

Case IPR2024-00965
U.S. Patent No. 11,768,200

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ILLUMINA, INC.,
Petitioner

v.

MOLECULAR LOOP BIOSCIENCES, INC.,
Patent Owner

Case IPR2024-00965

U.S. Patent No. 11,768,200

PATENT OWNER'S PRELIMINARY RESPONSE

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Patent Trial and Appeal Board
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77 Fed. Reg. 48,612 (Aug. 14, 2012)	19

All citations to 35 U.S.C. §§102 and 103 in this paper refer to the pre-AIA statute.

All emphases are added unless otherwise noted.

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U.S. Patent No. 11,768,200

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All citations to exhibits refer to stamped exhibit page numbers.

I. Introduction

U.S. Patent No. 11,768,200 (the “’200 Patent”) solved significant problems in the field of sequencing by improving efficiency and accuracy with scalable technologies. Prior to the ’200 Patent, errors were often introduced during sequencing workflows, such as during amplification and sequencing when many samples were pooled together. For example, nucleic acid molecules from different samples that were analyzed together could overlap during the process of amplifying the nucleic acid, creating erroneous molecules that were sequenced and assigned to incorrect samples as a result of the errors introduced during amplification. Thus, there was a need for sequencing approaches that could avoid these errors and ensure accuracy while providing scalable and cost-effective sequencing technology for widespread adoption, for example by maintaining accuracy during multiplex sequencing when many patient samples were pooled together to increase throughput. *See, e.g.*, EX1001, 1:35-62.

The inventors of the ’200 Patent discovered that preparing nucleic acid samples with certain identifier sequences before the nucleic acid was analyzed through multiplex sequencing reactions allowed for downstream errors to be recognized and corrected during data analysis to increase the accuracy of the process. The inventors developed methods that incorporated pairs of identifier sequences corresponding to specific individual samples so that the samples could be pooled

and sequenced together to increase throughput (e.g., increase the number of samples that can be analyzed in a single sequencing run). *See, e.g.*, EX1001, 2:12-29. The pairs of identifier sequences allowed for amplicons produced through amplification and then sequenced during a run to be accurately traced back to the original sample from which they originated, ensuring that different sequences were accurately identified and analyzed for their particular samples after the multiplexed sequencing run. *Id.*

The Petition should be denied because it is deficient in several respects.

First, Petitioner relies heavily on Gloor in anticipation and obviousness grounds and touts Gloor as a reference not previously considered by the Office. But Petitioner fails to even show there was a reasonable likelihood that Gloor is prior art to the '200 Patent, rendering null Petitioner's argument that Gloor anticipates, or in combination with other references renders obvious, the '200 Patent.

Second, Petitioner invites the Board to revisit the Patent Office's examination and allowance of the Challenged Claims with repackaged prior art and arguments. The Board should exercise its discretion under 35 U.S.C. § 325(d) and deny Petitioner's attempts to resurrect the same issues that were addressed during prosecution. Petitioner asserts that the references in the Petition shine a new light on the validity of the Challenged Claims. But Petitioner fails to persuasively explain

how they differ in meaningful ways from the numerous references that were before the Examiner during prosecution.

While Patent Owner reserves the right to present additional arguments, the deficiencies of the Petition noted herein are sufficient for the Board to deny institution.

II. Background

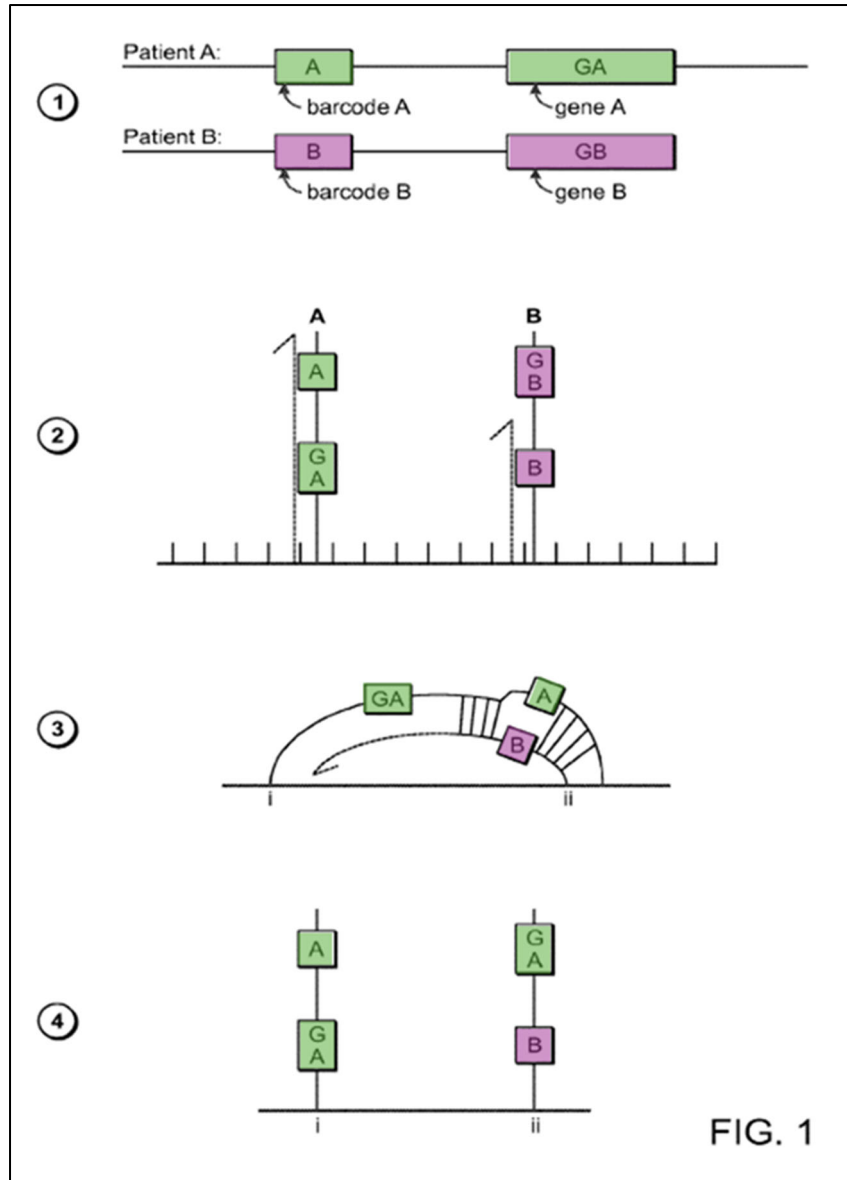
A. Overview Of The '200 Patent

The '200 Patent relates to “validating the results of a molecular detection assay and for enabling the detection of errors introduced in sample preparation.” EX1001, 1:66-2:1. During multiplex sequencing reactions, “the sample preparation phase frequently introduce[d] errors into the subsequent sequencing reaction.” *Id.*, 1:37-39. The '200 Patent addressed those problems in next-generation multiplex sequencing reactions, including addressing errors that could arise when “template molecules may physically overlap on a substrate; and in some cases result in a detectable erroneous signal.” *Id.*, 1:39-41. As the '200 Patent notes, “[i]n any sequencing process that requires high accuracy, such errors can have a significant impact on results.” *Id.*, 1:41-43.

An error that can be introduced during next-generation sequencing results from “improper pairing of template strands from different samples,” which can “form during the amplification of the multiplexed samples.” *Id.*, 1:52-54. As the '200

Patent notes, “such errors can have a significant [e]ffect on the results.” *Id.*, 1:59-60.

Some efforts had been taken to address these sources of error, for example by using single “barcodes” to identify samples from which nucleic acid was obtained prior to multiplexing, but those efforts had not sufficiently addressed the problems. The ’200 Patent explains that when single barcode identifiers were used to identify different samples, “improper molecular overlap” occurring between samples during amplification could lead to a high-quality signal being obtained and the overlap not being detected, meaning that ultimately “the data will be assigned to the wrong sample because it has become associated with the wrong barcode.” EX1001, 4:17-63. The ’200 Patent illustrates this phenomenon in Figure 1.



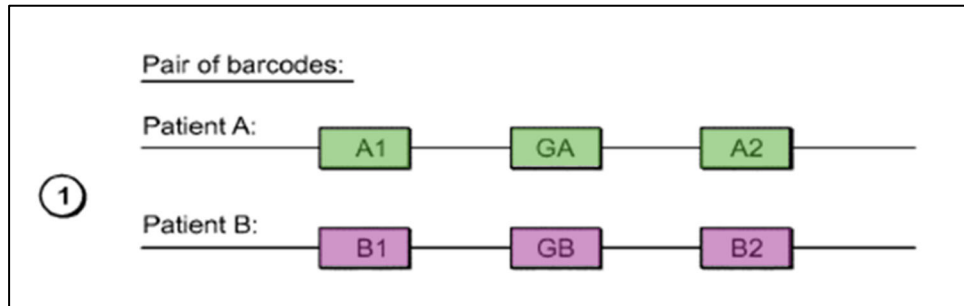
EX1001, FIG. 1 (annotated). As a result of the molecular overlap shown during amplification, an erroneous molecule is produced because “[s]trand ii contains the barcode for patient B but the gene fragment for patient A.” *Id.*, 4:53-55. The prior single-barcode approach was unable to detect this erroneous molecule, and thus “[d]uring the sequencing process, patient A’s sequence data will be improperly and incorrectly associated with patient B.” *Id.*, 4:55-57; 4:60-63.

The '200 Patent addressed the shortcomings of prior approaches by “utiliz[ing] two or more identifiers that are uniquely associated with an analyte of interest, such that the identifiers will only be present when the analyte of interest is detected” and “requiring concomitant detection of two or more independent markers associated with the analyte to be detected” to avoid “false positive and/or false negative results.” EX1001, 2:4-11; 2:16-18 (“The invention is based upon using *two or more identifiers*, such as nucleic acid barcodes that are uniquely associated with an analyte to be detected.”). By using at least two identifiers for each template (e.g., for each sample), the '200 Patent increased the ability to detect and eliminate error because “template containing only one identifier or an incorrect pair (i.e., a pair or more of identifiers not associated with the same template) will be excluded from analysis.” *Id.*, 2:23-25.

For example, as shown in Figure 2 of the '200 Patent, the inventive methods include identifying template nucleic acids from different samples by incorporating pairs of identifiers before the samples are pooled for a multiplex sequencing reaction. *Id.*, FIG. 2. “Each template has a gene fragment from that patient (e.g., GA), and a pair of sequence identifiers (first and second) specific to that patient (e.g., A1 and A2).” *Id.* 5:2-5. “[A] first identifier can be incorporated into a 5' end of the template and a second identifier can incorporated into a 3' end of the template. The first and second identifiers are designed such that each set of identifiers is correlated

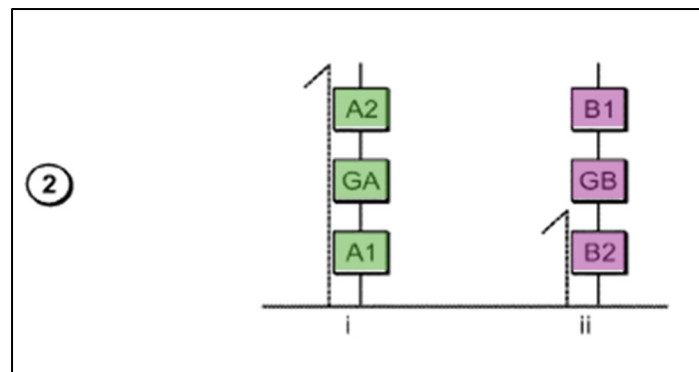
to a particular sample ... allowing samples to be distinguished and/or validated.”

Id., 3:12-19; 5:6-8.



EX1001, FIG. 2(1) (annotated).

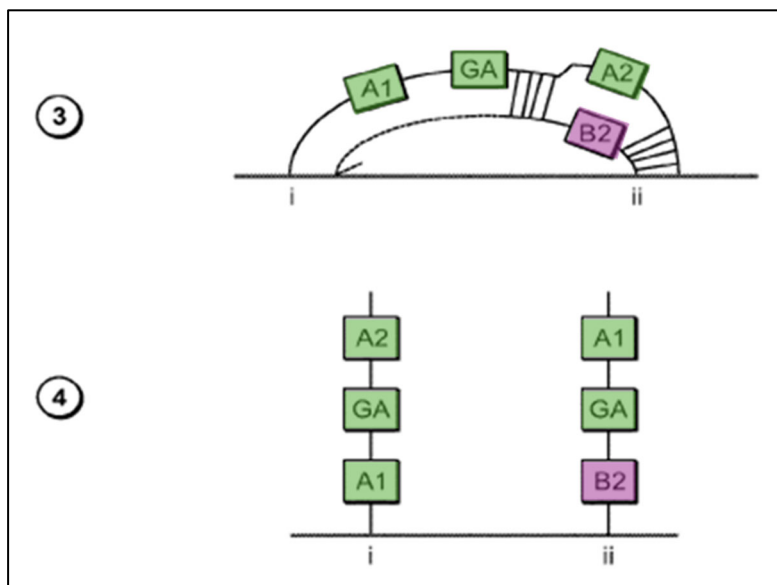
After nucleic acid samples are pooled together for multiplexed sequencing, “the samples are then hybridized to primers at discrete locations on a flow cell,” and in some instances “the nucleic acid from patient A and the nucleic acid from patient B land within a cluster radius on the solid support.” *Id.*, 5:28-40.



EX1001, FIG. 2(2) (annotated).

The pooled nucleic acid is then amplified to facilitate sequencing and analysis, and the amplification can again result in improper molecular overlap occurring between samples (e.g., between nucleic acid from patient A and nucleic acid from

patient B). “However, in the case of two barcodes, only one of patient B’s barcodes (B2) will be contained in the copied strand,” and “[t]he other barcode will be one of patient A’s barcode sequences (A1).” *Id.*, 5:41-55. Thus, “[u]nlike the example in FIG. 1, the chimeric molecule formed in this example includes one barcode sequence from patient A (A1) and one barcode sequence from patient B (B2).” *Id.*, 5:55-58.



EX1001, FIG. 2(3)-(4) (annotated).

Because two identifiers are now being used for each sample, the resulting chimeric molecule contains mismatched barcodes (i.e., “A1” paired with “B2” in strand ii above). “While each barcode sequence [A1 and B2] on its own is a valid barcode sequence, taken together, the two barcode sequences do not form a valid barcode sequence pair.” *Id.*, 5:62-65. The erroneous molecule produced from amplification can thus be detected even though “[d]uring the sequencing process, this would yield a high-quality signal,” because “during data analysis the molecules

would be recognized as invalid” and “the data can then be excluded from final analysis.” *Id.*, 5:65-6:6. Using the methods described in the ’200 Patent, “[s]equencing of the barcodes then validates detection of the analyte” because “the presence of two or more barcodes in association with the binder must be detected in order to validate the detection.” *Id.*, 3:51-54.

By increasing the ability to detect and exclude errors, the inventive methods described in the ’200 Patent “dramatically reduce false positives in a multiplex sequencing reaction” and address the problems that previously hampered next-generation multiplex sequencing reactions. EX1001, 6:53-57; 7:24-38; FIG. 3.

Petitioner asserts that the inventions in the ’200 Patent were copied from others, including from Petitioner (*see* Pet., 20), but that accusation is not well taken. Inventions in the ’200 Patent are shown in the three figures included in the patent and described in at least the corresponding detailed description of the figures. *See, e.g.*, EX1001, 3:65-7:38; FIGS. 1-3. Petitioner does not contend that any of those figures or corresponding description appear in any other publications, whether from Petitioner or third parties. Pet., 20 (citing EX1001, 1:25-31; 3:37-43; 7:45-10:2). And Petitioner’s overstated accusations of “copying” refer only to text discussing general considerations relevant to the invention, including text that is incorporated into the ’200 Patent from prior publications that were cited to the Patent Office, ***including some that are incorporated by reference in their entirety*** into the patent’s

specification. *See, e.g.*, EX1001, 3 (listing Steinmann et al. U.S. Patent Publication No. 2011/0301042, which is a national phase application that shares the same specification with WO2010/056728 that Petitioner cited as EX1037); 7:39-44 (noting “[t]he following sections discuss general considerations” for concepts related to the inventions); 10:4-10 (identifying and incorporating by reference in its entirety Sabot et al. U.S. Patent Publication No. 2009/0226975, which Petitioner cited as EX1036); 10:34-41 (same); 20:50-54 (“References and citations to other documents ... have been made throughout this disclosure. *All such documents are hereby incorporated herein by reference in their entirety* for all purposes.”); *see also id.*, 8:6-13; 8:65-9:4; 9:17-20; 15:46-50; 16:32-42; 18:9-14; 19:26-31; 19:66-20:4.

B. Overview Of The '200 File History

The '200 Patent's application was filed on June 4, 2021 as Application No. 17/339,527, claiming priority to December 23, 2010. EX1007 at 1, 41, 45, 51; EX1001, 1. Petitioner uses December 23, 2010 as the effective priority date of the '200 Patent for purposes of the Petition. Paper 1 (“Pet.”), 17.

In an Office Action dated June 1, 2023, the Examiner rejected the pending claims on the ground of nonstatutory double patenting as being unpatentable over Molecular Loop's U.S. Patent No. 11,041,852 in view of Parameswaran (EX1004).

EX1007, 272-276. In response, Applicant filed a terminal disclaimer over the '852 Patent. EX1007, 371, 381.

Following the terminal disclaimer, the Examiner deemed the claims to be allowable. A Notice of Allowance was issued on July 27, 2023, stating that “no references were found teaching or suggesting claims 66-71 [issued claims 1-6].” EX1007, 395, 399-401.

III. Overview Of The References¹

A. Gloor (EX1005)

Gloor is titled “Microbiome profiling by Illumina sequencing of combinatorial sequence-tagged PCR products.” Gloor, 1. Gloor discloses using “combinatorial sequence tagging” to analyze samples for microbiome profiling. *Id.* Gloor noted that “[c]ombinatorial sequence tagging can be used to examine hundreds of samples with far fewer primers than is required when sequence tags are incorporated at only a single end.” *Id.* Gloor “suggest[s] that this method will be useful for the deep sequencing of any short nucleotide region that is taxonomically informative....” *Id.* Gloor used Illumina sequencing in its methods and noted that

¹ Patent Owner does not concede that the references cited in the Petition are prior art to the '200 Patent. Patent Owner reserves its right to raise additional challenges to the prior art status of the references in future proceedings.

“[t]he Illumina sequencing platform is currently restricted to read lengths of ~100 nucleotides from each end of a DNA fragment, and was limited to ~75 nt at the time of experimental design.” *Id.*, 3.

Gloor added primers and combinatorial barcodes to nucleic acids prior to sequencing. For the barcodes, Gloor “chose sequence tags to ensure all 4 nucleotides were represented in each of the first four positions of the primers using parameters similar to those in the *barcrawl* program.” *Id.*, 5. For the barcode tags, Gloor “var[ied] the length of the tags between 3 and 6 nucleotides long.” *Id.*; *see also id.*, Table 2. “The tag length variation was expected to reduce the likelihood that adjacent spots on the Illumina solid support would be scored as one during the sequencing of the amplification primers.” *Id.*

After sequencing, Gloor identified sequences that contained “incorrect sequence tags” and inspected those sequences to determine that “the single largest contributor to the difference between the number of reads with proper primer sequences and the number of reads with proper sequence tag sequences was an N-1 truncation of the sequence tag, *which presumably arose during the primer synthesis.*” *Id.*, 7. “The next largest class of sequence tag error was complete lack of the left or right end sequence tag.” *Id.* For remaining errors, Gloor states that “remaining missing reads are composed of a large number of classes of sequence tag sequences each containing small numbers of errors including additional 5’ bases,

misincorporated bases or *difficult to classify errors* that presumably arose during the PCR amplification.” *Id.*

B. Parameswaran (EX1004)

Parameswaran is titled “A pyrosequencing-tailored nucleotide barcode design unveils opportunities for large-scale sample multiplexing.” Parameswaran, 1. The “pyrosequencing” Parameswaran describes is sequencing performed on “454/Roche Genome Sequencers.” *Id.*, 1. Parameswaran noted “[t]hree major high-throughput sequencing platforms” in use at the time and explained that “the Solexa and SOLiD systems provide many more sequence reads, but render much shorter read lengths than the 454/Roche Genome Sequencers.” *Id.* Parameswaran determined that “[t]his *makes the 454/Roche platform appealing for use with barcoding technology*, as the enhanced read length facilitates the unambiguous identification of both complex barcodes and sequences of interest.” *Id.*

Parameswaran discusses using pyrosequencing with “a high-information-content barcoding approach in which each sample is associated with two uniquely designed, 10-nucleotide barcodes.” *Id.*, 2. Parameswaran compared its barcode approach with prior methods that required physical separation between nucleic acids from different samples, stating that “[b]y not relying on physical separators, this procedure maximizes sequence space and multiplexing capabilities.” *Id.*

In addition to barcodes, Parameswaran incorporated forward and reverse cloning linkers into nucleic acids. *Id.*, 2, 3 (Fig. 1). Parameswaran used the cloning linkers to increase the accuracy of its methods. In particular, during analysis, because “six of the forward barcodes are exact reverse complements of six reverse barcodes,” Parameswaran “added a number of adjoining nucleotides in the Cloning-Linker (0-17) to the barcode query to reduce ambiguity while segregating the sequences into independent datasets.” *Id.*, 7. Parameswaran refers to the combination of 10-nucleotide barcodes and additional nucleotides from the cloning linkers as “barcode motifs” (or “search motifs”) that were ultimately used for sample identification. *Id.* Parameswaran’s study aimed to determine “how much of the (fixed) linker sequence will be required in addition to the (variable) barcode for definitive sample assignment,” and ultimately decided that “a search motif of 13 nt was determined to be ideal for our studies in minimizing false-discovery rate[.]” *Id.*, 7-8, Table 3.

When using 13-nt barcode motifs, Parameswaran found that approximately 94% of sequences had “perfect” forward and reverse barcode motifs. *Id.*, 7. Parameswaran attributed sequence reads that contained one perfect motif sequence unexpectedly paired with a second perfect motif sequence to “rare coincidental sequence matches (due to multiple fortuitous errors during barcode synthesis or sequencing), to contamination in PCR primer stocks, or to cross-contamination of template DNAs in the second round of PCR.” *Id.* The percentage of these “perfect

and unexpected” motif pair occurrences was less than 0.005% when 13-nt motifs were used, and Parameswaran did not exclude any such occurrences from its analysis. *Id.*, 8. Instead, “*all sequences with a match to one of the two expected sequence motifs were considered as true members* of the corresponding dataset.” *Id.*

Parameswaran was considered by the Examiner during prosecution of the ’200 Patent. Parameswaran was identified in an Information Disclosure Statement, and the Examiner signed the Statement indicating Parameswaran was considered on May 23, 2023. EX1007, 141 (Reference 2), 365. The Examiner also referenced Parameswaran in a substantive rejection, but the ’200 Patent was allowed after the Applicant overcame that rejection. *See supra* Section II.B.

C. Binladen (EX1029)

Binladen is titled “The Use of Coded PCR Primers Enables High-Throughput Sequencing of Multiple Homolog Amplification Products by 454 Parallel Sequencing.” Binladen, 1. Binladen describes the use of “5’-nucleotide tagged primers to generate homologous DNA amplification products from multiple specimens” that are sequenced by pyrosequencing. *Id.* Binladen describes multiplex sequencing reactions using DNA from thirteen species and attributes sequence errors to “artefacts of the current GS20 pyrosequencing chemistry,” “errors in the original primer synthesis process,” “contamination arising during the extraction or PCR

setup,” and “the fact that many species are closely related in the targeted 16S mtDNA region.” *Id.*, 3, 8.

Binladen was considered by the Examiner during prosecution of the '200 Patent. Binladen was identified in an Information Disclosure Statement, and the Examiner signed the Statement indicating Binladen was considered on July 21, 2023. EX1007, 389 (Reference 6), 410.

D. Bentley (EX1006)

Bentley is titled “Accurate whole human genome sequencing using reversible terminator chemistry.” Bentley, 1. Bentley describes massively parallel synthetic sequencing used to analyze whole human genomes. *Id.*, 3. Bentley explained that it “generated high-density single-molecule arrays of genomic DNA fragments attached to the surface of the reaction chamber (the flow cell) and used isothermal ‘bridging’ amplification to form DNA ‘clusters’ from each fragment.” *Id.*, 1.

IV. The Level Of Ordinary Skill In The Art

Petitioner proposes a level of ordinary skill in the art. Pet., 18. For the purposes of this Preliminary Response, Patent Owner does not set forth an alternative level of skill for a POSA because the Petition should be denied even under Petitioner’s proposal. Patent Owner’s silence regarding the appropriate level of skill of a POSA is not an agreement with Petitioner’s proposal. Patent Owner

reserves the right to challenge Petitioner's proposal, and to propose an alternative or additional level or ordinary skill, in future proceedings.

V. Claim Construction

Petitioner claims to apply the plain and ordinary meaning to each claim term. Pet., 24. For the purposes of this Preliminary Response, Patent Owner does not set forth any alternative claim constructions because the Petition should be denied even under Petitioner's apparent interpretations. Patent Owner's silence regarding the appropriate construction of any term is not an agreement with Petitioner's apparent interpretation of any such term. Patent Owner reserves the right to challenge Petitioner's apparent interpretation, and to propose alternative or additional claim constructions, in future proceedings.

VI. Petitioner Fails To Establish A Reasonable Likelihood That Gloor Is Prior Art.

Petitioner uses December 23, 2010 as the priority date of the '200 Patent for purposes of the Petition (Pet., 17) but fails to show a reasonable likelihood that Gloor (EX1005) was publicly accessible as of that date. "[T]he burden is on the petitioner to identify with particularity evidence sufficient to establish a reasonable likelihood that the reference was publicly accessible before the critical date of the challenged patent, and therefore that there is a reasonable likelihood that it qualifies as a printed publication." *Hulu, LLC v. Sound View Innovations, LLC*, IPR2018-01039, Paper 29 at 15 (PTAB Dec. 20, 2019) (precedential).

The Petition dedicates only two sentences to Gloor’s public accessibility and does not mention or cite any evidence other than Dr. Gloor’s purported recollection in an attempt to establish a reasonable likelihood that Gloor was publicly accessible before the ’200 Patent. Petitioner argues that Gloor was publicly accessible by July 29, 2010 through “arXiv.org,” and cites as purported support to a declaration by Dr. Gloor, arguing that he “received confirmation from the archive that *Gloor* was published on July 29, 2010, recalls his paper being published promptly after submission, and recalls discussing the publication with other scientists at the Human Microbiome Research Conference in St. Louis, Missouri, in September 2010.” Pet., 11 (citing EX1002, ¶¶12-19). That bare-bones assertion is insufficient to establish a reasonable likelihood that Gloor was publicly available under the Board’s precedent. *Hulu, LLC*, IPR2018-01039, Paper 29 at 13 (“***[T]he petition must identify, with particularity, evidence sufficient to establish a reasonable likelihood that the reference was publicly accessible*** before the critical date of the challenged patent and therefore that there is a reasonable likelihood that it qualifies as a printed publication.”). And to the extent Petitioner invites the Board to sift through the paragraphs of Dr. Gloor’s declaration and additional exhibits attached to the declaration—exhibits that are never cited or discussed anywhere in the Petition—the Board should decline to do so because Petitioner improperly attempts to incorporate by reference arguments and evidence without explanation, or even

citation, in violation of the Board’s regulations. *See* 37 C.F.R. § 42.6(a)(3); *Parus Holdings, Inc. v. Google LLC*, 70 F.4th 1365, 1371-73 (Fed. Cir. 2023) (affirming Board decision declining to consider evidence and argument alleged to antedate prior art that was improperly incorporated by reference); *General Access Solutions, Ltd. v. Sprint Spectrum L.P.*, 811 F. App’x 654, 657 (Fed. Cir. 2020) (The “prohibition against incorporation of arguments from other documents serves various policy goals, including to ‘minimize the chance that an argument may be overlooked’ and to ‘eliminate[] abuses that arise from incorporation and combination.’”) (quoting Rules of Practice for Trials Before the Patent Trial and Appeal Board and Judicial Review of Patent Trial and Appeal Board Decisions, 77 Fed. Reg. 48,612, 48,617 (Aug. 14, 2012)).

Even if the Board considers the additional evidence attached to Dr. Gloor’s declaration—evidence that Petitioner does not cite, explain, or even reference—it is still insufficient to show public availability. Dr. Gloor purports to support his testimony and recollection of events from fourteen years ago with documentation that at best indicates his article was ***submitted***, but does not show if and when it was actually ***published***, much less published in July 2010. Dr. Gloor’s Exhibits A-C and E-F show at best that the article was submitted in July 2010, but say nothing about its date of publication or public availability. Dr. Gloor’s Exhibits D and I are websites that he claims show arXiv’s announcement practices, but the websites are

from 2024 and say nothing about arXiv’s practices in July 2010, when Petitioner claims Gloor was publicly available. And Dr. Gloor’s Exhibits G and H are abstracts and a poster that he claims relate to a conference from 2010, but neither Petitioner nor Dr. Gloor even contend that the abstracts or poster actually include any of the details of Dr. Gloor’s article that are relevant to Petitioner’s challenge here. That evidence is wholly inadequate, particularly when compared to at least one prior case where the Board accepted an arXiv publication, relying on testimony from a Cornell University Library employee who was actually responsible for arXiv.org and knowledgeable regarding its practices. *Great West Casualty Company v. Intellectual Ventures II LLC*, IPR2015-01706, Paper 10 at 11 (PTAB Feb. 9, 2016) (“Mr. Warner testifies that he is an employee of the Cornell University Library (‘CUL’), and the Directory of Repository Architecture/Services within CUL Information Technology, which is responsible for arXiv.org, and explains that the data logs of arXiv.org indicate that MyLibrary was available, and arXiv.org users were notified of its availability via e-mail, as of February 3, 1999.”). Petitioner provides no testimony from any Cornell employee or any other custodian with any personal knowledge of arXiv.org or its regular practices. The Petition thus fails to provide even the minimum evidence previously found by the Board to be sufficient for showing public availability at the institution stage. *Hulu*, IPR2018-01039, Paper 29 at 13; *see*

Accordingly, Petitioner has failed to meet its burden to show that there was a reasonable likelihood that Gloor is prior art.

VII. The Board Should Exercise Its Discretion To Deny Institution Because The *Advanced Bionics* and *Becton* Factors Favor Denial Of Institution.

The Board has discretion under 35 U.S.C. § 325(d) to deny institution of a petition that raises the same or substantially the same art or arguments as was previously presented to the Patent Office. *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 at 17 (PTAB Dec. 15, 2017) (informative). The relevant factors considered by the Board favor denial of the Petition here under 35 U.S.C. § 325(d).

The Board uses a two-prong test to determine whether it will deny institution under 35 U.S.C. § 325(d): (1) whether the same or substantially the same art or arguments were previously presented to the Office; and (2) if the first part of the framework is satisfied, whether the Office erred in a manner material to the patentability of the challenged claims. *See Advanced Bionics LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 6-9 (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.*

The six non-exclusive factors described in *Becton* that the Board considers within the *Advanced Bionics* framework include:

- “(a) the similarities and material differences between the asserted art and the prior art involved during examination;
- (b) the cumulative nature of the asserted art and the prior art evaluated during examination;
- (c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection;
- (d) the extent of the overlap between the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art;
- (e) whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the asserted prior art; and
- (f) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of the prior art or arguments.”

Becton, Paper 8 at 17-18.

Here, the Petition presents art and arguments that are substantially the same as the art and arguments previously presented to the Office. Petitioner’s Grounds 1-3 rely on Gloor, which Petitioner has not shown is prior art for the reasons discussed above in Section VI, and Parameswaran, which was already substantively considered

by the Office during prosecution. Petitioner's Ground 4 relies on Parameswaran combined with Binladen, which was also already considered during prosecution. And Petitioner's Ground 5 (addressing only a single dependent claim) relies on Parameswaran and Binladen with Bentley. Petitioner fails to show how the Examiner materially erred in finding that the Challenged Claims were patentable. Thus, the Petition should be denied under the Board's § 325(d) discretion.

1. *Advanced Bionics* Part One: The Petition Relies On The Same Or Substantially The Same Art And Arguments Previously Presented To The Patent Office.

"Factors (a), (b), and (d) of the Becton, Dickinson factors relate to whether the art or arguments presented in the Petition are the same or substantially the same as those previously presented to the Office." *Roku, Inc. v. Universal Elecs., Inc.*, IPR2019-01619, Paper 17, at 4 (PTAB May 25, 2021) (citing *Advanced Bionics*). *Becton* Factors (a), (b), and (d) favor discretionary denial of the Petition.

i. *Becton* Factors (a) And (b) Weigh Against Institution.

Becton factors (a) and (b) weigh against institution because the only new reference that Petitioner has even arguably established as prior art is Bentley, but that reference has minimal impact on the analysis even in view of Petitioner's own assertions, which apply Bentley for only one dependent claim in the '200 Patent. Two other references applied in Petitioner's Grounds (Parameswaran and Binladen) were provided to and considered by the Examiner, and Petitioner has not shown that

its remaining reference (Gloor) is prior art. Thus, for factors (a) and (b), the Petition fails to raise new, materially-different prior art in its Grounds.

Petitioner's Grounds 1 and 3 rely on Gloor, either alone or in combination with other references. But Petitioner has not shown that Gloor is actually prior art to the '200 Patent for the reasons explained above in Section VI. Thus, Gloor cannot raise any new and material differences over the prior art considered during prosecution.

Petitioner's Grounds 2, 3, 4, and 5 rely on Parameswaran, either alone or in combination with other references. But Parameswaran was considered and substantively addressed by the Examiner during the prosecution of the '200 Patent. Parameswaran is listed in the "References Cited" in the '200 Patent. EX1001, 8. Parameswaran was provided to the Office by the Applicant in a September 2, 2021 Information Disclosure Statement. EX1007, 141 (Reference 2). The Examiner substantively addressed Parameswaran, applying it in a nonstatutory double patenting rejection during prosecution of the '200 Patent. EX1007, 272-276.

Petitioner's Grounds 4 and 5 rely on Binladen, combined with other references. But Binladen was also considered by the Examiner during the prosecution of the '200 Patent. Petitioner states—without any explanation, citation, or support—that "Binladen ... was not considered by the Examiner." Pet., 2; *see also id.*, 69. That assertion is incorrect. Binladen is listed in the "References Cited"

in the '200 Patent. EX1001, 9. Binladen was provided to the Office by the Applicant in a June 14, 2023 Information Disclosure Statement. EX1007, 389 (Reference 6). The Examiner signed the Statement indicating Binladen had been considered on July 21, 2023. *Id.*, 410.

Petitioner's Ground 5 relies on Bentley, combined with other references, but alleges Bentley is only minimally relevant, applying it in combination for only one dependent claim (Claim 6). Specifically, Petitioner cites Bentley in Ground 5 only for its alleged disclosure of "Illumina sequencing of template nucleic acids after bridge amplification on the surface of the flow cell." Pet., 66. Petitioner does not argue that Bentley is relevant to the majority of the challenged claims, including the only independent claim (Claim 1). Thus, in view of Petitioner's own assertions, Petitioner cannot argue that Bentley raises material differences over art considered during prosecution for the challenged claims.

ii. *Becton* Factor (d) Weighs Against Institution.

Becton factor (d) weighs against institution because Petitioner simply repeats and repackages the arguments that were considered by the Examiner and overcome during prosecution.

Petitioner uses Parameswaran to repeat arguments considered by the Examiner during prosecution of the '200 Patent. During prosecution of the '200 Patent, the Examiner asserted that "[i]t would have been *prima facie* obvious to one

of ordinary skill in the art at the time of the invention to have *used the barcodes of Parameswaran* et al. in the method of the '852 patent.” EX1007, 276. In Grounds 2-5, Petitioner argues that *Parameswaran’s barcodes* anticipate or render obvious (in combination with other references) the claims of the '200 Patent. *See* Pet., 35-67. Petitioner relies on different combinations of references, two of which were considered by the Examiner, merely repackaging the issues already addressed and overcome during prosecution. Therefore, factor (d) weighs against institution.

2. *Advanced Bionics* Part Two: Petitioner Fails To Demonstrate That The Office Erred In A Manner Material To The Patentability Of The Challenged Claims.

“Factors (c), (e), and (f) ‘relate to whether the petitioner has demonstrated a material error by the Office’ in its prior consideration of that art or arguments.” *Roku*, Paper 17, at 4 (citing *Advanced Bionics*).

i. *Becton* Factor (c) Weighs Against Institution.

Becton factor (c) weighs against institution because after setting aside Gloor, which Petitioner did not establish as prior art, Petitioner relies almost entirely on prior art that was previously presented to the Examiner. As explained in Section VII.1, Parameswaran and Binladen were presented to the Examiner during prosecution of the '200 Patent, and Parameswaran was relied on by the Examiner in a substantive nonstatutory double patenting rejection. And Petitioner’s use of

Bentley—applied only for dependent Claim 6—does not change the analysis on this factor for the reasons discussed above in Section VII.1.i.

ii. *Becton* Factor (e) At Worst Weighs Only Slightly In Favor Of Institution.

Becton factor (e) at worst weighs only slightly in favor of institution because Petitioner fails to convincingly show that the Examiner erred in its analysis of Parameswaran and Binladen.

Petitioner argues only that the Examiner erred in evaluating Parameswaran, never mentioning Binladen, ostensibly because Petitioner mistakenly believed Binladen was not disclosed during prosecution. Pet., 69-70. And for Parameswaran, Petitioner focuses solely on disclosure of “different” identifiers in Parameswaran, contrasting with “same” identifiers in an earlier patent application. *Id.* But Petitioner never shows that the “different identifiers” were the reason the Examiner determined that the ’200 Patent claims were patentable over Parameswaran and does not address that the Examiner expressly considered Parameswaran, addressed its disclosure, and determined that the claims were patentable over Parameswaran (either alone or in combination with any other reference) after using Parameswaran in a substantive rejection. *See supra* Section II.B.

“[I]f the record of the Office’s previous consideration of the art is not well developed or silent, then a petitioner may show the Office erred by overlooking something persuasive under factors (e) and (f). On the other hand, if the alleged error

is a disagreement with a specific finding of record by the Office, then ordinarily the petitioner's required showing of material error must overcome persuasively that specific finding of record." *Advanced Bionics*, IPR2019-01469, Paper 6, at 10-11. Petitioner does not persuasively argue that the Examiner erred in finding that the claims of the '200 Patent were not anticipated by Parameswaran. Additionally, Petitioner does not assert that the Examiner made a material error in finding that the claims of the '200 Patent were not rendered obvious by Parameswaran in view of Binladen. Therefore, *Becton* factor (e) at worst weighs only slightly in favor of institution.

iii. *Becton* Factor (f) Weighs Against Institution.

Becton factor (f) weighs against institution because the additional references asserted by Petitioner offer no new evidence to warrant reconsideration of the patentability of the Challenged Claims. Petitioner characterizes Gloor, Binladen, and Bentley as new evidence warranting the Board's reconsideration of the Examiner's findings. *See* Pet., 1-2, 16-17. However, as explained in Section VI, Petitioner has failed to show that Gloor was prior art to the '200 Patent. And as explained in Section VII.1.i, and contrary to the incorrect assertions in the Petition, Binladen was presented to the Office and considered by the Examiner during prosecution of the '200 Patent. Further, applying Petitioner's own characterizations of its references, Bentley—used for a very limited purpose in the Petition applying

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to only one dependent claim—does not materially change the Examiner’s prior evaluation of the art presented to the Office. Accordingly, factor (f) weighs against institution.

VIII. Conclusion

For the foregoing reasons, Patent Owner respectfully requests that the Board deny institution of the Petition.

Dated: October 31, 2024

Respectfully submitted,

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CERTIFICATION UNDER 37 C.F.R. § 42.24(d)

I hereby certify that this paper, excluding the portions exempted under 37 C.F.R. § 42.24(a), has 5,822 words as counted by Microsoft Word 365, the word-processing system used to prepare this paper.

Dated: October 31, 2024

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CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e), the undersigned certifies that on October 31, 2024, a complete copy of the foregoing was served on counsel of record for Petitioner by filing this document through P-TACTS and by sending this document via electronic mail to the following addresses:

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