

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

10X GENOMICS, INC.,
Petitioner,

v.

THE UNIVERSITY OF CHICAGO,
Patent Owner.

Case IPR2015-01158
Patent 8,329,407 B2

Before DONNA M. PRAISS, CHRISTOPHER L. CRUMBLEY, and
TINA E. HULSE, *Administrative Patent Judges*.

PRAISS, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

A. Background

10X Genomics, Inc. (“Petitioner”) filed a Petition to institute an *inter partes* review of claims 1–13 of U.S. Patent No. 8,329,407 B2 (“the ’407 patent”). Paper 2 (“Pet.”). University of Chicago (“Patent Owner”) timely filed a Preliminary Response. Paper 9 (“Prelim. Resp.”).

We have authority to determine whether to institute an *inter partes* review under 35 U.S.C. § 314 and 37 C.F.R. § 42.4(a). Based on the record before us, we are not persuaded that the information presented in the Petition demonstrates a reasonable likelihood that Petitioner will prevail in proving that at least one challenged claim would have been obvious under 35 U.S.C. § 103(a) based on the cited references. Accordingly, we decline to institute an *inter partes* review.

B. Related Proceedings

In addition to this Petition, Petitioner has filed five Petitions challenging the patentability of related U.S. Patent Nos. 8,822,148, 8,889,083, 8,273,573, 8,304,193, and 7,129,091 in IPR2015-01156, IPR2015-01157, IPR2015-01162, IPR2015-01163, and IPR2015-01560, respectively.¹ See Pet. 55; Prelim. Resp. 5. Petitioner states that the ’407 patent is presently asserted against Petitioner in *RainDance Techs., Inc. v. 10X Genomics, Inc.*, Civil Action No. 1:15-cv-00152-RGA (D. Del.) filed February 2, 2015. Pet. 55; Paper 6. Raindance Technologies, Inc. is a licensee of the ’407 patent. Pet. 50; Prelim. Resp. 47; Paper 13.²

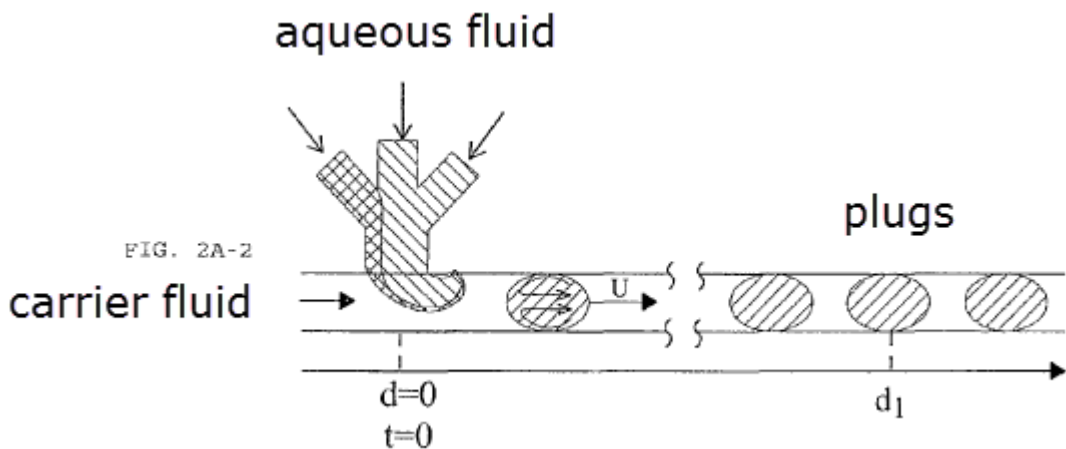
¹ Each of the challenged patents issued from a continuation or a continuation-in-part of U.S. Patent 7,129,091.

² Petitioner refers to Raindance Technologies, Inc. as the exclusive licensee of the ’407 patent (Pet. 50), however, Patent Owner refers to the ’407 patent

C. The '407 Patent

The '407 patent (Ex. 1001), titled “METHOD FOR CONDUCTING REACTIONS INVOLVING BIOLOGICAL MOLECULES IN PLUGS IN A MICROFLUIDIC SYSTEM,” generally relates to methods “for forming plugs, generating gradients in a series of plugs, varying the concentration of reagents inside plugs, rapid mixing in plugs, and scaling of mixing times.” Ex. 1001, 12:1–5. Applications for the method of the invention include “particle separation/sorting, synthesis, investigation of nonlinear and stochastic systems, nonlinear amplification using unstable autocatalytic mixtures, use of stochastic chemical systems for chemical amplification, kinetic measurements, time control of processes, increasing the dynamic range of kinetic measurements, ultrafast measurements, crystallization of proteins and dynamic control of surface chemistry” in addition to “a wide-range of other applications.” *Id.* at 12:13–21.

Figure 2A-2, an embodiment of the microfluidic plug system, is annotated and reproduced below:



among other patents being “licensed by RainDance” (Prelim. Resp. 47) and Raindance Technologies, Inc. as “a licensee” of the '407 patent (Paper 13).

Figure 2A-2 depicts the formation of plugs in laminar flow (U is the flow velocity), 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 18:26–35. The plug volumes, which are dependent on channel size, can range from about 1 femtoliter to about 250 nanoliters. *Id.* at 20:21–30.

In a preferred scheme, the plug-fluids initially coflow before coming into contact with the carrier fluid and the middle aqueous plug-fluid “preferably initially separates the two other aqueous plug-fluids before the aqueous plug fluids come into contact with the carrier-fluid.” *Id.* at 18:41–45. The purpose of the intervening aqueous plug-fluid is to “prevent, delay or minimize the reaction or mixing of the two outer aqueous plug-fluids before they come in contact with the carrier-fluid.” *Id.* at 18:41–48.

D. Illustrative Claim

Claim 1 is the sole independent claim. Each of claims 2 through 13 depends, directly or indirectly, from claim 1. Claim 1 illustrates the claimed subject matter and is reproduced below:

1. A method for conducting a 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;
continuously flowing an aqueous fluid containing at least one biological molecule and at least one reagent for conducting the reaction between the biological molecule and the at least one reagent through a first channel of the at least two channels;
continuously flowing a carrier fluid immiscible with the aqueous fluid through the second channel of the at least two channels;

forming at least one plug of the aqueous fluid containing the at least one biological molecule and the at least one reagent by partitioning the aqueous fluid with the flowing immiscible carrier fluid at the junction of the at least two channels, the plug being substantially surrounded by the immiscible carrier fluid flowing through the channel, wherein the at least one plug comprises at least one biological molecule and the at least one reagent for conducting the reaction with the at least one biological molecule; and

providing conditions suitable for the reaction in the at least one plug involving the at least one biological molecule and the at least one reagent to form a reaction product.

E. The Alleged Grounds of Unpatentability

Petitioner contends that the challenged claims are unpatentable on the following grounds.³

References	Basis	Claim(s) Challenged
Haff ⁴ and Quake ⁵	§ 103(a)	1–10, 12, and 13
Haff, Quake, and Ramsey ⁶	§ 103(a)	11

³ Petitioner supports its challenge with a Declaration of Wilhelm T. S. Huck, Ph.D., dated May 6, 2015 (Ex. 1002, “Huck Decl.”).

⁴ US 6,033,880, issued Mar. 7, 2000 (Ex. 1021, “Haff”). Petitioner asserts that Haff is prior art to the ’407 patent under 35 U.S.C. § 102(b).

⁵ US 2002/0058332 A1, published May 16, 2002 (Ex. 1004, “Quake”). Petitioner asserts that Quake is prior art to the ’407 patent under 35 U.S.C. § 102(e) because it was filed on Sept. 14, 2001.

⁶ US 6,524,456 B1, issued Feb. 25, 2003 (Ex. 1006, “Ramsey”). Petitioner asserts that Ramsey is prior art to the ’407 patent under 35 U.S.C. § 102(e) because it was filed on Sept. 29, 1999.

II. ANALYSIS

A. *Person of Ordinary Skill in the Art*

The parties dispute the proper definition of a person of ordinary skill in the art. Petitioner contends that a person of ordinary skill in the art would have had a Ph.D. in chemistry, biochemistry, mechanical engineering, or a related discipline, with two years of experience in using, designing or creating microfluidic devices. Pet. 3. Alternatively, Petitioner asserts that a skilled artisan would have had an M.S. or bachelor's degree in one of those disciplines with four or five years of additional relevant experience, respectively. *Id.* Patent Owner disagrees with Petitioner's definition, arguing that Petitioner overstates the level of ordinary skill in the art in the 2002 time frame. According to Patent Owner, a person of ordinary skill in the art would have been a researcher interested in microfluidics with at least a bachelor's degree in a "hard science," such as chemistry, physics, chemical engineering, bioengineering, or mechanical engineering. Prelim. Resp. 15.

For purposes of this Decision, we do not discern an appreciable difference between Petitioner and Patent Owner's proposed levels of ordinary skill in the art that would impact our ultimate conclusions. Patent Owner does not indicate how many years of experience a "researcher interested in microfluidics" would have. Accordingly, we determine that a person of ordinary skill in the art would have at least a bachelor's degree in chemistry, physics, chemical engineering, bioengineering, or mechanical engineering, or a related discipline, with at least four or five years of relevant experience. We also consider the cited prior art as representative of the level of ordinary skill in the art. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (finding the absence of specific findings on

“level of skill in the art does not give rise to reversible error ‘where the prior art itself reflects an appropriate level and a need for testimony is not shown’”) (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 163 (Fed. Cir. 1985)).

B. Claim Construction

In an *inter partes* review, claim terms in an unexpired patent are interpreted according to their broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 42.100(b); *see also In re Cuozzo Speed Techs., LLC*, 793 F.3d 1268, 1278 (Fed. Cir. 2015) (“Congress implicitly approved the broadest reasonable interpretation standard in enacting the AIA.”). Claim terms are given their ordinary and customary meaning as would be understood by a person of ordinary skill in the art at the time of the invention and in the context of the entire patent disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). If the specification “reveal[s] a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess[,] . . . the inventor’s lexicography governs.” *Phillips v. AWH Corp.*, 415 F.3d 1303, 1316 (Fed. Cir. 2005) (en banc) (citing *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002)). We apply this standard to the claims of the ’407 patent.

Petitioner requests that the following claim terms be given the proposed constructions below (Pet. 11–18):

Term (Claim)	Petitioner’s Proposed Construction
Preamble “[a] method for conducting a reaction in plugs in a microfluidic system.” (claim 1)	Requires that the reaction is conducted within the plugs while they are in the microfluidic system.

Term (Claim)	Petitioner's Proposed Construction
"plug of the aqueous fluid" (claim 1)	"Volumes of an aqueous fluid surrounded by a carrier fluid in which it is substantially immiscible, such as a nonpolar or hydrophobic fluid, e.g., an oil, and the diameter of a plug is substantially similar to the cross-section of the channel in which it is formed and the aqueous fluid is separated from the channel wall by a thin film of carrier fluid."
"reaction involving at least one biological molecule and at least one reagent to form a reaction product" (claim 1)	Encompasses at least PCR
"conditions suitable for the reaction" (claim 1)	Encompasses at least providing a stimulus such as radiation, heat, temperature or pressure change, ultrasonic wave, or a catalyst to induce a reaction that gives rise to the transformation of the reagent to another reagent, intermediate, or product
"substantially surrounded" (claim 1)	Includes "encapsulated" since used interchangeably
"autocatalytic reaction" (claim 3)	Encompasses at least PCR

We conclude that only the following terms require construction for purposes of this decision because the plain language of the remaining terms does not exclude the more specific constructions sought by Petitioner. See *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) (only terms in controversy need to be construed, and only to the extent necessary to resolve the controversy).

1. Plug of the Aqueous Fluid

Independent claim 1 recites the step of “forming at least one plug of the aqueous fluid containing the at least one biological molecule and the at least one reagent” According to Petitioner, descriptions of the plug that appear in the Specification should be included in the definition, such as examples of the carrier fluid, the diameter, and the relationship to the channel wall. Pet. 11–13. Patent Owner contends that the proposed construction imports non-essential attributes from the Specification that are exemplary options. Prelim. Resp. 18. Patent Owner proposes that the term be construed to mean “volumes of aqueous fluid formed when a stream of aqueous fluid is introduced into the flow of a substantially immiscible carrier-fluid.” *Id.* at 19.

We determine the appropriate construction by initially looking to the specification. *In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364 (Fed. Cir. 2004) (Claim limitations must be read “in light of the specification as it would be interpreted by one of ordinary skill in the art.”). The Specification describes the plug broadly as being “formed in a substrate when a stream of at least one plug-fluid is introduced into the flow of a carrier-fluid in which it is substantially immiscible.” Ex. 1001, 10:3–6. We agree with Patent Owner that this is a defining attribute of the claimed plug and that the Specification describes further details as preferred embodiments. According to the Specification, the size of the plug may vary depending on the relative flowrates of the aqueous fluid and the carrier fluid, but “should be substantially similar to the cross-section of the channels in which they are formed.” *Id.* at 10:10–13, 22:35–37. Separation of the aqueous fluid from the channel wall is also described in an optional manner as occurring when

the preferred condition of the carrier-fluid wetting the walls is satisfied. *Id.* at 21:35–41. The carrier fluid is described as “substantially immiscible” with the plug optionally being “surrounded by a non-polar or hydrophobic fluid such as an oil” or “encased by one or more layers of molecules that comprise both hydrophobic and hydrophilic groups or moieties.” *Id.* at 10:5–6, 22–31.

Accordingly, for purposes of this decision, we adopt Patent Owner’s proposed construction for the term “plug of the aqueous fluid” because it includes the property of the carrier fluid for the plug being substantially immiscible without also incorporating specific embodiments described in the Specification.

2. Conditions Suitable for the Reaction

Independent claim 1 recites the step of “providing conditions suitable for the reaction in the at least one plug.” According to Petitioner, this term requires an explicit construction to specify that the conditions “encompass at least providing a stimulus such as radiation, heat, temperature, or pressure change, ultrasonic wave, or a catalyst to induce a reaction.” Pet. 14–15.

Patent Owner contends that “the provision of a single stimulus such as those listed in the Petition would not necessarily, in itself, be sufficient to induce a reaction (including PCR) in a microfluidic plug.” Prelim. Resp. 20.

According to Patent Owner, this term would be understood by a skilled artisan to refer to “a global set of physical and chemical conditions that allows one to conduct a reaction (including PCR) in droplets.” *Id.* at 21.

At this stage of the proceeding, we determine that Patent Owner’s interpretation is most consistent with the Specification, which broadly describes the term “reaction” as “a physical, chemical, biochemical, or

biological transformation” and further describes the chemical, biochemical, and biological transformations as generally involving the breaking or formation of bonds. Ex. 1001, 11:25–31. Accordingly, for purposes of this decision, we adopt Patent Owner’s proposed construction for the term “conditions suitable for the reaction” because it broadly includes physical and chemical conditions to conduct a reaction that is a physical or chemical transformation as described in the Specification.

C. Obviousness over Haff and Quake

We turn now to Petitioner’s asserted grounds of unpatentability to determine whether Petitioner has met the threshold standard of 35 U.S.C. § 314(a). We begin with a description of Haff and Quake, which are asserted in each ground argued in the Petition.

1. Overview of Haff

Haff relates to automated machines for performing amplification reactions for nucleic acids, such as a polymerase chain reaction (“PCR”). Ex. 1021, 1:12–15. Haff states that PCR has been performed in disposable reaction tubes such as small, plastic microcentrifuge tubes or test tubes that are placed in an instrument containing a thermally controlled heat exchanger. *Id.* at 1:50–53. Haff explains that rapid, small-scale PCR capillary tube instruments have appeared in which the reaction mixture is placed in capillary tubes. *Id.* at 2:7–12. The Specification describes various capillary tube PCR instruments that use different means to heat and cool the PCR reaction mixture and different tube and fluid-handling means to move the reaction mixture.

Figure 2 of Haff is one embodiment and is reproduced below:

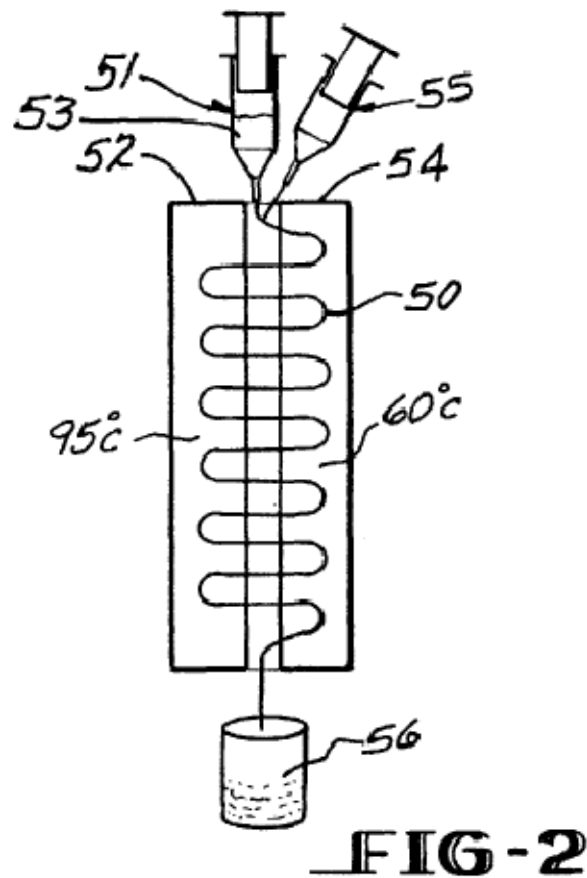


Figure 2 depicts a system that uses a length of capillary tubing 50 that is routed in and out of hot zone 52 and cool zone 54 a number of times. *Id.* at 9:58–65. Syringe 51, which contains PCR reaction mixture 53, and syringe 55, which contains air or an immiscible fluid, are connected in parallel with tubing 50. *Id.* at 10:20–32. Syringe 55 is operated intermittently to inject air bubbles or immiscible fluid bubbles into the flow stream of reagent mixture 53 in tubing 50. *Id.* at 10:32–35. The use of bubbles between samples results in “slug” flow where sample “slugs” are passed through the capillary tubes. *Id.* at 9:50–52. According to Haff, “[th]e length of the tubing [], its internal diameter, the length of tubing in each of the hot and cool zones, and

the flow rate of the reaction mixture inside the tube are all factors in the control of the amplification.” *Id.* at 10:15–19.

2. Overview of Quake

Quake relates to microfluidic devices designed to compartmentalize small droplets of aqueous solution within microfluidic channels filled with oil. Ex. 1004 ¶ 3. The devices comprise a main channel, through which a pressurized stream of oil is passed, and at least one sample inlet channel, through which a pressurized stream of aqueous solution is passed. *Id.* A junction joins the main channel with the sample inlet channel. *Id.* By adjusting the pressure of the oil and/or the aqueous solution, a pressure difference can be established such that the stream of aqueous solution is sheared off at a regular frequency as it enters the oil stream, thereby forming droplets. *Id.* Figure 16A of Quake is reproduced below:

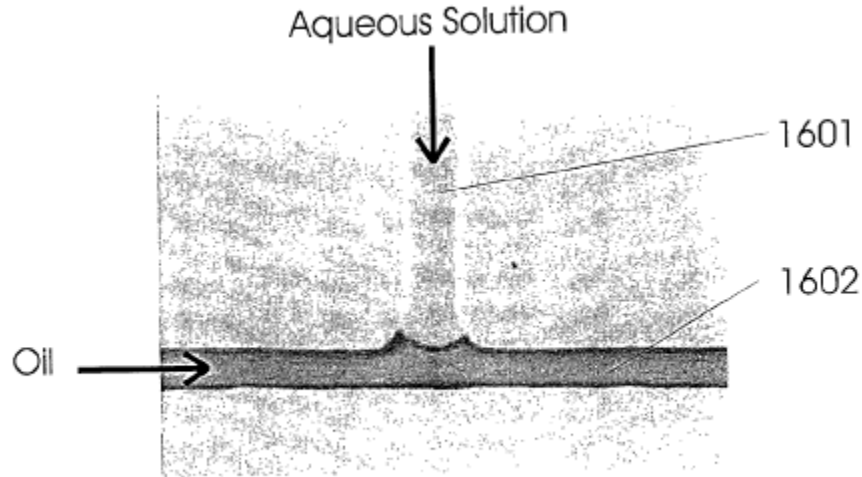


FIG. 16A

Figure 16A depicts the channel architecture for the droplet extrusion region. Channel 1601 containing an aqueous solution intersects with main channel 1602 containing oil. *Id.* ¶ 292.

In preferred embodiments, the droplets have a volume of approximately 0.1 to 100 picoliters. *Id.* According to Quake, microfabrication of the device “permits other technologies to be integrated or combined with flow cytometry on a single chip, such as PCR.” *Id.* ¶ 80.

3. Analysis

Petitioner asserts that claims 1–10, 12, and 13 would have been obvious over the combination of Haff and Quake. Pet. 18.

Regarding claim 1, Petitioner asserts that “Quake’s microfluidic device would use a lesser amount of reagents than Haff’s capillary system” (citing Ex. 1002 ¶ 72) and that one of ordinary skill in the art would have had a reason to modify Haff’s method to use the droplet system taught by Quake in order to conserve reagents, reduce costs, and minimize the amount of sample DNA needed. Pet. 31. Additionally, Petitioner argues that a skilled artisan would have modified Haff’s method by using Quake’s microfluidic system because Quake teaches that the microfluidic system overcomes the drawbacks of slug adherence to channel walls and mixing of reagents between slugs associated with PCR methods. *Id.* at 33. The reason to combine Quake with a PCR method also comes from Quake itself contends Petitioner (Pet. 35), which teaches that “[m]icrofabrication permits other technologies to be integrated or combined with flow cytometry on a single chip, such as PCR.” Ex. 1004 ¶ 80.

According to Petitioner, a skilled artisan “would have had a reasonable expectation of success in so doing because Quake teaches that his microfluidic device designs can be used to perform PCR.” *Id.* at 31 (citing Ex. 1002 ¶ 73); *id.* at 35. Petitioner argues that “it would have required no more than routine skill and knowledge in the art to adapt Haff’s capillary

PCR device to use Quake's method of creating encapsulated plugs comprising a target DNA sequence . . . and PCR specific reagents" *Id.* at 35 (citing Ex. 1002 ¶ 73). The Huck Declaration explains that Quake teaches controlling the flow of oil and the flow of the aqueous sample fluid to generate an encapsulated stream of droplets. Ex. 1002 ¶ 73. Dr. Huck also states that Quake teaches adjusting the concentration of the biological molecule to ensure that the droplets contain no more than a single biological molecule and teaches that the device and method can be integrated with PCR. *Id.* Accordingly, Dr. Huck concludes:

[I]t would have required no more than routine skill and knowledge in the art for a [skilled artisan] to adapt Haff's device to form a stream of PCR reaction mixture droplets encapsulated, i.e., substantially surrounded by an oil, which droplets comprise a single substrate DNA molecule, and to conduct PCR amplification, a reaction, in the droplets to form amplified DNA, a reaction product.

Id.

Patent Owner argues that Haff is not analogous art because the field of the '407 patent is microfluidic devices and Haff is "directed to a system for dealing with 'larger volumes' of fluids." Prelim. Resp. 26–28. Patent Owner also argues that Haff is not reasonably pertinent to the problems being addressed in the '407 patent. *Id.* at 28–29. We are not persuaded. Although Haff does not disclose the use of PCR in microfluidic devices, we do not believe such disclosure is necessary to consider Haff to be analogous art. "A reference is reasonably pertinent if, even though it may be in a different field from that of the inventor's endeavor, it is one which, because of the matter with which it deals, logically would have commended itself to an inventor's attention in considering his problem." *In re ICON Health &*

Fitness, Inc., 496 F.3d 1374, 1380–81 (Fed. Cir. 2007). On the current record, we find that Haff’s disclosure of PCR in larger-volume capillary tube devices logically would have commended itself to the inventors’ attention when considering methods of conducting PCR in smaller microfluidic devices. In other words, we find that the inventors logically would have considered how PCR is conducted in capillary tube devices to figure out how to scale down the reaction for microfluidic devices.

Patent Owner also argues that Petitioner has not shown that either Haff or Quake individually teaches the limitation of “providing conditions suitable for the reaction in the at least one plug involving the at least one biological molecule and the at least one reagent to form a reaction product” as required by claim 1. Prelim. Resp. 23–24. Although we agree with Patent Owner that neither reference alone teaches this limitation, that is not the test. Patent Owner cannot show nonobviousness by attacking the Haff and Quake references individually where the challenge is based on what the combination of Haff and Quake would have suggested to a person of ordinary skill in the art. *See In re Keller*, 642 F.2d 413, 426 (CCPA 1981) (rejecting appellant’s challenge to the prior art references individually where the test was what the combination of references would have suggested to one of ordinary skill in the art).

Patent Owner further argues that one of skill in the art would not have combined Quake with Haff for the purpose of conserving reagent because Haff’s system is designed to increase output, therefore large volumes of reagent is not a drawback. Prelim. Resp. 33. Patent Owner also argues that Haff and Quake are not both directed to performing enzymatic reactions, such as PCR, in small volumes of aqueous liquids, as asserted by Petitioner.

Id. at 35–37. Patent Owner asserts that Haff is directed to increasing the volume of PCR reactions, rather than conducting them in small volumes. *Id.* at 35. Patent Owner additionally argues that Quake teaches microfluidic sorting as an alternative to PCR because Quake only twice mentions PCR, describes the risk of cross-contamination between samples as a disadvantage of PCR as a diagnostics tool, and repeatedly teaches sorting of molecules using the microfluidic system. *Id.* at 35–37.

Finally, Patent Owner asserts that the modifications required by the combination of Haff’s method and Quake’s microfluidic plug system “require overcoming numerous engineering challenges” and would not be routine. *Id.* at 38. Patent Owner identifies as such a hurdle Haff’s use of a bulk reaction mixture while Quake does not describe packaging reagents into microfluidic droplets. *Id.* at 40. Patent Owner also points to Quake’s channels, which are carved into a single substrate and orders of magnitude smaller than Haff’s, and compares them to Haff’s capillary tubes passing in and out of liquid baths that create hot and cool zones. *Id.* at 38–39 (citing Ex. 1021, 1:12–15, 7:36–38, 9:65–10:6; Ex. 1004 ¶¶ 133–39). Patent Owner further identifies surface chemistry in a microfluidic device as being important to control because the surface-to-volume ratio increases as the system dimensions are reduced as in Quake. *Id.* at 42–43 (citing Ex. 1001, 36:32–34).

Whether a patent claiming the combination of prior art elements would have been obvious is determined by whether the improvement is more than the predictable use of prior art elements according to their established functions. *KSR Int’l v. Teleflex Inc.*, 550 U.S. 398, 417 (2007). To reach this conclusion, however, requires more than a mere showing that the prior

art includes separate references covering each separate limitation in a claim under examination. *Unigene Labs., Inc. v. Apotex, Inc.*, 655 F.3d 1352, 1360 (Fed. Cir. 2011). Rather, obviousness requires the additional showing that a person of ordinary skill at the time of the invention would have selected and combined those prior art elements in the normal course of research and development to yield the claimed invention. *Id.*

We are not persuaded that the combination of Haff's reactants and conditions for a PCR method with Quake's aqueous plugs in a microfluidic system likely would have been obvious based on the evidence of record.

We acknowledge that the Petition and Dr. Huck provide an overview of the state of the art as of May 2002. Pet. 4–10; Ex. 1002 ¶¶ 16–26. For example, the Petition describes a microfluidic system for performing chemical reactions in droplets. Pet. 6 (citing Ex. 1011). And the Petition describes the development of PCR, including microfluidic devices that could perform PCR on a nanoliter scale. *Id.* at 6–9; *see, e.g.*, Ex. 1017 (describing continuous-flow PCR on a chip). According to Petitioner's declarant, "[i]n each of these systems, a stream of a single PCR reaction mixture is injected into a microfluidic PCR reaction chamber, where it is thermocycled to achieve amplification of the target sequence." Ex. 1002 ¶ 22.

Despite that background information, we determine that Petitioner has not explained why a person of ordinary skill in the art would have had a reasonable expectation of success combining Haff's capillary tube PCR device with Quake's microfluidic system to amplify a substrate in droplets. Simply stating that it would have been "routine" is insufficient. To the extent Petitioner relies on the background information to support a reasonable expectation of success, Petitioner fails to explain any connection

between the two. For example, if conducting PCR in a stream of reaction mixture in a microfluidic device was known, Petitioner has not explained why, with that knowledge, it would have been routine to conduct PCR in droplets in a microfluidic device. Moreover, even though Haff describes conducting PCR in a capillary tube device, neither Petitioner nor its declarant explains how the conditions for conducting PCR in microfluidic droplets would differ, or why a person of ordinary skill in the art would consider conducting PCR in microfluidic droplets to be “routine.”

Petitioner contends that a skilled artisan would have had a reasonable expectation of success because Quake teaches how to obtain encapsulated aqueous plugs with a single substrate molecule. Pet. 35. But even with that teaching, Petitioner has not explained why that—or any teaching in Haff or Quake—would establish a reasonable expectation of success in providing conditions that are suitable to conduct a reaction with a biological molecule in a microfluidic plug.

The unexplained opinion of Dr. Huck that it would have required no more than routine skill and knowledge in the art “to adapt Haff’s device to form a stream of PCR reaction mixture droplets . . . and to conduct PCR amplification, a reaction, in the droplets . . . to form amplified DNA” (Ex. 1002 ¶ 73) also is not persuasive. See 37 C.F.R. § 42.65(a) (“Expert testimony that does not disclose the underlying facts or data on which the opinion is based is entitled to little or no weight.”); *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 294 (Fed. Cir. 1985) (stating a lack of objective support for an expert opinion “may render the testimony of little probative value in [a patentability] determination”).

Without a sufficient explanation regarding the combination of Haff and Quake, we determine that Petitioner has failed to establish a reasonable likelihood that it would prevail in its assertion that claim 1, or dependent claims 2–10, 12, and 13, are unpatentable as obvious over Haff and Quake.

D. Obviousness over Haff, Quake, and Ramsey

Petitioner asserts that claim 11 would have been obvious over the combination of Haff, Quake, and Ramsey. Pet. 45–48. Claim 11 depends indirectly from claim 1 and further requires that the immiscible carrier fluid is fluorinated oil. Ex. 1001, 80:11–12. For the same reasons stated above with respect to claim 1, we determine that Petitioner has failed to sufficiently show that claim 11 is unpatentable as obvious over the cited references.

III. CONCLUSION

For the foregoing reasons, we conclude that Petitioner has not established a reasonable likelihood of prevailing on its assertions that claims 1–13 of the '407 patent are unpatentable as obvious.

IV. ORDER

In consideration of the foregoing, it is hereby ordered that the Petition is *denied*.

IPR2015-01158
Patent 8,329,407 B2

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