IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BIOMÉRIEUX, S.A. and BIOMÉRIEUX, INC.,	:	
	:	
Plaintiffs,	:	
	:	
v.	:	C.A. No. 18-21-LPS
	:	
HOLOGIC, INC., GRIFOLS S.A., and GRIFOLS DIAGNOSTIC SOLUTIONS INC.,	:	
	:	
Defendants,	:	

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MEMORANDUM OPINION

June 11, 2019
Wilmington, Delaware

STARK, U.S. District Judge:

Plaintiffs bioMérieux, S.A. and bioMérieux, Inc.'s (together, "Plaintiffs" or "bioMérieux") assert in their February 3, 2017 Complaint (D.I. 1) that Defendants Hologic, Inc. ("Hologic"), Grifols Diagnostic Solutions Inc. ("GDS"), and Grifols, S.A. ("GSA") (together, "Defendants") infringe claims 1-6 of Plaintiffs' U.S. Patent No. 8,697,352 ("the '352 patent") and claims 1-15 Plaintiffs' U.S. Patent No. 9,074,262 ("the '262 patent") (together "the asserted patents"). The asserted patents describe "nucleotide sequences . . . that can be used as primers and probes in the amplification and detection of HIV-1 nucleic acid." ('352 patent at 3:19-21) The parties completed briefing of their claim construction disputes on December 14, 2018 (D.I. 156, 157, 165, 167) and the Court held a claim construction hearing on January 31, 2018 (D.I. 191) (Tr.). Thereafter, the parties submitted supplemental briefing on certain issues. (D.I. 179, 180, 182, 183)

I. LEGAL STANDARDS

The ultimate question of the proper construction of a patent is a question of law. *See Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 837 (2015) (citing *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 388-91 (1996)). "It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (citation and internal quotation marks omitted). "[T]here is no magic formula or catechism for conducting claim construction." *Id.* at 1324. Instead, the court is free to attach the appropriate weight to appropriate sources "in light of the statutes and policies that inform patent law." *Id.*

"[T]he words of a claim are generally given their ordinary and customary meaning. . . . [which is] the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application."

Id. at 1312-13 (internal citations and quotation marks omitted). "[T]he ordinary meaning of a claim term is its meaning to the ordinary artisan after reading the entire patent." *Id.* at 1321 (internal quotation marks omitted). The patent "specification is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996).

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

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

It is also possible that "the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Phillips*, 415 F.3d at 1316. It bears emphasis that "[e]ven when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." *Hill-Rom Servs., Inc. v. Stryker*

Corp., 755 F.3d 1367, 1372 (Fed. Cir. 2014) (quoting *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004)) (alteration in original) (internal quotation marks omitted).

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

"In some cases, . . . the district court will need to look beyond the patent's intrinsic evidence and to consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art during the relevant time period." *Teva*, 135 S. Ct. at 841. "Extrinsic evidence consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." *Markman*, 52 F.3d at 980. For instance, technical dictionaries can assist the court in determining the meaning of a term to those of skill in the relevant art because such dictionaries "endeavor to collect the accepted meanings of terms used in various fields of science and technology." *Phillips*, 415 F.3d at 1318. In addition, expert testimony can be useful "to ensure that the court's understanding of the technical aspects of the patent is consistent with that of a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field." *Id.* Nonetheless, courts must not lose sight of the fact that "expert reports and testimony [are] generated at the time of and for the purpose of litigation and thus can suffer

from bias that is not present in intrinsic evidence." *Id.* Overall, while extrinsic evidence "may be useful to the court," it is "less reliable" than intrinsic evidence, and its consideration "is unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence." *Id.* at 1318-19. Where the intrinsic record unambiguously describes the scope of the patented invention, reliance on any extrinsic evidence is improper. *See Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1308 (Fed. Cir. 1999) (citing *Vitronics*, 90 F.3d at 1583).

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

II. CONSTRUCTION OF DISPUTED TERMS

Claim 1 of the '262 patent recites the disputed terms (highlighted below) and is exemplary of the other asserted claims:

> 1. A method for amplifying HIV-1 nucleic acid in a sample, comprising:
>
> a) contacting the sample with a pair of oligonucleotide primers that bind to a first primer binding site and a second ***primer binding site*** located within the LTR region of ***the HIV-1 genome***; and
>
> b) performing a nucleic acid amplification under conditions wherein said oligonucleotide primers bind only to said first and second ***primer binding sites***, thereby amplifying HIV-1 nucleic acid in the sample;
>
> wherein said pair of oligonucleotide primers ***consists of a first primer and a second primer***,

wherein said first primer consists essentially of a first oligonucleotide that is ***fully complementary to a sequence of the LTR region*** at the first ***primer binding site***, said oligonucleotide being 15-26 nucleotides in length and comprising at least 15 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO: 1:
G GGC GCC ACT GCT AGA GA;

said first oligonucleotide being operably linked to a promoter; and

wherein said second primer consists essentially of a second oligonucleotide that is ***fully complementary to a sequence which is the reverse complement of a sequence of the LTR region*** at the second ***primer binding site***, said oligonucleotide being 10-26 nucleotides in length and comprising at least 10 sequential nucleotides of the nucleotide sequence of:

SEQ ID NO: 5:
CTC AAT AAA GCT TGC CTT GA.

A. "HIV-1 genome" / "HIV-1 nucleic acid"[1]

Plaintiffs' Proposed Construction	Defendants' Proposed Construction	Court's Construction
"the genetic sequence of an HIV-1 strain" "nucleic acid derived from the genetic sequence of an HIV-1 strain"	"all sequences of HIV-1 strains"	"the genetic sequence of an HIV-1 strain" "nucleic acid derived from the genetic sequence of an HIV-1 strain"

The parties present two issues: (1) whether the patentee intended to limit the claims to "all sequences of HIV-1" strains, and (2) whether "nucleic acid" has the same meaning as "genome." The Court sides with Plaintiffs on both disputes.

On point one, as Plaintiffs observe, "the claims refer to 'a sequence'" of HIV-1 to mean the genome, but nowhere require Defendants' limitation of "all sequences" of HIV-1 strains. (D.I. 157 at 11) Defendants contend that the "Titles, Abstracts, and written descriptions [of the

[1] '352 patent claims 1, 3, and 5; '262 patent claims 1, 6, and 11.

asserted patents] make crystal clear that the invention is directed to assays that can amplify and detect 'all' ***variants*** [or ***strains***] of HIV-1." (D.I. 156 at 5-6) (emphasis added) The specification, however, does ***not*** impose such a narrow limitation, but at most limits the patents to being capable of detecting "all presently known ***subtypes*** of HIV-1 . . . with high accuracy and sensitivity." ('352 patent at 3:26-31 (emphasis added); *see also id.* at 3:31-33, 7:26-30)[2] Defendants emphasize the text associated with Table 4, which reads "[i]n contrast, the assay using the gag primers probes combination as described in example 3 ***failed to detect*** subtype A and subtype E ***each from one of the samples*** and all samples containing HIV-1 RNA from group O members" ('352 patent at 12:50-53) (emphasis added), but Plaintiffs are correct that this means "the gag primers did not fail to detect Subtypes A and E, but just a single variant from both of them." (D.I. 180 at 2) Furthermore, "[f]ar from using 'subtype' and 'variant' interchangeably, the text associated with Example 5, from beginning to end, kept the concepts distinct." (*Id.*) Both Plaintiff and Defendants find support for their respective position in the prosecution history, which does not alter the Court's conclusion. (*Compare* D.I. 180 at 2-3 *with* D.I. 182 at 2-3) While it may be an advantage of the patent that "the nucleic acid of all presently known subtypes of HIV-1 can be detected with high accuracy and sensitivity," there is no basis to read this advantage into the claims. (*See* D.I. 156 at 7) (citing *C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 863-66 (Fed. Cir. 2004); *Virnetx, Inc. v. Cisco Sys., Inc.*, 767 F.3d 1308, 1318 (Fed. Cir. 2014))

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[2] Defendants clarified at the hearing that their view is the patent expressly requires detection of all ***subtypes*** of HIV-1 ***known at the time of filing*** (Tr. at 33-34), which according to Defendants requires detection of ***all strains within that subtype*** (Tr. at 32-34) ("[W]hen they said to be able to detect all subtypes of HIV-1, they were really talking about strains recognizing there is a distinction between the two, but they were concerned that if you missed even a single strain within a subtype, you missed the subtype.").

On the second point of dispute, "HIV-1 genome" and "HIV-1 nucleic acid" have different meanings within the context of the patent. The specification strongly supports Plaintiffs' construction of "nucleic acid" (*see, e.g.*, '352 patent at 1:30-33, 2:44-47, 2:55-57); by contrast, replacing both terms with the same definition would create incoherence (Tr. at 22).

B. "Fully Complementary" Terms:[3]

- **"fully complementary to a sequence of the LTR region"**
- **"fully complementary to a sequence which is the reverse complement of a sequence of the LTR region"**

Plaintiffs' Proposed Construction	Defendants' Proposed Construction	Court's Construction
"fully complementary to a sequence of the LTR region of an HIV-1 strain"	"each nucleotide of the oligonucleotide is a match of the Watson-Crick base pair (that is adenine is a match to thymine or uracil and guanine is a match to cytosine) to the sequence of the LTR region of all strains of HIV-1"	"fully complementary to a sequence of the LTR region of an HIV-1 strain"
"fully complementary to a sequence which is the reverse complement of a sequence of the LTR region of an HIV-1 strain"	"each nucleotide of the oligonucleotide is a match of the Watson-Crick base pair (that is, adenine is a match to thymine or uracil and guanine is a match to cytosine) to the sequence which is the reverse complement of a sequence of the LTR region of all strains of HIV-1"	"fully complementary to a sequence which is the reverse complement of a sequence of the LTR region of an HIV-1 strain"

The dispute with respect to these terms is largely the same as that already addressed in connection with the first term: must the oligonucleotide be "fully complementary" to "***an*** HIV-1 strain" (Plaintiffs' position) or to "***all*** strains of HIV-1" (Defendants' proposal)? (Tr. at 46-50,

[3] '352 patent claims 1, 2, 3, 4, and 5; '262 patent claims 1, 2, 6, 7, 11, and 12.

53-60)[4] The Court concludes that the term relates to "***an*** HIV-1 strain" not "***all*** strains," as "[t]he specification ***neither states nor suggests*** that the claimed primers must be ***fully*** complementary to ***every*** known strain of HIV-1." (D.I. 157 at 7) (emphasis added)

Plaintiffs argue that "H SEQ ID NO: 1, one of the specification's two 'most preferred' oligonucleotide primers . . . was not fully complementary to several published strains of HIV-1." (*Id.*) (citing '352 patent at 7:31-34) Thus, adoption of Defendants' proposed construction would lead to exclusion of a preferred embodiment, which is not a preferred result. *See, e.g.*, *Kaneka Corp. v. Xiamen Kingdomway Grp.*, 790 F.3d 1298, 1304 (Fed. Cir. 2015).

C. "consisting of a first primer and a second primer"[5]

Plaintiffs' Proposed Construction	Defendants' Proposed Construction	Court's Construction
Plain and ordinary meaning, in light of the specification and file history	consisting of a first primer and second primer, and no other HIV-1 primers	Plain and ordinary meaning, in light of the specification and file history

In this term, the word "consisting" merely "requires that the recited 'pair of oligonucleotide primers' contain only two HIV-1 primers (a first and second primer) with the specified characteristics," ***but does not limit the number of pairs*** of such primers. (D.I. 157 at 15; Tr. at 61-62) Limiting the claim to a single pair of primers would import a limitation that the patentee did not intend. (*See* D.I. 157 at 14) (citing *Williamson v. Citrix Online, LLC*, 792 F.3d 1339, 1346 (Fed. Cir. 2015)) The parent to the asserted patents, U.S. Patent No. 6,881,537 ("the '537 patent"), "expressly recites the limitation Defendants urge the Court to add here – 'a pair of

[4] At the hearing, Plaintiffs clarified that they agree with Defendants that "fully complementary" means a 100% match, adding that what has to match 100% is the oligonucleotide and a single strain of any given subtype. (*See* Tr. at 55-56) ("'Fully complementary' means, as used in the claim, it has to be 100 percent sequence identical to, not to every strain that is going to be amplified, but to a single strain, to the LTR sequence.")

[5] '352 patent claim 3; '262 patent claims 1, 6, and 11.

oligonucleotide primers, for use as ***a single primer set***.'" (D.I. 165 at 10 (quoting '537 patent at 15:61-16:65); Tr. at 71) The patentee removed this limitation from the asserted patents.

Defendants contend that the prosecution history and specification teach that the patent solved a problem in the prior art by allowing the detection of HIV-1 with ***a single*** primer pair. (D.I. 156 at 14-17 (citing D.I. 149-4 at BMX_00001389, BMX_00001486, BMX_00001390; '352 patent at 8:49-14:15); *see also* Tr. at 68-69 ("[T]his comes up multiple times where they say it's a single primer pair, the Examiner comes back and has this language about, well, maybe you could do this multiplexing amplification where you use other primer pairs and then they come back and dispute that.")) However, while the patentee discussed a single primer pair as an advantage of the invention, the patentee did not disavow the full scope of the claim, which allows for multiple primer pairs in the detection of HIV.[6] As the examiner noted during prosecution, "the asserted claims 'do not prohibit the combining of the resultant primer pairs with other primer pairs in a multiplexed reaction.'" (D.I. 165 at 12) (quoting D.I. 149-4, Ex. D at BMX_00001595-1598)

[6] The asserted claims require one primer pair for the amplification of the LTR region of the HIV-1 genome but allow for multiple primer pairs in the detection of HIV generally. (*See* Tr. at 73) (Plaintiffs: "[Y]ou have to have only one primer pair in the detection of HIV by amplifying the LTR, which is what our claims are directed to, . . . [but] you [] can have other HIV-1 primers that detects other regions" of the HIV genome)

D. "primer binding site"[7]

Plaintiffs' Proposed Construction	Defendants' Proposed Construction	Court's Construction
A location on the HIV-1 genome, or the sequence complementary thereto, to which an oligonucleotide can anneal	a site to which a primer binds	A location on the HIV-1 genome, or the sequence complementary thereto, to which an oligonucleotide can anneal

The Court's construction is supported by the specification, which makes clear the scope of the claims:

> The location ***on the HIV-genome (or the sequence complementary thereto) to which both oligonucleotides*** comprised in such a pair according to the invention ***can anneal, will together define the sequence of the nucleic acid that is amplified. The amplified sequence is located between the 'primer-binding sites'*** within the LTR region of the HIV-genome.

('352 patent at 7:19-25; '262 patent at 7:50-56) (emphasis added) Plaintiffs' proposed construction tracks this statement by allowing for binding on the sequence complementary to the HIV-1 genome. The patentee unambiguously intended to define a primer binding site as both a location on the HIV-1 genome and the sequence complementary thereto.

By contrast, Defendants' proposed construction could exclude a preferred embodiment of the patent. (Tr. at 80-81; D.I. 179 at 3 ("Claim 1 of each of the '352 and '262 patents do not cover the embodiment in column 7.")) The Court also finds unpersuasive Defendants' contention that claim 1 of the asserted patents, which recite "a sequence which is the reverse complement of a sequence of the LTR region at a second primer binding site" ('352 patent at claim 1; '262 patent at claim 1), ignores the limitations of these claims and renders them superfluous. (D.I. 167 at 1) The Court agrees with Plaintiffs that the specification clearly

[7] '352 patent claims 1, 3, and 5; '262 patent claims 1, 6, and 11.

intends "primer binding site" to include both a location on the HIV-1 genome or a location on a complementary sequence thereto, and a "POSA would readily understand which of those two strands was intended depending on the context of the claim." (D.I. 165 at 14)

III. CONCLUSION

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