IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GUARDANT HEALTH, INC., Plaintiff, v. FOUNDATION MEDICINE, INC., Defendant.	)	Civil Action No. 17-1616-LPS-CJB
GUARDANT HEALTH, INC., Plaintiff, v. PERSONAL GENOME DIAGNOSTICS, INC., Defendant.	)	Civil Action No. 17-1623-LPS-CJB

REPORT AND RECOMMENDATION

In these two related actions filed by Plaintiff Guardant Health, Inc. ("Guardant" or "Plaintiff") against Defendants Foundation Medicine, Inc. ("FMI") and Personal Genome Diagnostics, Inc. ("PGDx" and collectively with FMI, "Defendants"), Guardant alleges infringement of United States Patent Nos. 9,598,731 (the "'731 patent"), 9,834,822 (the "'822 patent"), 9,840,743 (the "'743 patent") and 9,902,992 (the "'992 patent" and collectively with the other patents, "the asserted patents"). Presently before the Court is the matter of claim construction. The Court recommends that the District Court adopt the claim construction-related decisions set forth below.

I. BACKGROUND AND STANDARD OF REVIEW

The Court hereby incorporates by reference the summary of the background of this matter set out in its September 6, 2019 Report and Recommendation ("September 6 R&R").

(D.I. 354 at 1-3)[1] It additionally incorporates by reference the legal principles regarding claim construction set out in the September 6 R&R. (*Id.* at 3-5)

II. DISCUSSION

The parties had claim construction disputes regarding 13 terms or sets of terms (hereinafter, "terms"). The Court has addressed three of these terms in the September 6 R&R. The Court addresses two of the remaining 10 terms herein.

A. "consensus sequence"

The claim term "consensus sequence" appears in claim 1 of the '731 patent. (D.I. 53, ex. B at 13) This claim is reproduced below, with the disputed term highlighted:

> **1.** A method for quantifying single nucleotide variant tumor markers in cell-free DNA from a subject, comprising:
>
> (a) providing at least 10 ng of cell-free DNA obtained from a bodily sample of the subject;
>
> (b) attaching tags comprising barcodes having from 5 to 1000 distinct barcode sequences to said cell-free DNA obtained from said bodily sample of the subject, to generate non-uniquely tagged parent polynucleotides, wherein each barcode sequence is at least 5 nucleotides in length;
>
> (c) amplifying the non-uniquely tagged parent polynucleotides to produce amplified non-uniquely tagged progeny polynucleotides;
>
> (d) sequencing the amplified non-uniquely tagged progeny polynucleotides to produce a plurality of sequence reads from each parent polynucleotide, wherein each sequence read comprises a barcode sequence and a sequence derived from cell-free DNA;
>
> (e) grouping the plurality of sequence reads produced from each non-uniquely tagged parent polynucleotide into families based on i) the barcode sequence and ii) at least one of: sequence information at a beginning of the sequence derived from cell-free

[1] For simplicity's sake, the Court will refer to the "D.I." number in Civil Action No. 17-1623-LPS-CJB, unless otherwise indicated.

DNA, sequence information at an end of the sequence derived from cell-free DNA, and length of the sequence read, whereby each family comprises sequence reads of non-uniquely tagged progeny polynucleotides amplified from a unique polynucleotide among the non-uniquely tagged parent polynucleotides;

(f) comparing the sequence reads grouped within each family to each other to determine *consensus sequences* for each family, wherein each of the *consensus sequences* corresponds to a unique polynucleotide among the non-uniquely tagged parent polynucleotides;

(g) providing one or more reference sequences from a human genome, said one or more reference sequences comprising one or more loci of reported tumor markers, wherein each of the reported tumor markers is a single nucleotide variant;

(h) identifying *consensus sequences* that map to a given locus of said one or more loci of reported tumor markers; and

(i) calculating a number of *consensus sequences* that map to the given locus that include the single nucleotide variant thereby quantifying single nucleotide variant tumor markers in said cell-free DNA from said subject.

('731 patent, col. 62:8-54 (emphasis added)) The parties' competing proposed constructions for "consensus sequence" are set out in the chart below:

Term	**Plaintiff's Proposed Construction**	**Defendants' Proposed Construction**
"consensus sequence"	No construction necessary.	"[t]he string of nucleotides that represents a set of multiply aligned sequence reads derived from the same parent polynucleotide"

(D.I. 59 at 13)

The Court finds that this term does not require construction, at least not at this time. The purpose of claim construction is to "determin[e] the meaning and scope of the patent claims asserted to be infringed." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir.

1995). However, claim construction is required only when "the parties raise an *actual dispute* regarding the proper scope of the[] claims[.]" *02 Micro Int'l Ltd. v. Beyond Innovation Tech. Co.*, 521 F.3d 1351, 1360 (Fed. Cir. 2008) (emphasis added); *see also, e.g.*, *Warner Chilcott Co. v. Mylan Inc.*, Civil Action Nos. 11-6844 (JAP), 11-7228(JAP), 2013 WL 3336872, at *3 (D.N.J. July 2, 2013) ("A court is not required to construe a claim term where there is not an actual dispute with respect to that term."). Upon review of the parties' briefing and after further probing the issue during the *Markman* hearing, it does not appear to the Court that the parties have an actual ripe dispute regarding the meaning of "consensus sequence."

Guardant asserts that "consensus sequence" need not be construed because additional language in step (f) of claim 1 of the '731 patent tells us that a consensus sequence: (1) corresponds to a unique polynucleotide; and (2) is determined by comparing sequence reads grouped within each family to each other. (D.I. 59 at 13)[2] During the *Markman* hearing, it became clear that the last portion of Defendants' proposed construction ("derived from the same parent polynucleotide") means the same thing as (and is therefore is redundant of) the language in the claim stating that the consensus sequence corresponds to a unique polynucleotide. (D.I. 85 (hereinafter, "Tr.") at 59-60) And with respect to the "multiply aligned" language in Defendants' proposed construction, Guardant asserted that such language was confusing. (D.I. 59 at 13-14; Tr. at 53-54) In response, Defendants suggested that this language simply means

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[2] During the *Markman* hearing, Guardant's counsel noted that this information regarding a "consensus sequence" is consistent with what is said in the specification. (D.I. 85 at 52, 54, 67) The specification teaches that "the set of sequence reads is collapsed to produce a set of *consensus sequences* corresponding to unique tagged parent polynucleotides. . . . By comparing sequences of progeny in a family, a *consensus sequence* of the original parent polynucleotide can be deduced. This produces a set of *consensus sequences* representing unique parent polynucleotides in the tagged pool." ('731 patent, col. 43:23-25, 33-37 (emphasis added))

that a consensus sequence is determined by comparing more than one sequence read. (D.I. 74 at 9; Tr. at 60-61) Yet Guardant agrees that a consensus sequence is determined by comparison of a group of sequence reads, (Tr. at 68-70), and other claim language already makes this point clear, as noted above.[3]

In sum, the parties have not established that construction of the term "consensus sequence" is necessary (at least at this time). Thus, the Court declines to construe this term. *See, e.g.*, *Endoheart AG v. Edwards Lifescis. Corp.*, C.A. No. 14-1473-LPS, 2016 WL 1270127, at *4 (D. Del. Mar. 31, 2016) (declining to construe a claim term where the parties failed to "actually articulate[] a fundamental disagreement about the scope of the disputed term"); *Warner Chilcott Co.*, 2013 WL 3336872, at *3 (declining to construe a claim term where "no party has been able to adequately articulate how, based upon the claim term 'tablet,' the meaning or proper scope of any of the asserted claims is in dispute"). The Court recommends that the term be afforded its plain and ordinary meaning.

B. "collapsing sequence reads in each family"

The claim term "collapsing sequence reads in each family" appears in claim 1 of the '822 patent and claim 1 of the '992 patent. (D.I. 53, ex. B at 15-17) Accordingly, these claims are reproduced below, with the disputed term highlighted:

> **1.** A method, comprising:
> a) providing a population of cell free DNA ("cfDNA") molecules obtained from a bodily sample from a subject;
>
> b) converting the population of cfDNA molecules into a population of non-uniquely tagged parent polynucleotides, wherein each of

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[3] In supplemental briefing, Defendants assert that "Guardant is trying to broaden the scope of 'consensus sequence' far beyond its ordinary meaning in an attempt to establish literal infringement." (D.I. 139 at 2) But on this record, it is just not clear to the Court how that is so.

the non-uniquely tagged parent polynucleotides comprises (i) a sequence from a cfDNA molecule of the population of cfDNA molecules, and (ii) an identifier sequence comprising one or more polynucleotide barcodes;

c) amplifying the population of non-uniquely tagged parent polynucleotides to produce a corresponding population of amplified progeny polynucleotides;

d) sequencing the population of amplified progeny polynucleotides to produce a set of sequence reads;

e) mapping sequence reads of the set of sequence reads to one or more reference sequences from a human genome;

f) grouping the sequence reads into families, each of the families comprising sequence reads comprising the same identifier sequence and having the same start and stop positions, whereby each of the families comprises sequence reads amplified from the same tagged parent polynucleotide;

g) at each genetic locus of a plurality of genetic loci in the one or more reference sequences, *collapsing sequence reads in each family* to yield a base call for each family at the genetic locus; and

h) determining a frequency of one or more bases called at the locus from among the families.

('822 patent, col. 62:18-48 (emphasis added))

1. A method for detecting genetic aberrations in cell-free DNA ("cfDNA") molecules from a subject, comprising:

a) providing cfDNA molecules obtained from a bodily sample of the subject;

b) attaching tags comprising barcodes having a plurality of different barcode sequences to the cfDNA molecules to tag at least 20% of the cfDNA molecules, which attaching comprises ligating adaptors comprising the barcodes to both ends of the cfDNA molecules, wherein ligating comprises using more than 10x molar excess of the adaptors as compared to the cfDNA molecules, thereby generating tagged parent polynucleotides;
c) amplifying the tagged parent polynucleotides to produce amplified tagged progeny polynucleotides;

d) sequencing the amplified tagged progeny polynucleotides to produce a plurality of sequence reads from each of the tagged parent polynucleotides, wherein each sequence read of the plurality of sequence reads comprises a barcode sequence and a sequence derived from a cfDNA molecule of the cfDNA molecules;

e) mapping sequence reads of the plurality of sequence reads to one or more reference sequences from a human genome;

f) grouping the sequence reads mapped in e) into families based at least on barcode sequences of the sequence reads, each of the families comprising sequence reads comprising the same barcode sequence, whereby each of the families comprises sequence reads amplified from the same tagged parent polynucleotide;

g) at each of a plurality of genetic loci in the one or more reference sequences, *collapsing sequence reads in each family* to yield a base call for each family at the genetic locus; and

h) detecting, at one or more genetic loci, a plurality of genetic aberrations, wherein the plurality of genetic aberrations comprises two or more different members selected from the group of members consisting of a single base substitution, a copy number variation (CNV), an insertion or deletion (indel), and a gene fusion.

('992 patent, col. 64:2-41 (emphasis added)) The parties' competing proposed constructions for "collapsing sequence reads in each family" are set out in the chart below:

Term	**Plaintiff's Proposed Construction**	**Defendants' Proposed Construction**
"collapsing sequence reads in each family"	No construction necessary.	"[c]onverting the polynucleotide sequence reads in each family into a single polynucleotide sequence that represents the sequence reads in the family"

(D.I. 59 at 19)

Here again, even following claim construction briefing and the *Markman* hearing, the Court does not understand there to be a discernible, specific dispute with respect to this claim

term. In the briefing, Guardant raised two issues with Defendants' proposed construction: (1) Defendants' substitution of the term "converting" for "collapsing[,]" which Guardant asserted is unnecessary; and (2) the possibility that Defendants' proposed construction could be read to wrongly suggest that "collapsing" leads to a sequence that represents *each* of the reads in the family (as opposed to a sequence that represents the *collection* of reads in the family). (D.I. 59 at 19-20; D.I. 72 at 12)

As for the first issue regarding "converting," Guardant's counsel agreed at the *Markman* hearing that that language was the most problematic portion of Defendants' proposed construction. (Tr. at 74) Yet Defendants' counsel then asserted that there was no dispute with respect to that word and Defendants would be "[f]ine" with leaving "collapsing" in their proposed construction (instead of "converting"). (*Id.* at 78) And any dispute with respect to the second issue seemed to be quickly dispelled by Defendants' responsive brief, where they appear to agree that collapsing leads to a sequence that represents the *collection* of reads in the family. (D.I. 68 at 13-14)

Beyond those particular two issues, Guardant's counsel was not "sure what [Defendants] are trying to get at with all this" additional language in their proposed construction. (Tr. at 81-82) Both parties seem to agree that the collapsing process results in the grouped sequence reads generating "a single representative sequence"—i.e., the base call. (D.I. 68 at 13 (Defendants explaining that "the base call is made in a particular way—by *collapsing* the grouped sequence reads into a single representative sequence") (certain emphasis in original, certain emphasis omitted); *see also* D.I. 59 at 19-20 (Guardant asserting that "[a]t most, the 'collapsing' process leads to a sequence that represents the collection of reads in a family") (emphasis omitted)) Indeed, claim 1 of the '822 patent expressly conveys that the sequence reads in each family are

collapsed "to yield a base call for each family at the genetic locus[.]" ('822 patent, col. 62:44-46) And so while Plaintiff and Defendants may each be skeptical about what is prompting the other side to take their respective positions here, being skeptical is not the same thing as articulating an actual dispute about the proper scope of the claim.

Because it is not clear to the Court that there is a real dispute with respect to "collapsing sequence reads in each family," (or if there is, what the nature of that dispute is), the Court declines to construe the term at this stage.[4] Accordingly, the Court recommends that the term be afforded its plain and ordinary meaning.

III. CONCLUSION

For the foregoing reasons, the Court recommends that the District Court adopt the following decisions:

1. "consensus sequence" should be afforded its plain and ordinary meaning

2. "collapsing sequence reads in each family" should be afforded its plain and ordinary meaning

This Report and Recommendation is filed pursuant to 28 U.S.C. § 636(b)(1)(B), Fed. R. Civ. P. 72(b)(1), and D. Del. LR 72.1. The parties may serve and file specific written objections within fourteen (14) days after being served with a copy of this Report and Recommendation. Fed. R. Civ. P. 72(b)(2). The failure of a party to object to legal conclusions may result in the loss of the right to de novo review in the district court. *See Henderson v. Carlson*, 812 F.2d 874, 878-79 (3d Cir. 1987); *Sincavage v. Barnhart*, 171 F. App'x 924, 925 n.1 (3d Cir. 2006).

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[4] Defendants assert that the term should be construed in light of, *inter alia*, a "[k]ey non-infringement issue[,]" (Defendants' Markman Presentation, Slide 35), but they have not made clear to the Court how any such issue relates to a dispute about the meaning of the term.

The parties are directed to the Court's Standing Order for Objections Filed Under Fed. R. Civ. P. 72, dated October 9, 2013, a copy of which is available on the District Court's website, located at http://www.ded.uscourts.gov.

Dated: September 11, 2019

Christopher J. Burke
UNITED STATES MAGISTRATE JUDGE