

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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DROPWORKS, INC.,  
Petitioner,

v.

BIO-RAD LABORATORIES, INC.,  
Patent Owner.

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IPR2021-00212  
Patent 9,127,310 B2

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Before CHRISTOPHER M. KAISER, MICHELLE N. ANKENBRAND,  
and AVELYN M. ROSS, *Administrative Patent Judges*.

ROSS, *Administrative Patent Judge*.

DECISION

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

## I. INTRODUCTION

Dropworks, Inc. (“Petitioner”) filed a Petition (Paper 2, “Pet.”) requesting an *inter partes* review of claims 1–6, 8–10, and 23 of U.S. Patent No. 9,127,310 B2 (Ex. 1001, “the ’310 patent”). Pet. 1. Bio-Rad Laboratories, Inc. (“Patent Owner”) filed a Preliminary Response (Paper 6, “Prelim. Resp.”).

We have authority to determine whether to institute an *inter partes* review. 35 U.S.C. § 314 (2018); 37 C.F.R. § 42.4(a) (2020). The standard for instituting an *inter partes* review is set forth in 35 U.S.C. § 314(a), which provides that an *inter partes* review may not be instituted “unless the Director determines . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least [one] of the claims challenged in the petition.”

For the reasons set forth below, upon considering the Petition, the Preliminary Response, and the evidence of record, we determine the information presented in the Petition fails to sufficiently establish a reasonable likelihood that Petitioner would prevail with respect to at least one of the challenged claims. Accordingly, we deny the Petition, and decline to institute an *inter partes* review.

### A. *Real Parties in Interest*

According to Petitioner, “Dropworks, Inc. is . . . the real party-in-interest in this [*inter partes* review].” Pet. 3. Patent Owner identifies Bio-Rad Laboratories as the real party-in-interest. Paper 3, 1 (Patent Owner’s Mandatory Notices).

*B. Related Proceedings*

The parties identify the pending lawsuit between the parties, styled *Bio-Rad Laboratories, Inc. v. Dropworks, Inc.*, 1:20-cv-00506-RGA (D. Del.) (“the district court litigation”) as a related proceeding in which Patent Owner asserts the ’310 patent. Pet. 3; *see* Paper 3, 1. Petitioner also identifies co-pending petitions for *inter partes* review, i.e., IPR2021-00100 and IPR2021-00218, “challenging two other patents asserted against it” in the district court litigation. Pet. 3. Patent Owner asserts that the ’310 patent is also being asserted in a second district court lawsuit captioned *Bio-Rad Laboratories, Inc. v. Stilla Technologies, Inc.*, 1:19-cv-11587-WGY (D. Mass.). Paper 3, 1.

*C. The ’310 Patent (Ex. 1001)*

The ’310 patent, titled “Digital Analyte Analysis,” issued on September 8, 2015. Ex. 1001, codes (45), (54). The ’310 patent describes a method for performing multiplexed polymerase chain reactions (“PCR”) on microfluidic droplets. *Id.* at 2:34–3:15. According to the ’310 patent,

multiplexing primers in droplets enables the simultaneous increase in the number of PCR droplets while keeping the amount of input DNA the same or lower and generate the same or greater amplicon yield. This results in an overall increase in the amount of PCR positive droplets and amplicon yield without the consumption of more DNA.

*Id.* at 2:48–54. The ’310 patent specification explains that “[e]ven though the number of PCR primer pairs per droplet is greater than one, there is only one template molecule per droplet, and thus, in some implementations, there is only one primer pair per droplet that is being utilized at one time” and “the advantages of droplet PCR for eliminating bias from either allele specific PCR or competition between different amplicons is maintained.” *Id.*

at 2:54–58. In addition, “other implementations advantageously allow detection of multiple loci on a single template using multiple primer pairs, preferably designed to minimize bias.” *Id.* at 2:62–64.

*D. Illustrative Claims*

Petitioner challenges claims 1–6, 8–10, and 23 of the ’310 patent. Claim 1 is illustrative of the subject matter of the ’310 patent and is reproduced below.

1. A method for detecting target sequences from a sample, the method comprising:

providing a plurality of droplets each comprising a nucleic acid molecule, reagents for an amplification reaction comprising a plurality of different primer types each specific to amplify a different target sequence, and a plurality of optically labeled probe types each specific for a different target sequence;

amplifying a single target sequence from the nucleic acid molecule in each droplet; and

detecting light emitted from an optically labeled probe type specific to the amplified target sequence in the droplets.

Ex. 1001, 51:15–27; *see also* Ex. 1004, 518 (certificate of correction replacing “droplets” with “partitions” in the second and last clauses of the claim).

*E. Prior Art and Asserted Grounds of Unpatentability*

Petitioner contends that claims 1–6, 8–10, and 23 are unpatentable based on the following grounds:

<b>Claim(s) Challenged</b>	<b>35 U.S.C. §</b>	<b>Reference(s)/Basis</b>
1–5, 8–10, 23	103	Davies, <sup>1</sup> Warren <sup>2</sup>
6	103	Davies, Warren, Chen <sup>3</sup>
1–5, 8–9, 23	103	Beer, <sup>4</sup> Warren
6	103	Beer, Warren, Chen

Pet. 5. Petitioner also relies on declaration testimony of Bernhard H. Weigl, Ph.D. (Ex. 1002).

## II. ANALYSIS

### A. Legal Standards

“In an [*inter partes* review], the petitioner has the burden from the onset to show with particularity why the patent it challenges is unpatentable.” *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016) (citing 35 U.S.C. § 312(a)(3) (requiring *inter partes* review petitions to identify “with particularity . . . the evidence that supports the grounds for the challenge to each claim”)). This burden of persuasion never shifts to Patent Owner. *See Dynamic Drinkware, LLC v. Nat’l Graphics*,

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<sup>1</sup> Mark Davies, et al., US 2010/0092973 A1, published April 15, 2010 (Ex. 1005, “Davies”).

<sup>2</sup> Luigi Warren, et al., *Transcription factor profiling in individual hematopoietic progenitors by digital RT-PCR*, 103 PNAS 47, 17807–17812 (November 21, 2006) (Ex. 1006, “Warren”).

<sup>3</sup> Ke-Lian Chen et al., *Duplication and De Novo Deletions of the SMN1 Gene Demonstrated by Fluorescence-Based Carrier Testing for Spinal Muscular Atrophy*, 85 Am. J. Med. Genetics 463–469 (1999) (Ex. 1031, “Chen”).

<sup>4</sup> N. Reginald Beer et al., *On-Chip, Real-Time, Single-Copy Polymerase Chain Reaction in Picoliter Droplets*, 79 Anal. Chem. 22, 8471–8475 (2007) (Ex. 1007, “Beer”).

*Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015) (discussing the burden of proof in an *inter partes* review).

A claim is unpatentable under 35 U.S.C. § 103(a) if “the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) objective evidence of nonobviousness.<sup>5</sup> *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

To show obviousness, it is not enough to merely show that the prior art includes separate references covering each separate limitation in a challenged claim. *Unigene Labs., Inc. v. Apotex, Inc.*, 655 F.3d 1352, 1360 (Fed. Cir. 2011). “This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.” *KSR*, 550 U.S. at 418–419. On the other hand, an obviousness analysis “need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.” *Id.* at 418; *accord In re Translogic Tech., Inc.*, 504 F.3d 1249, 1259 (Fed. Cir. 2007). However, Petitioner cannot satisfy its burden of proving

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<sup>5</sup> The parties have not asserted or otherwise directed our attention to any objective evidence of nonobviousness. Pet. 70; *see generally* Prelim. Resp.

obviousness by employing “mere conclusory statements.” *In re Magnum Oil Tools Int’l, Ltd.*, 829 F.3d 1364, 1380 (Fed. Cir. 2016).

Instead, Petitioner must articulate a reason why a person of ordinary skill in the art would have combined or modified the prior art references. *In re NuVasive, Inc.*, 842 F.3d 1376, 1382 (Fed. Cir. 2016); *see also Metalcraft of Mayville, Inc. v. The Toro Co.*, 848 F.3d 1358, 1366 (Fed. Cir. 2017) (“In determining whether there would have been a motivation to combine prior art references to arrive at the claimed invention, it is insufficient to simply conclude the combination would have been obvious without identifying any reason why a person of skill in the art would have made the combination.”); *Belden Inc. v. Berk-Tek LLC*, 805 F.3d 1064, 1073 (Fed. Cir. 2015) (“[O]bviousness concerns whether a skilled artisan not only *could have made* but *would have been motivated to make* the combinations or modifications of prior art to arrive at the claimed invention.”) (citing *InTouch Techs., Inc. v. VGO Commc’ns, Inc.*, 751 F.3d 1327, 1352 (Fed. Cir. 2014)). In addition, the law also “requires that the skilled artisan would have perceived a reasonable expectation of success in making the invention in light of the prior art.” *Amgen v. F. Hoffman-La Roche Ltd.*, 580 F.3d 1340, 1362 (Fed. Cir. 2009) (citing *In re Kubin*, 561 F.3d 1351, 1360 (Fed. Cir. 2009)). However, “only a reasonable expectation of success, not a guarantee, is needed.” *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007); *In re Longi*, 759 F.2d 887, 897 (Fed. Cir. 1985) (“[A] reasonable expectation of success, not absolute predictability” supports a conclusion of obviousness).

At this preliminary stage, we determine whether the information presented shows a reasonable likelihood that Petitioner would prevail in

establishing that at least one of the challenged claims would have been anticipated by the proposed prior art.

We analyze the challenges presented in the Petition in accordance with the above-stated principles.

*B. Level of Ordinary Skill in the Art*

We review the grounds of unpatentability in view of the understanding of a person of ordinary skill in the art at the time of invention.

*Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). Petitioner contends

a [person of ordinary skill in the art] at the relevant time would have been a researcher interested in microfluidics with an advanced degree, *e.g.*, a Ph.D. or master's degree, in bioengineering, chemical engineering, chemistry, physics, mechanical or aeronautical engineering, or biochemistry; or a bachelor's degree and significant experience in the relevant field.

Pet. 8 (citing Ex. 1002 ¶¶ 54–56). Petitioner further asserts that a person of ordinary skill in the art “may have worked as part of a multidisciplinary team, which may have included a biochemist, biologist, or a PCR specialist.”

*Id.* Finally, Petitioner states that the prior art and background art “demonstrates information with which a [person of ordinary skill in the art] would have been familiar at the relevant time.” *Id.*

At this stage in the proceeding, Patent Owner does not address Petitioner's definition of the person of ordinary skill in the art. *See generally* Prelim. Resp.

In light of the record before us, and for purposes of this Decision, we adopt Petitioner's proposed definition of the level of ordinary skill in the art. We also find that the prior art itself is sufficient to demonstrate the level of ordinary skill in the art at the time of the invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001).



*C. Claim Construction*

There are no claim terms in dispute or that we need to construe for purposes of this decision. *See* Pet. 8–9; *see generally* Prelim. Resp.

*D. Petitioner’s challenges to claims 1–6, 8–10, 23*

Petitioner contends claims 1–5, 8–10, and 23 are unpatentable over Davies in view of Warren. Pet. 15. Petitioner also asserts that claims 1–5, 8–9, and 23 are unpatentable over Beer in view of Warren. *Id.* at 42. Petitioner additionally contends that either of Davies or Beer in combination with Warren and Chen would have rendered obvious the subject matter of claim 6. *Id.* at 37, 65. Petitioner directs us to portions of Davies, Warren, Beer, and Chen that purportedly teach or suggest each of the limitations in the challenged claims. *Id.* at 15–70. Petitioner also relies on the declaration testimony of Dr. Weigl to support its arguments. *See id.*

The parties’ dispute at this stage of the proceeding centers on whether a person of ordinary skill in the art would have had a reason to modify Davies to include the “plurality of different primer types” and “plurality of optically labeled probe types” taught by Warren and whether the person of ordinary skill in the art would have had a reasonable expectation of success in the combination. Accordingly, we focus our discussion below on whether Petitioner has shown that a person of ordinary skill in the art would have had reason to modify the prior art, which is dispositive. First, however, we provide a brief summary of Davies, Warren, and Beer.

*1. Davies (Ex. 1005)*

Davies discloses a method and device for performing digital PCR using “‘droplet-in-oil’ technology, wherein a sample is segmented in droplets placed to a continuous flow of carrier fluid through a microfluidic channel.” Ex. 1005 ¶ 7. The droplets contain “on average about one or

fewer copies of a target nucleic acid and reagents sufficient to perform a polymerase chain reaction.” *Id.* ¶ 10. The “droplets are fully wrapped in the carrier fluid [e.g., oil] throughout the reaction and detection.” *Id.* ¶¶ 7, 10. “The sample may be pre-mixed with the primer, or the primer may be added to the droplet . . . [or] the starting sample[s] are merged with a second set of droplets comprising one or more primers for the target nucleic acid.” *Id.* ¶ 40. The droplets in Davies’ method “have volumes of 0.1 p1–500 nl.” *Id.* ¶ 13. Davies “detect[s] the presence or absence of, and/or determin[es] the amount of, the amplified target nucleic acid in the droplets while in the flow.” *Id.* ¶¶ 12, 30.

2. *Warren (Ex. 1006)*

Warren describes a method using a microfluidic chip-based digital multiplex PCR assay, which “partition[s] individual cDNA molecules into discrete reaction chambers before PCT amplification.” Ex. 1006, 17807. In contrast to traditional PCR assays, “digital PCR[] quantitation relies on binary, positive/negative calls for each subreaction within the partitioned analyte, affording an absolute readout of DNA copy number with single-molecule resolution.” *Id.* Warren’s technique employs multiple primer pairs and different probes that target different target sequences. *Id.* at 17808. As a result, Warren “measure[s] the levels of two transcripts within every cell: a transcription factor, PU.1, and a housekeeping gene, GAPDH.” *Id.* According to Warren, the cDNA is quantitated in the digital PCR chip and a scan is produced, shown below in Figure 1a.

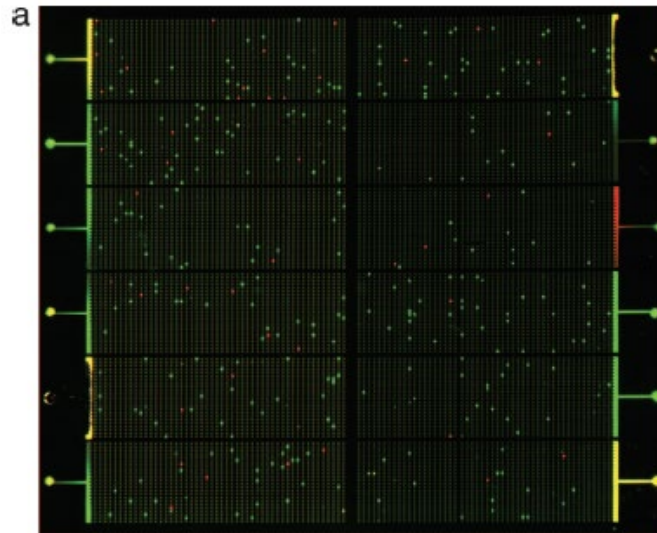


Figure 1a is “[a] PCR end-point scan of a chip” where “the FAM signal (GAPDH) is shown in green and the Cy5 signal (PU.1) is shown in red.” *Id.* at 17808.

### 3. *Beer (Ex. 1007)*

Beer discloses an on-chip instrument for picoliter droplet generation and PCR amplification and detection. Ex. 1007, 8471; *see also id* at 8472 (describing “real-time PCR in isolated picoliter droplets containing single-copy nucleic acids”). Beer explains that “[r]educing digital PCR reactor volumes . . . to the picoliter scale would allow earlier detection due to decreased diffusion distances, a wider range of sample concentrations, reduced reagent consumption, and improved statistics if all reactors are processed.” *Id.* at 8471–8472.

### 4. *Analysis*

Petitioner contends that the subject matter of claims 1–6, 8–10, and 23 of the ’310 patent would have been obvious over (1) Davies and Warren, (2) Beer and Warren, or (3) either combined with Chen. Pet. 15–42, 42–70. Patent Owner disagrees and focuses its argument on whether a person of ordinary skill in the art would have had reason to combine either Davies and

Warren or Beer and Warren as Petitioner contends. Prelim. Resp. 20–32. Patent Owner further asserts that the person of ordinary skill in the art would not have had a reasonable expectation of success in either combination. *Id.* at 32–41.

Below, we address whether Petitioner has sufficiently established that a person of ordinary skill in the art would have been motivated to combine Warren with Davies or Beer.

Petitioner’s allegations regarding the reasons to combine Davies and Warren are substantially similar to those for combining Beer and Warren. *Compare* Pet. 15–19, *with id.* at 43–46. Accordingly, we discuss Petitioner’s allegations regarding the reasons for combining Davies and Warren below. We also separately discuss any differences in Petitioner’s allegations that are relevant to the analysis of Beer and Warren.

Petitioner contends that “a [person of ordinary skill in the art] would have had good reason to employ the digital multiplex PCR approach taught by Warren in digital PCR droplets, as taught by Davies” because “both references are directed to quantify[ing] DNA by performing digital PCR using small partition reaction volumes, each comprising, on average, one or fewer target nucleotide sequences,” i.e., “to achieve their shared aim.” Pet. 17 (citing Ex. 1002 ¶ 106); *see also id.* at 43 (similar argument regarding reason to combine Beer and Warren).

Petitioner’s argument is not persuasive. Petitioner’s reasoning, while relevant to showing that the references *could* have been combined, i.e., that they may be analogous art, nevertheless falls short of establishing *what would have prompted* the ordinarily skilled artisan to make the proffered combination to yield the claimed method of detecting target sequences in a droplet including a plurality of different primer types and a plurality of

optically labeled probe types. *Wyers v. Master Lock Co.*, 616 F.3d 1231, 1238 (Fed. Cir. 2010); *see also In re Kahn*, 441 F.3d 977, 987–88 (Fed. Cir. 2006) (noting that the inquiry as to whether a person of ordinary skill in the art would have sought to combine the references “picks up where the analogous art test leaves off”).

Next, Petitioner alleges that a person skilled in the art would have had reason to combine the teachings of Davies and Warren “to obtain the benefits of droplet PCR combined with the benefits of using multiple different primer types in each reaction volume.” *Id.* at 17; *see also id.* at 44 (similar argument regarding reason to combine Beer and Warren). Specifically, the combination would allow “screening for multiple targets using the same stock solution in different partitions[, which] is more efficient, decreases the amount of the starting target sample needed, and reduces measurement noise” according to Warren, and to increase “throughput and ease of scalability” as Davies teaches. *Id.* at 17–18 (citing Ex. 1002 ¶¶ 106–108; Ex. 1006, 17807–17810; Ex. 1005 ¶¶ 5–13; Ex. 1010 ¶¶ 4–8); *see also id.* at 44–45 (similar argument regarding reason to combine Beer and Warren).

Petitioner’s argument is unconvincing. A “[d]etermination of obviousness can not be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention.” *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 546 (Fed. Cir. 1998). Instead, “[t]here must be a teaching or suggestion within the prior art, or within the field of the invention, to look to particular sources of information, to select particular elements, and to combine them in the way they are combined by the inventor.” *Id.*

Here, each of Davies and Warren describes different PCR processes having distinct advantages—Davies increases throughput and ease of scalability, whereas Warren allows for scanning multiple target sequences simultaneously, utilizes the same stock solution, and reduces the amount of starting sample needed. *See* Ex. 1005 ¶¶ 7–12; Ex. 1007, 8471; Ex. 1006, 17807–17810. Petitioner purports to combine Davies and Warren to achieve each of these distinct advantages in a single process. Pet. 17. Indeed, these are the same improvements the '310 patent identifies. *See* Ex. 1001, 1:33–2:64. For example, the '310 patent explains that

[m]ultiplexing primers in droplets enables the simultaneous increase in the number of PCR droplets while keeping the amount of input DNA the same or lower and generate the same or greater amplicon yield. This results in an overall increase in the amount of PCR positive droplets and amplicon yield without the consumption of more DNA.

*Id.* at 2:48–54. However, “[t]he invention must be viewed not after the blueprint has been drawn by the inventor, but as it would have been perceived in the state of the art that existed at the time the invention was made.” *Sensonic, Inc. v. Aerosonic Corp.*, 81 F.3d 1566, 1570 (Fed. Cir. 1996) (citing *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1138 (Fed. Cir. 1985)). Critically lacking from Petitioner’s analysis is what would have led the skilled artisan, in the absence of the '310 patent disclosure, to include multiple different primer and optical probe types in Davies’s method. *See* Pet. 17–18; Ex. 1002 ¶¶ 106–108. Only after review of the '310 patent disclosure does a reason to combine become clear and the use of hindsight become apparent. “[T]he simplicity of new inventions is oftentimes the very thing that is not obvious before they are made.” *In re Van Wanderham*, 378 F.2d 981, 987 (CCPA 1967). Thus, on this record,

Petitioner has failed to identify what would have suggested to the ordinarily skilled artisan the desirability of adding multiple primer types and multiple probe types to Davies's droplets.

Petitioner additionally contends that “applying Warren’s methodology to droplets amounted to a simple substitution of one known element—a droplet—for another—a microvial—to obtain predictable results.” Pet. 19 (citing Ex. 1002 ¶ 110); *see also id.* at 45–46 (similar argument regarding reason to combine Beer and Warren). According to Petitioner, both Davies and Warren utilize small reaction volumes and Warren teaches “that using diluted partitions with tiny reaction volumes mitigates problems otherwise observed in multiplex PCR reactions.” *Id.* at 18; *see id.* at 45 (same arguments as to Beer and Warren). Petitioner explains that “[e]ven Bio-Rad readily admits that ‘droplets serve essentially the same function as individual test tubes or wells in a plate in which the PCR reaction takes place.’” *Id.* at 19 (citing Ex. 1017, 3; Ex. 1001, 5:48–50, 8:5–18); *see also id.* at 46 (similar argument regarding reason to combine Beer and Warren).

We are similarly unpersuaded by Petitioner’s arguments relating to a simple substitution of elements. A patent claim may be obvious where “a patent claims a structure already known in the prior art that is altered by the mere substitution of one element for another known in the field,” if the combination must yield a predictable result. *KSR*, 550 U.S. 398, 416 (2007) (citing *United States v. Adams*, 383 U.S. 38, 50–51 (1966)). The combination Petitioner asserts, however, is not a simple substitution of a droplet for a microvial as a reaction vessel to contain an analyte. Rather, Petitioner proposes to substitute the *contents* of Warren’s microvial—containing a plurality of different primer types and plurality of optically labeled probe types—for the *contents* of Davies’s droplet—containing a

single primer type and single optically labeled probe type. *See* Pet. 23–25. Neither Petitioner nor Dr. Weigl directs our attention to any record evidence or argument to suggest that a person of ordinary skill in the art would have understood the *plurality* of different primer and probe types in Warren’s microvial to be a known substitute for the *single* primer and probe type in Davies’s droplet. *See generally* Pet.; Ex. 1002.

With respect to the combination of Beer and Warren, Petitioner advances an additional separate and distinct argument. *Id.* at 43–44. Petitioner explains that “Beer cites to Ottesen<sup>6</sup> as an example of a dilute digital PCR assay that would benefit from Beer’s picoliter-sized droplet technique.” *Id.* (citing Ex. 1007, 8471; Ex. 1008; Ex. 1002 ¶ 213; Ex. 1011). Ottesen was published by the Quake group, the same group that published Warren. *Id.* Petitioner, relying on the testimony of Dr. Weigl, reasons that a person of ordinary skill in the art “would have understood Beer’s citation and description of Ottesen, as well as its proposed improvements thereto, as a suggestion to employ multiple primer types and probes each specific to a different target sequence, as taught by Ottesen and as taught in Warren, in Beer’s dilute, picoliter-scale PCR droplets.” *Id.* at 44 (citing Ex. 1002 ¶¶ 213–214).

Petitioner’s arguments based on Ottesen are unpersuasive. Beer does not reference Ottesen “as an example of a dilute digital PCR assay that would benefit from Beer’s picoliter-sized droplet technique,” as Petitioner contends. *Id.* at 43–44. Rather, Beer cites to Ottesen to show that digital

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<sup>6</sup> Ottesen et al., *Microfluidic Digital PCR Enables Multigene Analysis of Individual Environmental Bacteria*, 314 *Science* 1464 (2006) (Ex. 1008, “Ottesen”).



PCR techniques have evolved and permit use of smaller sample volumes.

Ex. 1007, 8471. Specifically, Beer states that

[t]he advantages of digital PCR are well-known, principally the ability to detect a single copy of target nucleic acid in a complex background, and it has been used to detect a low concentration of mutations in alleles associated with colorectal cancer. . . . The method has since evolved with commercial arrays, Taqman-based FRET probes, smaller sample volumes, and the 40-cycle PCR protocol; for example, single-molecule sensitivity has recently been shown in 6.25-nL reaction chambers for multigene analysis of individual environmental bacteria.

*Id.* Beer continues to focus its discussion on sample size stating that further reducing “reactor volumes another [three] orders of magnitude to the picoliter scale would allow earlier detection due to decreased diffusion distances, a wider range of sample concentrations, reduced reagent consumption, and improved statistics if all reactors are processed.” *Id.* at 8471–8472. Further, Beer does not incorporate Ottesen’s teachings by reference nor does Beer discuss Ottesen further.<sup>7</sup> *See generally* Ex. 1007. As a result, Dr. Weigl’s testimony that simply “[b]y citing Ottesen, Beer thus suggested employing digital multiplex PCR in Beer’s digital PCR droplets” (Ex. 1002 ¶ 213), is conclusory and unsupported. *KSR*, 550 U.S. at 418 (quoting *Kahn*, 441 F.3d at 988) (explaining that a conclusion of obviousness “cannot be sustained by mere conclusory statements”).

On this record, Petitioner does not show sufficiently, that a person of ordinary skill would have had a reason combine the individual elements of Davies and Warren or Beer and Warren in the way the ’310 patent claims. Accordingly, we determine Petitioner has not established a reasonable

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<sup>7</sup> None of Petitioner’s challenges to the claims of the ’310 patent include Ottesen as a prior art reference. *See* Pet. 5.

likelihood that it would prevail in its assertion that claims 1–6, 8–10, and 23 would have been obvious over Davies and Warren or Beer and Warren, with or without Chen.

### III. CONCLUSION

For the foregoing reasons, we conclude that the information presented in the Petition and supporting evidence fails to establish a reasonable likelihood that Petitioner would prevail with respect to demonstrating at least one claim of the '310 patent is unpatentable. Accordingly, we decline to institute an *inter partes* review.

### IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that the Petition is denied and no trial is instituted.

IPR2021-00212  
Patent 9,127,310 B2

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