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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

10X GENOMICS, INC.,
Petitioner,

v.

BIO-RAD LABORATORIES, INC.,
Patent Owner.

IPR2021-00132
Patent 10,190,115 B2

Before SHERIDAN K. SNEDDEN, ZHENYU YANG, and CHRISTOPHER G. PAULRAJ, *Administrative Patent Judges.*

SNEDDEN, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
35 U.S.C. § 314, 37 C.F.R. § 42.4

I. INTRODUCTION

A. Background and Summary

10X Genomics, Inc. ("Petitioner") filed a Petition requesting an *inter partes* review of claims 1–26 of U.S. Patent No. 10,190,115 B2 ("the '115 patent," Ex. 1001). Paper 2 ("Pet."). Bio-Rad Laboratories, Inc. ("Patent Owner") filed a Preliminary Response to the Petition. Paper 7 ("Prelim. Resp.").

To institute an *inter partes* review, we must determine that the information presented in the Petition shows "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). The Supreme Court has held that a decision to institute under 35 U.S.C. § 314 may not institute on less than all claims challenged in the petition. *SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348, 1359–60 (2018). After considering the evidence and arguments presented in the Petition, we determine that Petitioner has not demonstrated a reasonable likelihood of success in proving that at least 1 claim of the '115 patent is unpatentable.

B. Real Parties in Interest

Petitioner 10X Genomics, Inc. and Patent Owner Bio-Rad Laboratories, Inc. each asserts it alone is the real party in interest. Pet. 57; Paper 5, 1.

C. Related Matters

Petitioner has filed a second petition for *inter partes* review in IPR2021-00133 for U.S. Patent No. 10,190,115. The parties indicate the '115 patent is asserted against Petitioner in *Bio-Rad Laboratories, Inc., et al v. 10X Genomics, Inc.*, 3:20-cv-03207-VC (N.D. Cal.). Pet. 57; Paper 5, 1.

D. The '115 Patent (Ex. 1001)

The '115 patent discloses "methods, compositions, and kits for assays, many of which involve amplification reactions such as digital PCR or droplet digital PCR." Ex. 1001, Abstract. The assays may be used for applications such as sequencing. *Id*.

The '115 patent discloses that "[s]eparate library preparations can be prepared for each sample, and each sample can have its own unique barcode. *Id*. at 3:67–4:2. When the prepared libraries are pooled and sequenced, "[e]ach sequence read of the resulting dataset can be traced back to an original sample via the barcode in the sequence read." *Id*. at 4:2–6. Pooling samples reduces the cost of sequencing per sample while retaining the ability to determine from which sample a sequence read is derived. *Id*. at 3:64–67.

More specifically, the '115 patent discloses separating polynucleotides in a sample into a plurality of partitions, e.g., droplets, and supplying adaptors with oligonucleotide barcode sequences (or tags) to each of a plurality of partitions comprising polynucleotides. *Id*. at 4:7–9, 10:26–43. The adaptor with a barcode can then be attached to a polynucleotide by ligation. *Id.* at 7:38–39. When polynucleotides with barcode adaptors are sequenced, "the barcodes can be used determine if two or more sequence reads were generated from one or more polynucleotides in the same partition." *Id*. at 4:11–14.

The '115 patent discloses "[b]arcode adaptors can be bundled within a partition, e.g., an aqueous phase of an emulsion, e.g., a droplet." *Id*. at 4:15–16. Barcode tagging is accomplished by merging partitions filled with adaptors and partitions containing sample polynucleotide. *Id*. at 4:15–16. Figure 1A, reproduced below, shows a method "of merging droplets

comprising a sample with droplets comprising adaptors with barcodes." *Id.* at 3:40–42.

FIG. 1A

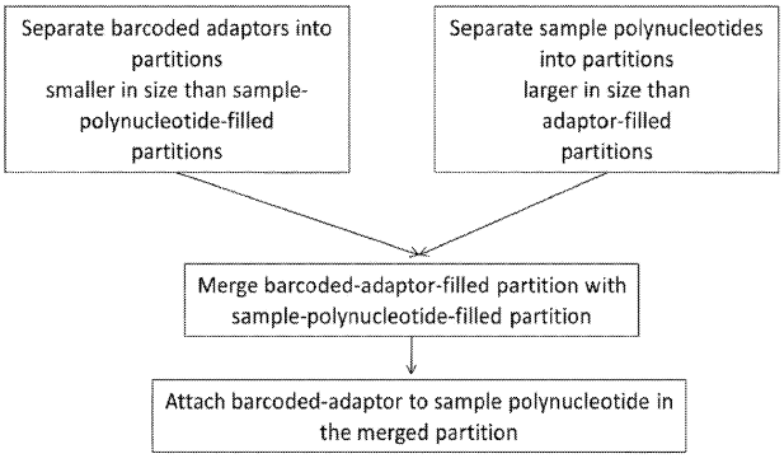

Figure 1A shows an adaptor-filled partition/droplet that is merged with a sample-polynucleotide-containing partition/droplet, resulting in an adaptor attached to a polynucleotide. *Id.* at 4:19–27. As illustrated in FIG 1A, partitions containing sample polynucleotide may be greater than (e.g., 1.5-fold or 100,000-fold) the average volume of adaptor-filled partitions. *Id.* at 4:27–32.

In some cases, sample-polynucleotide-containing partitions contain adaptor-filled partitions. *Id.* at 4:39–41. For example, adaptor-filled partitions "can be emulsified with a polynucleotide sample so that sample-polynucleotide-containing partitions (e.g., droplets) end up containing adaptor-filled partitions." *Id.* at 4:41–45. The '115 patent discloses "[t]he adaptor-filled droplets can be burst (e.g., through [a stimulus such as a] temperature adjustment) to release reaction components (e.g., PCR or ligation components) that can be used for library preparation." *Id.* at 4:45–48.

E. Illustrative Claim

Independent claims 1 and 14, reproduced below, are illustrative of the claimed subject matter of the '115 patent.

> 1. A composition comprising a plurality of second partitions containing first partitions, wherein:
>
> a. said first partitions are degradable upon the application of a stimulus to said first partitions such that contents of a first partition is mixed with contents of a second partition; and
>
> b. said first partitions are contained within the second partitions;
>
> c. said first partitions contain an oligonucleotide barcode; and
>
> d. the first partitions have on average a first average volume and the second partitions have on average a second average volume, wherein the second average volume is at least twice as large as the first average volume.
>
> 14. A device comprising a plurality of second partitions, wherein:
>
> a. at least one second partition of the plurality of second partitions contains a first partition comprising an oligonucleotide barcode, and the first partition has a first volume and the at least one second partition has a second volume, wherein the second volume is at least twice as large as the first volume; and
>
> b. said first partition is degradable upon the application of a stimulus to said first partition such that contents of a first partition is mixed with contents of a second partition.

Ex. 1001, 49:2–50:41.

Claims 2–13 depend from independent claim 1. *Id.* Claims 15–26 depend from independent claim 14. *Id.*

F. Evidence

Petitioner relies upon information that includes the following.

Ex. 1005, Hindson et al., US 2014/0155295 A1, published June 5, 2014 ("Hindson").

Ex. 1006, Anderson et al., US RE41,780 E, issued Sept. 28, 2010 ("Anderson").

Petitioner also relies upon the Declaration of Dr. John Quakenbush (Ex. 1004) to support its contentions.

G. Asserted Ground of Unpatentability

Petitioner asserts that claims 1–26 would have been unpatentable on the following grounds:

Ground	Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1	1–26	102	Hindson (with Anderson incorporated-by-reference)

II. ANALYSIS

A. Claim Construction

We interpret a claim "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) (2019). Under this standard, we construe the claim "in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent." *Id.*

Petitioner proposes construction for several claimed terms, including "first partition" and "droplet." Pet. 28–30. Patent Owner does not address claim construction in its Preliminary Response. Having considered the parties' positions and evidence of record, we determine that no express

construction of any claim term is necessary to determine whether to institute *inter partes* review. *Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) ("[W]e need only construe terms 'that are in controversy, and only 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))). To the extent further discussion of the meaning of any claim term is necessary to our decision, we provide that discussion below in our analysis of the asserted grounds of unpatentability.

B. Summary of Cited Prior Art

1. Summary of Hindson (Ex. 1005)

Petitioner's anticipation challenges rely on Hindson, which incorporates-by-reference Anderson. Pet. 31, 37; Ex. 1005 ¶ 32.

Hindson relates to microwell capsule array devices capable of performing one or more sample preparation operations. Ex. 1005, Abstract. Hindson discloses that the device is an assembly of partitions (e.g., droplets) that are loaded with microcapsules. *Id.* at ¶ 26.

Hindson discloses a composition for the device including a first microcapsule, a gel bead, which comprises an oligonucleotide barcode. *Id.* at ¶ 5. The microcapsule is degradable upon the application of a stimulus (i.e., a biological, chemical, thermal, electrical, magnetic, or photo stimulus, and combinations thereof). *Id.* at ¶ 6. Hindson discloses a second microcapsule, which may comprise the first microcapsule. *Id.* at ¶ 7.

Figure 1B, reproduced below, shows a microcapsule. *Id.* at ¶ 36.

Fig. 1B

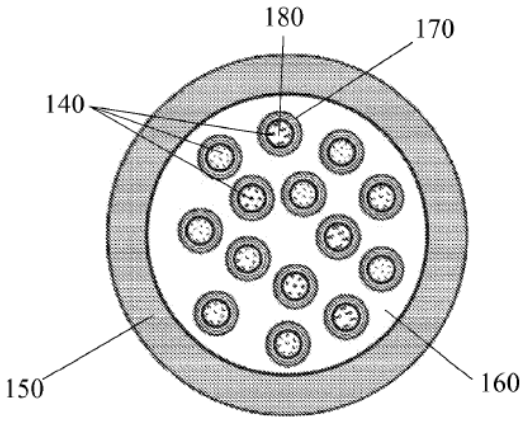

Figure 1A shows a plurality of smaller microcapsules, or compartments **140**, that are contained within the larger microcapsule. *Id*. at ¶ 37. Compartments **140** have polymerized shells, and each compartment can hold a different reagent. *Id*.

The release of reagents, such as oligonucleotide barcodes, can be controlled. *Id*. at ¶¶ 38, 56. For example, a reagent designed to be released upon a heat trigger may be contained within compartments having heat activatable polymerized shells, while reagents to be released upon a different trigger may be present in compartments with different types of polymerized shells. *Id*. at ¶ 37.

Hindson further discloses that the second microcapsule, which comprises the first microcapsule, may be a droplet. *Id*. at ¶ 7. Hindson refers to and incorporates-by-reference Anderson, which describes droplets and methods for droplet generation. *Id*. at ¶ 32.

2. Summary of Anderson (Ex. 1006)

Hindson incorporates Anderson by reference, and, in the following excerpt, specifically relies upon Anderson for its disclosure of droplets:

> Droplets and methods for droplet generation, for example, are described in U.S. Pat. No. RE41,780, which is incorporated herein by reference in its entirety for all purposes.

Ex. 1005 ¶ 32.

Anderson discloses a "system for nucleic acid amplification of a sample compris[ing] partitioning the sample into partitioned sections and performing PCR on the partitioned sections of the sample." Ex. 1006, Abstract. Anderson describes partitioning into droplets. *Id.* at 3:24, 5:8. Regarding droplet volume, Anderson discloses, for example, droplets of "picoliter type volumes," "microdroplets (each with a volume of $5x10^{-9}$ liters)," and "[a] pL microdroplet." *Id.* at 5:4–6, 7:40–44, 8:22–23.

C. Anticipation of Claims 1–26 by Hindson, with Anderson Incorporated-By-Reference

Petitioner contends claims 1–26 of the '115 patent are anticipated by Hindson. Pet. 31–56. Hindson was filed August 13, 2013 with an earliest effective filing date of August 14, 2012 and published as Publication No. 2014/0155295 on June 5, 2014. Ex. 1005. The '115 patent, however, claims the benefit of priority to Patent Application No. 13/456,121 ("the '121 application"), filed April 25, 2012. Ex. 1001. Petitioner contends that Hindson is prior art to the '115 patent because the claims lack written description support and thus the '115 patent is not entitled to the benefit of priority to the '121 application. Pet. 19–20. In particular, Petitioner contends that Patent Owner's infringement contentions filed in the related parallel litigation assert that the first partition is a dissolvable gel bead (*id.* at 18–19), however, "[t]here is no disclosure in the 115 Patent that partitions—or first partitions in particular—are beads or that beads are degradable upon the application of a stimulus" (*id.* at 2). Thus, according to Petitioner,

"under the constructions applied in Bio-Rad's infringement assertions in district court, the claims of the 115 Patent would only be entitled to a priority date of September 22, 2014," the filing date of the '115 patent. Pet. 6.

In its Preliminary Response, Patent Owner contends, "[b]ecause this specification of the '115 patent is the same specification as the specification of [the '121 application] to which the '115 patent claims priority, and because the '121 filing precedes the filing of Hindson, the '115 patent claims cannot be anticipated by Hindson." Prelim. Resp. 7.

We have considered the parties' arguments, summarized above, but determine that Patent Owner has the better position. In particular, we are not persuaded by Petitioner's contentions that the claims fail the written description requirement for the claimed "partitions" because the term "gel beads" are not adequately described. Pet. 19–20. The claims do not recite the term "gel beads". Ex. 1001, 49:2–50:41. Rather, the claims of the '115 patent are directed to compositions (claim 1–13) and devices (clam 14–26) having a plurality of second partitions containing first partitions, wherein the second partitions may be droplets (claims 4–6 and 18–20). *Id.* To the extent that Petitioner contends that the '115 patent does not provide adequate written description support for those elements of the challenged claims, we disagree. For example, claim 1 recites a composition "comprising a plurality of second partitions containing first partitions" where "first partitions are contained within the second partitions." Support for those elements is found, for example, in the following portions of the '115 patent:

> In general, described herein are methods, *compositions*, and kits for library preparation for sequencing polynucleotides. The methods, *compositions*, and kits can be used to separate a

> sample of polynucleotides into a plurality of partitions, and each of the plurality of partitions can be provided with a unique set of adaptors comprising a barcode.

Ex. 1001 at 3:50–55 (emphasis added);

> "In some cases, sample-polynucleotide-containing *partitions are formed so that they contain* adaptor-filled *partitions*. For example, adaptor-filled partitions (e.g., droplets) can be emulsified with a polynucleotide sample so that sample-polynucleotide-containing partitions (e.g., droplets) end up containing adaptor-filled partitions."

Id. at 4:39–45 (emphasis added); and

> "In some cases, the first partitions are first droplets and the second partitions are second droplets; and prior to the merging, the at least one second droplet comprises the at least one first droplet."

Id. at 2:1–4.

As another example, claim 1 recites, "first partitions are degradable upon the application of a stimulus to said first partitions such that contents of a first partition is mixed with contents of a second partition." Support for that element is found, for example, in the following portions of the '115 patent:

> In some cases, sample-polynucleotide-containing partitions are formed so that they contain adaptor-filled partitions. For example, adaptor-filled partitions (e.g., droplets) can be emulsified with a polynucleotide sample so that sample-polynucleotide-containing partitions (e.g., droplets) end up containing adaptor-filled partitions. The adaptor-filled droplets can be burst (e.g., *through a temperature adjustment*) to release reaction components (e.g., PCR or ligation components) that can be used for library preparation.

Id. at 4:39–48 (emphasis added);

> In some cases, an inner droplet (or partition) can be fused with an outer droplet (or partition) by heating/cooling to change

> temperature, applying pressure, altering composition (e.g., via a chemical additive), applying acoustic energy (e.g., via sonication), exposure to light (e.g., to stimulate a photochemical reaction), applying an electric field, or any combination thereof.

Id. at 6:44–50; and

> This disclosure provides methods that can be used in sequencing and other applications. In some instances, this disclosure provides a method comprising: a. subdividing a plurality of adaptors into a plurality of first partitions . . . wherein the adaptors comprise unique barcodes; b. subdividing a sample comprising multiple polynucleotides into a plurality of second partitions . . . c. merging at least one of the first partitions with at least one of the second partitions to form a merged partition; and d. tagging one of the multiple polynucleotides, or fragment thereof, with at least one of the adaptors.

Id. at 1:31–44.

Accordingly, in view of the above, we are not persuaded by Petitioner's arguments that the claims of the '115 patent lack written description support and, thus, are not entitled to claim the benefit of priority to the '121 application. Consequently, we determine that Hindson does not qualify as prior art to the '115 patent and therefore cannot anticipate the claims of the '115 patent.

III. CONCLUSION

Petitioner has failed to establish a reasonable likelihood of prevailing in demonstrating that claims 1–26 are unpatentable over prior art set forth in the asserted ground.

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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