

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

10X GENOMICS, INC.
Petitioner,

v.

BIO-RAD LABORATORIES, INC.
Patent Owner

Case IPR2020-00086
U.S. Patent No. 9,562,837

PATENT OWNER RESPONSE

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I. INTRODUCTION

Pursuant to 35 U.S.C. § 316, Patent Owner Bio-Rad Laboratories, Inc. (“Patent Owner”) respectfully submits this Response to the Petition for Inter Partes Review, IPR2020-00086 (Paper No. 2) (“the 086 Petition”) filed by Petitioner 10X Genomics, Inc. (“Petitioner”). The 086 Petition seeks *Inter Partes* Review (“IPR”) of claims 1-4, 7-13, and 19-20 of U.S. Patent No. 9,562,837 (“the ‘837 patent”) and includes five grounds¹: (1) alleged anticipation based on U.S. Patent No. 7,129,091 to Ismagilov et al. (“Ismagilov”) (Ex. 1004); (2) alleged obviousness based on Ismagilov and U.S. Published Application 2002/0058332 to Quake et al. (“Quake”) (Ex. 1006); (3) alleged obviousness based on U.S. Published Application 2006/0094119 to Ismagilov et al. (“Ismagilov 119”) (Ex. 1005); (4) alleged obviousness based on Ismagilov 119 and U.S. Published Application 2007/0243634 to Pamula et al. (“Pamula 634”); and (5) alleged obviousness based on Ismagilov 119 and U.S. Published Application 2015/0148238 to Pamula et al. (“Pamula 238”) (Ex. 1008). With respect to Grounds 3-5, the Board found that “Petitioner has not shown a reasonable likelihood of prevailing.” Patent Owner respectfully submits that on a complete record the Board should also find that the

¹ Petitioner does not challenge claims 3, and 7-9 in Ground 1, and does not challenge claims 3 and 8 in Ground 2.

Challenged Claims of the '837 patent are novel and non-obvious over Grounds 1 and 2.

First, Grounds 1 and 2 of the 086 Petition are based entirely on the false premise that, because the 10X Accused Device in the parallel Delaware Litigation infringes the '837 patent, all structures with an outlet opening that ever existed in the prior art anticipate and/or render obvious the Challenged Claims. That is incorrect. Just because certain structures in the 10X Accused Device constitute “separation chambers” within the meaning of the '837 patent does not mean that any and all structures with an opening from the prior art necessarily meet that definition as well. For example, the ports and outlets allegedly disclosed in Ismagilov are not “separation chambers.” To the extent the minimal disclosure of these particular elements of the devices in Ismagilov discloses an open structure at all, Ismagilov indicates they would have been fabricated by “punching” holes in the microchip itself at the channel ends, as was standard practice at the time. These structures with a “hole punched” opening would have been well known in the art during prosecution of the '837 patent and are very different than the “separation chambers” claimed in the '837 patent and found in the 10X Accused Device. The “separation chambers” of the '837 patent and 10X Accused Device are structures that sit atop the standard “hole punches” of the prior art, including those hole

punches that are alluded to but not ever actually shown or described in any detail in Ismagilov.

Second, Ismagilov does not disclose a “separation chamber” under the proper construction of that term, and by extension also does not disclose any of the limitations of the Challenged Claims of the ‘837 patent related to the “separation chamber.” Ismagilov does not disclose any intended functionality for the outlet of its device, besides general references to “collect[ing] or dispens[ing]” fluid none of which are sufficient to disclose a “separation chamber.” Ismagilov’s minimal, generic description of outlets simply does not contain any disclosure of a structure capable of accumulating fluid at the outlet of the device in order to separate multiple droplets from an immiscible fluid.

It is also undisputed that Ismagilov never expressly discloses separation of the droplets from an immiscible fluid. Ismagilov’s failure to teach anything about separating droplets from an immiscible fluid also substantiates that the reference in no way teaches any of the characteristics of the claimed separation chamber that are necessary to perform separation in a device like that claimed. Given the complete lack of any teaching regarding separation, Petitioner relies solely on the concept of inherency, which requires a very high standard of proof, to show invalidity. As explained in detail below, however, emulsion droplets do not

necessarily separate from surrounding immiscible fluid (typically oil) in the embodiments Ismagilov describes.

Petitioner has cobbled together a series of assumptions, nowhere explicitly disclosed in Ismagilov, and used those assumptions to arrive at the invention using hindsight. Those assumptions include, with no actual disclosure, that there is an outlet well in Ismagilov, though the patent specifically steers away from describing an outlet well. The assumptions also include claims about the size and shape of the outlet well that are nowhere described in Ismagilov. Last, the assumptions also include properties of the fluids, that are not described, which would always and necessarily lead to droplets separating from the immiscible fluid. This series of assumptions built on assumptions are not consistent with the law of inherency and Ismagilov, therefore, is not an anticipatory reference. *See Par Pharm., Inc. v. TWI Pharm., Inc.*, 773 F.3d 1186, 1195 (Fed. Cir. 2014) (“Inherency ... may not be established by probabilities or possibilities.”) .

Ismagilov also cannot anticipate the “droplet receiving outlet” limitations of the Challenged Claims. Under the proper construction of this term, a “droplet receiving outlet” is the “portion of the separation chamber where droplets are collected.” If droplets cannot be collected from a particular location, then that location cannot not be considered a “droplet receiving outlet.” Petitioner’s argument concerning the structures allegedly disclosed in Ismagilov ignores that

the standard hole punches described in Ismagilov would not necessarily always be large enough to use a micropipette in the way that Petitioner asserts. Indeed, as Dr. Fair explained in his deposition, the smallest available micropipettes are 1mm, which is far too large to fit into the much smaller holes that would have been created by the hole punching method disclosed in Ismagilov. Moreover, despite Petitioner's repeated arguments that a person of ordinary skill ("POSA") would necessarily use a pipette to collect droplets from "outlet wells" that are nowhere mentioned or actually described in Ismagilov and that Petitioner assumes could be there, Dr. Fair testified in no uncertain terms that, in his over 25 years of experience with microfluidic chips, he has never performed such a collection. (Ex. 2017 at 43:9-12 ("Q. When is the first time you used a pipette to remove a droplet from a chip and move it off chip? A. I don't think I've done that.")).

Finally, a POSA would not have been motivated to combine the various disclosures cited by Petitioner in Ismagilov with those in Quake. As Petitioner's expert Dr. Fair readily admitted, the devices disclosed in these two references are directed to very different use cases, and a POSA would not assume that the well structures used to hold samples in a specific sorting embodiment in Quake, where no droplets are even being formed, would be well structures, or obvious modifications, that would be used for the droplet generation devices disclosed in Ismagilov. Indeed, a POSA would understand that to accomplish the intended use

of Ismagilov, well structures of the type disclosed in Quake would be detrimental, not useful.

For all of these reasons, as explained in more detail below, the Board should find the Challenged Claims of the ‘837 patent novel and non-obvious.

II. BACKGROUND

A. The ‘837 Patent

The ‘837 patent is entitled “Systems for Handling Microfluidic Droplets” and issued on February 7, 2017. The ‘837 patent was filed on April 2, 2013, and claims priority to several provisional applications, the earliest of which (Provisional Application Nos. 60/799,833 and 60/799,834) were filed on May 11, 2006.²

The ‘837 patent is directed generally to systems and methods for forming, separating and collecting emulsion droplets. (Ex. 2016 at ¶22). The ‘837 patent explains that claimed assemblies offer an improvement over the prior art by minimizing operator handling and exposure of the sample to possible contamination. (Ex. 1001 at 2:35-39 (“The invention provides systems and methods that are designed to minimize sample contact and exposure of the sample to the surrounding environment, thereby minimizing or eliminating the

² As the Board noted in its Decision, Patent Owner is not attempting to swear behind the asserted prior art references for purposes of this proceeding, and therefore the issue of whether or not the AIA applies to the ‘837 patent is moot.

introduction of contaminants into an amplification reaction.”); *see also* Ex. 2016 at ¶24). The way that it does this is by creating droplets that act as reaction chambers. Once the droplets are formed that contain the reactants, those reactants are isolated from the outside world. (*Id.* at ¶23-28).

The ‘837 patent has 1 independent claims and 19 dependent claims.

Independent claim 1 recites:

1. An assembly, the assembly comprising:

a microchannel in a horizontal plane;

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

at least one downstream separation chamber comprising a droplet receiving chamber inlet and at least one droplet receiving outlet, wherein the separation chamber is upright to the microchannel and out of the horizontal plane;

wherein the droplet formation module and the separation chamber are in fluid communication with each other via the microchannel; 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 is of a volume sufficient to separate the plurality of droplets comprising the sample from the immiscible fluid within the separation chamber.

As recited in claim 1, the ‘837 patent covers systems for generating sample-containing droplets, or emulsions, through the use of “a microchannel in a

horizontal plane” with “at least one droplet formation module.” (Ex. 2016 at ¶30).

Emulsions are formed when the instrument drives fluids through the microchannel into a droplet formation module that contains both a “sample inlet” and an “immiscible fluid inlet” to a “junction” that creates droplets comprising the sample fluid surrounded by the immiscible fluid. (*Id.*). The patent further teaches the use of a novel “separation chamber” that is “out of the horizontal plane” of the microchannel and has a wider cross-section than the microchannel cross-section. (*Id.*). The “separation chamber” is designed to be of a volume “sufficient to separate the plurality of droplets comprising the sample from the immiscible fluid.” (*Id.*).

B. Ismagilov

Ismagilov is titled “Device and Methods for Pressure-Driven Plug Transport and Reaction.” (Ex. 1004). The Abstract teaches that the invention disclosed “provides microfabricated substrates and methods of conducting reactions within these substrates.” (*Id.*; *see also* Ex. 2016 at ¶32). As the 45 figures (many of which include sub-figures) in Ismagilov make clear, the focus of the invention and the description of the same in the specification is on the configuration of channels within the substrate in order to prepare droplets or plugs, and conduct the reactions being described. (*Id.* at ¶33). What is not disclosed in any detail, including in the 45+ figures, is the configuration, structure, or design of the outlet in any of the

devices. (*Id.* at ¶34). The off-hand references to “outlet ports” or “wells or reservoirs” relied upon by Petitioner relies on do not disclose any new design or configuration, such as the claimed separation chamber, but are merely referencing commonly known elements of microfluidic devices from the time of the disclosed invention in the early 2000’s, as evidenced by the reference to the use of cork borers or syringe needles to cut holes into the PDMS when preparing the devices. (Ex. 1004 at 9:5-8, 14:36-40, 16:35-36, 17:18-30; *see also* Ex. 2016 at ¶35). Indeed, a POSA would understand that to the extent Ismagilov provided any description of the outlets that were employed in the devices, the reference was merely describing standard off-the-shelf techniques for having droplets flow out of the device that were already well known in the art and distinct from the separation on the device that is the focus of the ‘837 patent. (Ex. 2016 at ¶36).

C. Quake

Quake discloses “a chip with an inlet channel and reservoir, a detection region a branch point, and two outlet channels and reservoirs.” (Ex. 1006). Quake further discloses that the apparatus embodying this configuration “is mounted on an inverted microscope for optical detection” and that “[e]lectrodes are used to direct virions or cells in response to the microscope detection.” (*Id.* at ¶ 31, Fig. 8). As Dr. Fair admitted, “Quake did not use droplets, he injected dye, which then he sorted based upon red or green. ***And this is not a droplet-based system.***” (Ex.

2017 at 141:12-142:2). This is consistent with the described use case of the device shown Figures 6 and 8 in Quake, which makes clear that the device was used to conduct “Sorting Experiments” where “[t]hree platinum electrodes were each inserted into separate wells” and then the device “was used to sort fluorescent beads of different emission wavelengths in different ratios up to 33,000 beads per hour.” (Ex. 1006 at ¶¶ 192-214; Ex. 2016 at ¶40).

III. LEGAL STANDARDS

A. Claim Construction

In an IPR, claims are to be “construed using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. 282(b), including construing the claim in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent.” *See* 37 C.F.R. § 42.100(b).

B. Anticipation

“A determination that a patent is invalid as being anticipated under 35 U.S.C. § 102 requires a finding that each and every limitation is found either expressly or inherently in a single prior art reference. *Transclean Corp. v. Bridgewood Servs., Inc.*, 290 F.3d 1364, 1370 (Fed. Cir. 2002). “Inherency ... may not be established by probabilities or possibilities.” *Par*, 773 F.3d at 1195. “The mere fact that a certain thing may result from a given set of circumstances is not sufficient.” *Id.*

“To serve as an anticipating reference, the reference must enable that which it is asserted to anticipate.” *Elan Pharmaceuticals, Inc. v. Mayo Foundation*, 346 F.3d 1051, 1054 (Fed. Cir. 2003). “A claimed invention cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled.” *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354 (Fed. Cir. 2003). Enablement requires that “the prior art reference must teach one of ordinary skill in the art to make or carry out the claimed invention without undue experimentation.” *Minnesota Mining and Manufacturing Co. v. Chemque, Inc.*, 303 F.3d 1294, 1301 (Fed. Cir. 2002). Further, the Federal Circuit has explained that determination of whether the requisite amount of experimentation is undue may include consideration of the so-called “*Wands* factors”: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.” *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

C. Obviousness

“An analysis of obviousness must be based on several factual inquiries: (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the art at the time the invention

was made; and (4) objective evidence of nonobviousness, if any.” *Leo Pharm.*

Prods. v. Rea, 726 F.3d 1346, 1353 (Fed. Cir. 2013) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966)). Further, “there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *KSR, Int’l. Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007). Moreover, the patent challenger must demonstrate a “reasonable expectation of success” of combining the prior art references to achieve the claimed invention. *Id.*

“Though less common, in appropriate circumstances, a patent can be obvious in light of a single prior art reference if it would have been obvious to modify that reference to arrive at the patented invention.” *Arendi S.A.R.L. v. Apple Inc.*, 832 F.3d 1355, 1361 (Fed. Cir. 2016).

In evaluating prior art, a POSA must avoid the trap of hindsight. *See KSR*, 550 U.S. at 421 (“A factfinder should be aware . . . of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning.”). “Even an obvious solution . . . does not render an invention obvious if the problem solved was previously unknown.” *Novartis Pharmaceuticals Corp. v. Watson Laboratories, Inc.*, 611 Fed. Appx. 988, 995 (Fed. Cir. 2015); *see also Mintz v. Dietz & Watson, Inc.*, 679 F.3d 1372, 1377 (Fed. Cir. 2012) (“Often the inventive contribution lies in defining the problem in a new revelatory way.”); *Leo*, 726 F.3d at 1356–57 (finding that the claimed invention would not have been obvious to try

to persons of ordinary skill in the art “because they would not have recognized the problem”). Further, a reference that teaches away cannot serve as a basis for obviousness. *See, e.g., In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994). “A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant.” *Id.*

Finally, “evidence rising out of so-called ‘secondary considerations’ when present must always be considered en route to a determination of obviousness.” *Stratoflex v. Aeroquip Corp.*, 713 F.2d 1530, 1538 (Fed. Cir. 1983). “The objective considerations, when considered with the balance of the obviousness evidence in the record, guard as a check against hindsight bias.” *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1079 (Fed. Cir. 2012).

IV. STATE OF THE ART

Microfluidics is the study of the behavior and flow of liquids inside micrometer-sized channels or other structures. (Ex. 2016 at ¶58-61). It has practical application in a number of fields, in particular, biotechnology where biomedical applications are increasingly relying on high throughput assays of small amounts of sample material and reagents. (*Id.* at ¶58). For example, high

throughput genetic tests may combine a small amount of genetic or other biological material with reagents to provide high-quality information about samples for drug discovery, biomarker discovery, and clinical diagnostics, among other things. (*Id.* at ¶58-59).

Emulsions have helped to revolutionize the field of high throughput assays. (*Id.* at ¶60). Emulsification can create tens to hundreds of thousands of aqueous droplets formed when a water based substance (such as a biological sample) becomes surrounded by a hydrophobic substance (such as oil). (*Id.*). Each tiny droplet formed through emulsification has the ability to act as a separate, miniature test tube in which biological reactions may occur. (*Id.*).

A microfluidic “chip” or “plate” can contain a set of micro-reservoirs and channels formed into a material (typically, glass, silicon or a polymer such as polydimethylsiloxane (“PDMS”)) and connected together according to the needs of the particular assay or other biomedical application. (*Id.* at ¶61). The chip or plate can be small and held in one hand. (*Id.*). Due to its ability to precisely and accurately control the movement of small amounts of fluid, however, a “chip” is capable of integrating several laboratory functions into a very small space. (*Id.*).

The technology at issue here involves microfluidic chips with a “separation chamber” that facilitates the collection and transfer of droplets for further “off chip” processing. (*Id.* at ¶62). By substantially separating the droplets from the

immiscible carrier fluid and directing them to a desired location, the novel chips of the '837 patent make collection of the droplets much easier to avoid contamination that can corrupt further downstream processing. (*Id.*).

During the timeframe prior to May 11, 2007, microfluidics researchers were largely focused on two major aspects of on-chip emulsification: (i) best methods of formation of uniformly-sized droplets of a desired size, frequency, and number; and (ii) using droplets as in-line reactors in which samples and reagents could be visualized. (*Id.* at ¶63). The collection of droplets after formation for further processing or analysis was not a common focus, and the separation of droplets from the surrounding oil fluid was also not widely reported or considered. (*Id.*).

Although emulsification outside microfluidic devices has been well studied for decades, emulsification in microfluidic devices did not gain popularity until the early 2000's when several academic research groups developed methods for forming uniform droplets in microfluidic chips. (*Id.* at ¶64). Thorsen presented a method using two channels oriented perpendicular to one another to shear off droplets of one immiscible liquid into a surrounding liquid. (*Id.* at ¶64, Ex. 1003, Chapter 3). Anna, Bontoux and Stone presented a different method for breaking off droplets using a "flow focusing" method that draws a narrow jet of one immiscible liquid into an accelerating stream of a surrounding liquid. (*Id.*, Ex. 2031). Other methods of droplet formation were also presented in the literature around that time,

and many were summarized in a review article that was published shortly after the stated priority date (*Id.*, Ex. 2029).

In many of the examples of microfluidic droplet formation in that time period, microfluidic devices were fabricated using a standard rapid prototyping method called soft lithography. (Ex. 2016 at ¶65, Ex. 2039). This involved creating a raised stamp from a two dimensional design of interconnected channels that were typically tens of micrometers in width and millimeters to centimeters in length. (*Id.*). Channels of rectangular cross-section were created with a depth determined by the depth of the stamp or mold, and this depth could be a few to tens of micrometers. (*Id.*).

PDMS and other elastomers used for soft lithography typically created hydrophobic surfaces, which promoted the formation of aqueous droplets surrounded by an immiscible oil. (*Id.* at ¶66). In order to generate flow in microfluidic devices, fluid needed to be introduced via an external pumping mechanism, and fluid also needed to be able to exit the channels. (*Id.* at ¶67). This is necessary because of the basic physical principle of conservation of mass: in a channel with a single inlet and a single outlet, what goes in must come out. (*Id.*).

To 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 ¶68, Ex. 2033). These holes were commonly punched

using sharpened syringe needles. (*Id.*). This was sufficient to press fit a piece of flexible tubing into the punched hole, allowing for fluid to be directed into the channel at the entrance, or diverted away from the channel at the exit. (*Id.*).

In addition to forming droplets and characterizing their size and formation frequency, researchers were also using droplets at that time as on-chip vessels for generating and monitoring reactions. (*Id.* at ¶69). It was common to use long segments of microchannels to generate many sequential droplets and observe reactions within them as they travel along the length of the channel. (*Id.*).

Examples of this type of application are described in a review article published in 2006 (*Id.*, Ex. 2035). However, in the time period prior to the priority date of the patent there was not a focus on collecting and separating droplets formed in microfluidic devices. (Ex. 2016 at ¶70). Instead, most droplet microfluidic applications focused on in-line production and manipulation of droplets, without considering removal of the droplets from the chip. (*Id.* at ¶71).

V. PERSON OF ORDINARY SKILL IN THE ART

A POSA at the time of the '837 patent 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. Additional training or study could substitute for work

experience and additional work experience or training could substitute for formal education. (Ex. 2016 at ¶72-74).

VI. CLAIM CONSTRUCTION

In its Decision, the Board adopted preliminary claim constructions for the terms “separation chamber” and “droplet receiving outlet” found in independent claim 1. Patent Owner discusses below its positions with respect to these terms, as well as the additional term “coupled.”³

A. “separation chamber” (all Challenged Claims)

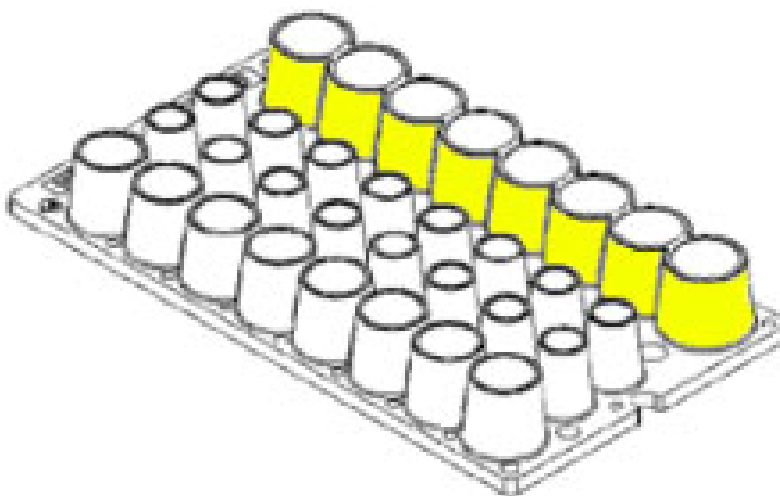
In the parallel district court litigation, Patent Owner proposed that the claim term “separation chamber” should be construed as a “chamber sized to accommodate multiple droplets and an immiscible fluid in separated form.” (Ex. 2032). Petitioner’s proposal adopted by the Board for purposes of its Institution Decision is not actually a formal construction for “separation chamber,” but rather an argument that “Bio-Rad’s interpretation of this term must be broad enough to include an open well.” (Pet. at 19, 35-37). The Board should adopt Patent Owner’s construction of “separation chamber” and reject Petitioner’s “open well” argument to the extent that it would turn all open structures into separation chambers. While

³ In the parallel district court action, Patent Owner has provided proposed constructions for “sample,” and “polymerase chain reaction(PCR)” and disputes Petitioner’s proposed constructions of those terms. (Ex. 2032). However, Patent Owner agrees with the Board that for purposes of the Board’s final decision those terms do not require express construction in these proceedings.

a separation chamber can cover an open structure, it does not follow then that all open structures are separation chambers as Petitions would have it. The Board should also affirm its rejection of the alternative construction offered by Petitioner of “a space that is substantially enclosed.”

First, the Board should adopt Patent Owner’s proposed construction of “separation chamber” because it is fully supported by the ‘837 claims and specification. (*See, e.g.*, Ex. 1001 at 88:18-23; 2:45-50, 3:37-58, 53:21-41; Ex. 2016 at ¶¶75-81). It is also fully supported by the prosecution history where the Applicants stated numerous times that their claimed separation chamber distinguished over the prior art because it was sized to allow multiple droplets to separate from the immiscible fluid. (*See, e.g.*, Ex. 1002 at 1114 (“Lee’s conduit differs from the claimed chamber because Lee’s conduit accommodates only one droplet across its width at a time. In contrast, 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.”); *id.* at 1168-69 (“Lee’s cross-intersection is different from the separation chamber in amended claim 1 because Lee’s cross-intersection is not a vertical chamber to separate droplets from an immiscible fluid carrier fluid. Nor does Lee’s cross-intersection . . . accumulate droplets in an immiscible fluid or have a specific volume to separate droplets from an immiscible fluid.”); Ex. 2016 at ¶¶ 82-83).

Second, although Petitioner does not explicitly say so, the implication from Petitioner’s “open well” argument is that Bio-Rad’s interpretation of “separation chamber” is so broad that it must include **all** open structures. (Ex. 2016 at ¶¶84-85). Specifically, Petitioner references Patent Owner’s Infringement Contentions from the Delaware Litigation where Patent Owner asserts that the open-top chamber from the 10X Accused Device infringes the ‘837 patent. (Pet. at 35-37 (citing Ex. 1026)). For ease of reference, the image of the 10X Accused Device from Patent Owner’s Infringement Contentions is shown below, with the chambers highlighted in yellow.



(Ex. 1026 at 1 (annotated)).

According to Petitioner, if the yellow chamber in the 10X Accused Device shown above is a “separation chamber” within the meaning of the ‘837 patent, then the term “separation chamber” must include any and all open structures. (Pet. at

35). This argument does not follow. The open top chambers in the 10X Accused Device meet the requirements of a “separation chamber” because they are “chambers sized to accommodate multiple droplets and an immiscible fluid in separated form.” While some open structure” (like those of the structures found on the 10X Accused Device) may satisfy that limitation, others (like those Petitioner assumes are present in Ismagilov but which are not described or shown anywhere, and those shown in Figure 6 of Quake which are found in devices that are not used to form droplets) will not under the proper construction of the term. (Ex. 2016 at ¶¶84-87). This is discussed in more detail in Section VII(A) below.

Finally, the Board should affirm its rejection of Petitioner’s alternative construction for “separation chamber” requiring “a space that is substantially enclosed.” (*See* Pet. at 19, 21-22). As the Board correctly found, Petitioner’s alternative construction would exclude the host of examples provided in the specification, which describe suitable containers that may act as a separation chamber when that term is properly construed, in favor of a description of a preferred embodiment that itself does not limit the scope of the term “chamber.” (Dec. at 11 (citing Ex. 1001, 53:35-38); Ex. 2016 at ¶¶88-96). Moreover, as the Board also found, claim 1 must be broader than claims 7 and 8, and 10X’s limiting construction of “separation chamber” would be inconsistent with the added

limitation in these claims requiring that the separation chamber be sealably coupled to a vessel. *Id.* at 12.

B. “droplet receiving outlet” (all Challenged Claims)

In the parallel district court litigation, Bio-Rad proposed that the claim term “droplet receiving outlet” should be construed as a “portion of the separation chamber where droplets are collected.” (Ex. 2032). Petitioner argues that “Bio-Rad’s interpretation of this term must be broad enough to include the opening at the top of an open well.” (Pet. at 18, 35-37). Petitioner is wrong, and the Board should adopt Patent Owner’s construction of “droplet receiving outlet,” reject Petitioner’s “open well” argument, and further affirm its prior rejection of Petitioner’s alternative proposals for the construction of this term.

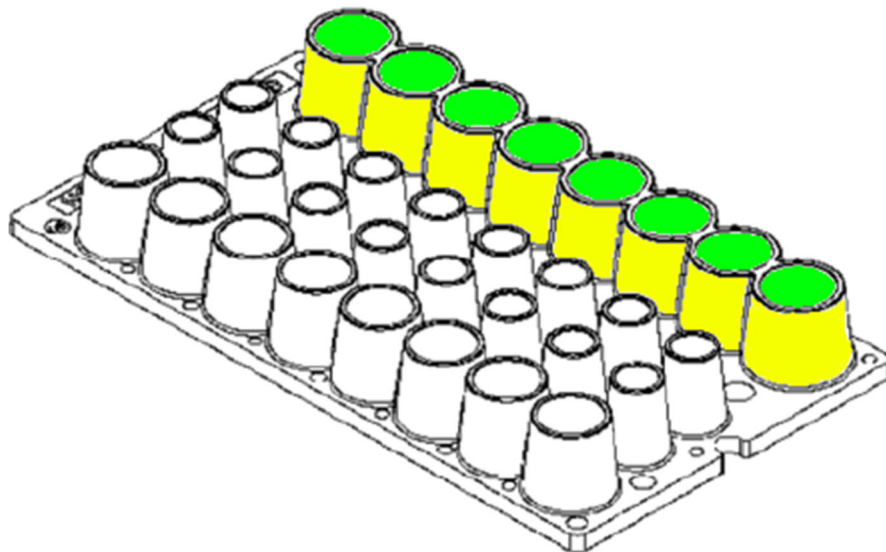
First, Bio-Rad’s proposed construction of “droplet receiving outlet” is supported by the ‘837 specification. For example, the ‘837 specification explains that the “droplet receiving outlet” is part of the separation chamber. (Ex. 1001 at 3:48-51 (“The outlet may be positioned at any place in the chamber and it is positioned based upon the densities of the partitioned portions and the immiscible fluid.”); Ex. 2016 at ¶¶97-100). The ‘837 specification also discusses specific locations of the “droplet receiving outlet” within the chamber. For example, the ‘837 specification explains that when the droplets are less dense than the immiscible fluid, they rise, and the “droplet receiving outlet” may be located at the

top of the separation chamber. (*Id.* at 3:51-58 (“[I]n certain embodiments, [the outlet] is positioned in a top portion of the chamber. In this embodiment, the partitioned portions and immiscible fluid flow into the chamber. The immiscible fluid is of a greater density than the partitioned portions and the partitioned portions rise in the chamber while the immiscible fluid sinks. The partitioned portions then flow into the outlet.”); *id.* at 4:12-13 (“Accordingly, an outlet for collecting the displaced droplets can be positioned at the top of the chamber.”)). When the droplets are more dense than the immiscible fluid, they fall, and the “droplet receiving outlet” may be located at the bottom of the chamber. (*Id.* at 4:12-16 (“In another example, aqueous droplets placed in a chamber of certain mineral oils will tend to sink due to their greater density. Accordingly, an outlet for collecting the displaced droplets can be positioned at the bottom of the chamber.”)). The ‘837 specification also explains that the “droplet receiving outlet” may be placed in between the top and bottom of the chamber. (*Id.* at 3:51-58 (“The outlet may be at the top, middle, or bottom of the chamber”)).

Further, the ‘837 specification explains that, wherever located, the “droplet receiving outlet” is the place in the separation chamber where droplets are collected while oil is left behind. *Id.* at 3:46-48 (“The chamber includes an outlet that is positioned to receive substantially only the partitioned portions of sample.”);

id. at 53:28-29 (“The outlet can be positioned accordingly to collect the droplets.”);
id. at 54:41-44).

Second, as with its “open well” argument in the context of “separation chamber,” Petitioner is wrong that Patent Owner’s interpretation of “droplet receiving outlet” is so broad that it includes **any and all openings at the top of any and all open wells**. (Ex. 2016 at ¶101). Again, Petitioner’s argument is based solely on Patent Owner’s Infringement Contentions from the Delaware Litigation where Patent Owner asserts that the open tops of the chambers that sit atop the 10X Accused Device are “droplet receiving outlets.” (Pet. at 35). For ease of reference, the image of the 10X Accused Device from Patent Owner’s Infringement Contentions is shown below, with the chambers highlighted in yellow and the open tops highlighted in green.



According to Petitioner, if the green open top in the 10X Accused Device shown above is a “droplet receiving outlet” within the meaning of the ‘837 patent, then the term “droplet receiving outlet” must include any and all open tops of any and all “open wells.” (Pet at 35). Again, this argument does not follow. The open tops of the chambers in the 10X Accused Device are “droplet receiving outlets” because they are the “portion of a separation chamber where droplets are collected” and oil is left behind. While some openings at the top of some open wells (like those of the structures found on the 10X Accused Device) may satisfy a “droplet receiving outlet,” others will not. (Ex. 2016 at ¶¶101-104). This is discussed in more detail in Section VII(A) below.

Finally, the Board should affirm its rejection of Petitioner’s multiple alternative constructions for “droplet receiving outlet.” (*See* Pet. At 19, 21-22). The Board correctly held that that “droplet receiving outlet” conveys sufficiently definite structure in which the droplets are collected inside the separation chamber, not the function of retrieving (or “receiving”) the droplets from the separation chamber at Petitioner contended. (Dec. at 13-14; Ex. 2016 at ¶¶105-108). Furthermore, the Board correctly rejected Petitioner’s second alternative construction requiring that “substantially only droplets” exit the chamber through the outlet because it is inconsistent with the specification and dependent claim 10 of the ‘837 patent. (*Id.* at 14-15).

C. “coupled” (dependent claims 7 and 8)

In the parallel district court litigation, Bio-Rad proposed that the claim term “coupled” should be construed as a “operably linked.” (Ex. 2032). Petitioner argues that “Bio-Rad’s interpretation of this term must be broad enough to include the use of a pipette to move droplets from an outlet to a vessel.” (Pet. at 19, 47-48). The Board should adopt Patent Owner’s construction of “coupled” and reject Petitioner’s “pipette” argument as well as affirm its prior rejection of 10X’s alternative construction that “coupled” means “fastened or jointed.”

First, Patent Owner’s proposed construction of “coupled” is supported by the intrinsic evidence. (Ex 2016 at ¶¶109-112). The term arises in two dependent claims where one states that the droplet receiving outlet of the separation chamber is coupled to a vessel (claim 7) and the other says it is sealably coupled to the vessel (claim 8). The “coupling” between the droplet receiving outlet and the vessel is to effectuate transfer of droplets from the separation chamber to the vessel. (*See, e.g.*, Ex. 1001 at 4:17-36). One method of doing this is to connect a slide sloping downward from the top of the separation chamber, where the droplet outlet is, to a “second location,” which could be a vessel. Droplets flow downward to the vessel, which can be any vessel known in the art, such as PCR tubes, test tubes, vials, Eppendorf tubes, and the like. (*Id.* at 4:17-29). The inventors considered this slide example to illustrate a vessel coupled to the outlet even

though there was no physical or mechanical connection between them. The inventors offered another example of the vessel being coupled to an outlet without the slide to facilitate droplet collection. (*Id.* at 4:27-29).

Second, Bio-Rad’s proposed construction of “coupled” is also consistent with the extrinsic evidence, in particular, the conventional use of the term. *See Johnson Worldwide Assocs., Inc. v. Zebco Corp.*, 175 F.3d 985, 992 (Fed. Cir. 1999) (construing “coupling” broadly and noting that the general term is “not limited to a mechanical or physical coupling”); *Oceaneering Int’l, Inc. v. Trendsetter Eng’g, Inc.*, No. 16-2797, 2016 WL 7388390, at *7 (S.D. Tex. Dec. 20, 2016) (declining to construe the common term “coupled to” and noting that the term may refer to direct or indirect coupling, and rejecting the proposed construction “directly joined”).

Third, as with its “open well” argument in the context of “separation chamber” and “droplet receiving outlet,” Petitioner is wrong that Patent Owner’s interpretation of “coupled” is so broad that it must include **all** uses of a pipette to facilitate movement of liquid off of a chip through an outlet to a vessel. While the transfer of droplets from a “droplet receiving outlet” through the use of a pipette in a manner that would leave oil behind in the chamber (as in the 10X Accused Device) may constitute “coupling,” other transfers, such as the reference to the use of a “micropipette” in Ismagilov, will not.

Finally, the Board should reject Petitioner’s alternative proposed construction requiring that “coupled” mean “fastened or joined.” (Pet. at 19, 22-23). Petitioner’s construction implies a physical or mechanical connection narrower than the conventional use of the term “coupled” referenced above. Moreover, Petitioner’s proposed construction would read out certain embodiments of the invention in favor of others. Petitioner’s reference to an embodiment in which the outlet is “sealably coupled” ignores other examples described in the specification where the distal end can have an output nozzle 807 that “may lead to a vessel or container for collecting the droplets, for example, a PCR tube or a test tube.” (Ex. 1001 at 54:57-59). In that embodiment, the distal end is not described as connected to the vessel and thus the vessel would not be connected to the outlet of the separation chamber, only coupled to it.

VII. ARGUMENT

Petitioner has failed to show that claims 1-2, 4, 10-13, and 19-20 are allegedly anticipated by Ismagilov (Ground 1) or alternatively that claims 1-2, 4, 7, 9-13, and 19-20 are obvious in view of Ismagilov when combined with Quake (Ground 2). The Board also correctly found in the Institution Decision that Petitioner failed to demonstrate claims 1-4, 7-13, and 19-20 are obvious in view of

Ismagilov 119, either alone (Ground 3), or in combination with either Pamula 634 (Ground 4) or Pamula 238 (Ground 5).

A. Ground 1: Ismagilov Anticipation

In Ground 1, Petitioner alleges that claims 1-2, 4, 10-13 and 19-20 are anticipated by Ismagilov. As explained in detail below, Ismagilov is missing critical elements of the Challenged Claims.

1. “at least one downstream separation chamber comprising a droplet receiving inlet and at least one droplet receiving outlet”

Petitioner misinterprets and conflates several separate disclosures in Ismagilov that discuss “ports” and “outlets,” and further applies improperly broad constructions of the terms “separation chamber” and “droplet receiving outlet” in order to stretch the description of the device in Ismagilov to teach the claimed “separation chamber comprising a droplet receiving inlet and at least one droplet receiving outlet.” (Ex. 2016 at ¶¶115-117). 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.” *See Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008) (“[T]he prior art reference—in order to anticipate under 35 U.S.C. § 102—must

not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements ‘arranged as in the claim.’”)

Petitioner argues that the “outlet port . . . that *collects* or dispenses the plug fluid” teaches a separation chamber. (Pet. at 36 (citing Ex. 1004 at 9:5-8) (emphasis in original)). Absent from this disclosure in Ismagilov is any description of a “well or reservoir” as part of the “collection” process at the outlet port. (Ex. 2016 at ¶118). In the same section of the specification, Ismagilov separately explains that the “*inlet port* may contain an inlet channel, *a well or reservoir*, an opening, and other features *that facilitate the entry of chemicals into the substrate*.” (Ex. 1004 at 8:41-44, Ex. 2016 at ¶119). A POSA reading these definitional descriptions of the inlet and outlet ports of the device in Ismagilov would not assume that fluids were being accumulated in a well or reservoir at the outlet port, or that a well or reservoir would even exist at the outlet port of the device. (Ex. 2016 at ¶120). To the contrary, given the separate disclosure of wells or reservoirs facilitating the introduction of fluids at the inlet port, had the named inventors of the Ismagilov patent intended to explain that a “well or reservoir” would facilitate the accumulation of fluids at the outlet port they clearly would have been able to do so. (*Id.* at ¶121). The absence of wells and reservoirs from the definition of outlet port, when they are included in the definition of an inlet port

just a few paragraphs earlier, indicates to a POSA that they are not part of the outlet port. *Id.*

Petitioner attempts to overcome this deficiency in the definition of the “outlet port” by pointing to a separate disclosure in Ismagilov describing that the outlet port “may also communicate with a well or reservoir.” (Pet. 36 (citing Ex. 1004 at 14:36-38)). However, this separate disclosure does not teach that the “well or reservoir”—which *may* be in communication with an outlet port—is functioning as a separation chamber at the outlet of the device. (Ex. 2016 at ¶122). Nor does this section of the specification, or any other portion of the specification, provide a description of the structure, function, or operation of any wells or reservoirs that may communicate with an outlet port. (*Id.* at 123). Furthermore, like the definitions of inlet and outlet ports discussed above, this paragraph in the specification includes additional functional description of the inlet port, but not the outlet port. (Ex. 1004 at 14:41-42 (“Fluid can be **introduced** into the channels **via the inlet** by any means.”)). A POSA reading this disclosure would therefore understand there to be a specific intended operation for introducing fluids at the **inlet** well or reservoir, but no similar intended function at the **outlet**, as Petitioner contends. (Ex. 2016 at ¶124-125). And again, had the named inventors intended there to be a specific function for a well or reservoir at the outlet of the device—namely to accumulate fluids rather than to simply facilitate movement of fluids out

of the device using standard customary techniques known in the art—they clearly could have and would have done so. *Id.*

Petitioner then relies on yet another separate disclosure in Ismagilov explaining “the outlet can be adapted for receiving, for example, a segment of tubing or a sample tube” or, alternatively, a “micropipette.” (Pet. at 36). Relying on its expert, Dr. Fair, Petitioner then assumes without any citation to support in Ismagilov, that “[c]ollecting fluids by micropipette *requires* a container with a volume of liquid to pipette and an opening to insert the pipette” and thus the devices in Ismagilov that include these manifolds would necessarily include a “collection well.” (Pet. at 36; Fair ¶¶ 129-132). However, nowhere in this section discussing this particular “solution outlet” at the end of the group of manifolds is there any reference to the previously disclosed “outlet port” or to “wells or reservoirs,” and there is no further discussion of the “solution outlet” of the manifold anywhere in the specification. (Ex. 1004 at 17:18-30; Ex. 2016 at ¶¶127-128). Petitioner improperly equates the term “outlet,” i.e., the “manifold outlet” with Ismagilov’s prior disclosure of an “outlet port” even though Ismagilov does not actually refer to the “manifold outlet” as a “port” of any kind. (Ex. 2016 at ¶129). Indeed, the “manifold outlet” is only described as “facilitating the movement of plugs” from different analysis units. (Ex. 1004 at 17:18-22). In other words, to the extent any connection can be made, it is clear that the “outlet ports”

of Ismagilov typically act as conduits that allow for collection of the entirety of the “solution” outside of the device following analysis within the manifolds, not as a “chamber” that maintains the entirety of the solution contents in a well or reservoir. (Ex. 2016 at ¶129).

Petitioner’s assumption that collection “using micropipettes” needs a certain volume or an open port also has no basis in Ismagilov, as demonstrated by Petitioner’s failure to cite any disclosure in Ismagilov in support of this assertion. (Pet. at 36). The reference does not describe creating a collection well, or any type of well, after the manifold outlet to facilitate the use of micropipettes. (Ex. 2016 at ¶130). The only support Petitioner cites for these statements is the testimony of its expert, not any disclosure in Ismagilov. (Pet. at 36-37). However, Dr. Fair readily admitted that he has never actually collected plug fluid from a device using a pipette, and thus he would have no basis on which to assume what structure or volume would be necessary to facilitate such a collection:

Q. When is the first time you used a pipette to remove a droplet from a chip and move it off chip?

A. I don't think I've done that.

Q. You've never done that?

A. Not on electrowetting chips, no.

Q. On any other chips?

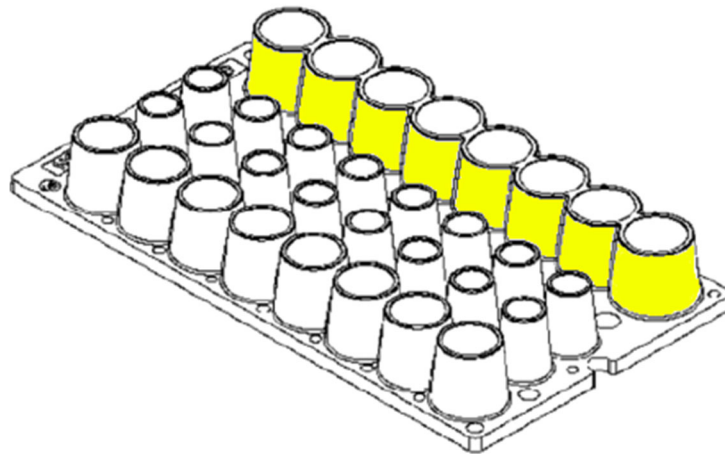
A. Not that I can recall.

(Ex. 2017 at 43:9-16).

There is simply no disclosure in Ismagilov that teaches any chamber with the dimensions and configuration claimed in the '837 patent, which is unsurprising given that the only functionality disclosed for the "outlet ports" is solution extraction, as explained above. (Ex. 2016 at ¶133). A POSA knowledgeable about the state of the art from this time frame would have understood that a micropipette tip could not be placed in much smaller diameter holes, such as those described in Ismagilov as being created by syringe needles and cork borers, at the end of the chip to collect the "slugs" directly through the tip region of the micropipette. (Ex. 2016 at ¶134). Indeed, other references showing the use of a pipette from the same timeframe, including an article written by Ismagilov, show precisely that. (Ex. 2020, Ex. 2021).

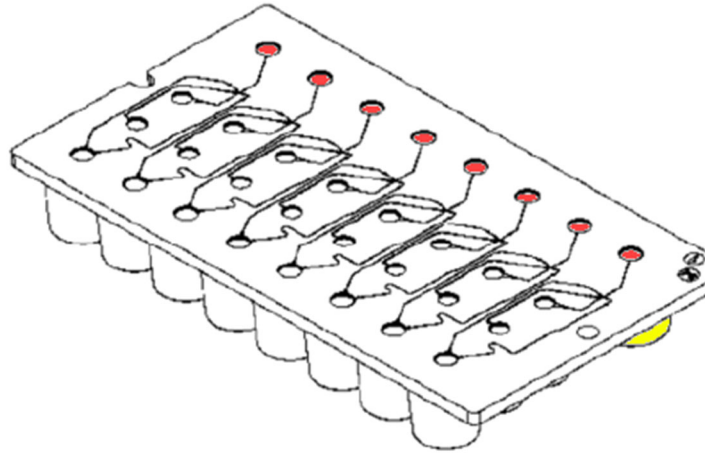
Petitioner's attempts to mix and match disclosures in Ismagilov to piece together a disclosure of a "separation chamber" with "at least one droplet receiving outlet" is also flawed because it is undisputed that Ismagilov does not expressly disclose separation of droplets from immiscible fluid within the alleged "outlet port," "wells or reservoirs," or "solution outlet" and subsequent collection of droplets that is intended to leave behind oil. Again, Ismagilov never provides any structural or functional description of an outlet in any detail, and "wells or reservoirs" are never shown in the 45+ images in Ismagilov. To overcome this

failure, Petitioner argues instead that Ismagilov “discloses the separation chamber . . . under Bio-Rad’s interpretations by disclosing a well or reservoir . . . [and] a well with an opening into which a pipette can be inserted meets this limitation.” (Pet. at 36-37). Specifically, Petitioner argues that if the chambers which are being accused of infringement in the 10X Accused Devices, highlighted in yellow in the image below, constitute “separation chambers” within the meaning of the ‘837 patent, then so too must the “outlet ports,” “wells or reservoirs,” or “solution outlet” allegedly disclosed in Ismagilov:



(Ex. 1026 at 1 (annotated)). Petitioner is wrong. The yellow highlighted chamber in the image above sits atop a “hole punched” outlet well in the 10X Accused Device. (Ex. 2016 at ¶136). Although the “hole punch” is not shown in the above

image of the **top** of the 10X device, it is highlighted in red in the below image of the **bottom** of the 10X device⁴:



The red “hole punches” in the 10X device are critical for purposes of the 086 Petition. (Ex. 2016 at ¶¶135-137). While there is no image of the “outlet ports” or “wells or reservoirs,” which are defined only with respect to the inlet port, referenced in Ismagilov, a POSA reading the explanation from Ismagilov that “[h]oles may be cut into the PDMS [substrate] using, for example, a tool such as a cork borer or a syringe needle” would understand the structures being fabricated simply included the “hole punches” in the 10X Accused Device that would have been well known to a POSA at the time, not the yellow accused “separation chamber.” (*Id.*).

⁴ Although this image of the bottom of the 10X device is also provided in Patent Owner’s Infringement Contentions from the Delaware Litigation, Petitioner did not show it in the 086 Petition. (Ex. 1026 at 1).

Furthermore, such a collection in Ismagilov is based on an assumption that a micropipette tip would even fit inside the holes as Ismagilov explains they would be created, because Ismagilov provides any further description beyond the offhand reference to micropipettes that Petitioner cites. Although Dr. Fair shows an image of a micropipette in his declaration, he never discloses the size of the “polypropylene disposable tip” or discusses whether it would fit into the opening of the Ismagilov purportedly operating as outlet wells. (Ex. 2016 at ¶131). Nor do the brochures of the micropipette attached to Dr. Fair’s declaration disclose these dimensions. (*Id.*). In fact, the only evidence concerning this issue is Dr. Fair’s own testimony that the smallest micropipette is 1 mm (1000 μ m), which is larger than the size of a hole that would be created by a syringe tip, for example. (Ex. 2017 at 159:13-16 (“Q. What is the minimum dimension of a micropipette? A. The ones we have, which are the smallest, are 1 millimeter.”); Ex. 2016 at ¶132).

In sum, the 086 Petition is based on a fundamental misconception (or misrepresentation) of Bio-Rad’s Infringement Contentions from the Delaware Litigation. Bio-Rad is not arguing in the Delaware Litigation that the “hole punches” in the 10X Accused Device are “separation chambers.” Rather, Bio-Rad is arguing that the separate yellow chamber that Petitioner places atop the standard “hole punch” is a “separation chamber.” (Ex. 2016 at ¶138). Petitioner is using these chamber to facilitate separation and collection of its droplets while

minimizing contamination, *i.e.* the same problem addressed in the ‘837 patent.

Ismagilov teaches nothing of the sort.

2. “wherein the separation chamber is upright to the microchannel and out of the horizontal plane”

As set forth above, Petitioner has not identified a separation chamber in Ismagilov. Petitioner cites disclosures of an “outlet port” that can “collect,” but does not cite to any disclosures actually showing a “well or reservoir” in Ismagilov collecting anything. (Ex. 2016 at ¶139). Nevertheless, according to Petitioner, “[b]ecause Ismagilov describes forming the substrate and closing the channels with a glass coverslip, the well or reservoir would extend [vertically and perpendicular to the] plane of the microchannels.” (Pet. at 40-41). Petitioner is again improperly mixing and matching different disclosures from the reference in order to construct a separation chamber that would meet this limitation where none is disclosed in Ismagilov. *See Net MoneyIN*, 545 F.3d at 1369 (“[T]he prior art reference—in order to anticipate under 35 U.S.C. § 102—must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements ‘arranged as in the claim.’”)

Petitioner also assumes that collecting with a micropipette requires a “well or reservoir” extending “out of the horizontal plane.” (Pet. at 41). Again, Petitioner cites no disclosures in Ismagilov supporting this assumption, relying instead on the same disclosure concerning the collection by pipette at the “manifold outlet.” (Pet.

at 40). Petitioner argues, without any citation from Ismagilov for support, that this disclosure requires a “volume . . . deep enough for a pipette to extend into it, and so the wells or reservoirs will extend out of the horizontal plane to permit that.” (Pet. at 41). However, a POSA with knowledge of the state of the art would just as easily understand this disclosure 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. (Ex. 2016 at ¶140). Indeed, to the extent anything can be gleaned about the device outlets in Ismagilov from the figures provided, it would appear that Ismagilov envisioned the “outlet port” in the horizontal plane. (See Ex. 1004 at 39:57-40:2, Figure 22D; Ex. 2016 at ¶141). In contrast, none of the 45+ figures describing an “outlet port,” show a well or reservoir upright to the microchannel or out of the horizontal plane. There are simply no disclosures supporting Petitioner’s assumptions that undisclosed vertical wells or reservoirs must necessarily exist in the devices disclosed in Ismagilov. (Ex. 2016 at ¶140).

Moreover, the disclosure of wells or reservoirs (which in Ismagilov are only part of the definition of the inlet port, not the outlet port) alone does not lend itself to the conclusion that they would extend upright and out of the horizontal plane in the device. For example, Petitioner’s expert testified it was not necessary for a well or reservoir to extend out of the horizontal plane, and that, in fact, he had designed

and used wells in the same plane as the microchannels in his own devices. Dr. Fair further explained that when the well is in the same plane as the microchannel, the droplet will **not** separate from the surrounding oil.

Q. If I asked you to design a system where the outlet well was in the same plane as the channel, could you do that?

A. You could you do that, but if the collection well that you're describing has the same height as the channel, then it would be very difficult to do separation of oil and liquid and droplets. So the early waste reservoirs that we built were, in fact, designed to have the same height as the channels in our devices. And they were just holding – they just were there to hold the droplets, not to separate from the oil.

Q. You did not put the outlet wells vertical to the channel until you decided you wanted to separate?

A. That's correct.

(Ex. 2017 at 69:2-18).

Petitioner also argues, again based on an assumption with no supporting disclosure in Ismagilov, that a well or reservoir must have a volume that “permit[s] collecting multiple droplets” because the channels do not have a “cross-section that can accommodate multiple droplets.” (Pet. at 41). As with Petitioner’s other unsupported assumptions, here too a POSA would not assume that there were outlet wells or reservoirs at the outlet port given that Ismagilov left those structures out of the definition of an outlet port. (Ex. 2016 at ¶143). More reasonably, given the totality of the disclosure in Ismagilov, a POSA would understand that the

droplets at the outlet port in Ismagilov were being collected by inserting “sample tube,” “centrifuge tube,” or “micropipette” into the end of the outlet port in the horizontal plane to facilitate movement of fluids off of the device. (*Id.*).

3. “wherein the droplet formation module and the separation chamber are in fluid communication with each other via the microchannels” (all challenged claims)

The Challenged Claims require that the “droplet formation module” is in “fluid communication” with a “separation chamber” via “microchannels” in the device. For the same reasons discussed above in Section VII(A)(1) that Ismagilov does not disclose a separation chamber as that term is properly construed, this limitation is also missing from Ismagilov.

4. “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 is of a volume sufficient to separate the plurality of droplets comprising the sample from the immiscible fluid within the separation chamber”

Like the other elements in claim 1 relating to a “separation chamber,” Petitioner’s argument rests on the assumption that the single reference to micropipette collection is sufficient for a POSA to understand that Ismagilov requires a certain volume that would be found in an “outlet port,” “wells or reservoirs” or a “solution outlet.” (Pet. at 44-46). For the same reasons these arguments fail with respect to the other separation chamber limitations in claim 1 they similarly fail for this element. (Ex. 2016 at ¶146).

Petitioner includes an argument for this limitation, based on the legal doctrine of inherency, that such structures—which again are not described in any detail or shown in any figures in Ismagilov—would nevertheless be used to separate droplets from immiscible fluid. Namely, petitioner asserts that the droplets and oil will necessarily separate because of their different densities. (*See* Pet. at 46 (“[T]he droplets floating or sinking relative to the oil is at least inherent because it necessarily occur with liquids of different densities”)). Petitioner must rely on this argument because, as noted above, it is undisputed that Ismagilov has no disclosure that discusses separating droplets from the immiscible fluid in wells, reservoirs, outlet ports, or anywhere else on the device. Petitioner argues that inherency applies because “Ismagilov discloses aqueous droplets in fluorinated oil . . . meaning they will separate.” (*Id.*) Ismagilov lists fluorinated oils as a preferential selection, but does not exclude all other oils as carrier fluids. (Ex. 1004 at 20:37-38). Depending on the density of the particular oil that is selected, the droplets will not necessarily separate “each and every time,” as required for Ismagilov to serve as an anticipatory disclosure. *Par*, 773 F.3d at 1195. For example, even if one were to assume, contrary to the definition Ismagilov supplies, that the outlet port is a reservoir of sufficient volume and design that fluids could pool, the drops will not necessarily separate if the selected oil has substantially the same density as water,

rather the droplets will be mixed with the oil as they are dispersed throughout the reservoir. (Ex. 2016 at ¶147-148).

5. “wherein an aqueous fluid from the sample inlet is segmented with an immiscible fluid from the immiscible fluid inlet at the junction” (dependent claim 2)

Claim 2 of the ‘837 patent depends from claim 1. For the same reasons discussed above in Section VII(A)(1)-(4), Ismagilov does not anticipate claim 2 of the ‘837 patent.

6. “wherein at least one droplet receiving outlet is located on the upper portion of the separation chamber” (dependent claim 4)

Claim 4 of the ‘837 patent depends from claim 1. For the same reasons discussed above in Section VII(A)(1)-(4) Ismagilov does not anticipate claim 4 of the ‘837 patent.

7. “wherein the droplet receiving outlet receives substantially one or more droplets” (dependent claim 10)

Claim 10 of the ‘837 patent depends from claim 1. For the same reasons discussed above in Section VII(A)(1)-(4), Ismagilov does not anticipate claim 10 of the ‘837 patent.

8. “wherein the reagent inlet is in fluid communication with the junction or the microchannel” (dependent claim 11)

Claim 11 of the ‘837 patent depends from claim 1. For the same reasons discussed above in Section VII(A)(1)-(4), Ismagilov does not anticipate claim 11 of the ‘837 patent.

- 9. “wherein the reagent inlet introduces one or more amplification reagents to the junction or the microchannel” (dependent claim 12)**

Claim 12 of the ‘837 patent depends from claim 11. For the same reasons discussed above in Section VII(A)(1)-(4) and (8), Ismagilov does not anticipate claim 12 of the ‘837 patent.

- 10. “wherein the one or more amplification reagents are for a polymerase chain reaction” (dependent claim 13)**

Claim 13 of the ‘837 patent depends from claim 12. For the same reasons discussed above in Section VII(A)(1)-(4) and (9), Ismagilov does not anticipate claim 13 of the ‘837 patent.

- 11. “a sorting module to direct the flow of droplets, wherein the sorting module is located between the droplet formation module and the separation chamber” (dependent claim 19)**

Claim 19 of the ‘837 patent depends from claim 1. For the same reasons discussed above in Section VII(A)(1)-(4), Ismagilov does not anticipate claim 19 of the ‘837 patent.

- 12. “wherein the sorting module comprises an apparatus to generate an electric force” (dependent claim 20)**

Claim 20 of the ‘837 patent depends from claim 19. For the same reasons discussed above in Section VII(A)(1)-(4) and (11), Ismagilov does not anticipate claim 20 of the ‘837 patent.

B. Ground 2: Ismagilov and Quake Obviousness

In Ground 2, Petitioner argues that the combination of Ismagilov and Quake renders claims 1-2, 4, 7, 9-13, and 19-20 of the ‘837 patent obvious. (Pet. at 24). However, Petitioner has not identified a sufficient motivation to combine Ismagilov and Quake, which are directed to two entirely different types of systems. Moreover, as set forth in detail above, there are critical differences between Ismagilov and the Challenged Claims and Quake cannot be used to fill those gaps. Finally, several secondary considerations of non-obviousness with a nexus to the ‘837 patent favor a finding of non-obviousness.

1. A POSA Would Not Have Had a Motivation to Combine Ismagilov and Quake

Petitioner has not identified a motivation to combine Ismagilov and Quake. As explained above, the Ismagilov reference is focused on microfabricated substrates for forming droplets or “plugs”. (See Ex. 1004 at Abstract; Ex. 2016 at ¶160). The examples of Quake on which Petitioner relies, on the other hand, were focused on cell sorting and did not use droplets or “plugs.” (Ex. 1006 at ¶31). While Petitioner states a “POSA would know to combine Ismagilov and Quake,” Petitioner provides no basis for combining two references with different purposes. (Ex. 2016 at ¶160)).

Petitioner also argues that a POSA would have been motivated to combine Ismagilov with Quake because “[t]he differences between Ismagilov and Quake

are minor and relate to additional structural details provided by Quake.” (Pet. at 39). The identification of similarities between two prior art references, however, is also not enough to satisfy Petitioner’s burden. *Free-Flow Packaging Int’l, Inc. v. Automated Packaging Sys.*, IPR2016-00350, Paper 7 at 12-13 (June 27, 2016). Moreover, it is undisputed that the differences between the two disclosures are not “minor” but actually relate to two completely different structures and assemblies with two completely different intended uses. (Ex. 2016 at ¶161). Specifically, Figures 6 and 8 of Quake are not droplet formation devices at all. Rather, Figures 6 and 8 disclose a “cell-sorting device.” (Ex. 1006 at ¶197). Dr. Fair admitted in his deposition that “Quake did not use droplets ***And this is not a droplet-based system.***” (Ex. 2017 at 141:12-142:2). Indeed, there is nothing in Quake’s sorting embodiment depicted in Figures 6 and 8 that includes an “extrusion region,” which is what Quake calls the place where droplets are formed in other disclosed embodiments. (Ex. 1006 at ¶¶ 29, 70). In fact, Quake states that in the sorting embodiment utilizing the devices disclosed in Figures 6 and 8, the first step is filling one of the wells with buffer, allowing that buffer to fill “all the channels . . . to avoid the formation of air pockets,” and then filling each of the wells with buffer. (*Id.* at ¶ 220). The “input or sample well is typically loaded last” and the “flow of material” is “driven by the electrodes.” (*Id.*) There are no disclosures of forming droplets or of an “extrusion region” and these droplet sorting

embodiments are not relevant to forming droplets. (Ex. 2016 at ¶162). Petitioner fails to explain why a POSA would look to the sorting embodiment in Quake in order to incorporate wells into the droplet formation devices of Ismagilov where hole punches were described as being created with syringes or cork borers. (*Id.*).

Petitioner also 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. (*Id.* at ¶163). Conclusory arguments such as this are insufficient to meet Petitioner’s burden. *See, e.g., Harmonic v. Avid Technology*, 815 F.3d 1356,1364-65 (Fed. Cir. 2016) (holding that Petitioner’s “single sentence without any elaboration” was improperly conclusory); *In re Magnum Oil Tools Int’l Ltd.*, 829 F.3d 1364, 1380 (Fed. Cir. 2016) (finding petitioner’s “mere conclusory statements” insufficient to satisfy its burden of proving obviousness); *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006) (a rejection on the ground of obviousness must include “articulated reasoning with some rational underpinning to support the legal conclusion of obviousness”).

Finally, Petitioner’s argument that a POSA would combine the wells and channels of Ismagilov and Quake, and then “[b]ased on this combination, a droplet receiving chamber inlet was obvious” is purely impermissible hindsight. Indeed, Dr. Fair admitted that he “started with looking at the claim language” and then

“found appropriate references to cite in an invalidity analysis.” (Ex. 2017 at 53:5-8). As the Federal Circuit has explained, “[i]t is impermissible to use the claimed invention as an instruction manual or ‘template’ to piece together the teachings of the prior art so that the claimed invention is rendered obvious.” *In re Fritch*, 972 F.2d 1260, 1266 (Fed. Cir. 1992); *InTouch Techs., Inc. v. VGO Commc’ns, Inc.*, 751 F.3d 1327, 1338 (Fed. Cir. 2014) (holding that Defendant’s expert testimony was nothing more than impermissible hindsight because she “relied on the patent itself as her roadmap for putting what she referred to as pieces of a ‘jigsaw puzzle’ together ... consist[ing] of conclusory references to her belief that one of ordinary skill in the art could combine these references, not that they would have been motivated to do so.”); *see also 10X Genomics, Inc. v. Bio-Rad Laboratories, Inc.*, Case IPR2018-00692, Paper No. 11 at 16 (July 10, 2018) (“The number of mental steps and physical modifications necessary to achieve the proposed Combined System suggests it is proposed out of hindsight, and not in view of the knowledge and skill in the art as of the earliest priority date of the ’844 patent.”). .

2. Differences Between the Combination of Ismagilov and Quake and the Challenged Claims

(a) “separation chamber” (and related limitations from all challenged claims)

Quake also does not disclose a “separation chamber” and the related limitations in claim 1. Petitioner argues that because Figures 6 and 8 show “wells

or reservoirs as large, open structures” they are necessarily operating as a “separation chamber.” (Pet. at 38-40). Petitioner is misreading the disclosures, which do not disclose a separation chamber as properly construed. (Ex. 2016 ¶165).

Petitioner cites paragraphs 198-200 as disclosing wells intended for separation but this portion of Quake teaches nothing of the sort. The “wells” in Quake are used for “sorting experiments” where “cells can be directed to either side of the ‘T’ channels depending upon the voltage potential settings” created by inserting platinum electrodes into the disclosed “wells.” (Ex. 1006 at ¶¶197-198; Figs. 6 and 8). While Figure 6 includes “collection wells,” there are no disclosures of separating droplets and immiscible fluid in these wells. (*Id.* at ¶197). In fact, there are no droplets even present in this embodiment. Thus, even if a POSA were motivated to combine Ismagilov with Quake, which Petitioner has failed to establish, the combination would still fail to teach the claimed separation chamber and related limitations of the ‘837 patent. (Ex. 2016 at ¶166).

(b) “wherein an aqueous fluid from the sample inlet is segmented with an immiscible fluid from the immiscible fluid inlet at the junction” (dependent claim 2)

Petitioner presents no analysis of this limitation under Ground 2 separate from its analysis under Ground 1. For the same reasons discussed above in Section

VII(A)(5) above, Claim 2 is non-obvious in light of the combination of Ismagilov and Quake.

(c) “wherein at least one droplet receiving outlet is located on the upper portion of the separation chamber” (dependent claim 4)

Petitioner presents no analysis of this limitation under Ground 2 separate from its analysis under Ground 1. For the same reasons discussed above in Section VII(A)(6) above, Claim 4 is non-obvious in light of the combination of Ismagilov and Quake.

(d) “wherein the droplet receiving outlet is coupled to a vessel” (dependent claim 7)

Claim 7 of the ‘837 patent depends from and includes all of the same limitations as claim 1, plus the additional limitation that “the droplet receiving outlet is coupled to a vessel.” Petitioner presents no analysis of this limitation separate from its analysis of claim 1. For the same reasons discussed above in Section VII(A)(1)-(4) above, Claim 7 is non-obvious in light of the combination of Ismagilov and Quake. Indeed, because neither Ismagilov nor Quake disclose a separation chamber with one or more droplet receiving outlets, as those terms are properly construed, there is also no disclosure of a “droplet receiving outlet” being “coupled,” or “operably linked,” to another vessel. Furthermore, in simply incorporating its arguments for claim 1 with no further analysis or detail, Petitioner

also fails to identify any disclosure of a “separate vessel” in either Ismagilov or Quake.

**(e) “wherein the vessel is a PCR tube or a test tube”
(dependent claim 9)**

The Petition states that “Claim 9 is only challenged under Grounds 3-5. (Pet. at 70). However, Petitioner’s chart and the Board’s Decision both identify claim 9 as part of Petitioner’s Ground 2 assertions. Nevertheless, Petitioner’s arguments concerning this additional limitation simply incorporate Petitioner’s arguments for claims 1 and 7. Thus, to the extent Petitioner has sufficiently identified claim 9 in the challenged claims for Ground 2, for the same reasons discussed above in VII(A)(1)-(4), Ismagilov in combination with Quake does not render obvious dependent claim 9.

**(f) “wherein the droplet receiving outlet receives
substantially one or more droplets” (dependent claim
10)**

Petitioner presents no analysis of this limitation under Ground 2 separate from its analysis under Ground 1. For the same reasons discussed above in Section VII(A)(7) above, Claim 10 is non-obvious in light of the combination of Ismagilov and Quake.

(g) “wherein the reagent inlet is in fluid communication with the junction or the microchannel” (dependent claim 11)

Petitioner presents no analysis of this limitation under Ground 2 separate from its analysis under Ground 1. For the same reasons discussed above in Section VII(A)(8) above, Claim 11 is non-obvious in light of the combination of Ismagilov and Quake.

(h) “wherein the reagent inlet introduces one or more amplification reagents to the junction or the microchannel” (dependent claim 12)

Petitioner presents no analysis of this limitation under Ground 2 separate from its analysis under Ground 1. For the same reasons discussed above in Section VII(A)(9) above, Claim 12 is non-obvious in light of the combination of Ismagilov and Quake.

(i) “wherein the one or more amplification reagents are for a polymerase chain reaction” (dependent claim 13)

Petitioner presents no analysis of this limitation under Ground 2 separate from its analysis under Ground 1. For the same reasons discussed above in Section VII(A)(10) above, Claim 2 is non-obvious in light of the combination of Ismagilov and Quake.

(j) “a sorting module to direct the flow of droplets, wherein the sorting module is located between the

droplet formation module and the separation chamber” (dependent claim 19)

While the Petition includes separate sub-sections for Grounds 1 and 2 for this limitation, Petitioner presents no additional analysis of this limitation under Ground 2 separate from its analysis under Ground 1 and simply incorporates its arguments for Ground 1. For the same reasons discussed above in Section VII(A)(11) above, Claim 19 is non-obvious in light of the combination of Ismagilov and Quake.

(k) “wherein the sorting module comprises an apparatus to generate an electric force” (dependent claim 20)

Petitioner presents no analysis of this limitation under Ground 2 separate from its analysis under Ground 1. For the same reasons discussed above in Section VII(A)(12) above, Claim 2 is non-obvious in light of the combination of Ismagilov and Quake.

3. Several Secondary Considerations Support A Finding Of Non-Obviousness

Several secondary considerations weigh in favor of a finding of nonobviousness of the '837 claims, including long-felt need, commercial success, praise, and acquiescence and licensing. 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. (Ex. 2014; Ex. 2016 at ¶178). Bio-Rad's ddPCR™ platform—including the QX100 and

QX200 Droplet Digital PCR systems and AutoDG Droplet Generator—practices the ‘837 patent. (Ex. 2022 (“The Bio-Rad Digital PCR Systems and/or their use is covered by claims of U.S. patents, and/or pending U.S. and non-U.S. patent applications owned by or under license to Bio-Rad Laboratories, Inc., including, but not limited to, U.S. Patent Nos. 9,089,844; 9,126,160; 9,216,392; 9,347,059; 9,500,664; 9,562,837; 9,636,682; 9,649,635; and 9,896,722.”); Ex. 2016 at ¶179). The ‘837 patent includes numerous novel elements, including multi-step processes and apparatus designed to improve the ability to easily and reliably remove the droplets from the separation chamber while minimizing the removal of unwanted continuous phase fluid. (Ex. 2016 at ¶182.) This ability is facilitated by a particular orientation for the separation chamber (one that is upright or perpendicular to the microchannel) of a certain width. (*Id.*). The patented features from the ‘837 patent are repeatedly referenced in Bio-Rad’s instruction manuals and are critical to the Bio-Rad products’ workflows. (Ex. 2010, Ex. 2011)). Thus, the secondary considerations cited herein related to Bio-Rad’s products have a sufficient nexus to the claims of the ‘837 Patent. *Polaris Indus., Inc. v. Arctic Cat, Inc.*, 882 F.3d 1056, 1072 (Fed. Cir. 2018) (quoting *Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1130 (Fed. Cir. 2000)) (“We presume that such a nexus applies for objective indicia 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.’”). (Ex. 2016 at ¶181).

(a) Long-Felt Need

When RainDance Technologies, Inc. (“RainDance”) was founded, it helped transform disease research by making innovative tools using its proprietary technologies that simplify complex genetic analysis. 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. (Ex. 2016 at ¶182).

Bio-Rad’s ddPCR™ platform was heralded as a breakthrough that greatly advanced the capabilities of PCR. Shortly after its launch, Bio-Rad’s first-generation ddPCR™ product, the QX100, was widely acknowledged as an innovative design that contributed to the progression of PCR technology. The new product was an easy-to-use alternative to the existing technology, such as real-time or quantitative digital PCR, for users looking for more precise and accurate methods of detecting rare mutations and small copy number variations. (*See, e.g.*, Ex. 2001). Bio-Rad’s ddPCR™ products were rapidly adopted in the industry and led to an explosion of research. Just one year after the QX100 launch, the number of cancer research papers citing ddPCR™ nearly quintupled. (Ex. 2002). Since

launching Bio-Rad's ddPCR™ platform, there have been more than 4,400 published studies describing research breakthroughs using this technology, including 1034 publications in 2019. (Ex. 2003). With the help of ddPCR™, researchers were able to detect rare targets with a level of precision that was just not possible with previous technologies. (*See, e.g.*, Ex. 2004). The 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. (Ex. 2016 at ¶183-186).

(b) Commercial Success

Patent Owner's products that embody the '837 patent have also been a commercial success, with the inventions disclosed in the '837 patent contributing to this success. They allow for the utilization of differences in density of the different fluids to concentrate the droplets in a particular part of the chamber. This greatly improved the ability to easily and reliably remove the droplets from the separation chamber while minimizing the removal of unwanted continuous phase fluid. These developments represented a significant improvement on the prior art that greatly advanced the capability of PCR and NGS. (*See, e.g.*, Ex. 2005; Ex. 2006; Ex. 2007; Ex. 2008; Ex. 2009; Ex. 2016 at ¶187).

Similarly, 10X's products embodying the invention have been a commercial success. (*See, e.g.*, Ex. 2012 ("Since launching our first product in mid-2015, and

as of June 30, 2019, we have sold 1,284 instruments to customers around the world, including 93 of the top 100 global research institutions by publications, and 13 of the top 15 global pharmaceutical companies by 2018 revenue. . . . Revenue increased 106% to \$146.3 million in the year ended December 31, 2018 as compared to \$71.1 million in the prior year, and increased 85% to \$109.4 million for the six months ended June 30, 2019 as compared to \$59.2 million for the six months ended June 30, 2018, primarily due to the adoption of our platform by customers as reflected by the doubling in size of our installed base to more than 1,000 instruments as of December 31, 2018 and more than 1,280 instruments as of June 30, 2019, and the associated consumables pull-through on those instruments.”); Ex. 2016 at ¶188).

(c) Praise by Others

Patent Owner’s innovative ddPCR™ products have also received repeated accolades for their contributions to the field. (Ex. 2016 at ¶¶ In 2012, just one year after its launch, the QX100 ddPCR™ product was awarded *R&D Magazine*’s 100 Award, which is given to the 100 most technologically significant products introduced into the marketplace over the past year. (Ex. 2005). The QX100 ddPCR™ product was also awarded the *Laboratory Equipment* Readers’ Choice Award in the biotech category, which is given to celebrate excellence in product design and performance for the tools and materials used by scientists and engineers

in research laboratories. (*See* Ex. 2006). Similarly, the QX200 ddPCR™ product—Patent Owner’s second-generation ddPCR™ system—received the Scientists’ Choice Award for Best New Life Sciences Product of 2013 from *SelectScience* because of its significant contribution in 2013. (*See* Ex. 2007). The following year, the QX200 ddPCR™ product received the 2014 Frost & Sullivan New Product Innovation Award for the Digital PCR Market in recognition of its innovation, value-added features/benefits, and the return on investment to customers. (*See* Ex. 2008). Similarly, 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. (Ex. 2023, 2024, 2025, 2026).

Patent Owner’s investment and development efforts led to a new generation of products to be used in the preparatory steps of creating thousands of microdroplets that are then evaluated in Next Generation Sequencing (“NGS”) applications, such as in those provided by Illumina Corporation. Bio-Rad’s next generation product that is used in NGS is called the ddSEQ™ system. It was launched in January 2017 and it consists of both a newly-optimized microfluidic device (cartridge/chip) and a droplet generator instrument. As with its prior droplet products, the ddSEQ™ system has also received wide acclaim. (*See, e.g.*, Ex. 2009).

Both Bio-Rad's and 10X's products have received praise because of their turn-key, easy-to-use workflows. (*See, e.g.*, Ex. 2013). The patented inventions allow users to easily remove the droplets by collecting them on the microfluidic chip, where they can separate from the continuous fluid. This feature allows users to more efficiently and easily subject the contents of the droplets to further downstream reactions and analysis.

C. Grounds 3-5: Ismagilov 119 and Pamula Obviousness

With respect to Grounds 3-5, the Board correctly found that "Petitioner has not shown a reasonable likelihood of prevailing on these grounds." (Dec. at 43-44; *see also id.* at 48, 51).

First, the Board correctly found that "Petitioner presents no analysis of [Ismagilov 119 or Pamula] based on the claim constructions that Petitioner attributes to Patent Owner" in its purported Grounds 3a, 4a, and 5a, and therefore Petitioner's Grounds 3-5 were properly limited to Petitioner's proposed constructions. (Dec. at 44). As explained above, the Board correctly rejected Petitioner's alternative proposed constructions. Thus, Grounds 3-5 can be rejected on that basis alone.

Second, the Board correctly found that Petitioner's obviousness analysis of Ismagilov 119 in Ground 3 "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.” (Dec. at 46). Indeed, as the Board found, Petitioner’s reference to a single sentence in Ismagilov 119 that “plugs can be sorted by their density relative to that of the carrier fluid” (Ex. 1005, ¶ 123) describes *sorting* plugs based on relative density of those plugs, “not separating plugs from carrier fluid.” (Dec. at 45-47). Nor does this single sentence permit a POSA to extrapolate that a separation chamber must exist in order for such sorting to occur. (*Id.* at 45). The Board’s finding that Ground 3 is based on improper hindsight is also further confirmed by Dr. Fair, who admitted that he “started with looking at the claim language” and then “found appropriate references to cite in an invalidity analysis.” (Ex. 2017 at 53:5-8). Thus, the Board correctly held that Petitioner failed to show that claims 1–4, 7–13, and 19–20 are unpatentable over Ismagilov 119 because Petitioner failed to provide sufficient evidence that a “separation chamber” in which droplets are separated from immiscible fluid in a chamber that “is upright to the microchannel and out of the horizontal plane,” “has a wider cross-section than the microchannel cross-section” and “is of a volume sufficient to separate the plurality of droplets . . . from the immiscible fluid . . . ” as required by claim 1 of the ‘837 patent exists in Ismagilov 119. (Dec. at 48).

Finally, the Board also correctly held that Grounds 4 and 5, based on combinations of Ismagilov 119 and the Pamula references, are also “motivated by

impermissible hindsight, rather than reasoning that would have been employed upon by a POSA who had not seen claim 1 and the supporting disclosure of the '837 Patent.” (Dec. at 50). Petitioner’s contention that a POSA “would have been able to apply Pamula’s teachings . . . to Ismagilov’s system” (Pet. 61; Ex. 1008 ¶ 156) 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) (*See also* Ex. 2017 at 53:5-8). Furthermore, the Board correctly found that Petitioner and Dr. Fair failed to 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. (Dec. at 50). *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.”). Thus, Petitioner failed to show that claims 1–4, 7–13, and 19–20 are unpatentable over Ismagilov 119 and Pamula in either Ground 4 or Ground 5.

VIII. CONCLUSION

In view of the foregoing, Patent Owner respectfully submits that the Board should reject all grounds of the 086 Petition and uphold the patentability of the Challenged Claims.⁵

Date: August 11, 2020

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⁵ Patent Owner expressly reserves its right to present constitutional arguments pending resolution of *Arthrex, Inc. v. Smith and Nephew, Inc.*, No. 2018-2140.

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CERTIFICATE OF COMPLIANCE

I, the undersigned, certify that the above Patent Owner Preliminary Response complies with the applicable type-volume limitations of 37 C.F.R. § 42.24 (b)(1). Exclusive of the portions exempted by 37 C.F.R. § 42.24(a), this Preliminary Response, including footnotes, contains 13,942 words, as counted by the word count function of Microsoft Word. This is less than the limit of 14,000 words as specified by 37 C.F.R. §§ 42.24(a)(1)(i) and (b)(2).

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CERTIFICATION OF SERVICE (37 C.F.R. §§ 42.6(E), 42.105(A))

The undersigned hereby certifies that the foregoing document was served in its entirety on August 11, 2020 upon the following parties via Electronic Mail.

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