

**IN THE UNITED STATES DISTRICT COURT  
FOR THE DISTRICT OF DELAWARE**

BIO-RAD LABORATORIES, INC.	)	
	)	
Plaintiff,	)	
	)	C.A. No. 18-1679-RGA
v.	)	
	)	
10X GENOMICS, INC.	)	
	)	
Defendant.	)	

**JOINT CLAIM CONSTRUCTION BRIEF**

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**TABLE OF CONTENTS****Page**

I.	INTRODUCTION .....	1
A.	Plaintiff's Introduction .....	1
B.	Defendant's Introduction .....	1
II.	AGREED CONSTRUCTIONS .....	2
III.	DISPUTED CONSTRUCTIONS .....	2
C.	Disputed Term: "sample" .....	2
1.	Plaintiff's Opening Position .....	2
2.	Defendant's Answering Position .....	5
3.	Plaintiff's Reply Position .....	9
4.	Defendant's Sur-Reply Position .....	12
D.	Disputed Term: "separation chamber" .....	14
1.	Plaintiff's Opening Position .....	14
2.	Defendant's Answering Position .....	16
3.	Plaintiff's Reply Position .....	23
4.	Defendant's Sur-Reply Position .....	27
E.	Disputed Term: "droplet receiving outlet" .....	29
1.	Plaintiff's Opening Position .....	29
2.	Defendant's Answering Position .....	32
3.	Plaintiff's Reply Position .....	35
4.	Defendant's Sur-Reply Position .....	39
F.	Disputed Term: "coupled" .....	41
1.	Plaintiff's Opening Position .....	41
2.	Defendant's Answering Position .....	42
3.	Plaintiff's Reply Position .....	46
4.	Defendant's Sur-Reply Position .....	48
G.	Disputed Term: "polymerase chain reaction (PCR)" .....	49
1.	Plaintiff's Opening Position .....	49
2.	Defendant's Answering Position .....	50
3.	Plaintiff's Reply Position .....	53

4.	Defendant’s Sur-Reply Position .....	53
H.	Disputed Term: "providing an immiscible fluid flowing through a main channel that is in fluid communication with the sample inlet" .....	53
1.	Plaintiff’s Opening Position.....	53
2.	Defendant’s Answering Position .....	55
3.	Plaintiff’s Reply Position.....	61
4.	Defendant’s Sur-Reply Position .....	64
I.	Disputed Term: "main channel" .....	66
1.	Plaintiff’s Opening Position.....	67
2.	Defendant’s Answering Position .....	68
3.	Plaintiff’s Reply Position.....	71
4.	Defendant’s Sur-Reply Position .....	73
J.	Disputed Term: "continuous phase carrier fluid" .....	75
1.	Plaintiff’s Opening Position.....	75
2.	Defendant’s Answering Position .....	76
3.	Plaintiff’s Reply Position.....	79
4.	Defendant’s Sur-Reply Position .....	81

\*Exhibits A-Y were attached to the Joint Claim Construction Chart, D.I. 88. Exhibits Z-XX are attached to the Joint Appendix filed contemporaneously hereto.

LLC, Civil Action No. 14-1250-RGA, 2016 WL 158031, at \*8 (D. Del. Jan. 13, 2016) (finding application “listed as prior art on the face of the ’926 patent” intrinsic evidence). *OSRAM* is not to the contrary and is inapplicable because it concluded that references not cited by the examiner are rarely “probative of an intent to *depart* from the plain technical meaning,” but 10X cites evidence *confirming* the plain meaning. 505 F.3d 1351 at 1357-58; *see also*, *Archerdx*, 2019 WL 6785546, at \*8 n.3 (describing *OSRAM* and that “extrinsic” argument was undisputed).

Bio-Rad cites testimony from a prior litigation in which it agreed to the construction now proposed by 10X. Ex. Z, Chart 2, 2. Bio-Rad’s agreement is most probative, but the testimony also support 10X’s construction. 10X’s expert testified that “the word ‘sample,’ typically, I associate with an analyte, like something I want to analyze.” Ex. SS at 23:1-10. Bio-Rad is incorrect that 10X’s expert described “sample” without analysis. 10X’s expert said that “*in [Kumacheva’s] research* it would be a sample” because Kumacheva was “*varying conditions*” as part of “research” to “get the best result,” showing “it’s a *compound of -- of interest*, yeah, to *her*.” *Id.*, at 24:3-21.

Finally, 10X’s construction was adopted by the PTAB in a recent institution decision on the 837 Patent. Ex. UU, 10-12. The PTAB concluded that 10X’s construction was supported by the specification, the sample/contamination distinction, and the sample/reagent distinction. *Id.*

#### **D. Disputed Term: "separation chamber"**

U.S. Patent No. 9,562,837 (Claims 1, 4) and U.S. Patent No. 9,896,722 (Claims 1, 14)	
Bio-Rad's Proposed Construction	10X's Proposed Construction
chamber sized to accommodate multiple droplets and an immiscible fluid in separated form	a space that is substantially enclosed

#### **1. Plaintiff’s Opening Position**

Bio-Rad's proposed construction of "separation chamber" is consistent with the claim language, the specification, and the file history. 10X's definition ignores the term in the context of the claim, the specification, and the clarifying remarks in the file history. 10X's definition ignores the word "separation" and then imposes a requirement of "substantially enclosed" that appears nowhere in the intrinsic evidence. The description of "chamber" in the patents' specifications does not comport with 10X's requirement for a "substantially enclosed" space.

Both the '837 and '722 patents provide examples of chambers: "It 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." '722 Patent Col. 53:44-47; '837 Patent Col. 53:35-38 (emphasis added). The chamber examples follow the description of the droplet formation module being connected to a chamber and an explanation that "the chamber is configured to receive droplets and an immiscible fluid from the droplet formation module." '722 Patent Col. 53:30-33; '837 Patent Col. 53:21-24. Nowhere in the chamber examples is there any mention of the chamber being substantially closed. Rather, the only requirement is that the vessel be suitable for holding droplets.

Bio-Rad's construction adheres to the description of a "chamber" with additional requirements necessitated by the word "separation" and statements made during the prosecution of the patent. As fundamental tenets of claim construction mandate, a construction cannot render a term superfluous. *Aero Prod. Int'l, Inc. v. Intex Recreation Corp.*, 466 F.3d 1000, 1013 (Fed. Cir. 2006). 10X's construction does just that. It gives no meaning to the word "separation." Therefore, it cannot be correct.

Bio-Rad's construction, on the other hand, accounts for separation by requiring the chamber to be sized to allow multiple droplets and immiscible fluid to separate. This is

consistent with the claims, the specification, and the file history. For example, the '837 claims contain the requirement that the separation chamber containing droplets and immiscible fluid be of sufficient volume to allow them to separate. *See, e.g.*, '837 Patent Col. 88:18-23 (claim 1 "wherein" clause); '722 Patent Col. 88:20-22 ("separating" clause). Similar descriptions are contained in the specifications. *See, e.g.*, '837 Patent Col. 2:45-50, 3:37-58, 53:21-41; '722 Patent Col. 2:45-50, 3:35-43, 53:30-50, 54:43-50.

Last, the Applicants stated numerous times in the file history 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.*, JCCC Ex. N at BRL00001606 ("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 BRL00001660-61 ("As acknowledged by the Examiner . . . 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.").

Because Bio-Rad's construction is consistent with the intrinsic evidence and 10X's is not, Bio-Rad's construction should be adopted.

## **2. Defendant's Answering Position**

A POSA understands a "chamber," especially the claimed "separation chamber" as read in the context of the claims and specification of the Asserted Patents, to be "a space that is substantially enclosed." Bio-Rad's construction, in contrast, does not provide the Court or a jury

the claim language that requires the separation of droplets from the immiscible fluid in the separation chamber.

Bio-Rad's construction should also be rejected for failing to give meaning to the claim term "chamber." *Kara Tech, Inc. v. Stamps.com, Inc.*, 582 F.3d 1341, 1348-49 (Fed. Cir. 2009). That failure also means Bio-Rad's construction would not resolve the dispute between the parties about whether an open-topped well from which a user can use a pipette to remove droplets is the claimed "separation chamber," as Bio-Rad's infringement contentions allege. Exs. LL-MM; *O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co.*, 521 F.3d 1351, 1361-62 (Fed. Cir. 2008).

### **3. Plaintiff's Reply Position**

10X's argument that the separation chamber must be substantially enclosed is another attempt to read limitations for particular embodiments into the claims. 10X's construction is inconsistent with the broad definition of "chamber" in the specification. Additionally, 10X's logic for insisting that the separation chamber must be closed rests on a misreading of the ways in which contamination can be minimized in the invention compared to the prior art.

10X claims that the only way to minimize contamination is to have a system that is completely closed to the atmosphere at every step. *See, e.g.*, Ex. XX (Fair), ¶ 51. 10X is wrong. As Dr. Anna explains, one major advantage of droplet-based systems is that they minimize contamination compared to prior systems where reactions were carried out in bulk volume systems like test tubes. Ex. RR ¶ 73. As the specification explains, techniques using bulk volumes involve multiple handling steps where contamination can be easily introduced. '837 Patent Col. 2:4-31; Ex. RR ¶ 73. When droplets are used, however, each droplet acts as a tiny sealed reaction vessel that minimizes contamination. '837 Patent Col. 2:4-31; Ex. RR ¶¶ 73-75.



In droplets, sample molecules can be diluted according to statistics that ensure that each droplet contains one or few sample molecule. '837 Patent Col. 1:64-2:3. This droplet-based dilution minimizes contamination compared to bulk volume systems. Ex. RR ¶¶ 73-75. Thus, the use of an assembly that creates droplets with sample molecules sequestered therein reduces contamination compared to non-droplet systems. *Id.* While sealing an entire system may further reduce contamination, it is not the only way to decrease contamination in general.

While first claiming that vessels and chambers are different, 10X then points to examples of sealed vessels being used to reduce contamination as proof that the separation chamber must be sealed. These citations either refer to embodiments where the vessel is part of secondary assemblies that are collecting droplets from the separation chamber or are simply embodiments in which the vessel acting as a separation chamber is closed to **further** reduce contamination, not to provide the only contamination reduction. *See* '837 Patent Col. 4:23-47 (the vessel may be sealed or unsealed, and noting that sealably coupling the outlet [of the separation chamber] to the vessel "**further**" minimizes contamination); *id.* Col. 55:55-64 (describing an alternate embodiment); *id.* Col. 56: 30-39 (same); *id.* Col. 59:64-60:43 (describing an embodiment where, after amplification in droplets, the droplets are returned to the assembly for analysis).

The embodiments described in 10X's last three citations discuss Figure 39. The description of Figure 39 shows that the vessel which is the separation chamber 903 need not be closed. *Id.* Col. 55:60-62 ("In certain embodiments, the assembly includes a PCR tube cap **904** that locks[s] the vessel **903** into a sealed position."). In any event, limitations from embodiments may not be read into the claims. *Ericsson, Inc. v. D-Link Sys., Inc.*, 773 F.3d 1201, 1218 (Fed. Cir. 2014).

10X's theory that everything must be sealed to reduce contamination is also belied by multiple examples in the specification. For example, the specification describes transporting droplets from the separation chamber outlet to a vessel on a slide. '837 Patent Col. 4:17-23. The slide is shown open to the atmosphere. *See id.* Col. 54:47-67, Fig. 38B ("806"), Ex. RR ¶¶ 81-82. The specification also states that by "sealably coupling the outlet to the vessel, contamination can be "further minimized." *Id.* Col. 4:28-31. Sealing provides further minimization of contamination, not the only minimization. Ex. RR ¶¶ 73-76.

Contrary to what 10X argues, this is consistent with Col. 2:4-39 of the '837 which describes nucleic acids within droplets, which are therefore sealed off from the environment, being amplified outside the assembly. The droplets are then returned to the assembly to analyze the amplified nucleic acids within them. '837 Patent Col. 2:50-57. This portion of the specification shows that the droplets are what minimizes contamination, not the closed system. Ex. RR ¶ 74. 10X's claim that in an open separation chamber "the droplets will be exposed to contamination and sample loss defeating the purpose of the invention" (Ex. XX (Fair), ¶¶ 52, 54) fails to recognize the protection the droplets provide. Ex. RR ¶¶ 73-76.

10X is also incorrect that the separation chamber must be closed to be consistent with descriptions of the oil displacing droplets and oil not spilling out the top. Ex. XX (Fair), ¶¶ 53-54. As the specification describes, it is possible to locate an outlet near the "upper portion of the chamber to collect rising droplets." '837 Patent Col. 53:29-31. This does not require a sealed chamber. When droplets float to the top, they could be displaced through an outlet near the very top of the chamber. They could also be collected at the top of the chamber. Since there is generally a limited amount of oil being used in the system, the chamber is designed so that it has a volume sufficient to accommodate oil and droplets without spilling over. Ex. RR ¶ 77.

10X further argues that the file history teaches that the chamber must be closed because when the separation chamber was added to the claims, the applicants cited '837 Col. 52:27-54:46 for support and all the descriptions in these sections show chambers that are substantially closed. This too is incorrect. At Col. 53:35-38, the inventors state, "It 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." None of these vessels is described as having a cover or being closed. 10X claims one of skill in the art would have to read these containers as including their sealing devices because of the contamination and spillage issues. As described above, neither of these points require a closed vessel. Ex. RR ¶¶ 73-76.<sup>9</sup>

Dependent claim 8 of the '837 Patent is also inconsistent with 10X's argument. This claim adds a limitation to dependent claim 7 and requires the coupling the separation chamber's outlet to vessel (claim 7) be sealed (claim 8). Claim 1 must be broader than claims 7 and 8 and is not limited to a chamber that is closed by being sealably coupled to a vessel.

10X's reliance on extrinsic evidence in the form of dictionary definitions for "chamber" is also unfounded. Those definitions, which point to a judge's chamber and a gun chamber,<sup>10</sup> are inconsistent with the intrinsic evidence here regarding droplet microfluidics to the extent they call for a chamber to be closed. Therefore, the extrinsic definitions are irrelevant and must be disregarded. *Tempo Lighting, Inc. v. Tivoli, LLC*, 742 F.3d 973, 977 (Fed. Cir. 2014).

Last, 10X claims that the portions of Bio-Rad's definition that refer to the chamber being sized to accommodate droplets and immiscible fluid in separated form is unnecessary because

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<sup>9</sup> The PTAB also rejected 10X's argument, without any argument or evidence being presented by Bio-Rad, that the separation chamber must be sealed. Ex. VV at 10-12.

<sup>10</sup> It is not even clear that a gun chamber is closed as it appears to be integral to the barrel, which is open to the atmosphere.

this is already described elsewhere in the claim and incorrectly "contradict[s] claim language that requires the separation of droplets from immiscible fluid in the separation chamber." 10X is wrong on both accounts. The claims of the '837 Patent are directed to an assembly. They do not require separation to occur. And while the '837 claims do contain language that states the separation chamber has to be sized to accommodate droplets and immiscible fluid, the '722 claims do not contain that same language.

#### **4. Defendant's Sur-Reply Position**

Bio-Rad relies heavily on the incorrect assertion that the purported benefits of the invention described in the specifications (reduced contamination, reduced sample loss, and elimination of pipettes) result from the mere use of droplets rather than the use of a substantially enclosed system. *See supra* at 23-24; Ex. RR (Anna), ¶¶ 73-75. However, neither Bio-Rad nor its expert identify any intrinsic support connecting these benefits to the use of droplets, nor is there any, which is unsurprising given that droplet systems were already well-known prior art by the time of the Asserted Patents.

During prosecution, the applicant admitted that droplet-based systems were already known, ultimately distinguishing the asserted claims based on the claimed separation chamber. Ex. WW [3/16/2016 Applicant Remarks] at BRL00001630 ("FIG. 21A clearly shows that the coil sections, conduits, and detecting region of Lee have a width sized to receive a single droplet at a time such that the droplets flow through the coils, conduit, and detecting regions in a single file line."). The specifications also confirm that droplet-based systems were well-known. 722 Patent at 9:29-31 ("Technologies for precise and efficient formation of the various fluidic systems and devices of the invention from silicone are known."); *see also id.* at 9:16-10:56,

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