

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ABS GLOBAL, INC.,
GENUS, PLC,
Petitioner,

v.

CYTONOME/ST, LLC,
Patent Owner.

IPR2021-00088
Patent 10,583,439 B2

Before LYNNE H. BROWNE, SCOTT A. DANIELS, and
JAMES A. WORTH, *Administrative Patent Judges*.

WORTH, *Administrative Patent Judge*.

DECISION
Final Written Decision
Determining No Challenged Claims Unpatentable
35 U.S.C. § 318(a)

I. INTRODUCTION

This is a Final Written Decision in an *inter partes* review that addresses claims 1, 2, 6, 8, and 9 (the “challenged claims”) of U.S. Patent No. 10,583,439 B2 (Ex. 1001, “the ’439 patent”). We have jurisdiction under 35 U.S.C. § 6(b). This Final Written Decision is issued pursuant to 35

U.S.C. § 318(a). Having reviewed the arguments of the parties and the supporting evidence, we find that Petitioner has not demonstrated by a preponderance of the evidence that claims 1, 2, 6, 8, and 9 are unpatentable.

A. Background and Summary

On October 26, 2020, ABS Global, Inc. and Genus, PLC (collectively, “Petitioner”) filed a Petition (Paper 1, “Pet.”) requesting an *inter partes* review of claims 1, 2, 6, 8, and 9 of the ’439 patent. On February 10, 2021, Cytonome/ST, LLC (“Patent Owner”) filed a Preliminary Response (Paper 8, “Prelim. Resp.”). With authorization, the parties filed further pre-institution briefing related to the construction of the term “fluid focusing region” and collateral estoppel, as follows. On March 5, 2021, Petitioner filed a reply to the Preliminary Response (Paper 12, “Prelim. Reply”). On March 12, 2021, Patent Owner filed a sur-reply (Paper 14, “Prelim. Sur-Reply”).

On May 4, 2021, we instituted an *inter partes* review of claims 1, 2, 6, 8, and 9 of the ’439 patent. Paper 18 (“Dec. Inst.”).

On July 29, 2021, Patent Owner filed a Response to the Petition. Paper 21 (“PO Resp.”). On October 21, 2021, Petitioner filed a Reply. Paper 23. On December 10, 2021, Patent Owner filed a Sur-reply. Paper 27.

On February 2, 2022, an oral argument was held in the proceeding, a transcript of which has been entered in the record. Paper 37 (“Tr.”).

On February 4, 2022, we issued an Order (Paper 34) inviting supplemental briefing on claim construction for claim 1, e.g., on whether claim 1 requires that the device of claim 1 be in any particular orientation to meet the claim.

On February 11, 2022, Petitioner filed a supplemental brief on claim construction. Paper 35 (“Pet. Supp. Br.”). On February 18, 2022, Patent Owner filed a supplemental brief on claim construction. Paper 38 (“PO Supp. Br.”).

Petitioner relies on the declaration and supplemental declaration of David Issadore, Ph.D. Ex. 1003; Ex. 1054. Patent Owner relies on the declaration and supplemental declaration of Don W. Arnold, Ph.D. Ex. 2001; Ex. 2006.

B. Real Parties-in-Interest

Petitioner identifies ABS Global, Inc. and Genus PLC as real parties-in-interest. *See* Pet. 3. Patent Owner identifies Cytonome/ST, LLC as the real-party-in-interest. Paper 5, 1.

C. Related Matters

The parties note as related litigation in federal district court, *Inguran, LLC v. ABS Global, Inc.*, No. 3:20-cv-00085-wmc (W.D. Wis., filed Mar. 18, 2020) and *Inguran, LLC v. ABS Global, Inc.*, No. 3:20-cv-00349-wmc (W.D. Wis., filed Apr. 15, 2020). *See* Pet. 3–4; Paper 5, 1.

D. The ’439 Patent

The ’439 patent is titled “Hydrodynamic Focusing Apparatus and Methods” and relates to “hydrodynamic focusing, in particular, in a microfluidic device,” and more specifically relates to “systems and methods for producing a sheath flow in a flow channel and, in particular, in a micro channel in a microfluidic device.” Ex. 1001, code (54), 1:14–19.

According to the ’439 patent, sheath flow is a particular type of laminar flow in which one layer of sample fluid, or a particle, is surrounded by another layer of focusing fluid on more than one side. *Id.* at 1:23–25. The ’439 patent discloses that the process of confining a particle stream in a

fluid is referred to as a “sheath flow” configuration. *Id.* at 1:25–27. The ’439 patent describes an example with a single file row:

For example, in a sheath flow configuration, a sheath fluid may envelop and pinch a sample fluid containing a number of particles. The flow of the sample fluid containing particles suspended therein may be narrowed almost to the outer diameter of particles in the center of the sheath fluid. The resulting sheath flow flows in a laminar state within an orifice or channel so that the particles are aligned and accurately pass through an orifice or channel in a single file row.

Id. at 1:29–35.

In its Background section, the ’439 patent states that then-conventional devices that had been employed to implement sheath flow had relatively complex designs and were relatively difficult to fabricate. *Id.* at 1:54–56.

Figure 3A of the ’439 patent, reproduced below, depicts an embodiment of such a device:

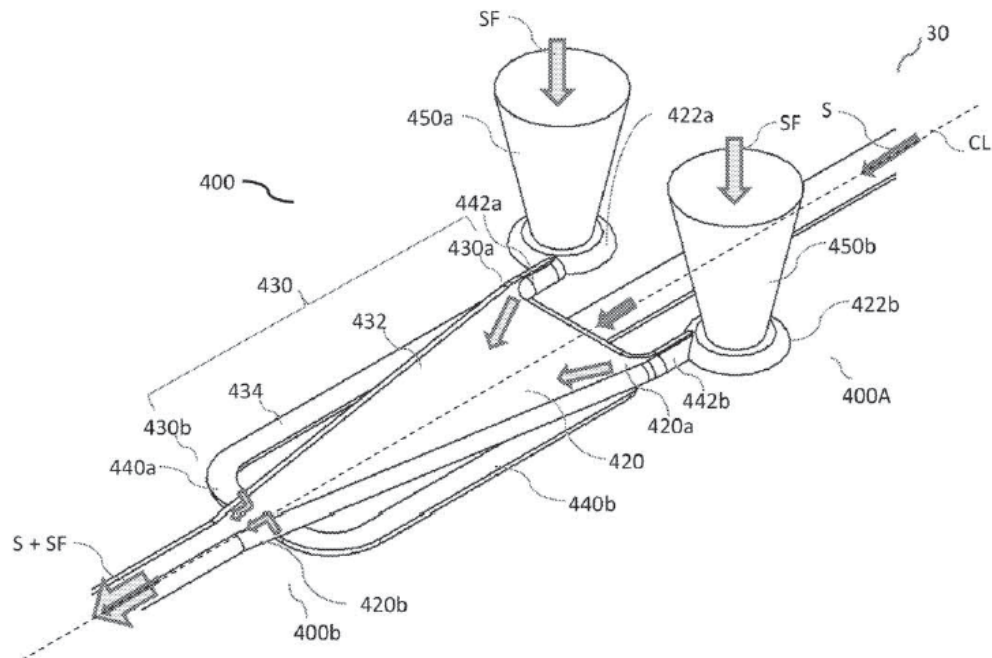


Figure 3A is a top perspective view of a portion of a flow channel geometry with arrows schematically depicting flow of sample fluid S along centerline CL and focusing fluid SF. *Id.* at 4:7–10.

Figure 3A shows a portion of micro channel 30 having core stream forming geometry 400. *Id.* at 10:11–12. Core stream forming geometry 400 may be fabricated in plastics, polycarbonate, glass, metals, or other suitable materials using microfabrication, injection molding, stamping, machining, 3D printing or by other suitable fabrication techniques. *Id.* at 10:38–41. As such, core stream forming geometry 400 may be formed in a single substrate layer, or by a plurality of stacked layers. *Id.* at 10:41–43.

Sample fluid S flowing through micro channel 30 may enter core stream forming geometry 400 along longitudinal centerline CL. *Id.* at 10:13–17. Focusing fluid may enter the core stream forming geometry 400 at upstream region 400a of the core stream forming geometry and also at downstream region of the core stream forming geometry 400b. *Id.* at 10:20–24.

Two sheath inlet ports 450a, 450b are associated with micro channel 30. *Id.* at 10:54–55. Sheath fluid channels 440a and 440b extend, respectively, from sheath fluid inlet ports 450a and 450b. *Id.* at 10:58–60. Each sheath fluid channel 440 extends from upstream region 430a of the fluid focusing region 430 to downstream region 430b of the fluid focusing region 430. *Id.* at 10:60–62. Each sheath fluid channel 440 is configured to transport focusing fluid SF from sheath inlet port 450 to micro channel 20. *Id.* at 10:63–66.

Lateral fluid focusing chamber 420 is widest at its upstream end 420a and narrowest at its downstream end 420b. *Id.* at 11:24–26. Between upstream end 420a and downstream end 420b, the chamber 420 substantially

linearly tapers symmetrically with respect to the centerline CL in the lateral direction. Between upstream end 420a and downstream end 420b, the chamber 420 has a substantially constant thickness. *Id.* at 11:26–32.

Sample fluid S enters focusing chamber 420 from below via a symmetrically centered opening having a length equal to overlap OL region and a width equal to the width of micro channel 30. *Id.* at 11:60–63. As the chamber 420 narrows or tapers in the lateral direction as the fluid travels downstream, an increasing inward force from the lateral sides of the chamber 420 acts on the fluid within the chamber, thus tending to focus (e.g., constrict) sample S in the middle of the lateral fluid focusing chamber 420. *Id.* at 12:3–8. The increasing inward force further tends to accelerate both the sheath and the sample within fluid focusing region 430 in flow channel 30. *Id.* at 12:8–11.

At downstream end 420b of lateral fluid focusing chamber 420, the vertical fluid focusing component provides a vertical upwardly-directed focusing force. *Id.* at 12:12–14. Specifically, vertical fluid focusing channels 440a, 440b introduce focusing fluid SF¹ from inlet ports 450a, 450b into lateral fluid focusing chamber 420 at downstream end 420b. *Id.* at 12:14–17. Thus, the vertical fluid focusing channels 440a, 440b introduce focusing fluid SF into fluid focusing chamber 420 at vertical focusing flow inlet 446 from below. *Id.* at 12:23–26.

¹ The Specification uses the term “FS” here but we understand this to be a typographical error and to refer to focusing fluid SF, as is used elsewhere. *See id.*

Figure 3D of the '439 patent, reproduced below, depicts a cross-sectional view of the same embodiment as Figure 3A (*see id.* at 4:19–21):

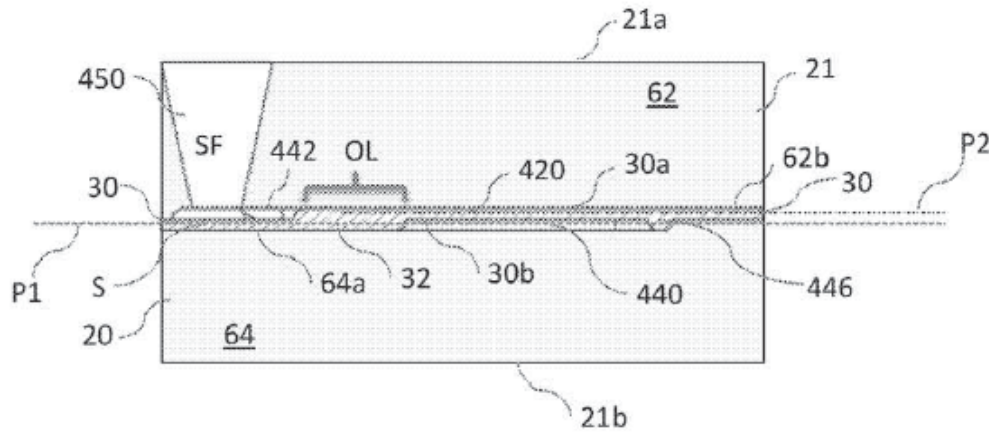


Figure 3D is a cross-sectional view through a line marked in Figure 3C (which is not reproduced here), i.e., a cross-sectional view through what appears to be a line down the middle of the microfluidic unit. *See id.* at 4:19–21, Fig. 3C.

As depicted in Figure 3D, sample S enters the fluid focusing region 430 at upstream end 430a in plane P1 below plane P2 in which the lateral fluid focusing chamber 420 is located. *Id.* at 12:37–40. Sample S is directed upward from plane P1 into plane P2 of lateral focusing chamber 420 in the overlapped region OL. *Id.* at 12:40–43. Then, at downstream end 430b of fluid focusing region 430, the laterally focused sample within a sheath of focusing fluid (S+SF) is vertically focused upward by the introduction of focusing fluid SF at vertical focusing flow inlet 446 from below. *Id.* at 12:43–47.

Figure 6A of the '439 patent is reproduced below, with coloring and annotations added (*see* Pet. 15):

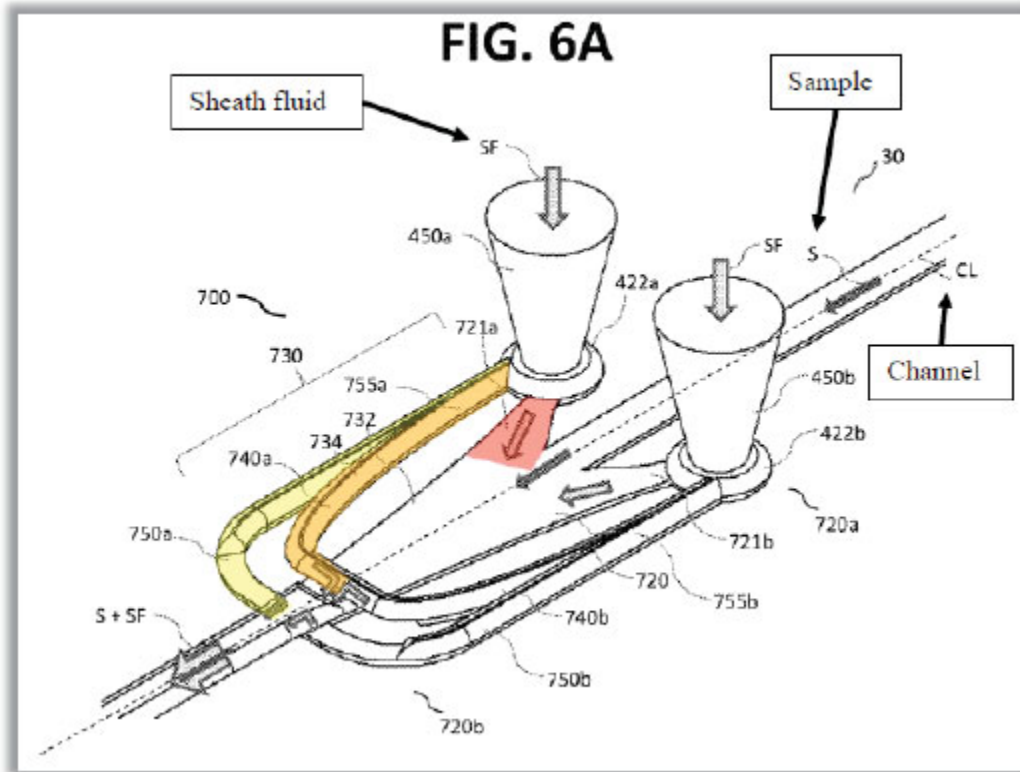


Figure 6A is a top perspective view of a portion of a flow channel geometry with arrows schematically depicting flow of sample fluid and focusing fluid in accordance with certain embodiments. *Id.* at 4:46–49. This figure has, among other features, lateral fluid focusing chamber 720 with tapered inlet 721 (shown with red highlighting), as well as first and second sets of vertical fluid focusing channels 740, 750 (shown with orange and yellow highlighting). *See id.* at 17:1–8.

E. Illustrative Claim

Claim 1, reproduced below, is the sole independent claim challenged in the Petition and is illustrative of the subject matter:

1. A microfluidic assembly for use with a particle processing instrument, the microfluidic assembly comprising:

a substrate; and

a flow channel formed in the substrate, the flow channel having:

- an inlet configured to receive a sample stream;
- a fluid focusing region ***configured to focus the sample stream***, the fluid focusing region having a lateral fluid focusing feature, a first vertical fluid focusing feature, and a second vertical fluid focusing feature, the lateral, the first vertical, and the second vertical fluid focusing features provided at different longitudinal locations along the flow channel, wherein a bottom surface of the flow channel lies in a first plane upstream of the first and second vertical fluid focusing features and the bottom surface of the flow channel shifts vertically upward to lie in a second plane downstream of the first and second vertical focusing features; and
- an inspection region at least partially downstream of the fluid focusing region.

Ex. 1001, 18:43–63 (emphasis added).

F. Prior Art and Asserted Grounds

Petitioner asserts that claims 1, 2, 6, 8, and 9 would have been unpatentable on the following grounds (Pet. 4):

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1, 2, 6, 8	102 ²	Simonnet ³

² The Leahy-Smith America Invents Act (“AIA”), Pub. L. No. 112-29, 125 Stat. 284, 287–88 (2011), amended 35 U.S.C. §§ 102 and 103. It is undisputed on this record that the priority date of the ’439 patent is March 14, 2013. *See* Pet. 5–6. Because the application leading to the ’439 patent was filed before the effective date of the relevant amendment, the pre-AIA version of §§ 102 and 103 applies.

³ Claire Simonnet and Alex Groisman, *High-Throughput and High-Resolution Flow Cytometry in Molded Microfluidic Devices*, 78 Anal. Chem. 5653–5663 (2006) (Ex. 1005, “Simonnet”).

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1, 2, 6, 8	103	Simonnet
8	103	Simonnet, Kim ⁴
9	103	Simonnet, Kummrow ⁵

II. ANALYSIS

A. Legal Standards

A “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.’” *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008) (quoting *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983)). “A single prior art reference may anticipate without disclosing a feature of the claimed invention if such feature is necessarily present, or inherent, in that reference.” *Allergan, Inc. v. Apotex Inc.*, 754 F.3d 952, 958 (Fed. Cir. 2014).

A patent claim is unpatentable under 35 U.S.C. § 103 if the differences between the claimed subject matter and the prior art are such that the subject matter, as a whole, would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. 35 U.S.C. § 103; *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). “[W]hen a patent claims a structure already known in the prior art that is altered by the mere substitution of one element for

⁴ Dong Sung Kim et al., *An efficient 3-dimensional hydrodynamic focusing microfluidic device by means of locally increased aspect ratio*, 86 *Microelectronic Engineering* 1343–1346 (2009) (Ex. 1015, “Kim”).

⁵ A. Kummrow et al., *Microfluidic structures for flow cytometric analysis of hydrodynamically focussed blood cells fabricated by ultraprecision micromachining*, 9 *Lab Chip* 972–981 (2009) (Ex. 1006, “Kummrow”).

another known in the field, the combination must do more than yield a predictable result.” *KSR*, 550 U.S. at 416 (citing *United States v. Adams*, 383 U.S. 39, 50–51 (1966)). The question of obviousness is resolved based on underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) objective evidence of non-obviousness.⁶ *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

B. Level of Ordinary Skill in the Art

Petitioner argues that a person of ordinary skill in the art (POSA) at the relevant time would have had a bachelor’s or master’s degree in the field of bioengineering, mechanical engineering, chemical engineering, or analytical chemistry, or a related field and at least three years of experience in designing or developing microfluidic systems. Pet. 4. Petitioner also argues, *inter alia*, that a skilled artisan would have been familiar with the asserted art and would have known how to configure those systems to focus particles in a variety of directions. *See id.* at 5 (citing Ex. 1003 ¶ 75).

In the Decision on Institution, we set forth our preliminary determination that a person of ordinary skill in the art at the relevant time would have had a bachelor’s or master’s degree in the field of bioengineering, mechanical engineering, chemical engineering, or analytical chemistry, or a related field and at least three years of experience in designing or developing microfluidic systems. *See* Dec. 10–11. Patent Owner does not dispute this definition. *See* PO Resp. 4.

⁶ The parties do not present or address objective evidence of non-obviousness in this proceeding.

After considering all evidence and arguments anew, we determine that it is proper to maintain our definition of the level of skill in the art.

C. Claim Construction

We construe each 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.” 37 C.F.R. § 42.100(b). Under this standard, claim terms are generally given their plain and ordinary meaning as would have been understood by a person of ordinary skill in the art at the time of the invention and in the context of the entire patent disclosure. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (*en banc*).

Petitioner requests construction of the terms “focusing” and “fluid focusing feature.” Pet. 17–22. In the Decision on Institution, we provided preliminary construction of the terms “focusing” and “fluid focusing region.” Dec. Inst. 11–21. Patent Owner requests that the Board revise its construction of “focusing” and also makes certain arguments about focusing in the claim phrase “configured to focus the sample stream”; requests that the Board revise its construction of “focusing region”; and argues that it is not necessary to construe “fluid focusing feature” but provides arguments in the event that the Board reaches that issue. PO Resp. 4–17. We address the construction of “focusing,” “configured to focus the sample stream,” and “fluid focusing region” below. *See Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) (claims are construed only to the extent necessary to resolve a dispute).

We also solicited post-hearing briefing on the following questions, which we also address, in part, to the extent necessary to resolve this dispute:

1. Does the language from the Specification of the '439 patent (Ex. 1001, 6:4–10) mean that a device can meet the claim if oriented in any manner, as a matter of claim construction?

2. If not, and a device can only meet the claim in one orientation, does that create a problem under *IPXL*, i.e., where there would be a mixing of a device and method of use in a claim? See *IPXL Holdings, L.L.C. v. Amazon.com, Inc.*, 430 F.3d 1377, 1384 (Fed. Cir. 2005).

3. If a device can only meet the claim in one orientation, does that create uncertainty as a matter of notice to the public about whether a device meets the claim, e.g., if the same device has been made, used, or sold in a different orientation?

4. Is the “wherein” clause part of the “configured to” clause? If so, does that support an understanding that the device meets the claim in any orientation?

Paper 34, 3.

1. “*focusing*”; “*configured to focus the sample stream*”

Petitioner argues that “focusing” should be construed to mean “narrowing, pinching, or otherwise confining a sample fluid with sheath fluid.” Pet. 17 (citing Ex. 1003 ¶¶ 98–101). Petitioner asserts that focusing was a term commonly used in the art with this meaning. *Id.* at 17–18 (citing Ex. 1003 ¶ 101; Ex. 1031, 167; Ex. 1013⁷, 247; Ex. 1007⁸, 3863; Ex. 1011⁹,

⁷ Albert Folch, *Introduction to BioMEMS*, CRC Press (2013) (Ex. 1013, “Folch”). It is unclear on this record whether Folch is prior art or merely a reference that is contemporaneous with the '439 patent. In either event, we determine that Folch may be used as evidence of the meaning of the term “focus” to a person of ordinary skill at the time of the invention.

⁸ Knight et al., *Hydrodynamic Focusing on a Silicon Chip: Mixing Nanoliters in Microseconds*, 80(17) *Physical Review Letters* 3863 (Apr. 27, 1998) (Ex. 1007, “Knight”).

⁹ Wada et al., U.S. Patent No. 6,506,609 B1, iss. Jan. 14, 2003 (Ex. 1011).

8:11–14). Petitioner argues that the ’439 patent uses the term “focusing” in a manner consistent with its ordinary meaning and that the applicants gave no indication that they intended to depart from the ordinary meaning. *Id.* at 18 (citing Ex. 1001, 1:27–29, 10:29–31, 12:5–7, 12:12–14, 15:42–46; Ex. 1003 ¶¶ 98–101).

In the Decision on Institution, we set forth our preliminary construction of “focusing” to mean “pinching, confining, squeezing, or constricting.” Dec. 14. In particular, we reviewed contemporaneous and prior art usages where “focusing” was variously referred to as “pinching” or “squeezing” and found this to be consistent with the disclosure in the Specification that an increasing force from the lateral sides is “*tending to focus (e.g., constrict)*” the sample. *See* Dec. Inst. 14 (citing Ex. 1001, 12:3–8; Ex. 1013, 247; Ex. 1011, 8:11–14) (emphasis in Decision).

Patent Owner argues that “focusing” requires a “sheath flow” with only a single sample stream, and requests that the Board revise its construction to “pinching, confining, squeezing, or constricting a single sample stream with sheath flow.” PO Resp. 5–11.

a) Whether “focusing” requires “sheath flow”

Patent Owner argues that the Specification describes using “sheath flow” to focus a sample stream in every embodiment (citing Ex. 1001, 12:62–13:2, 13:36–38; Ex. 2006 ¶¶ 39–47); that the background section of the Specification contains a definition of sheath flow (citing Ex. 2006 ¶¶ 10, 35 (quoting Ex. 1001, 1:23–25); that Dr. Issadore conceded during cross-examination that he could not see or imagine focusing without sheath flow (citing Ex. 2008, 92:11–20, 187:14–188:9, 189:14–24; 190:16–191:3); that an authority relied on by Petitioner’s expert uses the terms hydrodynamic focusing and sheath flow interchangeably (citing Ex. 2006 ¶¶ 11, 38, 48–52;

Ex. 1032, 148); and that a person of ordinary skill sought to achieve sheath flow so that the particles in a sample can be accurately inspected in a flow cytometer (citing Ex. 2006 ¶¶ 12–14, 38). PO Resp. 4–7.

Petitioner argues that “sheath flow” is used in different ways in the art, where sometimes it is used interchangeably with “sheath fluid” and other times it is used to refer to a laminar-flow configuration where one layer of fluid surrounds another on more than one side. Pet. Reply 2, 4–5 (citing Ex. 1054 ¶¶ 4, 6–8; Ex. 1038 ¶ 135; Ex. 1053, 88:4–15, 95:7–14; Ex. 1055, 4555; Ex. 1003 ¶ 47).¹⁰ Petitioner argues that Dr. Issadore testified that “focusing” requires “sheath fluid,” and “insomuch as sheath flow is sheath fluid . . . flowing in a laminar way,” then you “couldn’t have focusing without—without that” (citing Ex. 2008, 92:11–20, 92:24–95:10). Pet. Reply 3. Petitioner argues that Dr. Issadore did not testify that “focusing” requires surrounding a sample on multiple sides with sheath, or that it forecloses a split sample. *Id.*

Petitioner argues that skilled artisans routinely used the term “focusing” to describe introducing sheath fluid to confine a sample from just one side, which would not meet the sheath flow requirement advanced by Patent Owner. Pet. Reply 4–5 (citing, e.g., Ex. 1054 ¶¶ 8–9; Ex. 1039, Fig. 3; Ex. 1040, 26–27, Fig. 1, 2; Ex. 1041, 3746, Figs. 2, 3; Ex. 1042, 6:54–57, Fig. 4). Petitioner argues that Wada is an example of the prior art where there was “focusing” but only sheath fluid on one side and thus not sheath flow. Pet. Reply 4 (citing, e.g., Ex. 1011, 9:40–45, Figs. 16, 23, 24).

¹⁰ Petitioner argues that Patent Owner argues for a third definition of sheath flow, i.e., one and only one layer of sample fluid surrounded by sheath fluid. Pet. Reply 2–3. We address below whether focusing requires a single stream.

Before we address whether “focusing” requires sheath flow, we first address what is meant by sheath flow. We use the definition of “sheath flow” found in the Specification, i.e., sheath flow is a particular type of laminar flow in which one layer of sample fluid, or a particle, is surrounded by another layer of focusing fluid on more than one side. Ex. 1001, 1:23–25.

Nevertheless, just because the Specification contains a definition of sheath flow does not mean that “focusing” requires sheath flow. In other words, the Specification does not contain a definition of “focusing” that defines “focusing” as requiring “sheath flow.” As discussed above, the Specification does state “focusing (e.g., constricting).” *See also* Tr. 41:22–42:8 (discussing the Specification of the ’439 patent). Whether or not this disclosure rises to the level of a definition, it indicates that focusing is understood to be constricting and does not mention “sheath flow.” Although sheath flow may, in certain cases, be a natural result of having multiple fluid focusing features (*see* Ex. 1001, 14:6), the claim itself does not require that focusing include sheath flow.¹¹

¹¹ In terms of resolving the dispute between the parties, the real question appears to be whether the sample stream that exits the focusing region must be a single sample stream or whether it may encompass split sample streams, a question that we address in the next subsection. Patent Owner’s ultimate argument appears to be that “focusing” requires a single sample stream because “focusing” requires sheath flow and sheath flow requires a single sample stream. However, we agree with Petitioner that persons of ordinary skill could still refer to split streams as having “sheath flow” (*see* Ex. 1054 ¶ 11; Ex. 1043, 2215, Fig. 10 and caption (“separated two-sample 3D sheath flow”); Ex. 1044, 2 (“multiple core-sheath flow”), and therefore, even if we agreed with Patent Owner that focusing requires sheath flow, that would not clarify whether “focusing” precludes split sample streams. In any event, we conclude that focusing does not require sheath flow.

We recognize that there are examples in the Specification where there is sheath flow. *E.g.*, Ex. 1001, 5:30–32 (“Certain embodiments described herein relate [to] systems and methods for producing a sheath flow . . .”), 10:35–37 (“The illustrated core stream forming geometry 400 provides improved sheath flow capabilities and thus improved sample focusing capabilities.”). However, case law generally counsels against importing limitations from the Specification into the claims. *See, e.g., Phillips v. AWH Corp.*, 415 F.3d 1303, 1323 (“To avoid importing limitations from the specification into the claims, it is important to keep in mind that the purposes of the specification are to teach and enable those of skill in the art to make and use the invention and to provide a best mode for doing so.”).¹² We, therefore, do not import “sheath flow” into the definition of focusing.

Further, as Petitioner observes (Pet. Reply 5 n.3), the applicant in the prosecution history considered but ultimately did not use claim language that would have expressly limited a claim to “sheath flow.” *See* Ex. 1002, 1074 (claim 12). The original claim proposed during prosecution read “The microfluidic assembly of claim 1, wherein the flow channel further

¹² We recognize that there are certain instances in the case law where the Specification could give rise to an implied disclaimer, *e.g.*, where the Specification disparages the presence of a feature in the prior art and where there is the absence of the feature in every embodiment. *See In re Abbott Diabetes Care Inc.*, 696 F.3d 1142, 1149 (Fed. Cir. 2012). However, it is preferred that the Specification expressly define a special usage of a claim term and expressly disclaim features. Here, the Specification states “*Certain* embodiments described herein relate [to] systems and methods for producing sheath flow” (Ex. 1001, 5:30–32) (emphasis added), and although this discussion appears to relate to the claimed embodiment, we note that the language “[c]ertain embodiments” is not the language of a disclaimer that would apply to all cases.

comprises a sheath inlet in fluid communication with the sheath source, and wherein a sample inlet is positioned within a sheath flow created by the sheath inlet to facilitate a co-axial flow of sheath and sample.” *Id.* Thus, the applicant could have chosen to expressly claim “sheath flow” and did not do so.

Our conclusion is consistent with the usage in the art, such as Wada, where focusing is described to occur even with sheath fluid being applied on one side of a sample stream to pinch the sample stream. *See* Ex. 1054 ¶ 7 (discussing Ex. 1011, 7:15–17, 9:40–45, Fig. 16); Ex. 1011, 9:40–52. Figure 16 of Wada, annotated by Dr. Issadore (Ex. 1054 ¶ 7), is reproduced below:

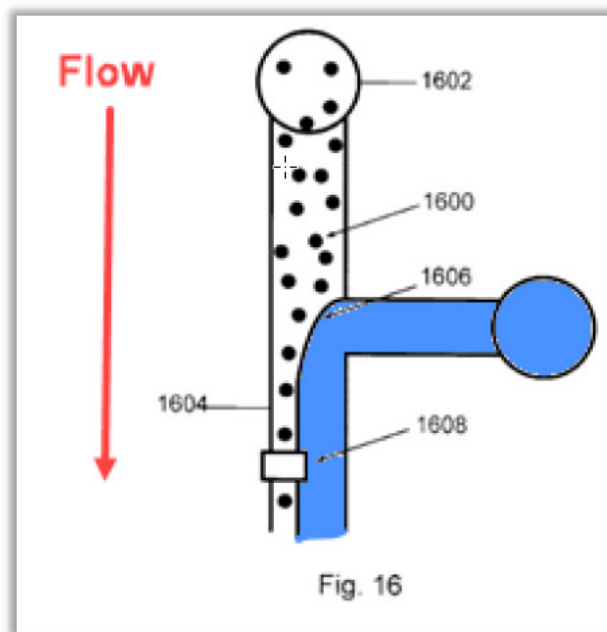


Figure 16 of Wada shows a T-junction microchannel configuration for hydrodynamically focusing cells for use in, e.g., flow cytometry. Ex. 1011, 7:15–17. Dr. Issadore’s annotation shows an arrow designating the direction of flow in red, and stream 1606 in blue that is used to focus particles 1600. *See* Ex. 1011, 9:40–52.

Patent Owner relies on its cross examination of Dr. Issadore to contend that “focusing” requires “sheath flow.” However, based on our review of the deposition testimony, Dr. Issadore’s concession is not as clear as Patent Owner argues. The discussion of “sheath flow” occupies several pages, but the central passage appears to be as follows:

[COUNSEL] . . . Using your understanding of “sheath flow” and “focusing,” can a microfluidic device focus a sample without using sheath flow?

[DR. ISSADORE] Under the definition I give in Paragraph 98, you couldn’t have focusing without sheath fluid. And insomuch as sheath flow is sheath fluid in a -- you know, flowing in a laminar way, as described in the previous paragraph we discussed, then I -- then you couldn’t. You couldn’t have focusing without -- without that.

Ex. 2008, 92:11–20. Dr. Issadore’s reference to paragraph 98 appears to refer to paragraph 98 of his initial declaration, which is the subject of the deposition. *See* 37 C.F.R. § 42.51(b)(1)(ii). Paragraph 98 of the declaration contains a definition of “focusing” as follows: “The ordinary meaning in the context of the ’439 Patent of the term ‘*focusing*’ is ‘narrowing, pinching, or otherwise confining a sample fluid with sheath fluid.’” Ex. 1003 ¶ 98. It is true that earlier in the deposition, Dr. Issadore agreed to apply a definition of sheath flow for the deposition: “‘Sheath flow is a particular type of laminar flow in which one layer (for example, the sheath) surrounds another layer (for example, a sample) on more than one side.’” *See* Ex. 2008, 90:23–91:9. However, in the portion of the deposition reproduced and indented above, Dr. Issadore appears to use a different definition of “sheath flow,” i.e., “insomuch as sheath flow is sheath fluid in a -- you know, flowing in a laminar way.” *See* Ex. 2008, 92:11–20. Further, the definition that Dr. Issadore refers back to, i.e., “in the previous paragraph we discussed,”

appears to be the definition of “focusing” in paragraph 98 of the declaration and not the definition of “sheath flow” discussed earlier in the deposition. Accordingly, all that Dr. Issadore clearly concedes to is that focusing involves sheath fluid flowing in a laminar manner. We agree with Petitioner that Dr. Issadore did not indicate agreement with Patent Owner that “focusing” requires sheath flow in the sense that sheath fluid must surround a layer of sample on more than one side.

We also agree with Petitioner that the Specification uses “SF” to refer to both sheath flow and sheath fluid, and thus uses the terms interchangeably in places. For example, the Specification refers to fluid SF sometimes as “focusing fluid SF” and sometimes as “sheath flow SF.” *See, e.g.*, Ex. 1001, 10:17 (“focusing fluid SF”), 12:65 (“sheath flow SF”), 13:11 (“sheath flow SF”), 13:16 (“sheath flow SF”). Therefore, the Specification is of limited assistance in determining whether it is only sheath fluid or also sheath flow that is required.

Thus, we determine that there is insufficient evidence to import a requirement of sheath flow into the definition of focusing.

b) Whether “focusing” requires a single stream

Patent Owner also argues that focusing requires focusing into a single stream based on its arguments that every embodiment in the Specification produces a focused core stream along the centerline of the channel (citing Ex. 1001, 5:27–29, 10:12–16, 10:28–31, 12:65–13:2, 13:48–58, 16:62–65, Figs. 4A–6D; Ex. 2006 ¶¶ 19, 44, 54, 56–60, 63); that the presence of a second stream would block the sorting of the selected particle in a subsequent particle sorting region (citing Ex. 1001, 5:15–29, 18:6–11; 13:53–58; Ex. 2001 ¶¶ 67, 86–89, 141; Ex. 2006 ¶¶ 14, 19, 20, 36, 65); and that in the presence of a second stream, particle detection accuracy decreases

as the sheath fluid flow rate increases (citing Ex. 2006 ¶ 17). PO Resp. 8–10. Patent Owner also argues that the language of claim 2 referring to “a centerline of the sample stream” indicates that the sample stream of claim 1, from which claim 2 depends, is a single sample stream, and that it would be absurd to have a centerline of two sample streams. PO Resp. 11 (citing *Wright Med. Tech., Inc. v. Osteonics Corp.*, 122 F.3d 1440, 1445 (Fed. Cir. 1997); *AIA Eng’g Ltd. v. Magotteaux Int’l S/A*, 657 F.3d 1264, 1276 (Fed. Cir. 2011) (“We strive, where possible, to avoid nonsensical results in construing claim language.”); Ex. 2006 ¶¶ 61–64). Patent Owner also argues that the term “the sample stream” in claim 1 is singular. PO Sur-reply 2.

Petitioner argues that skilled artisans have long recognized that a device can “focus” a sample even if it splits the sample into multiple sub-streams, and that this may even be desirable for certain applications. PO Resp. 5–6 (citing Ex. 1054 ¶ 10; Ex. 1014, 1483; Ex. 1020, 114104-2; Ex. 1005, 5657; Ex. 1039, 326). Petitioner argues that “sheath flow” is not part of a proper construction of “focusing,” but even if “sheath flow” were required, skilled artisans routinely used “sheath flow” to describe devices with split- or multiple-core samples surrounded by sheath fluid. Pet. Reply 6 (citing Ex. 1054 ¶ 11; Ex. 1043, Fig. 10, 2215; Ex. 1044, 2; Ex. 1045, 14:55–57).

Petitioner argues that dependent claim 2 provides no justification for departing from the ordinary meaning of “focusing” because, according to Petitioner, even a split sample has a centerline, which can be “at the center of flow channel,” i.e., between the two branches of the split sample. Pet.

Reply 7 (citing Pet. 58; Ex. 1003 ¶ 194; Ex. 1054 ¶ 12; Ex. 1005, 5657; Ex. 1020, 114104-2; Ex. 1014, 1483)).¹³

¹³ Patent Owner also makes certain arguments that a split stream would be disfavored if the purpose of the device were to detect sample or to accelerate the rate of flow. *See, e.g.*, PO Resp. 1 (“accuracy in the system decreases sharply as the sheath flow rate increases which is the opposite of what happens with focusing”), 7 (citing, *e.g.*, Ex. 2006 ¶¶ 12–14, 38). Petitioner disagrees, and points to testimony of Dr. Issadore that a measure of accuracy increased as the relative sheath flow rate increased. Pet. Reply 18–19 (Ex. 1054 ¶ 27); Ex. 2006 ¶ 80. We agree that f_d/f_0 [the ratio of the number of particles detected per second to the total particle fluxes] is greatest for the highest relative sheath flow rate [the flow rate of the sheath fluid relative to the flow rate of the sample] as described in Dr. Issadore’s Reply Declaration. *See* Ex. 1054 ¶¶ 23–24, 26–27 (citing, *e.g.*, Ex. 1005, 5659). In any event, we determine that Patent Owner’s arguments regarding accuracy go to the purpose of the claimed invention but do not, on their own, limit the claims.

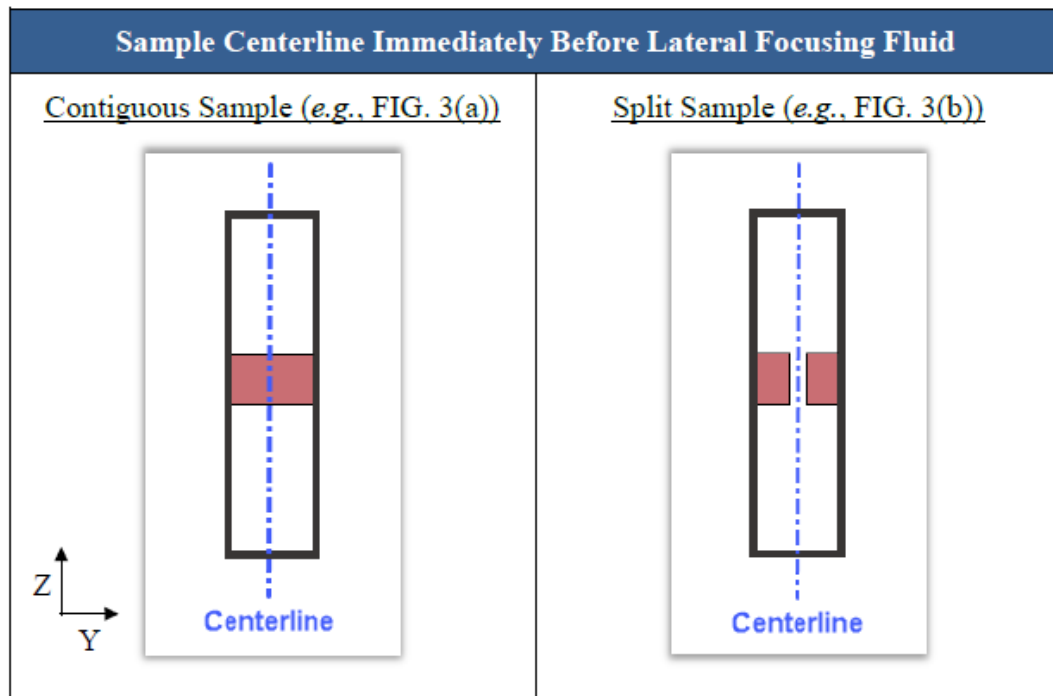
We recognize Patent Owner’s arguments that increasing the flow rate may cause split streams to drift further apart and that this would not be “focusing.” PO Resp. 10 (“when there are multiple sample streams in a channel, increasing the sheath fluid flow rate will cause the sheath fluid to split the sample streams farther apart) (citing Ex. 2006 ¶ 17). However, the claim is silent as to changes in flow rate, and although the burden rests with Petitioner, Patent Owner has not adequately explained why there could not be a narrowing of the sample overall (“focusing”) when there is a split stream. We have reviewed paragraph 17 of the Arnold Declaration and although Dr. Arnold explains that in a split stream, the two sample streams move away from the center of the channel, Dr. Arnold does not adequately explain why this would necessarily prevent constricting of the sample overall. We recognize that the flow rate may increase, for example, as a device narrows. *See, e.g.*, Ex. 2006 ¶ 17 (citing Ex. 1031, 166–168). We regard the issue of whether the sample narrows as a factual issue with respect to the application of the claim term “focusing” to each prior art device, rather than a claim construction issue.

As above, we do not agree with Patent Owner that the claims are limited to “sheath flow.” However, we are persuaded by Patent Owner’s argument that “the sample stream” is singular in this case.

Although we recognize the rule that the article “a” or “an” is presumed to mean one or more absent a clear intent to limit “a” or “an” to one, *Convolve, Inc. v. Compaq Computer Corp.*, 812 F.3d 1313 (Fed. Cir. 2016), and the Specification also states that “a” or “an” means “one or more” (*see* Ex. 1001, 18:27–30), we agree with Patent Owner that such an interpretation would not be consistent with the claim language in this case.¹⁴

For example, in claim 2, there is “a centerline of the sample stream.” We do not agree with Petitioner that there can be a “centerline” of the sample stream in the case of a split sample. Petitioner’s contentions are illustrated with further reference to the figures below.

¹⁴ Further, our interpretation is consistent with the plain and ordinary meaning of “the sample stream” as singular. *Cf. Apple Inc. v. MPH Techns. Oy*, Case 28 F.4th 254, 261–262 (Fed. Cir. 2022) (presumption that a plural refers to two or more items is an application of the general rule that claim terms are usually given their ordinary meaning). We do acknowledge that in *Apple*, there was no rule of construction provided in the Specification. *See id.* at 262.



These are figures reproduced from paragraph 34 of Dr. Issadore's Reply Declaration (Ex. 1054), which show where Dr. Issadore would draw a centerline in a contiguous sample and a split sample, e.g., in a cross section of Simonnet's device immediately before the symmetrical introduction of sheath from the sides, and where the outer black represents the channel walls. Ex. 1054 ¶ 34. Dr. Issadore opines, in the context of the prior art, that when the sample is split, the centerline of the stream is in the middle of the flow channel. Ex. 1054 ¶ 12 (citing Ex. 1003 ¶ 194). Dr. Issadore also opines that a person of ordinary skill in the art would simply draw a centerline through the center of the device where the sample enters, which in Simonnet is through port B. *See* Ex. 1054 ¶ 36. However, the claim refers to the centerline of the sample stream, and not simply the center of the device.¹⁵

¹⁵ We note that Dr. Issadore does not provide a basis for his opinion that the centerline of the sample stream would be the centerline of the flow channel

Although dependent claims 2 and 23 recite a “centerline of the sample stream,” by contrast dependent claim 5 recites “a centerline of the flow channel” and dependent claim 20 recites “a centerline of the microfluidic channel.” This difference in language indicates that the “centerline of the sample stream” is different than the “centerline of the flow channel” or “centerline of the microfluidic channel.” Dr. Issadore’s testimony is more consistent with dependent claims 5 and 20 than dependent claim 2 (at issue here) or dependent claim 23.¹⁶

Dr. Issadore also opines that in the case of a split stream (in the context of the prior art), the centerline would be through a gap between the streams, in which case the drawn centerline runs through the sheath fluid (instead of the sample). *See* Ex. 1054 ¶¶ 33–34; Ex. 2009, 401:23–402:3. We determine that this would not be a centerline of the sample stream because it runs through sheath fluid. Even if this could be considered a centerline of the sample, it is not a centerline of the sample stream.

We observe that “the sample stream” in the phrase “a centerline of the sample stream” in claim 2 (Ex. 1001, 18:67) refers back, as a matter of antecedent basis, to “a sample stream” in claim 1, i.e., “an inlet configured

or the centerline of the device at the point where the sample enters. Paragraph 12 of Exhibit 1054 refers to paragraph 194 of Exhibit 1003, where Dr. Issadore draws such a line, but Dr. Issadore does not provide underlying evidence for his opinion that this would have been the understanding of a person of ordinary skill in the art. Patent Owner challenges this interpretation for the situation where there is a split sample, which we discuss below.

¹⁶ The Specification refers, *inter alia*, to the “centerline CL of the core stream forming geometry 400” (Ex. 1001, 10:14–17) and the “center of the lateral fluid focusing channel 520” (Ex. 1001, 15:6–7), which is consistent with dependent claims 5 and 20 rather than dependent claims 2 and 23.

to receive a sample stream” (Ex. 1001, 18:48). One might argue that the sample stream is limited to the sample that enters the device, and such an interpretation would on its face be consistent with Dr. Issadore’s opinion that a person of ordinary skill would understand the centerline to be a centerline of the device where the sample enters. *See* Ex. 1054 ¶ 36.

However, the claims use the term “stream” to refer to the entire stream that flows through the device, and not simply the portion of the stream that enters the device. For example, claim 1 refers to a plane that is “upstream” and a plane that is “downstream.” *See* Ex. 1001, 18:57–61 (“wherein a bottom surface of the flow channel lies in a first plane upstream of the first and second vertical fluid focusing features and the bottom surface of the flow channel shifts vertically upward to lie in a second plane downstream of the first and second vertical focusing features”). The Specification is also consistent with this understanding of the sample stream as the particles of sample flowing through the device (as opposed to only the sample that enters the device). *See* Ex. 1001, 11:13 (“both of which may contribute to shaping sample stream S”), 12:1–3 (“As the sample stream and the focusing fluid progress along the lateral fluid focusing chamber **420**”), 13:7–9 (“A first downwards influence on the sample stream is created upon entry into the lateral fluid focusing chamber **420**”), 14:17 (“Thus, after being laterally focused, the stream is vertically focused downward and then vertically

focused upward”), 14:33 (“The focused stream exits the fluid focusing region **530** in the P2 plane”).^{17 18}

Further, if the term “stream” were plural such that there are two streams, then the term “centerline” might also be plural with each stream having its own centerline, in which case it would not be possible to “introduce fluid into the flow channel symmetrically with respect to a centerline of the sample stream,” as claimed in claim 2. *See* Ex. 2006 ¶ 62 (opining that each stream would have its own centerline).

This case resembles *Wonderland Nurserygoods Co., Ltd. v. Baby Trend, Inc.*, 727 F. App’x 1017, 1019 (Fed. Cir. 2018), where the ordinary language of the claims indicated that the terms “a fabric member” and “an enclosure member” were singular. In that case, a plural reading of “fabric member” or “enclosure member” would have erased a meaningful distinction between “side panels” and these other terms. *Id.* Further, the “fabric member” and “enclosure member” had to be unitary structures capable of delineating or surrounding an enclosed space. *Id.* Similarly, in this case, a plural interpretation of “stream” would be inconsistent with the claim language, e.g., because it might not be possible to draw a centerline of a sample stream and to introduce focusing fluid symmetrically with respect

¹⁷ In one instance, the Specification states: “There may be certain efficiencies gained in several stream lined aspects relating to the sheath fluid flow illustrated in FIGS. 5A-5D.” Ex. 1001, 15:57–60. However, we do not understand this to require several streams but merely to refer to stream-lined aspects where the *aspects* in *several* figures are referred to in the plural. Also, the Specification refers to stream forming geometries in the plural. *See* Ex. 1001, 18:3.

¹⁸ In multiple places the Specification also refers to a “core stream” or “core stream forming geometry.” Ex. 1001, *passim*.

to a centerline of the sample stream when there is more than one stream (i.e., in the case of a split sample).

Therefore, we construe “the sample stream” in the claim phrase “configured to focus the sample stream” to refer to a singular stream.

c) Conclusion as to “focusing” and “configured to focus the sample stream”

We maintain our construction of “focusing” as “pinching, confining, squeezing, or constricting” and decline to import additional requirements such as sheath flow into the term “focusing.” Nevertheless, we construe “the sample stream” in the claim phrase “configured to focus the sample stream” to refer to a singular stream.

2. “fluid focusing region”

In the Decision on Institution, we set forth our preliminary construction of the focusing region to mean “a portion of the microfluidic unit in which fluid is focused.” Dec. Inst. 21.

Patent Owner argues that the Board’s construction of “fluid focusing region” should be revised to “a region where focusing is achieved and maintained.” PO Resp. 12. Patent Owner argues that if the “fluid focusing region” did not need to achieve and maintain focusing throughout the region, the term would serve no purpose in the claims such that it would read words out of the claim and would lead to an absurd result. *See id.* at 12–13 (citing *Info-Hold, Inc. v. Muzak LLC*, 783 F.3d 1365, 1374 (Fed. Cir. 2015); *AIA Engineering Ltd. v. Magotteaux Intern. S/A*, 657 F.3d 1264, 1276 (Fed. Cir. 2011); Ex. 2006 ¶ 70). Patent Owner also argues that if a “fluid focusing region” needed only to achieve some focusing somewhere in it, regardless of subsequent widening or defocusing, it would be redundant of the term “fluid focusing features.” *Id.* at 12 (citing Ex. 2006 ¶ 69). Patent Owner argues

that a “fluid focusing region” cannot defocus. PO Sur-reply 7. Patent Owner argues that each vertical fluid focusing region in Figure 1 of Kim ends when the channel widens. PO Resp. 14 (citing Ex. 2006 ¶¶ 72–74).

Petitioner replies, *inter alia*, that “fluid focusing region” is not redundant over “fluid focusing features” because the “fluid focusing features” are the components used to achieve focusing within the “fluid focusing region.” Pet. Reply 8. Petitioner argues that the region’s purpose of focusing is satisfied if the sample flow arrives at the inspection region with the desired characteristics. *Id.* Petitioner argues that in Kim, the vertical focusing regions include the portion of the channel that widens after the introduction of fluid. *Id.* at 9 (citing Ex. 1054 ¶ 16, Fig. 1). Petitioner’s contentions are illustrated with further reference to the figures below.

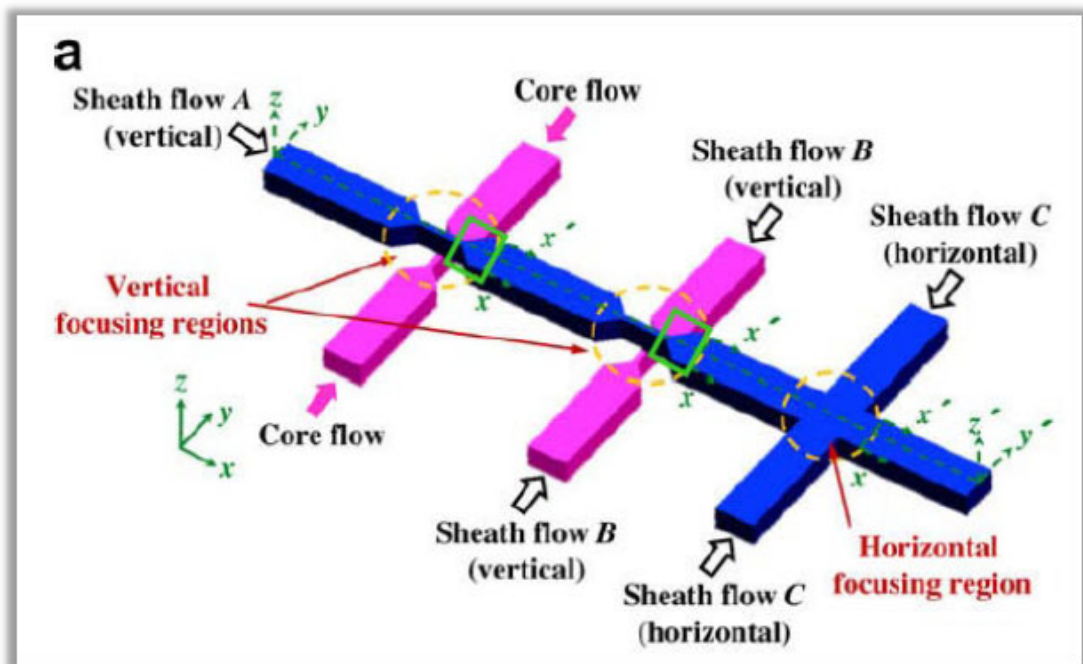


Figure 1 is a schematic diagram of the three-dimensional hydrodynamic focusing device proposed in Kim with an overall view (a). Ex. 1015, 1344. The above annotated figure from Dr. Issadore’s Reply Declaration shows Figure 1 of Kim with green rectangle annotations added, i.e., to show areas

where the sample stream widens and which Dr. Issadore avers to be part of the vertical focusing region. *See* Ex. 1054 ¶ 16.

Petitioner also argues, in the context of the prior art, that Patent Owner's arguments depend on the assumption that focusing must be achieved and maintained in all directions at once, which is in tension with the claim requirement that the lateral and vertical fluid focusing features be located at "different longitudinal locations along the flow channel." Pet. Reply 20 (citing Ex. 1054 ¶ 32). Petitioner also argues that even if the sample flow widens (e.g., in the horizontal direction during the process of horizontal focusing), vertical focusing that has been achieved may be maintained. *Id.* (citing Ex. 1054 ¶ 31).

Upon review of the arguments and evidence presented during the trial, we maintain our construction of "fluid focusing region" as "a portion of the microfluidic unit in which fluid is focused." We agree with Petitioner that the claimed "fluid focusing region" is composed of a horizontal fluid focusing region and two vertical fluid focusing regions and therefore the term "fluid focusing region" is not redundant over the component "fluid focusing features." We are also persuaded by Petitioner that the focusing may be achieved or maintained in one direction while being loosened in another direction, as long as by the end of the fluid focusing region, focusing has been achieved in both the horizontal and vertical directions.

We agree with Dr. Issadore that Kim supports the notion that a focusing region may contain areas of widening (designated in Dr. Issadore's Figure as green rectangles, Ex. 1054 ¶ 16) within the yellow circles marked in Kim as vertical focusing regions (*see* Ex. 1015, 1344 & Fig. 1).

Further, based on the claim language, we understand the claimed "fluid focusing region" to provide an output of focused sample fluid to the

claimed “inspection region.” The “fluid focusing region” is “configured to focus the sample stream.” Ex. 1001, 18:49. Thus, “focusing” is the objective for which the region is configured, which is designed to be accomplished by the action of the three “fluid focusing features.” *Cf. Aspex Eyewear Inc. v. Marchon Eyewear, Inc.*, 672 F.3d 1335, 1349 (Fed. Cir. 2012) (“the phrase ‘adapted to’ is most naturally understood to mean that the arms and magnetic members are designed or configured to accomplish the specified objective, not simply that they can be made to serve that purpose.”). Thus, although the claim does not simply encompass any region that is merely capable of focusing and requires focusing features that are designed to focus, the claim does not contain a limitation of continuous narrowing within the region.

3. *Additional claim construction issues addressed in post-hearing briefing*

We address the additional issues together to the extent necessary to resolve the present dispute.

The key passage in the Specification is as follows:

As used herein the terms “vertical,” “lateral,” “top,” “bottom,” “above,” “below,” “up,” “down,” and other similar phrases should be understood as descriptive terms providing general relationship between depicted features in the figures and not limiting on the claims, especially relating to flow channels and microfluidic chips described herein, which may be operated in any orientation.

Ex. 1001, 6:4–10.

Petitioner argues that this passage is definitional and is lexicography by the applicant in the Specification. *See* Pet. Supp. Br. 2–5. Petitioner asserts that this language shows that the terms referenced in the passage are intended to be relative terms. Patent Owner responds, *inter alia*, that the parties agree that claim 1 is not limited to one orientation, provided that the

components of the microfluidic chip are positioned relative to one another as claimed, i.e., in view of the cited passage from the Specification. PO Supp. Br. 2–5. We agree with Petitioner that the applicant in the Specification was acting as its own lexicographer with the language “as used herein,” and that the terms “bottom” and “up” are relative such that the claimed device can be in any orientation. We need not reach any further claim construction issue on the facts of this case.

D. Anticipation of Claims 1, 2, 6, and 8 over Simonnet

Petitioner contends that claims 1, 2, 6, and 8 are anticipated by Simonnet. Pet. 29–62. Patent Owner disagrees. *See* PO Resp. 18–31.

1. Simonnet

Simonnet is an article which describes a design, fabrication, and operation of two types of flow cytometers based on microfluidic devices, and presents some experimental results obtained therewith. *See* Ex. 1005, 5653.¹⁹

Simonnet discloses a molded microfluidic chip that allows tight hydrodynamic focusing in both in-plane and out-of-plane directions, i.e., three dimensional focusing. *Id.* at 5654. Simonnet discloses devices made of a single cast of PDMS sealed with a cover glass, which are disposable and compatible with standard short-working-distance microscope objectives. *Id.* Figure 1 depicting Simonnet’s high-throughput device is reproduced below:

¹⁹ Petitioner appears to rely on the first type of device described in Simonnet, which is a high-throughput device. *See* Pet. 23–24.

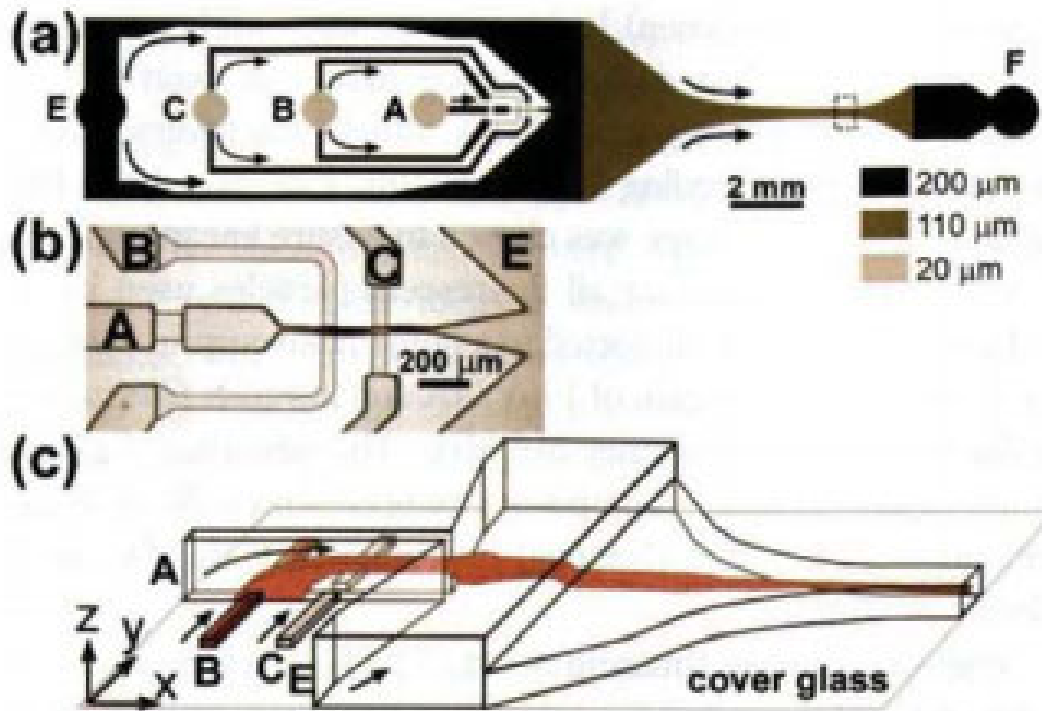


Figure 1 of Simonnet depicts a high-throughput device with arrows showing the direction of flow. Ex. 1005, 5655. A suspension of particles (the sample) is injected into port B. *Id.* Flow focusing in the out-of-plane (z) direction is provided by the liquids injected into ports A (focusing from the top) and C (focusing from the bottom). *Id.* Flow focusing in the in-plane direction is provided by the liquid injected into port E. *Id.* Port F is the device outlet. *Id.* The dashed line box on the top right of the figure indicates the cytometry channel. *See id.*

2. Analysis of Independent Claim 1

a) Preamble: “[a] microfluidic assembly for use with a particle processing instrument, the microfluidic assembly comprising”;

b) “a substrate”;

c) flow channel: “a flow channel formed in the substrate”;

d) sample stream inlet: “the flow channel having: an inlet configured to receive a sample stream”

Petitioner argues, *inter alia*, that Simonnet describes a microfluidic device having an assembly formed by multiple layers of materials and used to focus a stream of particles and/or to image the focused particle stream in an interrogation region. Pet. 29–30 (citing Ex. 1005, 5653–5654, 5656–5657; Ex. 1003 ¶ 126). Petitioner argues that Simonnet discloses a “substrate” because its microfluidic chips are made of “PDMS”—a plastic-based material in which channels are formed—and a “cover glass” used to enclose such channels and which serves as the bottom or top boundary of the microchannels formed in the chip. Pet. 30 (citing Ex. 1005, 5653–5655; Ex. 1003 ¶ 131). Petitioner argues that Figure 1(a) of Simonnet shows numerous channels into which fluids are introduced at inlets ports A, B, C, and E, and that there is a primary channel that permits the flow of fluid from the sample inlet (at port B) along the direction labeled “X” in Figure 1(c). Pet. 31–33 (citing Ex. 1005, 5654; Ex. 1003 ¶¶ 134, 140–141).

Patent Owner does not separately dispute Petitioner’s contentions as to these recitations. See PO Resp. 18–31. We accept Petitioner’s undisputed

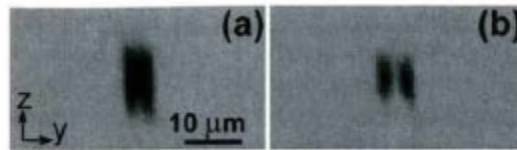
assertions as factual findings. *See generally In re NuVasive*, 841 F.3d at 974.^{20 21}

e) fluid focusing region: “fluid focusing region configured to focus the sample stream”;

f) fluid focusing features: “the fluid focusing region having a lateral fluid focusing feature, a first vertical fluid focusing feature, and a second vertical fluid focusing feature”

For these limitations, Patent Owner disputes whether “focusing” occurs for Petitioner’s asserted fluid focusing features (and whether there is a single stream) and also disputes whether the asserted fluid focusing features are arrayed in a single fluid focusing region as required. PO Resp. 19–27.

As context, the parties disagree on the interpretation of Figures 3(a) and 3(b) of Simonnet, reproduced below:



Figures 3(a) and 3(b) are confocal micrographs showing the flow structure near the central axis of the cytometry channel in HTD (the High throughput device depicted in Figure 1), at conditions typical for cytometry assays,

²⁰ Although Simonnet’s device receives a sample stream, the sample subsequently splits as it flows through the device. We note that below Patent Owner disputes the limitation “focus the sample stream” because the sample splits and does not remain a unitary sample stream.

²¹ Regardless of whether the preamble is limiting, Petitioner has shown that the recitation in the preamble is satisfied by the prior art. *See Allen Eng’g Corp. v. Bartell Indus., Inc.*, 299 F.3d 1336, 1346 (Fed. Cir. 2002) (“Generally, the preamble does not limit the claims.”).

where dark areas correspond to the stream from port B. *See* Ex. 1005, 5657 (caption to Figure 3); *see also id.*, 5655 (caption to Figure 1).

Petitioner argues that sheath flows from ports A, C, and E all contribute to focusing sample flow from port B. Pet. 35–36 (citing Ex. 1005, 5652, 5654–5655, 5657, Fig. 3; Ex. 1003 ¶ 146). Petitioner argues, with respect to the fluid focusing features, that when the flow of particles reaches the downstream cytometry channel, the flow is confined to a width of 5 μm (or 5–10 μm). *Id.* at 38 (citing, e.g., Ex. 1005, 5654, 5657, 5662, Fig. 3; Ex. 1003 ¶ 151). Petitioner relies on statements in Simonnet describing “focusing” (citing Ex. 1005, 5656–5660) and statements in other publications stating that Simonnet focused a sample (citing Ex. 1046, 1875; Ex. 1047, 3155; Ex. 1006, 973; Ex. 1018, 621; Ex. 1048, 3035; Ex. 1003 ¶ 59; Ex. 1013, 250; Ex. 1049, 120–121, Ex. 1051, 319–320). Pet. Reply 11–12.

Patent Owner argues that Simonnet’s device does not focus the sample stream because the resulting sample stream is split. PO Resp. 19–25. Patent Owner asserts that although Simonnet’s Figure 1 does not depict the sample stream in any detail, the accompanying text indicates that “the [sample] stream from inlet B is split into two parts, with a gap in the middle.” PO Resp. 20 (citing Ex. 1005, 5657). Patent Owner asserts that Figure 3(b) is an image of a cross-section of the Figure 1 device downstream of the alleged “fluid focusing region,” and it depicts two sample streams flowing side-by-side, divided by sheath fluid. PO Resp. 20 (citing Ex. 2001 ¶¶ 134–135; Ex. 2006 ¶ 76). Patent Owner argues that Simonnet also discloses another cross section of the sample streams in Figure 3(a), for which Simonnet admits a “residual gap can also be seen.” Ex. 1005, 5657.

Petitioner argues that Figure 3(a) depicts a single, contiguous, focused sample. Pet. Reply 14. Petitioner argues that Simonnet distinguishes Figure 3(b)'s "gap in the middle" from Figure 3(a)'s "residual gap," which skilled artisans would understand to refer to the cross section shape of 3(a)'s sample: it has a "notch" in the bottom but is not split through the middle. *Id.* (citing Ex. 1054 ¶ 18).

Petitioner also argues that the "gap" between streams in Figure 3(b) is much smaller than the diameter of a typical mammalian cell, so that cells would be expected to flow single-file, and were associated with the highest accuracy. Pet. Reply 13 n.6 (citing Ex. 1054 ¶¶ 21, 27).

Patent Owner argues that contrary to Petitioner's argument, Simonnet's experiments did not use 10-µm mammalian cells, but rather used much smaller beads instead. PO Sur-reply 12 n.2 (citing Ex. 1005, 5657).

We agree with Patent Owner that Simonnet discloses split sample streams because Simonnet discloses that the stream of Figure 3(b) is "split into two parts, with a gap in the middle" and "[a] residual gap can also be seen in Figure 3a." Ex. 1005, 5657.

Petitioner argues that Simonnet still discloses a device "configured to" focus the sample stream because an apparatus claim covers what a device is and not what it does. Pet. Reply 14–15 (citing *Paragon Solutions, LLC v. Timex Corp.*, 566 F.3d 1075, 1090 (Fed. Cir. 2009)). Apparently referring to Figure 3(a), Petitioner argues that the so-called "gap" occurs only for certain ratios of flow rates between channel A (first sheath) and channel B (sample). *Id.* at 14 (citing Ex. 1005, 5657). Petitioner argues that Simonnet cites

earlier work in Simonnet 2005²² (Ex. 1005, 5657 (citing Ex. 1020), which shows how varying flow-rate ratios can produce or avoid a gap. Pet. Reply 14 (citing Ex. 1020, 114104-2; Ex. 1014, 1483 & Fig. 7(a)). Petitioner argues that skilled artisans reading Simonnet alone would understand that Simonnet discloses a device configured to produce a “single sample with sheath flow” under a wide range of conditions, even if there are some conditions that will lead to a split sample. *Id.* at 15 (citing Ex. 1054 ¶ 19).

Patent Owner replies that Simonnet makes only a brief citation to Simonnet 2005 and does not specifically or expressly incorporate any part of that paper. PO Sur-reply 13 n.3. Patent Owner cites *Callaway Golf* for the proposition that “[m]ere reference to another . . . publication is not an incorporation of anything therein.” *Id.* (citing *Callaway Golf Co. v. Acushnet Co.*, 576 F.3d 1331, 1346 (Fed. Cir. 2009)).

We agree with Patent Owner that Petitioner has not adequately shown that Simonnet would have been understood to incorporate Simonnet 2005 for purposes of an anticipation analysis. In particular, Petitioner has not shown that the device in Simonnet 2005 is the same device, nor adequately explained how the teachings of Simonnet 2005 would apply to the device of Simonnet. We agree with Patent Owner that Simonnet merely refers to Simonnet 2005 without clearly identifying material that is incorporated. *See Callaway Golf Co.*, 576 F.3d at 1346. Indeed, as relevant to Petitioner’s contentions, Simonnet 2005 is used in a footnote as a citation for the proposition that the gap occurs when the flow emerging from the channels B is small compared with the flow in channel A, and the streams from

²² Simonnet, C.: Groisman, *Two-dimensional hydrodynamic focusing in a simple microfluidic device*, 87 APPL. PHYS. LETT. 114104 (2005) (Ex. 1020, “Simonnet 2005”).

channels B do not reach the middle of channel A. Ex. 1005, 5657.

Petitioner has not shown that Simonnet would incorporate an embodiment from Simonnet 2005 with no gap.

Applying our claim construction which requires a single sample stream, we determine that Simonnet's split sample does not satisfy "the sample stream" limitation.²³

"fluid focusing region"

Petitioner sets forth its contentions that Simonnet discloses a fluid focusing region with a lateral fluid focusing region and two vertical fluid focusing regions. Pet. 37–50. Patent Owner disputes that Simonnet discloses a single fluid focusing region because, according to Patent Owner, Simonnet discloses a widening in the lateral fluid focusing feature. PO Resp. 2, 26. To provide context, we first reproduce Petitioner's contentions for the three fluid focusing features as follows.

For a first vertical focusing feature, Petitioner argues that Simonnet discloses that inlet port A introduces focusing fluid into the flow channel of the device, which narrows or confines the sample in a vertical direction. Pet.

²³ In addition, Petitioner argues in a footnote in its Reply brief that mammalian cells could be used, i.e., in Simonnet's system in place of beads, and citing Dr. Issadore's Reply Declaration. Pet. Reply 13 n.6 ("... and the 'gap' between streams is much smaller than the diameter of a typical mammalian cell, so that cells would be expected to flow single-file") (citing Ex. 1054 ¶ 21). Although we address this argument in more detail in the obviousness section below, we also address this argument as an argument for anticipation as follows. Simonnet suggests that cells can be used (*see* Ex. 1005, 5662), but does not disclose a single stream of cells. Dr. Issadore avers that cells would not "typically" arrive at the inspection region at once (i.e., side by side) (Ex. 1054 ¶ 21), but this stops short of a statement that there is a single stream.

38 (citing Ex. 1005, 5654). Petitioner's contentions are illustrated with further reference to the annotated figure below.

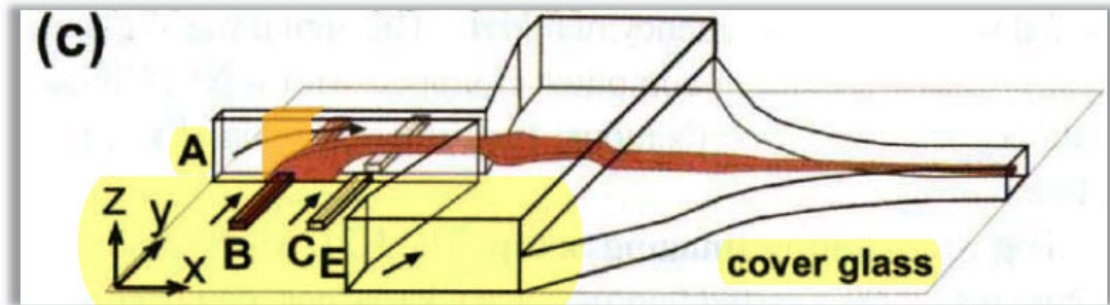


Figure 1(c) of Simonnet annotated by Petitioner is provided above, with yellow and orange color added. *Id.* at 39. Petitioner asserts that this figure illustrates that focusing fluid from port A enters the flow channel and pushes vertically downward against the sample flow from port B to focus that fluid from the top. *Id.* at 39 (citing Ex. 1005, 5652, 5657, 5662; Ex. 1003 ¶ 152).

Petitioner asserts that the vertical focusing is confirmed in Simonnet's experimental results, which show that the sample is confined to a cross section of 5–10 μm near the central axis of a cytometry channel. *Id.* (citing Ex. 1005, 5654, 5657, 5662, Fig. 3).

For a second vertical focusing feature, Petitioner argues that Simonnet discloses that the pair of sheath fluid inlets (at C) introduces focusing fluid into the flow channel of the device, to focus the sample in the vertical direction. Pet. 39–40 (citing Ex. 1005, 5654). Petitioner argues that Simonnet discloses that “flow focusing in the out-of-plane (z) direction is provided by the liquid[] injected into port[] ... C (focusing from the bottom).” *Id.* at 40 (citing Ex. 1005, Fig. 1). Petitioner's contentions are illustrated with further reference to the annotated figure below.

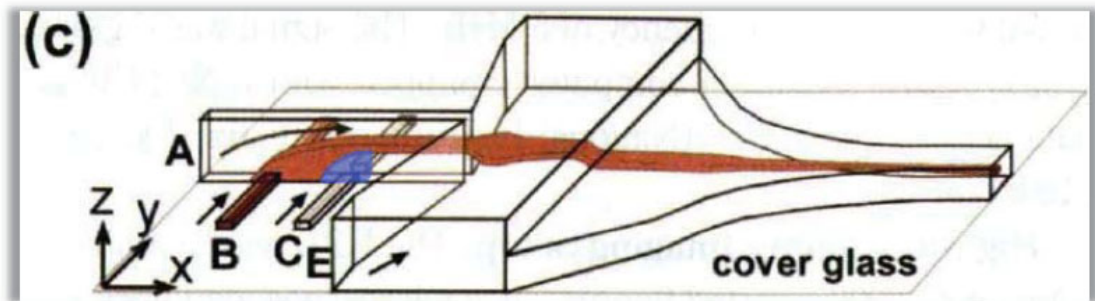


Figure 1(c) of Simonnet annotated by Petitioner, is provided above, with blue color added. *Id.* at 40. Petitioner argues that Simonnet’s experimental results show that the sample is confined to a cross section of “5-10 μm near the central axis of a cytometry channel, which has a cross section of 300 x 100 μm .” *Id.* (citing, e.g., Ex. 1005, 5654). Petitioner argues that focusing fluid from port C helps to confine the sample to near the center of the channel by pushing upward on the sample from below. *Id.* at 40–41 (citing Ex. 1003 ¶ 153).

For a lateral fluid focusing feature, Petitioner argues that Simonnet’s device includes a component that introduces sheath fluid (a focusing fluid) through the channels labeled “E” to narrow or constrain the sample in a lateral direction (corresponding to the “y” direction in the axis shown on FIG. 1(c), illustrated with arrows below). Pet. 37 (citing Ex. 1005, Fig. 1).

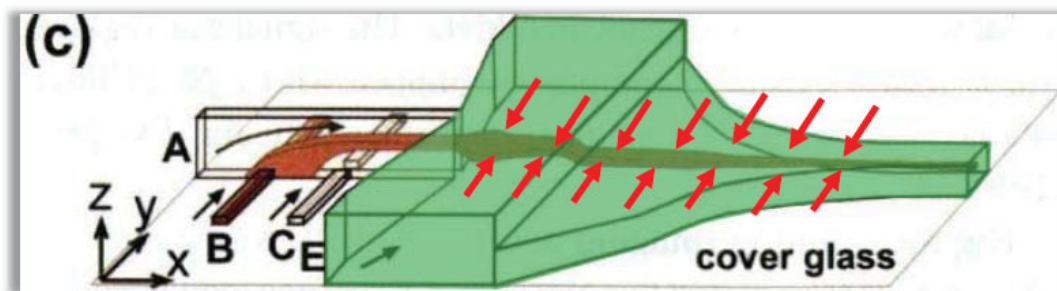


Figure 1(c) of Simonnet annotated by Petitioner is reproduced above, with green color and red arrows added. *Id.* Petitioner asserts that Simonnet discloses that “[f]low-focusing in the plane of the device (in the y-direction)

is achieved by squeezing the stream carrying particles between the streams emerging from the two channels, E.” *Id.* (quoting Ex. 1005, 5656; citing Ex. 1005, 5652, 5654, 5657).²⁴

Patent Owner argues that Petitioner fails to establish that Simonnet discloses a “fluid focusing region” because, in the alleged region, the sample stream “plumes” and thus fails to maintain focusing. *See* PO Resp. 25. Patent Owner’s contentions are illustrated with further reference to the annotated figure below.

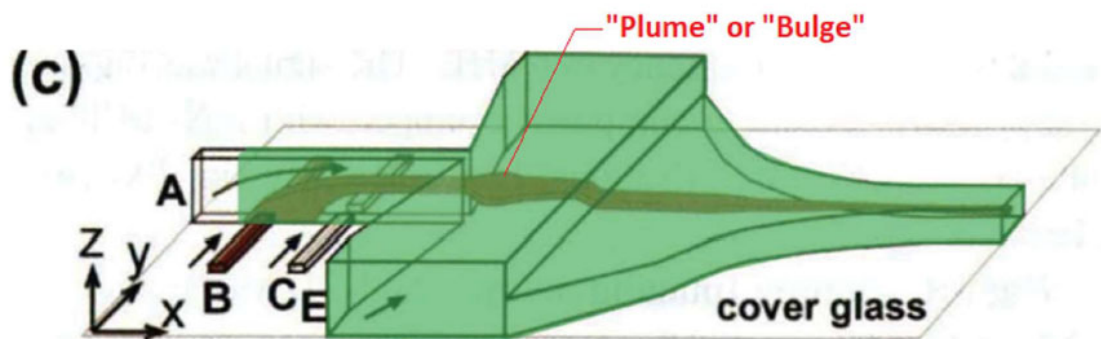


Figure 1(c) of Simonnet annotated by Patent Owner, is provided above, with green color added and a label for part of the sample as “Plume” or “Bulge.” *Id.* at 26. Patent Owner argues that while Dr. Issadore refers to the “plume” as a “slight bulge” (Ex. 2008, 175:22–55), Dr. Arnold fully analyzed the device and concluded that the sample stream widens by about eight times its original width at that location. *Id.* (citing Ex. 2001 ¶¶ 122–127, 147–148).

²⁴ Although the Petition identifies certain alternative parts of Simonnet’s device as potential fluid focusing features (*see* Pet. 49–50), counsel for Petitioner represented at the hearing that it is not necessary for the Board to evaluate these alternative theories “because patent owner hasn’t disputed that each of the identified features in the primary theory, if the device focuses at all, is a fluid focusing feature.” Tr. 5:13–17.

Beyond disputing that the fluid focusing features combine in one fluid focusing region (and otherwise disputing the limitations of “focusing” and “the sample stream”), Patent Owner does not dispute that Simonnet discloses a lateral fluid focusing feature and two vertical fluid focusing features.

Petitioner argues that the lateral fluid focusing region would be part of one fluid focusing region with the vertical fluid focusing features under the Board’s claim construction of fluid focusing region as “the portion in which fluid is pinched, confined, squeezed, or constricted.” Pet. Reply 19–20. Petitioner also argues that, even under Patent Owner’s proposed construction, skilled artisans would readily understand that, if the sample flow “widens” or “plumes,” the vertical focusing that had been “achieved” upstream would be “maintained,” because the channel remains the same height as it widens laterally. *Id.* at 20 (citing Ex. 1054 ¶ 31).

Applying our claim construction for “fluid focusing region,” we determine that the Simonnet’s two vertical fluid focusing features and lateral focusing feature are part of a fluid focusing region because the sample is “squeezed” and “confined” as a result of its flow through the three portions of Simonnet’s microfluidic channel identified by Petitioner. *See* Ex. 1005, 5654 (“The flow of particles is confined to a region with a diameter of 5–10 μm near the central axis of a cytometry channel, which has a cross section of 300 x 110 μm ”); 5655 (caption to Figure 1 states that flow focusing occurs); 5656 (“Flow-focusing in the plane of the device (in the y-direction) is achieved by squeezing the stream carrying particles between the streams emerging from the two channels, E”). However, as above and applying our definition of “the sample stream,” we determine that Simonnet’s fluid focusing region is not “configured to focus the sample stream” because Simonnet does not disclose a single sample stream.

g) Different longitudinal locations: “the lateral, the first vertical, and the second vertical fluid focusing features [are] provided at different longitudinal locations along the flow channel”

Petitioner argues that the '439 patent uses the terms “longitudinal” or “longitudinally” to refer to the direction along which the sample flow travels in the chip. Pet. 51 (citing Ex. 1001, 13:26–30, Fig. 3D).

Petitioner relies on the locations marked below in orange, blue, and green for the recited fluid focusing features (see Pet. 51–52). Petitioner’s contentions are illustrated with further reference to the annotated figure below.

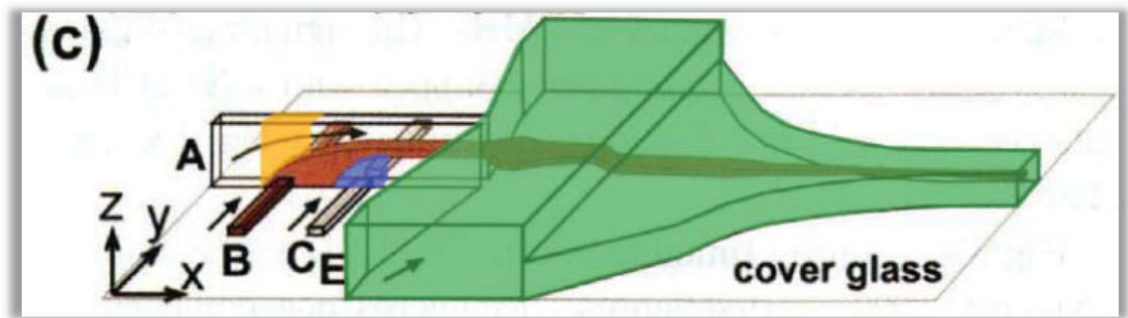


Figure 1(c) of Simonnet annotated by Petitioner, is provided above with color added (see Ex. 1005, Fig. 1). *Id.* at 52.

Patent Owner does not separately dispute Petitioner’s contentions that the asserted flow focusing features are at different longitudinal locations. See PO Resp. 18–31.

We determine that Simonnet’s Figure 1(c) demonstrates the recited relationship.

h) Upward vertical shift: “wherein a bottom surface of the flow channel lies in a first plane upstream of the first and second vertical fluid focusing features and the bottom surface of the flow channel shifts vertically upward to lie in a second plane downstream of the first and second vertical focusing features”

Petitioner relies on the vertical shift in the annotated figure (see Pet. 54). Petitioner’s contentions are illustrated with further reference to the annotated figure below.

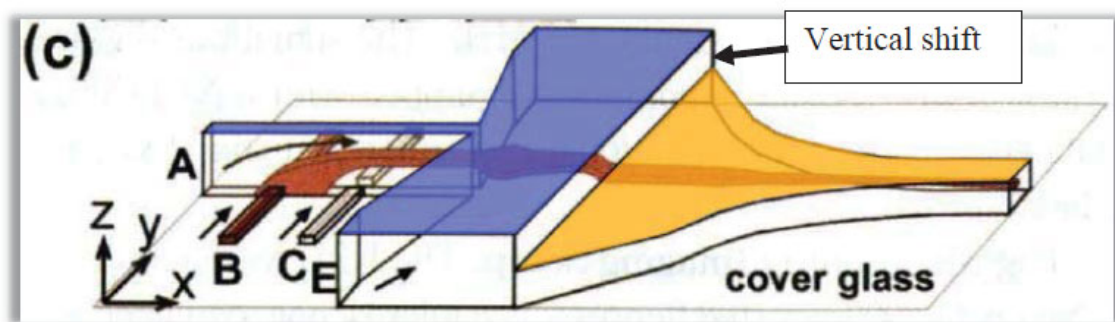


Figure 1(c) of Simonnet annotated by Petitioner, is provided above with color and annotation added (see Ex. 1005, Fig. 1). Petitioner asserts that the top height of the device shifts its height downward at the location of the vertical step, i.e., just before the flow channel starts to taper. Pet. 54. However, Petitioner argues that this is equivalent to an upward shift because the '439 patent states that “flow channels . . . may be operated in any orientation” (citing Ex. 1001, 6:8–10) and “bottom . . . should be understood as [a] descriptive term[] providing general relationship between depicted features in the figures and not limiting on the claims” (citing *id.* at 6:4–8). *Id.* at 53–54. According to Petitioner, fluid forces in a chip are stronger than gravity. *Id.* at 54 (citing Ex. 1027, 47). Petitioner argues that a person of ordinary skill would have known that this device could be viewed from (or operated in) a different orientation than that of the image. *Id.* at 55 (citing Ex. 1003 ¶¶ 181–182).

Patent Owner argues that “[a]nticipation requires Simonnet to expressly or inherently disclose each limitation arranged [as] claimed, and the claim expressly requires the ‘bottom surface of the flow channel’ to ‘shift vertically *upward*.’” PO Resp. 27. Patent Owner argues that anticipation by inherency “may not be established by probabilities or possibilities.” *Id.* at 28 (citing *Bettcher Indus. v. Bunzl USA, Inc.*, 661 F.3d 629, 639 (Fed. Cir. 2011)). Patent Owner argues that Petitioner must show that Simonnet “necessarily functions in accordance with, or includes, the claimed limitations.” *Id.* (citing *Brassica Prot. Prods. LLC v. Sunrise Farms (In re Cruciferous Sprout Litig.)*, 301 F.3d 1343, 1349 (Fed. Cir. 2002)). Patent Owner argues that Petitioner made no attempt to establish such inherency. *Id.* Patent Owner asserts that Dr. Issadore admitted at his deposition that, though Simonnet “could be operated in a vertically flipped orientation,” such vertical flipping would not occur as a “natural result of its normal operation.” *Id.* (citing Ex. 2008, 240:11–241:13; Ex. 2006 ¶¶ 100–101).

Petitioner replies that Patent Owner’s expert merely testified that the Simonnet chip would not spontaneously flip on its own. Pet. Reply 21 (citing Ex. 2006 ¶ 100). Petitioner argues that Simonnet’s device needs no modification, that “top” and “bottom” are relative terms, and that Dr. Issadore testified without contradiction that a skilled artisan looking at Simonnet would recognize that the device “could be analyzed (and operated) in a vertically flipped orientation” relative to what is illustrated in Simonnet Figure 1. Pet. Reply 21–22 (citing Ex. 1003 ¶¶ 179, 181). Petitioner argues that if Patent Owner’s contrary understanding were adopted, potential infringers could avoid infringement simply by operating their otherwise-

infringing chips in a different orientation—where a shift “up” is no longer a shift up relative to Earth’s surface. *Id.* at 22.

Applying our claim construction of the “wherein” clause, where the terms “bottom surface” and “vertically upwards” are understood to be terms of relative position, we determine that Simonnet’s Figure 1(c) both expressly and inherently discloses this limitation of claim 1. In particular, Figure 1(c) depicts a top surface shifting downward, and where these are relative terms, this is the same as a bottom surface shifting upward. Further, as argued elsewhere by Petitioner (*see* Pet. Reply 15), this is a claim for an assembly, not a process, and the device is the same in any orientation regardless of how it is operated.

i) Inspection region: “an inspection region at least partially downstream of the fluid focusing region.”

Petitioner argues Simonnet discloses that the flow cytometer design it implements is used to detect “optical properties” of the focused sample particles. Pet. 56 (citing Ex. 1005, 5653). Petitioner argues Simonnet describes “imaging systems” used with its flow cytometry devices, including particle detection, using a camera, microscope, and laser light. *Id.* at 56–57 (citing Ex. 1005, 5654, 5656). Petitioner argues that Simonnet detects particles, which requires inspecting them. *Id.* at 57 (citing Ex. 1003 ¶ 187).

Petitioner also argues that Simonnet refers to a “cytometry channel” as the location where the microscope and camera inspects and detects particles, and that this is downstream of the fluid focusing region. *Id.* (citing Ex. 1005, 5656–5657). Petitioner argues that Simonnet also expressly states that it contains an “interrogation region, where flow cytometry assays were carried out, [] in the central area of the cytometry channel (Figure 1a)” and

argues that this is at least partially downstream of the fluid focusing region. *Id.* at 57–58 (citing Ex. 1005, 5656–5657).

Patent Owner does not separately dispute this limitation. We determine that Simonnet discloses this limitation. Figure 1(a) of Simonnet is depicted below.



Figure 1(a) of Simonnet is a schematic drawing of the microchannel network, where the dashed line box (on the right) indicates the cytometry channel. *See* Ex. 1005, 5655; Pet. 57. Based on the arrows in Figure 1(a) of Simonnet, the cytometry channel is at least partially downstream of the microfluidic channel. Using confocal microscopy, Simonnet measures fluorescence across the cytometry channel. Ex. 1005, 5656.

j) Summary for claim 1

For the reasons above, we determine that Petitioner has not established that claim 1 is anticipated by Simonnet because Simonnet does not disclose the recited “fluid focusing region configured to focus the sample stream.”

3. Analysis of Dependent Claims 2, 6, and 8

Claims 2, 6, and 8 depend from claim 1. Because we find that Petitioner has not established that claim 1 is anticipated by Simonnet, we find that Petitioner has not established that claims 2, 6, and 8 are anticipated by Simonnet for the same reason.

E. Obviousness of Claims 1, 2, 6, and 8 over Simonnet

Petitioner sets forth its contentions that claims 1, 2, 6, and 8 are obvious over Simonnet. Pet. 62–64.

1. Independent claim 1

a) “fluid focusing region configured to focus the sample stream”

Above, we find that Petitioner has not shown that Simonnet anticipates independent claim 1 because Simonnet produces a split sample with more than one stream, which does not qualify as “the sample stream,” which we construe to be singular.

Petitioner asserts that Patent Owner has admitted that skilled artisans “would have been encouraged” to follow Simonnet’s “suggestion” to “address [the split-stream] issue” by “decreas[ing] the relative flow rate of the sheath fluid.” Pet. Reply 15 (citing PO Resp. 33). Petitioner asserts that Simonnet on its face teaches that the “gap” occurs only under certain relative flow conditions (i.e., “when the flow emerging from channels B is small compared with the flow in channel A”) (citing Ex. 1005, 5657), and argues that skilled artisans would have readily adjusted those conditions to eliminate any gap, if doing so was desirable for a particular application (citing Ex. 1054 ¶¶ 20–21). Pet. Reply 15–16.²⁵

Patent Owner argues that Petitioner has not provided a motivation to combine Simonnet with Simonnet 2005 and has not shown a reasonable expectation of success in doing so. *See* PO Sur-reply 15–20. Patent Owner

²⁵ Paragraph 20 of the Issadore Reply Declaration tracks Petitioner’s statement in this regard and does not add additional reasoning. *See* Ex. 1054 ¶ 20. We address paragraph 21 of the Issadore Reply Declaration in the discussion of mammalian cells below.

argues that Petitioner does not disclose what the other relative flow conditions would be, what particular applications might call for those other flow conditions, nor how or why those undisclosed conditions would meet the other requirements for focusing. PO Sur-reply 16. Patent Owner argues that Petitioner also does not identify any reason or motivation for modifying the Simonnet device to arrive at the claimed invention. *Id.* Patent Owner argues that, if anything, Petitioner is improperly relying on the '439 patent as a blueprint for its obviousness analysis. *See id.* at 16–17 (citing *Orexo AB v. Actavis Elizabeth LLC*, 903 F.3d 1265, 1271 (Fed. Cir. 2018); *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 113 (Fed. Cir. 1985)).

Patent Owner argues that Dr. Issadore admitted in deposition that his opinion only extended to how a person would purportedly avoid splitting the sample stream in Simonnet, not why a person would do so. PO Sur-reply 17–18 (citing Ex. 2009, 345:19–346:7, 340:13–18, 341:8–15). Patent Owner points, *inter alia*, to the following exchange at the deposition:

[Counsel for Patent Owner] Okay. And -- so they would have known how to do it, but -- in your opinion -- ***but why would they want to eliminate such a split stream?***

[Dr. Issadore] ***I'm not sure I can speak to why, you know, in general an artisan would want to do something.*** Like I said before, there are so many applications of microfluidic, it would really be -- it would really depend on the context of a particular application.

PO Sur-reply 17 (quoting Ex. 2009, 345:19–346:7) (emphasis in brief).

Patent Owner also appears to dispute Petitioner's contention that reducing the flow rate would prevent the sample from splitting. *See* PO Sur-reply 16–17 n.4 (citing PO Resp. 33). Patent Owner also argues that Petitioner's Reply is completely silent on why a person of skill in the art

would have any success in doing so while still achieving the invention claimed in the '439 Patent. PO Sur-Reply 19.

We agree with Patent Owner that Petitioner has not provided adequate reasoning as to why a person of ordinary skill would have sought to modify the teachings of Simonnet, e.g., to vary the flow rate ratios and eliminate the gap in the sample streams. *See* Pet. Reply 14–16. Indeed, Petitioner even states to the contrary that a split sample may be desirable for certain applications. Pet. Reply 5–6 (citing Ex. 1039, 326; Ex. 1054 ¶ 10).²⁶

Simonnet does state that “[t]he gap occurs when the flow emerging from channels B is small compared with the flow in channel A” (Ex. 1005, 5657), but Simonnet stops short of suggesting a change in the flow rate ratios and Petitioner and Petitioner’s expert do not sufficiently explain why a person of ordinary skill would have sought to decrease the relative flow rate of sheath fluid. *See* Pet. Reply 15. Further, although Petitioner states that Simonnet 2005 “shows how varying flow-rate ratios can produce or avoid a gap,” Petitioner has not explained why a person of ordinary skill in the art using the device of Simonnet would have done so. *See* Pet. Reply 14. Dr. Issadore does not provide additional reasoning in the declaration, and as quoted above in the deposition Dr. Issadore was candid that he was not providing reasoning as to “why” a skilled artisan would have wanted to eliminate the split stream. *See* Ex. 1054 ¶¶ 20–21; Ex. 2009, 345:19–346:7, 340:13–18, 341:8–15. Dr. Issadore opines that a person of ordinary skill would have eliminated the gap “if doing so was desirable for a particular application.” Ex. 1054 ¶ 20. This statement is conclusory.

²⁶ Further, Dr. Issadore states that “the split sample allowed for the most ‘accurate’ particle detection” (in discussing Dr. Arnold’s opinion that “ f_d/f_0 ” is a measure of “accuracy”). Ex. 1054 ¶ 27; *see id.* ¶ 23; *supra* n.13.

As to Petitioner's assertion that Patent Owner has admitted that skilled artisans would have decreased the relative flow rate of the sheath fluid based on a suggestion from Simonnet (Pet. Reply 15 (citing PO Resp. 33)), we disagree. Rather, Patent Owner's argument at page 33 of its Patent Owner Response is that even with a decreased flow rate, a gap would still exist. *See* PO Resp. 33.

Petitioner additionally mentions in a footnote in its Reply brief that mammalian cells could be used, i.e., in Simonnet's system in place of beads, and citing Dr. Issadore's reply declaration. Pet. Reply 13 n.6 ("... and the 'gap' between streams is much smaller than the diameter of a typical mammalian cell, so that cells would be expected to flow single-file") (citing Ex. 1054 ¶ 21). Patent Owner replies that Petitioner has not provided any evidence to show that a skilled artisan would have any reason to use the same device and flow configuration with mammalian cells or would have had a reasonable expectation of success when using cells that are five times the size of the beads used in Simonnet's experiments. PO Sur-reply 12 n.2 (citing Ex. 1005, 5657 ("we seeded the liquid . . . with 1.9- μ m polystyrene beads . . ."); Ex. 2009, 320:23-321:13).

In context, Dr. Issadore avers that if mammalian cells were used, "the focused split sample *typically* would not allow two cells to arrive at the inspection region at once, because there is not enough space for two 10- μ m cells to travel side by side." *See* Ex. 1054 ¶ 21 (citing Ex. 1005, 5662) (emphasis added). The qualifier "typically" for two cells not arriving at the same time does not indicate that there would be no split stream. And Dr. Issadore seems to concede there could be a split sample. *Id.* Further, Dr. Issadore does not state which dimensions of which of Simonnet's channels

that he is using as a reference.²⁷ We determine that Dr. Issadore provides insufficient evidence and reasoning for an understanding that there would be a single stream if mammalian cells were used, in addition to making a statement that stops short of that conclusion.

Although not argued by Petitioner nor discussed by Dr. Issadore, Simonnet does state: “we expect the HTD to be compatible with cells up to ~15 μm in size.” Ex. 1005, 5662. Simonnet also states: “We expect that with the improvements in optics and detection electronics, a cytometry system based on the HTD would match the throughput, sensitivity, and accuracy of commercial flow cytometers and would be an adequate tool for assaying fluorescently marked live cells.” *Id.* These statements can be fairly read as a statement of reasonable expectation of success of using mammalian cells in the device. However, Simonnet is silent as to whether the mammalian cells would be in a single stream, and if anything, Simonnet appears to be inviting further experimentation.

Accordingly, Petitioner has not provided adequate reasoning to modify Simonnet to form a single sample stream.

²⁷ For example, Simonnet states that “The smallest channels in the HTD (the shallow channels connected to the tall-and-narrow channel; Figure 1b) have a cross section of 60 x 20 μm ” (Ex. 1005, 5662) but Simonnet also states that “[t]he 200- μm -deep channels connecting the inlets A, B, and C with the 3D focusing element are 150 μm wide” (Ex. 1005, 5655 (caption to Fig. 1)).

b) “wherein a bottom surface of the flow channel lies in a first plane upstream of the first and second vertical fluid focusing features and the bottom surface of the flow channel shifts vertically upward to lie in a second plane downstream of the first and second vertical focusing features”

Petitioner argues that to the extent that the limitation relating to shifting vertical planes was not met as a matter of anticipation, it would have been obvious to modify the device to meet those limitations, e.g., by flipping the device. Pet. 63 (citing, e.g., Ex. 1003 ¶ 184). Petitioner argues that it would have been obvious to a skilled artisan that Simonnet could be flipped vertically, without changing the characteristics of the device, and would have been a trivial step. *Id.* (citing *Sealy Tech., LLC v. SSB Mfg. Co.*, No. 2019-1872, 2020 WL 5033045, at *4 (Fed. Cir. Aug. 26, 2020); Ex. 1003 ¶¶ 179, 184; Ex. 1001, 6:8–10).

Patent Owner argues that there is no reason why a person of ordinary skill would have modified Simonnet to achieve the “shifts vertically upward” limitation in claim 1. PO Resp. 33–34 (citing *InTouch Techs. Inc. v. VGo Communs. Inc.*, 751 F.3d 1327, 1352–54, n.8 (Fed. Cir. 2014)). Patent Owner argues that the only authority Petitioners cite for side-stepping a reason to modify Simonnet is “an inapposite non-precedential opinion addressing obviousness of a design patent.” *Id.* at 34 (citing *Sealy Tech., LLC v. SSB Mfg. Co.*, 825 F. App’x 801, 807 (Fed. Cir. 2020)). Patent Owner argues that in that case, the primary reference had only a trivial difference from the patented design and a similarity in appearance between the primary and secondary references supported a motivation to combine them, whereas here Petitioner fails to explain how such reasoning applies to this ground of obviousness. *Id.*

For the same reasons as for the ground of anticipation by Simonnet, we find that Simonnet expressly and inherently discloses this limitation even without modifying Simonnet's device.

c) Other arguments and conclusion as to claim 1

Petitioner also argues that to the extent the limitation of an inspection region at least partially downstream from a fluid focusing region was not met as a matter of anticipation because fluid is still being focused at the inspection region, it would have been obvious to elongate the device further. Pet. 63–64 (citing, e.g., Ex. 1003 ¶ 191).

Patent Owner argues that Petitioner's arguments do not address the other deficiencies in the ground of anticipation of claim 1. *See* PO Resp. 32.

With respect to the “inspection region,” above we find no deficiency in the “inspection region” limitation. However, we determine above that Simonnet fails to disclose “focusing region configured to focus the sample stream,” and Petitioner has failed to show that it would have been obvious to modify Simonnet to arrive at this limitation. We, therefore, determine that Petitioner has not established that independent claim 1 would have been obvious over Simonnet.

2. Dependent claims 2, 6, and 8

Because we determine that Petitioner has not established that claim 1 is obvious over Simonnet, we determine that Petitioner has not established that claims 2, 6, and 8 are obvious over Simonnet for the same reason.

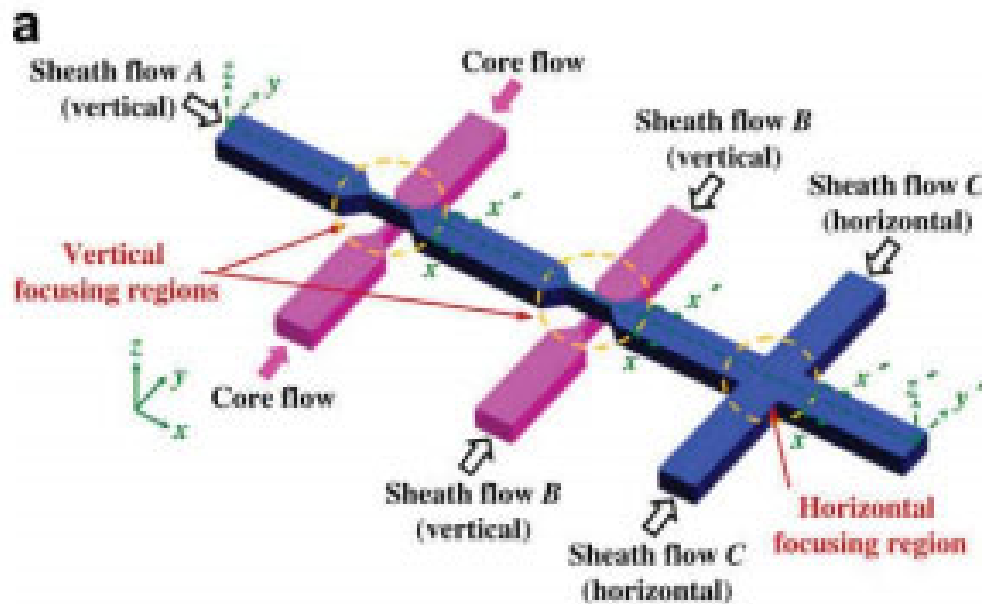
F. Obviousness of Claim 8 over Simonnet and Kim

Petitioner contends that claim 8 would have been obvious over Simonnet and Kim. Pet. 64–66. Patent Owner disagrees. *See* PO. Resp. 35–36.

1. Kim

Kim is an article that describes the author's design, fabrication, and characterization of an efficient three-dimensional hydrodynamic focusing microfluidic device, with experimental results. Ex. 1015, 1343. Kim states that to achieve a high aspect ratio, previous microfluidic devices required extravagantly high channel height (more than 100 μm) or very narrow width, which can develop expensive fabrication costs or increased pressure drop, respectively. *Id.* Kim describes a device where hydrodynamic focusing of core sample flow is effectively achieved in the pressure driven flow owing to a locally increased aspect ratio of thickness to width even below the global aspect ratio of 0.5. *Id.*

Figure 1 of Kim is reproduced below:



b



Figure 1 is a schematic diagram of the three-dimensional hydrodynamic focusing device proposed in Kim with an overall view (a) and a vertical view (z-z') (b). Ex. 1015, 1344. The channel width at two vertical focusing regions is locally reduced to 50 μm to achieve the high aspect ratio. *Id.*

2. Analysis of Claim 8

Claim 8 depends from independent claim 1 and further recites “wherein within the fluid focusing region the fluid flow channel transitions from a first cross section shape to a second cross section shape different from the first cross section shape.” Ex. 1001, 19:36–38.

Petitioner does not rely on Kim to remedy the deficiency in the ground of obviousness of claim 1 over Simonnet, which we have addressed above. Accordingly, we determine that Petitioner has not established that claim 8 would have been obvious over Simonnet and Kim.

G. Obviousness of Claim 9 over Simonnet and Kummrow

Petitioner contends that claim 9 would have been obvious over Simonnet and Kummrow. Pet. 67–70. Patent Owner disagrees. *See* PO Resp. 37–39.

1. Kummrow

Kummrow is an article that describes three-dimensional microfluidic structures with integrated optical fibers, mirrors, and electrodes for flow cytometric analysis of blood cells, and experimental results obtained therewith. Ex. 1006, 972. Most of the fluidic channels had constant height resulting in the confinement of sample flow in one direction. *Id.* at 973. Kummrow's flow cells feature one inlet for the sheath flow, cascaded hydrodynamic focusing, an optical interaction region to detect light scatter and fluorescence, and an interaction region to detect impedance change induced by each cell. *Id.* According to Kummrow, since only one sheath inlet is necessary, easy handling of the structures is ensured. *Id.*

Figure 1(a) of Kummrow is reproduced below:

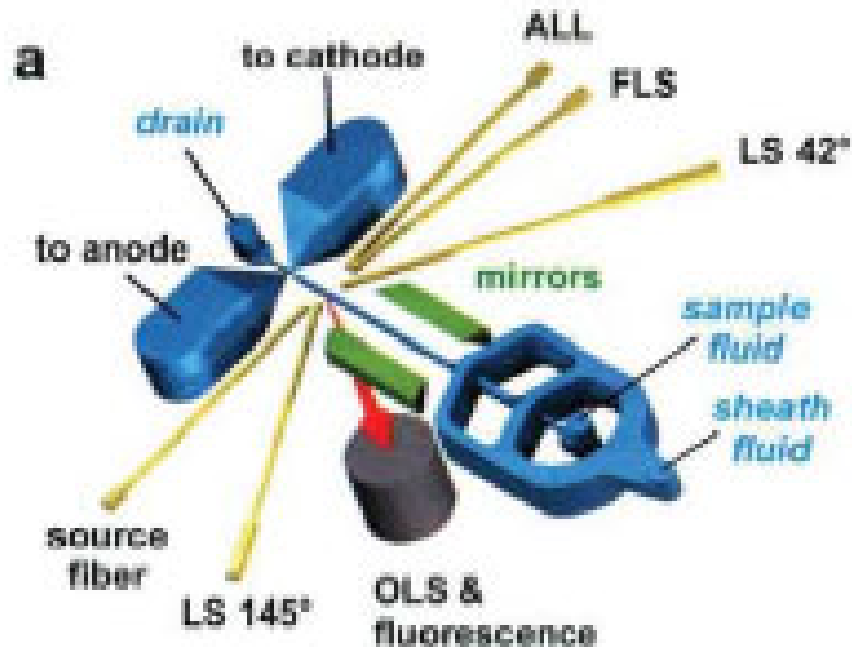


Figure 1(a) of Kummrow is a schematic diagram of a micro-fluidic flow cell featuring two stage cascaded hydrodynamic focusing, integrated mirrors (green), grooves for optical fibers (yellow), and fluidic connections (blue) to externally mounted platinum electrodes. *Id.*

2. Analysis of Claim 9

Claim 9 depends from independent claim 1 and further recites “wherein each of the fluid focusing features is in fluid communication with a first focusing fluid inlet port provided on a top surface of the substrate.” Ex. 1001, 19:40–43.

Petitioner does not rely on Kummrow to remedy the deficiency in the ground of obviousness of claim 1 over Simonnet, which we have addressed above. Accordingly, we determine that Petitioner has not established that claim 9 would have been obvious over Simonnet and Kummrow.

III. CONCLUSION

We conclude that Petitioner has not established that any of the challenged claims are unpatentable.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that on the record before us, Petitioner has not shown by a preponderance of the evidence that claims 1, 2, 6, 8, and 9 of the '439 patent are unpatentable; and

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

In summary:

Claims	35 U.S.C. §	Reference(s)/Basis	Claims Shown Unpatentable	Claims Not Shown Unpatentable
1, 2, 6, 8	102	Simonnet		1, 2, 6, 8
1, 2, 6, 8	103	Simonnet		1, 2, 6, 8
8	103	Simonnet, Kim		8
9	103	Simonnet, Kummrow		9
Overall Outcome				1, 2, 6, 8, 9

IPR2021-00088
Patent 10,583,439 B2

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