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Paper 51
Entered: November 15, 2016

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 IPR2015-01157
Patent 8,889,083 B2

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

CRUMBLEY, *Administrative Patent Judge*.

FINAL WRITTEN DECISION
35 U.S.C. § 318 and 37 C.F.R. § 42.73

I. INTRODUCTION

In this *inter partes* review trial, instituted pursuant to 35 U.S.C. § 314, Petitioner 10X Genomics, Inc. ("10X") challenges the patentability of claims 1–31 of U.S. Patent No. 8,889,083 B2 ("the '083 patent," Ex. 1001), owned by The University of Chicago ("Chicago").

We have jurisdiction under 35 U.S.C. § 6(b). This Final Written Decision, issued pursuant to 35 U.S.C. § 318(a), addresses issues and arguments raised during trial. For the reasons discussed below, we determine that 10X has not proven, by a preponderance of the evidence, that claims 1–31 of the '083 patent are unpatentable.

A. Procedural History

On May 6, 2015, 10X requested an *inter partes* review of claims 1–31 of the '083 patent. Paper 1, "Pet." Chicago filed a Patent Owner Preliminary Response. Paper 9, "Prelim. Resp." In a Decision on Institution of *Inter Partes* Review (Paper 14, "Dec. on Inst."), we instituted trial as to claims 1–31 on the following grounds of unpatentability:

1. Whether claims 1–31 are unpatentable under 35 U.S.C. § 103(a) as having been obvious over Quake[1] and Ramsey;[2]
2. Whether claims 18 and 24 are unpatentable under 35 U.S.C. § 103(a) as having been obvious over Quake, Ramsey, and Green.[3]

Dec. on Inst. 21.

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[1] Quake et al., US 2002/0058332 A1, published May 16, 2002 (Ex. 1004).

[2] Ramsey et al., US 6,524,456 B1, issued Feb. 25, 2003 (Ex. 1006).

[3] Green, S.W. et al., *Perfluorocarbon Fluids*, Organoflourine Chemistry: Principles and Commercial Applications (1994) (Ex. 1007).

Following institution of trial, Chicago filed a Patent Owner Response (Paper 19, "PO Resp."), and 10X filed a Reply (Paper 25, "Pet. Reply").

10X supported its Petition with the Declaration of Wilhelm T.S. Huck, Ph.D. Ex. 1002. Chicago took cross-examination testimony of Dr. Huck via deposition on January 7–8, 2016, and submitted the transcript of that deposition. Exs. 2026, 2027.

With its Response, Chicago submitted the Declaration of Samuel Sia, Ph.D. Ex. 2028. 10X cross-examined Dr. Sia via deposition on March 25, 2016, and submitted the transcript. Ex. 1073.

With its Reply, 10X submitted a Second Declaration of Dr. Huck (Ex. 1087), and submitted the declaration testimony of a second witness, Peter David Olmsted, Ph.D. (Ex. 1085). Chicago took cross-examination testimony via deposition of Dr. Huck on May 17, 2016, and of Dr. Olmsted on May 13, 2016, and submitted the transcripts to the Board. Exs. 2051 (Olmsted), 2052 (Huck).

Chicago filed Observations on the Cross-Examination of Drs. Olmsted and Huck (Paper 35), and 10X filed a Response (Paper 39). As authorized by the Board (Paper 30), Chicago also filed an Identification of Testimony from Dr. Huck that allegedly exceeds the proper scope of reply (Paper 34), and 10X filed a Response to that list (Paper 38).

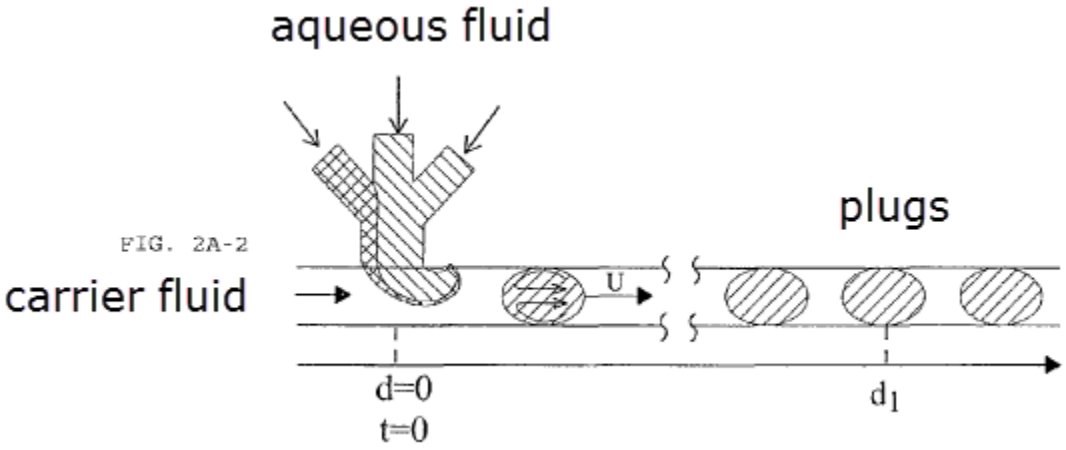
Chicago filed a Motion to Exclude various exhibits submitted by 10X (Paper 36, "Mot."), to which 10X filed an Opposition (Paper 40) and Chicago filed a Reply (Paper 43).

Oral hearing was requested by both parties (Papers 31, 33), and argument before the Board was held June 30, 2016. A transcript of the oral hearing is included in the record. Paper 50, "Tr."

B. The '083 Patent

The '083 patent, entitled "Device and Method for Pressure-Driven Plug Transport and Reaction," issued November 18, 2014. Ex. 1001, (45), (54). Microfluidic systems transport fluids through networks of channels, typically having micrometer dimensions. *Id.* at 1:18–20. According to the specification, the main advantages of microfluidic systems are high speed and low consumption of reagents. *Id.* at 1:23–25. The 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 '083 patent specification describes using microfluidic droplets, or "plugs" in the system. 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 17:17–23.

In one disclosed embodiment, the walls of the channels are not fluorinated, while the carrier fluid is a fluorinated oil that contains a fluorinated surfactant. *Id*. at 20:63–21:2. According to the specification, "[b]ecause the walls of the channels (PDMS, not fluorinated) and the carrier-fluid (fluorinated oil) are substantially different chemically, when a fluorinated surfactant is introduced, the surfactant reduces the surface tension at the oil-water interface preferentially over the wall-water interface." *Id*. This difference in surface tension results in the carrier fluid preferably wetting the walls of the channels, as opposed to wetting the plugs, meaning that the plugs typically do not contact the walls of the channel. *Id*. at 20:41–45. "This allows the formation of plugs that do not stick to the channel walls." *Id*. at 21:1–2.

C. Illustrative Claim

Of the challenged claims, 1, 20, and 31 are independent, with claims 1 and 31 directed to microfluidic systems and claim 20 directed to a method of conducting a reaction within a plug in a microfluidic system. Claim 1 is illustrative and is reproduced below:

> 1. A microfluidic system comprising:
>
> a non-fluorinated microchannel;
>
> a carrier fluid comprising a fluorinated oil and a fluorinated surfactant comprising a hydrophilic head group in the microchannel;
>
> at least one plug comprising an aqueous plug-fluid in the microchannel and substantially encased by the carrier-fluid,

> wherein the fluorinated surfactant is present at a concentration such that surface tension at the plug-fluid/microchannel wall interface is higher than surface tension at the plug-fluid/carrier fluid interface.

Ex. 1001, 73:11–21.

II. ANALYSIS

A. Claim Construction

For purposes of our Decision on Institution, we analyzed each claim term in light of its broadest reasonable interpretation, as understood by one of ordinary skill in the art and consistent with the specification of the '083 patent. 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2144–46 (2016). Under the broadest reasonable interpretation standard, and absent any special definitions, claim terms are given their ordinary and customary meaning, as would be understood by one of ordinary skill in the art in the context of the entire disclosure. *In re Translogic Tech. Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms or phrases must be set forth with reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

In the Decision on Institution, we evaluated the parties' proffered constructions for the claim terms "at least one plug comprising an aqueous plug fluid" (claims 1 and 31) and "at least one plug." Dec. on Inst. 7–8. We determined that, based on the record at the time, the broadest reasonable interpretation is "at least one volume of aqueous fluid formed when a stream of aqueous fluid is introduced into the flow of a substantially immiscible carrier-fluid." *Id*. at 8. We also evaluated the other constructions proffered

by the parties,[4] and determined that the remaining terms did not require express construction. *Id*. at 8–10. During the instituted trial, neither party disputed our preliminary claim constructions as set forth in the institution Decision or raised additional claim construction arguments. Upon review of the entire record, we maintain our prior constructions.

B. Obviousness over Quake and Ramsey

10X contends that claims 1–31 are unpatentable under 35 U.S.C. § 103(a), as they would have been obvious over the combined disclosures of Quake and Ramsey. Pet. 18–50. An obviousness inquiry involves four underlying determinations: the scope and content of the prior art; the differences between the prior art and the claims at issue; the level of ordinary skill; and any objective indicia of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966).

Quake relates to microfluidic devices and methods for analyzing and/or sorting biological materials that "offer several advantages over traditional flow cytometry devices and methods." Ex. 1004, Abstract, ¶ 14. The devices are designed to compartmentalize small droplets of aqueous solution within microfluidic channels filled with oil. *Id.* ¶ 3. The devices comprise a main channel, through which a pressurized stream of oil is

[4] Specifically, both parties proffered constructions for "fluorinated surfactant comprising a hydrophilic head group" and "surface tension at the plug-fluid/microchannel wall interface is higher than the surface tension at the plug-fluid/carrier fluid interface." Pet. 13–15; Prelim. Resp. 22–30. 10X proffered a construction for two additional claim terms: "non-fluorinated microchannel" (Pet. 10–13) and "substantially encased/substantially surrounded on all sides" (*id*. at 15–17).

passed, and at least one sample inlet channel, through which a pressurized stream of aqueous solution is passed. *Id.* The channels of the device may be formed from a silicon elastomer, including polydimethylsiloxane (PDMS), or urethane. *Id*. ¶¶ 118, 216.

A junction joins the main channel with the sample inlet channel. *Id.* ¶ 3. 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:

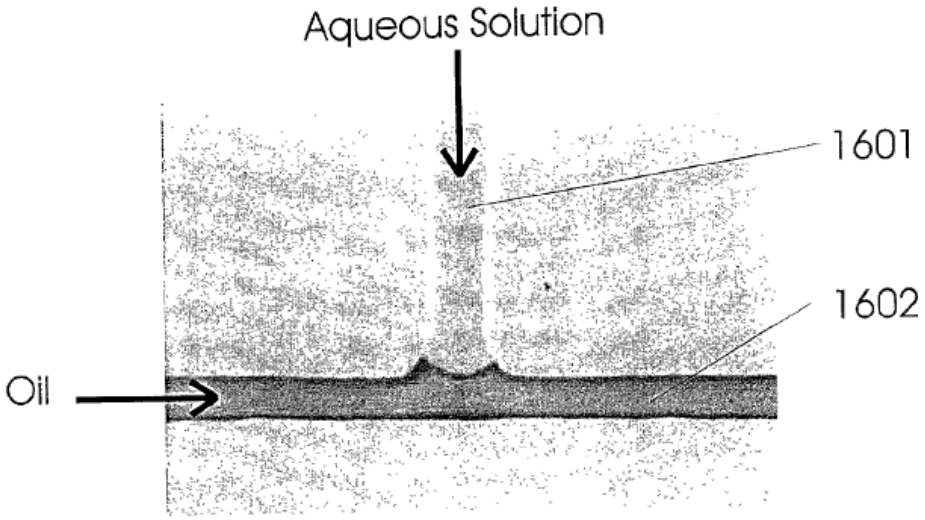


FIG. 16A

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

Quake discloses that the fluid that forms the droplet is typically an aqueous buffer solution that is physiologically compatible with the molecules in the

droplet. *Id*. ¶ 116. The carrier fluid[5] in which the droplets are formed is a fluid that is not miscible with the droplet fluid, preferably a nonpolar solvent such as decane or another oil. *Id*. The fluids may contain additives, such as surfactants, which Quake teaches "may aid in controlling or optimizing droplet size, flow and uniformity." *Id*. ¶ 117. Quake discloses that the surfactant may be contained in the carrier fluid, such that when the fluid flows through the channels of the microfluidic device, the surfactant coats the channel walls. *Id*. ¶ 96. Such a coating minimizes adhesion, preventing material such as "cells, virions and other particles or molecules" from adhering to the sides of the channels. *Id*. ¶ 94.

Ramsey relates to "a microfabricated channel device that can manipulate nanoliter or subnanoliter biochemical reaction volumes in a controlled manner to produce results at rates of 1 to 10 Hz per channel." Ex. 1006, Abstract. Ramsey discloses separating volume segments using a segmenting material that "is preferably a liquid that is immiscible in . . . the reaction fluid(s)." *Id.* at 3:63–67, 6:36–37. Ramsey also discloses that "the segmenting fluid should be biocompatible with [the] biological reagents that are used" in the reaction fluid and, specifically, that "[p]erfluorocarbons may also be suitable because they are widely used where biocompatibility is required." *Id*. at 6:37–39, 49–50.

[5] Quake uses the term "extrusion" or "barrier" fluid to refer to the fluid that surrounds the droplets (Ex. 1004 ¶ 20); we use the terminology of the '083 patent.

1. Content of the Record

Before turning to the merits of the parties' arguments, we address Chicago's contention that the Second Declaration of Dr. Huck (Ex. 1087) exceeds the proper scope of reply. As summarized in our May 26, 2016 Order, Chicago requested authorization to file a motion to strike Dr. Huck's Second Declaration as improper reply testimony. Paper 30, 2. We declined to authorize a motion to strike, because the Board is capable of determining at the close of evidence whether new arguments were raised and disregarding any improper reply. We permitted Chicago to file a short list setting forth the allegedly improper testimony. *Id*. Chicago filed its list (Paper 34), and 10X filed a responsive paper (Paper 38).

"It is of the utmost importance that petitioners in [*inter partes* review] proceedings adhere to the requirement that the initial petition identify 'with particularity' the 'evidence that supports the grounds for the challenge to each claim.'" *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1369 (Fed. Cir. 2016) (quoting 35 U.S.C. § 312(a)(3)). For this reason, our Rules require that "[a] reply may only respond to arguments raised in the corresponding opposition . . . or patent owner response." *See* 37 C.F.R. § 42.23(b). This reasoning applies equally to reply declarations, submitted to support a party's reply brief. *See Intelligent Bio-Sys., Inc*., 821 F.3d at 1369–70 (affirming exclusion of reply brief and supporting declaration). Our Trial Practice Guide provides that "a reply that raises a new issue or belatedly presents evidence will not be considered. . . . The Board will not attempt to sort proper from improper portions of a reply."

Office Patent Trial Practice Guide, 77 Fed. Reg. 48,756, 48,767 (Aug. 14, 2012) ("Trial Practice Guide").

Of course, "the introduction of new evidence in the course of the trial is to be expected in *inter partes* review trial proceedings." *Genzyme Therapeutic Prod. Ltd. P'ship v. Biomarin Pharm. Inc.*, 825 F.3d 1360, 1366 (Fed. Cir. 2016). That new evidence, however, must be responsive to an argument raised by the opposing party in its opposition brief. By contrast, when "new evidence necessary to make out a prima facie case for . . . unpatentability" or "new evidence that could have been presented in a prior filing" is introduced, these are indications that a new issue has been raised improperly. *See* Trial Practice Guide, 77 Fed. Reg. at 48,767.

Chicago identifies four general topics of testimony, and supporting exhibits, that allegedly exceed the proper scope of reply. We address each in turn below.

a. Testimony on State of the Art of Microfluidics

First, Chicago challenges ¶¶ 24–39 of Dr. Huck's Second Declaration, pertaining to various "microfluidics conferences, journals, companies, and products." Paper 34, 1. Several exhibits supporting this testimony are also identified: Exs. 1041–1045, 1047, 1051–1056, 1068, 1071–1072, 1081–1082, and 1088–1092. *Id*. at 1–2. In this portion of his testimony, Dr. Huck is testifying regarding the state of the art of microfluidics, and supporting this testimony with citations to various conferences, journals, and the like. 10X contends that this testimony is responsive to "Dr. Sia's allegation that microfluidics was a nascent field in 2002." Paper 38, 1.

Upon review, we determine this testimony and the supporting documents to be proper reply evidence. In his Declaration, Dr. Sia testifies that there was a "limited amount of research in this area," and disputes the familiarity that the skilled artisan would have with various microfluidics techniques. Ex. 2028 ¶ 30. 10X was entitled to introduce evidence responsive to this testimony. Furthermore, we note that Dr. Huck's testimony and the supporting documents are not being offered to establish 10X's proposed gorund of unpatentability, but rather to provide general background information for establishing the state of the art. *See Genzyme*, 825 F.3d at 1367 (permitting reply evidence "relevant to show the state of the art at the time of the inventions").

b. Testimony on Knowledge of Reactions in Droplets

Chicago also objects to ¶¶ 104–111 of Dr. Huck's Second Declaration, along with supporting Exhibits 1049–1050, 1059, 1078, and 1093. Paper 34, 1–2. This testimony and accompanying exhibits pertain to performing reactions in microfluidic droplets, particularly PCR in droplets. 10X argues that this testimony is responsive to Dr. Sia's testimony that a person of ordinary skill would have had limited knowledge of droplet PCR. Paper 38, 2.

This presents a closer question, because the knowledge of PCR in droplets—particularly, the expectation of success in performing PCR in droplets—is relevant to the ground of unpatentability as to claims 11 and 21, which expressly require performance of PCR in the droplets. The Petition, however, relies on Quake itself for this reasonable expectation of success. Pet. 45–46. Dr. Sia addresses the cited portion of Quake in his testimony,

contending that a "host of other problems and complications left unaddressed by both Quake and Ramsey would have prevented the skilled artisan from having a reasonable expectation of successfully being able to carry out PCR or other autocatalytic reactions in microfluidic droplets," and goes on to provide examples of these issues. Ex. 2028 ¶ 105. After reviewing the testimony of Dr. Huck, we determine that it properly replies to this testimony by Dr. Sia, and cites the supporting exhibits to dispute these alleged "problems and complications."

c. Testimony as to Paragraph 117 of Quake

Chicago objects to ¶¶ 45–48 and 71–74 of the Second Huck Declaration, which consist of testimony regarding ¶ 117 of Quake. Paper 34, 1. This testimony is closely tied to an allegedly new argument raised in 10X's Reply, which we address in the following section. For the reasons discussed below, we determine that Dr. Huck's testimony in these portions exceeds the proper scope of reply.

d. Testimony as to Routine Optimization

Finally, Chicago challenges ¶¶ 76–78 of Dr. Huck's Second Declaration, which explain Dr. Huck's assertion in ¶ 75 that "selecting the surfactant of choice and the amount of surfactant would have been a matter of routine optimization." After reviewing the testimony, we determine that this portion raises a new issue that alters the basis of Dr. Huck's testimony, and thus exceeds the proper scope of reply.

Dr. Huck's first Declaration does not rely on routine optimization of the surfactant concentration to achieve the claimed surface tension

relationship ("surface tension at the plug-fluid/microchannel wall interface is higher than surface tension at the plug-fluid/carrier fluid interface").[6] *See generally* Ex. 1002 ¶¶ 59–63. Rather, Dr. Huck contends that—in the terminology of the '083 patent—the surface tension relationship "merely represents a condition achieved when sufficient fluorinated surfactant is present in the carrier fluid such that the plugs do not adhere to the channel wall." *Id.* ¶ 44. Dr. Huck then testifies that because Quake discloses surfactants that coat the walls of its channels, a person of ordinary skill in the art "would have understood that Quake discloses the use of a fluorinated surfactant in the carrier fluid to prevent the plugs from adhering to the microchannel wall." *Id.* ¶ 61. As a result, Dr. Huck concludes, the person of ordinary skill in the art "would have understood that the combination of Quake and Ramsey discloses a microfluidics system where the surface tension" relationship is present. *Id.*

From this testimony, it is clear that Dr. Huck's theory in his first Declaration was that the behavior of Quake's droplets signifies that the surface tension relationship—and, therefore, sufficient surfactant—was *present* in the system. By contrast, routine optimization relies on a *modification* of the disclosed system to achieve a surfactant concentration that is not disclosed by the reference. *See* Ex. 1087 ¶ 76 ("Quake teaches a range of suitable surfactant concentrations from between 0.2 and 5%. . . . Following Quake's teaching of adding surfactant to the carrier oil, a [person of ordinary skill in the art] would have routinely optimized the amount of

[6] During trial, the parties adopted the shorthand of referring to this limitation as "the surface tension relationship." For brevity, we will do the same.

surfactant to achieve controlled or optimized plug flow."). Notably, Dr. Huck did not testify that concentrations between 0.2 and 5%, as disclosed by Quake, would achieve the claimed surface tension relationship. Ex. 2027, 256:2–257:4.

This, we conclude, is a change in Dr. Huck's rationale for unpatentability: from an actual disclosure in Quake of the claimed surface tension relationship, to a modification of Quake through routine optimization to achieve the surface tension relationship. As such, it is improper to raise this for the first time in a reply declaration. *See Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, Case IPR2013-00517, 2015 WL 996355, at *9 (PTAB Feb. 11, 2015) (excluding reply that "chang[ed] the unpatentability rationale from express reliance on . . . conditions, to asserting that those conditions would have been obvious to modify"). To permit 10X to present this changed theory for the first time in Dr. Huck's reply testimony would deprive Chicago of a meaningful opportunity to respond. *See Belden Inc. v. Berk-Tek LLC*, 805 F.3d 1064, 1080 (Fed. Cir. 2015) ("A patent owner . . . is undoubtedly entitled to notice of and a fair opportunity to meet the grounds of rejection."). We will not consider 10X's routine optimization argument[7] in evaluating the proposed ground of unpatentability.

[7] We note that even if we were to consider it, routine optimization is of dubious applicability in this case. At oral hearing, counsel argued that Example 12 of Quake tests "several different concentrations of surfactant and finds that 2 percent is best." Tr. 74:21–24, 76:5–10. This is not an accurate description of Example 12. Quake does not evaluate the effect of using different surfactant concentrations—it merely states that different

e. Conclusion

As we noted above, if the Board determines that a reply brief or testimony exceeds the proper scope of reply, we typically will not parse the paper in an attempt to separate proper from improper portions. Trial Practice Guide, 77 Fed. Reg. at 48,767. In this case, however, no such parsing is required because Chicago's paper identifying the allegedly improper testimony sets forth the particular paragraphs it contends are objectionable. For the reasons given, we agree that ¶¶ 45–48, 71–74, and 76–78 of Dr. Huck's Second Declaration exceed the proper scope of reply testimony, and will not consider those portions in reaching our decision in this trial.

2. New Argument in Reply

At oral hearing, counsel for Chicago contended that—in addition to the portions of Dr. Huck's Second Declaration discussed above—the Reply submitted by 10X contained new arguments and issues and therefore was an improper reply. Tr. 40–48. Before addressing these contentions, however, we summarize the relevant arguments and evidence as presented by 10X in its briefs, and in Dr. Huck's testimony.

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concentrations of 0.5, 1.0, or 2.0% were tried—and it does not characterize any concentration as "best." Ex. 1004 ¶ 300. Furthermore, even if Quake can be said to evaluate surfactant concentrations, there is no disclosure in the reference indicating that changing concentration resulted in a change in the claimed surface tension relationship. *See In re Antonie*, 559 F.2d 618, 620 (CCPA 1977) (variable must be recognized as result-effective before routine optimization applies).

a. 10X's Arguments Regarding Surface Tension Relationship

Central to the dispute between the parties are two limitations of the independent claims: first, "a fluorinated surfactant comprising a hydrophilic head group"; and second, that the surfactant is "present at a concentration such that surface tension at the plug-fluid/microchannel wall interface is higher than surface tension at the plug-fluid/carrier fluid interface." In its Petition, 10X argued that Quake discloses the first limitation in paragraphs 116 and 117, and in particular quoted paragraph 117: "**The fluids used in the invention may contain additives**, such as agents which reduce surface tensions (**surfactants**). **Exemplary surfactants include . . . fluorinated oils**, ..." (emphasis and ellipses in original). Pet. 19; *see also id.* at 22–23. Dr. Huck's Declaration supporting the Petition cited and quoted the same portion of Quake. Ex. 1002, claim chart following ¶ 53 (pg. 33).

For the surface tension relationship limitation, however, 10X relied on a different portion of Quake—namely, paragraphs 94 and 118, which discuss coating the channel walls with surfactant. From paragraph 94, 10X quoted Quake's statement that "[t]o prevent material (e.g., cells, virions and other particles or molecules) from adhering to the sides of the channels, the channels (and coverslip, if used) may have a coating which minimizes adhesion. . . . Alternatively, the channels may be coated with a surfactant." Pet. 20–21 (emphasis omitted). From paragraph 118, 10X includes the following quote: "The **channels may also be coated** with additives or agents, such as surfactants, TEFLON, or **fluorinated oils** such as octadecafluoroctane . . . or fluorononane." *Id*. (emphasis and ellipses in original). Again, Dr. Huck similarly relies on paragraphs 94 and 118 of

Quake to disclose the surface tension relationship. Ex. 1002, claim chart following ¶ 53 (pg. 35); *see id.* ¶ 61.

During cross-examination at his first deposition, Dr. Huck stated that paragraph 117 is the only portion of Quake that discloses "how a surfactant can be used to assist flow of a droplet." Ex. 2026, 150:23–151:6. Dr. Huck also agreed that he was not relying on the wall-coating surfactants disclosed in paragraphs 94 or 118 to support his obviousness theory. *Id*. at 156:8–13, 157:1–8. Rather, Dr. Huck repeatedly cited paragraph 117's disclosure that surfactants "aid in controlling or optimizing droplet size, flow, and uniformity" as evidence of the claimed surface tension relationship. *See, e.g., id.* at 99:25–100:4; 112:8–12; 133:16–20.

Similarly, in its Reply, 10X no longer cites the wall-coating surfactants of paragraphs 94 or 118 as disclosing the claimed surface tension relationship. Nor does 10X cite to Dr. Huck's first Declaration regarding these paragraphs. Pet. Reply 10–11. 10X instead relies on Dr. Huck's deposition testimony regarding paragraph 117's "controlling or optimizing droplet size, flow, and uniformity" statement. *Id*. (citing Ex. 2026). Nor does Dr. Huck's Second Declaration rely on paragraphs 94 and 118, instead citing to paragraph 117 as evidence of the surface tension relationship. Ex. 1087 ¶¶ 72–74.

b. Analysis

An *inter partes* review trial before the Board is a formal adjudication under the Administrative Procedure Act; as such, the parties to the trial are guaranteed certain procedural protections. *See Belden*, 805 F.3d at 1080. Significant among these is that parties must be given notice of the "matters

of fact and law asserted," and the opportunity to meaningfully respond. *Id*. For this reason, the Federal Circuit has held that we may not base our decision on patentability on late-arising factual assertions or theories. *See Dell Inc. v. Acceleron, LLC*, 818 F.3d 1293, 1301 (Fed. Cir. 2016). In *Dell*, "an opportunity to respond was needed when the petitioner, to make its anticipation showing, newly pointed to a previously unmentioned portion of the allegedly anticipatory prior-art patent, even though it had earlier focused extensively on other portions of that prior-art patent." *In re Nuvasive Inc.*, No. 2015-1672, 2016 WL 6608999, at *5 (Fed. Cir. Nov. 9, 2016) (discussing *Dell*, 818 F.3d at 1301).

To be sure, we are not "limited to citing only portions of the prior art specifically drawn to [our] attention" in a petition. *Id*. at *4. But where the newly cited portions are "sufficiently distinct" from those previously presented by a party, the opposing party is entitled to the opportunity to respond. *Id*. at *5. Therefore, while we must consider the disclosure of a prior art reference as a whole, this does not mean that we may permit 10X to change its theory of unpatentability during trial.

10X argues that it has not changed its position, and has consistently cited paragraph 117 of Quake from the outset. Tr. 71:13–24; Pet. Reply 23. According to 10X's counsel, the Petition cited paragraph 117 "in general, and [in] its entirety, repeatedly." Tr. 73:8–9. There is no dispute that the Petition cited paragraph 117 of Quake. But the proposition for which paragraph 117 was cited in the Petition was the disclosure of fluorinated surfactants in the carrier fluid. Pet. 19–20. The paragraph's statement that surfactants "aid in controlling or optimizing droplet size, flow, and

uniformity" is quoted nowhere in the Petition; nor is paragraph 117 relied upon in the sections of the Petition pertaining to the surface tension relationship, other than to establish the presence of the surfactant itself.

The change in 10X's position is not insignificant, or a mere change in emphasis from one portion of Quake to another. Rather, it signals a change in the theory of unpatentability advanced in the Petition upon which we instituted trial. In its Petition, 10X argued that the claimed surface tension relationship is met when droplets do not adhere to the walls of the channel, and cites Quake's disclosure (in paragraph 118) of surfactants *coating the walls* as evidence that the surfactant is causing the surface tension relationship. This is the theory of unpatentability upon which we instituted trial:

> Petitioner does not contend that Quake specifically discloses the relationship between surface tension at the plug-fluid/ microchannel interface and the plug-fluid/carrier fluid interface. Rather, Dr. Huck notes Quake's disclosure that a surfactant may be used to cause the surfactant to *coat the channel walls*. . . . According to Dr. Huck, a person of ordinary skill in the art would have understood this to mean that the surface tension at the plug-fluid/ microchannel wall interface is higher than surface tension at the plug-fluid/carrier fluid interface.

Dec. on Inst. 16–17 (emphasis added).

Starting with Dr. Huck's deposition and continuing through the Reply, however, 10X's theory is that the surface tension relationship is proven by the presence of "free-flowing droplets," and that Quake discloses in paragraph 117 that surfactants *in the carrier fluid* "aid in controlling or optimizing droplet size, flow and uniformity." As counsel for 10X conceded at oral hearing, paragraphs 117 and 118 "disclose two *separate* uses of

surfactants." Tr. 21:4–9 (emphasis added). It would be unfair to Chicago if we were to institute trial on one of these uses of surfactants, and then base our finding of unpatentability on the other, separate use.

We consider it of no moment that the change in theory was first signaled during Dr. Huck's deposition, prior to Chicago filing its Patent Owner Response. Nor do we find it significant that, in its Patent Owner Response, Chicago included a section preemptively addressing 10X's potential change in theory. PO Resp. 42–46. Until 10X filed its Reply, Chicago did not know whether 10X would adopt Dr. Huck's testimony on paragraph 117 and his abandonment of paragraphs 94 and 118. Furthermore, the Board does not consider arguments made only in witness testimony and not explained sufficiently in a paper. *Cf. Cisco Sys., Inc. v. C-Cation Techs., LLC*, Case IPR2014-00454, slip op. at 10 (PTAB Aug. 29, 2014) (Paper 12) (informative) (declining to consider arguments not made in a petition and only incorporated by reference from expert declaration). Chicago was not fully on notice of 10X's new theory of unpatentability until the Reply, when it adopted Dr. Huck's cross-examination testimony.

c. Conclusion

We have determined that the Reply and Dr. Huck's supporting Second Declaration raise new issues and arguments for the first time. The citation to the new sentence of paragraph 117 of Quake is a change in 10X's theory of unpatentability. Furthermore, as discussed above, both the Declaration and the Reply rely on a theory of routine optimization that is not set forth in the Petition. *See* Pet. Reply 11. The Reply and Second Declaration, therefore,

exceed the proper scope of reply permitted under our Rules. *See* 37 C.F.R. § 42.23(b).

We determined above that we would not rely on particular sections of Dr. Huck's Second Declaration objected to by Chicago. For similar reasons, we will not rely on the Reply to the extent it raises the new arguments discussed above. Though we would be permitted, under our Rules and precedent, to exclude the entirety of the Reply, on the facts of this case we consider it sufficient to not consider the the newly-raised theories of unpatentability regarding paragraph 117 of Quake and routine optimization raised in Sections II, III, and VIII of the Reply. *See Ariosa Diagnostics v. Verinata Health, Inc*., 805 F.3d 1359, 1367 (Fed. Cir. 2015) (affirming Board's exclusion of certain arguments raised for the first time in Reply). In evaluating 10X's asserted ground of unpatentability over Quake and Ramsey, we will rely on the theory of unpatentability as set forth in the Petition and Dr. Huck's first Declaration, on which we instituted trial.

3. Fluorinated Surfactant Having a Hydrophilic Head Group

Turning to the merits of the ground of unpatentability, we first focus on the limitation—present in all independent claims—that requires that the carrier fluid comprise "a fluorinated surfactant comprising a hydrophilic head group." 10X asserts that Quake discloses this element. Pet. 19–20 (citing Ex. 1004 ¶¶ 116–117). Quake discloses in those paragraphs that its carrier fluid "may contain additives, such as agents which reduce surface tensions (surfactants)" and that "[e]xemplary surfactants include Tween, Span, fluorinated oils, and other agents that are soluble in oil relative to water." Ex. 1004 ¶ 117.

Dr. Huck testifies that "[t]he term surfactant is a contraction of the descriptive phrase 'surface active agent.' . . . because they concentrate at interfacial regions such as oil-water or liquid-solid interfaces." Ex. 1002 ¶ 42. In aqueous systems such as those disclosed in the '083 patent and Quake, Dr. Huck testifies that the surfactant is understood to reside at the oil-water boundary because it has a hydrophilic head group and a hydrophobic tail group. *Id*. (citing Ex. 1022, 3). Dr. Olmsted, who has significant experience in interfacial phenomena including surfactants, agrees, and further notes that Tween and Span—mentioned in the same sentence of Quake cited by 10X—have hydrophilic head groups. Ex. 1085 ¶¶ 26–29.

In response, Chicago notes that Dr. Huck admits surfactants, by definition, do not require a hydrophilic head group. PO Resp. 27. Furthermore, Chicago argues that Quake's disclosure of surfactants are to coat the channel walls, meaning that they reside at the channel wall/carrier fluid interface. *Id*. at 28–29. In such situations—where the interface is between two hydrophobic materials—Dr. Huck agreed that he would not use a surfactant with a hydrophilic head group. *Id*. (citing Ex. 2026, 102:17–23). Dr. Sia's testimony supports these arguments. Ex. 2028 ¶¶ 71–87.

We agree with Chicago that Quake does not explicitly disclose that the surfactants of paragraph 117 have a hydrophilic head group, and that "surfactants" in general include surface active agents both with and without a hydrophilic head group. Nevertheless, we find that a person of skill in the art would understand the surfactants disclosed in paragraph 117 may include a hydrophilic head group. Dr. Olmsted notes, and Chicago does not dispute,

that the other surfactants listed as "exemplary"—namely, Tween and Span—have hydrophilic head groups. Ex. 1085 ¶ 27. Furthermore, the sentence characterizes the surfactants as "soluble in oil relative to water," from which Dr. Olmsted concludes that the oil-water boundary is the surface where the surfactants are expected to reside. *Id*. ¶ 29. While Chicago is correct that other portions of Quake—for example, as discussed extensively above, paragraph 118—disclose surfactants that coat the channel walls, we do not understand paragraph 117's surfactants to be so limited.[8]

For this reason, we find credible Dr. Huck's and Dr. Olmsted's testimony that a person of ordinary skill in the art would understand paragraph 117's disclosure to refer to surfactants having a hydrophilic head group. We find that Quake discloses fluorinated surfactants that reside at the droplet-carrier fluid interface, and which have a hydrophilic head group.

4. Surface Tension Relationship

Having found the claimed surfactant disclosed in Quake, we now address the challenged independent claims' requirement that the surfactant is "present in a concentration such that surface tension at the plug-fluid/microchannel wall interface is higher than surface tension at the plug-

[8] In any event, even if Quake's surfactants were limited to those coating the channel walls, Quake discloses that some channels may be made of hydrophilic materials such as urethane. Ex. 1004 ¶ 118 ("Channels of the invention may be formed from . . . urethane compositions" and "hydrophilic properties of urethane."); *see also id.* ¶ 216 ("PDMS device is placed in a hot bath of HCl to make the surface hydrophilic"). In such applications, the surfactant coating these hydrophilic channel walls would reasonably be expected to have a hydrophilic head group.

fluid/carrier fluid interface." 10X again relies on Quake for this disclosure, in particular paragraphs 94 and 118 of the reference.

10X concedes that Quake does not explicitly disclose the surface tension relationship. Tr. 8:13–20. Rather, 10X infers that the surface tension relationship is met because of the presence of droplets that do not adhere to the channel walls. *Id*. at 10:9–13; Pet. 24. 10X then ties this non-adhesion of droplets to the presence of surfactants coating the channel walls, as disclosed in paragraphs 94 and 118 of Quake. Pet. 25 ("The combination of Quake and Ramsey teaches how to avoid adhesion of plugs to the wall. Quake discloses use of fluorinated oils such as surfactants in carrier fluid and discloses use of such surfactants for coating the walls of microchannels."). As discussed at length above, Dr. Huck testified in his first Declaration in support of this inference of the surface tension relationship. Ex. 1002 ¶¶ 59–61.

The theory advanced by 10X—that the surface tension relationship can be inferred from the lack of adhesion of droplets—suffers from at least two failings. First, as discussed above, to establish the presence of fluorinated surfactants with a hydrophilic head group, 10X relies on paragraph 117 of Quake, which it argues discloses surfactants residing at the oil-water interface between the droplets and the carrier fluid. Indeed, this reliance is crucial to its inference that the surfactants have a hydrophilic head group. But when it comes to inferring that the claimed surface tension relationship is present, 10X points to a different disclosure of surfactants coating the channel walls. As counsel conceded, the disclosures of paragraphs 117 and 118 "disclose two separate uses of surfactants." Tr.

21:8–9. 10X cannot have it both ways, arguing that the hydrophilic head group is implied because the surfactant is at the oil-water interface, while also arguing that the surface tension relationship is implied because the surfactant coats the channel walls.

Furthermore, even if we were to accept 10X's reliance on the surfactant coating the channel walls, its proposed inference is not supported by the record or logic. While it may be the case that if the surface tension relationship is present, droplets do not adhere to the wall, to infer the reverse would be affirming the consequent.[9] In other words, we cannot infer from the fact that droplets do not adhere to the channel wall that the claimed surface tension relationship is necessarily present, because there are other possible causes of non-adherence. As Chicago correctly notes, Quake discloses multiple reasons why a droplet may not adhere to a channel wall, including droplet shape ("about four times as long as [it is] wide") and size ("[d]roplet adherence is overcome when the droplet is massive enough in relation to the channel size"). PO Resp. 24–25 (citing Ex. 1004 ¶ 92).

10X attempts to distinguish these causes of non-adherence in Quake's paragraph 92 by arguing that they pertain only to "a situation where a droplet has actually touched the channel wall and then breaks off. That is not a free-flowing droplet. A free-flowing droplet is one that doesn't adhere to the wall and flows through the channel." Tr. 11:15–12:5. The record does not support such a distinction. Indeed, paragraph 92 uses the exact

[9] The "fallacy of affirming the consequent" is the following logical fallacy: "If cause, then effect." "Effect, therefore cause." The fallacy occurs because there may be other causes that lead to the same effect.

term "free-flowing droplet," discussing a "typical free-flowing droplet" of a certain shape, such that it "overcome[s] channel adherence and move[s] freely through the microfluidic device." Ex. 1004 ¶ 92. In sum, we cannot infer from the evidence adduced by 10X—that Quake discloses droplets that do not adhere to channel walls—that the claimed surface tension relationship is present.[10]

For these reasons, we cannot conclude from the arguments advanced in the Petition that the claimed surface tension relationship is disclosed by Quake.

5. Conclusion

10X has not proven by a preponderance of the evidence that Quake teaches the surface tension relationship limitation of the challenged claims. Nor does 10X allege that Ramsey teaches or suggests this limitation. For these reasons, we cannot conclude that 10X has carried its burden of proving that claims 1–31 are unpatentable over the combined disclosures of Quake and Ramsey.

[10] We note that we would reach the same conclusion even if we had not excluded portions of 10X's Reply. 10X's new theory of unpatentability—which relies on paragraph 117 as evidence of the surface tension relationship—suffers from the same infirmity as its original theory; namely that we cannot infer from the fact that "[s]urfactants may aid in controlling or optimizing droplet size, flow and uniformity" (Ex. 1004 ¶ 117) that the claimed surface tension relationship is present.

C. Obviousness over Quake, Ramsey, and Green

Claims 18 and 24 further require particular fluorinated oils as the carrier fluid. Petitioner argues that these claims are unpatentable as having been obvious over the combined disclosures of Quake, Ramsey, and Green. Pet. 50–52. Petitioner contends that, given the disclosure in Ramsey of perfluorocarbon segmenting fluids, a person of ordinary skill in the art would have consulted Green, which lists perfluorocarbons used in various applications, including the perfluorocarbons recited in claims 18 and 24. *Id.* at 51.

10X does not contend, nor do we find, that Green remedies the deficiency in Quake noted above. In other words, the record does not establish that Green teaches or suggests the claimed surface tension relationship. For this reason, 10X has not met its burden of proving that claims 18 and 24 are unpatentable over the combined disclosures of Quake, Ramsey, and Green.

D. Motion to Exclude

Chicago moves to exclude various exhibits filed by 10X, namely Exhibits 1037, 1043, 1045, 1047, 1050, 1051–1056, 1072, 1081, 1088–1092, and portions of Dr. Huck's testimony (Exs. 1002 and 1087). Mot. 1. The basis for the Motion is Chicago's prior objections to these exhibits on grounds of hearsay (FRE 802), prejudice (FRE 403), or unreliability (FRE 702). Even having considered these objected-to exhibits, however, we have found in Chicago's favor on the merits of 10X's patentability challenge. As such, the grant or denial of Chicago's Motion would have no effect on the

outcome of the proceeding. We, therefore, dismiss the Motion to Exclude as moot.

III. CONCLUSION

For the foregoing reasons, based on a review of the complete record developed during trial, we conclude that 10X has not proven, by a preponderance of the evidence, that claims 1–31 are unpatentable.

IV. ORDER

Accordingly, it is:

ORDERED that claims 1–31 of U.S. Patent No. 8,889,083 B2 *have not been proven unpatentable*;

FURTHER ORDERED that, pursuant to 35 U.S.C. § 318(b), upon expiration of the time for appeal of this decision, or the termination of any such appeal, a certificate shall issue confirming the patentability of claims 1–31 of U.S. Patent No. 8,889,083 B2;

FURTHER ORDERED that Patent Owner's Motion to Exclude (Paper 36) is *dismissed as moot*; and

FURTHER ORDERED that, because this is a Final Written Decision, parties to the proceeding seeking judicial review of the decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

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