

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

TWINSTRAND BIOSCIENCES, INC.,
Petitioner,

v.

GUARDANT HEALTH, INC.,
Patent Owner.

IPR2022-00746
Patent 10,801,063 B2

Before SUSAN L. C. MITCHELL, TINA E. HULSE, and
MICHAEL A. VALEK, *Administrative Patent Judges*.

MITCHELL, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
35 U.S.C. § 314

I. INTRODUCTION

TwinStrand Biosciences, Inc. (“Petitioner”) filed a Petition requesting an *inter partes* review of claims 1–28 of U.S. Patent No. 10,801,063 B2 (Ex. 1001, “the ’063 patent”). Paper 2 (“Pet.”). Guardant Health, Inc. (“Patent Owner”) filed a Preliminary Response. Paper 8 (“Prelim. Resp.”). With our authorization, Petitioner filed a Reply to Patent Owner’s Preliminary Response (Paper 10), and Patent Owner filed a Sur-reply to the Reply (Paper 13).

We have authority under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted “unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” 35 U.S.C. § 314(a). Upon considering the argument and evidence presented by the parties, we determine that Petitioner has not established a reasonable likelihood that it would prevail in showing the unpatentability of at least one claim challenged in the Petition.

Accordingly, we decline to institute an *inter partes* review of any claim of the ’063 patent on any ground.

A. *Related Proceedings*

The parties state that the ’063 patent has been asserted in *TwinStrand Biosciences, Inc. v. Guardant Health, Inc.*, 1-21-cv-01126 (D. Del.). Pet 73; Paper 12, 1. The parties state that the ’063 patent is also the subject of *Illumina, Inc. v. Guardant Health, Inc.; Helmy Eltoukhy; and Amirali Talasaz*, 22-cv-00334 (D. Del.) (March 17, 2022). *Id.*

Petitioner filed concurrently a Petition requesting *inter partes* review of related patent U.S. Patent No. 10,889,858 B2 in IPR2022-00746.

On June 7, 2022—over two months after filing the instant Petition—Petitioner filed another petition requesting *inter partes* review of claims 1–

28 of the '063 patent in IPR2022-01115. Accordingly, Petitioner filed an Explanation of Multiple Petitions and Ranking of Petitions ranking the later-filed petition above the instant Petition. Paper 7. Because we deny the instant Petition on the merits, Petitioner's preference for the petition in IPR2022-01115 is moot.

B. The '063 Patent (Ex. 1001)

Genetic testing is useful for a number of diagnostic methods. Ex. 1001, 1:21–22. Disorders that are caused by rare genetic mutations (e.g., sequence variations) or changes in epigenetic markers, such as cancer and partial or complete aneuploidy, may be detected or more accurately characterized with DNA sequence information. *Id.* at 1:22–26.

Early detection and monitoring of genetic diseases is often useful and needed in the successful treatment or management of a disease. *Id.* at 1:27–29. According to the '063 patent, one approach may include monitoring a sample derived from cell-free nucleic acids, which are polynucleotides that can be found in different types of bodily fluids. *Id.* at 1:29–32. Cell-free DNA (“cfDNA”) has been known in the art for decades, and may contain genetic aberrations, such as copy number variation or sequence variation associated with a particular disease. *Id.* at 1:32–38.

The '063 patent explains that many methods have been developed to estimate copy number variation. *Id.* at 1:42–43. According to the Specification, most of those methods involve preparing a sample by converting the original nucleic acids into a sequenceable library, followed by massively parallel sequencing, and then conducting a bioinformatic analysis to estimate the copy number variation at one or more loci. *Id.* at 1:47–51.

The '063 patent states that although known methods for detecting cfDNA are able to reduce the errors introduced by the sample preparation

and sequencing processes for the molecules that are converted and sequenced, these methods are not able to infer the counts of molecules that were converted, but not sequenced. *Id.* at 1:56–59. The '063 patent states this inability to count converted but unsequenced molecules “can dramatically and adversely affect the sensitivity that can be achieved.” *Id.* at 1:59–63. Accordingly, the '063 patent relates to a method of tagging and counting both halves of double-stranded DNA and estimating the number of unseen molecules based on the number of detected Pairs (i.e., molecules where both strands were identified) and Singlets (i.e., molecules where only one strand was identified). *See id.* at 1:64–2:13.

C. *Illustrative Claims*

Petitioner challenges claims 1–28 of the '063 patent. Claims 1 and 15 are independent. Claim 1 is illustrative and reproduced below:

1. A method for classifying consensus sequences generated from sequencing reads derived from double-stranded cell-free deoxyribonucleic acid (cfDNA) molecules from a sample of a human subject, the method comprising:

- (a) non-uniquely tagging a population of double-stranded cfDNA molecules from the sample with more than a 10x molar excess of adapters comprising molecular barcodes, relative to the double-stranded cfDNA molecules in the population, to generate non-uniquely tagged parent polynucleotides,

wherein the double-stranded cfDNA molecules that map to a mappable base position of a reference sequence are tagged with a number of different molecular barcodes ranging from at least 2 to fewer than a number of double-stranded cfDNA molecules that map to the mappable base position, and

wherein at least 20% of the double-stranded cfDNA molecules are non-uniquely tagged with the adapters comprising the molecular barcodes at

both ends of a molecule of the double-stranded
cfDNA molecules;

- (b) amplifying a plurality of the non-uniquely tagged parent polynucleotides to produce progeny polynucleotides;
- (c) enriching a plurality of the progeny polynucleotides for target regions of interest to generate enriched progeny polynucleotides;
- (d) sequencing a plurality of the enriched progeny polynucleotides to produce a set of sequencing reads;
- (e) mapping a plurality of sequencing reads from the set of sequencing reads to the reference sequence;
- (f) grouping a plurality of the mapped sequencing reads into families of mapped sequencing reads based at least on
 - (i) sequence information from the molecular barcodes
 - and (ii) a beginning base position and an ending base position of the mapped sequencing reads;
- (g) generating a consensus sequence for each family from among one or more of the families to produce a set of consensus sequences; and
- (h) classifying one or more consensus sequences from among the set of consensus sequences as (1) paired consensus sequences generated from sequencing reads representing a Watson strand and a Crick strand of a non-uniquely tagged parent polynucleotides or (2) unpaired consensus sequences generated from sequencing reads representing only one of either a Watson strand or a Crick strand of a non-uniquely tagged parent polynucleotide.

Ex. 1001, 60:16–63. Independent claim 15 differs from claim 1 in that it describes a method for classifying unique sequencing reads. *See id.* at 62:1–34.

D. The Asserted Grounds of Unpatentability

Petitioner asserts that claims 1–28 would have been unpatentable on the following grounds:

Claims Challenged	35 U.S.C. §¹	References/Basis
1–7, 9–11, 15–18, 22–28	103	Murtaza ² , Schmitt ³ , and Meyer ⁴
8	103	Murtaza, Schmitt, Meyer, and Craig ⁵
12–14, 19–21	103	Murtaza, Schmitt, Meyer, and Kivioja ⁶

Petitioner also relies upon the Declaration of Dr. Paul T. Spellman (“Spellman Declaration,” Ex. 1002).

II. ANALYSIS

A. Person of Ordinary Skill in the Art

Petitioner asserts that a person of ordinary skill in the art at the time of the invention would have had

¹ The Leahy-Smith America Invents Act (“AIA”), Pub. L. No. 112–29, 125 Stat. 284 (2011), amended 35 U.S.C. §§ 102 and 103, effective March 16, 2013. Because the application from which the ’063 patent issued has an effective filing date after that date, the AIA version of § 103 applies.

² Schmitt et al., WO 2013/142389 A1, published Sept. 26, 2013 (“Schmitt,” Ex. 1009).

³ Murtaza et al., *Non-Invasive Analysis of Acquired Resistance to Cancer Therapy by Sequencing of Plasma DNA*, 497 NATURE 108–12 (2013) (“Murtaza,” Ex. 1004).

⁴ Meyer et al., *Parallel Tagged Sequencing on the 454 Platform*, 3 NATURE PROTOCOLS 267–78 (2008) (“Meyer,” Ex. 1005).

⁵ Craig et al., *Identification of Genetic Variants Using Bar-coded Multiplexed Sequencing*, 5 NATURE METHODS 887–93 (2008) (“Craig,” Ex. 1007).

⁶ Kivioja et al., *Counting Absolute Numbers of Molecules Using Unique Molecular Identifiers*, 9 NATURE METHODS 72–76 (2012) (“Kivioja,” Ex. 1006).

(i) a Ph.D. in molecular biology, genetics, bioinformatics, or a related field, and have at least about two years of experience in the use and development of sequencing technologies; or (ii) a Master's degree in one of the same fields with at least about five years of the same experience.

Pet. 18 (citing Ex. 1002 ¶¶ 26–29). Patent Owner does not offer a proposed definition of the level of ordinary skill in the art at this stage of the proceeding. *See generally* Prelim. Resp.

On this record, we adopt Petitioner's uncontested definition of the level of ordinary skill in the art. We further note that the prior art itself is sufficient to demonstrate the level of skill in the art at the time of the invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that specific findings regarding ordinary skill level are not required “where the prior art itself reflects an appropriate level and a need for testimony is not shown” (*quoting Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 163 (Fed. Cir. 1985))).

B. Claim Construction

In an *inter partes* review, the Board applies the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b). *See* 37 C.F.R. § 100(b) (2021). Under that standard, claim terms “are generally given their ordinary and customary meaning” as understood by a person of ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc).

Petitioner sets forth a proposed construction for “a number of double-stranded cfDNA molecules that map to the mappable base position,” recited in claim 1. Pet. 18–19. Petitioner asserts that a “POSA would understand that the number of double-stranded cfDNA molecules that map to the

mappable base position will vary, depending on the number of haploid genome equivalents (HGEs) in the sample.” *Id.* at 19 (citing Ex. 1002 ¶¶ 133–136). Patent Owner does not dispute Petitioner’s construction. Prelim. Resp. 25.

Having considered the parties’ respective arguments, we determine that it is unnecessary to expressly construe any claim terms for purposes of rendering this Decision. *See Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011) (“[C]laim terms need only be construed ‘to the extent necessary to resolve the controversy.’” (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999))).

C. Obviousness over Murtaza, Schmitt, and Meyer

Petitioner asserts that claims 1–7, 9–11, 15–18, and 22–28 are unpatentable as obvious over Murtaza, Schmitt, and Meyer. Pet. 25–64. Patent Owner opposes Petitioner’s assertions. Prelim. Resp. 25–47. On this record, we determine that Petitioner has not established a reasonable likelihood that it would prevail in showing the challenged claims are unpatentable as obvious over the cited references.

1. Murtaza (Ex. 1004)

Murtaza is a journal article entitled “Non-invasive analysis of acquired resistance to cancer therapy by sequencing of plasma DNA” that appears to have been published in May 2013. Ex. 1004. According to Murtaza, cancers can acquire drug resistance through clonal evolution and selection. *Id.* at 108.⁷ Murtaza states that genomic alterations of solid cancers can be characterized by massively parallel sequencing circulating

⁷ Unless stated otherwise, citations to page numbers refer to the reference page numbers.

tumor DNA (“ctDNA”) that has been released from cancer cells into plasma. *Id.* Murtaza teaches tagging ctDNA molecules with barcodes to create barcoded sequencing libraries, enriching the libraries, amplifying, sequencing, and mapping the sequences to a reference sequence. *Id.* at 111.

2. *Schmitt (Ex. 1009)*

Schmitt is an international patent application entitled “Methods of Lowering the Error Rate of Massively Parallel DNA Sequencing Using Duplex Consensus Sequencing,” published on September 26, 2013. Ex. 1009, code (43). Schmitt relates to a method called Duplex Consensus Sequencing (“DCS”) that, according to Schmitt, greatly reduces sequencing errors by independently tagging and sequencing each of the two strands of a DNA duplex. *Id.*, Abstract. Because the two strands of DNA are complementary, true mutations can be found at the same position on both strands, as opposed to on a single strand if PCR or sequencing errors occur. *Id.*

According to Schmitt’s DCS method, sheared double-stranded DNA that has been end-repaired and T-tailed is combined with A-tailed single molecule identifier (“SMI”) adapters and ligated. *Id.* ¶ 12, Fig. 1. In one embodiment, every adapter contains a unique, double-stranded, complementary n-mer random tag on each end, such that every DNA fragment becomes labeled with two distinct SMI sequences. *Id.* The labeled DNA fragments are amplified by PCR, resulting in two types of PCR products, each with a distinct SMI sequence. *Id.* In another embodiment, Schmitt discloses a hybrid method using a combination of sheared ends and shorter n-mer tags that serve as unique molecular identifiers. *Id.* ¶ 38.

For error correction through DCS, sequence reads sharing a unique set of SMI tags are grouped into paired families, each pair reflecting one

double-stranded DNA fragment. *Id.* ¶ 14. Mutations present in only one or a few family members, or mutations occurring in only one of the two strands, represent sequencing mistakes or PCR-introduced errors. *Id.* True mutations are present on both strands and appear in all members of a family pair. *Id.*

3. *Meyer (Ex. 1005)*

Meyer is a journal article entitled “Parallel tagged sequencing on the 454 platform” that appears to have been published online on January 31, 2008. Ex. 1005, 267. Meyer relates to a method called parallel tagged sequencing that allows for parallel sequencing of large numbers of double-stranded DNA samples on a next-generation sequencing system called the 454 Platform. *Id.*, Abstract. According to Meyer, the method involves blunt end repairing each DNA sample and then ligating sample-specific barcoding adapters to both ends of blunt-end repaired DNA molecules. *Id.* at 268, Fig. 1. The adapters “comprise single self-hybridized oligos containing a sequence tag and an *SrfI* restriction site.” *Id.* at 267. The barcoded samples are pooled in equimolar ratios, and untagged molecules are excluded from sequencing through dephosphorylation and restriction digestion. *Id.*, Fig. 1. The sample pool is then sequenced and the sequence reads are sorted according to their tag sequences and the source of each DNA can then be traced using the tag sequences. *Id.*

4. *Analysis*

A patent claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the claimed subject matter and the prior art are such that the subject matter, as a whole, would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406

(2007). The question of obviousness is resolved on the basis of underlying factual determinations, including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of skill in the art; and (4) objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

“[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.” *KSR*, 550 U.S. at 418. “[I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.” *Id.* Moreover, a person of ordinary skill in the art must have had a reasonable expectation of success of doing so. *PAR Pharm., Inc. v. TWI Pharms., Inc.*, 773 F.3d 1186, 1193 (Fed. Cir. 2014).

Petitioner asserts that each limitation of independent claims 1 and 15 is taught by the combination of Schmitt, Meyer, and Murtaza, and that a person of ordinary skill in the art would have been motivated to combine Murtaza’s cfDNA sequencing of cancer genes with Schmitt’s DCS method of error correction in view of Meyer’s teaching of 40–60% adapter-DNA ligation efficiency to reach the claimed invention with a reasonable expectation of success. Pet. 25–42, 55–58. Patent Owner disagrees, arguing, among other things, that Petitioner fails to show that the cited references teach or suggest that the tagging produces “at least 20% of the cfDNA molecules are ligated with the adapters comprising the molecular barcodes at both ends of a molecule of the double-stranded cfDNA

molecules”⁸ with a reasonable expectation of success, as required by independent claims 1 and 15. *See* Ex. 1001, 60:32–35 (claim 1), 62:12-15 (claim 15). On this record, we agree with Patent Owner.

Petitioner relies solely on Meyers for the 20% tagging efficiency limitation, asserting that Meyers teaches “successfully achieving 40–60% tagged DNA fragments” in a method that would only detect adapter-ligated DNA fragments tagged on both ends. *See* Pet. 30 (citing Ex. 1005, 274, Fig. 1; Ex. 1002 ¶¶ 179–180). Petitioner asserts that Meyer’s disclosure of 40–60% recovery falls within the claimed range of producing at least 20% of the double-stranded cfDNA molecules having adapters comprising the molecular barcodes ligated to both ends. *See id.* (citing Ex. 1005, 274); Ex. 1002 ¶¶ 179–180.

Petitioner asserts that a person of ordinary skill in the art would have been motivated by Schmitt and Meyer to ligate adapters efficiently to maximize sequenceable targets, especially with cfDNA. Pet. 38 (citing Ex. 1002 ¶¶ 221, 227–231; Ex. 1009 ¶ 92; Ex. 1005, 272–274). Petitioner further asserts that a “POSA would have expected to successfully tag ‘at least 20%’ of the DNA fragments” because Meyer teaches successfully tagging 40–60% of DNA fragments. *Id.* at 41 (citing Ex. 1002 ¶¶ 255–257; Ex. 1005, 274). And, according to Petitioner, Meyer’s disclosure of 40–60% tagging efficiency is consistent with other references. *Id.* For example, Petitioner cites the KAPA data sheet,⁹ which teaches “15–40% of input DNA is typically recovered as adapter-ligated molecules.” *Id.* (quoting

⁸ For ease of reference, we refer to this limitation as the “20% tagging efficiency limitation.”

⁹ KAPA Technical Data Sheet for KAPA HTP Library Preparation Kit. Ex. 1015 (“KAPA data sheet”).

Ex. 1015, 4). Petitioner also cites Fisher¹⁰ as disclosing “recovering 47% of the library as adapter-ligated DNA fragments.” *Id.* (citing Ex. 1031, Fig. 3). Finally, Petitioner asserts that a person of ordinary skill in the art “would have expected Schmitt’s sticky-end adapter-DNA ligation (using A- and T-overhangs) to be even more efficient than Meyer’s blunt-end adapter-DNA ligation, which nevertheless achieved 40–60% adapter-ligated DNA fragments.” *Id.* at 41 (citing Ex. 1002 ¶ 256; Ex. 1005, 273; Ex. 1009 ¶¶ 91–92). Even if the claimed amount is not expressly taught by the art, Petitioner asserts that the limitation of “at least 20%” tagging would have been an obvious optimization of a result-effective variable. *See id.* (citing Ex. 1002 ¶¶ 254–257).

We are not persuaded by Petitioner’s arguments. Although Meyer teaches that its particular protocol results in 40–60% tagging efficiency, Petitioner fails to sufficiently explain why a person of ordinary skill in the art would have expected Meyer’s tagging efficiency to apply to Schmitt’s DCS method when used with Murtaza’s sequencing of cfDNA. For example, Petitioner fails to address the differences between Meyer’s adapters and Schmitt’s adapters, and how those differences affect the tagging efficiency. Meyer’s barcodes comprise “single self-hybridized palindromic oligonucleotides, carrying an *Srf*I restriction site in the middle (GCCCCGGGC), a sequence tag at the 3’ end and the reverse complementary tag sequence at the 5’ end.” Ex. 1005, Fig. 1. Schmitt, on the other hand, teaches a “hybrid method” of tagging that uses a combination of the sheared

¹⁰ Fisher et al., *A Scalable, Fully Automated Process for Construction of Sequence-Ready Human Exome Targeted Capture Libraries*, 12:R1 GENOME BIOLOGY 1–15 (2011). Ex. 1031 (“Fisher”).

ends of the DNA fragments and a “shorter n-mer tag (such as 1 or 2 or 3 or 4 or more degenerate or semidegenerate bases) in the adaptor.” Ex. 1009 ¶ 38.

Moreover, as Patent Owner notes, Petitioner is also silent as to how the references’ different starting sample sizes affect tagging efficiency. Prelim. Resp. 28–29. According to the KAPA data sheet submitted by Petitioner, “[t]he proportion of fragmented DNA that is successfully converted to adapter-ligated molecules decreases as input is reduced.” Ex. 1015, 4. The KAPA data sheet states that “[w]hen starting library construction (end repair) with >100 ng fragmented DNA, 15–40% of input DNA is typically recovered as adapter-ligated molecules, whereas the recovery typically ranges from 0.5 to 15% for libraries constructed from 100 pg–100 ng DNA.” *Id.* Meyer teaches using DNA samples with 100–500 ng of DNA. Ex. 1005, 272 (“Transfer 100–500ng of each sample to a 96-well PCR plate.”). Murtaza, on the other hand, teaches generating sequencing libraries using amounts ranging from 2.3 to 40 ng cfDNA. Ex. 1004, 113 (“2.3–40 ng of DNA (Supplementary Table 2) was used to generate a sequencing library using manufacturer’s protocols.”). According to the KAPA data sheet, based on their respective sample sizes, the tagging efficiency for Meyer would be within the higher 15–40% range, whereas the tagging efficiency for Murtaza would be within the lower 0.5 to 15% range expected for a smaller sample size of 100 pg – 100 ng DNA. *See* Ex. 1015, 4. Petitioner, however, does not acknowledge these differences and why a person of ordinary skill in the art would have had a reasonable expectation of tagging at least 20% of the cfDNA molecules of Murtaza given the small cfDNA starting sample size.

In addition to the sample size, the KAPA data sheet states that tagging efficiency “can be significantly lower for DNA of lower quality.” Ex. 1015,

4. Fisher also explains that “the efficiency of adaptor ligation varies between samples, probably because of variation in input DNA quality.” Ex. 1031, 5–6. Petitioner does not address how the quality of the cfDNA of Murtaza compares to the quality of the genomic DNA samples of Meyer and Schmitt or how that would affect the expected tagging efficiency. As Patent Owner notes, the KAPA data sheet discloses sticky-end adapter DNA ligation, but KAPA teaches that only 0.5 to 15% tagging efficiency is expected when the starting sample is 100 pg–100 ng of “high quality DNA.” Ex. 1015, 4. Thus, as the KAPA data sheet makes clear, the use of sticky-end adapters, such as Schmitt discloses, does not in and of itself teach or suggest the recited at least 20% tagging efficiency for cfDNA.

Finally, Petitioner asserts that a person of ordinary skill in the art would have understood that adapter-DNA tagging efficiency is a result-effective variable, and the 20% tagging efficiency limitation “is nothing more than claiming an optimum value in a known process.” Pet. 41 (citing Ex. 1002 ¶ 254–257). Patent Owner contends that this is no more than a conclusory argument, and Petitioner fails to provide sufficient evidence to support its assertion. Prelim. Resp. 34–35.

We agree with Patent Owner. Petitioner’s expert states that a person of ordinary skill in the art would have understood that “increasing the concentration of adapters was a routine technique that could be used to maximize ligation efficiency such as by using a molar excess of adapters relative to DNA fragments in the ligation reaction.” Ex. 1002 ¶ 223. But the record evidence submitted by Petitioner suggests tagging efficiency is not as simple as varying the concentration of adapters. As explained above, the evidence suggests that tagging efficiency is also affected by the amount of starting sample and the quality of the DNA. *See* Ex. 1015, 4; Ex. 1031, 6.

Thus, we are not persuaded that Petitioner has shown sufficiently that adapter-DNA tagging efficiency, particularly for the cfDNA recited in the challenged claims, is a simple result-effective variable that can be determined by routine optimization.

Accordingly, having considered the parties' respective arguments and evidence, we determine Petitioner has not established a reasonable likelihood of prevailing on its assertion that independent claims 1 and 15—and therefore dependent claims 2–7, 9–11, and 16–18, and 22–28—would have been obvious over Murtaza, Schmitt, and Meyer.

D. Remaining Grounds

Petitioner asserts dependent claims 8 would have been obvious over Murtaza, Schmitt, Meyer, and Craig and dependent claims 12–14 and 19–21 would have been obvious over Murtaza, Schmitt, Meyer, and Kivioja. Pet. 64–75. In its analysis of the additional dependent limitations, Petitioner relies on Craig's disclosure of 6-mer barcodes (Pet. 65–66) and on Kivioja's methods for calculating unseen molecules (Pet. 68–69). Because Petitioner does not rely on either Craig or Kivioja to teach or suggest the 20% tagging efficiency limitation of independent claims 1 and 15, we determine Petitioner has not shown a reasonable likelihood of prevailing on these grounds for the same reasons stated above.

III. CONCLUSION

For the foregoing reasons, we conclude that Petitioner has not established a reasonable likelihood of prevailing on its assertions that claims 1–28 of the '063 patent are unpatentable over the cited art.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that the Petition is *denied* as to all challenged claims of the '063 patent and no trial is instituted.

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Patent 10,801,063 B2

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