

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ILLUMINA INC.,
Petitioner,

v.

MOLECULAR LOOP BIOSCIENCES, INC.,
Patent Owner.

IPR2024-00965
Patent 11,768,200 B2

Before ERICA A. FRANKLIN, ZHENYU YANG, and
ROBERT A. POLLOCK, *Administrative Patent Judges*.

YANG, *Administrative Patent Judge*.

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

I. INTRODUCTION

Illumina, Inc. (“Petitioner”) filed a Petition (Paper 1, “Pet.”), seeking *inter partes* review of claims 1–6 of U.S. Patent No. 11,768,200 B2 (Ex. 1001, “the ’200 patent”). Molecular Loop Biosciences, Inc. (“Patent Owner”) filed a Preliminary Response. Paper 6 (“Prelim. Resp.”).

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).

For the reasons provided below, we determine Petitioner has satisfied the threshold requirement set forth in 35 U.S.C. § 314(a). Accordingly, we institute *inter partes* review of all challenged claims based on the ground raised in the Petition.

A. Related Matters

According to the parties, the ’200 patent is involved in the following litigations: *Molecular Loop Biosciences, Inc. v. Illumina, Inc. et al.*, No. 1:24-cv-00680 (D. Del.) and *Illumina, Inc. et al. v. Molecular Loop Biosciences, Inc.*, No. 1:24-cv-11501 (D. Mass.). Pet. 70; Paper 3, 1.

Petitioner filed IPR2024-00964, challenging the claims of U.S. Patent No. 11,041,852, a patent in the same family as the ’200 patent. Pet. 70.

B. The ’200 patent

The ’200 patent relates generally to “methods for maintaining the integrity and identification of a nucleic acid template in a multiplex sequencing reaction.” Ex. 1001, Abstract. The methods include the steps of “obtaining a template nucleic acid, incorporating a pair of sequence identifiers into the template, and sequencing the template.” *Id.*

According to the '200 patent, maintaining accurate sample identification during a multiplex sequencing reaction is problematic because “the sample preparation phase frequently introduces errors into the subsequent sequencing reaction.” *Id.* at 1:37–39. “For example, template molecules may physically overlap on a substrate; and in some cases result in a detectable erroneous signal.” *Id.* at 1:39–41; *see also id.* at 1:52–54 (stating that errors can be introduced from “improper pairing of template strands from different samples,” which can “form during the amplification of the multiplexed samples”). Because these errors have a significant effect on the results, the '200 patent states that “methods for reducing or eliminating errors in such procedures are needed.” *Id.* at 1:60–62.

The '200 patent explains the undesired introduction of sequencing errors when using a single barcode identifier. *See id.* at 4:17–63, Fig. 1 (showing “one example of how molecular overlap can lead to apparent high quality, but incorrect sequence data”). The '200 patent states that its method uses “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.” *Id.* at 2:5–8. According to the '200 patent, “[i]n this way, false positive and/or false negative results are avoided by requiring concomitant detection of two or more independent markers associated with the analyte to be detected.” *Id.* at 2:8–11.

The '200 patent states that, using two or more nucleic acid barcodes as identifiers, its method is especially useful in multiplex next-generation sequencing. *Id.* at 2:12–18. The '200 patent explains that:

in sequencing applications, a pair of barcodes are placed such that they flank the sequence of interest. The identifiers are unique to the sample, so that valid sequence data are confirmed

by the presence of the pair of flanking identifiers. In contrast, 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. Thus, methods of the invention make it possible to determine whether the integrity of a sample was maintained during a multiplex sequencing reaction, and prevent the assigning of sequence data to the wrong sample.

Id. at 2:18–29; *see also id.* at 4:64–6:6 (describing Figure 2 show “how methods of the invention allow one to detect, during analysis, whether the integrity of a patient's sample was maintained during a multiplex sequencing reaction”), Fig. 2.

C. Illustrative Claim

Of the challenged claims, claim 1 is independent. Claim 1 is illustrative of the claimed subject matter and is reproduced below.

1. A method for validating the sequence of a nucleic acid analyte of interest in a multiplex sequencing reaction, the method comprising:

i) detecting the presence of two or more identifier sequences that are uniquely associated with the nucleic acid analyte of interest,

wherein at least a first identifier sequence is incorporated into a 5' portion of the nucleic acid analyte of interest and wherein at least a second identifier sequence is incorporated into a 3' portion of the nucleic acid analyte of interest, and

wherein the first and second identifier sequences have four or more nucleotides and are different;

ii) sequencing the first identifier sequence, the nucleic acid analyte of interest and the second identifier sequence; and

iii) validating the sequence of the nucleic acid analyte of interest by analyzing both identifiers and excluding the sequences of those nucleic acid analytes of interest containing only one identifier or an incorrect pair of

identifiers from sequence analysis of the multiplex sequencing reaction.

Ex. 1001, 21:2–22:6.

D. Asserted Challenges to Patentability

Petitioner asserts the following challenges to patentability:

Claims Challenged	35 U.S.C. § ¹	References
1–6	102	Gloor ²
1–6	102	Parameswaran ³
1–6	103	Parameswaran, Gloor
1–6	103	Parameswaran, Binladen ⁴
6	103	Parameswaran, Binladen, Bentley ⁵

As support for its patentability challenge, Petitioner relies on the Declarations of Gregory B. Gloor, Ph.D. (Ex. 1002) and Paul T. Spellman, Ph.D. (Ex. 1003).

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 and 103, effective March 16, 2013. On its face, the ’200 patent claims priority to several applications filed before the effective date of AIA. Ex. 1001, code (60). Accordingly, we apply the pre-AIA version of §§ 102 and 103.

² G.B. Gloor, et al., *Microbiome profiling by Illumina sequencing of combinatorial sequence-tagged PCR products*, Cornell University Library, arXiv:1007.5075v1 (2010) (Ex. 1005, “Gloor”).

³ P. Parameswaran, et al., *A pyrosequencing-tailored nucleotide barcode design unveils opportunities for large-scale sample multiplexing*, 35 NUCLEIC ACIDS RSCH, 19(e130) (2007) (Ex. 1004, “Parameswaran”).

⁴ J. Binladen, et al., *The use of coded PCR primers enables high-throughput sequencing of multiple homolog amplification products by 454 parallel sequencing*, 2 PLoS ONE 2:e197 (2007) (Ex. 1029, “Binladen”).

⁵ D.R. Bentley, et al., *Accurate whole human genome sequencing using reversible terminator chemistry*, 456 NATURE 6, 53–59 (2008) (Ex. 1006, “Bentley”).

II. ANALYSIS

A. *Claim Construction*

In an *inter partes* review, we construe a claim term “using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. [§] 282(b).” 37 C.F.R. § 42.100(b) (2020). Under that standard, the words of a claim “are generally given their ordinary and customary meaning,” which is “the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application.” *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc).

On this record and for purposes of this Decision, we see no need to expressly construe any claim term. *See Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) (stating that only claim terms that are in controversy need construed and only to the extent necessary to resolve the controversy).

B. *Alleged Anticipation by Gloor*

Petitioner asserts that claims 1–6 are anticipated by Gloor. Pet. 25–34. Based on this record, and for at least the following reasons, we determine Petitioner has established a reasonable likelihood that it would prevail in this assertion.

1. Gloor

Gloor is titled “Microbiome profiling by Illumina sequencing of combinatorial sequence-tagged PCR products.” Ex. 1005, 1. Gloor describes “a low-cost, high-throughput microbiome profiling method that uses combinatorial sequence tags attached to PCR primers that amplify the rRNA V6 region.” *Id.*; *see also id* at 2 (reporting “the methods used to perform

microbiome analysis of the V6 region of 272 clinical samples using the Illumina sequencing technology”). Gloor describes sequencing amplified PCR products “using an Illumina paired-end protocol to generate millions of overlapping reads.” *Id.* at 1. According to Gloor, “[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 added primers and sequence tags to nucleic acids prior to sequencing. *Id.* at 3–6. Gloor “var[ied] the length of the sequence tags between 3 and 6 nucleotides long” and “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.* at 5. Gloor describes developing custom programs “to identify the overlapping segments of the forward and reverse reads” and to extract “overlapping reads with proper primer sequences and correct sequence tags.” *Id.* at 7. Gloor inspected sequences with “incorrect sequence tags” to determine the sources of the errors. *Id.* at 7–8.

2. Analysis

Petitioner provides detailed analysis, mapping each limitation of claims 1–6 to Gloor’s disclosures. Pet. 25–34. At this time, Patent Owner does not dispute that Gloor discloses the limitations of the challenged claims. *See generally* Prelim. Resp. We find Petitioner’s analysis persuasive and adopt it as our own.

Patent Owner, however, challenges Gloor’s prior art status. *Id.* at 17–21. Relying on the Declaration of Dr. Gloor, the first named author, Petitioner contends that Gloor was published on July 29, 2010, and thus, “is

prior art under at least pre-AIA 35 U.S.C. §102(a).” Pet. 11 (citing Ex. 1002). Dr. Gloor testifies that he submitted Gloor to arXiv.org on July 28, 2010, and received an email from arXiv.org confirming the public availability of Gloor as of July 29, 2010. Ex. 1002 ¶¶ 16, 17 (citing Ex. 1002, Exhibit E). According to Dr. Gloor, “[r]ecently, arXiv Technical Support confirmed in an email to [him] that *Gloor*’s release ‘would have been announced on Thursday, July 29, 2010.’” *Id.* ¶ 17 (citing Ex. 1002, Exhibit F). Dr. Gloor also testifies that he presented a poster at a conference held between August 31 and September 2, 2010, and the poster “provides a complete citation to” the Gloor reference. *Id.* ¶ 18 (citing Ex. 1002, Exhibit H).

Patent Owner counters that Petitioner has failed to show a reasonable likelihood that Gloor was publicly accessible as of December 23, 2010, the alleged priority date of the ’200 patent. Prelim. Resp. 17–21. Patent Owner contends that the exhibits Dr. Gloor relies on in support of his declaration “at best indicate[] his article was *submitted*, but do[] not show if and when it was actually *published*, much less published in July 2010.” *Id.* at 19. Based on the current record, we find Petitioner has shown a reasonable likelihood that Gloor qualifies as prior art.

Indeed, Exhibit E to the Gloor declaration shows that the Gloor reference was assigned an arXiv identifier as of July 29, 2010. Ex. 1002, Exhibit E. It provides a hyperlink to the abstract and states that the abstract would appear in that day’s mailing. *Id.* In Exhibit F to the Gloor declaration, the arXiv Technical Support states that the submission with the same hyperlink “would have been announced on Thursday, July 29, 2010.” Ex. 1002, Exhibit F.

Patent Owner argues that Exhibit H to the Gloor declaration also does not support Dr. Gloor's testimony of the public availability of the Gloor reference. Prelim. Resp. 20. According to Patent Owner, neither Petitioner nor Dr. Gloor contends that Exhibit H "actually include[s] any of the details of Dr. Gloor's article that are relevant to Petitioner's challenge here." *Id.* As we understand it, however, Petitioner does not rely on the substantive teachings of Exhibit H to support its unpatentability argument. Instead, Petitioner relies on Exhibit H to support the public availability of the Gloor reference before the priority date. *See* Pet. 11; *see also* Ex. 1002 ¶ 18 (Dr. Gloor testifying that "the References section" of Exhibit H provides a complete citation to the Gloor reference).

Patent Owner asserts that Petitioner's evidence to show the public availability of Gloor is 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." Prelim. Resp. 20 (citing *Great West Casualty Company v. Intellectual Ventures II LLC*, IPR2015-01706, Paper 10 at 11 (PTAB Feb. 9, 2016)).

We agree with Patent Owner that testimony from a "custodian with any personal knowledge of arXiv.org or its regular practices" would have strengthened Petitioner's argument that Gloor is prior art. *See* Prelim. Resp. 20; *see also, e.g., Murray & Poole Enters. LTD v. Institut De Cardiologie De Montreal*, IPR2023-01064, Paper 49 (PTAB Jan. 14, 2025) (considering testimony regarding the internet archive service known as the Wayback Machine (<https://web.archive.org/>) in determining public accessibility). At the institution stage, however, Petitioner needs to show that

Gloor qualifies as prior art by “a reasonable likelihood” standard. *See Hulu, LLC, v. Sound View Innovations, LLC*, IPR2018-01039, Paper 29, 13 (PTAB Dec. 20, 2019) (precedential) (“[A]t the institution stage, the 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.”). We find that, for purposes of institution, Petitioner has met its burden to show a reasonable likelihood that Gloor was publicly accessible before the priority date of the ’200 patent.

To prevail in this *inter partes* review, Petitioner must meet the preponderance of the evidence standard. *See* 35 U.S.C. § 316(e). Thus, we encourage the parties to fully develop the record during trial to facilitate the ultimate resolution of this issue.

In sum, based on this record, we determine Petitioner has established a reasonable likelihood that it would prevail in its assertion that Gloor anticipates claims 1–6. Thus, we institute an *inter partes* review as to all challenges raised in the Petition. *See SAS Institute, Inc. v. Iancu*, 138 S. Ct. 1348, 1356 (2018); *see also* 37 C.F.R. § 42.108(a) (“When instituting *inter partes* review, the Board will authorize the review to proceed on all of the challenged claims and on all grounds of unpatentability asserted for each claim.”); Patent Trial and Appeal Board Consolidated Trial Practice Guide 64 (Nov. 2019)⁶ (“The Board will not institute on fewer than all claims or all challenges in a petition.”).

⁶ Available at <https://www.uspto.gov/sites/default/files/documents/tpgnovpdf>.

C. Other Challenges and Discretionary Denial

Petitioner asserts that the challenged claims are anticipated by Parameswaran, and are rendered obvious over the combination of Parameswaran and other prior art (Gloor, Binladen, or Binladen and Bentley). Pet. 34–67. At this time, Patent Owner does not dispute these assertions. *See generally* Prelim. Resp.

Patent Owner, however, argues that we should our discretion to deny institution under § 325(d). Prelim. Resp. 21–29. 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 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 Electromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 (“*Advanced Bionics*”), 8 (PTAB Feb. 13, 2020) (precedential).

Patent Owner contends that (1) Parameswaran and Binladen “were provided to and considered by the Examiner;” (2) Bentley, which does not appear to be presented or considered during the prosecution, “has minimal impact on the analysis” because the Petition applies Bentley for only one dependent claim; and (3) “Petitioner has not shown that its remaining reference (Gloor) is prior art.” Prelim. Resp. 23–24. Accepting, without deciding, Patent Owner’s argument on the first two issues, we nevertheless

decline to deny the Petition under § 325(d) in light of Petitioner's challenge to all 20 claims of the '200 patent based on Gloor.

It is undisputed that Gloor was not previously presented or considered by the Office. And Patent Owner does not presently dispute Petitioner's anticipation challenge based on Gloor other than with respect to its prior art status. As explained above, we find that, for purposes of institution, Petitioner has met its burden to show a reasonable likelihood that Gloor is prior art. *See supra* Section II.B.2.

Thus, we decline to deny the Petition under § 325(d). Instead, under *SAS*, we institute an *inter partes* review as to all challenges raised in the Petition. *See SAS*, 138 S. Ct. at 1356.

III. CONCLUSION

Based on the current record, and for the reasons explained above, we find Petitioner has demonstrated a reasonable likelihood that it would prevail with respect to at least one claim challenged in the Petition. We therefore institute an *inter partes* review of all challenged claims on all asserted grounds.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 314(a), *inter partes* review is hereby instituted on all challenged claims of the '200 patent based on the assert ground set forth in the Petition; and

FURTHER ORDERED, pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4(b), notice is hereby given of the institution of a trial commencing on the entry date of this decision.

IPR2024-00965
Patent 11,768,200 B2

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