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 constructions as set forth below.

I. BACKGROUND

Guardant commenced these actions on November 9, 2017. (Civil Action No. 17-1616-LPS-CJB, D.I. 1; Civil Action No. 17-1623-LPS-CJB, D.I. 1) The cases were thereafter referred to the Court to hear and resolve all pretrial matters, up to and including case-dispositive motions. (Civil Action No. 17-1616-LPS-CJB, D.I. 5; Civil Action No. 17-1623-LPS-CJB, D.I. 4)

In the currently-operative Third Amended Complaints, Guardant alleges that Defendants' liquid biopsy tests infringe claims of the asserted patents. (Civil Action No. 17-1616-LPS-CJB, D.I. 149 at ¶¶ 4, 14-24; Civil Action No. 17-1623-LPS-CJB, D.I. 280 at ¶¶ 6, 17-28) The asserted patents relate to methods for identifying genetic material harboring cancer-causing mutations from a patient's blood. (*See* D.I. 59 at 1)[1] Each of the patents is titled "Systems and Methods to Detect Rare Mutations and Copy Number Variation." (D.I. 53, exs. C-F)[2] The '731 patent, '822 patent and the '743 patent share a common specification ("the specification"), and the '992 patent has a similar specification. (*See* D.I. 75, ex. 1 at Slide 4)

The parties completed initial briefing on claim construction on November 16, 2018. (D.I. 59; D.I. 68; D.I. 72; D.I. 74)[3] The Court held a *Markman* hearing on December 14, 2018. (D.I. 85 (hereinafter, "Tr.")) Following the hearing, Defendants submitted a supplemental letter brief relating to a new argument asserted by Guardant during the *Markman* hearing. (D.I. 84) And the parties thereafter submitted supplemental briefs relating to *inter partes* review proceedings with respect to the '731 patent, which the parties assert have relevance to the construction of

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[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.

[2] The asserted patents appear on the docket in this action more than once. Citations to the patents will simply be to the '731 patent, '822 patent, '743 patent and '992 patent.

[3] FMI and PGDx filed joint claim construction briefs.

certain disputed terms. (D.I. 88; D.I. 90; D.I. 136; D.I. 139; D.I. 162; D.I. 173; D.I. 283; D.I. 286; D.I. 351)

II. STANDARD OF REVIEW

It is well-understood that "[a] claim in a patent provides the metes and bounds of the right which the patent confers on the patentee to exclude others from making, using, or selling the protected invention." *Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1257 (Fed. Cir. 1989). Claim construction is a generally a question of law, although subsidiary fact finding is sometimes necessary. *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 837-38 (2015).

The Court should typically assign claim terms their "ordinary and customary meaning[,]" which is "the meaning that the term[s] would have to a person of ordinary skill in the art ['POSITA'] 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). However, when determining the ordinary meaning of claim terms, the Court should not extract and isolate those terms from the context of the patent; rather it should endeavor to reflect their "meaning to the ordinary artisan after reading the entire patent." *Id.* at 1321; *see also Eon Corp. IP Holdings LLC v. Silver Spring Networks, Inc.*, 815 F.3d 1314, 1320 (Fed. Cir. 2016).

In proceeding with claim construction, the Court should look first and foremost to the language of the claims themselves, because "[i]t 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*, 415 F.3d at 1312 (internal quotation marks and citations omitted). For example, the context in which a term is used in a claim may be "highly instructive." *Id.* at 1314. In addition,

"[o]ther claims of the patent in question, both asserted and unasserted, can . . . be valuable" in discerning the meaning of a particular claim term. *Id.* This is "[b]ecause claim terms are normally used consistently throughout the patent, [and so] the usage of a term in one claim can often illuminate the meaning of the same term in other claims." *Id.* Moreover, "[d]ifferences among claims can also be a useful guide[,]" as when "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.

In addition to the words of the claims, the Court should look to other intrinsic evidence. For example, the Court should analyze the patent specification, which "may reveal a special definition given to a claim term . . . that differs from the meaning [that term] would otherwise possess" or may reveal an intentional disclaimer of claim scope. *Id.* at 1316. Even if the specification does not contain such revelations, it "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." *Id.* at 1315 (internal quotation marks and citation omitted). That said, however, the specification "is not a substitute for, nor can it be used to rewrite, the chosen claim language." *SuperGuide Corp. v. DirecTV Enters., Inc.*, 358 F.3d 870, 875 (Fed. Cir. 2004). And a court should also consider the patent's prosecution history, if it is in evidence, because it "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[.]" *Phillips*, 415 F.3d at 1317.

Extrinsic evidence, "including expert and inventor testimony, dictionaries, and learned treatises[,]" can also "shed useful light on the relevant art[.]" *Id.* (internal quotation marks and

citations omitted). Overall, while extrinsic evidence may be useful, it is "less significant than the intrinsic record in determining the legally operative meaning of claim language." *Id.* (internal quotation marks and citations omitted); *accord Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 981 (Fed. Cir. 1995).

In utilizing these resources during claim construction, courts should keep in mind that "[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).

III. DISCUSSION

The parties currently have disputes regarding 13 terms or sets of terms (hereinafter, "terms"). This Report and Recommendation addresses three such terms. The other terms will be addressed in one or more forthcoming Report and Recommendations.

A. "sequence read"

The claim term "sequence read" appears in certain claims of all four asserted patents. (D.I. 53, ex. B at 4-5) The use of the disputed term in claim 1 of the '731 patent and claim 1 of the '743 patent is representative. (*See* Defendants' Markman Presentation, Slide 3; Guardant's Markman Presentation, Slide 7) Accordingly, these claims are 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;
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> (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 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 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))

1. A method for detecting copy number variation, comprising:

a) sequencing extracellular polynucleotides from a bodily sample from a subject, wherein each of the extracellular polynucleotides generates a plurality of *sequence reads*;

b) filtering out reads that fail to meet a set accuracy, quality score, or mapping score threshold;

c) mapping the plurality of *sequence reads* to a reference sequence;

d) quantifying mapped reads or unique *sequence reads* in a plurality of predefined regions of the reference sequence; and

e) determining copy number variation in one or more of the plurality of predefined regions by:

i) normalizing a number of reads in the plurality of predefined regions to each other, or a number of unique *sequence reads* in the plurality of predefined regions to each other; and/or

ii) processing a number of reads in the plurality of predefined regions or a number of unique *sequence reads* in the plurality of predefined regions with numbers obtained from a control sample.

('743 patent, col. 62:43-65 (emphasis added))

The parties' competing proposed constructions for "sequence read" are set out in the chart below:

Term	**Plaintiff's Proposed Construction**	**Defendants' Proposed Construction**
"sequence read"	"[i]nformation obtained from a sequencer evidencing the order of bases in a nucleic acid molecule"	"[t]he order of the bases of a polynucleotide determined by a sequencer"

(D.I. 59 at 6) As reflected by the proposals, the parties' dispute is a narrow one. Both parties agree that: (1) a "sequence read" is obtained from a sequencer; (2) a "sequence read" reflects the order of bases of a polynucleotide; and (3) an accuracy, quality or mapping score threshold can

be *assigned* to a "sequence read." (D.I. 74 at 5; Tr. at 6, 12)[4] What the parties do not agree on is whether that additional information related to accuracy and quality "is actually part of a sequence read." (Tr. at 6-7; *see also* D.I. 59 at 6-7; D.I. 74 at 5) For the reasons set out below, the Court concludes that Defendants' proposed construction is better aligned with the intrinsic evidence.

Guardant asserts that the claim language supports its view that the term "sequence read" encompasses information beyond merely the order of the bases. (D.I. 59 at 6; D.I. 72 at 5; Tr. at 7, 15) To that end, Guardant points to the limitation of claim 1 of the '743 patent that recites "filtering out [sequence] reads that fail to meet a set accuracy, quality score, or mapping score threshold[.]" (D.I. 59 at 6 (quoting '743 patent, col. 62:49-50)) Guardant also points to dependent claim 5 of the '731 patent, which recites "[t]he method of claim **1**, further comprising filtering out sequence reads that fail to meet a set quality control threshold" and claim 10 of the '822 patent, which recites "[t]he method of claim **1**, further comprising filtering out sequence reads that fail to meet a quality threshold." (*Id.* (quoting '731 patent, col. 63:5-7; '822 patent, col. 63:9-10)) In the Court's view, however, this claim language does not demonstrate that the recited accuracy or quality threshold is *actually a part of* the sequence read itself (as opposed to being something that is assigned to or associated with the sequence read).

The specification underscores this conclusion. It first conveys that a "sequence read" is "[t]he output of a sequencer[.]" ('731 patent, col. 31:21) The specification then explains that "[a]fter sequencing, reads *are assigned a quality score*" and that such a score "may be a *representation* of reads that *indicates whether those reads may be useful in subsequent analysis based on a threshold.*" (*Id.*, col. 44:37-40 (emphasis added); *see also id.*, col. 44:50-51 ("After

[4] The parties also seem to agree that the accuracy and quality information can be used to determine how reliable the sequence read is. (Tr. at 9, 13-14)

mapping alignment, sequence reads *are assigned a mapping score*.") (emphasis added)) Furthermore, the specification explains that "[s]equencing reads *with a quality score* at least 90%, 95%, 99%, 99.9%, 99.99% or 99.999% may be filtered out of the data. In other cases, sequencing reads *assigned a quality score* less than 90%, 95%, 99%, 99.9%, 99.99% or 99.999% may be filtered out of the data set." (*Id.*, col. 44:42-47 (emphasis added)) Thus, the specification consistently demonstrates that a quality score is not part of the sequence read itself, but instead is something that is assigned to the sequence read, *after* the sequence read itself has already been generated. (*See* D.I. 68 at 5; D.I. 74 at 5; Tr. at 12 ("The sequence read is the sequence. In addition to that, the sequencer may assign a quality score. That is information about the quality of the sequence read. But that is not the sequence read."))[5]

For the above reasons, the Court recommends that "sequence read" be construed to mean "the order of the bases of a polynucleotide determined by a sequencer."

B. "barcode(s)"

The claim term "barcode(s)" appears in certain claims of all four asserted patents. (D.I. 53, ex. B at 1) The use of the disputed term in claim 1 of the '731 patent, reproduced above, is

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[5] Guardant further argues that the POSITA would understand that a "sequence read" includes quality and accuracy information, and in support points to the FASTQ file format, an industry standard for storing sequence reads. (D.I. 59 at 7 (citing *id.*, exs. 1-2); *see also* Tr. at 7-8) Guardant notes that the FASTQ file format "stores both sequence and quality information." (D.I. 59 at 7) Indeed, the documents that Guardant cites explain that "FASTQ is a text-based sequencing data file format that stores *both raw sequence data and quality scores*." (*Id.*, ex. 1 at 1 (emphasis added); *see also id.*, ex. 2 at 1 ("FASTQ format is a text-based format for storing both a biological sequence (usually nucleotide sequence) and its corresponding quality scores.") (emphasis omitted)) Rather than supporting Guardant's position, however, this extrinsic evidence merely reinforces that the sequence information (i.e., order of bases) and the corresponding quality information amount to *separate* information. Just because such information may be stored together in a file "does not mean that sequence read and corresponding quality information are not distinct items of information." (D.I. 68 at 5 n.6)

representative. (*See* Defendants' Markman Presentation, Slide 8) That claim recites, *inter alia*, "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[.]" ('731 patent, col. 62:12-17 (emphasis added))

The parties' competing proposed constructions for "barcode(s)" are set out in the chart below:

Term	**Plaintiff's Proposed Construction**	**Defendants' Proposed Construction**
"barcode(s)"	"[a] nucleic acid identifier"	"[a] nucleotide or a sequence of nucleotides used as a tag or identifier"

(D.I. 59 at 3) The parties agree that a "barcode" is something used to identify unique molecules. (*Id.*; D.I. 68 at 2-3; Tr. at 19) The crux of the dispute with respect to this term is whether a "barcode" must be made out of a "nucleotide or a sequence of nucleotides[,]" (Defendants' position), or whether a "barcode" may be made up of things other than nucleotides, such as a dye or metal isotope (Guardant's position). (D.I. 59 at 3-4; D.I. 68 at 3; Tr. at 18) Here, the Court again concludes that Defendants' position is best supported by the intrinsic evidence.

According to Guardant, one particular portion of the specification clearly conveys that a "barcode" may be composed of things other than nucleotides:

> C. Assignment of *Barcodes* to Cell Free Polynucleotide Sequences
> The systems and methods disclosed herein may be used in applications that involve the assignment of *unique or non-unique identifiers, or molecular barcodes*, to cell free polynucleotides. *Often, the identifier is a bar-code oligonucleotide that is used to tag the polynucleotide; but, in some cases, different unique identifiers are used. For example, in some cases, the unique identifier is a hybridization probe. In other cases, the unique*

> *identifier is a dye,* in which case the attachment may comprise intercalation of the dye into the analyte molecule (such as intercalation into DNA or RNA) or binding to a probe labeled with the dye. In still other cases, the unique identifier may be a nucleic acid oligonucleotide, in which case the attachment to the polynucleotide sequences may comprise a ligation reaction between the oligonucleotide and the sequences or incorporation through PCR. In other cases, the reaction may comprise addition of a metal isotope, either directly to the analyte or by a probe labeled with the isotope.

('731 patent, col. 38:8-25 (emphasis added)) Guardant asserts that this specification excerpt demonstrates that the patentee used the terms "identifier" and "barcode" interchangeably. (D.I. 72 at 3; Tr. at 20) In other words, Guardant reads the above-quoted phrase "unique or non-unique identifiers, or molecular barcodes" to mean "unique or non-unique identifiers, which is another way of saying molecular barcodes." Thus, according to Guardant, when this portion of the specification goes on to teach that a "dye" or "hybridization probe" could be utilized as a unique identifier, that means that a dye or hybridization probe could be utilized as a barcode (and that it would thus be improper to construe "barcode" as being limited to a nucleotide or a sequence of nucleotides). And the Court acknowledges that, when read in isolation, the above excerpt could seem helpful to Guardant's position. (*See* Tr. at 28 (Defendants' counsel noting that that this excerpt "is unclear, because there is nothing else that equates barcodes with a unique identifier"))

However, when the specification is viewed as a whole, it very clearly teaches that a "barcode" is a *particular type of identifier* that is made up of a single nucleotide or a sequence of nucleotides.[6] (D.I. 74 at 3 & n.3; Tr. at 26) For example, the specification explains that

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[6] This is also consistent with how the term "barcode" is used in the claims, as seen, for example, in claim 1 of the '731 patent. (*See* Tr. at 25 (noting that this claim refers to "barcodes" being comprised of nucleotides))

"[s]amples may be processed before sequencing with one or more reagents (e.g., enzymes, *unique identifiers (e.g., barcodes)*, probes, etc.)." ('731 patent, col. 30:37-39 (emphasis added); *see also, e.g.*, *id.*, col. 38:59-61 ("The unique identifiers (e.g., oligonucleotide bar-codes, antibodies, probes, etc.) may be introduced to cell free polynucleotide sequences randomly or non-randomly.")) These descriptions explicitly convey that a barcode is one example of a unique identifier (not that a barcode is synonymous with the term "unique identifier"). (*See* D.I. 74 at 3 n.3; Tr. at 24-25) Moreover, even the portion of the specification that Guardant relies upon in support of its proposal conveys that while a barcode is a type of identifier, there could be different unique identifiers utilized, such as a hybridization probe, dye, or metal isotope: "Often, the identifier is a bar-code oligonucleotide that is used to tag the polynucleotide; but, in some cases, different unique identifiers are used." ('731 patent, col. 38:11-13; *see* D.I. 68 at 3; Tr. at 29) Lastly, it is also notable that the specification otherwise repeatedly refers to a "barcode" as consisting of a single nucleotide or a sequence of nucleotides. (*See, e.g.*, '731 patent, col. 3:29-36 ("[i]n some embodiments, the barcode is a polynucleotide"); *id.*, col. 15:39-47 ("In some embodiments, the barcode is a polynucleotide. In some embodiments, the barcode comprises random sequence. In some embodiments, the barcode comprises a fixed or semi-random set of oligonucleotides[.]"))[7] Meanwhile, the specification never uses the term "barcode" to refer to dyes or other types of non-nucleotide barcodes. (*See* Tr. at 21-22)

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[7] During the *Markman* hearing, Guardant's counsel argued that because the specification states that "[i]n some embodiments" the "barcode is a polynucleotide" this means that in other embodiments, a barcode could be something other than a nucleotide. (Tr. at 19 ("This tells you that a barcode does not need to be limited to nucleotide.")) In response, Defendants' counsel noted that the specification states that a barcode may be a *single nucleotide or a polynucleotide*—that is, it states that "[i]n some cases, the unique identifiers may be a variety of lengths such that each barcode is at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 50, 100,

The intrinsic record, then, is consistent with Defendants' position that a "barcode" is made up of a nucleotide or sequence of nucleotides (while things such as dyes and isotopes are different types of unique identifiers). Accordingly, the Court recommends that "barcode(s)" be construed to mean "a nucleotide or a sequence of nucleotides used as a tag or identifier."

C. "non-uniquely tagged" / "non-uniquely tagging" / "barcode attached . . . is not unique" (the "non-uniquely tagged" terms)

The non-uniquely tagged terms appear in certain claims of all four asserted patents. (D.I. 53, ex. B at 6-9) The use of the disputed term in claim 1 of the '822 patent is representative. (*See* Defendants' Markman Presentation, Slide 15) Accordingly, this claim is 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 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;
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> 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;

1000 base pairs." ('731 patent, col. 39:11-13 (cited in Tr. at 26-27); Defendants' Markman Presentation, Slide 13) Therefore, the specification's "in some embodiments" language does not signal that in other embodiments, the barcode is *something other than* a nucleotide or sequence of nucleotides; rather, read in context, it conveys that there could be embodiments wherein the barcode consists of a single nucleotide (and others where it consists of a sequence of nucleotides).

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))

The parties' competing proposed constructions for the "non-uniquely tagged" terms are set out in the chart below:

Term	**Plaintiff's Proposed Construction**	**Defendants' Proposed Construction**
"non-uniquely tagged" / "non-uniquely tagging" / "barcode attached . . . is not unique"	"the number of different identifiers is at least 2 and fewer than the number of polynucleotides, such that neither every polynucleotide nor nearly every polynucleotide receives a unique identifier"	"the number of different identifiers is at least 2 and fewer than the number of polynucleotides"

(D.I. 59 at 7) The parties' dispute with respect to the non-uniquely tagged terms "is whether the number of 'non-unique' barcodes can approach the total number of polynucleotides." (*Id.*) In other words, Defendants' proposed construction would cover a situation where 1,000,000 polynucleotides were tagged with 999,999 barcodes. (*Id.*; *see also* D.I. 68 at 7-8 (Defendants explaining that "when the number of different identifiers is the same as the number of polynucleotides, the set is uniquely tagged, and when the number of identifiers is fewer than the

number of polynucleotides, the set is non-uniquely tagged")) For its part, Guardant contends such a construction cannot be correct "[a]s a matter of pure commonsense[.]" (D.I. 59 at 7) In Guardant's view, non-unique tagging encompasses circumstances where "neither every polynucleotide nor nearly every polynucleotide receives a unique identifier." (D.I. 72 at 7 (internal quotation marks and citation omitted))

The non-uniquely tagged terms should be construed as Defendants propose. After all, the patents expressly define the term "non-uniquely tagged," and Defendants' proposal tracks this express definition. (D.I. 68 at 5; D.I. 74 at 5; Tr. at 40, 43, 47-48; Defendants' Markman Presentation, Slide 16) To that end, the specification of the '731 patent explains that:

> Accordingly, this invention also provides compositions of tagged polynucleotides. The polynucleotides can comprise fragmented DNA, e.g. cfDNA. A set of polynucleotides in the composition that map to a mappable base position in a genome can be *non-uniquely tagged, that is, the number of different identifiers can be at least at least 2 and fewer than the number of polynucleotides that map to the mappable base position.*

('731 patent, col. 41:45-52 (emphasis added)) The patentee's use of "that is" here clearly signals an intent to define what it means to be "non-uniquely tagged." *See, e.g.*, *Edwards Lifescis. LLC v. Cook Inc.*, 582 F.3d 1322, 1334 (Fed. Cir. 2009) ("[T]he specification's use of 'i.e.' signals an intent to define the word to which it refers, 'malleable[.]'"); *Vitamix Corp. v. Blentec, Inc.*, CASE NO. 1:15 CV 1118, 2016 WL 2944150, at *4 (N.D. Ohio May 20, 2016) ("By using the phrase 'that is' the patentee demonstrated his intent to define the term 'not centered relative to the bottom surface.'").

Guardant nevertheless contends that the use of "that is" here "does not signal a definition where additional context makes clear that a particular definition is not intended." (D.I. 72 at 6) Yet, as Defendants note, "Guardant fails to point to any language in the specification or

prosecution history suggesting that the express definition was not intended or was limited to a single embodiment." (D.I. 74 at 5-6)

Guardant claims that, in the excerpt that follows, the specification actually describes Defendants' interpretation of non-unique tagging as *unique tagging* (and that the specification then goes on to criticize such form of tagging):

> [U]pon sequencing the genomic DNA, it may not be possible to determine which sequence reads are derived from which parent molecules. This problem can be diminished by tagging parent molecules with a sufficient number of unique identifiers (e.g., the tag count) such that there is a likelihood that two duplicate molecules, i.e., molecules having the same start and stop positions, bear different unique identifiers so that sequence reads are traceable back to particular parent molecules. *One approach to this problem is to uniquely tag every, or nearly every, different parent molecule in the sample.* However, depending on the number of haploid gene equivalents and distribution of fragment sizes in the sample, this may require billions of different unique identifiers.
>
> *This method can be cumbersome and expensive. . . .*

('731 patent, cols. 40:64-41:11 (emphasis added)) Accordingly, Guardant argues, "Defendants' construction should be rejected because it encompasses the very approaches that the specification describes as 'unique' barcoding, which are described as being 'cumbersome and expensive.'" (D.I. 59 at 7) To be sure, this passage does suggest that tagging nearly every molecule with a different tag (i.e., the reference to "uniquely tag[ing] . . . nearly every . . . parent molecule"—a form of *non-unique* tagging) would be cumbersome and expensive. But the fact that the patentee stated a criticism of this particular form of non-unique tagging does not necessarily wipe away the patentee's express definition of the term—a definition that could, at its extreme, allow for a

situation where 1,000,000 polynucleotides are tagged with 999,999 barcodes.[8] (*See* Tr. at 42 (Defendant's counsel noting that "the term as directly defined in the specification would encompass[,] at least at one extreme, a set of alternatives that have been criticized[,] but that doesn't mean [such alternatives] are not within the scope of the claim"))

Guardant also asserts that the embodiments using "non-unique" barcoding described in the specification "do[] not contemplate that virtually every polynucleotide will be given its own barcode" and that this further demonstrates that Defendants' proposal is wrong. (D.I. 59 at 8-9) In support, Guardant points to the specification's statement that a typical "sample comprising about 10,000 haploid human genome equivalents of cfDNA can be tagged with about *36 unique identifiers*." ('731 patent, col. 41:36-38 (emphasis added) (*cited in* D.I. 59 at 8-9)) But as Defendants retort: (1) it is improper to limit claims to an embodiment; and (2) just because a non-uniquely tagged set of polynucleotides *may have* substantially fewer barcodes than polynucleotides does not mean that the patents *require* this as to all forms of non-unique tagging. (D.I. 68 at 6)

In sum, the specification clearly defines "non-unique tagging," and Guardant's arguments to the contrary fail to overcome the patentee's express definition. For these reasons, the Court recommends that "non-uniquely tagged" / "non-uniquely tagging" / "barcode attached . . . is not

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[8] Defendants point out that even this "extreme" example would comport with the plain meaning of "not unique." That is, the plain meaning of "unique" is "'being the only one,'" (D.I. 68 at 6 (quoting *id.*, ex. 2 at 1288)), and in this example, the same barcode would be used to tag two different polynucleotides. Thus, these polynucleotides would not each be uniquely tagged. (*Id.*) And although this type of extreme example is criticized in the patent, it could well be that the patentee nevertheless chose a definition for the terms-at-issue that would encompass such an example, in part to avoid any concern about "creat[ing] hopeless indefiniteness" problems otherwise. (Tr. at 42)

unique" be construed to mean "the number of different identifiers is at least 2 and fewer than the number of polynucleotides."

IV. CONCLUSION

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

1. "sequence read" should be construed to mean "the order of the bases of a polynucleotide determined by a sequencer"

2. "barcode(s)" should be construed to mean "a nucleotide or a sequence of nucleotides used as a tag or identifier"

3. "non-uniquely tagged" / "non-uniquely tagging" / "barcode attached . . . is not unique" should be construed to mean "the number of different identifiers is at least 2 and fewer than the number of polynucleotides"

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).

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 6, 2019

Christopher J. Burke
UNITED STATES MAGISTRATE JUDGE