

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

DROPWORKS, INC.,
Petitioner,

v.

THE UNIVERSITY OF CHICAGO,
Patent Owner.

Case IPR2021-00100
Patent 8,304,193 B2

Before SHERIDAN K. SNEDDEN, CHRISTOPHER L. CRUMBLEY, and
WESLEY B. DERRICK, *Administrative Patent Judges*.

CRUMBLEY, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
35 U.S.C. §§ 314, 325(d)

I. INTRODUCTION

Dropworks, Inc. (“Petitioner”) filed a Petition requesting an *inter partes* review of claims 1–9 and 11 of U.S. Patent No. 8,304,193 B2 (Ex. 1001, “the ’193 patent”). Paper 2 (“Pet.”). The assignee of the ’193 patent, the University of Chicago (“Patent Owner”), filed a Preliminary Response to the Petition. Paper 6 (“Prelim. Resp.”). Pursuant to Board authorization, Petitioner filed a Pre-Institution Reply (Paper 7, “Reply”), and Patent Owner filed a Pre-Institution Sur-Reply (Paper 8, “Sur-Reply”), limited to addressing issues related to Patent Owner’s argument that institution should be denied under 35 U.S.C. § 325(d).

Institution of an *inter partes* review is authorized by statute when “the information presented in the petition . . . shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” 35 U.S.C. § 314(a) (2018). Nevertheless, we may deny institution when “the same or substantially the same prior art or arguments previously were presented to the Office. 35 U.S.C. § 325(d) (2018). Upon consideration of the parties’ briefing and the evidence of record, we determine that it is appropriate to exercise our discretion to deny institution of trial under § 325(d). Accordingly, we decline to institute an *inter partes* review.

A. Related Proceedings

The parties identify several related proceedings involving the ’193 patent. Patent Owner previously asserted the ’193 patent against an unrelated party, 10X Genomics Inc., in an action for patent infringement in district court. *Bio-Rad v. 10X Genomics, Inc.*, Case No. 15-cv-152-RGA (D. Del.). Following trial, the jury found the ’193 patent not invalid, and the

court denied a post-trial motion for judgment as a matter of law that the '193 patent is invalid. Ex. 1035, 2.¹ 10X Genomics also challenged the patentability of the claims of the '193 patent in a petition for *inter partes* review; the Board denied institution of trial. IPR2015-01163, Paper 14; Pet. 3. Following that denial, 10X Genomics also requested *ex parte* reexamination of claims 1–14 of the '193 patent, which resulted in a reexamination certificate confirming the patentability of all claims. Pet. 4; Ex. 1028, 7757–59.²

Patent Owner has asserted the '193 patent against Petitioner in *Bio-Rad Laboratories, Inc. et al. v. Dropworks, Inc.*, Case No. 1:20-cv-00506-RGA (D. Del.). Pet. 3; Paper 3, 1.

B. The '193 Patent (Ex. 1001)

The '193 patent, entitled “Method for Conducting an Autocatalytic Reaction in Plugs in a Microfluidic System,” issued November 6, 2012. Ex. 1001, codes (45), (54). Microfluidic systems transport fluids through networks of channels, typically having micrometer dimensions. *Id.* at 1:20–22. According to the patent, the main advantages of microfluidic systems are high speed and low consumption of reagents. *Id.* at 1:25–26. The

¹ On appeal, the Court of Appeals for the Federal Circuit reversed the court's claim construction as to the '193 patent and vacated the judgment of infringement. Ex. 1035, 2. The jury's findings on validity do not appear to have been appealed.

² Petitioner provided the file history of the reexamination application as Exhibit 1028, a multi-part PDF totaling 7759 pages. The citations in the Petition to Ex. 1028 do not appear to match the page numbers of the exhibit itself, however. *Compare* Pet. 4 (citing to page 3 of Ex. 1028 as the reexamination certificate), *with* Ex. 1028, 7757 (reexamination certificate).

microfluidic systems may be used for various chemical and biochemical processes, including autocatalytic reactions, such as the polymerase chain reaction (PCR). *Id.* at 44:38–61.

Rather than rely on laminar flow of liquids through microfluidic channels, the '193 patent describes using microfluidic droplets, or “plugs” in the system. *Id.* at 2:54–61, 3:39–45, 17:38–43, Figs. 2A-1, 2A-2. Figure 2A-2, an embodiment of the system, is annotated and reproduced below:

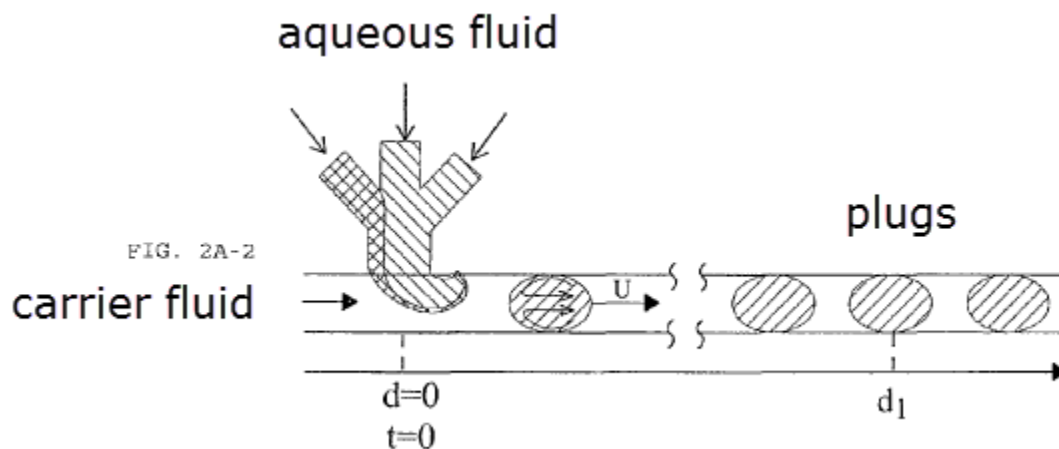


Figure 2A-2 depicts the formation of plugs, where the aqueous fluid containing a substrate and reagents enters a channel with an immiscible carrier fluid, such as an oil, to form a series of plugs. *Id.* at 17:38–43. The plug volumes, which are dependent on channel size, can range from about 1 femtoliter to about 250 nanoliters. *Id.* at 19:45–54.

C. The Challenged Claims

Petitioner challenges claims 1–9 and 11 of the '193 patent. Claim 1, the sole independent claim, is illustrative of the subject matter at issue and is reproduced below:

1. A method for conducting an autocatalytic reaction in plugs in a microfluidic system, comprising the steps of:
 - providing the microfluidic system comprising at least two channels having at least one junction;
 - flowing an aqueous fluid containing at least one substrate molecule and reagents for conducting an autocatalytic reaction through a first channel of the at least two channels;
 - flowing an oil through the second channel of the at least two channels;
 - forming at least one plug of the aqueous fluid containing the at least one substrate molecule and reagents by partitioning the aqueous fluid with the flowing oil at the junction of the at least two channels, the plug being substantially surrounded by an oil flowing through the channel, wherein the at least one plug comprises at least one substrate molecule and reagents for conducting an autocatalytic reaction with the at least one substrate molecule; and
 - providing conditions suitable for the autocatalytic reaction in the at least one plug such that the at least one substrate molecule is amplified.

Ex. 1001, 78:8–29.

D. The Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–9 and 11 of the '193 patent on the following grounds:

Claims Challenged	35 U.S.C. §³	References
1–9, 11	103(a)	Quake, ⁴ Holliger ⁵
1–9, 11	103(a)	Quake, Holliger, and Shaw Stewart ⁶
1–9, 11	103(a)	Quake and Litborn ⁷
1–9, 11	103(a)	Quake, Litborn, and Shaw Stewart

Petitioner asserts that all references asserted in the grounds of unpatentability are prior art as of the earliest claimed priority date of May 9, 2002. Pet. 7. Patent Owner does not contest the prior art status of any of the references in its Preliminary Response.

³ The Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) (“AIA”), included revisions to 35 U.S.C. §§ 102 and 103 that became effective on March 16, 2013. Because the '193 patent issued from an application filed before March 16, 2013, we apply the pre-AIA versions of the statutory basis for unpatentability.

⁴ International Patent Application Publication No. WO 02/23163 to Quake et al., published March 21, 2002 (Ex. 1005).

⁵ International Patent Application Publication No. WO 02/22869 to Holliger et al., published March 21, 2002 (Ex. 1006).

⁶ International Patent Application Publication No. WO 84/02000 to Shaw Stewart, published May 24, 1984 (Ex. 1008).

⁷ Litborn et al., “Synthesis and Analysis of Chemical Components in Nanoscale,” MICRO TOTAL ANALYSIS SYSTEMS 2000, 447–454 (2000).

II. DENIAL UNDER 35 U.S.C. § 325(d)

As noted above, the patentability of the '193 patent has been analyzed in numerous proceedings before the Office, including during initial examination, in a preliminary *inter partes* review proceeding, and in an *ex parte* reexamination. For this reason, Patent Owner asks that we exercise our discretion under 35 U.S.C. § 325(d) to deny institution of trial in this proceeding without reaching the merits of Petitioner's challenges to the claims. Prelim. Resp. 25–32. Upon review, we find Patent Owner's arguments persuasive, and exercise our discretion to deny institution of trial.

A. Discretion to Deny Institution

We have discretion to deny review when “the same or substantially the same prior art or arguments previously were presented to the Office.” 35 U.S.C. § 325(d). In that respect, section 325(d) provides that the Director may elect not to institute a proceeding if the challenge to the patent is based on matters previously presented to the Office.⁸ *Advanced Bionics, LLC v. Med-El Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 7 (PTAB Feb. 13, 2020) (precedential) (“*Advanced Bionics*”).

In evaluating the exercise of discretion to deny institution under § 325(d), the Board applies a two-part framework: (1) first, we determine whether the same or substantially the same art previously was presented to the Office, or whether the same or substantially the same arguments previously were presented to the Office; and (2) if either condition of the first part of the framework is satisfied, we examine whether the petitioner

⁸ By regulation, the Director has delegated the decision whether to institute trial to the Board. 37 C.F.R. § 42.4(a) (2020).

has demonstrated that the Office erred in a manner material to the patentability of challenged claims. *Advanced Bionics*, 8.

In applying the two-part framework, we consider several non-exclusive factors, including:

- (a) the similarities and material differences between the asserted art and the prior art involved during examination;
- (b) the cumulative nature of the asserted art and the prior art evaluated during examination;
- (c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection;
- (d) the extent of the overlap between the arguments made during examination and the manner in which petitioner relies on the prior art or patent owner distinguishes the prior art;
- (e) whether petitioner has pointed out sufficiently how the examiner erred in its evaluation of the asserted prior art; and
- (f) the extent to which additional evidence and facts presented in the petition warrant reconsideration of the prior art or arguments.

Becton, Dickinson & Co. v. B. Braun Melsungen AG, IPR2017-01586, Paper 8 at 17–18 (PTAB Dec. 15, 2017) (precedential as to Section III.C.5, first paragraph) (“*Becton, Dickinson*”).

Factors (a), (b), and (d) of the *Becton, Dickinson* factors relate to whether the art or arguments presented in the petition are the same or substantially the same as those previously presented to the Office. *Advanced Bionics*, 10. Factors (c), (e), and (f) “relate to whether the petitioner has demonstrated a material error by the Office” in its prior consideration of that art or arguments. *Id.* Only if the same or substantially the same art or arguments were previously presented to the Office do we then consider whether petitioner has demonstrated a material error by the Office. *Id.* “At

bottom, this framework reflects a commitment to defer to previous Office evaluations of the evidence of record unless material error is shown.” *Id.* at 9.

B. Same or Substantially the Same Art or Arguments

We first consider whether Petitioner has asserted substantially the same art or arguments presented to the Office during initial examination, the prior *inter partes* review petition, or *ex parte* reexamination. *Advanced Bionics*, 8. For the following reasons, we conclude that Petitioner has done so here.

Patent Owner contends that each of the prior proceedings before the Office involved Quake,⁹ the primary reference relied upon in the instant Petition. Prelim. Resp. 27. The jury trial in the District of Delaware also allegedly involved Quake as “the primary reference.” *Id.* Although Patent Owner acknowledges that the instant Petition asserts new secondary references, it contends these new references fail to address the previously-identified shortcomings in Quake and are applied under a rationale identical to those asserted in the prior challenges to the patent. *Id.* at 28–29. Patent Owner characterizes this rationale as “identify[ing] a reference that includes a disclosure of PCR and argu[ing] that the skilled artisan would be

⁹ We note that the version of Quake identified during examination and asserted in the prior *inter partes* review was the published US patent application US 2002/0058332 A1 (Ex. 1029), whereas the *ex parte* reexamination and the present Petition involve the PCT counterpart application (Ex. 1005). Neither party identifies any material difference between the disclosures of the two documents, however, and we will treat them interchangeably.

motivated to combine that disclosure with Quake to do PCR in droplets.” *Id.* at 29.

Petitioner does not address the fact that Quake was considered in the prior proceedings, or the degree to which the grounds in the instant case rely on the disclosures of Quake. Rather, Petitioner argues that the secondary references relied on in the instant Petition were not before the Office in the previous proceedings, and that they are sufficiently distinguishable from the previously-considered art that it cannot be said that the Petition presents substantially the same art or arguments as the preceding cases. Reply 2–3. Specifically, Petitioner contends that each of Holliger, Litborn, and Schneegaß¹⁰ “disclose successful (i.e., actual reduction to practice) PCR amplification in microscopic w/o (water in oil) droplets” that makes the references “materially different” in that they directly disprove prior statements made by the Patent Owner to the Office. *Id.* at 1–2. Petitioner contests Patent Owner’s characterization of the newly-cited secondary references as merely cumulative to the art presented to the Office in prior proceedings. *Id.* at 3–4.

There is no question that Quake is central to every ground of unpatentability set forth in the Petition. For example, in the first ground, Petitioner relies on Quake to teach all but one of the limitations of claim 1: a microfluidic system (Pet. 30–31); flowing an aqueous fluid (*id.* at 31–33); flowing an oil (*id.* at 33–34); and forming at least one plug . . . substantially

¹⁰ Schneegaß, Ivonne et al., “Flow-through Polymerase Chain Reactions in Chip Thermocyclers,” 82 REV. MOL. BIOTECH. 101–121 (2001) (Ex. 1009). Petitioner does not rely on Schneegaß as the basis for a ground of unpatentability, but does cite it as evidence of the background knowledge of a person of ordinary skill in the art. Pet. 21–22.

surrounded by an oil (*id.* at 34–38). The only limitation that requires reliance on a secondary reference is “providing conditions suitable for the autocatalytic reaction . . . such that the at least one substrate molecule is amplified.” *Id.* at 39–41. But even with respect to this limitation, Petitioner contends that Quake discloses conditions suitable for PCR amplification. *Id.* Similarly, for every challenged dependent claim, Petitioner primarily relies on Quake, with some additional teachings provided by the secondary references. *Id.* at 42–52.

We note that this is not a case where Quake was simply a peripheral or secondary reference in the prior proceedings before the Office, either. During prosecution, Quake was directly cited in the Examiner’s Notice of Allowance. Ex. 1004, 282–83. Quake was a part of every ground of unpatentability presented to the Office in the prior *inter partes* review petition. Ex. 1027, 5. And in the reexamination, the Examiner rejected all claims over a combination in which Quake allegedly disclosed all claim elements except conditions suitable for an autocatalytic reaction, similar to the grounds advanced in the present Petition. Ex. 1028, 5856–62.

In determining whether arguments asserted in a petition are substantially the same as those presented to the Office in a prior proceeding, we are to look to “the extent of the overlap between the arguments made” in the prior proceeding, and “the manner in which petitioner relies on the prior art.” *Becton, Dickinson*, 17–18; *see Advanced Bionics*, 10 (“this factor more broadly provides guidance as to whether the arguments presented in the petition are ‘the same or substantially the same’ as the arguments previously presented to the Office”). In this case, the manner in which Petitioner has relied on Quake is very instructive: Quake is the central focus of each of

Petitioner's patentability challenges, after the same reference was also central to the prior proceedings before the Office. Indeed, as discussed above, the reference is relied on to teach almost every element of the challenged claims, in the same "manner" as the reexamination rejection.

We also look to the "material differences between the asserted art" and the art in the prior proceedings, which involves consideration of the degree to which any newly-cited references are cumulative to the art cited previously. *Becton, Dickinson*, 17–18; see *Advanced Bionics*, 10 ("these factors more broadly provide guidance as to whether the art presented in the petition is the 'same or substantially the same' as the prior art previously presented to the Office"). Here, again, we are not convinced that the newly-cited references that Petitioner contends distinguish this proceeding from prior proceedings—namely, Holliger, Litborn, and Schneegaß—are in fact distinguishable in any material way.¹¹ Petitioner relies on these references to supply teachings of conditions suitable for performing PCR in microscopic quantities, in water-oil droplet systems. Pet. 39–41, 65–67; Reply 1 ("[E]ach of Holliger, Litborn, and Schneegaß disclose successful (i.e., actual reduction to practice) PCR amplification in microscopic w/o (water in oil) droplets."). But previously-presented secondary references, such as Kopp (during the reexamination) or Haff (in the *inter partes* review

¹¹ As noted above, the Petition also includes grounds involving Shaw Stewart as a secondary reference. Pet. 53–54, 70–71. Petitioner does not rely on Shaw Stewart as distinguishing the art cited in the Petition from that previously presented to the Office. In any event, we observe that Shaw Stewart was explicitly relied on as part of the basis for the Examiner's rejection of the claims during the reexamination. Ex. 1028, 5858.

petition), were relied on for the same proposition. *See* Ex. 1028, 5858; Ex. 1027, 13–14.

Petitioner’s attempts to distinguish the new secondary references from Kopp and Haff are unconvincing. According to Petitioner, neither previously-provided reference describes the use of PCR in microscopic aqueous volumes using “traditional hydrocarbons” such as those used in Quake. Reply 1. And Petitioner indicates that both Haff and Kopp were not droplet systems, but instead used air or aqueous blanks to separate slugs of reaction volumes. *Id.* at 1–2. But, as Patent Owner argues, the newly-cited references allegedly suffer from exactly the same shortcoming, in that none of Holliger, Litborn, or Schneegaß disclose performing PCR in a droplet system. Prelim. Resp. 36–39; Sur-Reply 2–4. For example, Patent Owner observes that Holliger performs its PCR method in an emulsion containing millions of various-sized vesicles, and is therefore even further afield from Quake than the previously-considered references. Sur-Reply 2. And Litborn and Schneegaß allegedly suffer from the same faults as Haff and Kopp, in that they are not droplet PCR reactions, but instead disclose segmented-flow systems. *Id.* at 3–4. On this record, Patent Owner’s arguments appear well-supported, and we agree that the new secondary references do not appear to disclose performing PCR in water-oil droplets, as Petitioner contends.

Accordingly, we agree that Petitioner has not sufficiently distinguished the new secondary references from those previously presented to the Office. To be clear, our conclusion is not that the newly-cited references of Holliger, Litborn, and Schneegaß are entirely cumulative of the references previously cited to the Office, such as Haff or Kopp. But our

analysis under § 325(d) does not require that the teachings be identical or entirely cumulative, only that they are substantially the same. And here, Petitioner advances grounds of unpatentability that are structured substantially identically to those previously considered by the Office, and relies on prior art that is similar to the art that the Office has considered on multiple prior occasions. We, therefore, conclude that the art and arguments presented in the Petition are substantially the same as those previously presented to the Office.

C. Material Error by the Office

Even if a Petition presents substantially the same art or arguments as previously presented to the Office, we may nevertheless institute trial if Petitioner demonstrates that the Office erred in its prior consideration, in a manner that is material to the patentability of the challenged claims. *Advanced Bionics*, 8, 10; *see Becton, Dickinson*, 24. For the following reasons, we cannot conclude that Petitioner has demonstrated such error in this case.

Petitioner addresses three potential errors in its Petition. First, Petitioner contends that the '193 patent issued based on the Examiner's "erroneous belief . . . that the Quake reference did not disclose droplet formation by flowing a continuous stream in aqueous fluid into a continuous stream of oil." Pet. 74. But, as Petitioner concedes, to the extent there was any error in the original allowance of the patent, it was subsequently "corrected . . . by Patent Owner and the reexamination Examiner." *Id.* (citing Ex. 1026 (Preliminary Response in IPR2015-01163), 13–14;

Ex. 1028, 1915–16¹²). Indeed, during reexamination, the Examiner observed that Quake discloses “[a]t least one plug of the aqueous fluid . . . formed by partitioning the aqueous fluid with the flowing oil at the junction of the at least two channels.” Ex. 1028, 5859. Even if Petitioner were correct that the Office erred during initial examination and issued the ’193 patent based on the Examiner’s mistaken belief regarding Quake, such an error would not be material to the patentability of the challenged claims, as it was subsequently addressed by the reexamination and the Examiner’s correct statement regarding the disclosure of Quake. Accordingly, the alleged error during initial examination identified by Petitioner cannot be material to the patentability of the challenged claims.

Second, Petitioner identifies the Board’s denial of institution of *inter partes* review based on the 10X Genomics’ prior petition in IPR2015-01163. Pet. 76. But Petitioner does not even assert any potential error in the Board’s analysis in that case. There, we concluded that the petition failed to sufficiently establish that a person of ordinary skill in the art would have believed there to be a reasonable expectation of success of combining Haff’s PCR system with Quake’s microfluidic system to successfully amplify a substrate molecule in a droplet. Ex. 1027, 15–17. Petitioner only argues that it should not be prejudiced by “[a] shortcoming of a completely different party.” Pet. 74. Our analysis under § 325(d), however, does not ask whether the same or substantially the same art or arguments were presented *by the same party*, but whether the Office has, in general, been

¹² Again, Petitioner’s pin citation to the reexamination file history appears to be in error, as pages 1915–16 are from the middle of the District Court’s claim construction order, not a statement by the Examiner.

presented with such art or arguments. Indeed, in the typical case involving § 325(d), the Board takes into account the art and arguments that were before the Office during original prosecution, a process that did not involve the petitioner. “At bottom, [the § 325(d)] framework reflects a commitment to defer to previous Office evaluations of the evidence of record unless material error is shown.” *Advanced Bionics*, 9.

Finally, Petitioner argues that, during reexamination, allowance of the claims was achieved due to Patent Owner’s erroneous argument that the “traditional hydrocarbons” used in Quake would be incompatible, making PCR impossible in the combined system of Quake and Kopp. Pet. 74–75. According to Petitioner, if the Office had been made aware of the art asserted in the current Petition, which allegedly shows “successful DNA PCR amplification in microfluidic [water/oil] droplets,” it would not have accepted Petitioner’s argument and confirmed the claims. *Id.* at 75.

Patent Owner’s response is that the newly-cited prior art references do not demonstrate material error during the reexamination, because none of the new disclosures call into question the conclusion that Petitioner identifies as allegedly erroneous: “that PCR could not be performed in water-in-oil emulsions where the oil comprised standard hydrocarbons such as mineral oil,” such as the system in Quake. Prelim. Resp. 30–31. According to Patent Owner, Litborn and Schneegaß do not pertain to droplets, and therefore cannot be found to teach that PCR can be performed in water-in-oil droplets in standard hydrocarbons. *Id.* at 31. Furthermore, Holliger is not a microfluidic system, and Patent Owner contends that given the varying sizes of its vesicles there is no reason to conclude that PCR was successfully

performed in vesicles having the same size as those involved in the droplet system of Quake. *Id.*

Our analysis of whether Petitioner has made a sufficient showing of material error takes into account the “extent to which the asserted art was evaluated” during the prior proceedings, “including whether the prior art was the basis for rejection.” *Becton, Dickinson*, 17–18. Here, there is no question that the Quake reference has been evaluated extensively by the Office: first during prosecution, then again before the Board in the first *inter partes* review petition, then again before the Office during the reexamination. Though the newly-cited secondary references of Holliger, Litborn, and Schneegaß have not themselves been evaluated in any of these proceedings, we have already found them to be substantially similar to previously-considered art, and that the proceedings raised substantially similar arguments. And that substantially similar art has been extensively considered in at least the decision denying the prior *inter partes* review and the reexamination.

We also take into account whether a petitioner has sufficiently identified an error, and the degree to which the newly-presented evidence warrants reconsideration of that alleged error. *Becton, Dickinson*, 17–18. Given how extensively the patentability of the challenged claims has been considered in prior proceedings before the Office over nearly identical art and arguments, the evidence that the error “warrants reconsideration” must be sufficient to outweigh the multiple prior considerations. In other words, because factor (c) of *Becton, Dickinson* weighs so heavily against a finding of material error, Petitioner’s showing under either factor (e) or (f) must weigh sufficiently in the other direction.

Petitioner has not made such a showing. Notably, the reexamination Examiner's findings in the Reasons for Allowance relied on the testimony from Dr. Samuel Sia that "instead of teaching biocompatible fluorinated oils and fluorosurfactants, Quake teaches traditional hydrocarbons," which would make any droplet system unsuitable for PCR. Ex. 2005, 4–5 (citing Sia Declaration ¶¶ 91–93 (Ex. 1028, 5950–51)). In his testimony, Dr. Sia states that Quake is not concerned with the issues associated with the droplet/carrier-fluid interface that would need to be addressed in order to carry out PCR in a droplet, and which distinguish droplet-based systems from those that use segmented flow. Ex. 1028, 5950–51. This is due to the fact that, because the droplets are substantially surrounded by the carrier fluid, and are so small, they have a high surface-to-volume ratio, and thus interactions at the droplet/carrier-fluid interface must be considered. *Id.* at 5944–45.

Although Petitioner submitted a declaration from its expert witness Dr. Carl D. Meinhart (Ex. 1002), his testimony does not directly address Dr. Sia's. Instead, Petitioner presented us with references such as Holliger, Litborn, and Schneegaß that allegedly demonstrate Dr. Sia's testimony to be in error. Pet. 75 ("Had the Office considered the asserted teachings of any of Holliger, Litborn, or Schneegaß, which actively contradict Patent Owner's arguments, the challenged claims would not have issued or would not have been confirmed."). We are not convinced. At best, Litborn and Schneegaß may contain references to droplet systems, but reasonably can be interpreted to pertain primarily to segmented flow systems where the aqueous phase is not substantially surrounded by the carrier fluid. For example, Litborn Figure 6B shows a "droplet" having significant contact

between aqueous phase and channel wall, and discusses conducting PCR only in system where samples are “interspaced” with hydrocarbon. *See* Ex. 1007, 452–53. And Holliger is not a microfluidic system at all, but rather an emulsion PCR method. *See* Ex. 1006, 59. We, therefore, find the statements in these references as to the types of oils are suitable for performing PCR in their systems to be of limited applicability in evaluating the testimony of Dr. Sia or the conclusions of the Examiner during reexamination. They certainly do not sufficiently demonstrate that the multiple prior evaluations of the validity of the claims warrant reconsideration.

III. CONCLUSION

As discussed above, the patentability of the ’193 patent has been considered on numerous occasions by the Office. All of these proceedings focused heavily on Quake, the primary prior art reference cited in the instant Petition. In these circumstances, Petitioner’s arguments are insufficient to show material error by the Office, and we are unwilling to subject the ’193 patent, and Patent Owner, to yet another proceeding before the Office. Such an outcome respects our “commitment to defer to previous Office evaluations of the evidence of record unless material error is shown.” *Advanced Bionics*, 9. For these reasons, we believe it is appropriate to exercise our discretion to deny institution of trial in this proceeding.

IV. ORDER

In consideration of the foregoing, it is hereby ORDERED that the Petition is *denied* and no *inter partes* review trial is instituted.

IPR2021-00100
Patent 8,304,193 B2

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