Trials@uspto.gov
571.272.7822

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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 IPR2015-01560
Patent 7,129,091 B2

Before CHRISTOPHER L. CRUMBLEY, TINA E. HULSE, and ELIZABETH M. ROESEL, *Administrative Patent Judges*.

HULSE, *Administrative Patent Judge*.

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

I. INTRODUCTION

10X Genomics, Inc. ("Petitioner") filed a Petition requesting an *inter partes* review of claims 1–14, 21–46, and 49–58 of U.S. Patent No. 7,129,091 B2 (Ex. 1001, "the '091 patent"). Paper 1 ("Pet."). The University of Chicago ("Patent Owner") filed a Preliminary Response to the Petition. Paper 11 ("Prelim. Resp.").

We have jurisdiction under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted "unless . . . 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). Upon considering the Petition and Preliminary Response, we determine that Petitioner has not established a reasonable likelihood that it would prevail in showing the unpatentability of claims 1–14, 21–46, and 49–58. Accordingly, we decline to institute an *inter partes* review of those claims.

A. Related Proceedings

Petitioner identifies as a related matter *RainDance Techs., Inc. v. 10X Genomics, Inc.*, No. 1:15-cv-00152-RGA (D. Del.). Pet. 59.

Petitioner also filed petitions for *inter partes* review of related patents in IPR2015-01163 (US 8,304,193), IPR2015-01162 (US 8,273,573), IPR2015-01158 (US 8,329,407), IPR2015-01157 (US 8,889,083), and IPR2015-01156 (US 8,822,148). The Board instituted *inter partes* reviews in IPR2015-01157 and IPR2015-01162, and denied the remaining petitions.

B. The ’091 Patent (Ex. 1001)

The ’091 patent relates to methods for conducting a reaction in plugs in a microfluidic system. Ex. 1001, Abstract. Microfluidic systems transport fluids through networks of channels, typically having micrometer dimensions. *Id.* at 1:15–17. According to the Specification, the main advantages of microfluidic systems are high speed and low consumption of reagents. *Id.* at 1:20–21.

Rather than rely on laminar flow of liquids through microfluidic channels, the ’091 patent Specification describes using microfluidic droplets, or “plugs” in the system. Figure 2A, is reproduced below:[1]

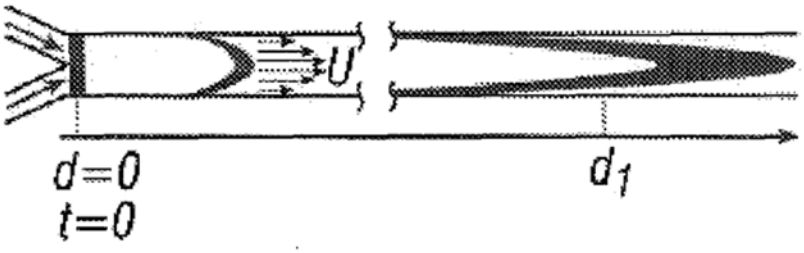

FIG. 2A-1

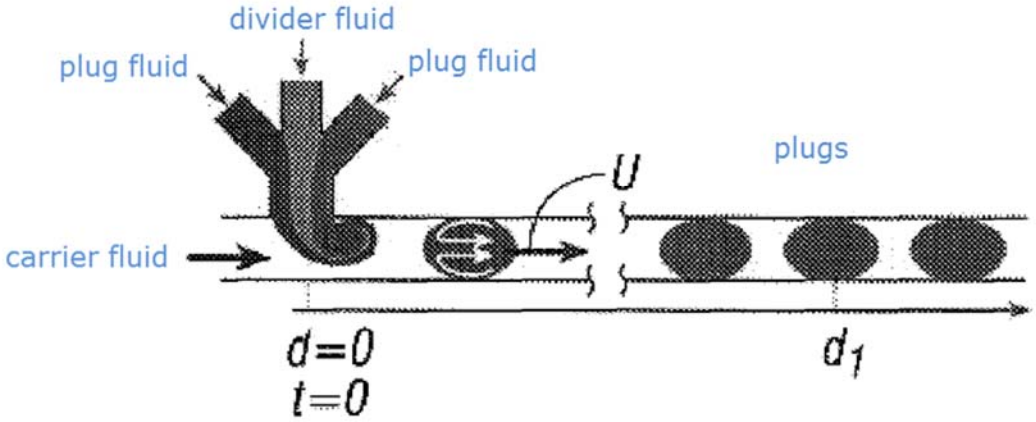

FIG. 2A-2

[1] We have added the annotations in blue to Figure 2A-2 to indicate the plug fluids, divider fluid, carrier fluid, and plugs.

Figure 2A is a diagram contrasting laminar flow transport (depicted in Figure 2A-1) with plug transport (depicted in Figure 2A-2) in a channel. Figure 2A-2 depicts the formation of plugs, where two aqueous plug fluids separated by a "divider" aqueous stream, enter a microchannel with a flowing immiscible carrier fluid, such as an oil, at which point a series of plugs form, and the plug fluids mix. *Id.* at 17:45–51. The plug volumes, which are dependent on channel size, can range from about 1 femtoliter to about 250 nanoliters. *Id.* at 19:59–20:1.

C. Illustrative Claim

Petitioner challenges claims 1–14, 21–46, and 49–58 of the '091 patent. Claims 1, 36, 37, and 57 are independent. Claim 1 is illustrative and is reproduced below:

> 1. A method for conducting a reaction within at least one plug comprising the steps of:
>
> introducing a carrier-fluid into a first microchannel of a device;
>
> simultaneously introducing at least two streams of plug-fluids into a first inlet in fluid communication with the first microchannel so that at least one plug forms in the carrier-fluid after the streams contact the carrier-fluid; wherein:
>
> a first plug-fluid comprises a first reagent;
>
> a second plug-fluid comprises a second reagent;
>
> each plug-fluid is immiscible with the carrier-fluid; and

each plug comprises both the first and second plug-fluids so that the reaction of the reagents substantially occurs in the plug;

each plug is substantially surrounded by carrier.

D. The Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–14, 21–46, and 49–58 of the '091 patent on the following grounds:

References	**Basis**	**Claims challenged**
Quake[2]	§ 103	1, 2, 5–11, 13, 14, 21–26, 28–43, 45, 46, and 49–58
Quake and Kenis[3]	§ 103	1, 2, 5–14, 21–26, 28–46, and 49–58
Quake and Ramsey[4]	§ 103	3
Quake, Ramsey, and Green[5]	§ 103	4 and 27
Quake, Kenis, and Ramsey	§ 103	3
Quake, Kenis, Ramsey, and Green	§ 103	4 and 27

[2] Quake et al., US 2002/0058332 A1, filed Sept. 14, 2001 and published May 16, 2002 (Ex. 1004).

[3] Kenis et al., *Microfabrication Inside Capillaries Using Multiphase Laminar Flow Patterning*, 285 SCIENCE 83–85 (1999) (Ex. 1008).

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

[5] Green et al., *Perfluorocarbon Fluids*, Organofluorine Chemistry: Principles and Commerical Applications 89–119 (Banks, Smart, Tatlow eds., 1994) (Ex. 1007).

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 at least 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 at least 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. 17.

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 experience in using, designing or creating microfluidic devices. 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, the Board interprets claim terms in an unexpired patent according to the broadest reasonable construction in light of the specification of the patent in which they appear. *See In re Cuozzo Speed Techs., LLC*, 793 F.3d 1268, 1276–80 (Fed. Cir. 2015); 37 C.F.R. § 42.100(b). Under that standard, and absent any special definitions, we give claim terms their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *See In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms must be set forth with reasonable clarity, deliberateness, and precision. *See In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

Based on the current record, we determine that none of the claim terms requires explicit construction for purposes of this Decision.

C. Obviousness over Quake

Petitioner asserts that claims 1, 2, 5–11, 13, 14, 21–26, 28–43, 45, 46, and 49–58 are unpatentable as having been obvious over Quake, which Petitioner asserts is prior art under 35 U.S.C. § 102(e) as of its September 14, 2001 filing date. Pet. 16–43. Petitioner relies

on the testimony of its declarant, Wilhelm T. S. Huck, Ph.D. Ex. 1002. Patent Owner opposes Petitioner's assertion. Prelim. Resp. 26–43. Based on the current record, we determine that Petitioner has not established a reasonable likelihood that it would prevail in showing the claims are unpatentable as having been obvious over Quake.

1. Quake (Ex. 1004)

Quake relates to microfluidic devices and methods for analyzing and/or sorting biological materials. Ex. 1004, Abstract. Quake states that its device and methods "offer several advantages over traditional flow cytometry devices and methods." *Id.* ¶ 14. Quake's 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 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 22 of Quake illustrates the preferred embodiment of Quake and is reproduced below:

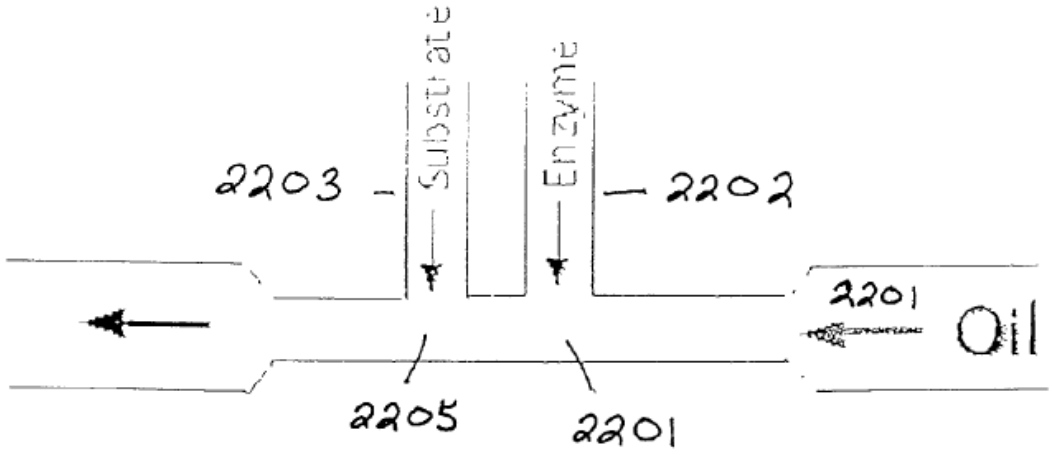

Figure 22 shows a channel design for compartmentalization of enzyme and substrate. Ex. 1004 ¶ 45. First inlet channel 2202 may introduce an aqueous solution containing an enzyme so that droplets are introduced into a stream of oil in main channel 2201 at the first droplet extrusion region 2204.[6] *Id.* ¶ 316. Second inlet channel 2203 may introduce an aqueous solution containing a substrate for the enzyme so that droplets containing the substrate are introduced into main channel 2201 at second droplet extrusion region 2205. *Id.* According to Quake, "[b]y timing release of these droplets to occur as a droplet of enzyme passes through the second droplet extrusion region, the two droplets are combined and the enzyme is able to react with the substrate." *Id.*

2. Analysis

Petitioner asserts that Quake alone teaches or suggests each limitation of claims 1, 2, 5–11, 13, 14, 21–26, 28–43, 45, 46, and 49–

[6] Figure 22 identifies both the main channel and the first droplet extrusion region as item 2201. We understand from the Quake specification, however, that the first droplet extrusion region should be labeled 2204. Ex. 1004 ¶ 316.

58. Regarding claim 1, Petitioner provides a claim chart identifying the disclosures of Quake that purportedly teach or suggest each limitation. Pet. 17–21. Petitioner acknowledges, however, that Quake differs from claim 1 in that Quake discloses introducing each plug fluid through its own inlet, instead of co-flowing each plug fluid through an inlet. Pet. 24. Petitioner, however, argues that "simultaneously introducing at least two fluids into a microchannel," as required by claim 1, "such that they co-flow in parallel, was well-known in the art by May 2002." *Id.* Petitioner also argues that a skilled artisan reading Quake would have known that simultaneously introducing at least two fluids would have allowed for rapid introduction of the reagents into the same plug without the need for merging plugs. *Id.*

According to Petitioner's declarant, Dr. Huck, modifying Quake to introduce plug fluids via the same inlet would have been a "predictable variation of Quake's method" as the modification "would simply bring the two inlets closer such that they meet at a single junction entering the main channel." Ex. 1002 ¶ 58. Dr. Huck also states that it would have required only common sense to implement such a modification and would not have been beyond the skill of a skilled artisan to do so. *Id.* ¶ 59. Thus, Dr. Huck concludes that a person of ordinary skill in the art would have had a reasonable expectation of success in modifying Quake. *Id.* ¶ 60.

In response, Patent Owner asserts that Petitioner has failed to provide the requisite reasoning to show that the challenged claims would have been obvious over Quake. Prelim. Resp. 27–37. We agree with Patent Owner.

In essence, Petitioner argues that because Quake discloses forming plugs containing a single fluid and because simultaneously introducing two fluids into a microchannel was known in the art, it would have been obvious to modify Quake to obtain the claimed invention. It is well established, however, that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR Int'l Co. v. Teleflex Inc*., 550 U.S. 398, 418 (2007). "[I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine elements in the way the claimed new invention does." *Id.* Moreover, a person of ordinary skill in the art must have had a reasonable expectation of success of doing so. *PAR Pharm., Inc. v. TWi Pharms., Inc.*, 773 F.3d 1186, 1193 (Fed. Cir. 2014).

We are not persuaded that Petitioner has shown sufficiently that a person of ordinary skill in the art would have modified the system of Quake to simultaneously introduce two plug fluids into an inlet to form plugs containing both fluids with a reasonable expectation of success. Although Petitioner asserts that simultaneously introducing two fluids into a microchannel such that they co-flow in parallel was well known in the art by May 2002, Pet. 24, Petitioner's assertion does not address whether it was known or would have been obvious to introduce two reagents into a microchannel inlet to form plugs, such that each plug contains both reagents and a reaction of the reagents substantially occurs in the plugs, as recited in the challenged claims. Furthermore, the references cited as teaching or suggesting simultaneous introduction of two fluids into a microchannel are not

directed to the formation of plugs, let alone to conducting reactions in plugs. Rather, each reference is directed to laminar flow of parallel streams of fluid such that any reaction that occurs is localized along the interface between the fluids. *See* Ex. 1008, 85 (describing "parallel streams of fluid [that] can maintain sharp boundaries . . . [such] that reaction can be localized at the interfaces"); Ex. 1016,[7] Abstract ("This paper describes the use of laminar flow of liquids in capillary systems . . . ."); Ex. 1019,[8] Fig. 5B (illustrating laminar flow of two fluids and diffusional mixing at the interface); Ex. 1018,[9] 2376 ("Laminar flow patterning occurs by a chemical reaction at the interface between two miscible fluids flowing through a channel."). The '091 patent, however, distinguishes such laminar flow transport and fluid mixing from plug transport and mixing of fluids within each plug. Ex. 1001, Fig. 2A, 17:45–54.

Petitioner also argues that a person of ordinary skill in the art reading Quake would have known that "simultaneously introducing at least two fluids in such a manner would have allowed for rapid introduction of the reagents into the same plug without the need for merging plugs—which can be favored when plugs have been stabilized against coalescence by the presence of surfactants." Pet. 24

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[7] Takayama et al., *Patterning Cells and Their Environments Using Multiple Laminar Fluid Flows in Capillary Networks*, 96 Proc. Natl. Acad. Sci. USA 5545–48 (1999) (Ex. 1016).

[8] Kopf-Sill et al., US 5,842,787, issued Dec. 1, 1998 (Ex. 1019).

[9] Ismagilov et al., *Experimental and Theoretical Scaling Laws for Transverse Diffusive Broadening in Two-Phase Laminar Flows in Microchannels*, 76 Applied Physics Letters 2376–78 (2000) (Ex. 1018).

(citing § III.A.1; Ex. 1015, Abstract, 168:1–169:2; Ex. 1028, 52–53; Ex. 1026, 2439–42; Ex. 1002 ¶ 55). Petitioner, however, offers nothing more than a string cite of references (sometimes to entire articles) with no accompanying explanation as to how those references support Petitioner's argument. Even if we were to overlook this lack of explanation, closer examination of the cited references reveals that they do not support Petitioner's argument. Each of the references appears to relate to the use of surfactants and their effect on droplet coalescence. Even if this suggests the need to avoid merging plugs, Petitioner does not explain adequately why a person of ordinary skill in the art would have known that simultaneously introducing two fluids into a microchannel inlet would address this need.

Petitioner further argues that modifying the system of Quake would have been a predictable variation that would not require an overall redesign of Quake's plug-generating structures or overall changes to Quake's methods. Pet. 25–26. According to Dr. Huck, the device of Quake "would be largely unchanged because it would use the same inlet and channel dimensions and fluids but with a modified inlet design." Ex. 1002 ¶ 58. The modification of Quake "would simply bring the two inlets closer such that they meet at a single junction entering the main channel." Ex. 1002 ¶ 58. Dr. Huck also contends that doing so "would have only required common sense . . . and it would not have been beyond the skill of a [person of ordinary skill in the art] to do so." *Id.* ¶ 59.

We are not persuaded by Dr. Huck's conclusory testimony. In short, Petitioner and Dr. Huck contend that a person of ordinary skill

in the art would have known and expected that merging the two inlets of Quake would have resulted in forming a series of plugs, each of which contains two reagents such that a reaction of the reagents substantially occurs in the plugs. But neither Petitioner nor Dr. Huck offers sufficient evidence in support of this contention. For example, neither Petitioner nor Dr. Huck provides persuasive reasoning, that does not rely on impermissible hindsight, explaining why one of ordinary skill in the art would have been led to introduce two fluids into an inlet to form plugs containing both fluids, especially given that the cited prior art discusses the use of a single inlet in laminar flow, as opposed to plug formation. Dr. Huck also does not explain why a person of ordinary skill in the art would have expected a "modified inlet design" in Quake to yield predictable results in a microfluidic device in May 2002. We are not persuaded that the generic statement in Quake that "[a] variety of channels for sample flow and mixing can be microfabricated on a single chip and can be positioned at any location on the chip" (Ex. 1004 ¶ 79) suggests that merging the two plug fluid inlets would predictably result in the formation of plugs in which a reaction might occur. We, therefore, give Dr. Huck's testimony little weight on this issue. *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").

As such, we find that Petitioner has not established a reasonable likelihood that a person of ordinary skill in the art would have found the subject matter of claim 1 obvious over Quake alone. Furthermore, Petitioner offers essentially the same arguments for independent claims 36, 37, and 57. Pet. 27–29. For the same reasons stated above for claim 1, we find that Petitioner has not shown sufficiently that a person of ordinary skill in the art would have had a reason to modify Quake to simultaneously introduce two plug fluids through an inlet to form a plug, as recited in the claims, with a reasonable expectation of success.[10]

Accordingly, we determine that Petitioner has failed to establish a reasonable likelihood that it would prevail in its assertion that independent claims 1, 36, 37, and 57, or dependent claims 2, 5–11, 13, 14, 21–26, 28–35, 38–43, 45, 46, 49–56, and 58, are unpatentable as obvious over Quake.

D. Obviousness over Quake and Kenis

Relying on the Huck Declaration for support, Petitioner argues that claims 1, 2, 5–14, 21–26, 28–46, and 49–58 are unpatentable as

[10] We note that claim 37 appears to be broader than the other independent claims, as it recites having an inlet for each plug fluid and forming at least one plug "after the first and second plug fluids contact the carrier fluid." Petitioner, however, only asserts that claim 37 "encompass[es] simultaneously introducing at least two plug-fluids that co-flow in parallel through an inlet." Pet. 28. Petitioner then asserts the same arguments for claim 37 as it does for claim 1. *Id.* at 28–29. Because Petitioner does not separately challenge claim 37 under a broader construction, we do not consider whether claim 37 is unpatentable under such a construction.

obvious over Quake and Kenis. Pet. 43–47. Patent Owner opposes the challenge. Prelim. Resp. 43–45.

Petitioner's arguments with respect to the combination of Quake and Kenis are largely the same as its obviousness challenge over Quake alone. Rather than rely on the knowledge of a person of ordinary skill in the art to teach or suggest the simultaneous introduction of plug fluids (which included knowledge of Kenis, Ex. 1008), Petitioner expressly relies on Kenis as part of the combination. *Compare* Pet. 24 *with id.* at 43.

Kenis discloses a system in which two fluids flow laminarly through separate inlets to join together at a "Y" junction. Ex. 1008, Fig. 1. Kenis states that parallel streams of fluid can maintain sharp boundaries such that reactions "can be localized at the interfaces." *Id.* at 85. Kenis, however, does not disclose the formation of plugs.

For the same reasons stated above with respect to Quake alone, we find that Petitioner has failed to show sufficiently that a person of ordinary skill in the art would have had a reason to modify Quake's system to include Kenis's inlet with a reasonable expectation of success.

Accordingly, we determine that Petitioner has failed to show a reasonable likelihood that it would prevail in its assertion that claims 1, 2, 5–14, 21–26, 28–46, and 49–58 are unpatentable as obvious over Quake and Kenis.

E. Remaining Obviousness Challenges

Petitioner argues that dependent claims 3, 4, and 27, which depend directly or indirectly from claim 1, are unpatentable as obvious over Quake and one or more other references. Petitioner does

not argue, nor do we find, that the additional references remedy the deficiencies of Quake or Quake and Kenis, as discussed above. For the same reasons stated above with respect to claim 1, we, therefore, determine that Petitioner has failed to show a reasonable likelihood that it would prevail in its challenge of any of those claims.

III. CONCLUSION

We conclude that Petitioner has not established a reasonable likelihood of prevailing on its assertions that claims 1–14, 21–46, and 49–58 of the ’091 patent are unpatentable as obvious.

IV. ORDER

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

PETITIONER:

Eldora L. Ellison
eellison-PTAB@skgf.com

Deborah A. Sterling
dsterlin-PTAB@skgf.com
STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

PATENT OWNER:

Adrian Percer
adrian.percer@weil.com

Elizabeth Weiswasser
elizabeth.weiswasser@weil.com
WEIL, GOTSHAL & MANGES, LLP