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Paper 15
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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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NEOGENOMICS LABORATORIES, INC.,
Petitioner,

v.

NATERA, INC.,
Patent Owner.

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IPR2024-00346
Patent 11,530,454 B2

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Before DEBORAH KATZ, ZHENYU YANG, and RYAN H. FLAX,
*Administrative Patent Judges*.

YANG, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
*35 U.S.C. § 325(d)*

# I. INTRODUCTION

NeoGenomics Laboratories, Inc. ("Petitioner") filed a Petition (Paper 1, "Pet."), seeking an *inter partes* review of claims 1–28 of U.S. Patent No. 11,530,454 B2 (Ex. 1001, "the '454 Patent"). Natera, Inc. ("Patent Owner") filed a Preliminary Response. Paper 6 ("Prelim. Resp."). With our authorization (Ex. 3002), Petitioner filed a Reply (Paper 12), and Patent Owner filed a Sur-reply (Paper 13).

For the reasons provided below, we exercise our discretion under 35 U.S.C. § 325(d), and deny institution of an *inter partes* review.

## *A. Related Matters*

According to the parties, Patent Owner asserted the '454 patent against Petitioner in *Natera, Inc. v. Inivata, Inc.*, No. 1:22-cv-01609 (D. Del.) (consolidated), and in *Natera, Inc. v. NeoGenomics Laboratories, Inc.*, No. 1:23-cv-00629 (M.D.N.C.) ("North Carolina case"). Pet. 14; Paper 4, 1.

In the North Carolina case, the district court granted Patent Owner's motion for a preliminary injunction and denied Petitioner's motion for a stay pending appeal. Ex. 2017; Ex. 2022. The court held a *Markman* hearing on May 14, 2024 and issued its Claim Construction Order three days later on May 17, 2024. *See* Ex. 2028. The trial date is set for March 10, 2025. Ex. 2021, 3.

In the consolidated Delaware case, which involves additional patents and parties, the parties stipulated and the court agreed to a stay because the resolution of the North Carolina case against Petitioner "is likely to simplify issues and to preserve judicial economy." *See* Ex. 2011.

*B. The '454 Patent and Related Background*

The '454 patent relates to "methods and systems for detecting ploidy of a chromosome segment, and methods and systems for detecting a single nucleotide variant [SNV]." Ex. 1001, 1:28–31.

In humans, most DNA is generally found in chromosomes within the nuclei of cells. Ex. 1028, 001. DNA, however, can be found outside of cells in cell-free bodily fluids, such as blood plasma. Ex. 1029, 002; Ex. 1030, 003. DNA located outside of the cells is referred to as cell-free DNA (cfDNA). Cell-free DNA can be derived from both normal cells and cancer cells. Ex. 1031, 002. Circulating tumor DNA (ctDNA) is the portion of circulating DNA specifically derived from cancer cells. *Id.* Tumor-derived cfDNA has been used for early detection of cancer. *Id.*

Cancer is associated with mutations in DNA and "[s]omatic (cancer-only) single nucleotide variants (SNVs) are the simplest class of mutation." Ex. 1039, 001. The '454 patent describes methods for detecting one or more SNVs in a test sample. Ex. 1001, 5:44–6:21, 67:33–68:14.

*C. Illustrative Claims*

Among the challenged claims, claims 1 and 14 are independent. Claim 1 is illustrative of the claimed subject matter and is reproduced below.

> 1. A method for preparing a plasma sample of a subject having cancer or suspected of having cancer useful for detecting one or more single nucleotide variant (SNV) mutations in the plasma sample, the method comprising:
>
> performing whole exome sequencing or whole genome sequencing on a tumor sample of the subject to identify a plurality of tumor-specific SNV mutations;
>
> performing targeted multiplex amplification to amplify 10 to 500 target loci each encompassing a different tumor-specific

> SNV mutation from cell-free DNA isolated from a plasma sample of the subject or DNA derived therefrom to obtain amplicons having a length of 50-150 bases, wherein the target loci are amplified together in the same reaction volume; and
>
> sequencing the amplicons to obtain sequence reads, and detecting one or more of the tumor-specific SNV mutations present in the cell-free DNA from the sequence reads, wherein the sequencing has a depth of read of at least 50,000 per target locus.

Ex. 1001, 171:25–43.

Claim 14 is similar to claim 1, except (1) it does not specify the length of the amplicons, and (2) instead of the sequencing depth recited in claim 1, it recites "wherein the method is capable of detecting an SNV mutation that is present in less than or equal to 0.015% of the cell-free DNA comprising the SNV locus." *Id.* at 172:10–31.

*D. Asserted Challenges to Patentability*

Petitioner asserts the following challenges to patentability:

| Claims Challenged | 35 U.S.C. §[1] | Reference(s) |
|---|---|---|
| 1–6, 8–20, 22–28 | 103 | Forshew[2] |

[1] The Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112-29, 125 Stat. 284, 287–88 (2011), amended 35 U.S.C. §§ 102, 103, effective March 16, 2013. As explained below, we deny institution under § 314(a) and § 325(d), regardless of which version of the law applies.

[2] Forshew et al., *Noninvasive Identification and Monitoring of Cancer Mutations by Targeted Deep Sequencing of Plasma DNA*, 4 SCI. TRANSLATIONAL MED. 1–12 (2012) (with Supplemental Materials, S1–S19) (Ex. 1003, "Forshew").

| Claims Challenged | 35 U.S.C. §[1] | Reference(s) |
|---|---|---|
| 3–5, 7, 17–19, 21 | 103 | Forshew, Bai,[3] Bashashati[4] |
| 14–20, 22–28 | 103 | Forshew, Bentley,[5] Narayan[6] |
| 17–19, 21 | 103 | Forshew, Bai, Bashashati, Bentley, Narayan |

Petitioner relies on the declaration of Niall Lennon, Ph.D., as support for its Petition. Ex. 1002.

## II. ANALYSIS

Institution of an *inter partes* review is discretionary. *See Cuozzo Speed Techs., LLC v. Lee*, 579 U.S. 261, 273 (2016) (explaining that because 35 U.S.C. § 314 includes no mandate to institute review, "the agency's decision to deny a petition is a matter committed to the Patent Office's discretion"); *see also Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1367 (Fed. Cir. 2016) (stating that under § 314(a), "the PTO is permitted, but never compelled, to institute an IPR proceeding").

Under 35 U.S.C. § 325(d), in determining whether to institute an *inter partes* review, "the Director may take into account whether, and reject the

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[3] Bai et al., *Detection and Clinical Significance of Intratumoral EGFR Mutational Heterogeneity in Chinese Patients with Advanced Non-Small Cell Lung Cancer*, 8(2): PLoS ONE e54170 (2013) (Ex. 1005, "Bai").
[4] Bashashati et al., *Distinct Evolutionary Trajectories of Primary High-Grade Serous Ovarian Cancers Revealed Through Spatial Mutational Profiling*, 231 J. PATHOLOGY 21–34 (2013) (Ex. 1004, "Bashashati").
[5] Bentley et al., *Accurate Whole Human Genome Sequencing Using Reversible Terminator Chemistry*, 456 NATURE 53–59 (2008) (Ex. 1056, "Bentley").
[6] Narayan et al., *Ultrasensitive Measurement of Hotspot Mutations in Tumor DNA in Blood Using Error-Suppressed Multiplexed Deep Sequencing*, 72 CANCER RSCH. 3492–98 (2012) (Ex. 1086, "Narayan").

petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office." Our § 325(d) analysis employs a two-prong framework: (1) whether the arguments presented in the petition are the same or substantially the same as those previously presented to the Office; and (2) if so, whether the petitioner has demonstrated a material error by the Office in its prior consideration of those arguments. *Advanced Bionics, LLC v. Med-El Electromedizinishe Geräte GmbH*, IPR2019-01469, Paper 6 ("*Advanced Bionics*"), 8 (PTAB Feb. 13, 2020) (precedential). "If a condition in the first part of the framework is satisfied and the petitioner fails to make a showing of material error, the Director generally will exercise discretion not to institute *inter partes* review." *Id.* at 8–9. "At bottom, this framework reflects a commitment to defer to previous Office evaluations of the evidence of record unless material error is shown." *Id.* at 9.

Petitioner contends that Forshew renders obvious claims 1–6, 8–20, and 22–28 of the '454 patent. Pet. 20–47. Petitioner also contends that claims 3–5, 7 and 14–28 would have been obvious over the combined teachings of Forshew and other prior art references. *Id.* at 47–56. Thus, all of Petitioner's asserted grounds foundationally rely on Forshew's teachings. Patent Owner argues that we should deny institution under § 325(d) because "Forshew was already thoroughly vetted, and overcome, during the original prosecution. [Petitioner] NeoGenomics has not identified any actual errors by the Examiner in allowing the claims, let alone a material error, meriting another go-around." Prelim. Resp. 17. For the reasons explained below, we find Patent Owner's arguments persuasive.

*A. Forshew*

As Petitioner acknowledges, Forshew "was front and center during examination" by the Patent Office. Pet. 59. It is also the cornerstone reference asserted by Petitioner here.

Forshew teaches "a method for tagged-amplicon deep sequencing (TAm-Seq) and screened 5995 genomic bases for low-frequency mutations." Ex. 1003, Abstract. Using this method, Forshew "identified cancer mutations present in circulating DNA at allele frequencies as low as 2%." *Id.*

In Forshew, "[a]n initial preamplification step was performed for 15 cycles using a pool of the target-specific primer pairs to preserve representation of all alleles in the template material." *Id.* at 003.[7] In this step, DNA molecules that carry mutations were amplified alongside wild-type molecules. *Id.* Forshew teaches that "[r]egions of interest in the preamplified material were then selectively amplified in individual (single-plex) PCR, thus excluding nonspecific products." *Id.*; *see also id.* at 004 (teaching its method includes "a limited-cycle preamplification step where all primer sets were used together to capture the starting molecules present in the template, followed by individual amplification to purify and select for intended targets").

Forshew explains that it "applied a two-step amplification process" because both single-plex amplification and multiplex amplification have shortcomings. *Id.* at 004. Specifically, Forshew states that "[m]ultiplex

[7] We cite the page numbers provided by the parties for each exhibit.

amplification using a large set of primers could result in nonspecific amplification products and biased coverage." *Id.*

Forshew's method includes an additional PCR step to attach sequencing adaptors and tag each sample by a unique molecular identifier or "barcode." *Id.*

*B. Prosecution History of the '354 Application*

The '454 patent issued from Application No. 17/738,354 ("the '354 application"). Ex. 1001, code (21).

During the prosecution of the '354 application, the examiner rejected all then-pending claims except claim 2 as obvious over Forshew and other prior art references. Ex. 1020, 005–009. Then-pending claim 2 depended from claim 1 and further recited "wherein the high-throughput sequencing has a depth of read of at least 50,000 per target locus." Ex. 1019, 001. Claim 2 was not a subject of the examiner's obvious rejection over the prior art. Ex. 1020, 005–009.

In response to the office action, the applicant amended claim 1 to incorporate the limitation of claim 2. Ex. 1021, 001. It argued that "[n]one of the cited references teaches or suggests sequencing each of the target loci with a depth of read of at least 50,000 per target locus." Ex. 1022, 003. In addition, the applicant rewrote then-pending claim 15 (eventually issued as independent claim 14) into independent form, requiring that "the method is capable of detecting an SNV mutation that is present in less than or equal to 0.015% of the cell-free DNA comprising the SNV locus." Ex. 1021, 002–003. The applicant argued that "Forshew's TAm-Seq workflow was only able to achieve a detection limit of 2%." Ex. 1022, 003.

The applicant further argued that

> Forshew's TAm-Seq process was rationally and deliberately designed to rely on single-plex, "*individual amplification to purify and select for intended targets*" (pg. 3). In fact, Forshew had considered but dismissed multiplex targeted amplification – "*Multiplex amplification using a large set of primers could result in nonspecific amplification products and biased coverage*" (Fig. lB, pg. 3). Forshew deliberately resorted to parallel single-plex amplification on Access Array, which physically separate individual primer pairs and individual reaction volumes to avoid issues such as nonspecific amplification and primer dimer formation. There was no reason or motivation for one of ordinary skill in the art to alter Forshew's TAmSeq process by substituting a step rationally and deliberately designed by Forshew for purpose of addressing the issue of nonspecific amplification, for a step already considered but dismissed by Forshew.

*Id.* at 004.

In an applicant-initiated interview (per its summary), "[t]he examiner stated that the limitations of a depth of read of at least 50,000 per target locus in independent claim 1 and detection of an SNV at 0.015% of cell-free DNA comprising the SNV in proposed independent claim 15 would require further search to determine obviousness of the claims." Ex. 2003, 431.

After considering the references cited in the IDS and conducting further searching (*id.* at 1087, 1094), the examiner withdrew all obviousness rejections and allowed all pending claims. Ex. 1024, 007. In the Reasons for Allowance, the examiner stated that

> The prior art does not show the limitation in independent claim 1 of a sequencing read depth of at least 50,000 per target locus in the context of the claimed subject matter. The prior art does not show the limitation in independent claim 15 of detecting a single nucleotide variant mutation that is present in

> less than or equal to 0.015% of the cell-free DNA comprising the single nucleotide variant locus in the context of the claimed subject matter.

*Id.* at 009.

*C. Same or Substantially the Same Prior Art or Arguments*

It is undisputed that Forshew "was front and center during examination" of the challenged claims by the Patent Office. Pet. 59. Petitioner also acknowledges that Bai, Bashashati, Bentley,[8] and Narayan were "of record during examination due to their inclusion in an IDS." *Id.* at 60–61. Thus, we find the first part of *Advanced Bionics* two-prong framework is satisfied.

*D. Material Error*

Having found that the condition required of the first part of the two-prong framework is satisfied, we next evaluate whether Petitioner has demonstrated a material error by the Office in its prior consideration of the previously presented art. *Advanced Bionics*, 8. Based on the current record, we determine Petitioner has not met its burden to show the examiner materially erred.

Petitioner argues that "[w]hile Forshew was of record and considered during examination, the Examiner made several critical errors." Pet. 57. According to Petitioner, "the Examiner erred materially, failing to appreciate that: (1) Forshew's preamplification step is multiplex amplification; and (2) a greater depth of sequencing and the resulting increased sensitivity

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[8] Petitioner states that Bentley was not apparently of record, but its parent application was presented in an IDS. Pet. 61. Thus, we consider it to have been of record, at least cumulatively so.

would have been obvious because sequencing depth was a known result effective variable for increased sensitivity." *Id.*

1. Multiplex Amplification

As explained above (*see supra* Section II.B), during prosecution, the examiner rejected all then-pending claims except claim 2 as obvious over Forshew. Ex. 1020, 005–009. Specifically, the examiner found

> Forshew et al. shows in the abstract and throughout analysis of cell-free DNA of individuals with tumors for mutation analysis by multiplex amplification using a pool of primer pairs followed by sequencing of amplicons. Forshew et al. outlines the process in Figure 1, which shows a preamplification step that uses a single multiplex amplification of regions of interest followed by a second amplification followed by barcoded amplification and sequencing.

*Id.* at 006. Thus, the examiner did not fail to appreciate that Forshew's preamplification step is multiplex amplification.

Petitioner also faults the examiner for accepting the applicant's "erroneous" and "false statement" that "Forshew had considered but dismissed multiplex targeted amplification." Pet. 57–58. According to Petitioner, Patent Owner's expert confirmed in the North Carolina case that "Forshew ***does*** disclose multiplex targeted amplification." *Id.* We are not persuaded by this argument.

Forshew "applied a two-step amplification process" because "[m]ultiplex amplification using a large set of primers could result in nonspecific amplification products and biased coverage." Ex. 1003, 004. Thus, it was not false for the applicant to argue, and not unreasonable for the examiner to accept, that "Forshew had considered but dismissed multiplex

targeted amplification."[9] Ex. 1022, 004 ("Forshew deliberately resorted to parallel single-plex amplification on Access Array, which physically separate individual primer pairs and individual reaction volumes to avoid issues such as nonspecific amplification and primer dimer formation.").

Indeed, each of independent claims 1 and 14 recites "performing targeted multiplex amplification . . . to obtain amplicons" and "sequencing the amplicons." Although Forshew teaches multiplex amplification in the preamplification step (*see* Ex. 1003, 003–004), it appears to only refer to the single-plex amplification products as amplicons to be sequenced (*id.* at 003). This tends to support the examiner's apparent finding that Forshew does not teach the recited multiplex-amplification limitation because that amplification does not result in the amplicons to be sequenced.

In fact, in the North Carolina case, Petitioner has taken the position that "sequencing the amplicons" should be construed to mean "[s]equencing the amplicons obtained from the targeted multiplex amplification step." Ex. 2028, 7–8 (citing Ex. 2030, 15); *see also* Ex. 2032, 15–16 (Petitioner arguing "intervening steps such as size selection or barcoding PCR would mean that the amplicons being sequenced are not the same amplicons obtained from performing the targeted multiplex amplification"). Forshew teaches the barcoding PCR step, and also the single-plex amplification step, which is after the multiplex amplification step. *See* Ex. 1003, 003–004.

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[9] Perhaps a more accurate statement would be that Forshew had considered but dismissed multiplex targeted amplification *alone*. In any event, though, the applicant, contrary to Petitioner's assertion, did not argue "Forshew *did not disclose* the use of the claimed 'multiplex targeted amplification.'" *See* Pet. 57 (emphasis added).

Thus, even under Petitioner's proposed claim construction in the North Carolina case, we are not persuaded that the examiner materially erred because, in Forshew, the amplicons sequenced are not those obtained from the targeted multiplex amplification step.

In sum, Petitioner has not demonstrated that the examiner materially erred when considering the multiplex-amplification limitation. *See Advanced Bionics*, 9 ("If reasonable minds can disagree regarding the purported treatment of the art or arguments, it cannot be said that the Office erred in a manner material to patentability."). Under the asserted grounds, Petitioner relies on Forshew as the sole reference to teach this limitation, which is required in all challenged claims. Thus, we exercise our discretion under § 325(d) and decline to institute *inter partes* review of the '454 patent.

For completeness, we address Petitioner's additional arguments below.

2. Sequencing Depth

Claim 1 requires "the sequencing has a depth of read of at least 50,000 per target locus." As explained above (*see supra* Section II.A.2), during prosecution, this limitation was incorporated from then-pending claim 2. Ex. 1021, 001.

Petitioner contends that "[t]he Examiner appears to have neglected claim 2 entirely during examination." Pet. 58 ("Allowing the claims on the basis of the sequencing 'depth' element after giving this topic no scrutiny was material error."). Evidence of the record, however, contradicts Petitioner's argument.

Indeed, in an applicant-initiated interview, the examiner stated that the sequencing-depth limitation "would require further search to determine

obviousness of the claims." Ex. 2003, 431. This evidence was not addressed, or even submitted, by Petitioner. Later during prosecution, in the Reasons for Allowance, the examiner specifically addresses the subject matter of claim 2, as incorporated into claim 1, stating that "[t]he prior art does not show the limitation in independent claim 1 of a sequencing read depth of at least 50,000 per target locus in the context of the claimed subject matter." Ex. 1024, 009. Thus, the examiner did not neglect the sequencing-depth limitation.

Petitioner argues that Forshew teaches "[h]igher read depth" can be used to achieve "enhanced mutation detection without change to protocols." Pet. 59 (citing Ex. 1003, 011). According to Petitioner, "[t]he Examiner utterly failed to recognize this teaching." We are not persuaded.

As an initial matter, in view of the examiner's attention to the sequencing-depth limitation, both during the interview and in the Reasons for Allowance, Petitioner's allegation that the examiner failed to recognize Forshew's teachings on this issue is unsupported by the record.

Moreover, substantively, Petitioner has not shown that the examiner materially erred when he found that Forshew does not teach a sequencing depth of at least 50,000 per target locus. Table 1 of Forshew shows the mean sequencing depth for several mutations, including a mean sequencing depth of 7,700 for one mutation. Ex. 1003, 006. Relying on the opinion of its declarant Dr. Lennon, Petitioner asserts that Table 1 shows "duplicate samples with mean sequencing depth of 7,700, for total sequencing depth of 15,400." Pet. 27 (citing Ex. 1002 ¶ 163); *see also* Ex. 1002 ¶ 163 (Dr. Lennon testifying that an ordinarily skilled artisan "would have

understood that the mean sequencing depth of 7,700 for duplicate samples is a total sequencing depth of 15,400 (*i.e.*, twice 7,700)").

Patent Owner counters that "[e]ven if Dr. Lennon's unsupported assertion were correct, Dr. Lennon never explains how he knows that Table 1 did not already double the read depths to account for one of skill's alleged understanding. *See* [Ex. 1002 ¶ 163.] Forshew certainly does not say one way or the other. *See* EX1003 at 6 (Table 1)." Prelim. Resp. 50–51.

Furthermore, even if Forshew teaches a sequencing depth of 15,400, Petitioner still has not shown the examiner materially erred in his finding on the sequencing-depth limitation. Petitioner argues that increasing the sequencing depth from 15,400 to 50,000 would have been an obvious change because both are on the order of tens of thousands. Pet. 27 (citing Ex. 1002 ¶ 164). But, as Patent Owner contends, Forshew only "vaguely mention[s]" that "[h]igher read depth" could be used, which "is not the same as disclosing a 'depth of read of at least 50,000 per target locus.'" Prelim. Resp. 24 (citing Ex. 1003, 011). In other words, Petitioner presents some evidence on the sequencing-depth limitation, but not enough to establish that the examiner materially erred in determining the full scope of the claims was not obvious.

Petitioner and Dr. Lennon rely on other prior art to show it was routine to increase sequencing read depth to obtain greater sensitivity. *See* Pet. 27–28; Ex. 1002 ¶¶ 168–169. For example, referring to Table 2 of Bentley, Dr. Lennon testifies that

> Bentley reflects a POSA's understanding that a sequencing depth of 40,000 would, with 95-99% confidence, successfully detect SNPs between a frequency of 0.014% and 0.018%.

> Bentley also reflects a POSA's understanding that a sequencing depth of 100,000 would, with 95-99% confidence, successfully detect SNPs between a frequency of 0.005 and 0.007%.

Ex. 1002 ¶ 168 (citations omitted).

Patent Owner counters that

> Bentley's Table 2 (EX1057 at 14) discloses high depths of read within the 50,000 range only for targeting 1-2 loci, EX1057 ¶88, not "10-500 target loci" as required by all the claims, EX1001 at 171:32-33, 172:18-19. Instead, Table 2 shows the read depths for 10 or more target loci fall far short of the 50,000 read depth limitation, and read depth only decreases as the number of target loci increases. EX1057 ¶88, Table 2.

Prelim. Resp. 53–54.

Similarly, Dr. Lennon testifies that Narayan "expressly discloses a sequencing depth of 108,467 reads per locus." Ex. 1002 ¶ 169 (citing Ex. 1086, 003). Patent Owner contends that Narayan also does not satisfy the "10-500 target loci" limitation, because, according to Patent Owner, Narayan used only four target loci. Prelim. Resp. 54 (citing Ex. 1086, 003).

On this record, we find Patent Owner's argument more persuasive that the examiner did not materially err in allowing the challenged claims over the asserted prior art. Under the statute, a claim is unpatentable if "the claimed *invention as a whole* would have been obvious." 35 U.S.C. § 103 (emphasis added). Petitioner's reliance on Bentley and Narayan does not sufficiently connect the "10-500 target loci" limitation with the requirement that "the sequencing has a depth of read of at least 50,000 per target locus." In other words, it does not address the invention as whole.

Petitioner further asserts that "Patent Owner has time and again explicitly argued that increasing sequencing 'depth' was routine,

conventional and obvious" because "higher sensitivity could be achieved by sequencing more molecules." Pet. 59 (citing Ex. 1002 ¶ 170). The statements Petitioner relies on, however, appear general. *See id.* at 59–60 (citing Ex. 1082 ¶¶ 91, 214; Ex. 1088, 032–033; Ex. 1094 ¶ 119). As such, we agree with Patent Owner that they "say[] nothing about a read depth of 50,000, much less in the context of the claims as a whole at issue here." Prelim. Resp. 55–57.

In sum, Petitioner has not demonstrated that the examiner materially erred in finding that "[t]he prior art does not show the limitation in independent claim 1 of a sequencing read depth of at least 50,000 per target locus in the context of the claimed subject matter." *See* Ex. 1024, 009.

3. Detection Sensitivity

Claim 14 requires "the method is capable of detecting an SNV mutation that is present in less than or equal to 0.015% of the cell-free DNA comprising the SNV locus." Petitioner does not allege material error regarding this limitation. *See* Pet. 57–61.

4. Other References

Petitioner argues that although Bai, Bashashati, Bentley, and Narayan were presented to the Office in an IDS, they were not the basis of a rejection. Pet. 60–61. In a single sentence, Petitioner asserts that "[f]ailure to reject claims over these references was also material error." *Id.* at 61.

Here, because "the record of the Office's previous consideration of the art is not well developed or silent," Petitioner "may show the Office erred by overlooking something persuasive." *Advanced Bionics*, 10. Petitioner, however, provides no analysis or evidence to support its allegation of material error.

## III. CONCLUSION

Because the same or substantially the same art previously were presented to the Office and Petitioner has not demonstrated that the examiner materially erred when considering the prior art, we exercise our discretion under § 325(d) and decline to institute *inter partes* review of the '454 patent.[10]

## IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that the Petition is denied, and no trial is instituted.

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[10] Patent Owner also argues that we should deny review for other reasons. *See* Prelim. Resp. 30–64. We do not address those contentions because we deny the Petition for reasons explained above.

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