IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ENZO LIFE SCIENCES, INC., Plaintiff. v. GEN-PROBE, INCORPORATED, Defendant.	)	C.A. No. 12-104-LPS
ENZO LIFE SCIENCES, INC., Plaintiff. v. LIFE TECHNOLOGIES, CORPORATION, Defendant.	)	C.A. No. 12-105-LPS
ENZO LIFE SCIENCES, INC., Plaintiff. v. ROCHE MOLECULAR SYSTEMS, INC., et al., Defendants.	)	C.A. No. 12-106-LPS
ENZO LIFE SCIENCES, INC., Plaintiff. v. ABBOTT LABORATORIES, et al., Defendants.	)	C.A. No. 12-274-LPS

ENZO LIFE SCIENCES, INC., Plaintiff. v. BECTON, DICKINSON AND COMPANY; et al., Defendants.	)	C.A. No. 12-275-LPS
ENZO LIFE SCIENCES, INC., Plaintiff. v. HOLOGIC, INC., Defendant.	)	C.A. No. 12-276-LPS
ENZO LIFE SCIENCES, INC., Plaintiff. v. AFFYMETRIX, INC., Defendant.	)	C.A. No. 12-433-LPS
ENZO LIFE SCIENCES, INC., Plaintiff. v. AGILENT TECHNOLOGIES, INC., Defendant.	)	C.A. No. 12-434-LPS

ENZO LIFE SCIENCES, INC., Plaintiff. v. ILLUMINA, INC., Defendant.	)	C.A. No. 12-435-LPS
ENZO LIFE SCIENCES, INC., Plaintiff. v. SIEMENS HEALTHCARE DIAGNOSTICS, INC., Defendant.	)	C.A. No. 12-505-LPS

Brian E. Farnan, FARNAN LLP, Wilmington, DE
John M. Desmarais, Michael P. Stadnick, Jordan Malz, Justin P.D. Wilcox, Peter C. Magic, Joseph C. Akalski, Jessica A. Martinez, Danielle A. Shultz, DESMARAIS LLP, New York, NY

Attorneys for Plaintiff.

Karen L. Pascale, Pilar G. Kraman, YOUNG CONAWAY STARGATT & TAYLOR LLP, Wilmington, DE
Matthew M. Wolf, ARNOLD & PORTER LLP, Washington, DC
Jennifer Sklenar, Wallace Wu, ARNOLD & PORTER LLP, Los Angeles, CA

Attorneys for Defendants Hologic, Inc. and Gen-Probe Incorporated

Jack B. Blumenfeld, Karen Jacobs, Michael J. Flynn, MORRIS, NICHOLS, ARSHT & TUNNELL LLP, Wilmington, DE
Ron E. Shulman, Terry Kearney, Michael R. Seringhaus, LATHAM & WATKINS LLP, Menlo Park, CA
Jennifer R. Saionz, LATHAM & WATKINS LLP, New York, NY
Ryan R. Owens, LATHAM & WATKINS LLP, Costa Mesa, CA
Jennifer Koh, LATHAM & WATKINS LLP, San Diego, CA
Katherine Nolan-Stevaux, THERMO FISHER SCIENTIFIC INC., Foster City, CA

Attorneys for Defendant Life Technologies Corporation

Frederick L. Cottrell, III, Katharine C. Lester, RICHARDS, LAYTON & FINGER, P.A., Wilmington, DE
William G. McElwain, Jamie T. Wisz, WILMER CUTLER PICKERING HALE AND DORR LLP, Washington, DC
Robert J. Gunther, Jr., Jane M. Love, PhD., Omar Khan, Christopher R. Noyes, WILMER CUTLER PICKERING HALE AND DORR LLP, New York, NY
Gregory P. Teran, WILMER CUTLER PICKERING HALE AND DORR LLP, Boston, MA
William W. Kim, WILMER CUTLER PICKERING HALE AND DORR LLP, Palo Alto, CA

Attorneys for Defendants Becton, Dickinson and Company, Becton Dickinson Diagnostics Inc., and Geneohm Sciences, Inc., Roche Molecular Systems, Inc., Roche Diagnostics Operations, Inc., Roche Diagnostics Corporation, and Roche NimbleGen, Inc.

Richard L. Horwitz, David E. Moore, Bindu A. Palapura, POTTER ANDERSON & CORROON LLP, Wilmington, DE
James F. Hurst, Maureen Rurka, Elizabeth Thompson, WINSTON & STRAWN LLP, Chicago, IL
Melinda Lackey, WINSTON & STRAWN LLP, Houston, TX

Attorneys for Defendants Abbott Laboratories and Abbott Molecular Inc.

Denise S. Kraft, Brian A. Biggs, DLA PIPER LLP, Wilmington, DE
John Guaragna, Aaron G. Fountain, DLA PIPER, Austin, TX
Stanley Panikowski, Erica Pascal, DLA PIPER, San Diego, CA

Attorneys for Intervenor-Defendant and Counterclaim-Plaintiff Luminex Corporation

Jack B. Blumenfeld, Maryellen Noreika, Derek J. Fahnestock, MORRIS, NICHOLS, ARSHT & TUNNELL LLP, Wilmington, DE
Michael J. Malecek, Peter E. Root, Sean M. Boyle, KAYE SCHOLER LLP, Palo Alto, CA

Attorneys for Defendant Affymetrix Inc.

Jack B. Blumenfeld, Maryellen Noreika, Derek J. Fahnestock, Paul Saindon, Ethan H. Townsend, MORRIS, NICHOLS, ARSHT & TUNNELL LLP, Wilmington, DE

Attorneys for Defendant Agilent Technologies, Inc.

Steven J. Balick, Lauren E. Maguire, ASHBY & GEDDES, Wilmington, DE
Kevin M. Flowers, Mark H. Izraelewicz, Cullen N. Pendleton, Amanda K. Antons, MARSHALL, GERSTEIN & BORUN LLP, Chicago, IL

Attorneys for Defendant Illumina, Inc.

Jack B. Blumenfeld, Derek J. Fahnestock, MORRIS, NICHOLS, ARSHT & TUNNELL LLP, Wilmington, DE
Nagendra Setty, George L. Kanabe, ORRICK, HERRINGTON & SUTCLIFFE LLP, San Francisco, CA
Anthony C. Kuhlmann, ORRICK, HERRINGTON & SUTCLIFFE LLP, Irvine, CA
Ryan C. Micallef, ORRICK, HERRINGTON & SUTCLIFFE LLP, New York, NY

Attorneys for Defendants Siemens Healthcare Diagnostics Inc.

MEMORANDUM OPINION

July 7, 2015
Wilmington, Delaware

STARK, U.S. District Judge:

Plaintiff Enzo Life Sciences, Inc. ("Plaintiff" or "Enzo") filed patent infringement actions against Defendants Abbott Laboratories, Abbott Molecular Inc., Luminex Corp., Becton, Dickinson and Company, Becton Dickinson Diagnostics Inc., Geneohm Sciences, Inc., Gen-Probe, Inc., Hologic, Inc., Life Technologies Corp., Luminex Corp., Roche Molecular Systems, Inc., Roche Diagnostics Corp., Roche Diagnostic Operations, Inc., and Roche Nimblegen, Inc. ("Defendants") for infringement of one or more of the following patents: U.S. Patent No. 7,064,197 ("the '197 patent"),[1] U.S. Patent No. 6,992,180 ("the '180 patent"),[2] and U.S. Patent No. 8,097,405 ("the '405 patent").[3] The '180 and '405 patents, which relate generally to nucleic acid detection technology, are part of the same family and share nearly identical specifications.

Pending before the Court is the issue of claim construction of various disputed terms of the patents-in-suit. The parties completed briefing on claim construction on July 22, 2014. (C.A. No. 12-274-LPS D.I. 133; C.A. No. 12-104-LPS D.I. 77) In addition to the briefing, the parties also submitted technology tutorials. (C.A. No. 12-274-LPS D.I. 163, 164; C.A. No. 12- 104-LPS D.I. 91, 92) The Court held a *Markman* hearing on August 18, 2014. (*See* C.A. No. 12-274-LPS D.I. 133; C.A. No. 12-104-LPS D.I. 77) ("Tr.")

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[1] The '197 patent is entitled "System, array and non-porous solid support comprising fixed or immobilized nucleic acids," issued on June 20, 2006, and claims priority to January 27, 1983.

[2] The '180 patent is entitled "Oligo- or polynucleotides comprising phosphate-moiety labeled nucleotides," issued on January 31, 2006, and claims priority to June 23, 1982.

[3] The '405 patent is entitled "Nucleic Acid Sequencing Processes Using Non-Radioactive Detectable Modified or Labeled Nucleotides or Nucleotide Analogs, and Other Processes For Nucleic Acid Detection and Chromosomal Characterization Using Such Non-Radioactive Detectable Modified or Labeled Nucleotides or Nucleotide Analogs," issued on January 17, 2012, and claims priority to June 23, 1982.

I. LEGAL STANDARDS

The ultimate question of the proper construction of the patent is a question of law. *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." *Phillips*, 415 F.3d 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." *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004) (internal quotation marks omitted), *aff'd*, 481 F.3d 1371 (Fed. Cir. 2007).

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 ordinary 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).

II. THE '197 PATENT[4]

A. Agreed-Upon Claim Terms

The parties agree on the proper construction for the following claim terms:

Claim Term/Phrase	**Agreed-Upon Construction**
hybridizable form	Capable of binding through Watson-Crick base pairing
Various	having different nucleotide sequences

The Court will adopt the agreed-upon constructions.

B. Disputed Claim Terms

1. "non-porous"

Plaintiff's Proposal:	No construction necessary.[5]
Or in the alternative	Not full of minute holes through which fluid may pass
Defendants'[6] Proposal:	Having no pores, *e.g.*,, having no nooks or crannies

[4] All citations in Section II are to C.A. No. 12-274-LPS, unless specified otherwise.

[5] Plaintiff's primary preference with respect to each of the disputed terms in the '197 patent is for the Court to simply adopt the plain language. However, as was made clear during the claim construction hearing, there are genuine disputes with respect to the proper construction of each of the terms discussed here. Under these circumstances, adopting an unspecified "plain meaning" would leave the door open to multiple reasonable constructions to be advocated later in the case, with the nearly-certain improper result that the parties would try claim construction to the factfinder.

Life Technologies' Proposal:	A solid support having an impermeable surface without pores, *e.g.*, without nooks and crannies[7]
Court's Construction:	Having no pores

The parties have two primary disputes with respect to "non-porous."[8] First, they dispute whether "non-porous" means "not full of holes," "having no pores," or "having an impermeable surface without pores." Second, the y dispute whether pores are "minute holes through which fluid may pass" or, instead, are "nooks and crannies."

The patent specification identifies "non-porous" materials "such as glass, or alternatively, plastic, polystyrene, polyethylene, dextran, polypropylene, and like" and contrasts these with "[c]onventional porous materials, e.g., nitrocellulose filters." ('197 patent, col. 6 ll. 4-9; *see also* D.I. 201 at 3 ("Enzo's construction is grounded in the intrinsic evidence, which cites glass, plastic, and polystyrene as examples of non-porous materials – none of which permit the passage of fluid – and a filter as an example of a porous material – which does permit the passage of fluid.")) Beyond this, however, the specification provides little additional guidance as to the proper construction of "non-porous."

The prosecution history makes clear that "[t]he key to the invention was getting nucleic acids to reliably bind in hybridizable form to the *surface* of a non-porous material . . ." (D.I. 161-62 Ex. B-8 at ENZO-0019424) (emphasis in original) "As the nucleic acids form a monolayer, saturating the surface . . . the nucleic acids are favorably placed to take part in

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[6] All Defendants except Life Technologies.

[7] Life Technologies takes the position that the larger phrase "non-porous solid support" should be construed as a whole, rather than in two separate parts, which is the position of Plaintiff and the remainder of the Defendants. Ho wever, since Life's proposal only construes the phrase "non-porous" and incorporates the term "solid support" into its proposal, the Court finds Life's construction is essentially a competing construction for "non-porous."

hybridization reactions. Interactions with the solutions phase are much faster, because molecules do not have to diffuse into and out of the pores." (*Id.* at ENZO-0019427) This history supports Defendants' contention that "non-porous" means "having no pores."

Enzo's alternative construction, adding "not full of minute holes," creates ambiguity. (*See* C.A. 12-106 D.I. 108 at 3) Under this construction, a glass plate with a single pore would not be considered porous (because it would not be "full" of pores), even thought it would allow fluid to travel into and out of the support. The Court also rejects Defendants' addition of "nooks and crannies," as this limitation is not required by any intrinsic evidence (including the prosecution history). (*See* D.I. 161-62 Ex. B-8 at ENZO-0019427 ("The uniformity of these non- porous solid supports, which stands in contrast to the nooks and crannies of porous supports in the prior art. . . ")) Lastly, Life Technologies' proposal would improperly read into the claim language a limitation based solely on the disclosed embodiments in the specification, a limitation that is not present in the claim itself.

2. "solid support"

Plaintiff's Proposal:	No construction necessary.
Or in the alternative:	solid structure
Defendants' Proposal:	a solid structure for containing fluid
Court's Construction:	a solid structure

The parties dispute whether a solid support must "contain[] fluid." As is evident from the plain language of the claims and the intrinsic evidence, the shape of the claimed support is not limited. Defendants' proposed limitation is based on the disclosed embodiments in the

specification, and the assumption that the support must "contain[] fluid" in order for the soluble signaling moiety to dissolve. (*See* C.A. 12-106 D.I. 98 at 12 ("The ability to contain fluid is critical because the hybridization assays of the '197 patent all involve the use of a soluble signal and the solid support must be able to contain the fluid solution in which the soluble signal is dissolved."))

But Defendants' proposed limitation is not supported by the claim language. Claims 33 and 40 refer to solid supports comprising "a plate or plates." ('197 patent, col. 17 ll. 9-10, 32-33) While Defendants argue that this must be in reference to the flat, plate-like surface of a petri dish,[9] that is not what is stated in the claims. The prosecution history also refers to a slide as solid support. (*See* D.I. 161-60 Ex. B-3 at ENZO-0017734) Defendants' construction would read disclosed embodiments out of the claims.[10]

3. "array"

Plaintiff's Proposal:	No construction necessary. *Or in the alternative*: an orderly grouping or arrangement
Defendants' Proposal:	one or more solid supports having a defined, ordered arrangement of separate fluid-containing areas
Court's Construction:	an orderly grouping or arrangement

[9] A petri dish, Defendants argue, contains liquid. Other examples of "plates" which contain fluid in the specification include: "[G]lass plates" with wells or depressions ('197 patent, col. 8 ll. 66-67); "microtiter well plates (*id.* at col. 12 ll. 54-58); and "polystyrene plates" (*id.* at col. 11 l. 58, col. 12 ll. 8-10).

[10] Defendants assume, and additionally argue, that the solid support must contain fluid because the soluble signal of the signaling moiety must be dissolved in liquid. This position is based on Defendants' proposed construction of "signaling moiety" which, as explained below, the Court has rejected.

The parties have two disputes related to the construction of "array": (1) whether an "array" is a "defined, ordered arrangement" or instead an "orderly grouping or arrangement," and (2) whether the "array" requires separate fluid-containing areas.

The phrase "orderly grouping or arrangement," as proposed by Enzo, comes from the prosecution history. (*See* D.I. 161-62 Ex. B-8 at ENZO-0019445 ("The everyday meaning of array is an orderly grouping or arrangement.")) Defendants contend that in order to identify the hybridized nucleic acids, the arrangement must be "defined, ordered." (*See id.* at ENZO-0019444) The support for Defendants' narrower proposal are statements in the prosecution history which do not refer to the present invention. (*See* D.I. 161-86 at ENZO-0019002, ENZO-0018989 ("ordered"); D.I. 161-62 at ENZO-0019444 ("defined")) The Court adopts Plaintiff's proposal of an "orderly grouping or arrangement."

The term "array" appears in claims 17, 18, 19, 20, 21, and 22 in reference to "an array comprising [various] . . . nucleic acids." ('197 patent, col. 15 l. 51 – col.16 l. 14) "Array" is also in claims 25 and 26, which are expressly limited to "an array comprising various . . . nucleic acids fixed or immobilized . . . to a non-porous support having wells or depressions." ('197 patent, col. 16 ll. 20-28) Defendants' effort to limit "array" based on the specification's reference to "glass plates provided with an array of depressions or wells" ('197 patent, col. 8 ll. 66-67) is inconsistent with the use of the term in the various claims noted above: claims 17-22 do not call out arrays having depressions or wells, unlike claims 25 and 26 (which do). It follows that the patentee limited some, but not all, claims to arrays having depressions or wells.[11]

[11] As suggested by the parties at the hearing, the Court's decision on this dispute is

4. "one or more amine(s) hydroxyl(s) or epoxide(s) thereon," "via said one or more amine(s), hydroxyl(s) or epoxide(s)"

Plaintiff's Proposal:	No construction necessary.
Or in the alternative:	one or more amine(s), hydroxyl(s) or epoxide(s) on the solid support; through said one or more amine(s), hydroxyl(s) or epoxide(s) on the solid support
Defendants' Proposal:	one or more amine(s), hydroxyl(s) or epoxide(s) present on the solid support; by said one or more amine(s), hydroxyl(s), or epoxide(s) that are present on the solid support
Court's Construction:	one or more amine(s), hydroxyl(s) or epoxide(s) present on the solid support; by said one or more amine(s), hydroxyl(s), or epoxide(s) that are present on the solid support

At the hearing, the parties indicated that this term is no longer in dispute. (*See* Tr. 69, 72)

5. "signaling moiety"

Plaintiff's Proposal:	that portion of a label which on covalent attachment or non-covalent binding to a polynucleotide or oligonucleotide sequence or to a bridging moiety attached or bound to that sequence provides a signal for detection of the label
Defendants' Proposal:	that portion of a label which on covalent attachment or non-covalent binding to a polynucleotide or oligonucleotide sequence or to a bridging moiety attached or bound to that sequence provides a soluble signal for detection of the label
Court's Construction:	that portion of a label which on covalent attachment or non-covalent binding to a polynucleotide or oligonucleotide sequence or to a bridging moiety attached or bound to that sequence provides a signal for detection of the label

The '197 patent defines the "signaling moiety" as "[t]hat portion of a label which on covalent attachment or non-covalent binding to a polynucleotide or oligonucleotide sequence or to a bridging moiety attached or bound to that sequence provides a signal for detection of

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largely compelled by its resolution of the earlier dispute over "solid support." (*See* Tr. 59, 60)

the label." ('197 patent, col. 2 ll. 1-5) The parties' dispute is whether that signal must be ***soluble***. Defendants argue that the specification and prosecution history clearly show that the present invention contemplates only a soluble signal.

"[A] definition set forth in the specification governs the meaning of the claims. When the specification explains and defines a term used in the claims, without ambiguity or incompleteness, there is no need to search further for the meaning of the term." *Sinorgchem Co., Shandong v. Int'l Trade Comm'n*, 511 F.3d 1132, 1138 (Fed. Cir. 2007) (internal citations omitted). In this case, while the specification language repeatedly mentions soluble[12] signals, it also contains a definition, which does not limit the signaling moiety to a soluble signal.

Defendants rely on *Trading Techs. Int'l, Inc. v. eSpeed, Inc.*, 595 F.3d 1340, 1353 (Fed. Cir. 2010), to argue that the Court can reconstrue a claim "based on its . . . understanding of the claims, specification, prosecution history, and record," notwithstanding an express definition in a specification. Even so, here Defendants provide no persuasive basis for the Court to reconstrue "signaling moiety" to mean anything other than the special definition it is given in the specification. Unlike in *Trading Technologies*, where the definition in the specification "expressly promise[d] to discuss [the relevant term] later in the specification," and the Court's construction took account of that later discussion (*id.*), here the definition of "signaling moiety" is set forth completely in one place in the specification.

Furthermore, during prosecution, the patentee removed the word "soluble" from its

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[12] The only explicit reference to an ***insoluble*** signal is in reference to prior art. ('197 patent, col. 4 l. 66 - col. 5 l. 4)

claims. (*See* D.I. D.I. 161-66 Ex. B-5 at ENZO-0018106) Claims 66 and 67 contain limitations requiring the signaling moiety to be "quantifiable in or from a fluid or solution," which would be redundant if signaling moiety were limited to soluble signals.

6. "double-stranded"

Plaintiff's Proposal:	No construction necessary.
Or in the alternative:	two nucleic acid strands hybridized to each other
Defendants' Proposal:	two nucleic-acid strands hybridized to each other throughout their entire length
Court's Construction:	two nucleic acid strands hybridized to each other

The parties dispute whether the individual strands of the "double-stranded" nucleic acid need to be "hybridized to each other throughout their entire length." Defendants contend that Enzo disavowed any partial double-strandedness during prosecution, so this claim term must be construed to mean that the two nucleic acid strands cannot be hybridized along just a portion of the entire length. Enzo responds that the amendments removing partial double-strandedness claims advanced the prosecution of the claims but do not constitute a disclaimer of claim scope.

The doctrine of prosecution history disclaimer applies to unambiguous disavowals. *See Grober v. Mako Prods., Inc.*, 686 F.3d 1335, 1341 (Fed. Cir. 2012) ("When a patentee makes a 'clear and unmistakable disavowal of scope during prosecution,' a claim's scope may be narrowed under the doctrine of prosecution disclaimer"). The burden of demonstrating such a disclaimer is a heavy one.

Here, the Examiner stated that "double-stranded lacks any specificity such as partial character for this limitation." (D.I. 161-92 Ex. B-83 at ENZO-018733) Enzo contends that it

did not accept this position when it cancelled claims covering "partially double-stranded" nucleic acids, and that it cancelled the claims solely to advance the prosecution of the application. (*See* D.I. 161-92 Ex. B-84 at ENZO-0018744 ("In yet another sincere effort, this time to advance prosecution of this application by reducing or simplifying the issues for possible appeal, Applicants have canceled pending claims 718-1265."))

Defendants have not shown a clear and unmistakable disavowal. The Court has found no express statement in the prosecution history indicating why the patentee made the amendments. The uncertainty and ambiguity in the prosecution history weighs against finding a disavowal. *See 01 Communique Lab., Inc. v. LogMeIn, Inc.*, 687 F.3d 1292, 1297 (Fed. Cir. 2012) ("There is no clear and unmistakable disclaimer if a prosecution argument is subject to more than one reasonable interpretation, one of which is consistent with a proffered meaning of the disputed term.") (internal quotation marks omitted) Defendants have failed to persuade the Court that the patentee's tactical decision to cancel claims expressly covering partial strandedness means that the claims it was issued require the Court to construe "double stranded" in a manner that excludes partial strandedness.

7. "double-stranded nucleic acid is fixed or immobilized" [and similar terms]

Plaintiff's Proposal:	No construction necessary.
Or in the alternative:	two hybridized nucleic acid strands bound
Defendants' Proposal:	two hybridized nucleic acid strands fixed to the non-porous solid support in which one strand is an (unlabeled) analyte and the other strand is a (labeled) probe
Court's Construction:	two hybridized nucleic acid strands bound

The parties dispute whether the two nucleic acid strands that comprise the claimed

"double-stranded nucleic acid" are limited to the preferred embodiment. The Court agrees with Plaintiff that the claim scope is not limited to the preferred embodiment and, therefore, adopts Plaintiff's alternative proposed construction. *See Kara Tech. Inc. v. Stamps.com Inc.*, 582 F.3d 1341, 1348 (Fed. Cir. 2009) ("The claims, not specification embodiments, define the scope of patent protection. The patentee is entitled to the full scope of his claims, and we will not limit him to his preferred embodiment or import a limitation from the specification into the claims.").

In addition, in each claim reciting a double-stranded nucleic acid, one of the strands is identified as having a signaling moiety attached thereto. (*See, e.g.,* '197 patent, col. 14 ll. 1-11 ("at least one double-stranded nucleic acid is fixed or immobilized . . . and wherein one nucleic acid strand of said . . . double-stranded nucleic acid has covalently attached" to a signaling moiety); *see also id.* at ll. 12-45) If the Court were to construe "double-stranded nucleic acid is fixed or immobilized" to include the limitation proposed by Defendants – identifying one strand as labeled and the other as unlabeled – the wherein clause contained in those claims would be rendered redundant.

8. "single-stranded nucleic acid is fixed or immobilized" and similar terms, "nucleic acid strand or sequence fixed or immobilized," "nucleic acid is fixed or immobilized," "DNA or RNA is fixed or immobilized"

Plaintiff's Proposal:	No construction necessary.
Or in the alternative:	single-stranded nucleic acid is bound; single-stranded nucleic acids bound; single-stranded nucleic acids are bound; nucleic acid strand or sequence bound; nucleic acid is bound; DNA or RNA is bound
Defendants' Proposal:	a non-hybridized nucleic acid strand of an analyte, or its complementary sequence (for indirect fixation of the analyte),

	that is fixed to the non-porous solid support
Court's Construction:	single-stranded nucleic acid is bound; single-stranded nucleic acids bound; single-stranded nucleic acids are bound; nucleic acid strand or sequence bound; nucleic acid is bound; DNA or RNA is bound

The parties' dispute is similar to the one just discussed with respect to the "double-stranded nucleic acid is fixed or immobilized" term. Defendants argue their construction is necessary to prevent the claims from being expanded beyond what is disclosed in the specification. Enzo counters that Defendants' extraneous limitations are not supported by the intrinsic evidence. The Court again agrees with Plaintiff.

Defendants assert that "[t]he specification does not make a single reference to any hybridization assay format in which the fixed single-stranded nucleic acid is anything other than an analyte or a complementary sequence to an analyte." (*See* C.A. 12-106 D.I. 98 at 21) This is not a persuasive basis for importing Defendants' proposed limitations into the claim. The claim language requires that a single-stranded nucleic acid is fixed or immobilized, but Defendants would narrow the claim scope substantially further, without justification.

9. "wherein one nucleic acid strand of said at least one double-stranded nucleic acid" [and similar terms]

Plaintiff's Proposal:	No construction necessary.
Or in the alternative:	a labeled polynucleotide or oligonucleotide which is hybridized with another polynucleotide or oligonucleotide
Defendants' Proposal:	a labeled polynucleotide or oligonucleotide which is complementary to and hybridized with an analyte
Court's Construction:	a labeled polynucleotide or oligonucleotide which is hybridized with another polynucleotide or oligonucleotide

The parties dispute whether this term should be construed to require that the labeled

polynucleotide or oligonucleotide be complementary to and hybridized with an analyte. Plaintiff argues that these are improper limitations on the claims, while Defendants point to several portions of the specification which disclose that the probe, or the complementary sequence, attaches to an analyte.

The background section of the specification defines analyte as "a substance or substances . . . whose presence is to be detected." ('197 patent, col. 1 ll. 37-38) The "probe" "is complementary to a polynucleotide or oligonucleotide sequence of a particular analyze and . . . hybridizes to said analyte sequence." ('197 patent, col. 1 ll.51-55) The "label" generates a "signal for detection of the hybridized probe and analyte." ('197 patent, col. 1 ll. 56-57) Defendants construct their proposal from these statements in the specification.

Enzo contends that Defendants are impermissibly seeking to limit the claim terms. Just as with other terms already discussed, the Court agrees. The Court does not read the portions of the specification on which Defendants rely as meaning to limit the scope of the claims to certain embodiments.

The parties agree that "wherein one nucleic acid strand" refers to "a labeled polynucleotide or oligonucleotide." But Defendants' proposed construction attempts also to identify the type of strand which should be labeled. The specification does not support such an additional limitation. (*See* '197 patent, col. 8 ll. 13-18 ("[T]he present invention provides for the novel product of a non-porous solid support to which a polynucleotide is directly fixed in hybridizable form. Such a fixed sequence may be hybridized to another polynucleotide sequence . . .").)

III. THE '180 PATENT[13]

A. Agreed-Upon Claim Terms

The parties agree on the proper construction of the following claim terms:

Claim Term/Phrase	
An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof	The preamble is limiting
said oligo- or polydeoxy-ribonucleotide	said oligo- or polynucleotide
Hybridized	bound through Watson-Crick base pairing

The Court will adopt the agreed-upon constructions.

B. Disputed Claim Terms

1. "modified nucleotide" / "modified nucleotide analog"

Plaintiff's Proposal:	No construction necessary.
Or in the alternative:	nucleotide [analog] that is labeled with a Sig.
Defendants' Proposal:	Mononucleotide [analog] that is labeled with a Sig moiety before incorporation into said oligo- or polynucleotide
Court's Construction:	nucleotide [analog] that is labeled with a Sig.

The parties have two primary disputes with respect to the "modified nucleotide" / "modified nucleotide analog" terms. First, they dispute whether the nucleotide has to be a ***mono***nucleotide. Second, they dispute whether this nucleotide must be labeled with a Sig moiety before it is incorporated into an oligo- or polynucleotide.

The disputed term appears in independent claims 1, 29, 59, and 87. In claim 1, a "modified nucleotide" is claimed as follows: "said oligo- or polynucleotide comprising at least one modified nucleotide or modified nucleotide analog having the formula Sig-PM-SM-

[13] All citations in Section III are to C.A. No. 12-104-LPS, unless otherwise specified.

BASE." ('180 patent, col. 59 ll. 63-67) Defendants seize upon the "at least one modified nucleotide" language to argue that a modified nucleotide must be a mononucleotide, distinguishing it from the oligo- and polynucleotides referenced earlier. The specification teaches preparing modified oligo- and polynucleotides along with modified mononucleotides. (*See, e.g.*, '180 patent, col.17 ll. 36-39 ("Modified oligo- or polynucleotides can also be prepared by chemical modification of existing oligo- or poly-nucleotides using the approach described previously for modification of individual nucleotides.")) If the patentee had intended to limit the modified nucleotide to a modified mononucleotide, the patentee could have done so.

Defendants further argue that the patentee clearly disclaimed claim scope and limited "modified nucleotide" to a mononucleotide during reexamination of the related U.S. Patent No. 5,241,060 ("the '060 patent"), by representing to the PTO that:

> the patent relates to hybridization probes that are formed by **first labeling a <u>mononucleotide</u>** with a detectable moiety (termed 'Sig' in the patent), **and *subsequently* incorporating the labeled mononucleotide** into an oligo- or polynucleotide probe using a polymerase (e.g., a terminal transferase).

(D.I. 93 at 10) (emphasis in original) However, while the '060 patent and the '180 patent share a common specification, the term "modified nucleotide" does not appear in the claims of the '060 patent, and the patentee did not limit the scope of the claims in the '180 patent in the context of the reexamination of the '060 patent.

Defendants also argue that the modified nucleotide must be modified, i.e., labeled, before being incorporated into an oligo- or polynucleotide. In support of this position, Defendants rely on what they assert is functional language in at least claim 1, that limits the claimed product ("an oligo- or polynucleotide"). Claim 1 recites:

> wherein said Sig comprises a non-polypeptide . . . label moiety which can be directly or indirectly detected when attached to PM or ***when said modified nucleotide is incorporated into said oligo- or polynucleotide*** or when said oligo- or polynucleotide is hybridized . . . .

('180 patent, col. 60 ll. 10-15) (emphasis added) The Court does not read the emphasized language as placing a temporal limitation on when a modified nucleotide is incorporated into an oligo- or polynucleotide. Instead, the emphasized language describes one of the three states in which the Sig must be detectable. The language most naturally recites the limitation that: the Sig can be directly or indirectly detected if it is attached to a PM, or if the modified nucleotide is incorporated into the oligo- or polynucleotide, or if the oligo- or polynucleotide is hybridized. Because neither the intrinsic record nor any extrinsic evidence limits the "modified nucleotide" or "modified nucleotide analog" terms in the manner proposed by Defendants, the Court will adopt Plaintiff's broader construction.

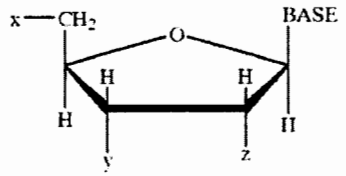
2. "said analog"

Plaintiff's Proposal:	Not indefinite under 35 U.S.C. §112(2). The "said analog" refers to "pyrimidine analog," "purine analog," or "deazapurine analog."
Defendant's Proposal:	Indefinite under 35 U.S.C. §112(2).
Court's Construction:	The "said analog" refers to "pyrimidine analog," "purine analog," or "deazapurine analog."

The parties dispute whether the "said analog" term is indefinite under 35 U.S.C. §112(2). Under §112(2), "[t]he specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention." According to Defendants, this term is indefinite because claims 1, 29, 59, and 87 – in which the "said analog" term appears -- recite four

different "analog" terms, each of which could potentially serve as the antecedent basis for "said analog."

Representative claim 29 recites:

> An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide comprising at least one modified nucleotide or a ***modified nucleotide analog*** having the structural formula
>
> 
>
>
> wherein BASE is a moiety comprising a pyrimidine, ***a pyrimidine analog***, a purine, ***a purine analog***, a deazapurine or ***a deazapurine analog***, wherein ***said analog*** can be attached to or coupled to or incorporated into DNA or RNA, wherein ***said analog*** does not substantially interfere with double helix formation or nucleic acid hybridization, and wherein said BASE is attached to the 1' position of the furanosyl ring from the N1 position when said BASE is a pyrimidine or a pyrimidine analog, or from the N9 position when said BASE is a purine, a purine analog, a deazapurine or a deazapurine analog;

('180 patent, col. 6 l. 52 – col. 62 l. 8) (all emphases added) Defendants contend that "said analog," which appears twice in the claim, could refer to "modified nucleotide analog," "pyrimidine analog," "purine analog," or "deazapurine analog." Plaintiff argues that in both instances, "said analog" refers to the listed BASE moieties, i.e., the purine analog, pyrimidine analog, or deazapurine analog.

"[A] patent is invalid for indefiniteness if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention." *Nautilus, Inc. v. Biosig Instruments,*

Inc., 134 S. Ct. 2120, 2124 (2014).

Defendants have failed to show by clear and convincing evidence that a person of ordinary skill in the art would fail to understand, with reasonable certainty, the meaning of "said analog" in the asserted claims. As Plaintiff has explained (*see* Tr. 127-34), the structure of the claim language, including the proximity of the analog limitations to the base analogs, as well as the prosecution history (in which the patentee made an amendment to overcome an indefiniteness challenge), all support Plaintiff's proposed construction. Accordingly, the Court finds that the "said analog" term is not indefinite and adopts Plaintiff's proposed construction.

3. "Sig being covalently attached to PM" / "Sig is covalently attached directly or through a non-nucleotidyl chemical linkage to at least one phosphate"

Plaintiff's Proposal:	No construction necessary
Or in the alternative:	Sig being covalently attached to a phosphate moiety/Sig is covalently attached directly or through a non-nucleotidyl chemical linkage to at least one phosphate moiety
Defendants' Proposal:	Sig being covalently attached to the phosphate moiety of a nucleotide/Sig is covalently attached . . . to at least one phosphate of a nucleotide
Court's Construction:	Sig being covalently attached to a phosphate moiety/Sig is covalently attached directly or through a non-nucleotidyl chemical linkage to at least one phosphate moiety.

The parties essentially dispute whether the Sig moiety must be attached to a full nucleotide (or nucleotide analog)[14] or whether the Sig moiety may be attached to the phosphate moiety before the Sig-phosphate complex is attached to an SM-Base nucleoside.

[14] Plaintiff argues that Defendants' construction would read out "or nucleotide analog" from the claim language but Defendants have represented that the omission was inadvertent. Defendants' amended construction would include "or nucleotide analogs." (*See* D.I. 106 at 1 n.2)

The disputed claim terms appear in claims 1, 13, 29, 41, 59, 71, 87, and 99. As a representative example, claim 1 recites:

> An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide or modified nucleotide analog having the formula
>
> Sig-PM-SM-BASE
>
> . . .
>
> attached to SM, said BASE being attached to SM, and said Sig being covalently attached to PM directly or through a non-nucleotidyl chemical linkage, and wherein said Sig comprises a non-polypeptide, non-nucleotidyl, non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is . . . incorporated into said oligo- or polynucleotide or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof . . . .

('180 patent, col. 59 l. 62 – col. 60 l. 21) Claim 1, like the other relevant claims, is a product claim directed to an oligo- or polynucleotide. The claim, and the specification, only disclose formulating this oligo- or polynucleotide by attaching the Sig moiety to a nucleotide. However, neither the claims nor the specification limit the claimed product to a process of making it. *See Hazani v. U.S. Int'l Trade Comm'n*, 126 F.3d 1473, 1479 (Fed. Cir. 1997) (distinguishing between product and product-by-process claims). Under Plaintiff's proposed construction, the final product would still be the claimed oligo- or polynucleotide.

Unlike in *Miken Composites, L.L.C. v. Wilson Sporting Goods Co.*, 515 F.3d 1331, 1337 (Fed. Cir. 2008), where the United States Court of Appeals for the Federal Circuit found that the term "insert" connoted both structure and function in a product patent, no analogous term here functionally limits the manner in which the final product is assembled. Because the claims simply require the eventual creation of a modified nucleotide or modified

nucleotide analog – without limiting the manner in which those modified nucleotides/nucleotide analogs are created – the Court will not read such a limitation into the claims. Accordingly, the Court will adopt Plaintiff's broader construction.

4. "complementary"

Plaintiff's Proposal:	Containing sufficient corresponding Watson-Crick bases to bind
Defendant's Proposal:	The corresponding Watson-Crick base(s)
Court's Construction:	The corresponding Watson-Crick base(s)

Plaintiff contends that the parties' dispute regarding the construction of the "complementary" term is based on whether a perfect match between each of the Watson-Crick bases of the oligo- or polynucleotide is needed for two oligo- or polynucleotides to hybridize. Plaintiff argues that a perfect match is not necessary; Defendants, in Plaintiff's view, contend that a perfect match is necessary. In actuality, however, Plaintiff's construction of "complementary" is more accurately directed at a construction of the entire "said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof" term instead of the standalone term "complementary." (*See* '180 patent, col. 59 l. 62 – col. 60 l. 21)

The parties have already agreed that "hybridized" means "bound through Watson-Crick base pairing." (D.I. 88-1 Ex. A at 15) Plaintiff essentially seeks to import the "or a portion thereof" language into the "complementary" term. Plaintiff argues that "the specification, like the claims, plainly does not require a 100% match for two strands of nucleic acids to be complementary." (D.I. 107 at 15) That is not entirely accurate. The claims and the specifications do not require a 100% match for two strands to ***hybridize***, but this does not necessarily mean a 100% match is unnecessary for two strands ***to be complementary***. (*See, e.g.*,

'180 patent, col. 54 ll. 33-42) Neither the specification nor the intrinsic record do anything to alter the plain and ordinary meaning of "complementary." (*See* D.I. 93 Ex. 4 at 177 ("James Watson and Francis Crick conceived the idea of specific interactions between complementary bases: A with T or U, and G with C."); '180 patent, col. 58 ll. 13-22 ("where A and B are complementary base pairs"); D.I. 88-10 Ex. A-10 at ENZO-0013420 (traversing but not contesting Examiner statement that "[t]he probe sequence will be at least substantially complementary to a gene coding for a product characteristic of a pathogen . . . . The probe need not have perfect complementarity to the sequence to which it hybridizes; there may be 30% or more of mismatched pairs")) "Complement," therefore, refers to the corresponding Watson-Crick base(s). Substantial complementarity or complementarity sufficient for hybridization may indeed require "contain[ing] sufficient corresponding Watson-Crick bases to bind" but those terms are not being construed here. Accordingly, the Court will adopt Defendant's more accurate construction of the term in dispute.

5. "nucleotide analog"

Plaintiff's Proposal:	No construction necessary.
Or in the alternative:	variant of a nucleotide
Defendants' Proposal:	Sugar, phosphate or base analog of a mononucleotide suitable as a substitute for a naturally occurring nucleotide
Court's Construction:	Variant of a nucleotide with a sugar analog, phosphate analog, and/or base analog.

The parties all agree that a nucleotide analog must comprise a sugar analog, phosphate analog, and/or base analog. (*See* D.I. 95 at 7; C.A. No. 12-274 D.I. 167 at 12) The only dispute is whether the "suitable as a substitute for a naturally occurring nucleotide" language is an "essential element" of a nucleotide analog. Defendants contend that this limitation is

essential because of the following passage in the specification:

> Several essential criteria must be satisfied in order for a modified nucleotide to be generally suitable as a substitute for a radioactively-labeled form of a naturally occurring nucleotide.

('180 patent, col. 5 ll. 42-45) Defendants read the foregoing passage as limiting "nucleotide analog" to "substitute[s] for . . . naturally occurring nucleotide." However, in context, the passage is not discussing "nucleotide analogs," but is instead discussing a "modified nucleotide." A few lines before the cited passage, the specification references modified nucleotide as "[n]ucleotides modified in accordance with the practices of this invention." (*Id.* at col. 5 ll. 27-28) A modified nucleotide is a nucleotide that has been modified so that it is labeled with a Sig moiety instead of being labeled radioactively, a practice taught in the prior art. The cited passage sheds no light on whether a "nucleotide analog" must be "suitable as a substitute for a naturally occurring nucleotide."

Because there is no evidence in the intrinsic record (including the prosecution history on which Defendants rely) that the patentee intended for "nucleotide analog" to mean anything other than its plain and ordinary meaning, the Court will not import the limitation proposed by Defendants into the term's construction. However, the Court's construction will clarify that a "nucleotide analog" must comprise a "sugar analog, phosphate analog, and/or base analog."

IV. THE '405 PATENT[15]

A. Disputed Claim Terms

1. "hybridizing specifically" terms

Plaintiff's Proposal:	Preferentially hybridizing to a nucleic acid of interest
Defendants' Proposal:	Complementary to over 90% of the nucleotides in the nucleic acid sequence of interest and hybridizing to the nucleic acid sequence of interest and no other nucleic acid
Court's Construction:	Hybridizing to the nucleic acid sequence of interest and no other nucleic acid sequence

The parties primarily dispute whether there was a clear disavowal of claim scope during prosecution of the '405 patent. As a representative example, claim 63 of the '405 patent states:

> 63. A process for determining whether the number of copies of a particular chromosome in a cell is normal or abnormal, the process comprising: providing at least one cell; contacting said cell under hybridizing conditions with one or more clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are capable of ***hybridizing specifically*** to a locus or loci of said particular chromosome or a portion thereof

('405 patent, col. 34 l. 62 – col. 35 l. 3) (emphasis added) Plaintiff contends that "hybridizing specifically" simply means that the oligo- or polynucleotides need to hybridize preferentially with as opposed to randomly with a nucleic acid of interest.

During prosecution of the '405 patent, the examiner rejected claims lacking the phrase "specific hybridization" as indefinite because they were:

> inclusive of all levels of stringency including conditions where hybridization is permitted to not only "nucleic acid of interest"

[15] All citations to the docket in Section IV refer to C.A. No. 12-274-LPS unless specified otherwise.

> but also to other nucleic acids that may be only 90% complementary, 70% complementary, or even only 20% complementary, etc. to the "oligo- or polynucleotide" . . . .

(D.I. 165-1 Ex. C-62 at ENZO-22777) The applicants did not challenge the examiner's rejection but overcame it by adding language requiring "oligo- or polynucleotides" that are capable of "hybridizing specifically." In rejecting the original claims, the examiner offered the applicants two options to overcome the indefiniteness rejection: either (1) claim a condition where hybridization is permitted only to the "nucleic acid of interest" or (2) specify a percentage of complementarity. Defendants seek to import both options (1) and (2) into the construction of the "hybridizing specifically" terms. However, the applicant chose option (1) – inserting the "hybridizing specifically" language but declining to specify an acceptable or necessary level of complementarity. Accordingly, the Court will construe "hybridizing specifically" so that hybridizing is permitted only to the nucleic acid of interest, but the Court will not additionally impose a level of complementarity between the oligo- or polynucleotides being hybridized.

2. "clone"

Plaintiff's Proposal:	A population of DNA molecules all carrying the same sequence
Defendants' Proposal:	The segment of chromosomal DNA inserted into a vector
Court's Construction:	A population of DNA molecules all carrying the same inserted sequence.

The term "clone" appears in independent claims 63-65 and 67, and dependent claims 68, 69, and 152. As a representative example, claim 63 states:

> 63. A process for determining whether the number of copies of a particular chromosome in a cell is normal or abnormal, the process comprising: providing at least one cell; contacting said cell under

> hybridizing conditions with one or more clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci of said particular chromosome or a portion thereof . . .

('405 patent, col. 34 l. 62 – col. 35 l. 3) During prosecution, the patentee addressed the meaning of the term "clone" by providing the examiner the following definition:

> **clone**: This term is used in a number of senses. As a noun, it may mean (i) a population of recombinant DNA molecules all carrying the same inserted sequence, or (ii) a population of cells or organisms of identical genotype. It is most frequently used to describe a colony of microorganisms which harbour a ***specific DNA fragment*** inserted into a vector molecule.

(D.I. 161-101 Ex. C-5 at ENZO-0022750) (emphasis in original). Plaintiff uses the first part of the definition to formulate its construction but leaves out the word "inserted." Defendants use the definition for their construction as well but instead emphasize the "specific DNA fragment inserted into a vector molecule" language. The Court is not persuaded by either approach.

Defendants' approach is problematic because the patentee explicitly distinguished "DNA fragments" from "clones" in the claim itself. By construing "clone" as "segment of . . . DNA," Defendants would effectively render the "or DNA fragments" language in the claims redundant.

Moreover, neither the patent nor the prosecution history limits "clone" to "chromosomal DNA." The claim is directed at "determining . . . the number of copies of a particular chromosome;" the claim requires that the clone "hybridiz[e] specifically to a . . . particular chromosome" but those limitations are expressly and distinctly laid out in the claim. These limitations need not be read into the construction of "clone."

Plaintiff's approach, however, is problematic because it reads out the word "inserted" even though it appears in the definition Plaintiff cited to the examiner during prosecution. Plaintiff provides no reason for why "inserted" should not be included in the construction of "clone."[16] Accordingly, the Court will modify Plaintiff's proposed construction to require that a "clone" contain an "inserted sequence."

3. "DNA fragments, or oligo- or polynucleotides derived from said clone(s)"

Plaintiff's Construction:	no construction necessary
Or in the alternative:	pieces of DNA, or oligo- or polynucleotides derived from said population or populations of DNA molecules all carrying the same sequence
Defendants' Construction:	All the pieces of the clone or clones
Court's Construction:	pieces of DNA, or oligo- or polynucleotides derived from said population or populations of DNA molecules all carrying the same inserted sequence

The parties' dispute here is largely resolved by the Court's construction of the "clone" term above. The only remaining dispute is whether "derived form said clone(s)" modifies both "DNA fragments" and "oligo- or polynucleotides" or just "oligo- or polynucleotides." The disputed term appears in claims 63-65 of the '405 patent. Claims 67 and 152 recite "providing sets of clones or DNA fragments or oligo- or polynucleotides derived from said clones." ('405 patent, col. 38 ll. 21-22; col. 44 ll. 7-8) Defendants contend that because the comma separating "DNA fragments" and "or oligo- or polynucleotides derived from said clone(s)" appears in some claims but does not appear in others, it is unclear from the claims whether the modifier "derived from said clone(s)" applies to both "DNA fragments" and "oligo- or

[16] During the claim construction hearing, Plaintiff agreed to modify its construction to include the word "inserted." (Tr. 186)

polynucleotides." In the Court's view, the opposite is true. Had none of the claims included the comma, it may have been unclear whether the modifier "derived from said clone(s)" was meant to modify both "DNA fragments" and "oligo- or polynucleotides" or just the latter. None of the claims read "clones, or DNA fragments or oligo- or polynucleotides derived from said clone(s)." Yet, that is the reading Defendants ask the Court to adopt. The claims make clear that "derived from said clone(s)" only modifies the "oligo- or polynucleotides" term.

The relevant prosecution history also does not support Defendants' proposed construction. During prosecution, the patentee stated:

> The elements, clones, DNA fragments and oligo- or polynucleotides, are basically equivalents for the purposes of the invention and these elements claimed alternatively do not introduce any uncertainty or ambiguity with respect to the scope or breadth of the chromosomal characterization claims.

(D.I. 161-101 Ex. C-5 at ENZO-0022750) Defendants seize upon the "basically equivalent for the purposes of the invention" language to argue that clones, DNA fragments, and oligo- or polynucleotides should all be construed more or less interchangeably. However, because DNA fragments, and oligo- or polynucleotides, are "basically equivalents" for the purposes of the invention does not necessarily mean they are the same exact thing in all respects. The patentee simply meant that any of these three elements may be used in practicing the invention.

4. "locus" or "loci"

Plaintiff's proposal:	Region(s) of a chromosome
Defendants' Proposal:	The region of a chromosome occupied by a particular gene and therefore determining a single biochemical function
Court's Construction:	The region(s) of a chromosome occupied by a gene or genes.

The term "locus or loci" appears in claims 63, 64, 65, and 67. As a representative example, claim 63 states "wherein said clones or fragments or oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci of said particular chromosome or a portion thereof." ('405 patent, col. 34 l. 67 – col. 35 l. 3) Plaintiff's proposed construction appears to read out a limitation that is contained in the claim. For their part, Defendants refer the Court to extrinsic evidence, and here the Court finds it appropriate to consult Defendants' cited "technical dictionaries," as here they enable the Court "to better understand the underlying technology and the way in which one of skill in the art might use the claim terms . . . [b]ecause dictionaries, and especially technical dictionaries, endeavor to collect the accepted meanings of terms used in various fields of science and technology . . . ." *Phillips*, 415 F.3d at 1318.

Various technical texts and dictionaries define a locus as "a gene, a part of a gene, or a DNA sequence which has some regulatory role" (D.I. 206-3 at 63 (Stephen G. Oliver and John M. Ward, A DICTIONARY OF GENETIC ENGINEERING 63, 1985)), or "the position that a gene occupies on a chromosome" (D.I. 169-7 at 24 (AMERICAN HERITAGE DICTIONARY (Second College Edition), 1984)). The specification suggests that the claimed process is designed to work with a sample "wherein the sample is suspected of containing a nucleic acid of interest associated with a genetic disorder . . . ." ('405 patent, col. 32 ll. 16-25) In context, then, the "locus" referred to in the claims is narrower than "a region of a chromosome" but broader than "the region of a chromosome occupied by a particular gene and therefore determining a single biochemical function." The extrinsic evidence and specification suggest that a definition that limits a locus to a gene without imposing the limitation that the gene or

genetic marker determine a single biochemical function is in keeping with the plain and ordinary meaning as well as the context of the "locus or loci" term.[17] Accordingly, the Court will construe "locus or loci" as "[t]he region(s) of a chromosome occupied by a gene or genes."

5. "covalently attached"

Plaintiff's proposal:	No construction necessary.
Alternatively:	connected by the sharing of electrons between atoms
Defendants' proposal:	Connected by sharing of electrons between two atoms with no linkage group
Court's Construction:	connected by the sharing of electrons between atoms

The parties primarily dispute whether "covalently attached" may encompass a connection through a linkage group.

The "covalently attached" language appears in several claims. Claim 63 recites that:

> PM is a phosphate moiety,
>
> SM is a furanosyl moiety,
>
> BASE is a base moiety, and
>
> Sig is a detectable non-radioactive moiety,
>
> wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group . . . .

('405 patent, col. 35 ll. 35-54) Defendants argue that claim 63 "makes clear that a covalent attachment between the signal and the attachment site is distinct from attachment through a

[17] During the claim construction hearing, Defendants agreed to amend their construction by eliminating the "determining a single biochemical function" limitation. (Tr. 177)

linkage group." (D.I. 167 at 11) Based on claim 63, Defendants argue that "[f]or attachments to the sugar or phosphate, the claims say 'covalently attached to [SM or PM] directly or through a linkage group.' For attachments to the base, the claims say 'covalently attached to BASE' and therefore exclude attachment through a linkage group." (D.I. 199 at 10) However, this argument cannot be reconciled with Claim 93 which reads:

> 93. The process according to any of claims 63, 64, 65, or 67, wherein any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group.

('405 patent, col. 41 ll. 1-4) Defendants' argument would only make sense if Claim 93 were rewritten to read "said Sig is covalently attached to BASE or SM, or PM through a linkage group." But that is not what the claim states.

In light of the language of claims 93 and 63, covalent attachment can occur through a linkage group. Accordingly, the Court disagrees with Defendants' position and adopts Plaintiff's broader construction.

6. "through a linkage group"

Plaintiff's proposal:	No construction necessary
In the alternative:	through a chemical linkage
Defendants' proposal:	Linked through a series of molecules that provides distance
Court's Construction:	through a chemical linkage

The parties primarily dispute whether connecting "through a linkage group" must "provide distance" between the linked moieties. The parties are in agreement that the plain and ordinary meaning of "through a linkage group" does not require "provid[ing] distance." However, Defendants argue that the specification of the U.S. Patent No. 4,711,955 ("the '955

patent"), which the '405 patent incorporates by reference (*see* '405 patent, col. 25 ll. 16-22), introduces the functional limitation that the linkage group must "provide[] distance."

The '955 patent specification states that

> The linkage or group joining moiety A to base B may include any of the well-known bonds . . . . However, it is generally preferred that the chemical linkage include an olefinic bond . . . [which] serves to hold the moiety A away from the base when the base is paired with another in the well known double-helix configuration. This permits interaction with polypeptide to occur more readily, thereby facilitating complex formation.

('955 patent, col. 8 l .63- col. 9 l. 6) This passage does not mandate the functional limitation that a linkage group must necessarily provide distance between the linked moieties. At most, it suggests that one particular bond (an olefinic bond) is a preferred chemical linkage because it has the benefit of holding the linked moieties away from each other. In this way, the passage cited above supports Plaintiff's construction, and not that proposed by Defendants.

7. "nucleotide analog"

Plaintiff's Proposal:	No construction necessary.
Or in the alternative:	variant of a nucleotide
Defendants' Proposal:	Sugar, phosphate or base analog of a mononucleotide suitable as a substitute for a naturally occurring nucleotide
Court's Construction:	Variant of a nucleotide with a sugar analog, phosphate analog, and/or base analog

For the reasons discussed in relation to the '180 patent above, the "nucleotide analog" term will be construed as "variant of a nucleotide with a sugar analog, phosphate analog, and/or base analog."

8. "modified or labeled nucleotides" or "modified or labeled nucleotide analogs"

Plaintiff's Proposal:	No construction necessary.
Or in the alternative:	nucleotide [analog] that is labeled with a Sig.
Defendants' Proposal:	Mononucleotide [analog] that is labeled with a Sig moiety before incorporation into said oligo- or polynucleotide
Court's Construction:	nucleotide [analog] that is labeled with a Sig.

For the reasons discussed in relation to the '180 patent above, the "modified or labeled nucleotides" or "modified or labeled nucleotide analogs" terms will be construed as "nucleotide [analog] that is labeled with a Sig."

V. CONCLUSION

An appropriate Order follows.