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

Case No. IPR2024-01451

U.S. Patent No. 11,827,921 B2

PATENT OWNER'S SUR-REPLY

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UPDATED EXHIBIT LIST

Exhibit No.	Description
2001	Declaration of Kevin Struhl, Ph.D.
2002	*Curriculum Vitae* of Kevin Struhl, Ph.D.
2003	File history of U.S. Patent No. 11,827,921
2004	U.S. Provisional Application No. 61/507,082
2005	Patent Scheduling Order dated March 8, 2024, Dkt No. 47, *ChromaCode, Inc. v. Bio-Rad Laboratories et al.*, Case No. 5:23-cv-06360, N.D. Cal.
2006	Petitioner's Amended Invalidity Contentions, *ChromaCode, Inc. v. Bio-Rad Laboratories et al.*, Case No. 5:23-cv-06360, N.D. Cal.
2007	Comparison of Saxonov and Saxonov Provisional
2008	Appendix M to Bio-Rad's Amended Invalidity Contentions
2009	Appendix I to Bio-Rad's Amended Invalidity Contentions
2010	Docket, *ChromaCode, Inc. v. Bio-Rad Laboratories et al.*, Case No. 5:23-cv-06360, N.D. Cal.
2011	Plaintiff's Opening Claim Construction Brief, *ChromaCode, Inc. v. Bio-Rad Laboratories et al.*, Case No. 5:23-cv-06360, N.D. Cal.
2012	Reply Claim Construction Brief, *ChromaCode, Inc. v. Bio-Rad Laboratories et al.*, Case No. 5:23-cv-06360, N.D. Cal.
2013	Notice Setting Claim Construction Hearing, Dkt. 83, *Chromacode Litig.*, Case No. 5:23-cv-04823, N.D. Cal.
2014	Joint Case Management Statement, Dkt. 80, *Chromacode Litig.*, Case No. 5:23-cv-04823, N.D. Cal.
2015	Minute Entry for Case Management Conference held on November 6, 2024, Dkt. 88, *Chromacode Litig.*, Case No. 5:23-cv-04823, N.D. Cal.
2016	*Dropworks, Inc. v. Lawrence Livermore Nat'l Sec., LLC*, No. IPR2021-00302, Ex. 2023.
2017	June 4, 2025 Cross Examination of Dr. Carl A. Batt.
2018	Supplemental Declaration of Kevin Struhl, Ph.D. in Support of the Patent Owner Response.
2019	QX ONE Droplet Digital PCR (ddPCR) System, available at https://www.bio-rad.com/en-us/life-science/digital-pcr/qx-one-droplet-digital-pcrddpcr-system (accessed June 19, 2025).

Exhibit No.	Description
2020	QX600 Droplet Digital PCR System, available at https://www.bio-rad.com/en-us/product/qx600-droplet-digital-pcr-system?ID=b07d12ac-0585-fc4c-a586-3ddf20d5c4a0 (accessed June 19, 2025).
2021	Bio-Rad SEC filing, available at https://www.sec.gov/Archives/edgar/data/12208/000119312520315015/d28972dex991.htm (accessed June 19, 2025).
2022	Plaintiffs ChromaCode, Inc. and California Institute of Technology's Opposition to Defendant's Motion to Transfer, Dkt. 29, *ChromaCode, Inc. et al. v. Bio-Rad Labs., Inc.*, No. 4:23-cv-06360-EKL (N.D. Cal. Nov. 20, 2023).
2023	Bio-Rad SEC filing, available at https://www.sec.gov/Archives/edgar/data/12208/000119312522053527/d901425dex991.htm (accessed June 19, 2025).
2024	*In re: ChromaCode Litig.*, No. 5:23-cv-04823-EKL, Dkt. 125 (Claim Construction Order) (N.D. Cal. July 22, 2025).
2025	October 9, 2025 Cross Examination of Dr. Carl A. Batt.

I. INTRODUCTION

Petitioner's Reply improperly introduces new arguments and embodiments from Larson and twists the record. The Board has been clear that petitioners must limit their reply briefs to addressing arguments raised in the PO's response. Even considering Petitioner's new arguments (which, per PO's concurrently filed motion to strike, the Board should not do), the evidence demonstrates Petitioner has failed to carry its burden to show the challenged claims are unpatentable.

For Ground 3 (obviousness based on Larson and Saxonov), Dr. Batt concedes he did not properly analyze either motivation to modify Larson or reasonable expectation of success, whether alone or in combination with Saxonov. EX2017, 184:18-185:15 ("Q. You didn't account for any of the reasons why it might not work, correct? A. Right."); EX2025, 70:22-79:5 ("Q. Is there any problem with the method in Larson with respect to multiple PCR that are cured or resolved by Saxonov? A. I can't answer that…I haven't done that analysis"). And instead of responding to PO's arguments explaining the deficiencies in Larson and in Petitioner's ostensible patentability analysis (Paper 17 at 40-62), Petitioner's Reply merely rehashes arguments from the Petition and improperly introduces new arguments and evidence to try to fill the gaps PO's Response identified. Paper 20 at 11-22 (relying on Larson's FIG. 11a and ¶131 and Saxonov's FIG. 4 and ¶¶20, 41 for the first time on Reply).

Additionally, Petitioner creates false narratives that it then protests. For example, for Grounds 1, 2, and 4, instead of responding to PO's actual arguments, Petitioner's Reply falsely accuses PO of relying on "the same litigation-driven claim constructions and an overly-narrow reading of Larson" as in Ground 3. *Id*. at 23. But, for Ground 3, PO explained how Petitioner failed to explain why a POSA would have been motivated to modify Larson with a reasonable expectation of success. Paper 17 at 54-62. For Ground 1, PO explained why Petitioner's reliance on PO's preliminary infringement contentions was misplaced, because they constitute merely extrinsic evidence. *Id.* at 33. Petitioner's Reply does not even attempt to rebut these arguments. Paper 20.

Indeed, to avoid substantively addressing PO's arguments, Petitioner attacks Dr. Struhl's credibility. Paper 20 at 2-6. But the fully-developed record, particularly the portions of Dr. Struhl's testimony Petitioner purposefully disregards, demonstrates Dr. Struhl's testimony is both credible and persuasive, and underscores Petitioner's failure to show the claims are unpatentable.

Accordingly, Petitioner has failed to demonstrate the claims are unpatentable.

II. PETITIONER HAS FAILED TO DEMONSTRATE THE CHALLENGED CLAIMS ARE UNPATENTABLE

A. Ground 3 Fails

The Board should reject Petitioner's argument that claims 1-10 and 12-19 would have been obvious over Larson and Saxonov because the record simply does not support Petitioner's position.

1. The evidence does not support Petitioner's position that modifying Larson would have been obvious

a. Dr. Batt agrees Larson's goal is one target per droplet and that Larson teaches many problems associated with multiple occupancy

Petitioner mischaracterizes Larson as allegedly teaching multiple occupancy, which the challenged claims require, when it is clear that Larson is directed to single-occupancy droplets. Petitioner asserts Larson teaches "limiting dilution" where some droplets contain "multiple molecules, following the Poisson distribution." EX1043, ¶¶18-19; EX2025, 31:18-33:13; Paper 20 at 13-14; *accord* EX2018, ¶61; EX2017, 134:24-135:20, 145:14-20; EX1044 160:25-161:14. However, Dr. Batt testified Larson's "goal" is obtaining only ***single-occupancy droplets***: "Q. That's how Larson sought to avoid the issues of having multiple alleles, right? A. Yes, digital PCR in general, Larson being an example of that, that is the goal of digital PCR." EX2017, 129:23-130:4; *id*, 106:6-22 ("you should

just have one" target), 107:18-108:3 ("aspirational statement"), 127:6-11 ("aspirational statements of a perfect world"), 129:13-130:4; *accord* EX2018, ¶76.

Additionally, Dr. Batt testified that Larson teaches that multiple-occupancy causes numerous problems:

> Q. Now we touched on this before, but Larson describes several downsides of detecting multiple analytes in a droplet; is that correct?
>
> A. As a general statement, yes.
>
> Q. And that includes bias from allele-specific PCR; is that correct?
>
> A. That is correct, yes….
>
> Q. One of the downsides Larson describes with detecting multiple analytes in a droplet is bias from competition between different amplicons, correct?
>
> A. [Larson ¶101] states specifically these result in varying yields between different -- I am sorry, these results in varying yields between competing amplicon which can result in a non-uniform amplicon yield. So in other words, yes, there is competition. I am not sure if this states it exactly the way you phrased it.
>
> Q. It is a complexity, correct?
>
> A. Yes, it is a consideration.
>
> Q. In paragraph 129 of Larson, Larson describes another challenge as the possibility of cross reactivity, correct?

> A. Yes, I don't like the word "cross reactivity," but yes.
>
> Q. And Larson in paragraph 129 describes the downside of an error that results from overlapping probes, correct?
>
> A. Yes, it does speak to overlapping, yes.

EX2017, 182:4-183:18; *accord* EX2018, ¶¶52, 55, 58, 105.

Further, Dr. Batt testified Larson increases dilution to alleviate such problems and ***minimize*** multiple-occupancy:

> [S]o the problem in PCR in general is that when you have multiple events going on, they… can compete for one another and the products of those reactions. So the more simplistic, the lower the number of targets you have in a sample, the less likely it is that those competing reactions would cause problems.

EX2017, 103:21-104:9, 168:21-169:23; *accord* EX2018, ¶¶ 52-63, 94, 105, 106, 121, 132.

Dr. Batt opined that to avoid these problems, Larson excludes "droplets with multiple targets":

> Critically, Larson teaches methods to detect these droplets with heterogeneous populations, *i.e.*, droplets with multiple targets from polymerase errors during PCR amplification, in order to ***exclude*** these variants. Identifying and ***removing*** these erroneous amplification

> products from the analysis ensures that only mutations in the original sample are detected, which enhances the reliability and specificity of mutation detection in highly sensitive applications.

EX1043, ¶25 (emphasis added) (citing EX1017, ¶¶15-18, 168-173); *accord* EX2018, ¶¶64-76, 106, 132. The Board should reject Dr. Batt's attempts to distinguish multiple-occupancy caused by polymerase errors from multiple-occupancy caused by Poisson loading, because neither he nor Petitioner has explained how Larson ostensibly supports such distinction. EX1043, ¶25; Paper 20 at 17-18. Indeed, the cited ¶¶15-18, 168-173 of Larson are entirely consistent with Dr. Batt's characterization during cross-examination in a "perfect world" Larson analyzes only ***single-occupancy*** droplets, and Larson teaches achieving this "goal" through dilution and exclusion. EX1017, ¶¶18 ("only one template strand"), 168 ("only a single nucleic acid molecule"), 173 ("at most a single target nucleic acid"); *accord* EX2018, ¶¶52, 55, 58, 105.

Accordingly, Dr. Batt himself confirms that Petitioner has not demonstrated Larson renders obvious detecting three targets in a droplet using two color channels.

b. Dr. Batt concedes the evidence does not support Petitioner's contentions

Dr. Batt further confirmed the evidence simply does not support Petitioner's positions expressed in its Reply. For example, Dr. Batt agreed that Larson's ¶¶35, 146, and 150 do not support the following proposition for which Petitioner's Reply cites them:

> Larson further explains that the intensity of signals from color labels can be adjusted to prevent ambiguous results, specifically to avoid overlap between signals from droplets containing different target analytes. These methods directly address the challenge of multiple occupancy and enable clear, unambiguous detection of all analyte combinations within a single droplet.

Paper 20 at 14 (citing EX1017, ¶¶35, 146, 150; EX1002, ¶163). Dr. Batt admitted in deposition that:

- ¶35 "doesn't speak to the issue of whether the targets exist in singular or more than one copy in a droplet." EX2025, 34:24-35:13; EX2017, 133:19-134:7; *accord* EX2018, ¶¶56-57.
- Nothing in ¶150 discloses identifying multiple-occupancy droplets. EX2025, 63:9-12; *accord* EX2018, ¶¶56-57.
- Of the nine labeled clusters in FIG. 15 discussed in ¶¶35 and 150, "[e]ach one is referring to a single" target, and the "probability of two

targets in a single droplet is infinitesimally small." EX2025, 40:15-19, 62:6-11; *accord* EX2018, ¶¶56-57.

- ¶146 and FIG. 14A are run at terminal dilution (vast majority of droplets have zero or one targets) and his comments for FIG. 15 and ¶35 apply equally. EX2025, 58:9-59:20, 62:12-19; *accord* EX2018, ¶¶56-57.
- ¶¶35, 146, 150 and FIGS. 14A and 15 also do not teach how to ***unambiguously*** distinguish multiple-occupancy droplets from single-occupancy droplets. Illustratively, for the highlighted cluster in annotated FIG. 15 below, Dr. Batt testified:

> Q. Why would you not label the cluster [in FIG. 15] at a 70 VIC and 95 FAM as both 815A and 815G or 5C?
> A. Because you're registering individual events. That's what I am trying to say.
> Q. Each individual event, the assumption is that there's only a single molecule in that droplet, correct?
> A. I can't say that.
> Q. Otherwise, you can't distinguish between double occupancy and single occupancy, correct?
> A. That's not the point of this. It doesn't exclude it. Doesn't include it.

EX2025, 50:9-23.

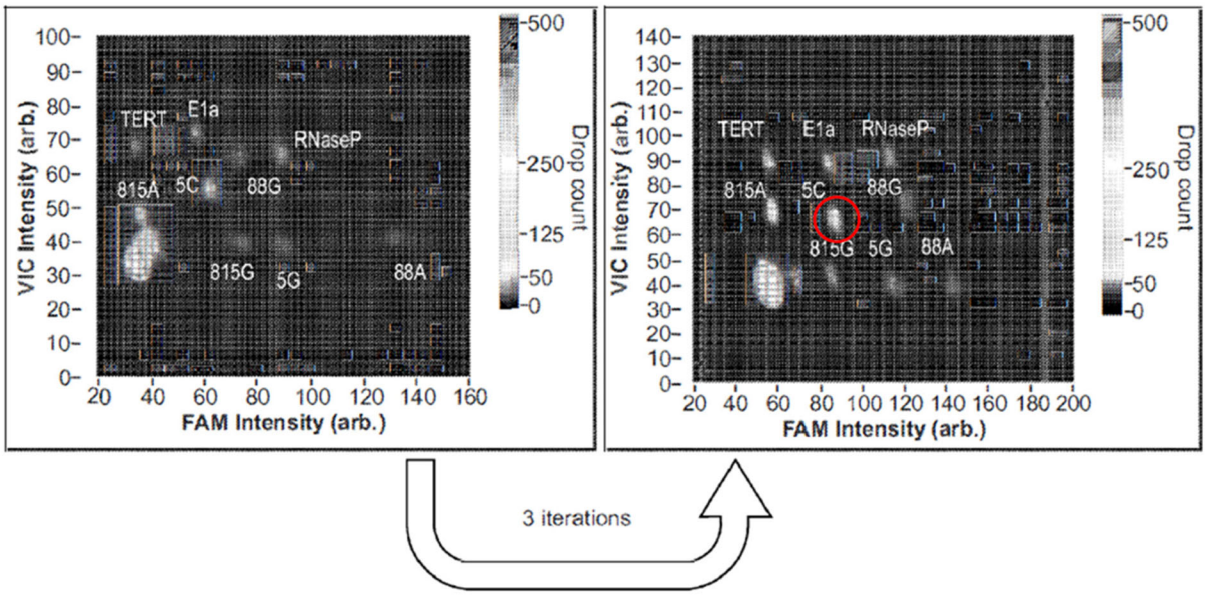

FIG. 15

EX1017, FIG. 15 (annotated); *accord* EX2018, ¶¶56-57.

When pressed on how to tell how many targets are in a droplet in this cluster, Dr. Batt admitted:

> So, you are, in principle, correct, that there could be a single droplet that has both of those [targets] in there that gave you a confusing signal, but you would not see it because it's .5 percent of the population… Each one of these white spots here represents a lot of droplets. So, if you had one single droplet that, as you want to point out and -- correct, it would not even show up here. You wouldn't see it.

EX2025, 54:23-56:11, 57:24-58:5 ("Q. [FIG. 15] doesn't teach you how to do that, correct? How to distinguish between the two targets and the one target droplets?

A. I can't determine that from this…information."), 58:6-8 ("Q. And paragraph 35 doesn't teach how to do that either, correct? A. I can't determine that, yeah.").

Accordingly, Dr. Batt admitted ¶¶35, 146, and 150 and FIGS. 14A and 15 do ***not*** teach how to distinguish multiple-occupancy from single-occupancy droplets. Indeed, Dr. Batt himself "can't determine that" from Larson. EX2025, 57:24-58:8; *accord* EX2018, ¶¶56-57. Thus, his testimony establishes Larson does ***not*** "directly address the challenge of multiple occupancy and enable clear, unambiguous detection of all analyte combinations within a single droplet." Paper 20 at 14.

Finally, in a last-ditch effort to show Larson teaches detecting multiple-occupancy droplets, Petitioner's Reply raises new arguments based on an embodiment from FIG. 11a of Larson not discussed in the Petition.[1] Paper 20 at 15-16; EX2025, 44:12-45:4. Particularly, citing this new figure in the Reply, Petitioner has added a new motivation-to-combine argument using Saxonov, and shifted its theory from embodiments in Larson and Saxonov purportedly detecting three targets using two colors, to arguing embodiments purportedly detecting two targets using one color.

[1] PO is moving to strike this subject matter but addresses it here for completeness.

Petitioner alleges Larson's purported disclosure of a "very small peak…at ~0.9 V…corresponded to droplets occupied by both genes" teaches the "unambiguous detection of multiple analytes in a single droplet" but conceded this peak is "***not visible on the scale of FIG. 11a***." Paper 20 at 15 (emphasis added). Moreover, FIG. 11a uses only ***one*** channel to ostensibly detect ***two*** targets. EX2025, 42:24-43:6, 72:9-73:5. This falls far short of what the '921 Patent claims require—using at least ***two*** channels to detect at least ***three*** targets—and impermissibly shifts Petitioner's invalidity theory to a new embodiment of Larson. Indeed, PO's Response points out, Petitioner couched its ***own invalidity theory*** on the assumption that F≥2 and M≥3, and relied on specific embodiments in Larson (and Saxonov) that purportedly disclosed F≥2 and M≥3. Paper 17 at 12-13 (citing Petition at 1, 24-26, 28-29, 35, 38-39, 49, 53, 55-58, 60; Paper 11 at 33). Now that Petitioner has recognized the strength of PO's arguments that the relied-upon embodiments in Larson do not disclose F≥2 and M≥3, Petitioner may not shift its theory to new evidence in Larson, or to argue the claims cover F=1 and M=2. *See Yita LLC v. MacNeil IP LLC*, 69 F.4th 1356, 1367 (Fed. Cir. 2023).

Moreover, the Board should reject Petitioner's argument that "'F' can be any value less than 'M,' including 1," because it is contrary to the claim language. Namely, the claims recite that the fluorescent signal comprises *plural* F wavelength *components*. There is a presumption that plural terms refer to two or

more items. *See Apple Inc. v. MPH Techs. Oy*, 28 F.4th 254, 261 (Fed. Cir. 2022) ("In accordance with common English usage, we presume a plural term refers to two or more items."). Where nothing in the claims or specification suggests otherwise, the plural does not include the singular. *Id.* at 262. Dr. Batt repeatedly confirmed that plural with "s" at the end means plural, not singular. EX2025, 13:17-14:14; 24:2-25:7. However, Dr. Struhl's opinion is that "F is at least 2, and…M is at least 3" and is based on both the claim language ***and*** the specification—the intrinsic record. EX1044, 199:15-200:9, 195:25-196:8, 197:7-14; *Allergan Sales, LLC v. Sandoz, Inc.*, 935 F.3d 1370, 1373 (Fed. Cir. 2019) ("[C]laim construction must begin with the words of the claims themselves."); *Bonutti Skeletal Innovations LLC v. Arthrex, Inc.*, No. 6:13-cv-00620, 2014 U.S. Dist. LEXIS 185178, at *27, 30 (M.D. Fl. Mar. 25, 2014) (claim language can be dispositive for claim construction); *Phillips v. AWH Corp.*, 415 F.3d 1303, 1315 (Fed. Cir. 2005) (en banc) (The specification is "always highly relevant to claim construction.").

Petitioner further complains that a "claim construction that excludes a preferred embodiment…is rarely, if ever correct…." Paper 20 at 9. But while Petitioner points to a "single color coding scheme" in the '921 Patent, Petitioner offers no evidence this is a ***preferred*** embodiment. Paper 20 at 8-9. Indeed, several embodiments described in the '921 Patent use multiple fluorophores

(colors) and thus are ***not*** F=1 embodiments, while ***other*** embodiments describe F=1. *Compare, e.g.*, EX1001, FIGS. 1-3, 8 (F>1), *with id.*, FIG. 7 (F=1). Contrary to Petitioner's attempt to corral PO into reciting all possible embodiments in claim 1, PO is entitled to pick and choose which embodiments to claim. *Intamin Ltd. v. Magnetar Techs., Corp.*, 483 F.3d 1328, 1337 (Fed. Cir. 2007) ("[A] claim need not cover all embodiments.").

Finally, there is no evidence the signal from the phantom peak in FIG. 11a actually exists, let alone discloses multiple-occupancy droplets, let alone droplets with M≥3. EX2017, 134:15-19 (FIG. 15 has "no labeled population of multianalyte droplets"); *id*., 115:8-23 ("I do not have powerful enough eyes to look at this histogram [FIG. 9D] and find individual droplets" with multiple targets.); *accord* EX2018, ¶¶56-57; EX1044 151:3-7, 151:25-152:2, 153:15-20.

Accordingly, Dr. Batt's testimony (in addition to Dr. Struhl's) confirms patentability.

2. Petitioner does not meet its burden to show obviousness

Petitioner's Reply alleges a POSA would have been motivated to combine the teachings of Larson's FIG. 11a and Saxonov's FIG. 4. Paper 20 at 22. However, this is a completely different obviousness theory than what Petitioner raised in the Petition or than what PO responded to in its Response and accordingly

should be stricken.[2] Paper 1 at 51-65. But even when considered on its face, the references do not support Petitioner's argument.

Petitioner's first obviousness theory in Ground 3 was based on Larson alone, relying on Larson's FIG. 9C and ¶121. Paper 1 at 55-57; EX1002, ¶¶333-36. But Dr. Batt now concedes Larson's ¶121 "doesn't account for" multiple-occupancy microdroplets containing targets 1+2, 1+3, 2+3, or 1+2+3." EX2017, 113:20-116:4. He also admits that FIG. 9C is a ***single-occupancy*** embodiment. EX2017, 108:4-109:4, 113:6-15, 114:13-115:23, 210:12-25; EX1017, ¶121, FIGS. 9A-9D; *accord* EX2018, ¶¶108-119. Even Dr. Batt could not tell if any multiple-occupancy droplets are present. EX2017, 113:6-115:23. According to Dr. Batt, Larson's "goal" is ***single-occupancy***, and Larson's "point" is finding the targets in the original sample, not distinguishing multiple-occupancy from single-occupancy. EX2025 39:12-19; 50:19-23, EX2017, 106:6-22; 107:18-108:3; 129:13-22; 127:6-11; *accord* EX2018, ¶¶108-119.

Dr. Batt concedes he did not properly analyze either motivation to modify Larson or reasonable expectation of success, whether alone or in combination with Saxonov, and indeed admits that his opinions did not even ***account*** for Larson's teachings on the downsides of multiple-occupancy. EX2017, 182:4-183:18;

[2] *See* PO's motion to strike.

103:21-104:9, 168:21-23; 184:18-185:15 ("Is that my responsibility?... your expectation is that I am going to sit here and discuss why it is not going to work, is that what you are asking me to do?" "Q. You didn't account for any of the reasons why it might not work, correct? A. Right."); EX2025, 70:22-79:5 ("Q. Is there any problem with the method in Larson with respect to multiple PCR that are cured or resolved by Saxonov? A. I can't answer that…I haven't done that analysis").

The Federal Circuit rejected Dr. Batt's approach in *Arctic Cat Inc. v. Polaris Industries, Inc.*, 795 Fed. App'x 827, 833 (Fed. Cir. 2019). There, while the petitioner had argued "the Board improperly required it to explain how drawbacks of [the] combination would be overcome," the Federal Circuit disagreed, holding "[t]he Board must weigh the benefits and drawbacks of the modification against each other, to determine whether there would be a motivation to combine." *Id.*

Moreover, Petitioner and Dr. Batt repeatedly fail to identify any specific reason to modify Larson as such, instead merely ***assuming*** some hypothetical reason. EX2025, 80:7-82:3 ("If for whatever reason you're running at a higher occupancy rate…"); *see W. Dig. Techs., Inc. v. Longitude Licensing Ltd.*, IPR2023-01230, Paper 31 at 76 (PTAB Jan. 21, 2025 (rejecting motivation to combine references because "Petitioner's reasoning…is not supported by sufficient factual evidence").

Petitioner proffered a second obviousness theory in Ground 3, based on Larson in view of Saxonov's FIG. 10. Paper 1 at 58-61; EX1002, ¶¶339-352. Yet Petitioner has repeatedly failed to establish FIG. 10 is prior art. Paper 11 at 29; Paper 1 at 13-17; Paper 9 at §II. Hence Petitioner's brand new theory based on Saxonov's ¶¶20 and 41 and FIG. 4. Paper 20 at 18-22.

And Petitioner has still failed to respond meaningfully to PO's arguments regarding Ground 3 (Paper 17 at 39-62), instead rehashing the same arguments from the Petition. Paper 20 at 13-14. Petitioner's Reply then improperly shifts its obviousness theory to Larson's FIG. 11a and Saxonov's FIG. 4, ¶20, and table at ¶41.[3] *Id.* at 15-22; EX1043, ¶¶28-30. But, just as it did for its initial invalidity theory, Petitioner fails to establish that Larson's FIG. 11a and Saxonov's FIG. 4, ¶20, and table at ¶41 (or anything else in Larson and Saxonov) would have motivated a POSA to modify Larson or that there would have been a reasonable expectation of success in doing so. Dr. Batt's complete opinion on the alleged motivation to combine these embodiments is:

> Most importantly, Saxonov FIG. 4 depicts the exact scheme taught by FIG. 11a. A POSA would have understood to combine these references and would have done so with a reasonable expectation of success.…

[3] *See* Motion to Strike.

> A POSA would be motivated to combine Saxonov and Larson because, in part, Saxonov discloses the same scenarios taught in Larson. A POSA would have a reasonable expectation of success because Saxonov and Larson both teach methods for unambiguous detection of multiple targets in a single droplet.

EX1043, ¶¶30, 37; Paper 20 at 22.

However, "[a]n obviousness determination cannot be reached where the record lacks explanation as to how or why the references would be combined to produce the claimed invention." *Apple Inc. v. Papst Licensing GMBH & Co. KG*, IPR2016-01863, Paper 35 at 10 (PTAB Apr. 13, 2018). Here, neither Petitioner nor Dr. Batt explain ***why*** any purported similarities between Larson's FIG. 11a and Saxonov's FIG. 4 would have motivated a POSA to combine Larson and Saxonov. Indeed, while Petitioner asserts in this respect that Larson and Saxonov disclose the same "exact" scheme, both Petitioner and Dr. Batt fail to demonstrate a POSA would have had a reason to combine them. Paper 20 at 21-22; *Microsoft Corp. v. Enfish, LLC*, 662 Fed. Appx. 981, 990 (Fed. Cir. 2016) (asserting references are similar is insufficient).

Dr. Batt's cross-examination established he did not do this analysis: "Q. You don't have any specific opinion in this declaration about a shortcoming in

Larson that would have motivated a person of ordinary skill in the art to combine it with Larson, do you? A. Again, I didn't do that analysis." EX2025, 74:5-79:5. And nothing else in Petitioner's arguments or Dr. Batt's opinions fills the gap to show a POSA would have been motivated (let alone based on purported similarities between Larson's FIG. 11a and Saxonov's FIG. 4) to modify Larson and Saxonov to achieve the claimed invention or had a reasonable expectation of success in doing so. Dr. Batt's opinions—upon which Petitioner's invalidity theor(ies) inextricably rely—do not account for Larson and Saxonov's shortcomings, and do not explain why a POSA would have expected that Petitioner's proposed modifications would overcome such shortcomings. EX2025, 71:3-72:8, 73:6-18, 78:9-22; *Arctic Cat*, 795 Fed. App'x at 833.

These failures are fatal to all of Petitioner's theories based on the modifying Larson or combining it with Saxonov.

Accordingly, the fully-developed record demonstrates Petitioner's obviousness theories are unsubstantiated, do not establish a POSA would have been motivated to modify Larson (alone or with Saxonov), and do not establish a POSA would have had a reasonable expectation of success in doing so or combining Larson and Saxonov.

Petitioner therefore has not shown the claims would have been obvious.

B. Grounds 1, 2, and 4 Fail

1. Larson does not anticipate the challenged claims

PO's Response explains that Larson does not anticipate (Ground 1) because FIG. 9C and ¶121 do not disclose using two or more colors to detect three or more analytes in the same single sample volume in which amplification occurs, which the '921 Patent claims require and on which Petitioner's arguments focus. Paper 17 at 12-13, 27-36; Paper 20 at 10; EX1043, ¶¶13, 20-21, 27; EX2025, 23:10-25. Petitioner accuses PO of taking "an overly-narrow reading of Larson that disregards the reference's explicit disclosures." Paper 20 at 23. But PO has done no such thing. Larson lacks such teachings, and even Dr. Batt ultimately conceded that Larson's ¶121 "doesn't account for" multiple-occupancy microdroplets containing targets 1+2, 1+3, 2+3, or 1+2+3" and that FIG. 9C is a ***single-occupancy*** embodiment. EX2017, 108:4-109:4, 113:6-15, 114:13-115:23, 210:12-25; EX1017, ¶121, FIGS. 9A-9D. Indeed, Dr. Batt could not tell if any multiple-occupancy droplets are present in such disclosure (they are not). EX2017, 113:6-115:23; 112:19-25. That is because Larson is silent regarding this claimed feature. Accordingly, Larson falls far short of disclosing how to use two or more colors to unambiguously detect any and all combinations of three or more analytes within multiple-occupancy droplets within which amplification is performed.

PO's arguments against Ground 1 differ from those against Ground 3 in critical ways. Paper 17 at 27-36, 39-62. Yet Petitioner's Reply for Ground 1 falsely accuses PO's Response of "reiterat[ing] the same arguments raised under Ground 3" and "relying on the same litigation-driven claim constructions" as in Ground 3. Paper 20 at 23. This is just noise. And while Petitioner's Reply accuses PO of arguing "Larson does not disclose amplification within a 'single sample volume'" and alleges Larson's ¶¶79 and 193 contradict this argument, this mischaracterizes and misses the point of PO's actual arguments, which is that Larson does not disclose detecting at least three targets in a droplet using fewer colors. Paper 20 at 23; Paper 17 at 34-36. Moreover, Dr. Batt's testimony fails to establish the portions of Larson relied upon in Ground 1 teach how to unambiguously detect any and all combinations of three or more analytes within multiple-occupancy droplets within which amplification is performed. EX2017, 108:4-109:4, 112:19-25, 113:6-115:23, 210:12-25; EX1017, ¶121, FIGS. 9A-9D.

Regardless, PO's preliminary infringement contentions in parallel litigation merely constitute extrinsic evidence that does not override the claim language and teachings of the '921 Patent.[4] *Great W. Cas. Co. v. Intell. Ventures II LLC*,

[4] The Board has approved additional briefing on construction of "single sample volume," so further discussion of this term beyond that in PO's Response will be in the context of such briefing.

IPR2015-01706, Paper 69 at 13 (PTAB Feb. 14, 2020). Dr. Batt was not even ***aware*** of the correct legal standard for interpreting the claims in view of PO's infringement contentions, so the Board should reject all of his testimony—and all of Petitioner's arguments in Grounds 1-4—that rely upon his interpretation. EX2017, 47:8-49:14; Paper 20 at 23; Paper 17 at 24-26. The Reply did not respond to PO's argument on this point.

Accordingly, Ground 1 fails.

2. Petitioner has not demonstrated claims 4 and 13 are anticipated or obvious

Claims 4 and 13 recite different, mutually exclusive features, but Petitioner improperly relies on a single embodiment from Larson to argue both claims are anticipated and obvious. Paper 20 at 23; Paper 1 at 34-35, 39, 62, 64. Per *Vizio, Inc. v. Polaris PowerLED Technologies, LLC*, a single disclosure from the prior art cannot satisfy two different, mutually exclusive claim features. IPR2020-00043, Paper 32 at 20-25 (PTAB Sept. 15, 2020) (denying institution and request for rehearing). Accordingly, Petitioner's arguments fail.

Claim 4 recites ***eliminating*** degenerate codes: the "coding scheme is made nondegenerate by enumerating every legitimate result that can be obtained from said coding scheme, identifying each legitimate result that is degenerate, and eliminating at least one potential analyte code from said coding scheme to

eliminate degeneracy." Claim 13's coding scheme is innately designed to be non-degenerate ***without*** removing any codes: the "coding scheme is innately nondegenerate or non-degenerate by construction." The '921 Patent specification explains this distinction. For claim 4, the specification explains "the full coding capability of a particular coding scheme may be enumerated, and certain potential analyte codes may be eliminated from the coding scheme to reduce or eliminate degeneracy." EX1001, 9:50-54. And for claim 13, the specification teaches "a coding scheme may be designed to be non-degenerate, so that a reduction or elimination of degeneracy is not necessary." *Id.* at 9:55-57; *id.* at 18:18-22; *compare, e.g.*, *id.* at Table 7 (crossing out codes as in claim 4) *with* Table 8 (no codes eliminated as in claim 13). The claim language and specification thus confirm these two embodiments are different and mutually exclusive.

Petitioner impermissibly relies on a single embodiment in Larson as disclosing ***both*** of these mutually exclusive features. For claim 4, Petitioner equates Larson's FIG. 15 scheme for adjusting intensity values to avoid ambiguous results with eliminating a code from the scheme. Paper 1 at 34-35 (citing EX1017 at ¶¶35, 140, 146, 150, FIG. 15). And for claim 13, Petitioner argues Larson's FIG. 15 scheme is innately non-degenerate or non-degenerate by construction. *Id.* at 39. But fine-tuning intensities per Larson FIG. 15 may not reasonably be

equated ***both*** with eliminating codes ***and*** being inherently non-degenerate, which as explained above are mutually exclusive embodiments.

PO raised this deficiency in its Response, and Petitioner's only responsive argument in its Reply—that the POR provided no authority for the contention that the same disclosure of Larson cannot invalidate both claims 4 and 13—should be rejected in view of at least *Vizio*.

3. Grounds 2 and 4 fail because Petitioner has not carried its burden for Grounds 1 or 3

Ground 2 identifies claims 2, 4, 6, 7, and 14-19 as allegedly being obvious over Larson. But, as discussed for Grounds 1 and 3, Petitioner does not establish the independent claims are anticipated by or obvious over Larson alone or combined with Saxonov. *Supra* §§II.A, II.B.1; Paper 17, §§V.A.1, V.A.3.

Ground 4 adds Silverbrook to invalidate claim 11. But Petitioner has not demonstrated Silverbrook cures Larson's and Saxonov's deficiencies. *Supra* §§II.A, II.B.1; Paper 17, §§V.A.1, V.A.3, V.A.4.

Accordingly, Grounds 2 and 4 likewise fail.

C. Petitioner's Arguments Regarding Objective Indicia of Nonobviousness Should Be Rejected

Petitioner argues there is no credible basis to conclude Bio-Rad's products infringe, and thus no evidence of commercial success or industry praise. Paper 20 at 24. This argument should be rejected because PO's infringement contentions

provide this very basis and Petitioner has not refuted that they show infringement. EX1012. Petitioner's attacks on PO's arguments for long-felt need are unpersuasive, because they rely on Petitioner's baseless attacks on Dr. Struhl's opinions. Paper 20 at 24-25. As explained herein, Dr. Struhl's opinions are reliable and should be credited. For these and the reasons set forth in PO's Response, objective indicia of nonobviousness support patentability.

III. DR. STRUHL'S DECLARATION TESTIMONY IS RELIABLE AND THE BOARD SHOULD CREDIT IT

Apparently lacking meaningful responses to PO's arguments, Petitioner resorts to attacking Dr. Struhl, arguing his testimony should be accorded no weight. Paper 20 at 1-6. But the purported issues Petitioner complains of, in view of the record, do not support disregarding Dr. Struhl's testimony. Rather, the record demonstrates Dr. Struhl's opinions are reliable and should be considered and adopted.

First, Petitioner complains Dr. Struhl did not know the '921 Patent's priority date or the importance of using it. Paper 20 at 3. But Dr. Struhl declared his understanding that the time of the invention is February 3, 2012, and that this is the "relevant timeframe" for his validity opinions. EX2018, ¶¶13, 14, 17, 20, 22, 23. Dr. Struhl relied on the 2012 priority date provided by counsel and used that date for his opinions. EX1044, 192:6-195:4.

Second, Petitioner complains that Dr. Struhl did not "do a historical perspective at all" and asserts "this is precisely what obviousness requires." Paper 20 at 4. Here, Petitioner constructed a soundbite to make it sound like Dr. Struhl thinks no normal person cares about a historical perspective: "I don't have the slightest idea… I didn't do a historical perspective. No normal person cares about that." *Id.* (quoting EX1044, 60:17-63:11). But this excerpt from Dr. Struhl's testimony must be viewed in context: Dr. Struhl was actually responding to a long line of questions about the specific years when different fluorophores became available for use with multiplex applications, and expressing his position that unless a POSA was "patenting individual dyes," they would not care about when specifically these dyes were invented. EX1044, 60:17-63:11. This is a ***very*** different proposition, and Petitioner's attempt to fabricate a different point from Dr. Struhl's testimony must fail.

Moreover, Petitioner faults Dr. Struhl for allegedly not knowing the timing of certain "key developments" or "significant advances," such as when FAM first became available. Paper 20 at 4 (citing EX1044, 52:9-53:7; 54:17-55:3; 55:8-25, 56:9-57:9, 57:13-20, 60:17-63:11, 163:11-16, 179:21-180:19, 181:6-9). Petitioner does not provide any evidence of why a POSA would consider these developments and events to actually be "key" or "significant" to the '921 Patent claims (they are not). Moreover, the law does ***not*** require the "historical perspective" Petitioner

asserts, instead requiring "to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field." *In re Kotzab*, 217 F.3d 1365, 1369 (Fed. Cir. 2000). That is exactly what Dr. Struhl did. *See, e.g.*, EX2018, ¶¶28 (techniques known in the art), 30 (subsequent multiplex PCR approach), 32 (known multiplexing techniques), 33 (known dilution regimes), 35 (solution of the '921 Patent compared to prior approaches), 38 (same). Furthermore, if the Board considers rejecting Dr. Struhl's testimony on this basis (it should not), the Board should also reject Dr. Batt's testimony because he did not consider a "historical perspective." EX2025, 19:6-18.

Third, Petitioner argues the Board should not consider Dr. Struhl's testimony because he allegedly did not understand the standard for claim construction or the patent's claims. Paper 20 at 5. This too is inconsistent with the record and should be rejected. Dr. Struhl explained his (correct) understanding of the claim construction standard in his declaration. EX2018, ¶¶20-21. Petitioner argues Dr. Struhl did not understand the claim term "component," but he included his understanding in his declaration and testimony. *See, e.g.*, Paper 20 at 4; EX2018, ¶38 (explaining "each analyte…is encoded as a value in each of two components of a signal (*e.g.*, intensity and wavelength)"); EX1044, 97:21-22. Finally, Petitioner's argument that it does not comprehend Dr. Struhl's testimony

concerning the dependent claims is not credible given Dr. Struhl's straightforward opinions supporting his analysis of those claims. EX2018, ¶¶96-97, 134.

Fourth, Petitioner argues the Board should disregard Dr. Struhl's testimony because he was allegedly not conversant in PO's infringement contentions. Paper 20 at 5-6. But Petitioner does not explain why Dr. Struhl's cross-examination testimony regarding infringement contentions purportedly renders any of his opinions unreliable. Moreover, at most the contentions constitute extrinsic evidence, which further dilutes any purported importance they would have to Dr. Struhl's opinion. *Great W. Cas.*, IPR2015-01706, Paper 69 at 13.

Finally, Petitioner argues the Board should disregard Dr. Struhl's testimony because he allegedly lacked familiarity with the Petition. Paper 20 at 6. But the record plainly shows Dr. Struhl understands the Petition and Petitioner's theories. During the portions of Dr. Struhl's cross-examination that Petitioner cites, Dr. Struhl was merely unsure that the document Petitioner's counsel was questioning him on was an authentic copy of the correct document, but Petitioner neglects to mention that Dr. Struhl clarified that "[m]y point was before that I didn't see it in my list, but now I'm seeing it in my document, so it's obviously there…it's exactly the same thing." EX1044 at 190:23-192:5.

Accordingly, Dr. Struhl's testimony is reliable and supports patentability, and the Board can and should credit the testimony. If the Board agrees with

Petitioner on any point addressed above (it should not), that should merely go to the weight of the testimony.

IV. CONCLUSION

For at least these reasons, the Board should uphold patentability of all of the challenged claims.

Respectfully submitted,

SHEPPARD, MULLIN,
RICHTER & HAMPTON LLP

/Jesse A. Salen/
Jesse A. Salen (Reg. No. 72,209)
Counsel for Patent Owner
California Institute of Technology

Date: October 24, 2025

12275 El Camino Real, Suite 100
San Diego, CA 92130
Tel: (858) 720-8900
Fax: (858) 509-3691

CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e), I hereby certify that on October 24, 2025, a copy of the foregoing document was served via E-Mail on the Petitioner at the following correspondence address provided by counsel of record for the Petitioner pursuant to 37 C.F.R. § 42.8(b)(4):

Derek C. Walter
dwalter@jonesday.com
Jones Day
555 California Street, 26th floor
San Francisco, CA 94104

Matthew W. Johnson
mwjohnson@jonesday.com
Jones Day
500 Grant Street, Suite 4500
Pittsburgh, PA 15219

/s/Jesse A. Salen

Jesse A. Salen (Reg. No. 72,209)
Counsel for Patent Owner
California Institute of Technology

12275 El Camino Real, Suite 100
San Diego, CA 92130
Tel: (858) 720-8900
Fax: (858) 509-3691

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Respectfully submitted,

SHEPPARD, MULLIN,
RICHTER & HAMPTON LLP

/s/Jesse A. Salen
Jesse A. Salen (Reg. No. 72,209)
Counsel for Patent Owner
California Institute of Technology

Date: October 24, 2025

12275 El Camino Real, Suite 100
San Diego, CA 92130
Tel: (858) 720-8900
Fax: (858) 509-3691