IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ARCHERDX, INC. and THE GENERAL HOSPITAL CORPORATION d/b/a MASSACHUSETTS GENERAL HOSPITAL,	)	
Plaintiffs,	)	
v.	)	C.A. No. 18-1019 (MN)
QIAGEN SCIENCES, LLC, QIAGEN LLC f/k/a QIAGEN INC., QIAGEN BEVERLY, LLC f/k/a QIAGEN BEVERLY, INC., QIAGEN GAITHERBURG, LLC f/k/a QIAGEN GAITHERSBURG, INC., QIAGEN GMBH, QIAGEN N.V. and JONATHAN ARNOLD,	)	
Defendants.	)	

MEMORANDUM ORDER

At Wilmington this 12th day of December 2019:

As announced at the hearing on November 12, 2019[1], IT IS HEREBY ORDERED that the disputed claim terms of U.S. Patent No. 10,017,810 ("the '810 Patent") are construed as follows:

1. "universal oligonucleotide tail adaptor" means "a nucleic acid molecule comprised of two strands (a blocking strand and an amplification strand) and comprising a first ligatable duplex end and a second unpaired end" ('810 Patent, claims 1, 15, & 16);

2. "blocking strand" means "a strand of the universal oligonucleotide tail adaptor that comprises a 5' duplex portion" ('810 Patent, claims 1-4 & 16);

3. "amplification strand" means "a strand of the universal oligonucleotide tail adaptor that comprises an unpaired 5' portion, a 3' duplex portion, and a 3' T overhang, and nucleic acid sequences identical to a first and second sequencing primers" ('810 Patent, claims 1-4 & 16);

[1] The construction of all the listed terms except the term "nested" were announced at the November 12, 2019 hearing.

4. "second target-specific primer" means "a single-stranded oligonucleotide comprising a 3' portion comprising a nucleic acid sequence that can specifically anneal to a portion of the known target nucleotide sequence comprised by the amplicon resulting from step (b), and a 5' portion comprising a nucleic acid sequence that is identical to a second sequencing primer" ('810 Patent, claims 1 & 16);

5. "known target nucleotide sequence" means "a portion of a target nucleic acid for which the sequence (e.g. the identity and order of the nucleotide bases comprising the nucleic acid) is known" ('810 Patent, claims 1, 13, 14, & 16); and

6. "second adaptor primer" means "a nucleic acid molecule comprising a nucleic acid sequence identical to a portion of the first sequencing primer and is nested with respect to the first adaptor primer" ('810 Patent, claims 1 & 16).

In addition, for the reasons set forth below,

7. "nested" means "annealed to a nucleic acid sequence 3' downstream and in the same direction as another molecule . . ." ('810 Patent, claim 1).

The parties briefed the issues (*see* D.I. 123) and submitted a Joint Claim Construction Chart containing intrinsic evidence (*see* D.I. 134, Ex. A[2]). They also submitted an extensive Appendix that included three expert declarations. (D.I. 124). Defendants submitted a tutorial describing the relevant technology (*see* D.I. 140). The Court carefully reviewed all submissions in connection with the parties' contentions regarding the disputed claim terms, heard oral argument and expert testimony (*see* D.I. 143), and applied the following legal standards in reaching its decision.

I. LEGAL STANDARDS

A. Claim Construction

"[T]he ultimate question of the proper construction of the patent [is] a question of law," although subsidiary fact-finding is sometimes necessary. *Teva Pharms. USA, Inc. v. Sandoz, Inc.*,

[2] The parties amended their original claim construction chart (D.I. 76) three times. (D.I. 90); (D.I. 93); (D.I. 134, Ex. A). The Court references the third, and final, amended claim construction chart.

135 S. Ct. 831, 837-38 (2015). "[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." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (en banc) (internal citations and quotation marks omitted). Although "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. *Id.* at 1314. "[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 . . . [as] 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). 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. "Even when the specification describes only a single embodiment, [however,] 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) (internal quotation marks omitted) (quoting *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004)).

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) (en banc), *aff'd*, 517 U.S. 370 (1996). The prosecution history, which is "intrinsic evidence, . . . consists of the complete record of the proceedings before the [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, courts "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. 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." *Phillips*, 415 F.3d at 1318. 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, although 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).

B. Indefiniteness

"The primary purpose of the definiteness requirement is to ensure that the claims are written in such a way that they give notice to the public of the extent of the legal protection afforded

by the patent, so that interested members of the public, *e.g.* competitors of the patent owner, can determine whether or not they infringe." *All Dental Prodx, LLC v. Advantage Dental Prods., Inc.*, 309 F.3d 774, 779-80 (Fed. Cir. 2002) (citing *Warner-Jenkinson Co. v. Hilton-Davis Chem. Co.*, 520 U.S. 17, 28-29 (1997)). Put another way, "[a] patent holder should know what he owns, and the public should know what he does not." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 535 U.S. 722, 731 (2002).

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).

Like claim construction, definiteness is a question of law, but the Court must sometimes render factual findings based on extrinsic evidence to resolve the ultimate issue of definiteness. *See, e.g.*, *Sonix Tech. Co. v. Publications Int'l, Ltd.*, 844 F.3d 1370, 1376 (Fed. Cir. 2017); *see also Teva*, 135 S. Ct. at 842-43. "Any fact critical to a holding on indefiniteness . . . must be proven by the challenger by clear and convincing evidence." *Intel Corp. v. VIA Techs., Inc.*, 319 F.3d 1357, 1366 (Fed. Cir. 2003); *see also Tech. Licensing Corp. v. Videotek, Inc.*, 545 F.3d 1316, 1338 (Fed. Cir. 2008).

I. THE COURT'S RULING

The Court's rulings regarding all of the disputed claim terms of the '810 Patent, except "nested," were announced from the bench at the conclusion of the hearing as follows:

> At issue is U.S. Patent No. 10,017,810, titled "Methods for Determining a Nucleotide Sequence Contiguous to a Known Target Nucleotide Sequence." There are seven terms in dispute. All of the terms but one – "nested" – appear in claims 1 and 16 of the '810 Patent. "Nested" appears only in claim 1.
>
> I am prepared to rule on six of those disputes. I will not be issuing a written opinion on those six, but I will issue an order stating my rulings. I will issue an opinion – either with that order or otherwise – regarding the term "nested."
>
> As to my rulings today, I want to emphasize before I announce my decisions that while I am not issuing a written opinion, we have followed a full and thorough process before making the decisions I am about to state. I have reviewed the '810 Patent and the portions of the prosecution history and parent prosecution history submitted. There was full briefing on each of the disputed terms. There was an extensive appendix that included two expert declarations from Niall Lennon on behalf of Plaintiffs and one from Michael Metzker on behalf of Defendants. Defendants submitted a tutorial. There has been argument here today, as well as testimony from Dr. Metzker and from Dr. Lennon. All of that has been carefully considered.
>
> Now as to my rulings. As an initial matter, I am not going to read into the record my understanding of claim construction law generally. I have a legal standard section that I have included in earlier opinions, including somewhat recently in *Omega Flex v. Ward Manufacturing*, C.A. No. 18-1004. I incorporate that law and adopt it into my ruling today, and will also set it out in the order that I issue.
>
> Additionally, I note that through Dr. Lennon, Plaintiffs define the person of ordinary skill in the art as someone having "a Ph.D. in Biology, Molecular Biology, Genetics, Biochemistry, Pharmacology, Biomedical Engineering or related fields, with 2 to 5 years of experience in next generation sequencing OR a BSc in Biology, Molecular Biology, Genetics, Biochemistry, Pharmacology, Biomedical Engineering, or related fields and 5 to 6 years of experience in next generation sequencing."

Defendants, through Dr. Metzker, define the person of ordinary skill as one having "either an M.D./Ph.D. or Ph.D. in Molecular Biology, Molecular Genetics, Chemistry, Engineering, or equivalent disciplines with two years of experience, or a Bachelor of Science in such fields with five years of experience, with such experience including library preparation methods, PCR, and next generation sequencing." The competing definitions differ as to whether the experience should be limited to next gen sequencing, but the parties appear to agree that the differences in the proposals are not relevant to claim construction.

First, we have three terms: "Universal oligonucleotide tail adaptor," "blocking strand," and "amplification strand," all of which appear in subsection little roman numeral "i" of claims 1 and 16. Plaintiffs propose that no construction is necessary for any of the three. In their briefing, in the alternative, for "universal oligonucleotide tail adaptor," Plaintiffs offer "[a] nucleic acid molecule comprised of two strands (a blocking strand and an amplification strand) and comprising a first ligatable duplex end and a second unpaired end." Today they offered a construction of amplification strand that "amplification strand comprises an unpaired 5' portion, a 3' duplex portion, and a 3' T overhang and nucleic acid sequences identical to a first and second sequencing primer."

For universal oligonucleotide tail adaptor, Defendants propose "[a] nucleic acid molecule comprised of two strands (a blocking strand and an amplification strand) and comprising a first ligatable duplex end and a second unpaired end. The blocking strand of the universal oligonucleotide tail adaptor comprises a 5' duplex portion. The amplification strand comprises an unpaired 5' portion, a 3' duplex portion, and a 3' T overhang and nucleic acid sequences identical to a first and second sequencing primers. The duplex portions of the blocking strand and the amplification strand are substantially complementary and form the first ligatable duplex end comprising a 3' T overhang and the duplex portion is of sufficient length to remain in duplex form at the ligation temperature." For the other two terms – "blocking strand" and "amplification strand" – they assert that these terms are "defined as part of the definition of 'universal oligonucleotide tail adaptor.'"

In column 11, lines 32 to 36 of the '810 Patent, the specification states "[a]s used herein, the term 'universal oligonucleotide tail adaptor' refers to a nucleic acid molecule comprised of two strands (a blocking strand and an amplification strand) and comprising a first ligatable duplex end and a second

unpaired end." It then continues [in lines 36 to 40] that the blocking strand "comprises a 5' duplex portion" and the "amplification strand comprises an unpaired 5' portion, a 3' duplex portion, and a 3' T overhang and nucleic acid sequences identical to a first and second sequencing primer."

Here, the first sentence of the paragraph provides a clear definition and lexicography for the term. The parties do not dispute that. Moreover, here today the parties agreed that two sentences discussing the "blocking strand" and "amplification strand" are acceptable definitions for those terms, and also agreed that whether those terms are included as part of the "universal oligonucleotide tail adaptor" or separately does not matter.

The dispute that remains is whether it is appropriate to add the last sentence of Defendants' proposal – that "[t]he duplex portions of the blocking strand and the amplification strand are substantially complementary and form the first ligatable duplex end comprising a 3' T overhang and the duplex portion is of sufficient length to remain in duplex form at the ligation temperature."

Here, the prosecution history is instructive. In the Notice of Allowability of the application that became the ['810's parent patent, U.S. Patent Number 9,487,828], the Examiner referred to the universal oligonucleotide tail as being one of the terms having an "explicit and limiting definition[] present in the specification." She then went on to say that "[t]he universal oligonucleotide tail adaptor must contain a blocking strand and an amplification strand as well as a ligatable duplex portion and an unpaired end [(Specification at page 14, paragraph 65)]. The blocking strand must contain a 5' duplex portion, and the amplification strand must contain an unpaired 5' portion, a 3' duplex portion, and a 3' T overhang, and sequences identical to the first and second sequencing primers [(Specification at page 14, paragraph 65)]."

Similarly, in the June 7, 2017 Office Action during the prosecution of the '810 Patent, the Examiner rejected several dependent claims as not further limiting because they recited structural features "required by the explicit definition of the 'universal tail adaptor' set forth in the specification." [June 7, 2017 Office Action at page 7]. Among the claims that were rejected on that basis were then claim 23, which claimed that the amplification strand must contain an unpaired 5' portion, and also then claim 24, which specified a 3' T overhang.

The Examiner, however, did not include the additional requirements that Defendants seek to add, i.e., that the strands be substantially complimentary and of sufficient length. In looking at the intrinsic evidence as a whole, I find that those requirements are not clearly part of the patentees' definition.

Thus, I will construe the term "universal [oligonucleotide] tail adaptor" to mean: "a nucleic acid molecule comprised of two strands (a blocking strand and an amplification strand) and comprising a first ligatable duplex end and a second unpaired end."

I will construe "blocking strand of the universal oligonucleotide tail adaptor" to comprise a 5' duplex portion.

I will construe the amplification strand to comprise an unpaired 5' portion, a 3' duplex portion, and a 3' T overhang, and nucleic acid sequences identical to a first and second sequencing primers.

Second, we have the term "second target-specific primer." Plaintiffs state that no construction is necessary, but "[t]o the extent the Court seeks to construe the term," proposes the construction: "A single-stranded oligonucleotide comprising a 3' portion comprising a nucleic acid sequence that can specifically anneal to a portion of the amplification product resulting from step (ii), and a 5' portion comprising a nucleic acid sequence that is identical to the second sequencing primer."

Defendants counter with "[a] single-stranded oligonucleotide comprising a 3' portion comprising a nucleic acid sequence that can specifically anneal to a portion of the known target nucleotide sequence comprised by the amplicon (amplification product) resulting from step (ii), and a 5' portion comprising a nucleic acid sequence that is identical to a second sequencing primer. The second target-specific primer is nested with respect to the first target-specific primer."

Here, again, the '810 Patent defines the term at issue, and the parties do not dispute that. In column 16, lines 33 to 39, the patent states: "As used herein, the term 'second target-specific primer' refers to a single-stranded oligonucleotide comprising a 3' portion comprising a nucleic acid sequence that can specifically anneal to a portion of the known target nucleotide sequence comprised by the amplicon resulting from step (b), and a 5' portion comprising a nucleic acid sequence that is identical to a second sequencing primer."

The parties do not dispute that this is a definition. Instead, Plaintiffs remove part of the definition – the words "the known target nucleotide sequence comprised by" before the word amplicon [–] and change other words, e.g., they change "a second sequencing primer." And Defendants add the sentence in the specification following the definition that I just read, i.e., that "[t]he second target-specific primer is nested with respect to the first target-specific primer."

It is settled that the specification may define a claim term and that, when it does, "the inventor's lexicography governs." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1316 (Fed. Cir. 2005). "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." *Cont'l Circuits LLC v. Intel Corp.*, 915 F.3d 788, 796 (Fed. Cir. 2019)[; *Pacing Techs., LLC v. Garmin Int'l, Inc.*, 778 F.3d 1021, 1024 (Fed. Cir. 2015); *Thorner v. Sony Comput. Entm't Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012); *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002)].

Here, I reject all of the changes proposed by the parties to the definition set forth in the specification.

Plaintiffs clearly set forth a definition in the specification. And they have not offered any compelling reason to diverge from that. Instead, they change the words asserting that it is not a difference in substance but rather will make it more jury friendly.

I cannot say whether that is true or not at this point, but the intrinsic evidence does not support the changes Plaintiffs suggest. For example, during the prosecution of the parent application, applicants submitted a new claim (claim 56), which claimed *inter alia* "[t]he method of claim 21, wherein the second target-specific primer comprises a 3' portion comprising a nucleic acid that can specifically anneal to a portion of the nucleic acid comprising the known target nucleotide sequence comprised by the amplification product of step (ii)." [June 16, 2015 Amendment at page 8.] The Examiner rejected that dependent claim because it was not further limiting because the added features were already required in claim 21 by the explicit definition in the specification. [September 22, 2015 Office Action at page 8.]

Similarly, in the prosecution of the '810 Patent itself, virtually the same proposed amendment was rejected for the same

reason. [May 2, 2017 Preliminary Amendment at page 3, claim 32; June 7, 2017 Office Action at page 7.]

Additionally, in connection with a double patenting rejection, the Examiner noted that "the second amplification . . . necessarily requires the second target-specific primer to be capable of annealing to a portion of the known target sequence present in the first amplification product." [June 7, 2017 Office Action at pages 10–11].

As to Defendants' proposal, I do not find that it is clear that the language they propose to add is part of the lexicography for the term. That this is not part of the definition is consistent with the prosecution history where the Patent Examiner referenced the "explicit" definition of "second target-specific primer," [in the June 7, 2017 Office Action at page 3,] and she did not include the "nesting requirement" that Defendants now propose.

Similarly, in the Notice of Allowability of the parent application, the Examiner referred to the definition of "second target-specific primer" as requiring "a 3' target-specific portion and a 5' portion comprising a nucleic acid sequence that is identical to a second sequencing primer." [Notice of Allowance at page 8]. Again, there is no requirement for nesting recognized by the Examiner as part of the construction.

Moreover, "nesting" is specifically included in claim 1, but is not included in claim 16. In the absence of a clear reason to do so, which I have not seen, I will not read into the claim a term that the patentee chose not to include.

To the extent that Defendants assert that the reference to a second sequencing primer in the construction renders the claim indefinite, for a claim to be held invalid for indefiniteness, there must be clear and convincing evidence. *See Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 912 n.10 [(citing *Microsoft Corp. v. i4i Ltd. P'ship*, 564 U.S. 91, 95 (2011))]. At this time, the Court finds that Defendants have not met their burden to show indefiniteness. Should there still be a disagreement regarding this claim in the future, Defendants may raise the issue later, if appropriate, after full fact and expert discovery.

The third disputed term is "nested." We have heard testimony and argument on this issue today. I need to review that testimony and argument, and as I stated at the beginning of this ruling, I will address that issue separately.

The fourth disputed term is "known target nucleotide sequence." Plaintiffs state that no construction is necessary, but then offer that to the extent the Court seeks to construe the term … "[a] portion of a target nucleic acid for which the sequence (e.g. the identity and order comprising the nucleotide bases comprising the nucleic acid) is known."

Defendants offer the same sentence at the start of their proposal and then tack on the sentence: "The known target nucleotide sequence can be of any length of 10 or more nucleotides."

Here, again the patent specification provides a definition of the term. In column 10, lines 55 to 59, it states: "As used herein, the term 'known target nucleotide sequence' refers to a portion of a target nucleic acid for which the sequence (e.g. the identity and order of the nucleotide bases comprising the nucleic acid) is known."

It is not clear that [Defendants'] additional sentence is part of the lexicography. And in the absence of that being clear, I will not read the limitation in.

The final term is "second adaptor primer." Here, again, Plaintiffs offer that no construction is necessary, and in the alternative propose the construction "[a] nucleic acid molecule comprising a nucleic acid sequence identical to a portion of the first sequencing primer."

Defendants propose the construction "[a] nucleic acid molecule comprising a nucleic acid sequence identical to a portion of the first sequencing primer and that is nested with respect to the first adaptor primer."

The specification again defines [the] term. In column 17, lines 5 to 8, it states: "As used herein, the term 'second adaptor primer' refers to a nucleic acid molecule comprising a nucleic acid sequence identical to a portion of the first sequencing primer and is nested with respect to the first adaptor primer."

Plaintiffs agree that the first portion of that sentence is definitional but omit the second portion. They support their argument [by] noting that during prosecution of the parent the Examiner in an Interview Summary noted that "new claim 79 does not require nesting of the adaptor primers." As Defendants point out, however, the term at issue in claim 79 was not "second adaptor primer" it was "an adaptor primer."

> Here, the patentees included a nesting requirement in the definition of "second adaptor primer." They did not refer to it as an embodiment. They included it in the definition. I will follow suit and define the term as the patentees did in the specification.

As noted above, the Court did not construe the term "nested" at the hearing. After further review of the papers submitted and the transcript of the argument and expert testimony, it will do so now. Claim 1 of the '810 Patent requires that "the second target-specific primer is relative to the first target-specific primer." Plaintiffs assert that "[a] second primer is nested relative to a first primer when the second primer is not identically positioned with respect to the first primer." (D.I. 134, Ex. A at 11). Defendants assert "[a] second primer is nested with respect to a first primer when the second primer anneals to a nucleic acid sequence 3' downstream and in the same direction as the first primer (inside)." (*Id.*). Thus, the primary dispute is whether the second primer must be downstream of and in the same direction as the first primer or may anneal anywhere that is different from the first primer's binding location.

The Court construes "nested" to mean "annealed to a nucleic acid sequence 3' downstream and in the same direction as another molecule." This construction is consistent with the ordinary and customary meaning of "nested" to a person of ordinary skill in the relevant art and is supported by the intrinsic evidence.

As already stated, "the 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." *Phillips*, 415 F.3d at 1312-13. The Federal Circuit has further instructed that "[b]roadening of ordinary meaning of a term" to "encompass relatively obscure definitions" "in the absence of support in the intrinsic record indicating that such a broad meaning was intended violates the

principles articulated in *Phillips*." *Nystrom v. Trex Co., Inc.*, 424 F.3d 1136, 1145-46 (Fed. Cir. 2005).

Both experts agree that, by far, the "most common" way in which "nested" is used in the relevant art is to describe a second primer 3' downstream from and in the same direction as a first primer. (*See, e.g.*, D.I. 143 at 85:6-20, 95:15-22; D.I. 124 Ex. 2 ¶ 42 (Metzker Declaration)). Plaintiffs, however, maintain that the "ordinary" meaning is broader. Setting aside any semantic argument regarding the difference between "most common" and "ordinary," in light of *Nystrom* the Court is hesitant to adopt Plaintiffs' construction without intrinsic support for such an expansion of the vastly more common definition. Yet Plaintiffs rely entirely on extrinsic evidence – the use of "nested" in three publications[3] and the personal experiences of their expert, Dr. Lennon. (*E.g.*, D.I. 123 at 47-49, 55-57).[4] Moreover, the intrinsic record here does not support Plaintiffs' construction; rather, it supports an "inside" construction of nested.

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[3] Defendants assert, and Plaintiffs do not dispute, that the three sources Plaintiffs cite are extrinsic. (*E.g.*, D.I. 123 at 55 & n.16 (Defendants' first articulation of "extrinsic" argument in Joint Claim Construction Brief); *id.* at 55-57 (Archer's Response)); D.I. 143 at 109:11-17, 121:6-7 (Defendants repeatedly describing Plaintiffs' references as "extrinsic")). Two of them – "Schuelke" and "Kanizay," (*e.g.*, D.I. 124 Ex. 1, Exs. 3-4) – indisputably are, as they are entirely external to the patent and prosecution history. The third – the "Illumina" or "Solexa" reference, (*e.g.*, D.I. 124 Ex. 1, Ex. 2), however, is cited on the face of the '810 Patent. ('810 Patent, at [56]). Although "prior art cited in a patent or cited in the prosecution history of the patent constitutes intrinsic evidence," *V-Formation v. Benetton Grp. S.P.A.*, 401 F.3d 1307, 1311 (Fed. Cir. 2005) (citations omitted), the Federal Circuit has also held that references included by a patentee in its disclosures but not otherwise cited by the applicant or the examiner during prosecution have little probative value in claim construction. *Osram GmbH v. Int'l Trade Comm'n*, 505 F.3d 1351, 1357-58 (Fed. Cir. 2007) (citations omitted). The dissenting judge in *Osram* even described such uncited references as "extrinsic evidence." *Id.* at 1361. Given this, along with Plaintiffs' failure to dispute Defendants' "extrinsic" argument or to articulate how the "Illumina/Solexa" patent application was utilized in the prosecution of the '810 Patent, the Court considers that reference to be extrinsic evidence.

[4] The parties dispute the import and disclosures of Plaintiffs' cited publications; however, the Court finds no need to resolve those issues in light of its other findings.

First, the articulated goals and advantages of the claimed invention require "internally" nested primers. The '810 Patent is directed towards increasing the specificity with which target oligonucleotide sequences are identified, ('810 Patent, at [57] (Abstract) ("The technology described herein is directed to methods of determining oligonucleotide sequences, e.g. by enriching target sequences prior to sequencing the sequences."); *id.* at col. 35 l. 60 – col. 36 l. 12 ("Advantages of the methods described herein include: . . . 3. High specificity . . . .")), and a second round of PCR with primers "internal" to those used in the first round is key to achieving that high specificity, (*see* '810 Patent col. 35 ll. 6-9 ("High specificity in this system is achieved with the unidirectional tandem, nested primers . . . ."); *id.* at col. 36 ll. 28-32 ("Additional specificity is achieved by using two unidirectional primers, with [the second] 3' downstream of [the first] . . . .")). Moreover, the Court finds compelling Dr. Metzker's testimony that the use of "externally" nested primers (one option under Plaintiffs' construction) would not increase specificity if utilized in a PCR reaction because the second, external primers would simply "amplify everything that's present" rather than target the desired sequence. (D.I. 143 at 117:18 – 119:23).

Second, the definitions and descriptions of "nested" that are incorporated into the '810 Patent define or describe that term to mean "3' downstream and in the same direction as." *See, e.g.*, Molecular Biology and Biotechnology: A Comprehensive Desk Reference 644 (Meyers et al eds., 1995) ("Another approach that can improve PCR specificity is to follow the initial amplification reaction with an additional PCR with internal, single, or double-nested primers. Like the use of oligonucleotide hybridization probes, this approach utilizes sequence information internal to the two 'outer' primers to identify the subset of amplification products that corresponds to the target fragment."); Sambrook & Russell, Molecular Cloning: A Laboratory Manual 8.61

(3d ed. 2001) ("If necessary, the products of the first PCR can be used as templates for a second, nested PCR, which is primed by a gene-specific sense oligonucleotide internal to the first, and a second antisense oligonucleotide . . . ."); Davis, Kuehl, & Battey, Basic Methods in Molecular Biology 117 (2d ed. 1995) ("'[N]ested' PCR can be used to increase the specificity of the amplification reaction. The nested PCR procedure involves two sequential PCR reactions. After 10 to 20 cycles of PCR with the first pair of gene-specific primers . . . a second 25- to 30-cycle PCR reaction [is conducted] with a new set of gene-specific primers that hybridize to sequences internal to, or nested between, the first pair."); (*see also* '810 Patent col. 9 l. 65 – col. 10 l. 19 (incorporating definitions of common cell and molecular biology terms or descriptions of "standard procedures" from, *inter alia*, Meyers, Sambrook, and Davis)). Additionally, Dr. Metzker testified that at least two of these incorporated resources would be used by someone of ordinary skill in the relevant art at the time of the invention. (D.I. 143 at 129:12 – 132:22).

Finally, although not definitive, Plaintiffs have failed to point to a single instance in the patent or elsewhere in the intrinsic evidence where "nested" is used in the manner they advocate. Rather, as they admit, the term is repeatedly used in the specification to mean "annealed to a nucleic acid sequence 3' downstream and in the same direction as another molecule." (*See* D.I. 123 at 49 (disputing the relevance of, but noting that "the examples of the '810 patent show the second primers nested downstream of the first")); *see also, e.g.*, '810 Patent fig. 1 & col. 5 ll. 56-59 (instructing that, in Figure 1, after being subjected to a first round of PCR with a first target-specific primer, "the sample is subjected to an additional 14 cycles of PCR amplification using multiplex nested gene specific primers (3' downstream of [the first target-specific primer] and in the same direction)"); *id.* at fig. 3A & col. 6 ll. 6-7 (describing Figure 3A, which shows a second target-specific primer 3' downstream and in the same direction as a first target-specific primer, as

"depict[ing] a schematic presentation of nested primer targeting strategy"); *id.* at fig. 8 & col. 6 ll. 22-23 (stating Fig. 8, which shows "nested adaptor primers and nested gene specific primers" 3' downstream and in the same direction as adaptor and gene specific primers used in an earlier round, as "a schematic presentation of the targeting sequencing approach described herein")).

In light of the foregoing, the Court does not adopt the broad construction Plaintiffs request. Instead, it construes "nested" to mean "annealed to a nucleic acid sequence 3' downstream and in the same direction as another molecule."

Maryellen Noreika

The Honorable Maryellen Noreika
United States District Judge