

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BIO-RAD LABORATORIES, INC.,
Petitioner,

v.

CALIFORNIA INSTITUTE OF TECHNOLOGY,
Patent Owner.

IPR2024-01451
Patent 11,827,921 B2

Before ERICA A. FRANKLIN, GRACE KARAFFA OBERMANN, and
TAWEN CHANG, *Administrative Patent Judges*.

FRANKLIN, *Administrative Patent Judge*.

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

I. INTRODUCTION

Petitioner, Bio-Rad Laboratories, Inc., filed a Petition requesting *inter partes* review of claims 1–19 of U.S. Patent No. 11,827,921 B2 (Ex. 1001, “the ’921 patent”). Paper 1 (“Petition” or “Pet.”). Patent Owner, California Institute of Technology, filed a Preliminary Response to the Petition. Paper 8 (“Prelim. Resp.”). With our authorization, Ex. 3001, Petitioner filed a Reply to the Preliminary Response and Patent Owner filed a Sur-reply in response. Paper 9 (“Pet. Reply”); Paper 10 (“PO Sur-reply”).

We have authority to determine whether to institute an *inter partes* review. 35 U.S.C. § 314. Upon considering the parties’ arguments and evidence, we determine that Petitioner has established a reasonable likelihood that it would prevail in showing the unpatentability of at least one claim challenged in the Petition, and, for the reasons discussed below, decline to exercise our discretion to deny institution under 35 U.S.C. § 314(a). Accordingly, we institute an *inter partes* review of the challenged claims.

A. *Real Parties-in-Interest*

Each party identifies itself as the real party-in-interest. Pet. 19; Paper 7, 2.

B. *Related Matters*

The parties relay that the ’921 patent is involved in district court litigation in *In Re: ChromaCode Litigation*, Case No. 5:23-cv-04823-EKL (N.D. Cal.). Pet. 20; Paper 7, 2. Patent Owner explains that case also involves related patents, U.S. Patent No. 10,770,170 (“the ’170 patent”) and U.S. Patent 10,068,051 (“the ’051 patent”). Paper 7, 2. The parties note that the ’051 patent was the subject of IPR2024-01177, and that the ’170 patent was the subject of IPR2024-01178. Pet. 20; Paper 7, 2.

C. The '921 patent

In one aspect, the '921 patent relates to methods and kits for the multiplexed detection of multiple analytes in a sample. Ex. 1001, 1:51–52, 8:63–64. The '921 patent describes that “[f]luorescence detection has been a preferred technique for multiplexed assays.” *Id.* at 8:33–34. A schematic representation of the detection of 6 analytes (including a control) with four fluorescent colors is shown below in Figure 2.

Fig. 2

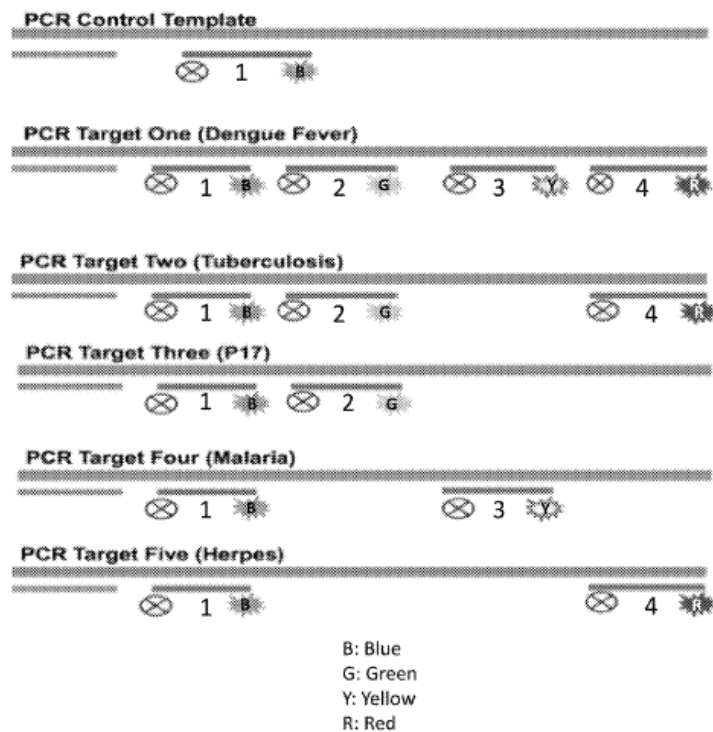


Figure 2 represents the detection of analytes “using hybridization probes attached to a fluorophore (B, G, Y, R; blue, green, yellow, and red, respectively) and a quencher (oval with ‘X’).” *Id.* at 8:2–5. The '921 patent describes that “[t]he control sequence and the five other sequences” specific for each analyte “are all detected using a probe labeled with a blue fluorophore.” *Id.* at 8:5–10. The '921 patent explains that “standard

fluorophores have wide emission spectra. Therefore, in order to avoid spectral overlap (i.e., to preserve spectral resolution) only a relatively small number of colors (e.g., 4 to 6) are typically used simultaneously in multiplexed fluorescent assays.” *Id.* at 8:40–44.

The Specification explains, “[t]he traditional encoding method for multiplexed fluorescent assays has been to encode each analyte with a single color: i.e., $M=N$, where M is the number of analytes that can be detected and N is the number of spectrally resolved fluorescent probes.” *Id.* at 8:45–49. Whenever the number of analytes that can be detected is greater than the number of spectrally resolved fluorescent probes, “fluorescence is generally combined with other techniques, such as aliquoting, spatial arraying, or sequential processing.” *Id.* at 8:49–52. However, “[t]hese additional processing steps are labor-intensive and frequently require relatively expensive and complex optical and mechanical systems.” *Id.* at 8:52–58. Thus, according to the ’921 patent, “there is a significant need for multiplexed encoding and decoding methods that can provide an inexpensive means of multiplexing while avoiding the use of expensive additional processing steps.” *Id.* at 8:58–62.

To address this need, the ’921 patent describes the detection of a number of analytes greater than the number of spectrally resolved fluorescent probes based on “encoding, analysis, and decoding methods.” *Id.* at 8:65–66. The ’921 patent explains that in some embodiments, “each analyte to be detected is encoded as a value in each of at least two components of a signal (e.g., intensity and wavelength).” *Id.* at 9:3–5.

These components may be “cumulatively measured for the sample” and the “presence or absence of an analyte may then be determined based on the values of each of the at least two components of the signal and the values used to encode the presence of the analyte (i.e., those values in the coding scheme).” *Id.* at 9:39–47.

The ’921 patent explains that the terms “degenerate” and “degeneracy,” as used in the Specification, “generally describe a situation where a legitimate result is not definitive, because it can indicate more than one possibility in terms of the presence or absence of an analyte.” *Id.* at 16:47–50. According to the ’921 patent, the claimed methods reduce or eliminate degeneracy from the coding scheme, “thereby increasing the confidence with which an analyte is detected.” *Id.* at 16:57–59. The ’921 patent describes different solutions for degeneracy, such as encoding individual analytes using intensity levels so that every possible combination of analytes has a unique cumulative intensity. *See id.* at 23:38–56.

D. Challenged Claims

Petitioner challenges claims 1–19 in the ’921 patent. Claim 1, the independent claim, is illustrative and set forth below.

1. An assay that is capable of unambiguously detecting the presence or absence of each of at least M analytes, wherein each of said at least M analytes is encoded as a value of one component of a fluorescent signal, thereby generating a coding scheme, wherein said fluorescent signal comprises F wavelength components, and wherein said assay is capable of unambiguously detecting the presence or absence of each of said at least M analytes, in any combination of presence or absence, in a single sample volume, based on detection of said F wavelength components, when M is greater than F,

wherein the assay does not require the use of mass spectrometry or immobilization of said at least M analytes, and
wherein the analytes are amplified in the single sample volume.

Ex. 1001, 67:10–26.

E. Asserted Grounds of Unpatentability

Petitioner asserts that the challenged claims are unpatentable on the following four grounds:

Claims Challenged	35 U.S.C. §¹	Reference(s)
1–10, 13–19	102	Larson ²
4, 6–7, 14–19	103(a)	Larson
1–10, 12–19	103(a)	Larson, Saxonov ³
11	103(a)	Larson, Saxonov, Silverbrook ⁴

Petitioner also relies upon the Declaration of Carl A. Batt, Ph.D. (Ex. 1002). Patent Owner relies on the Declaration of Kevin Struhl, Ph.D. (Ex. 2001).

¹ The Leahy-Smith America Invents Act (“AIA”), Pub. L. No. 112–29, 125 Stat. 284 (2011), amended 35 U.S.C. § 103, effective March 16, 2013.

Because the application from which the ’921 patent issued has an effective filing date prior to March 16, 2013, the pre-AIA version of §103 applies.

² Larson, U.S. Patent App. Pub. 2011/0250597 A1, published October 13, 2011 (Ex. 1017, “Larson”).

³ Saxonov, U.S. Patent App. Pub. 2013/0040841 A1, published February 14, 2013 (Ex. 1004, “Saxonov”).

⁴ Silverbrook, U.S. Patent App. Pub. 2011/0312704 A1, published December 22, 2011 (Ex. 1009, “Silverbrook”).

II. ANALYSIS

A. *Discretionary Denial Under 35 U.S.C. § 314(a)*

Patent Owner asserts that the Board should exercise its discretion to deny the Petition. Prelim. Resp. 63. We have discretion to deny institution of an *inter partes* review under the provisions of 35 U.S.C. § 314(a) (authorizing institution of an *inter partes* review under particular circumstances, but not requiring institution under any circumstances). *See Cuozzo Speed Techs., LLC v. Lee*, 579 U.S. 261, 273 (2016) (“[T]he agency’s decision to deny a petition is a matter committed to the Patent Office’s discretion.”); *SAS Inst. Inc. v. Iancu*, 138 S. Ct. 1348, 1356 (2018) (“[Section] 314(a) invests the Director with discretion on the question whether to institute review” (emphasis omitted)); *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1367 (Fed. Cir. 2016) (“[T]he PTO is permitted, but never compelled, to institute an IPR proceeding.”).

In *Apple Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper 11 (PTAB Mar. 20, 2020) (precedential) (“*Fintiv*”), the Board articulated a list of factors that we consider in determining whether to exercise discretion to deny institution based on an advanced stage of a parallel proceeding:

1. whether the court granted a stay or evidence exists that one may be granted if a proceeding is instituted;
2. proximity of the court’s trial date to the Board’s projected statutory deadline for a final written decision;
3. investment in the parallel proceeding by the court and the parties;
4. overlap between issues raised in the petition and in the parallel proceeding;
5. whether the petitioner and the defendant in the parallel proceeding are the same party; and

6. other circumstances that impact the Board’s exercise of discretion, including the merits.

Fintiv, Paper 11, 5–6. “These factors relate to whether efficiency, fairness, and the merits support the exercise of authority to deny institution in view of an earlier trial date in the parallel proceeding.” *Id.* In evaluating these factors, we take “a holistic view of whether efficiency and integrity of the system are best served by denying or instituting review.” *Id.* (citing Patent Trial and Appeal Board Consolidated Trial Practice Guide (“CTPG”) at 55 (November 2019)).⁵

Petitioner contends that the District Court case does not justify discretionary denial. Pet. 69. In particular, Petitioner asserts that *Fintiv* factors 1–4 and 6 weigh against discretionary denial under § 314(a) and that *Fintiv* factor 5 is neutral. *Id.* at 70–74; Reply 5. Patent Owner disagrees and contends that *Fintiv* factors 2–6 weigh in favor of discretionary denial. Prelim. Resp. 63–70; Sur-reply 5. In our analysis below, we address each *Fintiv* factor in turn.

1. Factor 1: Existence or Likelihood of Stay

As recognized by the parties, the District Court case has not been stayed. Indeed, a motion to stay has not been filed. Petitioner asserts that it will seek a stay if this *inter partes* review is instituted. Pet. 70. However, we decline to speculate how the judge would rule on such a motion in the District Court case at issue here.

Accordingly, we conclude that the first *Fintiv* factor is neutral with respect to exercising our discretion to deny institution.

⁵ CTPG is available at <https://www.uspto.gov/TrialPracticeGuideConsolidated>.

2. *Factor 2: Proximity of Trial Date to Final Written Decision*

A trial date has not been set for the District Court case. Pet. 71; Prelim. Resp. 64. Petitioner estimates a trial date in, approximately, October 2027, based on an asserted median time-to-trial of 48.9 months from the earliest filing date of the consolidated case. Pet. 71 (citing Ex. 1023,⁶ 66). Petitioner notes also that the original District Court schedule was vacated and the matter was transferred to a new judge. *Id.* at 72. Patent Owner asserts only that its proposed schedule has trial set for January 2026. Prelim. Resp. 64 (citing Ex. 2013; Ex. 2014, 18–20).

Based on the record, Petitioner has shown persuasively that the court’s trial date will not likely be earlier than the projected statutory deadline for a Final Written Decision in March 2026. *See Guidance on USPTO’s rescission of “Interim Procedure for Discretionary Denials in AIA Post-Grant Proceedings with Parallel District Court Litigation”* at 3 (Mar. 24, 2025),

https://www.uspto.gov/sites/default/files/documents/guidance_memo_on_interim_procedure_rescission_20250324.pdf (“[I]n applying *Fintiv*, the Board may consider any evidence that the parties make of record that bears on the proximity of the district court’s trial date, . . . including median time-to-trial statistics for civil actions in the district court in which the parallel litigation resides.”). Thus, this factor weighs against exercising our discretion to deny institution.

⁶ Federal Judicial Caseload Statistics (2023), <https://www.uscourts.gov/statistics-reports/analysis-reports/federal-judicial-caseload-statistics>.

3. *Factor 3: Investment in Parallel Proceeding*

Petitioner asserts that this factor weighs in favor of institution because there has only been a “modest investment in the district court case.” Pet. 72. Petitioner asserts also that no depositions have been scheduled and expert discovery has not begun. *Id.* at 73; Reply 5. According to Petitioner, although a *Markman* hearing has been conducted, no *Markman* Order has issued to date. Reply 5.

Patent Owner asserts that this factor favors denial because the parties and the court have invested significantly in the case. Prelim. Resp. 65–66. Specifically, Patent Owner notes that infringement and invalidity contentions have been served, damages contentions have been exchanged, an ESI⁷ order has been entered by the court, a *Markman* hearing has been held, and fact discovery is ongoing.⁸ *Id.* at 65. According to Patent Owner, “further investment *will be* made before institution, including substantial discovery and likely a *Markman* order.” Sur-reply 5.

Based on the foregoing, it is apparent that some investment has occurred in the District Court case, mainly with respect to the claim construction hearing. However, we understand from the parties’ assertions that much more work remains, including, expert reports, expert discovery, expert depositions, and pretrial motions and disclosures. *See* Pet. 72–73; Reply 5; Prelim. Resp. 65–66; Sur-reply 5. Indeed, as Petitioner notes, the court has not set any deadlines for those activities, other than the close of fact discovery. *See* Reply 5.

⁷ ESI refers to “electronically stored information.”

⁸ Patent Owner has submitted a docket entry from the District Court case, which states that close of fact discovery is set for March 12, 2025. Ex. 2015.

Upon weighing the amount and type of work completed in the District Court case by the court and the parties as of this time with the work that is yet to be completed, along with an absence of evidence (or allegation) that Petitioner delayed filing the Petition, we determine, on balance, that this factor weighs against exercising our discretion to deny institution.

4. *Factor 4: Overlap Between Issues Raised in Petition and in the Parallel Proceeding*

Patent Owner asserts this factor weighs in favor of denial because Petitioner makes the same contentions in the District Court case as in the Petition, i.e., asserting that the '921 patent claims are invalid as anticipated and obvious based on Larson alone, and as obvious based on combinations of Larson, Saxonov, and/or Silverbrook. Prelim. Resp. 66–67.

Petitioner asserts that this factor favors institution because in the district court “there are extensive additional art and issues being litigated and Claim 18 [is challenged in this proceeding but] is not being asserted [in the district court litigation].” Pet. 73. Petitioner does not identify any of the alleged additional art involved in the District Court case, nor does Petitioner describe any of the alleged additional issues involved, beyond the challenge of claim 18 being limited to this proceeding. *See id.*; *see also* Reply 5.

Considering the degree of overlap between the claims and art raised in the Petition and the District Court case, this factor weighs in favor of exercising our discretion to deny institution.

5. *Factor 5: Whether Petitioner and Parallel Proceeding Defendant Are the Same Party*

Patent Owner asserts that this factor weighs in favor of discretionary denial because Petitioner is the defendant in the District Court case. Prelim. Resp. 68. Petitioner contends that this factor is neutral “because it is often

the case for a patent asserted in district court to be challenged at the Board.” Pet. 73. Here, we determine this factor upon whether Petitioner is the defendant in the District Court case, which is the case. Accordingly, we weigh this factor in favor of exercising our discretion to deny institution.

6. *Factor 6: Other Circumstances (Including Merits)*

This final factor requires consideration of other circumstances that may impact our decision whether to exercise discretion to deny institution, for example, whether the merits of the challenges are particularly strong. *Fintiv*, Paper 11 at 14–16. As discussed in our analysis of the merits, we determine, based on the current record, that Petitioner demonstrates a reasonable likelihood of prevailing with respect to its challenge of at least one claim. Beyond that, we do not find the merits in this case to be of particular significance such as to weigh this sixth factor for or against exercising discretion to deny the Petition. *See Sotera Wireless, Inc. v. Masimo Corp.*, IPR2020-01019, Paper 12 at 20 (PTAB Dec. 1, 2020) (precedential as to § II.A) (“[O]n this preliminary record, Petitioner has met its burden of demonstrating a reasonable likelihood that it would prevail in showing that claims of the RE353 patent are unpatentable Although we recognize the record may change during trial, . . . Petitioner has made a sufficiently persuasive showing, on the record presently before us, that the prior art references cited in the Petition teach or suggest all limitations of at least one challenged claim We determine that this factor does not weigh for or against denying institution in this case.”).

Accordingly, we determine that the sixth factor is neutral with respect to exercising our discretion to deny institution.

7. *Conclusion on the Factors*

Because the analysis is fact-driven, no single factor is determinative of whether we exercise our discretion to deny institution under 35 U.S.C. § 314(a). Rather, when considering the *Fintiv* factors, we “take[] a holistic view of whether efficiency and integrity of the system are best served by denying or instituting review.” *Fintiv* at 6. Here, factors one and six are neutral, factors two and three weigh against discretionary denial, and factors four and five favor denial. We assign less weight to the existence of an overlap in asserted claims and prior art, in view of there being no trial date scheduled in the District Court case and no persuasive evidence that the court’s trial date would be expected to be significantly before the due date of our Final Written Decision. Therefore, after weighing all of the factors, we determine that the facts in this case that weigh against exercising discretion outweigh the facts that favor exercising discretion. Accordingly, we decline to exercise our discretion to deny institution under § 314(a).

B. *Level of Ordinary Skill in the Art*

The level of skill in the art is a factual determination that provides a primary guarantee of objectivity in an obviousness analysis. *Al-Site Corp. v. VSI Int’l Inc.*, 174 F.3d 1308, 1323 (Fed. Cir. 1999) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966)); *Ryko Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714, 718 (Fed. Cir. 1991)).

Petitioner asserts that a person of ordinary skill in the art at the time of the invention (also referred to as “POSA”) “would have had a Ph.D. in molecular biology, genetics, biochemistry, or a related discipline, with at least a year of experience in quantitative and/or [digital] PCR and fluorescence-based analyte detection.” Pet. 9 (citing Ex. 1002 ¶¶ 66–68).

Alternatively, Petitioner asserts that “a POSA would have been someone with greater relevant experience sufficient to compensate for having less relevant formal education.” *Id.* (citing Ex. 1002 ¶ 68). Additionally, Petitioner asserts:

A POSA would have understood the following technologies and techniques:

- Multiplex PCR and its application in detecting and measuring polynucleotide analytes.
- The design and use of fluorescent-labeled oligonucleotide probes, including use of quenchers, and use in conjunction with multiplex PCR.
- The quantitative detection and measurement of polynucleotide analytes using fluorescent-labeled oligonucleotides in multiplex applications.
- Techniques for labeling probes and detecting multiple targets using fewer differently colored fluorophores than polynucleotide targets.
- Quantitative PCR and digital PCR and their application in detecting and measuring polynucleotide analytes, including in multiplex applications.

Id. at 9–10 (citing Ex. 1002 ¶ 69).

At this stage in the proceeding, Patent Owner does not dispute Petitioner’s description of the person of ordinary skill in the art. Prelim. Resp. 27. In view of this, and because Petitioner’s uncontested description of one of ordinary skill in the art is reasonable and consistent with the ’921 patent and the cited art, we adopt Petitioner’s definition for purposes of this Decision. We note, however, that the open-ended language “at least” expands the range of experience indefinitely with no upper bound. Therefore, we do not apply this aspect of Petitioner’s formulation.

C. *Claim Construction*

In an *inter partes* review, the Board applies the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b). 37 C.F.R. § 100(b) (2019). Under that standard, claim terms “are generally given their ordinary and customary meaning” as understood by a person of ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc) (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). “In determining the meaning of the disputed claim limitation, we look principally to the intrinsic evidence of record, examining the claim language itself, the written description, and the prosecution history, if in evidence.” *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 469 F.3d 1005, 1014 (Fed. Cir. 2006) (citing *Phillips*, 415 F.3d at 1312–17).

Petitioner and Patent Owner appear to agree “degenerate” and “degeneracy” should be construed to mean “a situation where a legitimate result is not definitive, because it can indicate more than one possibility in terms of the presence or absence of an analyte.” Pet. 21–22; Prelim. Resp. 27. For all other terms, “Petitioner requests that the Board understand the claims consistent with the apparent interpretations that Patent Owner is pursuing in parallel district court litigation.” Pet. 22. In response, Patent Owner asserts that the Board should simply “construe the present claims in view of the construction[s of “degenerate” and “degeneracy”] provided above and the intrinsic record.” Prelim. Resp. 28–29.

We determine that there is no need to expressly construe any claim term to determine whether to institute an *inter partes* review. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017

(Fed. Cir. 2017) (noting that “we 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 that any discussion regarding the scope of a claim term is relevant to our decision, we address that issue in our analysis of the asserted grounds of unpatentability.

Any final written decision entered in this case may include express claim constructions, or may include discussion of claim scope that differs from that provided in our analysis below. Any final claim constructions will be based on the full trial record.

D. Obviousness over Larson and Saxonov

Petitioner asserts that claims 1–10 and 12–19 would have been obvious over Larson alone, or alternatively, in combination with Saxonov. Pet. 51–65. Patent Owner disagrees. Prelim. Resp. 29–42, 49–62.

1. Larson

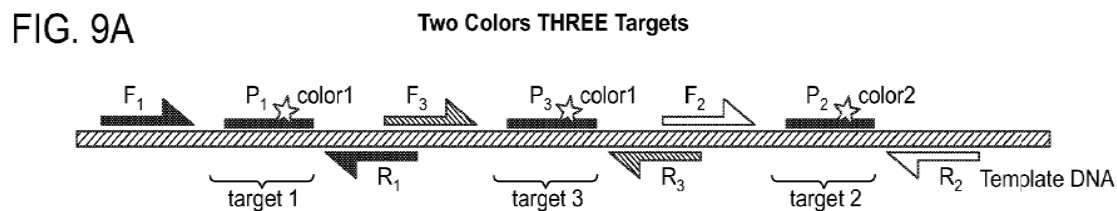
Larson, titled “Digital Analyte Analysis,” relates to “droplet based digital PCR and methods for analyzing a target nucleic acid using the same.” Ex. 1017, codes (54), (57). Larson was filed February 11, 2011. *Id.*, code (22).

Larson explains that digital analyte analysis is “based on the singular nature of amplifications at terminal or limiting dilution that arises because most often only a single target allele is ever present in any one droplet even when multiple primers/probes targeting different alleles are present.” *Id.*

¶ 45. Larson describes that “[d]igital PCR (dPCR) is an alternative quantitation method in which dilute samples are divided into many separate reactions.” *Id.* ¶ 6. “[A]t so called ‘terminal dilution[,]’ the vast majority of reactions contain either one or zero target DNA molecules.” *Id.* Larson

compares this situation with “so called ‘limiting dilution[,]’” in which “some reactions contain zero DNA molecules, some reactions contain one molecule, and frequently some other reactions contain multiple molecules, following the Poisson distribution.” *Id.*, see also *id.* ¶ 52.

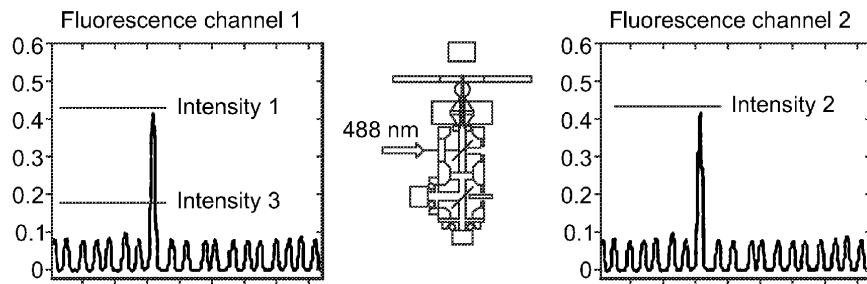
Larson’s Figure 9A, depicted below, is a schematic depicting two-color detection of three target genetic sequences:



Ex. 1017, Fig. 9A. Figure 9A shows “a template DNA amplified with three sets of primers: forward primers (F1, F2 and F3) and reverser primers (R1, R2 and R3).” *Id.* at ¶ 121. Larson further explains that “[p]robes (P1, P2 and P3) are labeled with fluorophores (color 1, color 2 and color 1) and bind the target genetic sequences (target 1, target 2 and target 3).” *Id.*

As discussed above, Larson teaches dividing diluted solution of such template DNA into microdroplets under conditions of limiting or terminal dilution. Ex. 1017 ¶ 121. Larson’s Figure 9C, depicted below, shows two graphs for the intensity detected in each of two fluorescence channels (color 1 and color 2):

FIG. 9C

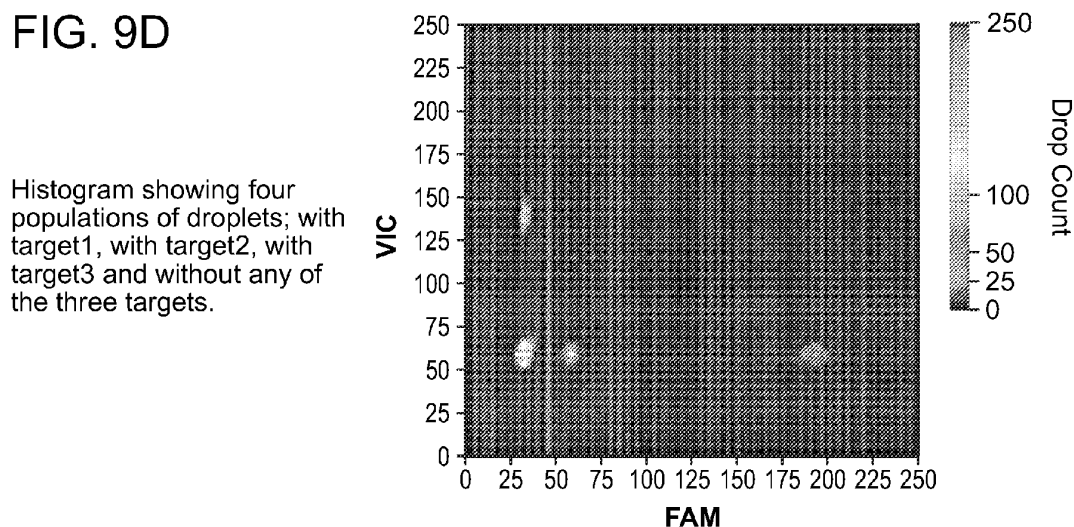


Ex. 1017, Fig. 9C. Microdroplets containing diluted template DNA solution, made under conditions of limiting or terminal dilution, emit fluorescence of color 1 at two different intensities if they contain target sequence 1 or 3. *Id.*

¶ 121. Microdroplets containing target sequence 2 emit fluorescence of color 2. *Id.*

Larson's Figure 9D, depicted below, is a histogram of the results of the assay discussed for Figures 9A and 9C:

FIG. 9D



Ex. 1017, Fig. 9D. Figure 9D shows a plot of four microdroplet populations representing the number of microdroplets containing target 1, target 2, target 3, or without any of the three targets. *Id.* ¶ 121.

Larson describes increasing the sample dilution as the number of analytes increases to reduce the probability that any droplet contains two or more analytes. *Id.* ¶¶ 79–84. According to Larson, having one allele per droplet avoids issues associated with traditional PCR, e.g., over representation of a single allele resulting from PCR efficiency differences between two alleles. *Id.* ¶¶ 99, 100. Larson states that “[h]igher degrees of multiplexing would require greater dilution,” because of the possibility for unintended “cross-reactivity” between analytes in any single droplet. *Id.* ¶ 129.

Larson explains also,
[w]ith multiple occupancy arises the complexity of simultaneous assays competing within the same reaction droplet, and also complexity of assigning the resulting fluorescence intensity that involves a combination of fluorescence from two different reaction products that may or may not be equal to the sum of the two fluorescence intensities of the individual reaction products.
Id. ¶ 141. According to Larson, “methods of the invention can accommodate these complications arising from multiple occupancy.” *Id.*

2. *Saxonov*

Saxonov, titled “Digital Assays with Multiplexed Detection of Two or More Targets in the Same Optical Channel,” relates to “performing a digital assay on a potentially greater number of targets through multiplexed detection of signals from reporters for two or more distinct targets in a common or shared channel.” Ex. 1004, code (54), ¶ 19. Saxonov was filed July 12, 2012, and claims the benefit of provisional application Nos. 61/507,082 and 61/510,013, filed July 12, 2011, and July 20, 2011, respectively. *Id.*, codes (22), (60).

Saxonov explains that digital assays

generally rely on the ability to detect the presence or activity of individual copies of an analyte in a sample. In an exemplary digital assay, a sample is separated into a set of partitions, generally of equal volume, with each containing, on average, less than about one copy of the analyte. If the copies of the analyte are distributed randomly among the partitions, some partitions should contain no copies, others only one copy, and, if the number of partitions is large enough, still others should contain two copies, three copies, and even higher numbers of copies. The probability of finding exactly 0, 1, 2, 3, or more copies in a partition, based on a given average concentration of analyte in the partitions, is described by a Poisson distribution.

Id. ¶ 3. Saxonov explains that “[d]igital assays frequently rely on amplification of a nucleic acid target in partitions to enable detection of a single copy of an analyte,” and such “[a]mplification may be conducted via the polymerase chain reaction (PCR).” *Id.* ¶ 5. Saxonov states that “[a]mplification of the target can be detected optically from a fluorescent probe included in the reaction,” and “the probe can include a dye that provides a fluorescence signal indicating whether or not the target has been amplified.” *Id.*

According to Saxonov, “[a] new approach is needed to increase the multiplex levels of digital assays,” because increasing multiplex levels of digital assays currently require “instruments with more optical channels, to detect emission from more dyes, [which] are more expensive than those with fewer channels.” *Id.* ¶¶ 6, 7. Moreover, Saxonov explains that “increasing the number of distinguishable dyes is expensive and becomes impractical beyond a certain number.” *Id.* at 6.

To that end, Saxonov describes using a “common or shared channel (‘the same optical channel’)” to detect signals from “reporters for two or more distinct targets.” *Id.* ¶ 19. Saxonov explains that “[t]he reporters may

include the same fluorophore, such as FAM or VIC, or different fluorophores with similar spectral characteristics, so that light from two or more reporters may be collected simultaneously in the same optical channel.” *Id.* According to Saxonov, “[t]he assays may be constructed so that data for each target are distinguishable, for example, by choosing assays for each target that have sufficiently distinct endpoints (or time courses).” *Id.* This allows a determination of the contents of each sample or sample partition, i.e., “those with no targets, those with a first assay (assay 1) target, those with a second assay (assay2) target, and those with both, in a two-target assay.” *Id.*

Saxonov explains that “[t]he assays may be extended in various ways,” for example, “to involve analysis of more than two targets in the same channel.” *Id.* ¶ 20. In this regard, Saxonov exemplifies an assay for three targets that may generate eight clusters or populations of data, separated by intensity. *Id.* Saxonov explains that “some targets may be analyzed in one channel (e.g., a FAM channel), and one or more other targets may be analyzed in one or more other channels (e.g., a VIC channel).” *Id.* In this example, “[t]hree targets, two in a first channel and one in a second channel, would again generate eight clusters or populations of data, but they would be separated in a two-dimensional intensity space and so in principle more easily resolvable.” *Id.*

The sample used in Saxonov’s system may be separated into partitions. *Id.* ¶ 28. “One or more signals may be created that are representative of light detected from the partitions.” *Id.* ¶ 36. Saxonov explains that “[t]he signal may represent an aspect of light, such as the intensity of the light, detected in the same optical channel from reporters for two or more distinct targets.” *Id.* Additionally, the signals “may include data

collected in one or more different channels (e.g., in different wavelength ranges (color regimes) from reporters for the same and/or different targets).”

Id.

Saxonov explains that “[t]he signal detected from each partition, and the partition itself, may be classified as being positive or negative for each of the reactions/targets contributing to the signal.” *Id.* ¶ 41. According to Saxonov, “[t]he data including all permutations of positives will generally fall into 2^N populations or clusters, where N is the number of targets, assuming that each population is distinguishable.” *Id.* The tables in Saxonov showing “[e]xemplary results for one, two, and three target systems in which data are collected in a single channel” are set forth below:

	Target A	Intensity
Population 2	+	Highest
Population 1	–	Lowest

	Target A	Target B	Intensity
Population 4	+	+	Highest
Population 3	+	–	Intermediate
Population 2	–	+	Intermediate
Population 1	–	–	Lowest

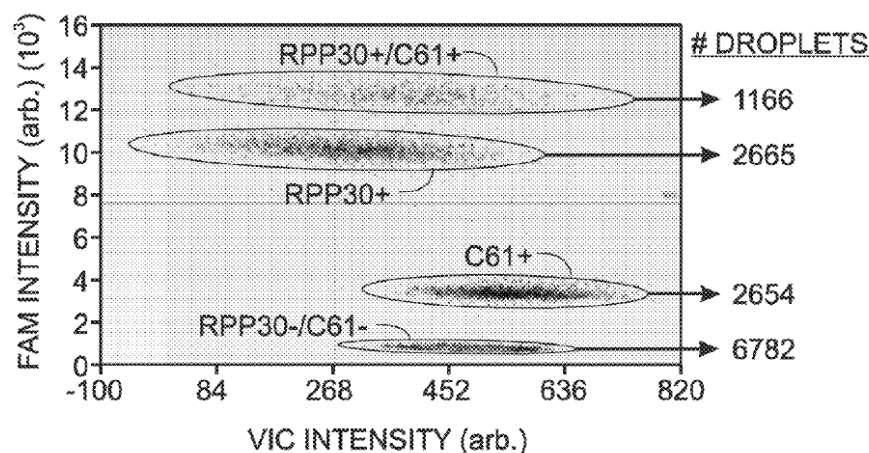
	Target A	Target B	Target C	Intensity
Population 8	+	+	+	Highest
Population 7	+	+	–	Intermediate
Population 6	+	–	+	Intermediate
Population 5	–	+	+	Intermediate
Population 4	+	–	–	Intermediate
Population 3	–	+	–	Intermediate
Population 2	–	–	+	Intermediate
Population 1	–	–	–	Lowest

Each of the three tables – one for each system – contains a first column listing separate populations, subsequent column(s) indicating whether the target(s) for that system is/are present or absent in each population, and a final column indicating the intensity detected, i.e., highest, intermediate or lowest, for each population. *See id.*

Saxonov exemplifies a “digital PCR assay, in which multiplexing in a single channel is used to assess copy number of the C61 gene.” *Id.* ¶ 60, Example 2. In this example, “signals from two probes, one for the gene of interest, C61, and one for a reference gene, RPP30, are collected together, as a single signal, in a single channel and used to assess the number of copies of the [C61] relative to the number of copies of the reference gene.” *Id.*

Saxonov states that Figure 5, set forth below, “is a graph showing data for the exemplary C61/RPP30 system.” *Id.* ¶ 63.

Fig. 5

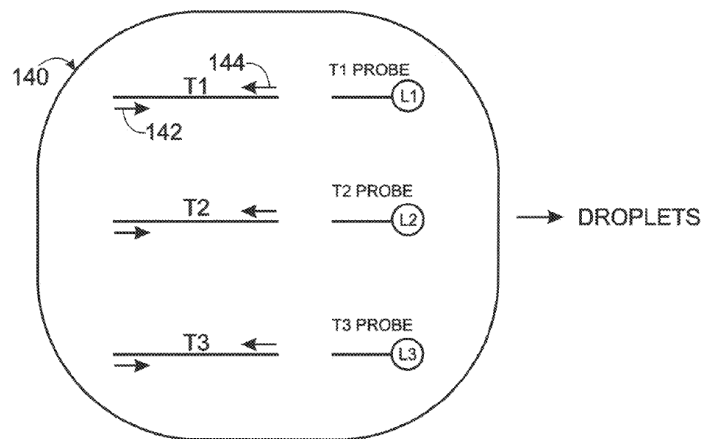


Ex. 1004, Fig. 5. Saxonov’s Figure 5 depicts a graph showing “droplet (or peak) intensities in arbitrary units (‘arb’) for a C61/RPP30 droplet assay, where data from reporters for C61 and RPP30 [genes] are collected together in the same optical channel and plotted as a function of intensity in a FAM

[fluorophore] channel (vertical axis) versus intensity in a VIC channel (horizontal axis).” *Id.* ¶ 13. The RPP30-/C61- cluster of 6782 droplets “corresponds to droplets that are negative for RPP30 and C61 (i.e., droplets that did not include either gene).” *Id.* ¶ 64. The C61+ cluster of 2654 droplets “corresponds to droplets that are positive for C61 and negative for RPP30 (i.e., droplets that included the C61 gene but did not include the RPP30 gene).” *Id.* ¶ 65. The RPP30+ cluster of 2665 droplets “corresponds to droplets that are positive for RPP30 and negative for C61 (i.e., droplets that included the RPP30 gene but did not include the C61 gene).” *Id.* ¶ 66. The RPP30+/C61+ cluster of 1166 droplets “corresponds to droplets that are positive for RPP30 and C61 (i.e., droplets that included both genes).” *Id.* ¶ 67.

Saxonov’s Figure 9, shown below, “is a schematic representation of an exemplary bulk phase mixture being separated into droplets during performance of an exemplary digital assay with multiplexed detection of three or more distinct targets (T1, T2, and T3).” *Id.* ¶ 17.

Fig. 9



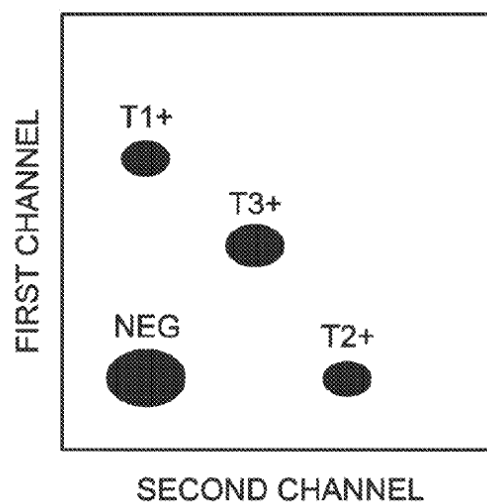
Ex. 1004, Fig. 9. Saxonov’s Figure 9 shows that “[m]ixture 140 may include a forward primer 142 and a reverse primer 144 for each target.” *Id.* ¶ 77.

Saxonov describes that “luminescence from the T1–T3 probes, and more particularly, the L1, L2, and L3 luminophores, may report whether or not target T1, T2, and T3, respectively, are present in each individual droplet.”

Id.

Saxonov’s Figure 10, shown below, “is a schematic representation of an exemplary graph showing droplet (or peak) intensities for a T1/T2/T3 droplet assay that may be performed with the droplets of FIG. 9.” *Id.* ¶ 18.

Fig. 10



Ex. 1004, Fig. 10. Saxonov’s Figure 10 shows that “[d]ata from the T1, T2, and T3 probes are collected in a first optical channel and a second optical channel and plotted as a function of intensity in the first channel (vertical axis) versus intensity in second channel (horizontal axis).” *Id.* ¶ 78.

Saxonov explains that the “[i]ntensities produced by exemplary populations or clusters of negative, T1-positive, T2-positive, and T3-positive droplets are identified by filled ellipses, with the size of each ellipse corresponding to the number of droplets in each population.” *Id.* According to Saxonov, “[t]o simplify the presentation, double-positive populations (T1+/T2+, T1+/T3+,

and T2+/T3+) and the triple-positive population (T1+/T2+/T3+) are not shown.” *Id.*

3. *Prior Art Status of Saxonov*

The parties disagree as to whether Saxonov is available as prior art under 35 U.S.C. 102(e). We address this contention here to provide the parties with our preliminary determination regarding this disputed issue. However, as noted below in the discussion of this ground, at this preliminary stage, we focus on Petitioner’s contention that the challenged claims are rendered obvious by Larson alone.

The ’921 patent issued on November 28, 2023, and claims the benefit of a provisional application filed on February 3, 2012. Ex. 1001, codes (45), (60), 1:6–15. For purposes of this proceeding, the parties agree that the ’921 patent is entitled to its earliest filing date of February 3, 2012. *See* Pet. 6; Prelim. Resp. 6. Saxonov was filed on July 12, 2012. Ex. 1004, code (22). To assert Saxonov as prior art to the ’921 patent, Petitioner relies on the filing date of the Saxonov provisional application, U.S. Provisional Patent Application Ser. No. 61/510,013, filed July 20, 2011 (Ex. 1007, “the ’013 provisional”). Pet. 13 (citing Ex. 1004, code (60)).

A reference patent or published application may be entitled to the benefit of its provisional application’s filing date for pre-AIA 35 U.S.C. § 102(e) prior art purposes when two conditions are met: (1) the provisional provides sufficient support for at least one claim in the reference patent or published patent application; and (2) the provisional application provides sufficient support for the subject matter relied upon for prior art purposes in the reference patent or application. *See Dynamic Drinkware, LLC v. Nat’l Graphics, Inc.*, 800 F.3d 1375, 1377, 1381–82 (Fed. Cir. 2015); MPEP §§ 2136 (I), 2136.03 (III), 2136 (Examples 2, 4, 7); *see, e.g., Google LLC v.*

Ikorongo Tech, LLC, IPR2021-00058, Paper 14 at 10–12 (PTAB May 10, 2021). The burden of production is on the Petitioner to show in its Petition that the asserted references qualify as prior art. *See Dynamic Drinkware*, 800 F.3d at 1380 (explaining that a petitioner bears the initial burden of production to establish that the asserted references qualify as prior art).

In the Petition, Petitioner asserts that “Saxonov is § 102(e) prior art as of at least the filing of the ’013 provisional, July 20, 2011, because the ’013 provisional supports Saxonov’s method of performing a digital assay recited in its claim 1.” Pet. 13. In support of that assertion, Petitioner provides a chart indicating disclosures in the ’013 provisional that Petitioner asserts support each limitation of claim 1 of Saxonov, i.e., the first condition noted above. *Id.* at 15–17. The issue here is whether Petitioner addressed sufficiently the second condition to show that Saxonov is entitled to the benefit of the ’013 provisional priority date for purposes of pre-AIA 35 U.S.C. § 102(e), i.e., that the provisional provides sufficient support for the subject matter relied upon in Saxonov for prior art purposes.

Patent Owner asserts that Saxonov is not prior art because the Petitioner has not demonstrated that the relied-upon subject matter in Saxonov was carried over from the Saxonov ’013 provisional. Prelim. Resp. 37. Further, Patent Owner contends that the ’013 provisional “does not actually disclose all of the relied-upon subject matter” because some of that subject matter was “newly added when Saxonov was converted to a non-provisional,” which was filed after the ’921 patent’s earliest priority date. *Id.* at 29. For example, Patent Owner alleges that Saxonov Figure 10, along with paragraphs 18 and 78–79, which are relied upon by Petitioner for Grounds 3 and 4, are not found in, or supported by, the Saxonov ’013 provisional. *Id.* at 42.

We authorized additional briefing for Petitioner to address Patent Owner's contention that Petitioner failed to demonstrate in the Petition that Saxonov is prior art. *See* Ex. 3001. In that briefing, Petitioner contends that "[Patent Owner's] contentions that ¶¶ 18, 78-79, and Figures 9 and 10 of Saxonov are not 'carried over' are without merit." Pet. Reply 4. Instead of identifying how the Petition explains how the '013 provisional application supports that material, Petitioner alleges that for Grounds 3 and 4, "[t]he critical point is that it is undisputed that the '013 provisional includes *identically* the content in ¶¶ 20 and 41 of Saxonov." *Id.* at 5. According to Petitioner, the Petition only relies materially on these paragraphs of Saxonov. *See id.* at 4-5.

Having considered the arguments and evidence, we agree with Patent Owner that Petitioner has not demonstrated sufficiently in the Petition, for purposes of institution, that all of the portions of Saxonov relied upon in the Petition are prior art. In particular, we determine that Petitioner has not established that the disputed portions of Saxonov are entitled to claim the benefit of the '013 provisional filing date because Petitioner has failed to satisfy the second condition for this benefit, i.e., by showing that the provisional application provides sufficient support for certain subject matter in Saxonov relied upon for prior art purposes in the Petition.

Specifically, contrary to Petitioner's assertion, we find that the Petition relies upon Saxonov Figure 10, and Saxonov paragraphs 18 and 78-79, with respect to Petitioner's obviousness contentions involving Saxonov. Petitioner's reliance on these disclosures in the Petition is apparent upon review of its discussion of how Saxonov allegedly teaches or suggests elements of the challenged claims. *See, e.g.,* Pet. 58-61. We also note that Patent Owner has provided a table in the Preliminary Response that itemizes

references to Saxonov in the Petition. *See* Prelim. Resp. 40–41. Petitioner does not establish that those disclosures are not relied upon in the Petition by shifting its focus in the Reply to other paragraphs of Saxonov. *See* Pet. Reply 2.

We next consider whether Petitioner has shown sufficiently in the Petition that Saxonov Figure 10 and Saxonov paragraphs 18 and 78–79, which are relied upon in the Petition to establish obviousness, are found in or supported by the '013 provisional. According to Petitioner, they have met the “carried over” requirement because the disputed disclosures in Saxonov appear substantially in the same form in the provisional application. Pet. Reply 3–4. Here, we do not focus on Petitioner’s parallel citations to the provisional for Saxonov disclosures that are identical or nearly identical in the provisional. Rather, Patent Owner’s contentions and our analysis focus on the disputed disclosures in Saxonov, i.e., the figures and paragraphs in Saxonov that do not appear, in any form, in the '013 provisional. Even though we authorized Petitioner to file additional briefing to explain how the Petition demonstrates that the disputed disclosures were carried over to Saxonov from the provision, Petitioner has made no effort to do so.

Thus, because Petitioner has not shown sufficiently that the Petition explains how each of the relied-upon disclosures in Saxonov Figure 10, and Saxonov paragraphs 18 and 78–79, which are not present in the '013 provisional, are supported by the '013 provisional, we determine that Petitioner has not shown that those cited portions of Saxonov are entitled to the priority date of the '013 provisional. Accordingly, on this record, we preliminarily determine that those relied-upon portions of Saxonov do not qualify as prior art to the '921 patent.

As noted above, we focus our discussion on whether Petitioner has established a reasonable likelihood of success in demonstrating that claim 1 is rendered obvious in view of Larson alone. Petitioner asserts how it alleges Larson teaches or suggests each element of claim 1. Pet. 52–62. In particular, Petitioner asserts that “Larson teaches a scheme wherein each of two or three analytes is encoded by an intensity of light in either one or two colors.” *Id.* at 53. As an example, Petitioner refers to Larson’s Figure 9A, reproduced above in Section II.D.1, and Larsen’s description that probes P1 and P3 for targets 1 and 3, are labeled with the same color (color 1), but provide different intensity signals, while probe P2 for target 2 is labeled with a different color (color 2). *Id.* (citing Ex. 1017 ¶ 121; Ex. 1002 ¶ 325)). Therefore, according to Petitioner and its declarant, Dr. Batt, Larson discloses an approach wherein each of three analytes are encoded as a value of one component of a fluorescent signal, e.g., an intensity of fluorescent light, in one of two wavelengths. *Id.* at 53–54 (citing Ex. 1002 ¶¶ 326–327).

For the claim element requiring the assay to be “capable of unambiguously detecting the presence or absence of each of said at least M analytes, in any combination of presence or absence in a single sample volume, based on detection of said F wavelength components, when M is greater than F,” Petitioner asserts that if “the ‘single sample volume’ is taken to be a portion of the original sample mixture prior to it being partitioned into droplets,” Larson discloses this element, and if the “single sample volume” refers to “an individual droplet generated by partitioning the sample mixture,” Larson renders this element obvious. *Id.* at 54.

Here, Petitioner asserts that Larson disclosed conducting a digital PCR assay “using two colors to identify three target analytes, relying on the combination of two colors as the multi-color label for one analyte, with each

of the two colors individually as a label for the other two targets.” *Id.* at 51, 54 (referring to Petitioner’s analysis for the anticipation ground), 28–29 (citing Ex. 1017 ¶ 140; Ex. 1002 ¶ 130). Petitioner asserts for this assay “M is three and F is two,” and “Larson . . . detect[s] whether . . . three targets are present in a ‘sample volume,’ specifically, a portion of a sample solution that is subsequently partitioned into droplets.” *Id.* at 29 (citing Ex. 1002 ¶¶ 131–132; EX1017 ¶¶ 11, 13–17, 21–23, 52–68, 154, 164, Figs. 1–3). Petitioner asserts that because Larson conducts the assay “under conditions of terminal dilution, where the probability of a single target molecule in droplets is much greater than, and overwhelms that of, multiple targets, . . . the detectable signal generated for each potential analyte is distinct and readily distinguishable, providing ‘unambiguous’ detection of the analytes.” *Id.* (citing Ex. 1017 ¶¶ 140–141, 6; Ex. 1002 ¶ 130). In other words, we understand Petitioner to assert that where the terminal dilution provides for a sample that is partitioned into droplets and each droplet contains only one analyte, Larson’s assay detects unambiguously which analyte is in each droplet.

Petitioner acknowledges, however, that “[w]hile Larson focuses on scenarios where droplets have only one target, it also teaches scenarios where individual droplets have multiple targets.” *Id.* at 54. Insofar as a single droplet in Larson’s assay has multiple targets, Petitioner asserts that Larson explains that complications may arise, but that its invention “can accommodate these complications arising from multiple occupancy.” *Id.* at 55 (quoting Ex. 1017 ¶ 141; citing Ex. 1002 ¶ 332).

In this regard, Petitioner and Dr. Batt refer to Larson’s assay depicted in Figures 9A and 9C, “involving three targets and two colors, wherein one color is used to identify two of the targets and a second color identifies the

third target.” *Id.* (citing Ex. 1017 ¶ 121, Fig. 9A; Ex. 1002 ¶ 333). According to Petitioner and Dr. Batt, Larson discloses in Figure 9C that “target 1 has a signal in a first color channel of a little above 0.4, target 3 has a signal in the same color channel of slightly less than 0.2, and target 2 has a signal in a different color channel of slightly greater than 0.4.” *Id.* (citing Ex. 1017 ¶ 121, Fig. 9C; Ex. 1002 ¶ 334). Petitioner asserts that with this coloring scheme, each target of the three targets “has its own unique color/intensity signature that is not overlapping with that of the other two targets.” *Id.* at 56 (citing Ex. 1002 ¶ 335). Specifically, Dr. Batt testifies that “because the slightly less than 0.2-intensity signal is not multipliable into the slightly more than 0.4-intensity signal, even a multiple of intensity 3 could be distinguished from intensity 1 because the various combinations of analytes would result in distinguishable signals for the three analytes.” Ex. 1002 ¶ 336. Therefore, according to Petitioner, “Larson alone renders obvious to a skilled artisan assays unambiguously determining the presence or absence of three different targets (and combinations thereof) in individual droplets.” Pet. 57 (citing Ex. 1002 ¶ 337).

Further, Petitioner asserts that a skilled artisan, in view of Larson, would have been motivated with a reasonable expectation of successfully “determining precisely which targets (or combinations of targets) are present or absent in an individual droplet as Larson teaches assays that perform this limitation” and doing so “adequately deals with the ‘multiple occupancy’ situations that arise with loading of targets into droplets with a Poisson distribution.” *Id.*

At this preliminary stage of the proceeding, we determine that Petitioner’s foregoing assertions are supported by the teachings and suggestions of Larson, along with the testimony of Petitioner’s declarant,

Dr. Batt, and that Petitioner has shown sufficiently for institution that Larson satisfies each element of challenged claim 1. In particular, based on the current record, we determine that Petitioner has shown sufficiently for institution that a person of ordinary skill in the art at the time of the invention would have understood that Larson teaches or suggests an assay that is capable of unambiguously detecting the presence or absence of three targets, i.e., $M=3$, in any combination of presence or absence, in a single volume, based on the detection of the two wavelength components, i.e., $F=2$, without the use of mass spectrometry or immobilization of the analytes, as required by claim 1.

The dispute between the parties centers on this claim element, and, in reaching our determination, we have considered Patent Owner's arguments. We address our reasoning in the context of Patent Owner's arguments in the following discussion.

To begin, we find no dispute between the parties with respect to the meaning of "single sample volume," recited in claim 1. Both parties agree that the '921 patent "contemplates both embodiments where the sample volume is separated and those where it is not." Pet. Reply 1–2; PO Sur-reply 3. Further, the parties agree that the "single sample volume" is not "limited to an individual 'droplet,' but rather includes any type or nature of volume, such as a 'tube or bottle.'" Pet. Reply 1; PO Sur-reply 3.

In Larson, whether or not we analyze its assay in terms of the single sample volume being a portion of the original sample solution (that is subsequently partitioned into multiple droplets) or being the droplet itself, ultimately, we must consider whether Larson's assay is capable of unambiguously detecting the presence or absence of each of the three possible targets, in any combination of presence or absence, in that volume.

This is because, even where the single sample volume is considered to be the original sample solution, Larson explains that its method of terminal dilution and partitioning the sample into single droplets for detection of an analyte may result in multiple analytes occurring in the same droplet, despite its efforts to avoid this multiple occupancy occurrence. *See* Ex. 1017 ¶¶ 52, 129, 141. Petitioner and Dr. Batt acknowledge this occurrence in Larson. *See* Pet. 52, 54; Ex. 1002 ¶¶ 321, 331. Thus, to meet the disputed claim limitation, Larson’s assay must be capable of doing more than identifying only a single analyte in a single droplet, as some of the droplets (prepared from an original single sample volume) may contain more than one analyte. As a result, based on our understanding of the current record at this preliminary stage of the proceeding, whether the single sample volume is considered to be the original sample solution or a single droplet, Larson’s assay must be capable of unambiguously detecting the presence or absence of each of the three possible targets, *in any combination of presence or absence*, in the ultimate volume analyzed. Patent Owner, in a timely-filed response, and Petitioner, to the extent permitted in a reply, may wish to address this assumption during the trial phase.

Patent Owner contends that Larson does not teach or suggest analyzing multiple targets in a single droplet. Prelim. Resp. 51. Patent Owner asserts that Petitioner and Dr. Batt merely “hypothesize what scenarios ‘would result in distinguishable signals’ from droplets containing different combinations of three analytes,” with respect to Larson’s assay discussed in connection with Figure 9, and “allege that the ‘foregoing coding scheme’ is ‘[c]ritically, consistent with Larson’s teaching that its assays can accommodate ‘multiple occupancy.’” *Id.* at 52 (quoting Pet. 56). According to Patent Owner, Larson instead accommodates multiple occupancy

situations by: (a) increasing the sample dilution to reduce the probability that any droplet contains more than one analyte; and/or (b) detecting, sorting away, and excluding droplets containing a heterogenous population of molecules based on how many signals (one or two) each droplet produces. *Id.* at 50–52 (citing Ex. 2001 ¶¶ 45–68, 115).

Regarding Larson’s Figure 9 assay, Patent Owner criticizes Petitioner and Dr. Batt for not addressing Larson’s Figure 9D, set forth above in Section II.D.1, which depicts a histogram showing only four populations of droplets, i.e., droplets containing only target 1, droplets containing only target 2, droplets containing only target 3, and droplets containing no targets. *Id.* at 53 (citing Ex. 1017, Fig. 9D, ¶ 121; Ex. 2001 ¶ 120). Patent Owner draws support from Larson’s omission from the histogram the depiction of “any clusters containing both target1 and target2, any clusters containing both target1 and target3, any clusters containing both target2 and target3, and any clusters containing all three targets.” *Id.* According to Patent Owner, the omission of any multiple occupancy populations in this “actual data from Larson” is consistent with Patent Owner’s interpretation of the Larson principle of operation to avoid droplets containing multiple targets by increasing sample dilution and excluding droplets with more than one target, rather than to unambiguously detect each target in a multiple occupancy droplet. *See id.* at 54.

Although we agree with Patent Owner, on this record, that Larson is focused primarily on using droplet based digital PCR to analyze a target nucleic acid, wherein the method provides for droplets that each contain only one target, we do not find merit in Patent Owner’s contention, at this stage, that a skilled artisan would not have been motivated to analyze a droplet that contains up to three targets using Larson’s assay method to

unambiguously detect and identify each of the three targets, in view of Larson's coding scheme for two-color detection of three genetic sequences depicted in Figure 9A and the results for such assay in Figure 9C. Although Larson does not disclose using this scheme to detect and distinguish among up to three targets in a single droplet, or depict such populations in Figure 9D, at this stage in the proceeding, we credit Dr. Batt's testimony that Larson's results in Figure 9C exemplify "an approach that differentiates three analytes by encoding them in one of two wavelengths of an intensity of fluorescent light (a part of the detecting signal) and allows for unambiguous detection of the three targets." Ex. 1002 ¶ 325.

In particular, as Dr. Batt explains, Larson's Figure 9C shows "the signal from target 1 has an intensity of slightly greater than 0.4, while the signal from target 3 has an intensity slightly less than 0.2." *Id.* ¶ 334; *see also* Ex. 1017, Fig. 9C. Further, as Dr. Batt continues, "because the slightly less than 0.2-intensity signal is not multipliable into the slightly more than 0.4-intensity signal, even a multiple of intensity 3 could be distinguished from intensity 1 because the various combinations of analytes would result in distinguishable signals for the three analytes." *Id.* ¶ 336. Thus, we are persuaded at this stage of the proceeding that in Larson's assay involving only three possible targets, each of the signals from probes P1, P2, P3, P1+P2, P1+P3, P2+P3, and P1+P2+P3 would have a different intensity, "as the combinations are additive and would each sum to unique values in each of the two colors used," as Dr. Batt testifies. *Id.* ¶ 336. In other words, Larson's assay would be "*capable of* unambiguously detecting the presence or absence of each of [three analytes], in any combination of presence or absence," as required by claim 1.

We also credit, on the current record, Dr. Batt’s testimony that a skilled artisan would have been motivated to use Larson’s assay to unambiguously detect up to three analytes in a single droplet, as an alternative to “limiting an experiment to only single-target droplets” because an “ability to acquire data not just from a fraction of the droplets, but from all droplets in the experiment would . . . be extremely cost effective” and improves the “total data collected” in an experiment. *Id.* ¶ 338. Further, Petitioner and Dr. Batt have established sufficiently for institution that a skilled artisan would have had a reasonable expectation of success using Larson’s assay to detect up to three analytes in a single droplet, because Larson’s disclosure exemplifies how the results of such an assay would provide unique values for each of the three analytes, in any combination of their presence or absence in the droplet.

Accordingly, we determine that Petitioner has shown a reasonable likelihood of prevailing on its assertion that at least one claim, i.e., independent claim 1, is rendered obvious by Larson.

E. Remaining Grounds

In the remaining grounds, Petitioner asserts that claims 1–10 and 13–19 are anticipated by Larson, claims 4, 6, 7, and 14–19 are rendered obvious by Larson, and claim 11 is rendered obvious by Larson, Saxonov, and Silverbrook. Pet. 21. We do not provide an analysis of these remaining grounds, as we have already determined that Petitioner has demonstrated a reasonable likelihood that it would prevail in showing the unpatentability of at least one of the challenged claims based upon Larson alone, and over similar arguments raised by Patent Owner. In view of that determination, we institute an *inter partes* review of all the challenged claims based upon all grounds raised in the Petition.

III. CONCLUSION

For the foregoing reasons, we conclude that Petitioner has established a reasonable likelihood of prevailing in its assertion that at least one challenged claim of the '921 patent is unpatentable. Accordingly, we institute the requested *inter partes* review on all grounds set forth in the Petition.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that pursuant to 35 U.S.C. § 314(a), an *inter partes* review of claims 1–19 of the '921 patent on all grounds set forth in the Petition is instituted, commencing on the entry date of this decision; and

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of review.

IPR2024-01451
Patent 11,827,921 B2

FOR PETITIONER:

Derek Walter
Adrian Percer
derek.walter@weil.com
adrian.percer@weil.com

FOR PATENT OWNER:

Jesse Salen
Martin Bader
Sheppard, Mullin, Richter &
Hampton LLP
jsalen@sheppardmullin.com
mbader@sheppardmullin.com