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Paper 39
Date: April 26, 2021

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

10X GENOMICS, INC.,
Petitioner,

v.

BIO-RAD LABORATORIES, INC.,
Patent Owner.

IPR2020-00086
Patent 9,562,837 B2

Before CHRISTOPHER M. KAISER, KIMBERLY McGRAW, and ELIZABETH M. ROESEL, *Administrative Patent Judges.*

ROESEL, *Administrative Patent Judge*.

DECISION
Final Written Decision
Determining Some Challenged Claims Unpatentable
35 U.S.C. § 318(a)

I. INTRODUCTION

A. Background and Summary

10X Genomics, Inc. ("Petitioner") filed a Petition (Paper 2, "Pet.") seeking *inter partes* review of claims 1–4, 7–13, 19, and 20 ("the challenged claims") of U.S. Patent No. 9,562,837 B2 ("the '837 Patent"). Bio-Rad Laboratories, Inc. ("Patent Owner") filed a Preliminary Response. Paper 7. On April 27, 2020, we instituted an *inter partes* review. Paper 8 ("Inst. Dec.").

After institution, Patent Owner filed a Patent Owner Response (Paper 26, "PO Resp."), Petitioner filed a Reply (Paper 29, "Pet. Reply"), and Patent Owner filed a Sur-reply (Paper 31, "PO Sur-reply"). An oral hearing was held on January 27, 2021, and a transcript of the hearing is included in the record. Paper 38.

We have jurisdiction under 35 U.S.C. § 6. This Final Written Decision is issued pursuant to 35 U.S.C. § 318(a). For the reasons that follow, we determine that Petitioner has shown by a preponderance of the evidence that some, but not all, of the challenged claims of the '837 Patent are unpatentable.

The Petition presents two theories of obviousness, one based on the disclosure of wells and another based on the disclosure of density sorters. Pet. 23–24, 31, 56. The parties' dispute concerning Petitioner's first theory centers on whether the asserted references teach or suggest a "separation chamber" and "droplet receiving outlet" as recited in the challenged claims. For the reasons that follow, we determine that Ismagilov 091, alone or in combination with Quake, discloses an open-topped outlet well or reservoir that satisfies Patent Owner's claim constructions for "separation chamber" and "droplet receiving outlet." The parties' dispute concerning Petitioner's

second theory centers on whether Ismagilov 119's disclosure of sorting droplets based on density would have suggested a "separation chamber" as recited in the challenged claims or would have been combined with Pamula's disclosure of separating one phase from another phase based on a difference in density. For the reasons that follow, we determine that Petitioner has not proven its case based on this second theory.

B. Real Parties in Interest

Pursuant to 37 C.F.R. § 42.8(b)(1), Petitioner identifies 10X Genomics, Inc. as the real party in interest. Pet. 71. Patent Owner identifies Bio-Rad Laboratories, Inc. as the real party in interest. Paper 24 (Updated Mandatory Notice).

C. Related Matters

Pursuant to 37 C.F.R. § 42.8(b)(2), the parties identify the following district court action: *Bio-Rad Laboratories, Inc. v. 10X Genomics, Inc.*, No. 1:18-cv-01679-RGA (D. Del.). Pet. 71; Paper 24.

There are three related cases before the Board involving the same parties and the same patent or a related patent. IPR2020-00087 involves the '837 Patent, and IPR2020-00088 and IPR2020-00089 involve U.S. Patent No. 9,896,722 B2, which is a continuation-in-part of the '837 Patent. The January 27, 2021, oral hearing transcript (Paper 38) pertains to all four cases.

D. The '837 Patent

The '837 Patent was issued on an application filed April 2, 2013, and lists a number of provisional and non-provisional priority applications, the

earliest of which were filed May 11, 2006. Pet. 3; Ex. 1001, codes (22), (60), (63).[1]

The '837 Patent is titled "Systems for Handling Microfludic [*sic*] Droplets." Ex. 1001, code (54). The '837 Patent discloses an assembly that includes a droplet formation module and a chamber. *Id.* at code (57); 3:11–12, 3:36–37, 52:38–39, 53:21–22. The droplet formation module is configured to form droplets surrounded by an immiscible fluid. *Id.* at code (57); 3:12–20, 52:38–48. The chamber is configured to receive droplets and immiscible fluid and has an outlet configured to receive substantially only droplets. *Id.* at code (57), 3:37–48, 53:22–25. According to the '837 Patent, the assembly is "particularly useful for reducing potential contamination associated with sample handing." *Id.* at 52:27–29.

[1] Petitioner argues that the America Invents Act ("AIA") applies to the '837 Patent because the application that led to the '837 Patent contained new matter and claims to that new matter with an effective filing date of April 2, 2013. Pet. 5. We do not need to determine whether or not the AIA applies because on this record, as discussed below, Petitioner's asserted references are prior art to the '837 Patent under either the AIA or pre-AIA version of 35 U.S.C § 102.

Figure 38 of the '837 Patent is reproduced below:

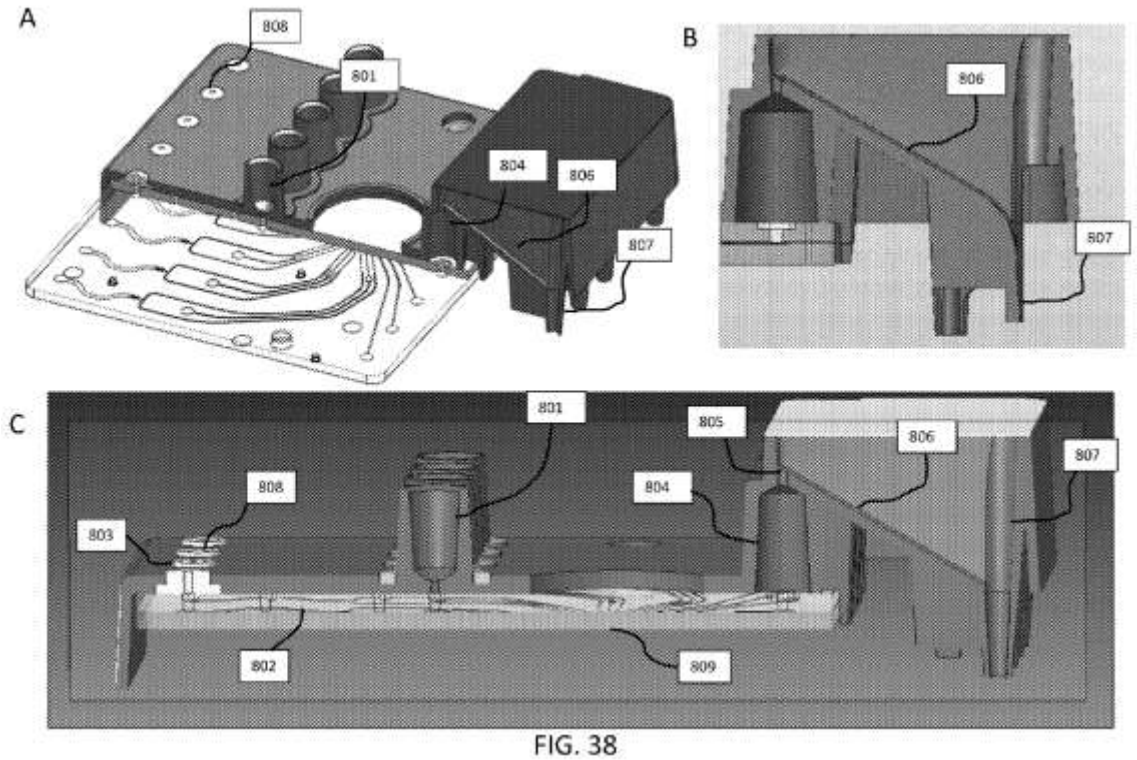

FIG. 38

Figure 38 shows a microfluidic assembly that includes a droplet formation module and a chamber. Ex. 1001, 8:22–23, 53:47–48, 53:62–65, 54:34–41. The droplet formation module includes sample input 801, channel 802, and oil input 803. *Id.* at 53:62–65. The assembly includes chamber 804 equipped with outlet 805, which is connected to slide 806, which is in turn connected to output nozzle or exit port 807. *Id.* at 54:34–41, 54:47–57, 54:61–63. The assembly also includes reagent input 808 and coalescence module 809. *Id.* at 54:4–6, 54:19–22.

An aqueous sample solution is introduced through sample input 801, and oil is introduced through oil input 803. Ex. 1001, 53:48–50, 53:59–60. The oil and aqueous solution meet at a junction in channel 802 such that the aqueous solution is segmented by the oil, thereby forming droplets. *Id.* at 53:60–62. "As the oil containing the droplets moves along the assembly

through the channel 802, the oil and droplets begin to enter the chamber 804." *Id.* at 54:37–39. "Due to the difference in their respective densities, the oil and droplets separate from each other in the chamber 804." *Id.* at 54:39–41. Droplets exit chamber 804 into outlet 805 "leaving a large part of the oil behind." *Id.* at 54:41–44. Droplets exiting chamber 804 through outlet 805 enter slide 806 and travel though the slide and nozzle 807, which leads to a vessel or container for collecting the droplets. *Id.* at 54:51–59.

E. Illustrative Claim

The '837 Patent includes 20 claims. Claim 1 is the sole independent claim and is reproduced below, with paragraph breaks adjusted and bracketed numbers added to correspond with Petitioner's identification of claim elements:

> 1. [1.0] An assembly, the assembly comprising:
>
> [1.1] a microchannel in a horizontal plane;
>
> [1.2] at least one droplet formation module comprising a sample inlet, an immiscible fluid inlet, and a junction, wherein the junction is located between the sample inlet and the microchannel and the droplet formation module is configured to produce droplets comprising the sample surrounded by the immiscible fluid; and
>
> [1.3] at least one downstream separation chamber comprising a droplet receiving chamber inlet and at least one droplet receiving outlet,
>
> [1.4] wherein the separation chamber is upright to the microchannel and out of the horizontal plane;
>
> [1.5] wherein the droplet formation module and the separation chamber are in fluid communication with each other via the microchannel;

> [1.6] and wherein the separation chamber has a wider cross-section than the microchannel cross-section to accumulate a plurality of droplets comprising the sample and
>
> [1.7] is of a volume sufficient to separate the plurality of droplets comprising the sample from the immiscible fluid within the separation chamber.

Ex. 1001, 88:2–23; *see also* Pet. 31–45 (identifying claim elements).

F. Asserted Grounds and References

Petitioner asserts the following grounds of unpatentability:

	Claims Challenged	35 U.S.C. §	Reference(s)
1	1, 2, 4, 10–13, 19, 20	102	Ismagilov 091[2]
2	1, 2, 4, 7, 9–13, 19, 20	103	Ismagilov 091, Quake[3]
3	1–4, 7–13, 19, 20	103	Ismagilov 119[4]
4	1–4, 7–13, 19, 20	103	Ismagilov 119, Pamula 634[5]
5	1–4, 7–13, 19, 20	103	Ismagilov 119, Pamula 238[6]

G. Testimonial Evidence

In addition to the prior art cited above, Petitioner relies on a Declaration of Richard B. Fair, Ph.D. (Ex. 1008) and a second declaration of Dr. Fair (Ex. 1071) filed with the Reply. Patent Owner cross-examined

[2]Ex. 1004, Ismagilov et al., US 7,129,091 B2, issued Oct. 31, 2006 ("Ismagilov 091").

[3]Ex. 1006, Quake et al., US 2002/0058332 A1, published May 16, 2002 ("Quake").

[4]Ex. 1005, Ismagilov et al., US 2006/0094119 A1, published May 4, 2006 ("Ismagilov 119").

[5]Ex. 1007, Pamula et al., US 2007/0243634 A1, published Oct. 18, 2007 ("Pamula 634").

[6]Ex. 1018, Pamula et al., US 2015/0148238 A1, published May 28, 2015 ("Pamula 238").

Dr. Fair twice and filed a transcript of the first deposition as Exhibit 2017 and the second deposition as Ex. 2041.

Patent Owner relies on a Declaration of Shelley Anna, Ph.D. Ex. 2016. Petitioner cross-examined Dr. Anna and filed a transcript of the deposition as Exhibit 1075.

II. DISCUSSION

A. Legal Standards

"In an [*inter partes* review], the petitioner has the burden from the onset to show with particularity why the patent it challenges is unpatentable." *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016) (citing 35 U.S.C. § 312(a)(3) (requiring *inter partes* review petitions to identify "with particularity . . . the evidence that supports the grounds for the challenge to each claim")); *see also* 37 C.F.R. § 42.104(b) (2019) (requiring a petition for *inter partes* review to identify how the challenged claim is to be construed and where each element of the claim is found in the prior art patents or printed publications relied upon).

A claim is anticipated under 35 U.S.C. § 102 only if "each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co.*, 814 F.2d 628, 631 (Fed. Cir. 1987). "In the context of anticipation, the question is not whether a prior art reference 'suggests' the claimed subject matter." *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1055 (Fed. Cir. 2010) (quoting party's argument). "Rather, the dispositive question regarding anticipation is whether one skilled in the art would reasonably understand or infer from a prior art reference that every claim element is disclosed in that reference." *Id.* (brackets and internal quotes omitted).

"[A]nticipation by inherent disclosure is appropriate only when the reference discloses prior art that must necessarily include the unstated limitation." *Rexnord Indus., LLC v. Kappos*, 705 F.3d 1347, 1355 (Fed. Cir. 2013).

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

Additionally, the obviousness inquiry typically requires an analysis of "whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue." *KSR*, 550 U.S. at 418 (*citing In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006) (requiring "articulated reasoning with some rational underpinning to support the legal conclusion of obviousness")). Furthermore, Petitioner does not satisfy its burden of proving obviousness by employing "mere conclusory statements," but "must instead articulate specific reasoning, based on evidence of record, to support the legal conclusion of obviousness." *In re Magnum Oil Tools Int'l, Ltd.*, 829 F.3d 1364, 1380 (Fed. Cir. 2016).

B. Level of Ordinary Skill in the Art

Relying on Dr. Fair's testimony, Petitioner asserts that a person of ordinary skill in the art ("POSA") would have had "a PhD in chemistry, biochemistry, mechanical or electrical engineering, or a related discipline with one year of experience related to systems for handling microfluidic droplets," "a Bachelor of Science in such fields with four years of such experience," or an equivalent level of education and practical experience. Pet. 3; Ex. 1008 ¶ 47. Petitioner and Dr. Fair assert that a "POSA would have knowledge of scientific literature concerning droplets (including emulsions), and systems and methods for handling them (including both their formation and handling downstream of formation), their applications, and chemistry, components, and reactions that occur within them." Pet. 3; Ex. 1008 ¶ 47. In addition, Petitioner and Dr. Fair assert that a "POSA may have worked on a multidisciplinary team and drawn on his or her own skills along with certain specialized skills of others; and a chemist, engineer, and biologist may have been part of the team." Pet. 3; Ex. 1008 ¶ 47.

Relying on Dr. Anna's testimony, Patent Owner asserts that a POSA "would have had at least the equivalent of a Bachelor's degree in engineering, physics, or chemistry and two years of academic, research, or industry experience related to fluid mechanics, fluid dynamics, or microfluidics." PO Resp. 17; Ex. 2016 ¶ 72. In addition, Patent Owner and Dr. Anna assert that "[a]dditional training or study could substitute for work experience and additional work experience or training could substitute for formal education." PO Resp. 17–18; Ex. 2016 ¶ 72.

Both sides' declarants represent that their opinions would not change based on their opponent's articulation of the level of ordinary skill in the art. Ex. 1071 ¶ 13; Ex. 2016 ¶ 74.

We find that Patent Owner's definition of a POSA is consistent with the scope and content of the '837 Patent and the asserted prior art. In addition, we find that Patent Owner's definition of a POSA is consistent with the legal standard for obviousness, which is to be determined from the viewpoint of a person of ordinary, not extraordinary, skill. *Stewart-Warner Corp. v. City of Pontiac, Mich.*, 767 F.2d 1563, 1570 (Fed. Cir. 1985) (section 103 is not concerned with the actual skill of the inventors—whose skill may be extraordinary—but rather with the level of ordinary skill in the art).

In contrast, Dr. Fair's opinion about the level of ordinary skill in the art is based on his own experience working in the field and "working with others in this field who consistently had that level of education and/or experience and worked with a multidisciplinary team." Ex. 1071 ¶ 10. Dr. Fair considers himself "an expert in the art of biomedical microfluidics and related applications, including handling microfluidic droplets." Ex. 1008 ¶ 48. We find that Petitioner and Dr. Fair have defined a POSA based on the level of skill possessed by Dr. Fair and others like him who are experts in the field. Ex. 1008 ¶¶ 47, 48; Ex. 1071 ¶¶ 9, 10. In our view, the level of skill in the art proposed by Petitioner and Dr. Fair is more akin to extraordinary, rather than ordinary skill in the art.

For these reasons, we apply Patent Owner's definition of a POSA. We also apply a portion of Petitioner's definition, namely that a POSA "would have knowledge of scientific literature concerning droplets (including emulsions), and systems and methods for handling them (including both their formation and handling downstream of formation), their applications, and chemistry, components, and reactions that occur within them." Pet. 3; Ex. 1008 ¶ 47; Ex. 1071 ¶ 12. This portion is

undisputed by Patent Owner and is consistent with the '837 Patent and the asserted prior art, as summarized below. In any event, our determinations regarding Petitioner's challenges do not turn on the differences between Petitioner's and Patent Owner's definitions of a POSA, and our conclusion would be the same under either party's definition.

C. Claim Construction

In an *inter partes* review, we apply the same claim construction standard as would be used by a district court to construe a claim in a civil action involving the validity or infringement of a patent. 37 C.F.R. § 42.100(b). Under that standard, claim terms are given their ordinary and customary meaning, as would have been understood by a person of ordinary skill in the art at the time of the invention, in light of the language of the claims, the specification, and the prosecution history of record. *Id.*; *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–19 (Fed. Cir. 2005) (en banc); *Thorner v. Sony Comput. Entm't Am. LLC*, 669 F.3d 1362, 1365–66 (Fed. Cir. 2012) (unless a claim term has been expressly defined by the patentee or has been limited by a clear and unmistakable disavowal of claim scope, it should receive its ordinary meaning).

The Petition is based on alternative claim constructions, with some grounds relying on Petitioner's proposed constructions and other grounds relying on constructions that Petitioner attributes to Patent Owner based on Patent Owner's infringement contentions in the related district court action. Pet. 18–20, 24–25. In the Institution Decision, we rejected Petitioner's proposed constructions for two claim terms, "separation chamber" and "droplet receiving outlet," and we applied the constructions relied upon by Patent Owner in its district court infringement contentions. Inst.

Dec. 10–17. In the Response, Patent Owner proposes its own constructions for these terms. PO Resp. 18, 22. In the Reply, Petitioner neither opposes Patent Owner's constructions, nor challenges our rejection of Petitioner's constructions. *See* Pet. Reply 2–3 (discussing Patent Owner's constructions).

Below we address the terms "separation chamber" and "droplet receiving outlet." We reject Petitioner's constructions for essentially the same reasons as set forth in the Institution Decision, and we adopt Patent Owner's constructions, which are unopposed by Petitioner. We determine that no other claim term requires express construction for purposes of resolving the controversy. *See Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) ("only those terms need be construed that are in controversy, and only to the extent necessary to resolve the controversy"); *see also Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (applying *Vivid Techs.* in the context of *inter partes* review).

1. "separation chamber"

Claim 1 recites that the claimed assembly comprises "at least one downstream separation chamber." Ex. 1001, 88:10. Claim 1 further recites that the separation chamber "is of a volume sufficient to separate the plurality of droplets comprising the sample from the immiscible fluid within the separation chamber." *Id*. at 88:18–23.

a) Petitioner's Construction

Petitioner contends that "separation chamber" should be construed as "a space that is substantially enclosed" and that a POSA "would not understand the term 'separation chamber' to include open containers."

Pet. 19, 21–22. As support for this construction, Petitioner cites dictionaries that define a "chamber" as an "enclosed space or cavity." Pet. 21 (citing Exs. 1027, 1028). Petitioner also cites the purpose of the '837 Patent's invention to eliminate the risk of contamination by avoiding operator handling of droplets. *Id.* (citing, e.g., Ex. 1001, 52:33–37). Petitioner acknowledges the Specification's disclosure that a chamber can "***include*** any vessel suitable for holding droplets, for example, test tubes, vials, beakers, jars, and PCR tubes," but argues that such chambers "are consistently and exclusively ***enclosed***—not open—when in use with a 'seal' to 'minimize potential contamination.'" Id. (quoting Ex. 1001, 53:45–47, 55:64–56:7 (emphasis added by Petitioner) and citing *id.* at Fig. 39).

We determine that Petitioner's proposed construction that excludes open containers is inconsistent with how the term "chamber" is used in the Specification. The Specification states "[i]t is to be understood that ***the chamber can include any vessel suitable for holding droplets***, for example, test tubes, vials, beakers, jars, and PCR tubes." Ex. 1001, 53:35–38 (emphasis added). As Petitioner's argument acknowledges, the disclosed examples—test tubes, vials, beakers, jars, and PCR tubes—are all open vessels, unless and until they are closed by a seal or other closure. *See* Pet. 21 (stating the vessels are enclosed "when in use with a 'seal'"). Although Petitioner directs us to the description of vessel 903 that is sealably connected to the assembly (*id.* (citing Ex. 1001, 55:55–65, Fig. 39)), the cited portion of the Specification is merely a description of a preferred embodiment that does not limit the scope of the claims. Moreover, the cited description does not limit the meaning of "chamber" to an "enclosed" space because vessel 903, within which oil is separated from droplets due to density differences, ***refers to the vessel alone, without the***

cap that seals it to the assembly. Ex. 1001, 55:60–62 ("In certain embodiments, the assembly includes a PCR tube cap 904 that lock[s] the vessel 903 into a sealed position."); *see also id.* at 57:38–41 (stating "vessels for use with the invention ***may*** be sealed. For example, the lid to a PCR tube . . . ***may*** be closed to prevent contamination" (emphasis added)).

Interpreting "chamber" as not requiring a space that is substantially closed and not excluding an open container is also consistent with the structure of the claims. Claim 1 recites a "separation chamber comprising . . . at least one droplet receiving outlet." Ex. 1001, 88:10–12. Claim 7 depends from claim 1 and recites: "the droplet receiving outlet is coupled to a vessel," and claim 8 depends from claim 7 and recites that "the droplet receiving outlet is sealably coupled to a vessel." *Id.* at 88:40–43. The subject matter of claim 1 is necessarily broader than the subject matter of dependent claims 7 and 8 and is not limited to a separation chamber that is closed by being sealably coupled to a vessel.

Accordingly, for these reasons, we do not adopt Petitioner's proposed construction for "separation chamber" as "a space that is substantially enclosed."

b) Patent Owner's Construction

Consistent with its position in district court, Patent Owner argues that "separation chamber" should be construed as a "chamber sized to accommodate multiple droplets and an immiscible fluid in separated form." PO Resp. 18 (citing Ex. 2032 (Joint Claim Construction Chart filed in district court)).

We find that Patent Owner's construction is supported by claim 1's recitation that the separation chamber "is of a volume sufficient to separate

the plurality of droplets comprising the sample from the immiscible fluid within the separation chamber." Ex. 1001, 88:18–23.

We find that the Specification supports Patent Owner's construction for "separation chamber." The Specification discloses that partitioned portions, i.e. droplets, and immiscible fluid flow into a chamber, where the partitioned portions sink, float, or are displaced from the chamber as a result of a difference in density between the partitioned portions and the immiscible fluid. Ex. 1001, 2:45–50, 3:37–46. Patent Owner's construction is further supported by the Specification's description of a "chamber . . . configured to receive droplets and an immiscible fluid from the droplet formation module," where "the immiscible fluid displaces the droplet from the chamber into the outlet due to the difference in density." *Id.* at 53:22–28. Patent Owner's construction is consistent with the Specification's disclosure that "the chamber can include any vessel suitable for holding droplets, for example, test tubes, vials, beakers, jars, and PCR tubes." *Id.* at 53:35–38.

We find that the prosecution history also supports Patent Owner's construction. Specifically, when distinguishing the "separation chamber" from a "conduit" disclosed in the prior art, Applicant argued that the conduit "accommodates only one droplet across its width at a time," whereas "the width of the claimed chamber is sized to accommodate multiple droplets, which allows for droplet concentration and removal of carrier fluid from between the droplets." Ex. 1002, 1114; *see also id.* at 1110 (amended claim 1: "the chamber has a width that is sized to accumulate a plurality of droplets across the width"). Similarly, Applicant distinguished the "separation chamber" of the claims from a "cross-intersection" disclosed in the prior art, arguing that the cross-intersection "is not a vertical chamber to

separate droplets from an immiscible carrier fluid" and does not "have a wider cross-intersection [*sic*, cross-section] than the channel cross-section to accumulate droplets in an immiscible fluid or have a specific volume to separate droplets from an immiscible fluid." *Id.* at 1168–69; *see also id.* at 1165 (amended claim 1: "the separation chamber is vertical to the channel" and "the separation chamber has a wider cross-section than the channel cross-section to accumulate a plurality of droplets and is of a volume sufficient to separate the plurality of droplets from an immiscible fluid.").

For these reasons, we adopt Patent Owner's proposed construction that "separation chamber" means "chamber sized to accommodate multiple droplets and an immiscible fluid in separated form."

2. "droplet receiving outlet"

Claim 1 recites that the separation chamber comprises "a droplet receiving chamber inlet and at least one droplet receiving outlet." Ex. 1001, 88:10–12.

a) Petitioner's Constructions

Petitioner first contends that "droplet receiving outlet" should be construed as a means-plus-function limitation pursuant to 35 U.S.C. § 112(f).[7] Pet. 18, 20. Petitioner next contends that, if the term is not subject to § 112(f), then a "droplet receiving outlet" should be construed as "a structure connected to the interior space of the chamber and configured so

[7] Although Petitioner refers to the post-AIA version of the statute (35 U.S.C. § 112(f)) and the case law discussed herein addresses the pre-AIA version of the statute (35 U.S.C. § 112 ¶ 6), the same principles apply under both versions of the statute.

that substantially only droplets flow into it when exiting the chamber." Pet. 18–19. As support for its constructions, Petitioner argues that "'droplet receiving outlet' . . . is not in the specification and has no well-understood meaning in the art." Pet. 20 (citing Ex. 1008 ¶ 80). In addition, Petitioner argues that the term is "described in functional terms" both in the claims and the Specification. *Id.* (citing Ex. 1001, code (57), 3:46–58, 53:21–35).

We first address Petitioner's contention that a "droplet receiving outlet" should be construed as a means-plus-function limitation. Under applicable law, if a claim term lacks the word "means," there is a rebuttable presumption that the term is not subject to 35 U.S.C. § 112(f) or § 112 ¶ 6. *MTD Prod. Inc. v. Iancu*, 933 F.3d 1336, 1341 (Fed. Cir. 2019); *Williamson v. Citrix Online, LLC*, 792 F.3d 1339, 1348 (Fed. Cir. 2015) (en banc). A challenger can rebut the presumption by demonstrating that "the claim term fails to recite sufficiently definite structure or else recites function without reciting sufficient structure for performing that function." *Williamson*, 792 F.3d at 1348 (internal quotes, brackets, and citation omitted). "One way to demonstrate that a claim limitation fails to recite sufficiently definite structure is to show that, although not employing the word 'means,' the claim limitation uses a similar nonce word that can operate as a substitute for 'means' in the context of § 112, para. 6." *MTD*, 933 F.3d at 1341 (internal quotes omitted); *Williamson*, 792 F.3d at 1350.

Here, the disputed claim term is "droplet receiving outlet." Because the term does not recite the word "means," there is a rebuttable presumption that it is not a means-plus-function term. We find that Petitioner has not rebutted that presumption. Petitioner's arguments and evidence do not persuade us that "droplet receiving outlet" fails to recite sufficiently definite structure. Petitioner does not argue that "outlet" is a "nonce word that can

operate as a substitute for 'means'" in the context of a patent claim. *Williams*, 792 F.3d at 1350. In our view, "outlet" is not a generic term, like "module," "mechanism," "element," or "device," that is commonly used as a verbal construct to claim a particular function rather than to describe a sufficiently definite structure. *Cf. MTD*, 933 F.3d at 1341.

The surrounding claim language suggests that a "droplet receiving outlet" is structural. Claim 1 recites "at least one downstream separation chamber comprising a droplet receiving chamber inlet and at least one droplet receiving outlet." Ex. 1001, 88:10–12. Despite the linguistic similarity of a "droplet receiving chamber inlet" and a "droplet receiving outlet," Petitioner makes no argument that the former term should be construed as a means-plus-function term. The dependent claims also suggest that § 112(f) (or pre-AIA § 112 ¶ 6) does not apply. Claim 3 recites that the droplet receiving outlet "is located on the lower portion of the separation chamber," claim 4 recites that the droplet receiving outlet "is located on the upper portion of the separation chamber," and claim 5 recites that the droplet receiving outlet "is connected to a proximal end of a slide." Ex. 1001, 88:27–35. Petitioner does not dispute that a "separation chamber" and a "slide" are structural limitations. We find that the surrounding language of claim 1 and the added limitations of dependent claims 3–5 support the structural nature of a "droplet receiving outlet" and do not help rebut the presumption against application of § 112(f) to this non-means term. *See TEK Global, S.R.L. v. Sealant Sys. Int'l, Inc.*, 920 F.3d 777, 785–86 (Fed. Cir. 2019) (relying on surrounding claim language and limitation of dependent claim when determining that "conduit" is not a means-plus-function term).

Although Dr. Fair opines that a POSA "would consider the term 'droplet receiving outlet' not to be a term used by persons of skill in the art to designate either a particular structure or a class of structures," he cites no persuasive evidence to support that opinion. Ex. 1008 ¶ 80. We find that Dr. Fair's opinion is undermined by his concession that a POSA "is familiar with numerous outlet structures." *Id.* Moreover, Dr. Fair refers to the term "outlet" as having a definite structure. *See id.* ¶ 81 (stating "the corresponding structure are the outlets"). In our view, "outlet" is not a nonce word, and the term "droplet receiving outlet" conveys sufficiently definite structure and is not subject to AIA 35 U.S.C. § 112(f) or pre-AIA § 112 ¶ 6.

We also reject Petitioner's argument that "droplet receiving outlet" should be construed as requiring that "substantially only droplets" exit the chamber through the outlet. Pet. 18–21. Petitioner directs us to several Specification passages that describe a chamber outlet in this manner. Pet. 20 (quoting Ex. 1001, code (57), 3:46–48, 53:24–25, 53:32–35, and citing 53:21–41, 54:34–46, 55:41–44). Petitioner provides no justification, however, for reading these descriptions from the Specification into the claim. *Thorner*, 669 F.3d at 1365–66 (absent an express definition or clear and unmistakable disavowal, claim terms should receive their ordinary meaning). Moreover, the Specification describes outlet 805, which is shown in Figure 38, as positioned where the rising droplets will exit chamber 804 into outlet 805 and "leav[e] a large part of the oil behind." Ex. 1001, 54:41–44. Because the Specification states that a "large part of the oil" is left behind, it can be presumed that at least part of the oil exits chamber 804 into outlet 805 with the droplets. *Id.*

Furthermore, Petitioner's proposed construction requiring that "substantially only droplets" exit the chamber through the outlet is inconsistent with dependent claim 10, which depends from claim 1 and recites: "wherein the droplet receiving outlet receives substantially one or more droplets." Ex. 1001, 88:46–47. Dependent claim 10 describes the function of the "droplet receiving outlet" in a manner similar to Petitioner's proposed construction, except that the word "only" is conspicuously missing from claim 10. As a matter of law, we cannot construe independent claim 1 more narrowly than dependent claim 10. 35 U.S.C. § 112(d) (corresponding to pre-AIA § 112 ¶ 4); *Trustees of Columbia Univ. v. Symantec Corp.*, 811 F.3d 1359, 1370 (Fed. Cir. 2016) ("[W]here dependent claims have no meaningful difference other than an added limitation, . . . construing the independent claim to exclude material covered by the dependent claim would be inconsistent.").

Accordingly, for these reasons, we do not adopt either of Petitioner's proposed constructions for "droplet receiving outlet."

b) Patent Owner's Construction

Consistent with its position in district court, Patent Owner argues that "droplet receiving outlet" should be construed as a "portion of the separation chamber where droplets are collected." PO Resp. 22 (citing Ex. 2032).

We find that the Specification supports Patent Owner's interpretation that a "droplet receiving outlet" is a "portion of the separation chamber." The Specification discloses that "[t]he chamber includes an outlet that is positioned to receive substantially only the partitioned portions of sample." Ex. 1001, 3:46-48. In addition, the Specification discloses that the outlet may positioned be "at the top, middle, or bottom of the chamber" depending

on the densities of the partitioned portions and the immiscible fluid. *Id.* at 3:48–52. For example, the Specification states that the outlet is positioned in a top portion of the chamber if the immiscible fluid is of a greater density than the partitioned portions, such that the partitioned portions rise in the chamber while the immiscible fluid sinks and the partitioned portions flow into the outlet. *Id.* at 3:52–58. These portions of the Specification show that a "droplet receiving outlet" is a portion of the separation chamber.

We find that the Specification also supports Patent Owner's interpretation that a "droplet receiving outlet" is a "where droplets are collected." For example, the Specification discloses that aqueous droplets tend to rise when placed in a chamber of fluorinated oil, and accordingly, "an outlet for collecting the displaced droplets can be positioned at the top of the chamber." Ex. 1001, 4:8–12. In another example, the Specification discloses that aqueous droplets tend to sink when placed in a chamber of certain mineral oils, and accordingly, "an outlet for collecting the displaced droplets can be positioned at the bottom of the chamber." *Id.* at 4:12–16. Both of these examples illustrate the role of an outlet as a structure for collecting droplets.

We find that Patent Owner's claim construction is supported by the Specification's description of Figure 38. The Specification states that "a chamber 804 equipped with an outlet 805" and "the outlet 805 can be positioned at an upper portion of the chamber 804 where the rising droplet will exit the chamber 804 into the outlet 805" or "the outlet 805 [can be] positioned at a lower portion of the chamber 804." Ex. 1001, 54:34–35, 54:41–46. When describing the Figure 38 embodiment, the Specification states that outlet 805 is positioned at the top of chamber 804 to collect droplets that are displaced by oil flowing into the chamber and that rise to

the top of the chamber. *Id.* at 59:55–63. These descriptions are consistent with Patent Owner's proposed construction for "droplet receiving outlet."

For these reasons, we adopt Patent Owner's proposed construction that a "droplet receiving outlet" means a "portion of the separation chamber where droplets are collected."

D. Petitioner's Ground 1: Ismagilov 091 Anticipation

Petitioner contends that Ismagilov 091 anticipates claims 1, 2, 4, 10–13, 19, and 20 of the '837 Patent. Pet. 31–56. We first provide an overview of Ismagilov 091 and then discuss the claims challenged in this ground.

1. Ismagilov 091 (Ex. 1004)

Ismagilov 091 is a U.S. Patent titled "Device and Method for Pressure-Driven Plug Transport and Reaction." Ex. 1004, codes (10), (54). Petitioner asserts that Ismagilov 091 is prior art to the '837 Patent under 35 U.S.C. § 102(a)(2) and pre-AIA § 102(e) as of its May 9, 2003 filing date and under § 102(a)(1) and pre-AIA § 102(a) as of its December 8, 2005 publication date. Pet. 12–13. Petitioner contends that Ismagilov 091 is prior art under pre-AIA § 102(b), if the challenged claims are not entitled to the benefit of any provisional applications filed between May 11, 2006 and December 12, 2006. Pet. 13, 15–16.

Patent Owner does not contest the prior art status of Ismagilov 091. We do not need to address Petitioner's contention under pre-AIA § 102(b) because Patent Owner does not attempt to show a date of invention earlier than Ismagilov 091's filing date or publication date. We find that Ismagilov 091 is prior art to the '837 Patent, regardless of whether the AIA applies to the patent.

Ismagilov 091 discloses microfabricated substrates and methods of conducting reactions in droplets ("plugs") in a flow of carrier fluid in a substrate. Ex. 1004, code (57).

Ismagilov 091 discloses that "'[p]lugs' . . . are 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. 1004, 9:20–23. According to Ismagilov 091, the "plugs" may be in the form of "an aqueous plug-fluid . . . surrounded by a non-polar or hydrophobic fluid such as an oil." *Id.* at 9:39–44. Ismagilov 091 discloses that an "inlet port" is "an area of a substrate that receives plug-fluids," and "[t]he inlet port can be in fluid communication with a channel." *Id.* at 8:41–42, 8:46–47. According to Ismagilov 091, a "channel" includes "microchannels." *Id.* at 7:46–48. Ismagilov 091 discloses that an "outlet port" is "an area of a substrate that collects or dispenses the plug-fluid, carrier-fluid, plugs or reaction product." *Id.* at 9:5–8.

In a section headed "Channels and Devices," Ismagilov 091 discloses a device that "includes one or more substrates comprising a first channel comprising an inlet separated from an outlet." Ex. 1004, 14:20–23. According to Ismagilov 091,

> The device may have one or more outlet ports or inlet ports. Each of the outlet and inlet ports may also communicate with a well or reservoir. The inlet and outlet ports may be in fluid communication with the channels or reservoirs that they are connecting or may contain one or more valves.

Id. at 14:36–40. In this section, Ismagilov 091 also discloses that a "plug-forming region generally comprises a junction between a plug-fluid inlet and a channel containing the carrier-fluid such that plugs form." *Id.* at 14:44–45.

In a section headed "Fabrication of Channels, Substrates, and Devices," Ismagilov 091 discloses methods for fabricating microfluidic devices, including a polymer casting method. Ex. 1004, 16:1–7, 16:23–41. According to this method, a negative image of the channels is etched into a crystalline silicon wafer, and the wafer is used as a mold for casting the channels from polydimethylsiloxane (PDMS). *Id.* at 16:23–28. In this method, the silicon wafer mold is placed in the bottom of a Petri dish, uncured PDMS is poured onto the mold, and the PDMS is then cured and removed from the mold. *Id.* at 16:30–35. Ismagilov 091 discloses that "[h]oles may be cut into the PDMS using, for example, a tool such as a cork borer or a syringe needle." *Id.* at 16:35–36. According to Ismagilov 091, the PDMS channels are treated with hydrochloric acid to render the surface hydrophilic. *Id.* at 16:37–38. Ismagilov 091 discloses that the PDMS channels can be "placed onto a microscope cover slip (or any other suitable flat surface), which can be used to form the base/floor or top of the channels." *Id.* at 16:38–41.

Ismagilov 091 discloses that "[a] substrate containing the fabricated flow channels and other components is preferably covered and sealed, preferably with a transparent cover, e.g., thin glass or quartz, although other clear or opaque cover materials may be used." Ex. 1004, 16:60–64. According to Ismagilov 091, the substrate can include "[a] variety of channels for sample flow" as well as "manifolds (a region consisting of several channels that lead to or from a common channel)." *Id.* at 17:10–11, 17:18–20. Such manifolds can "route[] the flow of solution to an outlet." *Id.* at 17:23–27. Ismagilov 091 discloses that "[t]he outlet can be adapted for receiving, for example, a segment of tubing or a sample tube, such as a

standard 1.5 ml centrifuge tube. Collection can also be done using micropipettes." *Id.* at 17:27–30.

Figure 3A of Ismagilov 091 is reproduced below.

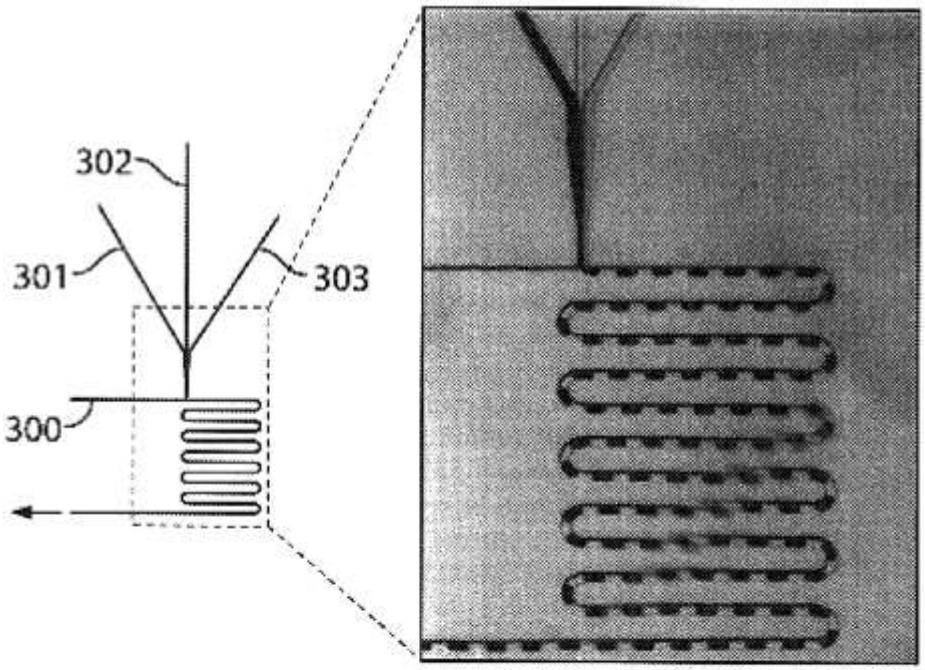

FIG. 3A

Ismagilov 091 Figure 3A includes a photograph (right side) and a schematic diagram (left side) depicting a stream of plugs formed from an aqueous plug-fluid and an oil (carrier-fluid) in curved serpentine channels. Ex. 1004, 4:6–10, 18:24–26, Fig. 3A. According to Ismagilov 091, the carrier-fluid is introduced into inlet port 300 of a substrate, and three aqueous plug-fluids are introduced in separate inlet ports 301, 302, and 303. *Id.* at 18:31–33.

2. Independent Claim 1

a) Element 1.0

It is undisputed that Ismagilov 091 discloses "an assembly" as recited in the preamble of claim 1. We find that Ismagilov 091 discloses "microsubstrates" that are, or are part of, an assembly, as Petitioner

contends. Pet. 31; Ex. 1004, code (57). Ismagilov 091 discloses that microfluidic substrates may be part of an assembly that includes, for example, syringe pumps, a microscope, a light source, a detector, a processor, a display monitor, and a printer. Ex. 1004, 14:42–43, 30:2–4, 31:20–27, 32:10–15, 32:60–63, 33:4–7, 33:25–35.

b) Element 1.1

There is no dispute that Ismagilov 091 discloses "a microchannel in a horizontal plane" as recited in claim element 1.1. We find that Ismagilov 091 discloses microchannels. For example, Ismagilov 091 discloses that "the term 'channel' includes microchannels that are of dimensions suitable for use in devices." Ex. 1004, 7:46–48; *see also id.* at 62:1–4 ("Example 3[;] Networks of microchannels with rectangular cross-sections were fabricated using rapid prototyping in PDMS.").

We find that Ismagilov 091's microchannels are in a horizontal plane. Our finding is supported by Ismagilov 091, which discloses that molded PDMS channels can be "placed onto a microscope cover slip (or any other suitable flat surface), which can be used to form the base/floor or top of the channels." Ex. 1004, 16:38–41; *see also id*. at 16:60–63 ("A substrate containing the fabricated flow channels and other components is preferably covered and sealed, preferably with a transparent cover, e.g., thin glass or quartz, although other clear or opaque cover materials may be used."). Petitioner shows persuasively that, when a glass cover slip is used as the "floor . . . of the channels," as Ismagilov 091 discloses, then a substrate containing the fabricated flow channels is placed channel-side down onto the cover slip, with the channels running parallel to the cover slip, i.e., horizontally. Pet. 31–32; Ex. 1004, 16:38–41.

c) Element 1.2

It is undisputed that Ismagilov 091 discloses claim element 1.2, which recites:

> at least one droplet formation module comprising a sample inlet, an immiscible fluid inlet, and a junction, wherein the junction is located between the sample inlet and the microchannel and the droplet formation module is configured to produce droplets comprising the sample surrounded by the immiscible fluid.

Ex. 1001, 88:4–9.

We find that Ismagilov 091 discloses a "droplet formation module" (Ismagilov 091's "plug-forming region") comprising a "sample inlet" (Ismagilov 091's "plug-fluid inlet" or "sample inlet"), an "immiscible fluid inlet" (Ismagilov 091's "carrier-fluid inlet," where the carrier-fluid is "a fluid that is immiscible with a plug-fluid"), and a "junction" (Ismagilov 091's "junction between a plug-fluid inlet and a channel containing the carrier-fluid"). Pet. 32; Ex. 1004, 7:31–32, 14:44–61, 15:53–60.

We find that Ismagilov 091 teaches "the junction is located between the sample inlet and the microchannel" as recited in claim element 1.2. For example, Ismagilov 091 discloses that a "plug-forming region generally comprises a junction between a plug-fluid inlet and a channel containing the carrier-fluid." Ex. 1004, 14:44–46.

We find that Ismagilov 091 discloses that "the droplet formation module is configured to produce droplets comprising the sample surrounded by the immiscible fluid" as recited in claim element 1.2. For example, Ismagilov 091 discloses that plugs "are 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. 1004, 9:20–23; *see also id.*

at 9:39–41 ("The plugs may be in the form of plugs comprising an aqueous plug-fluid containing one or more reagents . . . ."); *id.* at 14:44–49 ("A plug-forming region generally comprises a junction between a plug-fluid inlet and a channel containing the carrier-fluid such that plugs form . . . .").

d) Element 1.3

Claim element 1.3 recites: "at least one downstream separation chamber comprising a droplet receiving chamber inlet and at least one droplet receiving outlet." Ex. 1001, 88:10–12.

Petitioner contends that Ismagilov 091 discloses claim element 1.3 under an interpretation of "separation chamber" and "droplet receiving outlet" that Petitioner attributes to Patent Owner based on its infringement contentions. Pet. 35–36 (citing Ex. 1026, 11). Petitioner also contends that Ismagilov 091 discloses claim element 1.3 under Patent Owner's constructions as presented in the Response. Pet. Reply 4. Petitioner asserts that these constructions are "broad enough to encompass an open well and the opening at the top of an open outlet well." Pet. 35; Pet. Reply 2.

Petitioner contends that Ismagilov 091 discloses "at least one downstream separation chamber" in the form of a collection well or reservoir and that Ismagilov 091 discloses a "droplet receiving chamber inlet" in the form of an outlet of a manifold. Pet. 36 (citing Ex. 1004, 9:5–8, 14:36–40, 17:27–30). Petitioner asserts that Ismagilov 091 discloses a "droplet receiving outlet" by describing "a well or reservoir with an opening at the top" and "the ability to collect the fluids by micropipette." Pet. 36–37.

Patent Owner argues that Ismagilov 091 does not disclose a "separation chamber" or a "droplet receiving outlet." PO Resp. 29–38.

After considering Patent Owner's arguments and evidence, we find that Petitioner shows persuasively that Ismagilov 091 discloses a collection well or reservoir[8] at the outlet of a microfluidic device. Pet. 36. Our finding is supported by Ismagilov 091's definition of an "outlet port" as "an area of a substrate that collects . . . plugs" and Ismagilov 091's disclosure that the outlet port may "communicate with a well or reservoir." Ex. 1004, 9:5–8, 14:37–38. Taken together, these two disclosures plainly convey that Ismagilov 091's device may include an outlet well or reservoir for collecting droplets (plugs).

We find that Petitioner shows persuasively that Ismagilov 091's collection well or reservoir (corresponding to the claimed "separation chamber") is located downstream of Ismagilov 091's plug-forming region (corresponding to the claimed "droplet formation module"). Pet. 37. Our finding is supported by Ismagilov 091, which discloses that plugs flow from the plug-forming region through a channel to an outlet port, which may include a well or reservoir for collecting plugs. Ex. 1004, 9:5–8, 14:20–22, 14:36–40, 21:48–54; *see also id.* at 8:12–14 (defining "downstream" as "a position relative to an initial position which is reached after the fluid flows past the initial point").

We find that Petitioner shows persuasively that Ismagilov 091 describes a collection well that allows for collection of droplets using a micropipette. Pet. 36. Our finding is supported by Ismagilov 091's description of a "manifold" as "a region consisting of several channels that lead to or from a common channel," such that the manifold "facilitate[s] the

[8] In this Decision, we use the term "collection well" and "outlet well" interchangeably to refer to a well that collects droplets and is located at the outlet of a microfluidic device.

movement of plugs from different analysis units" and "routes the flow of solution to an outlet." Ex. 1004, 17:18–27. According to Ismagilov 091, "The outlet can be adapted for receiving, for example, a segment of tubing or a sample tube, such as a standard 1.5 ml centrifuge tube. Collection can also be done using micropipettes." *Id.* at 17:27–30. We are persuaded by Petitioner's contention that Ismagilov 091's disclosure of "[c]ollection . . . using micropipettes" refers to collecting droplets from a well using a micropipette. *Id.*; Pet. 36–37.

Our finding is supported by Dr. Fair's testimony, as follows:

> To permit the collection of fluids by micropipette, there must be a container with a volume of liquid that can be pipetted, and an opening into which the micropipette can be inserted, which describes a collection well.

Ex. 1008 ¶ 130 (citing Exs. 1040, 1041 as providing information about micropipettes).[9]

> [F]or a micropipette to be able to collect liquid, the liquid must first be collected in a container that (1) is of a sufficient volume for the pipette tip to be inserted, (2) has an opening through which the pipette can be inserted, and (3) the liquid is of a sufficient volume that the micropipette can collect it. This describes a collection well.

Id. ¶ 131. Our finding is further supported by Dr. Fair's testimony that "Ismagilov 091 also confirms there is an opening in the manifold outlet well by describing the ability to collect the fluids by micropipette." *Id.* ¶ 134 (citing Ex. 1004, 17:27–30).

[9] Exhibit 1040 is a Rainin Classic datasheet for "continuously adjustable digital microliter pipettes," and Exhibit 1041 is a web page titled, "Resource Materials: Use of Micropipetes [sic]."

We are persuaded that Ismagilov 091's collection wells or reservoirs satisfy our claim construction for "separation chamber" and "droplet receiving outlet." As discussed above, we adopt Patent Owner's proposed construction of "separation chamber" as meaning a "chamber sized to accommodate multiple droplets and an immiscible fluid in separated form." We adopt Patent Owner's proposed construction of "droplet receiving outlet" as meaning a "portion of the separation chamber where droplets are collected."

Petitioner shows persuasively that Ismagilov 091 teaches a collection well or reservoir sized to accommodate multiple droplets and immiscible fluid.[10] Pet. 36, 41. More specifically, Petitioner provides persuasive evidence that Ismagilov 091 teaches a well or reservoir large enough to allow collection of fluid by micropipette, which means that the well or reservoir has a volume greater than 0.1 μl. Pet. 41 (citing Ex. 1004, 17:27–30; Exs. 1040, 1041). Petitioner shows that a well or reservoir with a volume greater than 0.1 μl would accommodate multiple droplets of the size disclosed by Ismagilov 091. *Id.*; Ex. 1004, 19:61–64 (disclosing "plug volumes of between about 16 picoliters (pL) to 16 nanoliters (nL)"). Our findings are supported by the cited disclosures of Ismagilov 091, the sizes of commercially available micropipettes as shown in Exhibits 1040 and 1041, and Dr. Fair's testimony concerning the minimum volume that can be collected by micropipette compared with the volume of droplets disclosed in Ismagilov 091. Ex. 1008 ¶ 161 (citing Ex. 1004, 17:27–30, 19:61–66;

[10] The issue of whether Ismagilov 091's well or reservoir has a volume sufficient to separate the droplets from the immiscible fluid within the separation chamber such that the droplets and immiscible fluid are "in separated form" is addressed below in connection with claim element 1.7.

Exs. 1040, 1041). We observe that, even if the volume of Ismagilov 091's outlet well were only 0.1 µl, it would still be large enough to accommodate 2500 16 pL droplets and 0.06 µl of immiscible fluid. We also credit Dr. Fair's testimony that, to allow collection by micropipette, "the well will need to be larger than the 0.1 µl minimum volume that a micropipette can collect." *Id.*

Petitioner also shows persuasively that Ismagilov 091 teaches a collection well or reservoir that is open at the top to allow a micropipette to be inserted for the purpose of collecting droplets. Pet. 36–37; Ex. 1008 ¶¶ 129–131, 134. Patent Owner does not dispute that such an open top satisfies our claim construction for "droplet receiving outlet." *See generally* PO Resp. 24–25, 35–37.

Patent Owner argues that "Petitioner improperly attempts to piece together the disclosure of a 'separation chamber' using multiple disparate sections in Ismagilov that do not clearly connect to one another in any discernable arrangement or configuration that would be considered a 'separation chamber.'" PO Resp. 29; *see also id.* at 29–32 (elaborating on the separateness of Ismagilov 091's disclosures cited by Petitioner). We disagree. We are persuaded that Petitioner interprets Ismagilov 091 from the perspective of a POSA without mixing and matching unrelated disclosures, as asserted by Patent Owner. *Id.* at 34. Although Petitioner relies on disclosures from separate sections of Ismagilov 091, we find a POSA would understand that the cited disclosures all relate to an outlet or outlet port and can fairly be read together as disclosing that the outlet port may communicate with a well or reservoir for collecting droplets, where the well or reservoir allows for collection of the droplets using a micropipette. Ex. 1004, 9:5–8 (defining "outlet port" as "an area of a substrate that collects

. . . plugs . . . ."); *id.* at 14:37–38 ("Each of the outlet and inlet ports may also communicate with a well or reservoir . . . ."); 17:27–30 ("The outlet can be adapted for . . . [c]ollection . . . using micropipettes.").

Patent Owner disputes Petitioner's interpretation of Ismagilov 091's column 17 disclosure, arguing that "the 'outlet ports' of Ismagilov typically act as conduits that allow for collection of the entirety of the 'solution' outside of the device." PO Resp. 32–33 (citing Ex. 2016 ¶ 129); *see also id.* at 34 ("the only functionality disclosed for the 'outlet ports' is solution extraction" (citing Ex. 2016 ¶ 133)). In our view, however, the explanation provided by Patent Owner and Dr. Anna may be consistent with Ismagilov 091's disclosure that "[t]he outlet can be adapted for receiving, for example, a segment of tubing or a sample tube," but does not adequately account for the immediately succeeding disclosure that "[c]ollection can also be done using micropipettes." Ex. 1004, 17:27–30. Although Patent Owner and Dr. Anna cite Exhibits 2020 and 2021 to show how a POSA would have understood Ismagilov 091, they fail to direct us to any specific disclosures in these references. PO Resp. 34; Ex. 2016 ¶ 134 (citing Exs. 2020,[11] 2021[12]).

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[11] Ex. 2020, B. Zheng et al., *Using Nanoliter Plugs in Microfluidics to Facilitate and Understand Protein Crystallization*, 15 Current Opinion in Structural Biology 548 (2005). Figure 2(b) shows "Two funnel-shaped glass capillaries are used to couple the cartridge to the inlet and the receiving capillary to the outlet of the microfluidic channel." *Id.* at 550. Figure 3(b) shows "The receiving capillary is inserted into the outlet channel." *Id.* at 551.

[12] Ex. 2021, US 6,613,513 B1, issued Sept. 2, 2003, discloses microfluidic systems in which "a 'pipettor channel' (a channel in which components can be moved from a source to a microscale element such as a second channel or reservoir) is temporarily or permanently coupled to a source of material. The source can be internal or external to a microfluidic device comprising the pipettor channel." *Id.* at 32:47–52. Figure 2 shows an integrated system,

In our view, neither reference is pertinent to Ismagilov 091's disclosure of an "outlet . . . adapted for . . . [c]ollection . . . using micropipettes." Ex. 1004, 17:27–30.

We credit Dr. Fair's testimony that Ismagilov 091's disclosure of "[c]ollection . . . using micropipettes" describes an open-topped collection well. Ex. 1008 ¶¶ 130, 131, 134. Although Patent Owner relies on Dr. Fair's deposition testimony that he has not personally used a pipette to remove a droplet from a chip (PO Resp. 33–34 (quoting Ex. 2017, 43:9–16)), that testimony does not refute Ismagilov 091's express disclosure that "[c]ollection can also be done using micropipettes" (Ex. 1004, 17:27–30), nor undermine Dr. Fair's opinion that collection by micropipette requires an open-topped collection well (Ex. 1008 ¶¶ 130, 131, 134). We agree with Petitioner that Dr. Fair's testimony shows sufficient familiarity with the industry practice of using micropipettes to remove droplets from wells to provide an adequate basis for this opinion. Pet. Reply 7 n.2 (citing Ex. 1008 ¶¶ 130, 131, 160, 161, 170, 186; Ex. 2017, 42:21–43:4, 140:21–142:2).

Patent Owner argues that Ismagilov 091's "outlet ports" or "wells or reservoirs" differ from the "separation chamber" Patent Owner identifies in the accused products. PO Resp. 2–3, 35–36. In our view, however, Patent Owner's arguments reinforce, rather than refute, Petitioner's position that Ismagilov 091 discloses collection wells. Patent Owner asserts that the ports and outlets disclosed in Ismagilov 091 "would have been fabricated by 'punching' holes in the microchip itself at the channel ends, as was standard

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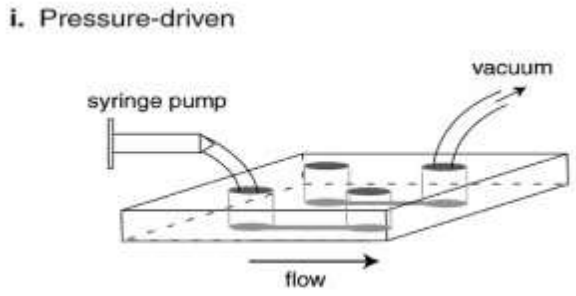
including body structure 202 with reservoirs 204, 208, and 214 and main channel 210, where reactants are flowed from pipettor channel 220 into main channel toward reservoir 214. *Id.* at 35:50–61, Fig. 2.

practice at the time." PO Resp. 2; *see also id.* at 9 (similar assertion). Patent Owner and Dr. Anna assert that "[t]o create inlets and outlets, it was common at the time to punch a hole through the PDMS at the ends of the channels where fluid was desired to be introduced and to exit." *Id.* at 16; Ex. 2016 ¶ 68 (citing Ex. 2033[13]). Patent Owner and Dr. Anna equate Ismagilov 091's "outlet ports" or "wells or reservoirs" with the "[h]oles" that Ismagilov 091 states "may be cut into the PDMS [substrate] using, for example, a tool such as a cork borer or a syringe needle," asserting that such "'hole punches' . . . would have been well known to a POSA at the time." PO Resp. 36 (quoting Ex. 1004, 16:35–36); Ex. 2016 ¶¶ 35, 137.

The evidence relied upon by Patent Owner and Dr. Anna to show commonly known inlet and outlet wells includes Figure 1A of Exhibit 2033, which is reproduced below:



Ex. 2033, Fig. 1A. The above figure shows a PDMS substrate layer with two microchannels (light gray) formed along the bottom of the PDMS layer and a cylindrical hole at each end (inlet and outlet) of the microchannel. *Id.*; Ex. 1071 ¶ 28. The parties' experts agree that the above figure shows inlet and outlet wells like those formed by Ismagilov 091's hole-punch technique

[13] Ex. 2033, S. Sia & G. Whitesides, *Microfluidic Devices Fabricated in Poly(Dimethylsiloxane) for Biological Studies*, 24 Electrophoresis 3563 (2003).

for making outlet wells or reservoirs. Ex. 1071 ¶¶ 27, 28; Ex. 2016 ¶¶ 35, 68, 137. Figure 1A of Exhibit 2033 and Dr. Anna's testimony that it was common to create inlets and outlets by punching a hole through the PDMS at the ends of the channels (Ex. 2016 ¶ 68) buttress Dr. Fair's opinion that a POSA "would understand the disclosure of an outlet 'well' [in Ismagilov 091] to refer to an open-topped, bucket-like structure from which the accumulated droplets could be extracted, e.g., by using a micropipette." Ex. 1008 ¶ 161; *see also* Ex. 1071 ¶ 35 (a POSA would understand "well" and "reservoir" in Ismagilov 091 "to be vertical, bucket-shaped storage areas").

The parties' experts also agree that a POSA would know that the smallest micropipette tip is 1 mm in diameter. Ex. 1071 ¶ 30; Ex. 2016 ¶ 132; Ex. 2017, 159:13–16. In view of Ismagilov 091's disclosure of an "outlet . . . adapted for . . . [c]ollection . . . using micropipettes" (Ex. 1004, 17:27–30), we credit Dr. Fair's testimony that a POSA would understand Ismagilov 091 as disclosing a collection well having a diameter greater than the 1 mm diameter micropipette tip, for example, a 2 mm or 4 mm diameter hole cut in the PDMS using a cork borer. Ex. 1071 ¶¶ 30, 31, 33, 37. Patent Owner does not dispute that a hole of this diameter cut in a substrate of the thickness disclosed in Ismagilov 091 ("about 1 micrometer to about 1 cm" (Ex. 1004, 8:5–6)) satisfies its constructions for "separation chamber" and "droplet receiving outlet." *See generally* PO Resp. 29–38 (addressing claim element 1.3); PO Sur-reply 4–13 (same). In fact, Patent Owner admits that these dimensions "match what Patent Owner accuses of infringement." PO Sur-reply 12–13.

e) Element 1.4

Claim element 1.4 recites: "wherein the separation chamber is upright to the microchannel and out of the horizontal plane." Ex. 1001, 88:12–14 (hereinafter, the "upright" limitation).

Petitioner contends that Ismagilov 091 discloses the "upright" limitation "[b]ecause Ismagilov describes forming the substrate and closing the channels with a glass coverslip" so that "the well or reservoir would extend up and out of the plane of the microchannels." Pet. 40–41 (citing Ex. 1004, 16:37–41, 30:2–9). Petitioner contends that "[t]he extension of the well or reservoir out of the horizontal plane of the microchannels is confirmed because the volume of an outlet well or reservoir in Ismagilov must permit collecting multiple droplets and must be large enough that the fluid can be collected by micropipette." Pet. 41 (citing Ex. 1004, 17:27–30).

Patent Owner argues that Ismagilov 091 does not disclose the "upright" limitation. PO Resp. 38–41.

We find that Petitioner shows persuasively that Ismagilov 091 discloses an outlet well or reservoir (corresponding to the claimed "separation chamber") that meets the "upright" limitation. Pet. 40–41. The parties agree that Ismagilov 091 discloses making wells or reservoirs at the ends of the channels by cutting a hole in the PDMS substrate using, for example, a cork borer. Ex. 1004, 16:35–36; PO Resp. 9, 36; Pet. Reply 7–8. Ismagilov 091 discloses that, after these holes are cut, the PDMS substrate containing molded channels is placed onto a microscope cover slip, which forms the base/floor or top of the channels. Ex. 1004, 16:38–41, 16:60–63, 30:5–8. Petitioner shows persuasively that this method results in a well or reservoir that is upright to the microchannel and out of the horizontal plane of the microchannels. Pet. 40–41; Ex. 1008 ¶ 160.

Our finding is confirmed by Figure 1A of Exhibit 2033 (reproduced above), which the parties' experts agree shows inlet and outlet wells like those formed by Ismagilov 091's hole-cutting process. Ex. 1071 ¶¶ 27, 28; Ex. 2016 ¶¶ 35, 68, 137. As shown in the figure, the cylindrical holes (wells) are upright to the microchannels and out of the horizontal plane of the microchannels. Ex. 2033, Fig. 1A. Petitioner also shows persuasively that Ismagilov 091's wells or reservoirs need to extend out of the horizontal plane of the microchannels so as to have sufficient volume and depth to permit collection of their contents by micropipette. Pet. 41 (citing Ex. 1004, 17:27–30; Ex. 1008 ¶ 161).

Patent Owner argues that a POSA "would just as easily understand this disclosure [in Ismagilov 091] could be describing a 'sample tube,' 'centrifuge tube,' or 'micropipette' inserted into the end of the outlet port in the horizontal plane, without the volume requirements petitioner asserts must be present." PO Resp. 39 (quoting Ex. 1004, 17:27–30 and citing Ex. 1004, 39:57–40:2, Fig. 22D; Ex. 2016 ¶¶ 140, 141).

We determine that, to the extent Patent Owner's argument pertains to collection using a micropipette, it is refuted by Dr. Anna's testimony that "in order for such a collection to be possible in the first place[,] a micropipette tip would need to fit inside the ***punch holes*** as Ismagilov explains they would be created." Ex. 2016 ¶ 131 (emphasis added). There is no dispute that the "punch holes" referenced by Dr. Anna (*id.*) and described by Ismagilov 091 as "[h]oles . . . cut into the PDMS" are perpendicular to the horizontal plane of the microchannels. Ex. 1004, 16:35–36; Ex. 1071 ¶¶ 27, 28, 37; Ex. 2016 ¶¶ 35, 68, 137; Ex. 2033, Fig. 1A.

The evidence of record does not support Patent Owner's argument that "[c]ollection . . . using micropipettes," as disclosed by Ismagilov 091

(Ex. 1004, 17:29–30), refers to inserting a micropipette into the end of the outlet port in the horizontal plane. PO Resp. 39, 41. Petitioner's undisputed evidence shows that a micropipette must be operated vertically, not horizontally, in order to collect fluids. Ex. 1040, 6 ("Tip angle is also important. Hold the pipette vertically, or within 20 degrees of vertical."); *id.* at 7 ("Never invert or lay the pipette down if liquid is in the tip."). The portions of Ismagilov 091 cited by Patent Owner (PO Resp. 39) do not relate to collection using a micropipette. Ex. 1004, 39:57–40:2, Fig. 22D (showing a device with "multiple outlets that can be closed or opened"). Although Patent Owner relies on Dr. Fair's testimony about devices he built (PO Resp. 40 (quoting Ex. 2017, 69:2–18)), that testimony is not related to Ismagilov 091 or the disclosures Petitioner relies upon to show the "upright" limitation of claim 1.

f) Element 1.5

Claim element 1.5 recites: "wherein the droplet formation module and the separation chamber are in fluid communication with each other via the microchannel." Ex. 1001, 88:15–17.

Petitioner contends that Ismagilov 091 discloses that the separation chamber (Ismagilov 091's outlet well) and droplet formation module are in fluid communication via a microchannel. Pet. 43 (citing Ex. 1004, 3:15–20, 14:21–35, 21:48–54). Patent Owner does not dispute Petitioner's contention about claim element 1.5 separate from its other arguments about a "separation channel." PO Resp. 41.

We find that Ismagilov 091 discloses a plug-forming region (corresponding to the claimed "droplet formation module") in fluid communication with an outlet well or reservoir (corresponding to the

claimed "separation chamber") via a first channel (corresponding to the claimed "microchannel"). Our finding is supported by the following disclosures in Ismagilov 091: "a device is provided that includes . . . a first channel comprising an inlet separated from an outlet" (Ex. 1004, 14:20–22); "[e]ach of the outlet and inlet ports may also communicate with a well or reservoir" (*id.* at 14:37–38); "plugs are formed by introducing the plug-fluid, at the plug-forming region, into the flow of carrier-fluid passing through the first channel" (*id.* at 21:48–50); and "[t]he force and direction of flow can be controlled . . . [to] permit[] the movement of the plugs into one or more desired branch channels or outlet ports" (*id.* at 21:50–54).

g) Element 1.6

Claim element 1.6 recites: "wherein the separation chamber has a wider cross-section than the microchannel cross-section to accumulate a plurality of droplets comprising the sample." Ex. 1001, 88:18–21 (hereinafter the "width" limitation).

Petitioner contends that Ismagilov 091's "wells or reservoirs 'collect' plugs." Pet. 44 (citing 8:41–44, 9:5–8, 14:36–38, 17:27–30). Petitioner asserts that, in Ismagilov 091, the droplets are not being accumulated single file in a structure with the cross-section of a channel, but instead are being pooled in a collection vessel that is deep and wide enough to permit removing the droplets with a micropipette. Pet. 44–45 (citing Ex. 1008 ¶ 170).

Patent Owner does not dispute Petitioner's contention about the "width" limitation separate from its other arguments about a "separation chamber." *See* PO Resp. 41–43 (addressing claim elements 1.6 and 1.7 together).

We credit Dr. Fair's testimony that Ismagilov 091 discloses pooling droplets in a vessel deep and wide enough to accommodate a micropipette. Ex. 1008 ¶ 170. As discussed above, we also credit Dr. Fair's testimony that a POSA would understand Ismagilov 091 as disclosing an outlet well with a diameter greater than the diameter of the smallest micropipette, i.e., a diameter greater than 1 mm. Ex. 1071 ¶¶ 30, 31, 33, 37. There is no dispute that such an outlet well has a wider cross-section than the microchannel cross-section. Ismagilov 091 discloses a channel diameters of 30 to 60 μm. Ex. 1004, 15:34–40.

h) Element 1.7

Claim element 1.7 recites that the separation chamber "is of a volume sufficient to separate the plurality of droplets comprising the sample from the immiscible fluid within the separation chamber." Ex. 1001, 88:21–23.

Petitioner contends that Ismagilov 091 discloses an outlet well or reservoir that "collects both a plurality of droplets and a volume of immiscible fluid." Pet. 45 (citing Ex. 1004, Figs. 2–10). According to Petitioner, Ismagilov 091 discloses aqueous droplets in fluorinated oil, and because there is a density difference between those two liquids, they will separate when the droplets and immiscible fluid are pooled in the outlet well or reservoir. Pet. 46.

Patent Owner relies on the same arguments for claim element 1.7 as it presented for the other separation chamber limitations of claim 1. PO Resp. 41. In addition, Patent Owner argues that, "[d]epending on the density of the particular oil that is selected, the droplets will not necessarily separate," for example, "the drops will not necessarily separate if the selected oil has substantially the same density as water." *Id.* at 42–43.

For the reasons discussed above in connection with claim element 1.3, we find that Ismagilov 091 discloses an outlet well or reservoir that collects both a plurality of droplets and a volume of immiscible fluid. Ex. 1004, 9:5–8, 14:37–38, 16:35–36, 21:48–54; *see also id.* at Fig. 3, 4:6–10 (depicting and describing "a stream of plugs from an aqueous plug-fluid and an oil (carrier-fluid) in curved channels"). Petitioner is correct that Ismagilov 091 discloses aqueous droplets with fluorinated oil as the immiscible fluid. Pet. 46; Ex. 1004, 9:38–44, 20:37–38, 20:64–67. Patent Owner does not challenge Petitioner's assertion that, because of a difference in density, aqueous droplets will necessarily float in fluorinated oil. Pet. 10–11; Ex. 1008 ¶ 57; PO Resp. 42; Ex. 2016 ¶ 148. Claim element 1.7 requires a "volume sufficient to separate," not actual separation. Nevertheless, because Ismagilov 091 expressly discloses an outlet well or reservoir that collects aqueous droplets and fluorinated oil (*see, e.g.*, Ex. 1004, 20:64–67), Petitioner has established that Ismagilov 091 inherently discloses separation of the droplets from the immiscible fluid. Pet. 46; Ex. 1008 ¶¶ 57, 174.

i) Conclusion for Independent Claim 1

Accordingly, after considering both parties' arguments and evidence, we are persuaded that Ismagilov 091 discloses all limitations of claim 1. We conclude that Petitioner has shown by a preponderance of the evidence that claim 1 is anticipated by Ismagilov 091.

3. Dependent Claims

a) Claim 2

Claim 2 depends from claim 1 and recites: "wherein an aqueous fluid from the sample inlet is segmented with an immiscible fluid from the immiscible fluid inlet at the junction." Ex. 1001, 88:24–26.

Relying on its explanation for claim element 1.2, Petitioner contends that Ismagilov 091 discloses aqueous droplets and segmenting by immiscible fluid at the junction. Pet. 47.

Patent Owner presents no arguments for dependent claim 2 separate from its arguments for independent claim 1. *See* PO Resp. 43.

We find that Ismagilov 091 discloses the limitation of claim 2 for the same reasons as discussed above for claim element 1.2.

b) Claim 4

Claim 4 depends from claim 1 and recites: "wherein the at least one droplet receiving outlet is located on the upper portion of the separation chamber." Ex. 1001, 88:30–32.

Relying on its explanation for claim 1, Petitioner contends that Ismagilov 091 describes the droplet receiving outlet on the upper portion of the separation chamber. Pet. 47.

Patent Owner presents no arguments for dependent claim 4 separate from its arguments for independent claim 1. *See* PO Resp. 43.

We find that Ismagilov 091 discloses the limitation of claim 4 for the same reasons as discussed above for claim element 1.3. More specifically, we find that Ismagilov 091 discloses an open-topped outlet well or reservoir from which droplets can be extracted using a micropipette, where the open top of the well or reservoir corresponds to the "droplet receiving outlet" and is located on the upper portion of the well or reservoir that corresponds to the "separation chamber." Ex. 1004, 9:5–8, 14:37–38, 16:35–36, 17:18–30; Ex. 1008 ¶¶ 130, 131, 134, 161.

c) Claim 10

Claim 10 depends from claim 1 and recites: "wherein the droplet receiving outlet receives substantially one or more droplets." Ex. 1001, 88:46–47.

Relying on its explanation for claim 1, Petitioner contends that Ismagilov 091 discloses a droplet receiving outlet that receives substantially one or more droplets. Pet. 48.

Patent Owner presents no arguments for dependent claim 10 separate from its arguments for independent claim 1. *See* PO Resp. 43.

We determine that Ismagilov 091 discloses the limitation of claim 10 for the same reasons as discussed above for claim element 1.3. More specifically, we find that Ismagilov 091 discloses an open-topped outlet well or reservoir from which substantially one or more droplets can be extracted using a micropipette, where the open top of the well or reservoir corresponds to the claimed "droplet receiving outlet." Ex. 1004, 9:5–8, 14:37–38, 16:35–36, 17:18–30; Ex. 1008 ¶¶ 130, 131, 134, 161.

d) Claim 11

Claim 11 depends from claim 1 and recites: "further comprising a reagent inlet, wherein the reagent inlet is in fluid communication with the junction or the microchannel." Ex. 1001, 88:48–50.

Petitioner contends that Ismagilov 091 discloses a reagent inlet in communication with the junction at which droplets are formed. Pet. 49–50 (citing Ex. 1004, 10:60–11:7, 18:49–58, 19:5–18, Figs. 4, 5). Petitioner contends that Ismagilov 091 also discloses a reagent inlet in communication with the microchannel in which the droplets merge. Pet. 51 (citing Ex. 1004,

3:14–33, 6:48–54, 15:10–23, 18:16–19, 27:37–39, 27:53–58, 49:18–19, 66:32–42, Figs. 37, 38).

Patent Owner presents no arguments for dependent claim 11 separate from its arguments for independent claim 1. *See* PO Resp. 43.

Claim 11 recites a reagent inlet in fluid communication with either the junction or the microchannel. We find that Ismagilov 091 discloses a reagent inlet in fluid communication with the junction at which droplets are formed. For example, Figure 4 of Ismagilov 091 shows inlet ports 401–405 in fluid communication with a junction with an oil channel, where oil is introduced into carrier fluid inlet port 400, multiple aqueous plug-fluid reagents or solvents are introduced into inlet ports 401–405, and droplets (plugs) are formed at the junction. Ex. 1004, 18:49–58, Fig. 4.

Because we find that Ismagilov 091 discloses a reagent inlet in fluid communication with the junction, we do not need to consider whether Ismagilov 091 discloses a reagent inlet in fluid communication with the microchannel.

e) Claim 12

Claim 12 depends from claim 11 and recites: "wherein the reagent inlet introduces one or more amplification reagents to the junction or the microchannel." Ex. 1001, 88:51–53.

Petitioner contends that Ismagilov 091 discloses devices and methods for conducting "autocatalytic reactions, and describes 'polymerase-chain reaction (PCR)' as such an autocatalytic reaction that 'is a ***very effective amplification method*** that has been widely used in the biological sciences.'" Pet. 53 (citing Ex. 1004, 45:57–46:5, 47:22–34). Petitioner contends that

"Ismagilov teaches that amplification reagents, including those for PCR, could be introduced through the reagent inlets." Pet. 54.

Patent Owner presents no arguments for dependent claim 12 separate from its arguments for independent claim 1. *See* PO Resp. 44.

We find that Ismagilov 091 discloses a reagent inlet that introduces one or more amplification reagents to the junction. More specifically, Ismagilov 091's Examples 7 and 9 and Figures 37 and 38 illustrate experiments in which chemical amplification reagents are introduced into the reagent inlets of a microfluidic device. Ex. 1004, 66:21–66:56, 67:40–68:55, Figs. 37, 38. In Example 7 and Figure 37, for example, a three-channel inlet introduces a first set of reagents through channels 3701–3703, which are in fluid communication with oil channel 3713 at a first plug-forming junction, and a five-channel inlet introduces a second set of reagents through channels 3705–3709, which are in fluid communication with oil channel 3714 at a second plug-forming junction. *Id.* at 66:32–43, Fig. 37. When plugs 3704 containing the first set of reagents merge with plugs 3710 containing the second set of reagents at contact region 3712, an autocatalytic amplification reaction is triggered. *Id.* at 66:49–56.

f) Claim 13

Claim 13 depends from claim 12 and recites: "wherein the one or more amplification reagents are for a polymerase chain reaction." Ex. 1001, 88:54–55.

Petitioner contends that Ismagilov 091 discloses that autocatalytic reactions such as PCR could be carried out using the disclosed microfluidic devices, which would involve introducing amplification reagents into the reagent inlets. Pet. 54.

Patent Owner presents no arguments for dependent claim 13 separate from its arguments for independent claim 1. *See* PO Resp. 44.

We find that a POSA reading Ismagilov 061 would "at once envisage" introducing amplification reagents for PCR into the reagent inlets of the microfluidic devices. *Kennametal, Inc. v. Ingersoll Cutting Tool Co.*, 780 F.3d 1376, 1381 (Fed. Cir. 2015) (A reference can anticipate a claim, even if it "'d[oes] not expressly spell out' all the limitations arranged or combined as in the claim, if a person of skill in the art, reading the reference, would 'at once envisage' the claimed arrangement or combination." (quoting *In re Petering*, 301 F.2d 676, 681 (CCPA 1962)). Although Ismagilov 091 does not disclose a specific example illustrating the introduction of amplification reagents for PCR into the reagent inlet of a microfluidic device, disclosure of such a specific example is not required for anticipation. *Kennametal*, 780 F.3d at 1383 ("Though it is true that there is no evidence in [prior art reference] of 'actual performance' of combining [claimed components], this is not required" for anticipation.). Ismagilov 091 discloses PCR as one of a limited number of specific examples of autocatalytic amplification reactions that can be carried out using microfluidic devices. Ex. 1004, 11:32–40, 46:2–5 (disclosing PCR as an "example of an autocatalytic reaction . . . which is a very effective amplification method that has been widely used in the biological sciences"); *id.* at 46:16–34 (disclosing a reaction between $NaClO_2$ and NaS_2O_3 "used for a highly sensitive amplification process"); *id.* at 46:46–47:9, 66:60–67:38 (disclosing an autocatalytic amplification involving the reaction of Co(III)-5-Br-PAPS) with $KHSO_4$). Furthermore, Ismagilov 091 discloses Examples 7 and 9, which illustrate two of these amplification reactions (*id.* at 66:21–66:56, 67:40–68:55) and describe introducing amplification reagents into the reagent inlets of a microfluidic

device (*id.* at 66:32–37, Fig. 37, 67:47–51, Fig. 38). In our view, a POSA reading Ismagilov 091 would "at once envisage" experiments in which amplification reagents ***for PCR*** are introduced into the reagent inlets, as recited in claim 13, because Ismagilov 091 discloses PCR as one of a limited number of specific amplification reactions and also discloses examples in which amplification reagents are introduced into the reagent inlets of a microfluidic device. *Kennametal*, 780 F.3d at 1381.

g) Claim 19

Claim 19 depends from claim 1 and recites: "further comprising a sorting module to direct the flow of droplets, wherein the sorting module is located between the droplet formation module and the separation chamber." Ex. 1001, 89:1–4.

Petitioner contends that Ismagilov 091 discloses a sorting module that meets the limitations of claim 19. Pet. 54–55 (citing Ex. 1004, 9:5–8, 14:36–38, 15:41–45, 15:46–52, 21:55–59, 31:20–33:18).

Patent Owner presents no arguments for dependent claim 19 separate from its arguments for independent claim 1. *See* PO Resp. 44.

We find that Ismagilov 091 discloses a sorting module to direct the flow of droplets. For example, Ismagilov 091 discloses a "detection region" defined as "a location in a substrate or channel wherein a chemical is identified, measured, ***or sorted*** based on a predetermined property or characteristic." Ex. 1004, 7:61–64 (emphasis added). Ismagilov 091 discloses that the "detection region" is located "downstream of the plug-forming region" and "upstream of the discrimination region or branch point." *Id.* at 15:46–52. Ismagilov 091 discloses that plugs are "sorted dynamically in a flow stream of microscopic dimensions" and that various

characteristics can be used to sort plugs. *Id.* at 21:55–59, 31:50–53. Ismagilov 091 discloses that a "variety of channels . . . can be fabricated . . . as the detection and discrimination or sorting points" and that these channels lead to an outlet that may include a well or reservoir and allow for collection of plugs using micropipettes. *Id.* at 14:37–38, 17:10–30. As discussed above, Ismagilov 091's outlet well or reservoir is a "separation chamber." Accordingly, we find that Ismagilov 091 discloses that the sorting module is located between the droplet formation module and the separation chamber.

h) Claim 20

Claim 20 depends from claim 19 and recites: "wherein the sorting module comprises an apparatus to generate an electric force." Ex. 1001, 89:5–6.

Petitioner contends that Ismagilov 091 discloses that the sorting module includes an apparatus—electrodes—to generate electrical force, which can move the droplets. Pet. 55–56 (citing Ex. 1004, 28:35, 29:31–39).

Patent Owner presents no arguments for dependent claim 20 separate from its arguments for independent claim 1. *See* PO Resp. 44.

We find that Ismagilov 091 discloses that the sorting module comprises an apparatus to generate an electric force. Our finding is supported by Ismagilov 091, which includes a section titled "Splitting and/or Sorting Plugs," which discloses that "electrodes can be fabricated onto a substrate" to control the movement of plugs using dielectrophoresis.

i) Conclusion for Dependent Claims

We conclude that Petitioner has shown by a preponderance of the evidence that dependent claims 2, 4, 10–13, 19, and 20 are anticipated by Ismagilov 091.

E. Petitioner's Ground 2: Ismagilov 091 and Quake

Petitioner contends that claims 1, 2, 4, 7, 9–13, 19, and 20 are unpatentable as obvious over Ismagilov 091 and Quake. Pet. 31–56. We first provide an overview of Quake and then turn to the parties' contentions and our analysis.

1. Quake (Ex. 1006)

Quake is a U.S. Patent Publication titled "Microfabricated Crossflow Devices and Methods." Ex. 1006, codes (10), (54). Petitioner asserts that Quake is prior art to the '837 Patent under 35 U.S.C. § 102(a)(2) and pre-AIA 35 § 102(e) as of its September 14, 2001 filing date and under § 102(a)(1) and pre-AIA § 102(a) and (b) as of its May 16, 2002 publication date. Pet. 14–15. Patent Owner does not contest the prior art status of Quake. We find that Quake is prior art to the '837 Patent, regardless of whether the AIA applies to the patent.

Quake discloses "microfluidic devices and methods," including devices "designed to compartmentalize small droplets of aqueous solution within microfluidic channels filled with oil." Ex. 1006 ¶ 3. More specifically, Quake discloses:

> The devices and methods of the invention 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. A junction or "droplet extrusion region" joins the sample inlet channel to the main channel such that the aqueous solution can be introduced to the

> main channel, e.g., at an angle that is perpendicular to the stream of oil. By adjusting the pressure of the oil and/or the aqueous solution, a pressure difference can be established between the two channels such that the stream of aqueous solution is sheared off at a regular frequency as it enters the oil stream, thereby forming droplets.

Id.; *see also id.* ¶ 84 (describing droplet extrusion region).

Figure 6 of Quake is reproduced below:

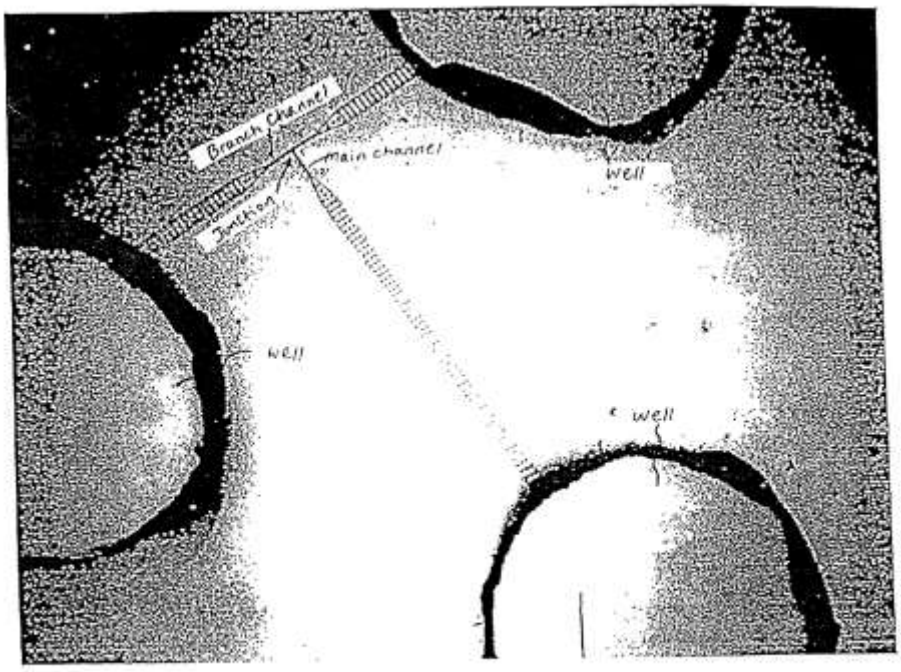


Fig 6

Quake Figure 6 is a photograph showing a microfabricated device ("chip") with an inlet channel and reservoir (labeled "well" at lower right side of Figure 6), a detection region (labeled "main channel" in Figure 6), a branch point (labeled "junction" in Figure 6), and two outlet channels and reservoirs (each labeled "well" at the left side and upper right side of Figure 6). Ex. 1006 ¶¶ 29, 196.

Quake discloses the process by which the chip of Figure 6 was molded from a silicone elastomer. Ex. 1006 ¶ 196. According to Quake, a negative master mold was made from a silicon wafer by standard photolithography and micromachining techniques. *Id.* ¶¶ 195, 196, Fig. 7 (showing etching process). Elastomer components were mixed together and poured onto the etched silicon wafer. *Id.* ¶ 196. After curing, the elastomer was peeled from the wafer. *Id*. The chip was treated to make the elastomer surface hydrophilic. *Id*. As shown in Figure 6, an inlet well and two collection wells were incorporated into the elastomer chip on three sides of a "T" arrangement of channels. *Id.* ¶ 197. The elastomer chip was then adhered to a glass coverslip. *Id.* ¶¶ 196, 197.

According to Quake, the device shown in Figure 6 has the following dimensions: The channels "are 100 μm wide at the wells, narrowing to 3 μm at the sorting junction (discrimination region). The channel depth is 4 μm, and the wells are 2 mm in diameter." Ex. 1006 ¶ 196. Quake discloses that the microfabricated device of Figure 6 can be used in sorting cells or biological materials. *Id.* ¶ 193.

Figure 8 of Quake is reproduced below.

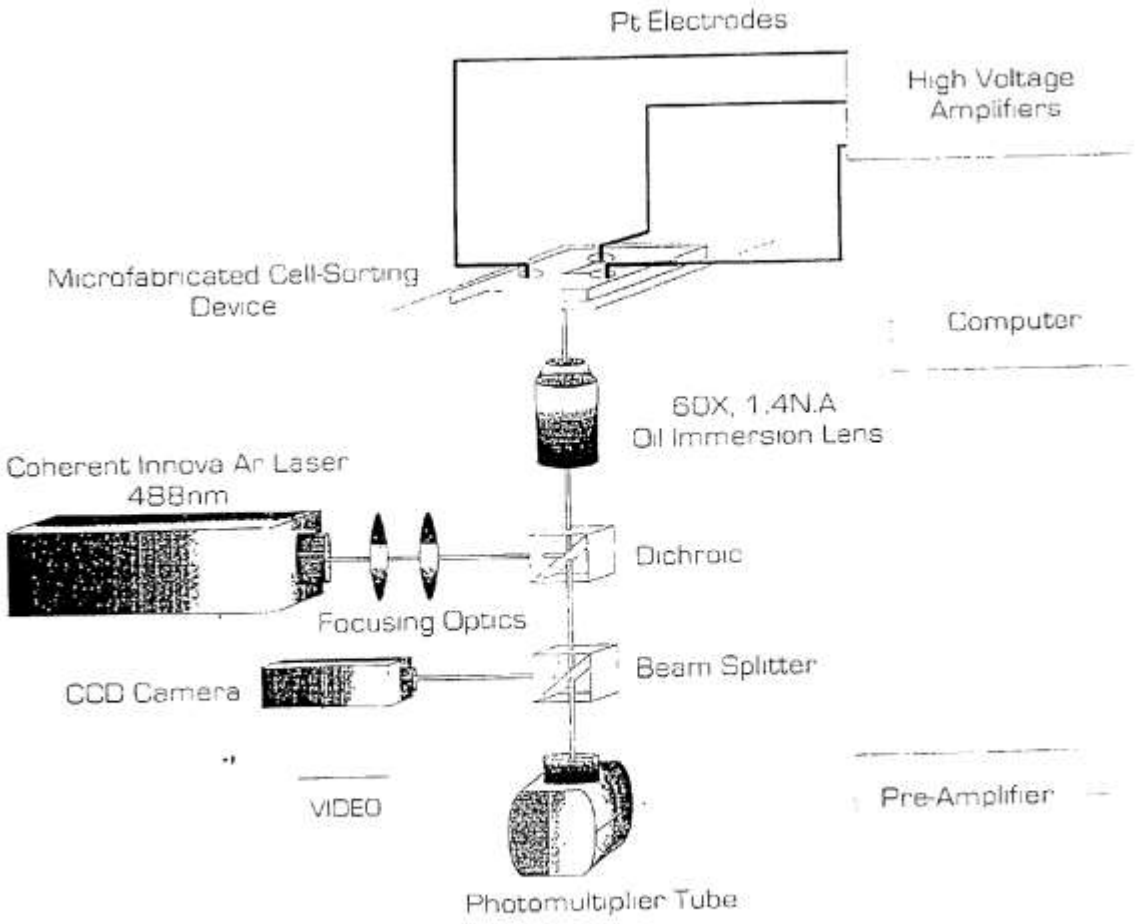


Fig 8

Quake Figure 8 shows a schematic representation of an apparatus for sorting cells or beads using the microfabricated device of Figure 6. Ex. 1006 ¶¶ 31, 197. As shown in Figure 8, the microfabricated cell-sorting device (silicone elastomer chip) was mounted on an inverted microscope for optical detection of fluorescence emission of laser-stimulated cells. *Id.* Electrodes were inserted into each of the three wells (the inlet well and two collection wells) to direct the flow of cells. *Id*. ¶¶ 197, 198, Fig. 8. Responsive to optical detection, voltages on the electrodes were used to direct the cells to

one or the other of the collection wells on each side of the "T" junction. *Id.* ¶¶ 31, 198.

2. Motivation to Combine

Petitioner contends that, to the extent a POSA would not have known the structure of features such as Ismagilov 091's wells, a POSA would have been motivated to look to art that further describes the structure of wells, namely Quake. Pet. 25. According to Petitioner, "[i]f a POSA with Ismagilov would want additional information regarding microfluidic structures, the POSA would have looked to the work of a leader in developing early microfluidic devices: Quake." Pet. 27–28 (citing Ex. 1008 ¶ 107). Petitioner contends that a POSA would have combined the microfluidic configurations, organizations, uses, substrate compositions, and fluids disclosed in Ismagilov 091—including placement of wells, reservoirs, or chambers—with the structures and dimensions for wells or reservoirs, their inlets and outlets, and channels disclosed in Quake. Pet. 39–40 (citing Ex. 1004, 16:2–47).

Patent Owner argues that a POSA would not have had a motivation to combine Ismagilov 091 and Quake because the references have "different purposes." PO Resp. 45–48. Patent Owner asserts that Ismagilov 091 is "focused on microfabricated substrates for forming droplets," and the examples of Quake relied upon by Petitioner are "focused on cell sorting and did not use droplets." *Id.* at 45. In addition, Patent Owner argues that Petitioner "fails to explain how a POSA would go about combining the disparate elements of the references, or what modifications a POSA would necessarily have made in order to combine the disparate elements." PO Resp. 47.

We are persuaded by Petitioner's argument that a POSA would have consulted Quake to obtain additional information about the structure and dimensions of the wells or reservoirs, inlets and outlets, and channels that are disclosed in somewhat less detail in Ismagilov 091. Pet. 25, 39–40. Petitioner is not combining "disparate elements," as argued by Patent Owner. PO Resp. 47. Instead, Petitioner is relying on Quake to provide explicit disclosure of the structure and dimensions of features, particularly outlet wells, that are already expressly described by Ismagilov 091. As support for a motivation to combine, Petitioner cites Ismagilov 091's description of fabrication of channels, substrates, and devices. Pet. 40 (citing Ex. 1004, 16:2–47). That description is very similar to Quake's description of fabrication of a microfabricated device that Petitioner relies upon to provide additional details regarding the dimensions and configuration of the wells or reservoirs, their inlets and outlets, and channels. Pet. 38–42, 45–46 (citing Ex. 1006 ¶¶ 196–200, Figs. 6–8).

In this instance, we view the similarities between Ismagilov 091 and Quake as strong support for combining the references' teachings relied upon by Petitioner. More specifically, Petitioner relies on Quake's disclosure of the manufacture and operation of a microfabricated device. Pet. 38–42, 45–46; Ex. 1006 ¶¶ 192–200. Quake's procedure for microfabrication is very similar to the procedure disclosed by Ismagilov 091. *Compare* Ex. 1004, 16:1–47 ("Fabrication of Channels, Substrates, and Devices"), *with* Ex. 1006 ¶¶ 194–197 ("Preparation of the microfabricated device"). For example, both references disclose that channels are molded from a silicone elastomer using an etched silicon wafer with a negative image of the channels as a mold. Ex. 1004, 16:23–25; Ex. 1006 ¶ 196. Ismagilov 091 discloses that "[h]oles may be cut into the PDMS using, for example, a tool such as a cork

borer or a syringe needle." Ex. 1004, 16:35–36. According to Patent Owner and Dr. Anna, a POSA would have understood that these "[h]oles" correspond to the "wells or reservoirs" that Ismagilov 091 discloses at the inlet and outlet ports. *Id.* at 14:37–38; PO Resp. 2, 9, 36; Ex. 2016 ¶¶ 35, 68, 137. Similar to Ismagilov 091's description of forming inlet and outlet wells, Quake describes an "inlet well and two collection wells . . . incorporated into the elastomer chip on three sides of the 'T' forming three channels." *Compare* Ex. 1004, 16:35–36 (quoted above), *with* Ex. 1006 ¶ 197 (quoted here). Quake's inlet and collection wells are shown in Figures 6 and 8. Ex. 1006, Figs. 6, 8.

Patent Owner argues that Ismagilov 091 and Quake would not have been combined because they "relate to two completely different structures and assemblies with two completely different intended uses," namely cell-sorting in Quake and droplet formation in Ismagilov 091. PO Resp. 45–47. We disagree. The Quake disclosure relied upon by Petitioner is part of Example 7, which demonstrates the manufacture and operation of a cell-sorting device that "can function as a stand-alone device or as a component of an integrated microanalytical chip." Ex. 1006 ¶ 193. More broadly than the specific examples, Quake discloses a "microfluidic device for analyzing and/or sorting biological materials," where the device includes a "droplet extrusion region." *Id.* at code (57), ¶¶ 3, 4, 15. Accordingly, although Example 7 demonstrates a cell-sorting, Quake plainly contemplates that the cell-sorting device can be integrated into a chip that includes a droplet extrusion region.

Accordingly, we find that Petitioner has shown that a POSA would have had a reason to combine the microfluidic configurations, organizations, uses, substrate compositions, and fluids disclosed in Ismagilov 091 with the

structures and dimensions for wells or reservoirs, their inlets and outlets, and channels disclosed in Quake.

3. Claim 1

Petitioner contends that claim elements 1.0, 1.1, 1.2, and 1.5 are disclosed by Ismagilov 091. Pet. 31–35, 43.

Regarding claim element 1.3, Petitioner contends that Quake describes and shows the wells or reservoirs as large, open structures with inlets from channels and electrodes inserted into the open wells. Pet. 38–39 (citing Ex. 1006 ¶¶ 198–200, Figs. 6, 8).

Regarding claim element 1.4, Petitioner contends that Quake confirms that the wells or reservoirs extend upright and out of the plane of the microchannels. Pet. 42. Petitioner relies on Quake's disclosed well and channel dimensions, a calculation of the height of Quake's wells, and Quake's description of how the microfluidic chip is fabricated and combined with electrodes and a microscope. *Id.* (citing Ex. 1006 ¶¶ 196–198, 200, Figs. 6–8).

Regarding claim element 1.6, Petitioner cites Quake's well and channel dimensions to show that, in the proposed combination of Ismagilov 091 and Quake, the wells have a wider cross-section than the channels and have a volume that can accumulate a plurality of droplets. Pet. 45 (citing Ex. 1006 ¶ 196).

Regarding claim element 1.7, Petitioner contends that, "given the large size of the wells specified by Quake, . . . the volume of the well or reservoir will be sufficient to separate droplets under Bio-Rad's contentions because it is sufficient to accumulate a plurality of droplets in a volume of

immiscible fluid where the droplets have a different density from the immiscible fluid." Pet. 46–47.

Patent Owner contends that Quake does not disclose a "separation chamber" and the related limitations of claim 1. PO Resp. 48–49.

For claim elements 1.0, 1.1, 1.2, and 1.5, we find that the limitations are disclosed by Ismagilov 091 for the same reasons as discussed in section II.D.2 above. Petitioner's combination of Ismagilov 091 with Quake does not change our analysis for these claim elements.

Regarding claim element 1.3, we find that Ismagilov 091 teaches an outlet well that is downstream from the droplet formation module. Ex. 1004, 9:5–8, 14:20–22, 14:36–40, 21:48–54. It is undisputed that Ismagilov 091's outlet wells are made by punching a hole in the PDMS substrate. PO Resp. 2, 9, 36; Pet. Reply 7–8; Ex. 1004, 16:35–36; Ex. 2016 ¶¶ 35, 137; Ex. 2033, Fig. 1A. In view of this undisputed evidence, there does not appear to be any dispute about whether Ismagilov 091's outlet wells are open-topped. Nevertheless, we agree with Petitioner that Quake confirms that Ismagilov 091's outlet wells are open-topped. Pet. 38. More particularly, Quake discloses collection wells made in the same way as Ismagilov 091's outlet wells. *Compare* Ex. 1006 ¶ 197 ("The inlet well and two collection wells were incorporated into the elastomer chip on three sides of the 'T' forming three channels (FIGS. 6 and 7)."), *with* Ex. 1004, 16:35–36 ("Holes may be cut into the PDMS using, for example, a tool such as a cork borer or a syringe needle."). Quake's inlet well and two collection wells are shown in Figure 6 and again in Figure 8, which depicts three open-topped wells with electrodes inserted into the wells. Ex. 1006, Fig. 8, ¶ 198 ("Three platinum electrodes were each inserted into separate wells.").

We are persuaded that our claim constructions for "separation chamber" and "droplet receiving outlet" are met by an outlet well as taught by Ismagilov 091 (Ex. 1004, 9:5–8, 14:36–40), having a 2 mm diameter as taught by Quake (Ex. 1006 ¶ 196), a depth within the range taught by both references (Ex. 1004, 16:46 (substrate can be "about 1 micron to about 1 cm in thickness"); Ex. 1006 ¶ 88 (same)), an inlet as described in Ismagilov 091 (Ex. 1004, 9:5–8, 14:36–40) and as shown in Quake Figure 6, and an open top produced by punching a hole as described by Ismagilov 091 (Ex. 1004, 16:35–36) and depicted in Quake Figures 6 and 8 (Ex. 1006 ¶¶ 197, 198). Pet. 40; Pet. Reply 21–22.

Regarding claim element 1.4, we agree with Petitioner that Quake confirms that the outlet wells or reservoirs, as disclosed in Ismagilov 091, have a significant dimension extending above the plane of the microchannels. Pet. 41–42. Patent Owner does not dispute Dr. Fair's calculation of the height of a cylindrical well having the diameter and capacity disclosed in Quake. Pet. 42; Ex. 1006 ¶¶ 196, 200; Ex. 1008 ¶ 164.

Regarding claim element 1.6, Petitioner shows persuasively that Quake teaches a collection well having a wider cross-section (2 mm diameter) than the microchannel cross-section (4 μm depth by 100 μm width at the wells, narrowing to 3 μm at the sorting junction). Pet. 45; Ex. 1006 ¶ 196, Fig. 6. Patent Owner does not dispute that the combination of Ismagilov 091 and Quake teaches this limitation.

Regarding claim element 1.7, Petitioner shows persuasively that Ismagilov 091 teaches an outlet well that collects droplets and immiscible fluid and, with the well dimensions and capacity specified by Quake (Ex. 1006 ¶¶ 196, 200), the volume of the outlet well will be sufficient to accumulate a plurality of droplets and to allow the droplets to separate from

the immiscible fluid based on their different densities. Pet. 42, 46–47; Ex. 1008 ¶ 176.

Patent Owner argues that Quake does not teach "wells intended for separation." PO Resp. 49. According to Patent Owner, Quake's "collection wells" are used for "sorting experiments" in which cells (not droplets) are directed by voltages. *Id.* Patent Owner argues there is no disclosure of separating droplets and immiscible fluid in Quake's wells. *Id.*

After considering Patent Owner's arguments, we are persuaded that Petitioner has established that the combination of Ismagilov 091 with Quake teaches the claimed "separation chamber" and related limitations. Whether Quake teaches "wells intended for separation" or "separating droplets and immiscible fluid in these wells" (PO Resp. 49) is not the correct test. Patent Owner's construction for "separation chamber," which we adopt here, does not require actual separation. Moreover, even if separation were required, Petitioner shows persuasively that, due to a difference in density, the droplets will necessarily separate from the immiscible fluid when the droplets accumulate in the outlet well. Pet. 10–11, 46–47; Ex. 1008 ¶¶ 57, 174, 176.

Accordingly, we are persuaded that the combination of Ismagilov 091 and Quake teaches all limitations of claim 1.

4. Dependent Claims

a) Claims 2, 4, 10–13, 19, and 20

Neither party presents an analysis of claims 2, 4, 10–13, 19, and 20 under Ground 2 separate from the analysis under Ground 1. Pet. 47–56; PO Resp. 49–53. For the reasons discussed in section II.D.3 above, we find that Ismagilov 091 discloses the limitations of claims 2, 4, 10–13, 19, and 20.

Petitioner's combination of Ismagilov 091 with Quake does not change our analysis for these claims.

b) Claim 7

Claim 7 depends from claim 1 and recites: "wherein the droplet receiving outlet is coupled to a vessel." Ex. 1001, 88:40–41.

Petitioner asserts that, according to Patent Owner's infringement contentions, "coupled" is "[b]road enough to encompass transporting by pipette between an alleged outlet/chamber and vessel." Pet. 19 (citing Ex. 1026, 21–22). Addressing claim 7, Petitioner contends "[i]t is understood by a POSA or obvious that the droplets collected from a well by pipette would be transferred to another vessel for downstream use" and that "such vessels were well known," quoting Ismagilov 091's disclosure of a "centrifuge tube." Pet. 48 (citing Ex. 1004, 17:27–30). According to Petitioner, removing the droplets by pipette and transporting them to another vessel meets the claim under Patent Owner's interpretation. *Id.* (citing Ex. 1008 ¶ 186).

Patent Owner argues that "coupled" should be construed as "operably linked." PO Resp. 26 (citing Ex. 2032). As support for this construction, Patent Owner argues that "[t]he 'coupling' between the droplet receiving outlet and the vessel is to effectuate transfer of droplets from the separation chamber to the vessel." *Id.* (citing Ex. 1001, 4:17–36). Addressing claim 7, Patent Owner argues that, "because neither Ismagilov nor Quake disclose a separation chamber with one or more droplet receiving outlets, . . . there is also no disclosure of a 'droplet receiving outlet' being 'coupled,' or 'operably linked,' to another vessel." *Id.* at 50. Patent Owner additionally

argues that Petitioner "fails to identify any disclosure of a 'separate vessel' in either Ismagilov or Quake." *Id.* at 50–51.

We determine that we do not need to provide an explicit construction for "coupled" in order to resolve the parties' dispute about claim 7. Patent Owner agrees that claim 7 requires no physical or mechanical connection between the droplet receiving outlet and a vessel and that transfer of droplets from the outlet to a vessel using a pipette may constitute "coupling." PO Resp. 26–27. For the reasons discussed above, we find that the combination of Ismagilov 091 and Quake teaches an outlet well that accumulates droplets and immiscible fluid and that Ismagilov 091 teaches collection of droplets from the outlet well using a micropipette. Ex. 1004, 9:5–8, 14:37–38, 16:35–36, 17:27–30, 21:48–54; Ex. 1006 ¶¶ 196, 197, Fig. 6. Patent Owner presents no effective rebuttal to Petitioner's contention that a POSA would have understood that a micropipette can be used to collect droplets from an outlet well and transfer them to another vessel and that such use meets the limitation of claim 7. We are persuaded by Petitioner's contention. Pet. 48; Ex. 1008 ¶ 186.

c) Claim 9

Claim 9 depends from claim 7 and recites: "wherein the vessel is a PCR tube or a test tube." Ex. 1001, 88:44–45.

Petitioner contends that it would have been obvious to place droplets in a centrifuge tube or PCR tube after the droplets have been transferred from the well by a pipette. Pet. 48 (citing Ex. 1008 ¶¶ 191, 192).

Patent Owner presents no arguments for dependent claim 9 separate from its arguments for independent claim 1. *See* PO Resp. 51.

We determine that Petitioner has established it would have been obvious to select a PCR tube or a test tube as the vessel for receiving the transfer of droplets collected by micropipette from an outlet well. Pet. 48; Ex. 1008 ¶ 192. The evidence shows that such vessels were known in the art. Ex. 1004, 17:27–29 (disclosing the use of a "sample tube" such as a "centrifuge tube" for collection); Ex. 1006 ¶ 148 (same). Our finding is further supported by the Examiner's determination that "it would have been obvious to one having ordinary skill in the art to use a test tube or a PCR tube as the vessel, as the claimed improvement on a device or apparatus is no more than 'the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for improvement.'" Ex. 1002, 1099 (quoting *Ex parte Smith*, 83 USPQ2d 1509, 1518–19 (BPAI 2007) (citing *KSR*, 550 U.S. at 417)). When responding to the Office Action, Applicant did not challenge this determination. *Id.* at 1115.

5. Secondary Considerations

Patent Owner contends that secondary considerations, including long-felt need, commercial success, praise, and acquiescence and licensing weigh in favor of a finding of nonobviousness of the '837 Patent claims. PO. Resp. 53–59.

a) Presumption of Nexus

Patent Owner asserts that its "ddPCR™ platform . . . practices the '837 patent." PO Resp. 53–54. As support for this assertion, Patent Owner relies on a statement that "[t]he Bio-Rad Digital PCR Systems and/or their use is covered by claims of U.S. patents," including the '837 Patent and eight other patents. *Id.* at 54 (citing Ex. 2022 (Patent Owner's standard

terms and conditions of sale)). Patent Owner also asserts that "[t]he patented features from the '837 patent are repeatedly referenced in Bio-Rad's instruction manuals and are critical to the Bio-Rad products' workflows." *Id.* (citing Exs. 2010, 2011). Dr. Anna directs us to portions of these manuals that instruct users how to transfer droplets out of the separation chamber of a cartridge. Ex. 2016 ¶ 180 (citing Ex. 2010, 18; Ex. 2011, 18). Based on these assertions, Patent Owner contends that "the secondary considerations . . . related to Bio-Rad's products have a sufficient nexus to the claims of the '837 Patent." PO Resp. 54.

"In order to accord substantial weight to secondary considerations in an obviousness analysis, the evidence of secondary considerations must have a nexus to the claims, i.e., there must be a legally and factually sufficient connection between the evidence and the patented invention." *Fox Factory, Inc. v. SRAM, LLC*, 944 F.3d 1366, 1373 (Fed. Cir. 2019) (internal quotes omitted); *see also Lectrosonics, Inc. v. Zaxcom, Inc.*, Case IPR2018-01129, Paper 33 at 32 (PTAB Jan. 24, 2020) (precedential) ("For objective indicia of nonobviousness to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the claimed invention."). There is a rebuttable presumption of nexus "when the patentee shows that the asserted objective evidence is tied to a specific product and that product 'embodies the claimed features, and is coextensive with them.'" *Fox Factory*, 944 F.3d at 1373 (citations omitted); *Lectrosonics*, Paper 33 at 32.

Patent Owner does not present an analysis demonstrating that its products are coextensive (or nearly coextensive) with the challenged claims of the '837 Patent. At best, Dr. Anna directs us to instructions for transferring droplets from outlet wells to a PCR plate. Ex. 2016 ¶ 180

(citing Ex. 2010, 18; Ex. 2011, 18). Even if these instructions were sufficient to establish that Patent Owner's products have a "separation chamber" and a "droplet receiving outlet," there are numerous other claim limitations that are not addressed by Patent Owner's evidence of nexus. Although Patent Owner relies on its standard terms and conditions listing the '837 Patent among eight other patents (PO Resp. 54 (citing Ex. 2022)), a simple patent listing is not enough to show coextensiveness or nexus.

Accordingly, Patent Owner has not shown that its products are entitled to a presumption of nexus.

b) Patent Owner's Acquisition of '837 Patent

Patent Owner asserts that "Bio-Rad acquired RainDance and all of its intellectual property in January 2017, including the '837 patent, demonstrating the value that has been placed on the protected features of the '837 patent." PO Resp. 53 (citing Ex. 2014 (press report titled, "Bio-Rad to Acquire RainDance Technologies")). Patent Owner does not present arguments or evidence as to the value that was ascribed to the '837 Patent or the technology covered by the challenged claims in the context of Patent Owner's acquisition of RainDance. Accordingly, we are not persuaded that Patent Owner has shown a nexus for this asserted secondary considerations evidence.

c) Long-Felt Need

Patent Owner asserts that "RainDance's patented droplet system, which included features embodied in the '837 patent, fundamentally enhances the way researchers and scientists study cell-based and cell-free biomarkers in cancer, infectious disease, and inherited disorders." PO Resp. 55 (citing Ex. 2016 ¶ 182).

According to Patent Owner, its "ddPCR™ platform was heralded as a breakthrough that greatly advanced the capabilities of PCR" and was "rapidly adopted in the industry and led to an explosion of research." PO Resp. 55 (citing Exs. 2001–2004). Based on this evidence, Patent Owner contends that "[t]he inventions of the '837 patent fulfilled a long-term need for a means of isolating sample from the surrounding environment for further analysis using microfluidic droplets by means of the claimed separation chamber." *Id.* at 56 (citing Ex. 2016 ¶¶ 183–186).

"A finding that a presumption of nexus is inappropriate does not end the inquiry into secondary considerations." *Fox Factory*, 944 F.3d at 1375; *Lectrosonics*, Paper 33 at 33. "To the contrary, the patent owner is still afforded an opportunity to prove nexus by showing that the evidence of secondary considerations is the 'direct result of the unique characteristics of the claimed invention.'" *Fox Factory*, 944 F.3d at 1373–74 (quoting *In re Huang*, 100 F.3d 135, 140 (Fed. Cir. 1996)); *Lectrosonics*, Paper 33 at 33. Patentee must show a "nexus to the merits of the claimed invention," meaning "some aspect of the claim not already in the prior art." *Lectrosonics*, Paper 33 at 33 (quoting *In re Kao*, 639 F.3d 1057, 1068–69 (Fed. Cir. 2011)).

We determine that Patent Owner has not demonstrated a nexus between the evidence relied upon to show long-felt need and the merits of the claimed invention. Patent Owner asserts that the evidence touts its ddPCR™ platform as "an easy-to-use alternative to the existing technology" that enabled researchers to publish numerous studies and "to detect rare targets with a level of precision that was just not possible with previous technologies." PO Resp. 55–56 (citing Exs. 2001–2004). Patent Owner makes no attempt to show a nexus between the technology discussed in

Exhibits 2001 to 2004 and the features recited in the challenged claims of the ’837 Patent.

d) Commercial Success

Patent Owner contends that its products that embody the ’837 Patent have been a commercial success, with the inventions disclosed in the ’837 Patent contributing to this success and representing “a significant improvement on the prior art that greatly advanced the capability of PCR and NGS [Next Generation Sequencing].” PO Resp. 56 (citing Exs. 2005–2009; Ex. 2016 ¶ 187).

Patent Owner also contends that Petitioner’s “products embodying the invention have been a commercial success.” PO Resp. 56–57 (citing and quoting Ex. 2012 (discussing number of instruments sold in total and to “top research institutions” and “global pharmaceutical companies” and associated revenue increases as of December 31, 2018 and June 30, 2019)).

For the reasons discussed above, Patent Owner has not shown that its products are entitled to a presumption of nexus. Nor has Patent Owner shown a nexus between the merits of the claimed invention and the evidence relied upon to show commercial success of its products or Petitioner’s products. Although Patent Owner relies on Exhibits 2005 to 2009 and 2012, it does not show a nexus between this evidence and the unique features of the challenged claims.

e) Praise by Others

Patent Owner asserts that its ddPCR™ products have received “repeated accolades for their contributions to the field” and that its “ddSEQ™ system has also received wide acclaim.” PO Resp. 57–58 (citing Exs. 2005–2009). According to Patent Owner, “prior to its acquisition by

Bio-Rad, Raindance received praise from the industry for its own systems that incorporated the patented features of the '837 patent." *Id.* at 58 (citing Exs. 2023–2026). Petitioner asserts that both Patent Owner's and Petitioner's products "have received praise because of their turn-key, easy-to-use workflows." *Id.* at 59 (citing Ex. 2013).

For the reasons discussed above, Patent Owner has not shown that its products are entitled to a presumption of nexus. Nor has Patent Owner shown a nexus between the merits of the claimed invention and the evidence relied upon to show industry praise of Patent Owner's products, RainDance's products, or Petitioner's products. Although Patent Owner relies on Exhibits 2005–2009, 2013, and 2023–2026, it does not show a nexus between this evidence and the unique features of the challenged claims. Furthermore, although Patent Owner discusses advantages of the patented inventions (PO Resp. 59), Patent Owner does not show that these advantages are the reasons Patent Owner's and Petitioner's products have received praise. Nor does Patent Owner show that the evidence of industry praise or other asserted secondary considerations is tied to the novel features of the claimed invention or the claimed combination as a whole. *WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1331 (Fed. Cir. 2016); *Lectrosonics*, Paper 33 at 33.

6. Conclusion for Ground 2

We conclude that Petitioner has shown by a preponderance of the evidence that claims 1, 2, 4, 7, 9–13, 19, and 20 are unpatentable as obvious over Ismagilov 091 and Quake.

F. Petitioner's Grounds 3–5: Ismagilov 119 alone or in view of Pamula

Petitioner contends that claims 1–4, 7–13, and 19–20 are unpatentable as obvious over Ismagilov 119, alone or in view of Pamula. Pet. 56–71. We first provide an overview of the asserted references and then turn to the parties' contentions and our analysis.

1. Ismagilov 119 (Ex. 1005)

Ismagilov 119 is a U.S. Patent Publication titled "Microfluidic System." Ex. 1005, codes (10), (54). Petitioner asserts that Ismagilov 119 is prior art to the '837 Patent under 35 U.S.C. § 102(a)(2) and pre-AIA § 102(e) as of its March 16, 2005 filing date and under § 102(a)(1) and pre-AIA § 102(a) as of its May 4, 2006 publication date. Pet. 13–14. Patent Owner does not contest the prior art status of Ismagilov 119. We find that Ismagilov 119 is prior art to the '837 Patent, regardless of whether the AIA applies to the patent.

Ismagilov 119 discloses a microfluidic system. Ex. 1005, code (54). Ismagilov 091 is incorporated by reference into Ismagilov 119. *Id.* ¶¶ 30, 118. Like Ismagilov 091, Ismagilov 119 refers to droplets as "plugs." *Id.* ¶ 22, Fig. 13b (showing "aqueous droplets, or plugs" being formed at the junction between "channel a" through which an aqueous stream is pumped and "channel b" though which a carrier fluid is pumped).

Petitioner relies on the following passage from Ismagilov 119:

> Plugs can be sorted. For example, the plugs can also be sorted according to their sizes. Alternately, the plugs can be sorted by their density relative to that of the carrier fluid. Alternately, plugs can also be sorted by applying a magnetic field if one group of the plugs contains magnetic materials such as iron or cobalt nanoparticles or ferrofluid.

Ex. 1005 ¶ 123.

2. Pamula 634 (Ex. 1007); Pamula 238 (Ex. 1018)

Pamula 634 and Pamula 238 are U.S. Patent Publications, both of which are titled "Droplet-based Surface Modification and Washing." Ex. 1007, codes (10), (54); Ex. 1018, codes (10), (54).

Petitioner asserts that Pamula 634 is prior art to the '837 Patent under 35 U.S.C. § 102(a)(2) and pre-AIA § 102(e) as of its December 15, 2006 filing date. Pet. 15. This assertion is based on Petitioner's contention that the '837 Patent claims are not supported by the provisional priority applications filed before Pamula 634's filing date. Pet. 15–16.

Petitioner asserts that Pamula 238 is prior art to the '837 Patent under 35 U.S.C. § 102(a)(2) and pre-AIA § 102(e) as of the April 18, 2006 filing date of a provisional application.[14] Pet. 16. According to Petitioner, the disclosures relied upon by Petitioner "are substantially identical between the publication and provisional" and "Pamula 238 includes claims supported by that provisional." *Id.* (citing Ex. 1018 ¶ 418; Ex. 1025, 8–9).

Patent Owner does not contest the prior art status of Pamula 634 or Pamula 238. We do not decide whether Petitioner has shown that either Pamula 634 or Pamula 238 is prior art to the '837 Patent because, for the reasons discussed below, we find that Petitioner has not established unpatentability based on the grounds that include these references.

Pamula 634 and Pamula 238 (collectively "Pamula")[15] disclose a droplet microactuator. Ex. 1007, code (57), ¶¶ 3, 13, 374, Fig. 1.

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[14] Ex. 1025, U.S. Provisional Application No. 60/745,058 ("Pamula 058").

[15] For the sake of simplicity, we cite only to Pamula 634 (Ex. 1007). Pamula 238 (Ex. 1018) contains the same disclosures as we cite in Pamula 634 (Ex. 1007).

By way of background, Pamula discusses two types of microfluidic systems. Ex. 1007 ¶ 12. According to Pamula, "continuous-flow systems rely on continuous flow of liquids in channels whereas discrete-flow systems utilize droplets of liquid either within channels or in a channel-less architecture." *Id.* Pamula identifies various limitations of continuous-flow systems. *Id*. Pamula indicates that a need remains for a system that uses droplet manipulations to carry out multiple tests on a single chip and that can be integrated into a handheld device for use at the point of sample collection, e.g., for bedside blood analysis. *Id.* ¶¶ 11, 12.

Pamula's droplet microactuator includes a substrate with electrodes arranged in arrays, paths, or networks for transporting droplets along the path or network of electrodes. Ex. 1007 ¶¶ 375–381. The droplet microactuator may include a pair of parallel substrates separated by a gap with an array of electrodes on one or both substrates. *Id.* ¶¶ 205, 377, Fig. 6. In that case, "droplets may be interposed in the space between the plates," and the "[s]pace surrounding the droplets typically includes a filler fluid." *Id.* ¶ 378. According to Pamula, "[t]he droplet microactuator operates by direct manipulation of discrete droplets, e.g., using electrical fields." *Id.* ¶ 381.

Pamula states that "[d]iscrete droplet operations obviate the necessity for continuous-flow architecture and all the various disadvantages that accompany such an architecture." Ex. 1007 ¶ 385. Nevertheless, Pamula discloses that "[t]he droplet microactuator may in some cases be supplemented by continuous flow components" and that "such combination approaches involving discrete droplet operations and continuous flow elements are within the scope of the invention." *Id.* Pamula states that "in certain other embodiments, various continuous flow elements are

specifically avoided in the droplet microactuator." *Id.* Pamula discloses "microchannels" as an exemplary component that may be excluded from a droplet microactuator. *Id.*

Petitioner relies on paragraph 418 of Pamula, which discloses in relevant part:

> The filler fluid may be selected to have a particular density relative to the droplet phase. A difference in density between the two phases can be used to control or exploit buoyancy forces acting upon the droplets. Examples of two-phase systems useful in this aspect of the invention include water/silicone oil, water/flourinert [*sic*, fluorinert], and water/fluorosilicone oil. When one phase is buoyant, then that effect can be exploited in a vertical configuration as a means to transport one phase through the other. For example, a waste or collection well can exist at the top or bottom of the droplet microactuator where droplets are delivered to that reservoir by simply releasing them at an appropriate point and allowing them to float or sink to the target destination. Such an approach may be suitable for use in removing reactant from a droplet microactuator, e.g. removing fluid containing amplified nucleic acid for use in other processes.

Ex. 1007 ¶ 418.

3. Ground 3: Ismagilov 119 Alone

Claim element 1.3 recites: "at least one downstream separation chamber comprising a droplet receiving chamber inlet and at least one droplet receiving outlet." Ex. 1001, 88:10–12.

Petitioner contends that claim element 1.3 is rendered obvious by Ismagilov 119's disclosure that "the plugs can be sorted by their ***density*** relative to that of the carrier fluid." Pet. 57 (quoting Ex. 1005 ¶ 123). More specifically, Petitioner contends:

> Based on the knowledge of one of ordinary skill, a POSA would already be familiar with the features of a system to sort droplets based on density. As described in section VI [of the

> Petition], droplets either float (cream) or sink (sediment) ***if they were placed in a large vessel*** such that the droplets and continuous phase liquid could move freely past each other if they had different densities. The above quote from Ismagilov 119 described a density difference between the carrier fluid and the droplets. Also, there was a density difference based on the fluids disclosed in Ismagilov, as described in section VI, and a POSA could have observed the droplets floating in the oil. ***The chamber itself would be a large volume*** to collect multiple droplets and allow them to move freely through the continuous oil phase to form a fraction enriched for droplets, as was well-known for emulsions. ***A chamber or reservoir would need to extend vertically*** to permit the density sorting to occur over the distance parallel with the force of gravity. For the chamber to operate to remove the fraction of floating droplets, ***an outlet is placed at the top of the chamber to collect the droplets***. This would allow the droplet enriched fraction to be collected, which would mean that substantially only droplets would be entering the outlet. There would also be an outlet on the bottom for unwanted fluids (e.g., immiscible fluid) to exit and avoid it overflowing into the outlet for the droplets.
>
> The space of the chamber would be enclosed ***except for the inlet and outlet*** to allow the droplets to be extracted (e.g., from the top of the chamber).

Id. at 57–58 (citing Ex. 1008 ¶¶ 136–144) (emphasis added).

Petitioner's contention is an attempt to extrapolate from a single sentence in Ismagilov 119—"the plugs can be sorted by their density relative to that of the carrier fluid"—a teaching or suggestion of a separation chamber comprising a droplet receiving chamber inlet and at least one droplet receiving outlet, as recited in claim element 1.3. In our view, however, this single sentence cited from Ismagilov 119 does not identify any particular structure at all, much less the recited "separation chamber" having a "droplet receiving chamber inlet" and a "droplet receiving outlet."

In our view, Petitioner's analysis improperly relies on hindsight and conclusory assertions about the knowledge of a POSA to supply multiple important claim limitations that are missing from the cited disclosure of Ismagilov 119. *See KSR*, 550 U.S. at 421 (in reaching a conclusion of obviousness, "hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning" must be avoided); *DSS Tech. Mgmt. v. Apple Inc.*, 885 F.3d 1367, 1374 (Fed. Cir. 2018) ("In cases in which 'common sense' is used to supply a missing limitation, as distinct from a motivation to combine, . . . our search for a reasoned basis for resort to common sense must be searching."); *Arendi S.A.R.L. v. Apple Inc.*, 832 F.3d 1355, 1367 (Fed. Cir. 2016) (reversing Board's determination of obviousness where "the missing limitation is not a 'peripheral' one, and there is nothing in the record to support the Board's conclusion that supplying the missing limitation would be obvious to one of skill in the art").

Petitioner misreads the sentence it relies upon as the lynchpin of its obviousness contention. Ismagilov 119 discloses that "plugs can be sorted by their density relative to that of the carrier fluid." Ex. 1005 ¶ 123. Dr. Fair opines "[t]his means that, based on the difference in densities between the droplets and the carrier fluid, the droplets are substantially separated from the carrier fluid." Ex. 1008 ¶ 136. According to Petitioner and Dr. Fair, this passage "refers to only two things in the sorting: the droplets that are referred to as having one density, and the carrier fluid that is referred to as having a different relative density." Pet. 57; Ex. 1008 ¶ 136.

We disagree with the hindsight-based interpretation advanced by Petitioner and Dr. Fair. The sentence from Ismagilov 119, paragraph 123 describes ***sorting*** plugs, ***not separating*** plugs from carrier fluid. Our

understanding is consistent with the entirety of Ismagilov 119, paragraph 123, which reads:

> Plugs can be sorted. For example, the plugs can also be sorted according to their sizes. Alternately, the plugs can be sorted by their density relative to that of the carrier fluid. Alternately, plugs can also be sorted by applying a magnetic field if one group of the plugs contains magnetic materials such as iron or cobalt nanoparticles or ferrofluid.

Ex. 1005 ¶ 123. Paragraph 123 begins with the general statement that "[p]lugs can be sorted." *Id.* Each sentence that follows that general statement is an "example" of how plugs can be sorted. *Id.* Accordingly, sorting plugs "by their density relative to that of the carrier fluid" is reasonably interpreted to mean separating the plugs ***from each other*** based on their density relative to the carrier fluid, as opposed to separating plugs from the immiscible fluid. For example, plugs that float in the carrier fluid can be sorted from plugs that sink in the carrier fluid without separating the plugs from the carrier fluid.

Petitioner's obviousness case hinges on the proposition that a POSA would have understood that a "separation chamber" would be necessary to carry out the "sorting by density" that is described in Ismagilov 119. *See, e.g.*, Pet. 57–60; Ex. 1008 ¶ 140 ("a person of ordinary skill in the art would know that all that would be required to perform such density-based sorting would be a relatively simple chamber with a sufficiently large volume to collect multiple droplets and allow them to move freely through the continuous oil phase to form a separate fraction enriched for droplets").

In our view, Petitioner's evidence does not justify a leap from density-based sorting, as disclosed in Ismagilov 119, to a "separation chamber" in which droplets are separated from immiscible fluid, as recited in claim 1.

Petitioner directs us to no disclosure or suggestion, either in Ismagilov 091 or Ismagilov 119, that the density-based sorting mentioned in paragraph 123 takes place in a chamber or reservoir. Moreover, Ismagilov 091 suggests that sorting occurs in microchannels, not in a separation chamber. Ex. 1004, 17:10–13 ("***A variety of channels*** for sample flow and mixing can be fabricated on the substrate and can be positioned at any location on the substrate, chip, or device as the detection and discrimination or ***sorting points***."); *id.* at 21:55–59 ("[O]ne or more plugs are detected, analyzed, characterized, or ***sorted*** dynamically ***in a flow stream of microscopic dimensions*** based on the detection or measurement of a physical or chemical characteristic, marker, property, or tag.") (emphases added). As such, Petitioner has not shown that Ismagilov 119 teaches a separation chamber comprising a droplet receiving chamber inlet and at least one droplet receiving outlet, as recited in claim element 1.3.

For these same reasons, Petitioner has not shown that Ismagilov 119 describes a separation chamber that is "is upright to the microchannel and out of the horizontal plane" as required by claim element 1.4, that "has a wider cross-section than the microchannel cross-section" as recited in claim element 1.6, or that "is of a volume sufficient to separate the plurality of droplets . . . from the immiscible fluid . . . " as recited in claim element 1.7. Ex. 1001, 88:10–14, 88:18–23; Pet. 64, 66–67.

The foregoing analysis for Ground 3 is essentially the same as set forth in our Institution Decision. Inst. Dec. 44–48. Patent Owner agrees with our analysis. PO Resp. 59–60. Petitioner presents two reply arguments. Pet. Reply 27–28.

First, Petitioner argues that we "misread Ismagilov 119's disclosure of sorting plugs/droplets" and that the first and third examples in paragraph 123

refer to sorting plugs from other plugs, e.g., "'according to their sizes' (plural)" and the second example refers "to only a singular 'density' of all plugs relative to the carrier fluid." Pet. Reply 27. We disagree. In our view, Petitioner places too much emphasis on the difference between the plural (sizes) and the singular (density). As discussed above, all three examples fall under the general statement that "[p]lugs can be sorted," which Petitioner does not dispute means sorting plugs from other plugs. Ex. 1005 ¶ 123. Petitioner's argument does not change our view that each sentence that follows that general statement is an "example" of how plugs can be sorted from other plugs. *Id.*

Second, Petitioner argues that "a POSA would recognize the need for a structure that would arrive at the density sorter of Grounds 3a/3b-5a/5b" and "[t]his is not an application of hindsight." Pet. Reply 27–28 (citing Pet. 56–71; Ex. 1008 ¶¶ 102, 108–114, 135–149, 155–159; Ex. 1071 ¶¶ 46–55). We are not persuaded by Petitioner's reply argument for both procedural and substantive reasons.

Regarding procedure, we agree with Patent Owner (PO Sur-reply 19–20) that Petitioner's Reply improperly incorporates argument by referring to eight pages from Dr. Fair's second declaration (Exhibit 1071) into the page-and-a-half of the Reply that addresses Grounds 3–5. *Compare* Pet. Reply 27–28, *with* Ex. 1071 ¶¶ 46–55. *See* 37 C.F.R. § 42.6(a)(3) ("Arguments must not be incorporated by reference from one document into another document."). Paragraph 50 of Dr. Fair's second declaration discusses how and why droplets separate from a continuous phase, providing opinions that are not discussed in Petitioner's Reply. Paragraph 53 of Dr. Fair's second declaration discusses whether Ismagilov 119's microchannels can be used as a density sorting structure, again providing

opinions that are not discussed in Petitioner's Reply. Paragraph 54 of Dr. Fair's second declaration discusses why a POSA would have combined the relevant teachings of Ismagilov 119 and Pamula, again providing opinions that are not discussed in Petitioner's Reply. Paragraph 55 of Dr. Fair's second declaration discusses the impact of Patent Owner's proposed claim constructions on Dr. Fair's opinions concerning Grounds 3–5, again providing opinions that are not discussed in Petitioner's Reply. We do not consider these portions of Dr. Fair's second declaration that are not discussed in Petitioner's Reply.

We are also not persuaded by the substance of Petitioner's reply argument. Petitioner argues that a POSA would have known that "multiple droplets would be pooled in the vertical chamber." Pet. Reply 27 (citing Ismagilov 119 ¶ 123). As stated above and in the Institution Decision (Inst. Dec. 48), Petitioner directs us to no disclosure or suggestion, either in Ismagilov 091 or Ismagilov 119, that the density-based sorting mentioned in paragraph 123 takes place in a chamber or reservoir. Moreover, Ismagilov 091 suggests that sorting occurs in microchannels, not in a separation chamber. *See id.*; Ex. 1004, 17:10–13, 21:55–59. Petitioner does not address whether the density-based sorting mentioned in Ismagilov 119 paragraph 123 refers to sorting that occurs in microchannels.

We conclude that Petitioner has not shown that claims 1–4, 7–13, and 19–20 are unpatentable based on Ismagilov 119 alone.

4. Grounds 4 and 5: Ismagilov 119 and Pamula

Petitioner contends that a POSA would have combined Ismagilov 119's teaching of "density separation" with Pamula's description of "sorting droplets based on a difference in density between the droplets

and the carrier fluid." Pet. 60–61 (citing Ex. 1007 ¶ 418; Ex. 1018 ¶ 418; Ex. 1025, 8–9). More specifically, Petitioner contends that a "POSA would have been able to apply Pamula's teachings of a density separation chamber with an outlet (collection well) at the top to Ismagilov's system which itself already included the use of both outlet wells and density-based sorting of droplets from oil." Pet. 61; Ex. 1008 ¶ 156 (same).

We are not persuaded by Petitioner's unpatentability contentions based on Ismagilov 119 and Pamula for several reasons.

First, Petitioner has not shown a reason why a skilled artisan would have combined the teachings of Ismagilov 119 and Pamula absent the use of impermissible hindsight. In contrast to Ismagilov 119, which discloses that droplets "can be sorted by their density relative to that of the carrier fluid" (Ex. 1005 ¶ 123), Pamula does not disclose sorting droplets. Instead, Pamula discloses separating aqueous droplets from the filler phase, e.g., silicone oil, by allowing them to float or sink to a target destination. *See, e.g.*, Ex. 1007 ¶ 418. In view of these differences, Petitioner's combination appears to be motivated by impermissible hindsight, rather than reasoning that would have been employed by a POSA who had not seen claim 1 and the supporting disclosure of the '837 Patent. *In re Gorman*, 933 F.2d 982, 987 (Fed. Cir. 1991) ("It is impermissible . . . simply to engage in a hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps.").

Second, it is unclear whether Petitioner contends that a POSA would have used Pamula's vertical collection well: (1) as Ismagilov 119's density sorter or (2) as Ismagilov 119's outlet well. *See* Pet. 61; Ex. 1008 ¶ 156. Either way, Petitioner and Dr. Fair do not explain sufficiently how and why

a POSA would have combined Ismagilov 119's channel-based flow elements with Pamula's discrete-flow system and vertical collection well. *See Metalcraft of Mayville, Inc. v. Toro Co.*, 848 F. 3d 1358, 1367 (Fed. Cir. 2017) ("Without any explanation as to how or why the references would be combined to arrive at the claimed invention, we are left with only hindsight bias that *KSR* warns against.").

Third, Petitioner's contention that a POSA "***would have been able to*** apply Pamula's teachings . . . to Ismagilov's system" (Pet. 61; Ex. 1008 ¶ 156, emphasis added) is improperly "focused on what a skilled artisan would have been *able* to do, rather than what a skilled artisan would have been *motivated* to do at the time of the invention." *Polaris Indus., Inc. v. Arctic Cat, Inc.*, 882 F.3d 1056, 1068 (Fed. Cir. 2018).

The foregoing analysis for Grounds 4 and 5 is essentially the same as set forth in our Institution Decision. Inst. Dec. 49–50. Patent Owner agrees with our analysis. PO Resp. 60–61. In reply, Petitioner presents the arguments addressed above for Ground 3. In addition, Petitioner argues that "[i]f additional structural information is required for either density-based sorting, a POSA would have been motivated to look to Pamula for the structure of a device that operated based on the droplet/oil density difference, and nothing precludes using Pamula's waste and collection wells for droplets." Pet. Reply 28 (citing Pet. 29–30, 60–64; Ex. 1008 ¶¶ 113–114, 155–158). In our view, Petitioner's reply argument suffers from the same deficiencies discussed above.

We conclude that Petitioner has not shown that claims 1–4, 7–13, and 19–20 are unpatentable as obvious over Ismagilov 119 and Pamula.

III. CONCLUSION

In summary:[16]

Claims	35 U.S.C. §	Reference(s)	Claims Shown Unpatentable	Claims Not Shown Unpatentable
1, 2, 4, 10–13, 19, 20	102	Ismagilov 091	1, 2, 4, 10–13, 19, 20	
1, 2, 4, 7, 9–13, 19, 20	103	Ismagilov 091, Quake	1, 2, 4, 7, 9–13, 19, 20	
1–4, 7–13, 19, 20	103	Ismagilov 119		1–4, 7–13, 19, 20
1–4, 7–13, 19, 20	103	Ismagilov 119, Pamula 634		1–4, 7–13, 19, 20
1–4, 7–13, 19, 20	103	Ismagilov 119, Pamula 238		1–4, 7–13, 19, 20
Overall Outcome			1, 2, 4, 7, 9–13, 19, 20	3, 8

[16] Should Patent Owner wish to pursue amendment of the challenged claims in a reissue or reexamination proceeding subsequent to the issuance of this decision, we draw Patent Owner's attention to the April 2019 *Notice Regarding Options for Amendments by Patent Owner Through Reissue or Reexamination During a Pending AIA Trial Proceeding*, 84 Fed. Reg. 16,654 (Apr. 22, 2019). If Patent Owner chooses to file a reissue application or a request for reexamination of the challenged patent, we remind Patent Owner of its continuing obligation to notify the Board of any such related matters in updated mandatory notices. *See* 37 C.F.R. § 42.8(a)(3), (b)(2).

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that Petitioner has shown by a preponderance of the evidence that claims 1, 2, 4, 7, 9–13, 19, and 20 of the ’837 Patent are unpatentable;

FURTHER ORDERED that Petitioner has not shown by a preponderance of the evidence that claims 3 and 8 of the ’837 Patent are unpatentable; and

FURTHER ORDERED that because this Decision is final, a party 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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