence, and its consideration "is unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence." *Id.* at 1318-19. Where the intrinsic record unambiguously describes the scope of the patented invention, reliance on any extrinsic evidence is improper. *See Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1308 (Fed. Cir. 1999) (citing *Vitronics*, 90 F.3d at 1583).

Finally, "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998). It follows that "a claim interpretation that would exclude the inventor's device is rarely the correct interpretation." *Osram GmbH v. Int'l Trade Comm'n*, 505 F.3d 1351, 1358 (Fed. Cir. 2007) (quoting *Modine Mfg. Co. v. U.S. Int'l Trade Comm'n*, 75 F.3d 1545, 1550 (Fed. Cir. 1996)).

B. INDEFINITENESS

A patent claim is indefinite if, "viewed in light of the specification and prosecution history, [it fails to] inform those skilled in the art about the scope of the invention with reasonable certainty." *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120, 2129 (2014). A claim may be indefinite if the patent does not convey with reasonable certainty how to measure a claimed feature. *See Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 789 F.3d 1335, 1341 (Fed. Cir. 2015). But "[i]f such an understanding of how to measure the claimed [feature] was within the scope of knowledge possessed by one of ordinary skill in the art, there is no requirement for the specification to identify a particular measurement technique." *Ethicon Endo–Surgery, Inc. v. Covidien, Inc.*, 796 F.3d 1312, 1319 (Fed. Cir. 2015).

II. CONSTRUCTION OF DISPUTED TERMS[1]

The '581 patent is entitled "Processes for Detecting Polynucleotides, Determining Genetic Mutations or Defects in Genetic Material, Separating or Isolating Nucleic Acid of Interest from Samples, and Useful Compositions of Matter and Multi-hybrid Complex Compositions." The claimed invention relates to "methods for the detection of a target genetic material having a desired base sequence or gene" and "methods for the detection of mutations, such as a point mutation or the detection of a gene or base." '581 patent, 1:18-23. It is "based upon techniques which utilize two labeled single stranded polynucleotide segments which are complementary to the same or the opposite strands of the target genetic material." *Id.* 1:24-27. According to the patent, this process "result[s] in the formation of a double hybrid and/or a

[1]Certain claim terms are no longer in dispute. (*See* D.I. 109; Tr. at 85) The Court will adopt the agreed-upon constructions.

multihybrid." *Id.* 1:27-29.

A. "A multihybrid complex composition which comprises three or more nucleic acid strands and two or more separate and mutually exclusive hybrids in said complex"[2]/"A process for forming the multihybrid complex composition of claim 123"[3]

Plaintiff the preamble is not limiting
Defendants the preamble is limiting
Court the preamble is limiting

Plaintiff argues that the preamble is not limiting because "the body of claim 123 provides a structurally complete formulation of the invention" (D.I. 84 at 4) and the preamble "is not necessary to understand[ing] the [claim] limitations" (D.I. 97 at 2). Defendants argue that the preamble is limiting because it provides an antecedent basis for an element recited in the body of the claim and "breathes 'life and meaning' into the claimed invention" (D.I. 83 at 4), as the "purported invention was a particularly defined multihybrid composition, not a generic composition with multiple hybrids" (D.I. 95 at 3).

"A preamble is generally construed to be limiting if it recites essential structure or steps, or if it is necessary to give life, meaning, and vitality to the claim." *Proveris Sci. Corp. v. Innovasystems, Inc.*, 739 F.3d 1367, 1372 (Fed. Cir. 2014) (internal quotation marks omitted). A preamble may be construed as limiting "when it recites particular structure or steps that are highlighted as important by the specification" and when "limitations in the body of the claim rely

[2]This term appears in claim 123.

[3]This term appears in claims 155 and 156.

upon and derive antecedent basis from the preamble, [which] then . . . may act as a necessary component of the claimed invention." *Id.*[4]

In the patent-in-suit, formation of a "multihybrid complex" is an important characteristic of the invention. It is mentioned in the title ("multihybrid complex compositions") and the abstract ("Double hybrid or multihybrid probes and compositions are usefully combined with capture assay and immobilization to provide for detection processes . . . ."). All three of the patent's figures illustrate the formation of a multihybrid and describe it as essential to the claimed invention. *See* '581 patent, Fig. 1 (showing "[h]ybridization to form the multihybrid" as final step); *id.* Fig. 2 (same); *id.* Fig. 3 (same); *see also id.* 2:45-3:18 ("Brief description of the Figures" describing figures depicting various embodiments and noting, "[w]hen the method of the invention is carried out . . . numerous single stranded polynucleotide segments . . . hybridize . . . to form the multihybrid").

Additionally, the specification expressly defines the multihybrid and makes numerous references to it. *See id.* 3:38-44 ("double hybrid can be interconnected so as to form a multihybrid (hereinafter referred to as the 'multihybrid')"); *see also, e.g.*, *id.* 5:37-43 ("formation of the multihybrid due to the particles bridging the double hybrids . . . [that] forms a precipitate or glob or glob-like structure which itself is much more readily detectable than the double hybrid"); *id.* 12:26-50 (explaining how invention can be used to detect different types of mutations and noting "utilizing the methods of the invention . . . result[s] in the formation of the double hybrid or multihybrid").

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[4]There are other instances as well, but they are not at issue here. *See Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 808 (Fed. Cir. 2002).

The preamble also provides an antecedent basis for an element recited in the body of the claim. Claim 123 recites "[a] multihybrid complex composition which comprises three or more ***nucleic acid strands*** . . . at least one strand being a nucleic acid . . . being capable of forming at least one hybrid with at least one of ***said other nucleic acid strands***" (emphasis added). As even Plaintiff agrees, the phrase "said other nucleic acid strands" derives antecedent basis from the "nucleic acid strands" described in the preamble. (D.I. 97 at 1) Further, the phrase "[t]he multihybrid complex" in asserted dependent claims 155 and 156 derives antecedent basis from "[a] multihybrid complex" described in independent claim 123.

B. "multihybrid"[5]

Plaintiff "an entity formed by more than two nucleic acid strands connected through hybridization"
Defendants "multiple, interconnected 'double hybrids,' with each double hybrid comprising two polynucleotides joined by their hybridization to the nucleic acid of interest"
Court "multiple, interconnected 'double hybrids,' with each double hybrid comprising two polynucleotides joined by their hybridization to the nucleic acid of interest"

The parties dispute whether the inventors acted as their own lexicographers in defining the term. While the parties agree that the term includes more than two nucleic acid strands connected through hybridization, they disagree on the additional limitations. In particular, Plaintiff objects to the use of the phrase "interconnected double hybrids" in Defendants' construction. (D.I. 84 at 6) For their part, Defendants contend that Plaintiff's construction "ignores the overwhelming intrinsic evidence demonstrating a special definition" for the term.

[5]This term appears in claim 123, 155, and 156.

(D.I. 95 at 4)

The Court agrees with Defendants. "[T]he inventor's lexicography governs" where "the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess." *Phillips*, 415 F.3d at 1316. "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." *Thorner v. Sony Computer Entm't Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012); *see also id.* at 1365-66 ("[An] inventor's written description of the invention, for example, is relevant and controlling insofar as it provides ***clear lexicography***.") (emphasis in original). Using phrases such as "defined below" or "refers to" in describing a limitation are examples of what usually constitutes clear lexicography. *See Vasudevan Software, Inc. v. MicroStrategy, Inc.*, 782 F.3d 671, 679 (Fed. Cir. 2015) ("An applicant's use of the phrase ***'refers to'*** generally indicates an intention to define a term.") (emphasis added); *Astrazeneca AB, Aktiebolaget Hassle, KBI-E, Inc. v. Mut. Pharm. Co.*, 384 F.3d 1333, 1340 (Fed. Cir. 2004) ("Certainly the '081 specification's statement that '[t]he solubilizers suitable according to the invention are ***defined below***' provides a strong signal of lexicography.") (emphasis added).

Here, the intrinsic evidence provides a "strong signal of lexicography." *Astrazeneca*, 384 F.3d at 1340. In describing the term, the specification uses the phrases "defined hereinbelow" and "referred to as." The "Summary of the Invention" explains that "[t]he methods of the invention result in the formation of a double hybrid and/or a multihybrid, ***defined hereinbelow***." '581 patent, 2:27-29 (emphasis added). Later, in the "Detailed description of the invention," the specification explains that "when the method of the invention is carried out, a double hybrid is formed which comprises two polynucleotide probes joined by their hybridization to the target

genetic material (***hereinafter referred to as the 'double hybrid'***)." *Id.* 3:35-38 (emphasis added). It then states that "the double hybrid can be interconnected so as to form a multihybrid (***hereinafter referred to as the 'multihybrid'***)." *Id.* 3:42-44 (emphasis added).

The prosecution history further supports this conclusion. In response to a rejection based on the terms "double-hybrid" and "multi-hybrid" being indefinite under § 112, the applicants stated that they "have ***defined those terms in the specification*** . . . and graphically in the figures . . . [and] [n]o further explanation is necessary as the meaning of those terms as so ***defined and represented*** would be obvious to one skilled in the art . . . ." (D.I. 77 Ex. 18 ENZOHOL-00001086) (emphasis added)

Plaintiff argues that the phrase "interconnected double hybrids" in Defendants' construction "create[s] unnecessary ambiguity in otherwise clear claim language." (D.I. 84 at 6) According to Plaintiff, this extra phrase in Defendants' construction would "require at least ***five*** nucleic acid strands and ***four*** hybrids" while the claim language only "require[s] ***three*** strands and ***two*** hybrids." (D.I. 97 at 5) (emphasis in original). But "interconnected double hybrid" are the words inventors used to define multihybrid. *See* '581 patent, 3:42-44 ("double hybrid can be interconnected so as to form a multihybrid"). Any purported "vague language cannot override the express definitional language." *Sinorgchem Co., Shandong v. Int'l Trade Comm'n*, 511 F.3d 1132, 1138 (Fed. Cir. 2007); *see also Trustees of Columbia Univ. in City of New York v. Symantec Corp.*, 811 F.3d 1359, 1366 (Fed. Cir. 2016) ("The patentee cannot rely on its own use of inconsistent and confusing language in the specification to support a broad claim construction which is otherwise foreclosed."). Moreover, the Court agrees with Defendants that "[Plaintiff's] accounting of 'no fewer than five strands' appears to be . . . the result of improperly including

non-unique polynucleotide probe strands in a multihybrid." (D.I. 95 at 6)

Plaintiff also relies on extrinsic evidence to support its proposal for a plain and ordinary meaning. (*See* D.I. 84 at 5-6) But extrinsic evidence cannot trump intrinsic evidence that unambiguously defines a term. *See Phillips* 415 F.3d at 1318 ("We have viewed extrinsic evidence in general as less reliable than the patent and its prosecution history in determining how to read claim terms, for several reasons."); *id.* at 1324 (noting that courts may rely on other sources for construing claims "as long as those sources are not used to contradict claim meaning that is unambiguous in light of the intrinsic evidence").

C. "capturing domain" and "capturing or collection domain . . ."

1. "capturing domain"[6]

Plaintiff "a region of the complex capable of separating or isolating said complex"
Defendants "a region of the formed complex that includes one member of a high specificity affinity binding pair"
Court "a region of the formed complex that includes one member of a high specificity affinity binding pair"

2. "capturing or collecting said complex to a solid support"/ "capturing or collecting said formed complex to a solid support"/ "capturing or collecting said first formed complex to a solid support"/"capturing or collecting said at least one first formed complex to a solid support"[7]

Plaintiff "bringing said [formed/first formed/said first formed/at least one first formed] complex into contact with a solid support"

[6]This term appears in claim 123.

[7]This term appears in claim 155, 156, 157, and 158.

Defendants "removing or isolating the complex/the formed complex/the first formed complex/the at least one first formed complex which previously was formed in solution onto a solid support using affinity binding and affinity binding pairs"
Court "removing or isolating the complex/the formed complex/the first formed complex/the at least one first formed complex which previously was formed in solution onto a solid support using affinity binding and affinity binding pairs"

The parties dispute whether a prosecution history disclaimer limits the scope of the terms. "In construing a claim term, [the Court] must look at the term's 'ordinary meaning in the context of the written description and the prosecution history . . . [except] when the patentee disavows the full scope of a claim term either in the specification or during prosecution." *Uship Intellectual Properties, LLC v. United States*, 714 F.3d 1311, 1313 (Fed. Cir. 2013). "[T]he entire prosecution history" is taken into account to determine whether there has been "a clear and unmistakable disclaimer of claim scope." *Id.* at 1315. "[S]tatements giving rise to a disclaimer may be made in response to a rejection over the prior art, but they may also take place in other contexts." *Id.*

Here, the prosecution history shows the applicant "clearly and unmistakably" limited the scope of the term. *Uship*, 714 F.3d at 1316. The applicant submitted an expert declaration to distinguish the patent's "capturing step" from a prior art reference describing an "immobilization" step. (*See* D.I. 77 Ex. 16 ENZOHOL-00000628) According to the expert's declaration, the capturing or collecting step involved "a single phase hybridization in solution," unlike the prior art reference, which used hybridization across a solid support. The declaration also explained that the patent used "high specificity affinity binding pairs" to capture the hybridization complex on a solid support, unlike the prior art reference, which used non-specific

binding. (*See id.* Ex. 17 ENZOHOL-00000650, 652-54) In response to the declaration, the Examiner allowed the pending claims. (*See id.* Ex. 29 Ex. 16 ENZOHOL-00000884)

Plaintiff argues that the statements regarding the prior art reference are not applicable to the asserted claims as they "were never rejected over that reference" but "were deemed allowable in the very office action that rejected other then-pending claims as unpatentable over [the prior art reference]." (D.I. 97 at 13) However, the representations made during prosecution reveal what the applicant understood the terms here to mean. *Uship*, 714 F.3d at 1315-16 ("Regardless of the examiner's motives, arguments made during prosecution shed light on what the applicant meant by its various terms."); *see also id.* at 1315 (noting that "prosecution history analysis focuses on what the applicant said, not on whether the representation was necessary or persuasive"); *Fenner Investments, Ltd. v. Cellco P'ship*, 778 F.3d 1320, 1325 (Fed. Cir. 2015) ("[T]he interested public has the right to rely on the inventor's statements made during prosecution, without attempting to decipher whether the examiner relied on them, or how much weight they were given."); *Microsoft Corp. v. Multi-Tech Sys., Inc.*, 357 F.3d 1340, 1350 (Fed. Cir. 2004) ("[A] patentee's statements during prosecution, whether relied on by the examiner or not, are relevant to claim interpretation."); *Laitram Corp. v. Morehouse Indus., Inc.*, 143 F.3d 1456, 1462 (Fed. Cir. 1998) ("The fact that an examiner placed no reliance on an applicant's statement distinguishing prior art does not mean that the statement is inconsequential for purposes of claim construction.").

Plaintiff further argues that there is no evidence of clear disavowal because the applicant distinguished the prior art reference "on the basis that the claims did not involve hybridization of the nucleic acid of interest across a solid support, but rather required a capturing step," and the

applicant "did not disclaim any particular types of capture." (D.I. 97 at 15) The Court does not agree. (*See* D.I. 17 Ex. 17 at ENZOHOL-0000650) (declaration explaining that patent using "specific affinity binding pairs" in capture step "altogether different and distinct" from prior art reference using "direct and non-specific immobilization step")

D. "wherein said formed complex is capable of providing a capturing domain, a signaling domain, or both"[8]

Plaintiff "capable of providing a region of the complex capable of separating or isolating said complex, a region of the complex capable of generating a signal, or both"/"wherein said formed complex includes a capturing domain, a signaling domain, or both""[9]
Defendants Indefinite/"wherein said formed complex of at least three nucleic acid strands has a component of those strands that is a capturing domain, a signaling domain, or both."[10]
Court "wherein said formed complex includes a capturing domain, a signaling domain, or both"

Defendants initially contended that the term is indefinite because it must contain a "preexisting" domain, yet "the claim language provides no guidance as to any preexisting structure that contributes or supplies a capturing domain, signaling domain, or both." (D.I. 83 at 19) They further argued that the term "presumably has a scope that differs from "comprising," "capable of forming," or "capable of generating" in other claims. (*Id.*) Plaintiff countered that the claim language does not require any preexisting domain or any particular structure. (D.I. 97 at 16-17)

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[8]This term appears in claim 123.

[9]This is Plaintiff's revised construction. (D.I. 127 at 1)

[10]This is Defendants' revised construction. (D.I. 127 at 1)

The record does not contain clear and convincing evidence of indefiniteness. While the specification does not use the term capturing domain or signaling domain, it does provide multiple examples of how capturing and signaling are achieved. *See e.g.*, '581 patent, Abstract ("The capture assay involves capturing a hybrid structure . . . or capturing a complex formed by reacting a hybrid structure with a complex forming moiety . . . . Capture and immobilization can be carried out using direct and indirect binding and attachment techniques. Targets can be detected directly or indirectly by using a signal generating moiety and labels."); *id.* 2:37-42 ("The label of each probe can be a particle, a moiety which is capable of generating a signal, either directly, e.g., a radioactive label, or indirectly, e.g., an enzyme-linked system . . . ."); *id.* 9:29-41 (describing capture assay). Based on these descriptions, a person of ordinary skill in the art ("POSA") would understand the scope of the term with reasonable certainty. This conclusion is supported by Plaintiff's expert. (*See* D.I. 98, Ex. F at 118:1-121:12)

After the claim construction hearing, the parties proposed revised constructions. (*See* D.I. 127) Defendants contend that under Plaintiff's revised construction, the "claimed complex can be essentially any entity formed through non-covalent binding in a manner that is inconsistent with the claim language." (*Id.* at 2) Plaintiff contends that Defendants' revised construction "improperly limits the terms 'capturing domain' and 'signaling domain' to components of a nucleic acid strand." (*Id.* at 3) The Court is adopting Plaintiff's revised construction. As explained below, the Court will be construing "complex" to include at a minimum multiple complementary nucleic acid strands held together through non-covalent binding. Nothing in the intrinsic evidence limits the capturing domain and the signaling domain to only components of nucleic acid strands. *See, e.g.*, '581 patent, 5:54-6:12 (noting nucleic acid strands could be

labeled with "any ligand and receptor" and providing examples of "[s]uitable ligands and receptors" such as biotin/avidin, antigen/antibody)

E. "(II) at least one strand"/ "a third strand (III)"/ "first nucleic acid strands"/"second nucleic acid strands"[11]

Plaintiff plain and ordinary meaning
Defendants "(II) at least one strand where no chemical modification has been made"/ "a third strand (III) where no chemical modification has been made" /"first nucleic acid strands where no chemical modification has been made"/"second nucleic acid strands where no chemical modification has been made"
Court "(II) at least one strand where no chemical modification has been made"/ "a third strand (III) where no chemical modification has been made" /"first nucleic acid strands where no chemical modification has been made"/"second nucleic acid strands where no chemical modification has been made"

As with the "capturing domain" and "capturing or collecting" terms, the prosecution history shows the applicant "clearly and unmistakably" limited the scope of this term to nucleic acid probes without chemical modifications. *Uship*, 714 F.3d at 1316. In response to a double patenting rejection, the applicant submitted a declaration from one of the inventors, stating that the claimed invention was different because the nucleic acid probes have not been chemically modified:

> Unlike the claims of either the '325 Patent or the '609 Patent, ***the present invention provides for useful capturing and signaling domains in processes and compositions for detecting target polynucleotides where no chemical modification has been made to the nucleic acid probes***. The agglutination method of the '325 Patent is directed to a modified probe bound to a particle. The capture sandwich invention of the '609 Patent is directed to two

[11]This term appears in claim 123, 155, 156, 157, and 158.

> covalent modifications to the nucleic acid probe, namely a label on the first probe and an entity for capturing on the second probe. ***The nucleic acid probes recited in the claims of the present invention have not been chemically modified in contrast to any of the issued claims in the '325 or '609 Patents***.

(D.I. 77 Ex. 13 at ENZOHOL-00000507) (emphasis added) Based on this declaration, the Examiner withdrew the double patenting rejections. (*See id.* Ex. 15 at ENZOHOL-00000581)

Plaintiff contends that "the term 'strand' would be readily understandable to a jury" and the term's "plain and ordinary meaning does not include the negative requirement proposed by Defendants." (D.I. 97 at 18) Prosecution history disclaimer is an exception to the general rule that a term is construed in accord with its plain and ordinary meaning. *See Uship*, 714 F.3d at 1313; *N. Am. Container, Inc. v. Plastipak Packaging*, Inc., 415 F.3d 1335, 1346 (Fed. Cir. 2005) ("[L]imitations may be construed to exclude a preferred embodiment if the prosecution history compels such a result.").

Plaintiff argues that the double patenting rejections are inapplicable to the asserted claims. (D.I. 84 at 17) However, Defendants have shown from the prosecution history that the asserted claims "mimic" and "correspond" to the claims which were the subject of the double patenting rejection and subsequently cancelled. (*See* D.I. 95 at 9-11; *see also* D.I. 77 Ex. 10 ENZOHOL-00000436) (noting that "[b]y and large, these claims ***mimic*** a great many of the previously pending claims" and showing table with columns "New Claim No." and "***Corresponding to Former Claim(s)***") (emphasis added); *id.* Ex. 10 ENZOHOL-00000447 (noting that new claims "have been added . . . ***in place of formerly pending claims*** . . . [and] are being presented for further examination on the merits") (emphasis added); *id.* Ex. 16 at

ENZOHOL-00000628 ("Applicants also acknowledge . . . that . . . Declaration submitted . . . was deemed sufficient to overcome three previous grounds of rejection.")) The record establishes that the claims at issue served as a replacement for the previously cancelled claims that had been the subject of the double patenting rejection during prosecution of the patent.

Plaintiff further contends that "the limitations at issue in the asserted claims are not the same as the terms that [applicant] allegedly disclaimed the scope of during prosecution." (D.I. 97 at 18) Specifically, Plaintiff contends that the asserted claims use the term "nucleic acid strand," but the cancelled claims used "nucleic acid probe." (*Id.*) But Plaintiff has not pointed to persuasive evidence that those two terms mean different molecular entities. To the contrary, the specification, in describing various embodiments of the invention, uses those terms interchangeably. *See e.g.*, '581 patent, 4:63-67 ("In this embodiment of the invention there are ***two polynucleotide probes***. ***Each single stranded polynucleotide*** segment is complementary to substantially mutually exclusive portions of the same or the opposite strands of the target genetic material.") (emphasis added); *id.* 3:34-37 ("[W]hen the method of the ***invention*** is carried out, a double hybrid is formed which comprises two ***polynucleotide probes*** joined by their hybridization to the target genetic material.") (emphasis added); *id.* 9:45-49 ("In this embodiment of the present invention there is only ***one polynucleotide probe***, but such polynucleotide probe comprises at least ***two single stranded polynucleotide*** segments of interest.") (emphasis added). Nor did the Examiner or applicant draw any distinction between these terms during prosecution. (*See, e.g.*, D.I. 77 Ex. 4 ENZOHOL-00000285 (claim 400 reciting "polynucleotide probe"); ENZOHOL-00000307 (claim 466 reciting "nucleic acid strands"); *see also* D.I. 95 at 12-13)

F. "solid support"[12]

Plaintiff "solid structure"
Defendants "solid matrix that is not dispersed in solution"
Court "solid structure"

The parties dispute whether the term includes a particle or a matrix (Plaintiff's position) or excludes particles and includes only a matrix (Defendants' position). Plaintiff contends that the "specification . . . discloses different types of solid supports, such as a 'particle' and a 'matrix'," to fix nucleic acids. (D.I. 84 at 10) Defendants contend that the patent distinguishes between a particle and a matrix. (D.I. 83 at 11)

Nothing in the patent limits the term to a matrix. According to the claim language, a solid support is used for fixing or immobilizing nucleic acid strands in the claimed composition. '581 patent, claim 123 ("at least one strand being fixed or immobilized to a solid support or being capable of fixation or immobilization to a solid support"). In describing multiple embodiments, the specification explains that either a particle or a matrix could be used for the this purpose. In a preferred embodiment, a particle is used. *See e.g.*, *id.* 2:48-61 ("FIG. 1 represents a preferred scheme for the assay system within the invention . . . [where] [e]ach ***particle*** . . . has ***attached*** thereto numerous (+) single stranded polynucleotide segments") (emphasis added); *id.* Fig. 1 (showing nucleic acid strands attached to particles). In other embodiments, a matrix is used. *See e.g.*, *id.* 8:28-36 (describing embodiment "wherein one of

[12]This term appears in claim 123, 155, 156, 157, and 158.

the labeled single stranded polynucleotide segments is ***fixed to a matrix***") (emphasis added).

According to the patent, the particle and the matrix could also be made from the same material. *See id.* 5:46-48 ("particles can be made from a variety of materials including glass, nylon . . . polystyrene, polyvinylchloride"); *id.* 8:31-33 ("matrix, such as . . . nylon, polystyrene, polyvinylchloride or . . . glass"). While the patent explains that a particle could act as a "label," *see id.* 3:59-61, nothing indicates that this is inconsistent with the use of particle as a solid support.

Defendants point out that the specification mentions the term only once, where it is used alternatively with the term matrix. (D.I. 83 at 11) The patent states that "a polynucleotide probe can be fixed to a ***matrix or solid support***." '581 patent, Abstract (emphasis added). Certain unasserted claims also use those two terms in this way. *See e.g.*, *id.* Claim 24 ("directly or indirectly captured or capturable to a ***matrix or solid support***") (emphasis added). But this does not mean that the patent uses the two terms synonymously. *See Thorner*, 669 F.3d at 1368 ("Simply referring to two terms as alternatives or disclosing embodiments that all use the term the same way is not sufficient to redefine a claim term.").

G. "complex"[13]

Plaintiff "an entity formed by non-covalent binding"
Defendants "multiple nucleic acid strands held together by noncovalent binding between complementary portions"
Court "at a minimum including multiple nucleic acid strands held together by noncovalent binding between complementary portions"

[13]This term appears in claims 123 and 155-58.

The parties agree that the "complex" formation occurs through the non-covalent binding of molecules, but dispute whether the non-covalent binding could be between any molecular entities (Plaintiff's position) or only between complementary portions of nucleic acid molecules (Defendants' position). Plaintiff contends that the "complex is not limited to nucleic acid strands, but rather may comprise 'any ligand and receptor.'" (D.I. 84 at 8) Defendants assert that Plaintiff's construction "is in clear conflict with the language of the claims and is nothing more than an attempt by [Plaintiff] to bring disclosed, but unclaimed subject matter within the metes and bounds of the claims through claim construction." (D.I. 95 at 16)

The claim language makes clear that the complex is formed, at a minimum, between complementary nucleic acid strands. *See .e.g.*, '581 patent, claim 123 ("said third strand being capable of forming a complex ***comprising at least*** two hybrids with at least two other strands") (emphasis added); *id.* claim 155 ("strands (I), (II) and (III) under hybridizing conditions to form a complex ***comprising at least*** two hybrids") (emphasis added); *id.* claim 156 ("strands (I) and (III) under hybridizing conditions to form a first complex ***comprising at least*** one hybrid") (emphasis added); *id.* claim 157 ("each such strand being capable of forming a complex ***comprising at least*** two hybrids with at least two other of said nucleic acid strands") (emphasis added); *id.* claim 158 ("under hybridizing conditions to form ***at least*** one first complex ***comprising*** one or more hybrids") (emphasis added).

The specification also describes formation of a complex through the interaction of nucleic acid segments that are complementary to each other. *See e.g.*, *id.* 3:28-29 ("Each single stranded polynucleotide segment is complementary to the same or the opposite strand of the target genetic material."); *id.* Figs. 1-3. Contrary to Defendants' construction, however, a complex is not

limited to only nucleic acid strands.[14]

The portion of the specification on which Plaintiff relies is part of a discussion of three methods by which "the double hybrid can be detected . . . depending upon the choice of the label of each polynucleotide probe." ('581 patent, 5:26-28; *see also* D.I. 84 at 8) This is different from what is described in the claims, which is the formation of a complex between nucleotide strands. The Court also agrees with Defendants that Plaintiff's construction is too broad, covering "something not claimed." *See Lehigh Valley R Co v. Mellon*, 104 U.S. 112, 118 (1881) ("[Patentee] cannot go beyond what he has claimed and insist that his patent covers something not claimed, merely because it is to be found in the descriptive part of the specification.").

III. CONCLUSION

The Court construes the disputed terms as explained above. An appropriate Order follows.

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[14]Notwithstanding their proposed construction, Defendants do not seem to dispute that a "complex" could include more than just nucleic acid strands. (*See* Tr. at 88) (Defendants' counsel noting during oral argument: "The claim tells us what is forming the complex. It's not limiting it. It says comprising. We understand what 'comprising' means. We're okay with that.")