Trials@uspto.gov
571-272-7822

Paper No. 47
Entered: April 16, 2019

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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ABS GLOBAL, INC.,
Petitioner,

v.

CYTONOME/ST, LLC,
Patent Owner.

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Case IPR2017-02097
Patent 8,529,161 B2

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Before SCOTT A. DANIELS, BEVERLY M. BUNTING, and TIMOTHY J. GOODSON, *Administrative Patent Judges.*

DANIELS, *Administrative Patent Judge.*

# FINAL WRITTEN DECISION
*35 U.S.C. § 318(a)*

# I. INTRODUCTION

## *A. Background*

ABS Global, Inc., ("Petitioner") filed a Petition to institute an *inter partes* review of claims 1– 20 of U.S. Patent No. 8,529,161 B2 ("the 161 patent"). Paper 1 ("Pet."). Cytonome/ST LLC. ("Patent Owner") filed a Preliminary Response. Paper 9 ("Prelim. Resp."). We instituted an *inter partes* review of claims 1– 20 of the '161 patent on all of the grounds asserted by Petitioner. Paper 11 ("Dec. on Inst."). Patent Owner timely filed a Patent Owner Response (Paper 25, "PO Resp."). Petitioner subsequently filed a Reply (Paper 30, "Pet. Reply"), and Patent Owner timely filed a Sur-Reply to Petitioner's Reply (Paper 40, "PO Sur-Reply").

Patent Owner filed a Motion to Exclude (Paper 38, "Mot. Exclude") and Petitioner filed an Opposition to Patent Owner's Motion to Exclude (Paper 41, "Opp. Mot. Exclude").

Oral argument was held on January 9, 2019 in San Jose, California. (Paper 46, "Tr.").

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 demonstrated by a preponderance of the evidence that challenged claims 1, 4, 8, 9, 12, and 16–20 of the '161 patent—are unpatentable. Petitioner has not demonstrated by a preponderance of the evidence that claims 2, 3, 5–7, 10, 11, and 13–15 are unpatentable.

## *B. Additional Proceedings*

Petitioner states that the '161 patent is asserted against ABS Global in Case No. 3:17-cv-446 in the United States District Court for the District of Wisconsin. Pet. 5.

At the Board, Petitioner filed petitions for *inter partes* review of certain claims of related U.S. Patent Nos. 7,611,309, 9,446,912, and 7,311,476, in Case Nos. IPR2017-02161, IPR2017-02162, and IPR2017-02163. *Id.* at 5–6. We instituted only in this proceeding and IPR2017-02162.

*C. The '161 Patent*

The '161 patent (Ex. 1001), titled "Multilayer Hydrodynamic Sheath Flow Structure," is directed to systems and methods for producing sheath flow in a microchannel in a microfluidic device. Ex. 1001, 1:20–24. By creating sheath flow, a microfluidic device can manipulate, process, and analyze a fluid often containing particles, such as a cell sample, and the device includes at least one channel having microscale dimensions. *Id.* at 4:18–21.

In its Background section, the '161 patent explains that "[s]heath flow is a particular type of laminar flow in which one layer of fluid, or a particle, is surrounded by another layer of fluid on more than one side." *Id.* at 1:28–31. When a sheath fluid with particles suspended therein flows within an orifice or channel, "the particles are lined [up] and accurately pass through the orifice or channel in a single file row." *Id.* at 1:38–39. Sheath flow is used in particle sorting systems, flow cytometers, and other systems for analyzing a particle because the sheath fluid protects the particles, enables positioning of the particles with respect to sensors, and allows for faster flow velocities. *See id.* at 1:44–57. According to the '161 patent, "[c]onventional devices that have been employed to implement sheath flow have relatively complex designs and are relatively difficult to fabricate." *Id.* at 1:57–59.

Figure 1 is reproduced below:

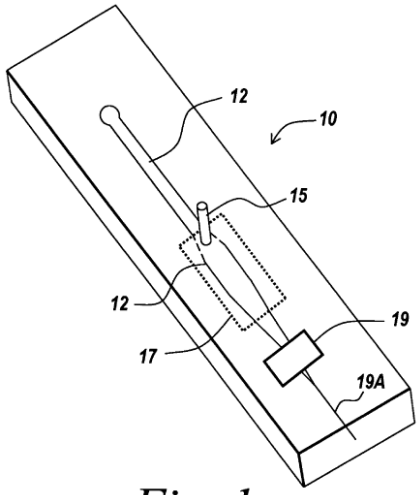



*Fig. 1*

Figure 1 illustrates microfabricated sheath flow structure 10, which includes primary sheath flow channel 12 and sample inlet 15. *Id.* at 3:31–32, 4:47–57. The '161 patent explains the operation of sheath flow structure 10 as follows:

> After introduction of the sample into the sheath fluid, a primary focusing region **17** accelerates and focuses the sheath fluid around the injected sample. Preferably, the primary focusing region **17** focuses the sheath fluid away from the sides and bottom of the sample. A secondary focusing region **19**, disposed downstream of the primary focusing region **17** along the primary sheath flow channel, provides additional focusing of the sheath fluid around the sample after the primary focusing region performs the primary focusing. Preferably, the secondary focusing region **19** focuses the sample in a vertical direction from above the sample.

*Id.* at 4:63–5:6.

Figures 7A and 7B are reproduced below:

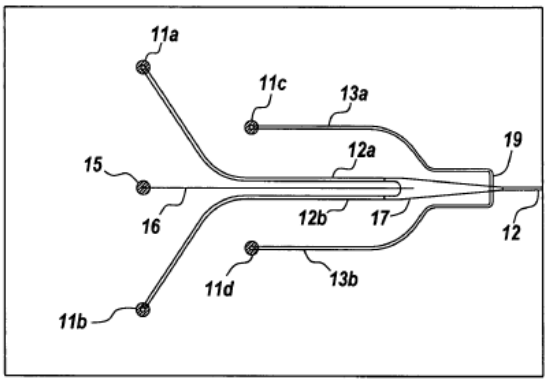



Fig. 7A

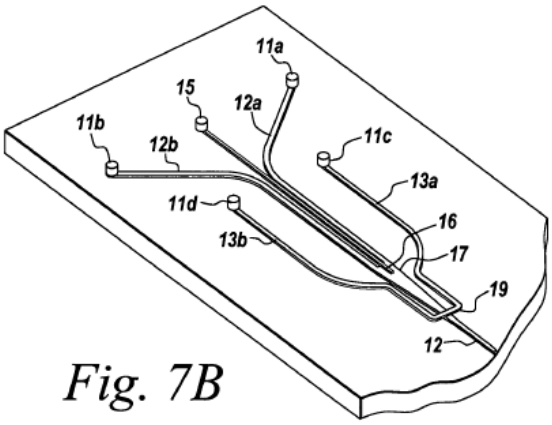



Fig. 7B

Figures 7A and 7B illustrate a sheath flow structure including sample inlet 15 provided upstream of a sheath flow inlet. *Id.* at 3:52–54. The upstream portion of primary sheath flow channel 12 includes separate subchannels 12a, 12b, which converge in primary focusing region 17. *Id.* at 8:34–37. Inlets 11a, 11b introduce sheath fluid to subchannels 12a, 12b, while inlets 11c, 11d introduce sheath fluid to secondary sheath channels 13a, 13b. *Id.* at 8:40–49. "[S]econdary sheath channels [13a, 13b] intersect the primary sheath flow channel **12** in the secondary focusing region [19] to provide focusing of a sample within a flowing sheath fluid in the primary sheath flow channel **12**." *Id.* at 8:41–45.

*D. Illustrative Claim*

Of the challenged claims, claims 1 and 9 are independent. Claim 1 illustrates the claimed subject matter and is reproduced below:

> 1. A microfluidic system comprising:
>
> a primary flow channel for flowing a sample having one or more particles suspended in a suspension medium;
>
> a primary adjustment region including a first set of one or more inlets intersecting the primary flow channel and

> adapted for introducing additional suspension medium into the primary flow channel, whereby the sample is adjusted in at least a first direction; and
>
> a secondary adjustment region downstream of the primary alignment region and including a second set of one or more inlets intersecting the primary flow channel downstream of the first set of one or more inlets and adapted for introducing additional suspension medium whereby the sample is adjusted in at least a second direction different from the first direction.

Ex. 1001, 10:63–11:10.

*E. The Alleged Grounds of Unpatentability*

Petitioner contends that the challenged claims are unpatentable on the following specific grounds.[1]

| References | Basis | Claims Challenged |
|---|---|---|
| Wada[2] | § 102 | 1–20 |
| Wada and Micronics 2001[3] | § 103 | 1–20 |

## II. CLAIM CONSTRUCTION

*A. Legal Standard*

In an *inter partes* review, claim terms in an unexpired patent are interpreted according to their broadest reasonable construction in light of the

[1] Petitioner supports its challenge with a Declaration of Dino Di Carlo, Ph.D. (Ex. 1003) and Patent Owner offers a Declaration of Dr. Ravi Kapur, Ph.D. (Ex. 2002). *See infra*.
[2] Ex. 1006, U.S. Patent No. 6,506,609 B1, issued Jan. 14, 2003.
[3] Ex. 1017, Bernhard H. Weigl et al., *Design and Rapid Prototyping of Thin-Film Laminate-Based Microfluidic Devices*, 3 Biomedical Microdevices 267 (2001).

specification of the patent in which they appear. 37 C.F.R. § 42.100(b) (2017); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2144–46 (2016) (upholding the use of the broadest reasonable interpretation standard).[4]

Claim terms are given their ordinary and customary meaning as would be 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. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007); *see also Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996) ("Although words in a claim are generally given their ordinary and customary meaning, a patentee may choose to be his own lexicographer and use terms in a manner other than their ordinary meaning, as long as the special definition of the term is clearly stated in the patent specification or file history."). We apply this standard to the claims of the '161 patent.

Central to the patentability determination in this proceeding is the construction of certain words and terms in the claims, including *inter alia*, "adjusted," "focusing," and "aligning." We address each of these words and terms, as well as others, in our discussion below.

*B. Adjusted* and *adjusting*

We determined in our Decision on Institution that the words, "adjusted" and "adjust[ing]" be accorded their plain and ordinary meaning as would have been understood by one of ordinary skill in the art, including,

[4] On October 11, 2018, the USPTO revised its rules to harmonize the Board's claim construction standard with that used in federal district court. Changes to the Claim Construction Standard for Interpreting Claims in Trial Proceedings Before the Patent Trial and Appeal Board, 83 Fed. Reg. 51,340 (Oct. 11, 2018)) (to be codified at 37 C.F.R. pt. 42). This rule change, however, applies to petitions filed on or after November 13, 2018, and therefore does not apply to this proceeding. *Id*.

"to move." Dec. on Inst. 8. Patent Owner argues that this is too broad a meaning, "because it allows the sample to be disrupted in a way that is inconsistent with the specification." PO Resp. 27. Patent Owner argues that the intrinsic evidence in the specification "requires a meaning of 'adjust' that is narrower than the overly broad term, 'move.'" *Id.* at 28. Patent Owner argues that "the most reasonable reading of 'adjust' requires that in addition to 'moving,' it at least preserve (i.e., not disrupt) the suspended sample core." *Id.* at 28–29.

Petitioner considers our original construction to be correct and argues that Patent Owner's proposed construction reads in limitations from the specification or, alternatively, renders the claims indefinite. Pet. Reply 3–5.

On the full record now before us, we find Patent Owner's proposed construction, which relies on portions of the specification describing "focusing" of the sample, to be untenable. PO Resp. 28 (citing Ex. 1001, 1:32–34, 2:2–5, 2:16–17, 5:10–14, 9:56–61, 10:12–16, 11:1–3). The specification is clear that the primary and secondary *focusing* regions 17 and 19, together, "provide[] three-dimensional focusing of the sheath fluid around the sample." Ex. 1001, 5:9–10. As Patent Owner points out, the specification describes that following the primary and secondary focusing regions 17 and 19, "[t]he resulting sheath flow **200** is a laminar flow that is *sample focused* hydrodynamically from all sides away from the walls at the channel center, as shown in FIG. **4D**." *Id.* at 7:57–63 (emphasis added). In every aspect of the written description, the specification describes "focusing region[s]" and "focus[ing] the sample," never, "adjustment regions" or "adjusting the sample." *Id.* at 2:12–16, 5:7–10. The term "adjustment region" never appears in the specification, except for in the claims.

Contrary to Patent Owner's argument, the specification does not explain how the sample would be "adjusted," as opposed to being "focused." *See* PO Resp. 28 (Patent Owner contends that "the specification requires a meaning of 'adjust' that is narrower than the overly broad term, 'move.'"). The first time we find the word "adjusted," it is recited in claim 1 as "the sample is adjusted." Ex. 1001, 11:2–3. Claim 6, which depends directly from claim 1, recites "adjusting the sample . . . includes focusing the sample." Ex. 1001, 11:24–26. It is reasonable based on claim differentiation, therefore, to understand that "adjusting" as used in the claims is broader than "focusing." All this, however, explains very little about a special meaning, or the complete scope, of the word "adjusted." It is not clear from the specification that "adjusting" or "adjusted" is narrower, broader, or otherwise, relative to the plain and ordinary meaning of "adjust" that means, as we previously determined, "to move." *See In re ICON Health and Fitness, Inc.*, 496 F.3d 1374, 1379 (Fed. Cir. 2007) ("[W]e look to the specification to see if it provides a definition for claim terms, but otherwise apply a broad interpretation.").

As we discussed in our Decision on Institution, the claims, on their face, provide little, if any, contextual evidence supporting a narrow meaning. We find Petitioner's construction to be the most convincing, that the words "adjusted" and "adjust[ing]" be accorded their plain and ordinary meaning as would have been understood by one of ordinary skill in the art, including "to move." Pet. 28; Dec. on Inst. 8 (citing Ex. 1003 ¶ 128). On the full record now before us, we are persuaded to maintain as our construction the plain and ordinary meaning of "adjusted," and "adjusting," which means, "to move." *Id.*

*C. Focusing*

Several dependent claims, e.g., claim 6, require that "adjusting the sample . . . includes focusing the sample." Ex. 1001, 11:24–26. We determined previously that "focusing" means "accelerating sheath fluid to exert a force on the particles, which narrows and aligns the particle stream in a desired direction relative to the boundaries of the channel, while achieving or maintaining laminar flow." Dec. on Inst. 17. Patent Owner agrees with our initial interpretation of "focusing." PO Resp. 31–35.

Petitioner initially proposed that "'focusing' does not appear to have a meaning that differs from 'adjusting' or 'adjusted,'" and the broadest reasonable interpretation of "focusing" is "moving" or "moved." Pet. 30. Petitioner now argues that the "plain and ordinary meaning—'pinching, narrowing, or otherwise confined'—is appropriate." Pet. Reply 7. Petitioner disagrees with the Board's initial construction, specifically, because it includes "accelerating" and "aligning" the sample particle stream. *Id.* at 8–13; *see* Tr. 24:13–16 (Petitioner's counsel asserted during oral argument that "you could take your construction, just remove the requirement that the sheath fluid be accelerating and that the -- that focusing results in alignment of the sample.").

With respect to "accelerating," Petitioner contends that even though the applicant argued to the Examiner during prosecution that "focusing" required "accelerating," this representation was "factually inaccurate" and was not, in fact, what was understood by those of ordinary skill in the art. *See* Ex. 2001, 48 (Applicant argued to the Examiner that "focusing of a particle in sheath fluid requires acceleration and removal of sheath fluid from around a particle."). Petitioner argues that, to the contrary, those of

ordinary skill in the art understand that "focusing" may include "accelerating" but that the sample stream does not have to be accelerated to be focused. Pet. Reply 8–11 (citing Ex. 1003 ¶¶ 41–42; Ex. 1026, 229:43–8, 229:25–230:6).

The disputed aspects of our construction are, therefore, whether "focusing" requires "accelerating" sheath fluid, and "align[ing]" the particle stream. Although in our Decision to Institute, we adopted the requirement that "focusing" requires both "accelerating and "align[ing]," we only need to address the issue of "align[ing]" because resolution of that part of the dispute disposes of all of Petitioner's challenges with respect to the claims including the "focusing" limitation.

With respect to "aligning," based on the complete record we are persuaded that "focusing" requires "align[ing] the sample particle stream in a desired direction relative to the boundaries of the channel." Initially, we determined in our Decision to Institute that a variety of extrinsic evidence compelled this determination. *See* Dec. on Inst. 14–16 (citing e.g., Ex. 1006, 8:22–25, 10:26–29; Ex. 1020, 74; Ex 1021, 133). The extrinsic and intrinsic evidence developed during this proceeding confirms our initial determination. For example, Petitioner's declarant, Dr. Di Carlo, although he did not use the word "align," explained in his declaration that

> [a]n example of three dimensional focusing involves injecting additional fluid into the flow channel through a pair of horizontal, orthogonal inlets (as in the two-dimensional focusing example above) and injecting additional fluid into the flow channel through a vertical inlet to confine the sample to the center of the flow channel.

Ex. 1003 ¶ 47. Based on a pragmatic and contextual understanding of this testimony, we are not apprised of a material difference between the sample

being "align[ed]" and "confine[d]" in the "center of the flow channel." It is further clear, in the context of Dr. Di Carlo's testimony that one purpose of hydrodynamic focusing is to position a sample in a flow channel.

Dr. Di Carlo agreed during his deposition that aligning cells in a sample to pass through a detector was at least one purpose of hydrodynamic focusing.

> Q. Do you understand the upstream channel to be injecting fluid?
>
> A. A skilled person would understand that the upstream channel is injecting sheath fluid to hydrodynamically focus the sample that's coming in at 2300.
>
> Q. Is one of the purposes of the upstream channel to move the cells such that they pass through the detector?
>
> A. So hydrodynamic focusing to align cells to pass through the detector, at relatively -- in uniform position and velocity would be -- would be one of the purposes to do hydrodynamic focusing, yes, although there are other purposes for hydrodynamic focusing, yeah.

Ex. 2004, 43:2–16. A reasonable reading of the specification of the '161 patent is consistent with Dr. Di Carlo's testimony, and describes the resulting relative positioning of the sample in a channel such that one of ordinary skill in the art would understand focusing to require aligning the sample. The written description states that

> the combination of the primary focusing region **17** and the secondary focusing region **19** provides three-dimensional focusing of the sheath fluid around the sample. The resulting sheath flow is sample-focused hydrodynamically on all sides of the sample away from the walls of the primary sheath flow channel **12,** with the sample being suspended as a focused core in the approximate center of the channel.

Ex. 1001, 5:7–14. We accord certain weight to this evidence as it is consistent in describing that the result of "focusing" includes positioning,

i.e., "aligning" the sample in a desired relationship to the channel in which it is flowing.

Petitioner argues that the claims "make clear that 'aligning' a sample, is distinct from 'focusing' a sample." Pet. Reply 13 (citing Ex. 1001, 11:11–13 (claim 2)). This argument is not persuasive because claim 1 from which claim 2 depends, does not require "focusing" a sample, but "adjusting" a sample. *See* Ex. 1001, 11:3–4 (Claim 1 recites "a primary adjustment region," not "a primary focusing region."). Petitioner also argues that "Dr. Gilbert testified that focusing ***may*** result in aligning the particle stream if the particle-stream diameter is narrowed to 'approach the diameter . . . of the particles,' but that otherwise the particle stream will be distributed across the sample stream." Pet. Reply 13 (citing Ex. 1026, 233:15–234:5). This argument misconstrues our construction. Our claim construction does not state anything about the specific alignment of relative particles, i.e., one particle relative to another particle, in a sample. Our claim construction clearly states that, focusing ". . . aligns the particle stream in a desired direction *relative to the boundaries of the channel*." Therefore, Petitioner's argument with respect to the relative alignment of particles with one another within the sample particle stream is misplaced.

Having the benefit of a complete record now before us, and for the reasons discussed, we need not resolve the issue of whether "focusing" requires "accelerating sheath fluid," and we determine that "focusing" requires "sheath fluid exerting a force on the particles, which narrows and aligns the particle stream in a desired direction relative to the boundaries of the channel, while achieving or maintaining laminar flow."

*D. Aligning*

Based on a general purpose dictionary definition, the parties agree that "aligning," as it is recited in dependent claim 2 and 10, means "to move into a line." Pet. 32 (citing Ex. 1009, 53); PO Resp. 31. Because the parties are in agreement as to the meaning of this term, and because it does not conflict with our determination as to the meaning of "focusing" discussed above, we accept and apply this meaning of "aligning" for purposes of this Decision.

*E. Orienting*

We determined initially, based on the parties' agreement, that "orienting" is understood to mean "moving the object of the phrase (the sample) into a specified position." Dec. on Inst. 18. Now, Patent Owner asserts that "orienting" means "providing directionality to asymmetric particles within a sample." PO Resp. 36.

The word "orienting" is not found in the specification, except in dependent claims 8 and 16, both of which recite, "wherein adjusting the sample in at least the first direction and adjusting the sample in at least the second direction includes orienting the sample." Ex. 1001, 11:30–33, 12:23–25. Dependent claims 8 and 16 are exactly the same as dependent claims 2 and 10, except that instead of "aligning the sample" they recite "orienting the sample."

Patent Owner argues that one of ordinary skill in the art would understand that "the term 'orienting' has a plain and ordinary meaning that applies in the art, and it requires that individual particles are pointed in the same direction." PO Resp. 37. Patent Owner argues that the "meaning of 'orient' is well-understood in microfluidics to refer to 'orienting' asymmetric particles (e.g., rod-shaped particles or sperm cells) with respect

to flow direction and/or channel walls." *Id.* (citing Ex. 2005 ¶ 13; Ex. 1003 ¶ 228; Ex. 2004, 26:10–14). Patent Owner contends that Petitioner's declarant, Dr. Di Carlo, testified that "[t]he term 'orient' is also sometimes used in the field of microfluidics to refer to providing directionality to asymmetric particles within a sample." *Id.* (citing Ex. 1003 ¶ 228). Although he did state this, Dr. Di Carlo concurrently opined that, "it does not appear to be used in this manner in the '161 Patent." Ex. 1003 ¶ 228. Patent Owner's declarant, Dr. Kapur, testifies that "[p]roviding directionality to asymmetric particles would be the plain and ordinary meaning of the term 'orienting' in the field of microfluidics." Ex. 2005 ¶ 13. Dr. Kapur further testifies that "'orienting the sample'. . . mean[s] that the entire sample directionally orients asymmetrical particles with respect to flow direction and/or channel walls." *Id.*

Arguably, the ordinary meaning of "orient" certainly *could* be used to describe a specific positioning of anything, e.g., particles in a sample, as both declarants recognize. We are not apprised, however, of any persuasive evidence in the specification that "orient" as recited in claim 6 and 18 is intended to apply to specific particle orientation (symmetric or asymmetric) within the sample. Patent Owner's declarant, Dr. Kapur, states that "[p]roviding directionality to asymmetric particles would be the plain and ordinary meaning of the term 'orienting' in the field of microfluidics." Ex. 2005 ¶ 13. This is, to an extent, commensurate with what Dr. Di Carlo says as well. Dr. Kapur, however, simply concludes without further explanation or basis, that a person of skill in the art would understand the claim language "orienting a sample" to include the additional limitations relating to asymmetric particles. Indeed, neither Dr. Kapur nor Patent

Owner describe or point to any reference to asymmetric particles and their specific orientation in the specification of the '161 patent or elsewhere. We give credit to Dr. Di Carlo's testimony, as he states that "sometimes," but not in the case of the '161 patent, the term "'orient' . . . refer[s] to providing directionality to asymmetric particles." Ex. 1003 ¶ 228. Moreover, even if one of ordinary skill in the art *could* understand "orient" in terms of particles, the claim is clear on its face that it is "the sample" that is oriented. *See Eastman Kodak Co. v. Goodyear Tire & Rubber Co.*, 114 F.3d 1547, 1552 (Fed. Cir. 1997) ("The claim language itself defines the scope of the claim."). It is important not to import into a claim any limitations that are not a part of the claim. For example, a particular embodiment appearing in the written description may not be read into a claim when the claim language is broader than the embodiment. *SuperGuide Corp. v. DirecTV Enters., Inc.*, 358 F.3d 870, 875 (Fed. Cir. 2004). Here, in the '161 patent, we are not apprised of any embodiment in the specification describing directionality of asymmetric particles.

We find Dr. Di Carlo's testimony, that the word "orient" is *not* used to describe asymmetric particle orientation, to be the most credible and consistent with the express recitations in claims 8 and 16. Therefore, we are not persuaded to limit our construction of "orienting" to "directionality of asymmetric particles."

On the full record now before us, we determine that "orienting" means "moving the object of the phrase (the sample) into a specified position."

*F. Other constructions*

The parties agree that "positioning" (claims 18 and 20) means "moving the object of the phrase (particles) 'to a particular place.'" Pet. 34 (citing Ex. 1009, 1508–09; Ex. 1003 ¶ 146); PO Resp. 38.

The parties agree that the broadest reasonable interpretation of "primary alignment region" (claim 1) is "primary adjustment region." Pet. 34–35; PO Resp. 38.

The parties agree that "a spatial characteristic" (claims 4 and 12) would be understood to mean changing "the position in space." Pet. 32; PO Resp. 38.

The parties agree that "increas[ing] a spatial uniformity . . . relative to the flow channel" (claims 5 and 13) means "increasing the similarity of the position in space of the object of the phrase (particles) relative to the flow channel." Pet. 32; PO Resp. 35.

The parties agree that "aligning" (Claims 2, 3, 10, and 11) means "to move into a line." Pet. 32 (citing Ex. 1009, 53); PO Resp. 31.

The parties' agreed upon constructions of these words and phrases are consistent with our understanding of the plain meaning of the claim language and relevant disclosure and written description in the specification of the '161 patent. Beyond the parties' agreed upon constructions, we do not provide explicit construction for any claim term. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co. Matal*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (noting that "we need only construe terms 'that are in controversy, and only to the extent necessary to resolve the controversy'") (citing *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

## III. ANALYSIS

We turn now to Petitioner's asserted grounds of unpatentability.

### *A. Legal Principles*

#### *1. Anticipation*

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. Inc., v. Union Oil Co.*, 814 F.2d 628, 631 (Fed. Cir. 1987). Moreover, "[b]ecause the hallmark of anticipation is prior invention, the 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). Whether a reference anticipates is assessed from the perspective of an ordinarily skilled artisan. *See Dayco Prods., Inc. v. Total Containment, Inc.*, 329 F.3d 1358, 1368 (Fed. Cir. 2003) ("[T]he dispositive question regarding anticipation [i]s whether one skilled in the art would reasonably understand or infer from the [prior art reference's] teaching that every claim element was disclosed in that single reference.").

#### *2. Obviousness*

In *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966), the Supreme Court set out a framework for assessing obviousness under § 103 that requires consideration of four factors: (1) the "level of ordinary skill in the pertinent art," (2) the "scope and content of the prior art," (3) the "differences between the prior art and the claims at issue," and (4) "secondary considerations" of non-obviousness such as "commercial success, long-felt but unsolved needs, failure of others, etc." *Id.* at 17–18.

"While the sequence of these questions might be reordered in any particular case," *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 407 (2007), the Federal Circuit has "repeatedly emphasized that an obviousness inquiry requires examination of all four Graham factors and that an obviousness determination can be made only after consideration of each factor." *Nike, Inc. v. Adidas AG*, 812 F.3d 1326, 1335 (Fed. Cir. 2016). We note that, with respect to the fourth *Graham* factor, the parties have not presented argument or evidence directed to secondary considerations of nonobviousness. The analysis below addresses the first three *Graham* factors.

*B. Level of Ordinary Skill in the Art*

In determining the level of skill in the art, we consider the type of problems encountered in the art, the prior art solutions to those problems, the rapidity with which innovations are made, the sophistication of the technology, and the educational level of active workers in the field. *Custom Accessories, Inc. v. Jeffrey-Allan Indus. Inc.*, 807 F.2d 955, 962 (Fed. Cir. 1986); *Orthopedic Equip. Co. v. U.S.*, 702 F.2d 1005, 1011 (Fed. Cir. 1983).

The parties agree that a person of ordinary skill in the art is "someone who has a bachelor's or master's degree in the field of bioengineering, mechanical engineering, chemical engineering, or analytical chemistry; or with a bachelor's or master's degree in a related field and at least three years of experience in designing or developing microfluidic systems." PO Resp. 24 (citing Pet. 23). Our review of the '161 patent, as well as the prior art in this proceeding is consistent with the parties agreement upon the level of

ordinary skill.[5] Accordingly, for purposes of this Decision, we find the level of ordinary skill in the art to be that described above and agreed upon by the parties and address our analyses in such terms.

*C. Claims 1–20 — Anticipation by Wada*

Petitioner argues that claims 1–20 are anticipated by Wada. Pet. 35–69. For the reasons set forth below, we determine that Petitioner has shown by a preponderance of the evidence that claims 1, 4, 8, 9, 12, 16, 18, and 20 are anticipated by Wada.

*1. Wada*

Wada is entitled "Focusing of Microparticles in Microfluidic Systems." Ex. 1006, (54). Figure 1A is reproduced below:

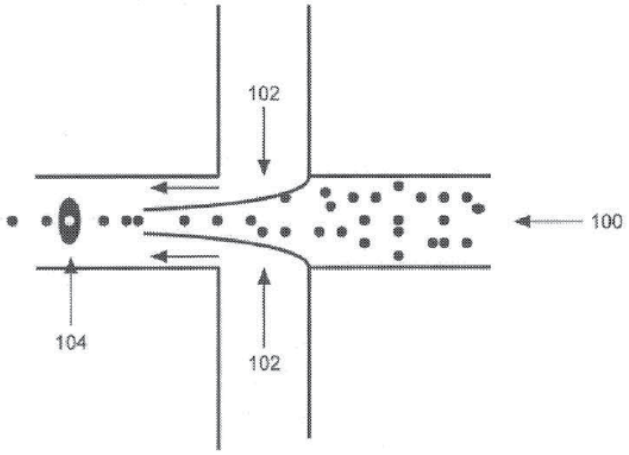



Fig. 1A

Figure 1A is a schematic showing focusing of cells in a microscale system. *Id.* at 6:14–17. Cells 100 flow from a microchannel into a cross-junction and are "focused by introducing hydrodynamic flows **102** from the

[5] Patent Owner states that it "does not concede" that certain references relied upon by Petitioner are prior art. PO Resp. 24. Patent Owner, however, provides no persuasive evidence or substantive argument that the references relied upon in the Petition, or in this Decision, namely Wada and Micronics 2001, are not prior art under 35 U.S.C. §102.

two orthogonal microchannels." *Id.* at 9:8–11. The patent describes that "[n]on-orthogonal (e.g., opposing or non-opposing) microchannels" can also be used. *Id.* at 9:12–14. Particles can be focused with a single focusing microchannel or "by using a series of offset focusing microchannels to achieve focusing by serial introduction of fluids from the offset channels." *Id.* at 9:14–17.

Wada's Figure 22 is reproduced below:

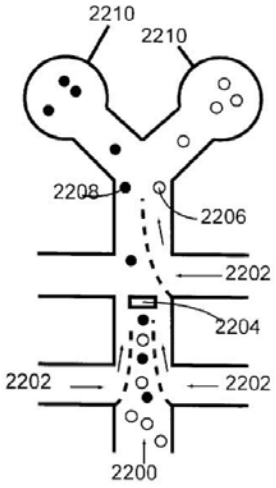



Fig. 22

Wada's Figure 22 depicts a microchannel configuration that includes detector 2204. *Id.* at 7:30–33; 13:1–16. Cells 2200 are flowed in a microchannel that intersects with a first hydrodynamic flow 2202 upstream of detector 2204. *Id.* at 13:2–7. A second hydrodynamic flow 2202 is also introduced at "[a] second set of opposing microchannels [] typically located downstream from detector **2204** . . . to direct selected cells **2208** (e.g., fluorescently-labeled cells) and non-selected cells **2206**" eventually into collections wells 2210. *Id.* at 13:10–16.

*2. Independent claims 1 and 9*

Petitioner argues that Wada meets every limitation recited in independent claims 1 and 9. Pet. 35. Claim 9 is a method claim reciting

similar limitations to apparatus claim 1. *Compare* Ex. 1001, 10:63–11:10, *with* 11:33–12:3. We address each independent claim in turn, below.

*Claim 1*

Petitioner argues that Wada discloses expressly the structure and systems recited in claim 1—namely, "a microfluidic system" having "a primary flow channel," as well as "a primary adjustment region" and a secondary adjustment region," where the adjustment regions include "inlets . . . adapted for introducing additional suspension medium." Pet. 35–55. Petitioner argues that Wada discloses a suspension of cells and molecules flowing in the system, including "flowing a sample having one or more particles suspended in a suspension medium" as recited in claim 1. *Id.* at 44–45 (citing Ex. 1006, 2:52–53, 2:60–63, 7:49–57, 23:21–22; Ex. 1003 ¶¶ 173, 175, 177).

According to Petitioner, Wada discloses the claimed structure, for example in Figures 1A–B, in which "cells 100 (or other particles) are typically flowed from one microchannel into the cross-junction and focused by introducing hydrodynamic flows 102 from the two orthogonal microchannels." *Id.* at 37 (citing Ex. 1006, 9:8–11; Ex. 1003 ¶ 159). Petitioner argues that Wada's "common intersection region" discloses the same structure and function as the claimed "primary adjustment region . . . whereby the sample is adjusted in at least a first direction," as recited in claim 1. *Id.* at 38–39. Petitioner argues further that Wada "describes one or more additional adjustment regions for further focusing the sample (and the particles in the sample) within the sheath fluid." *Id.* at 39 (citing Ex. 1006, 9:13–17; Ex. 1003 ¶ 159).

To meet the final limitation in claim 1, that "the sample is adjusted in at least a second direction different from the first direction," Petitioner relies on the embodiment shown in Figures 22 and 23 of Wada, reproduced below.

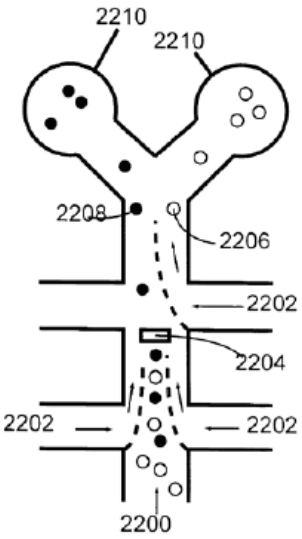



Fig. 22

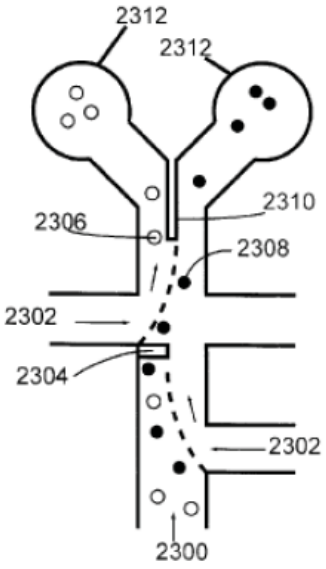


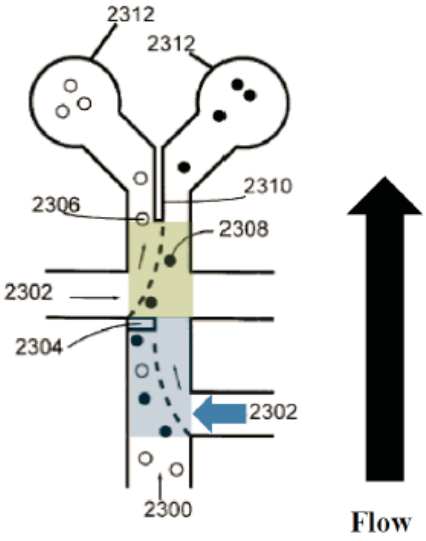

Fig. 23

Wada's Figures 22 and 23, above, illustrate alternative embodiments having different microchannel arrangements. Ex. 1006, 7:30–36. Figure 22 illustrates an embodiment having a pair of opposing microchannels downstream from a first pair of opposing microchannels. Figure 23 illustrates an embodiment having a pair of opposing microchannels downstream from a single microchannel. Both embodiments include collection wells for receiving particular cells. *Id.* at 13:10–16.

Patent Owner's argument is straightforward. Patent Owner argues that Wada does not disclose adjusting the sample in two different adjustment regions, in two different directions. PO Resp. 39. According to Patent Owner, e.g., observing Wada's Figure 23, "Wada's downstream channels . . . fail to adjust the sample because the left downstream channel ***disrupts***

the sample core by sorting—i.e., knocking out of the core—individual black-shaded particles on a selective basis." *Id.* at 40. In other words, Patent Owner's main argument is that "[t]his is a disruption and dispersion of the sample for sorting particles, not an adjustment." *Id.* at 41.

We are persuaded by Petitioner's evidence and comparison of the claim elements to the disclosure in Wada, because it is consistent with our own review of Wada revealing the same elements in a microfluidic system as recited in claim 1. For example, using Petitioner's annotated Figure 23, reproduced below (Pet. 51; PO Resp. 40), Wada discloses a microfluidic device in Figure 23 having a primary flow channel in which sample cells 2300 are flowing in a primary flow channel towards a first intersection, (blue), with a microchannel inlet introducing additional suspension medium.




Petitioner's annotated Figure 23 from Wada, above, illustrates an embodiment of a microfluidic system having cells 2300 flowing past detector 2304. Following detector 2304, sample cells 2300 flow through a second, downstream (green), intersection where additional suspension medium from at least a pair of opposing microchannel inlets moves, directs,

i.e., sorts, the sample cells into collection wells 2312. Indeed, Patent Owner does not dispute that Wada discloses these limitations in claim 1. *See* PO Resp. 39–49.

With respect to Patent Owner's position that "sorting" the cells in Wada's second intersection is not "adjusting" the sample, we disagree. We determined in our claim construction that the plain and ordinary meaning of "adjusting," means, "to move." *See supra* Section II.C. Even considering Patent Owner's description of Wada, that the downstream channel "***disrupts*** the sample core by sorting," the sample cells, as they are sorted, are being moved. PO Resp. 40. "Sorting," and thereby "moving," the sample, is therefore within with the scope of "adjusted," and "adjusting." Dr. Di Carlo testifies, persuasively, that "[t]he term '*adjusted*' and the term '*adjusting*,' as used in the independent claims from which those claims depend, are being used in a manner that is consistent with their plain and ordinary meanings, i.e., 'moved' or 'moving."' *See* Ex. 1003 ¶ 130. Dr. Di Carlo's testimony and Petitioner's argument are persuasive because even if one considers the sample to be "disrupted" and "sorted," at the second intersection—as Patent Owner alleges occurs in Wada, it is quite reasonable to understand that disrupting and sorting the sample is "moving" the sample. According to the proper claim construction, therefore, "adjusting" the sample at the second intersection is disclosed in Wada. We do not agree with Patent Owner's argument that the "difference between sorting particles and adjusting the

sample highlights a key difference between the '161 Patent and Wada." *See* PO Resp. 41.[6]

Petitioner has shown by a preponderance of the evidence that Wada discloses each limitation of the "microfluidic system" recited in claim 1. On the complete record now before us, we find that claim 1 is anticipated by Wada.

*Claim 9*

Claim 9 is very similar to claim 1 and recites "[a] method for configuring a sample microfluidic system." Ex. 1001, 11:33. Method claim 9 basically re-words the limitations of claim 1 to emphasize the functionality of the claimed system. For example, instead of "a primary flow channel for flowing a sample" as recited in claim 1, claim 9 recites "flowing a sample having one or more particles suspended in a suspension medium." *Id.* at 11:35–36. Also, claim 9 recites the steps of "introducing additional suspension medium into the primary flow channel at a primary [secondary] adjustment region." *Id.* at 11:37–44. And, exactly the same as claim 1, the final limitation in claim 9 recites that "the sample is adjusted in at least a second direction different from the first direction." *Id.* at 12:2–3.

Petitioner argues the two independent claims together and that claim 9 is anticipated for the same reasons as claim 1. *See* Pet. 40–55. Patent Owner similarly argues claims 1 and 9 together. Patent Owner argues, as discussed above, that Wada does not anticipate claim 9 because "Wada's

[6] It may be, as Patent Owner argues, that one aspect of "[t]he invention adjusts a sample in two regions to prepare the sample for detection." PO Resp. 41. This is not, however, what is recited in claims 1 or 9, neither of which include any such limitation to a detector, or the function of preparing a sample for detection.

downstream channels . . . fail to adjust the sample because the left downstream channel ***disrupts*** the sample core by sorting." PO Resp. 40.

We determine, for the same reasons as discussed above with respect to claim 1, that Wada, for example in Figure 23, discloses flowing sample cells through a microfluidic system that illustrates all the steps of independent claim 9 including, "flowing a sample . . . through a primary flow channel," and "introducing additional suspension medium . . . at a primary [secondary] adjustment region using a first [second] set of one or more inlets." Ex. 1001, 11:35–44. A comparison of these initial limitations in claim 9, apart from being written in a method form, reveals no substantive difference from any of the limitations in claim 1. Nor does Patent Owner argue that the limitations are substantively different. Therefore, our analysis above with respect to claim 1, holds true for claim 9 as well—that these method steps are disclosed by Wada.

Again, as discussed above, we determined in our claim construction that the plain and ordinary meaning of "adjusting," means, "to move." *See supra* Section II.C. Even considering Patent Owner's description of Wada, that the downstream channel "***disrupts*** the sample core by sorting," it is more than reasonable to understand that the sample cells, as they are sorted, are still being moved. *See* PO Resp. 40. "Sorting," and thereby "moving," the sample, is therefore commensurate with the scope of "adjusted," and "adjusting the sample." In light of our claim construction and our analysis of Wada's disclosure we do not agree with Patent Owner's argument that there is a difference between "sorting" sample particles as disclosed by Wada, and "adjusting" the sample as called for in independent claim 9.

We find that Petitioner has shown by a preponderance of the evidence that Wada discloses each step of the "method for configuring a sample microfluidic system" recited in claim 9. With the complete record now before us, we determine that claim 9 is anticipated by Wada.

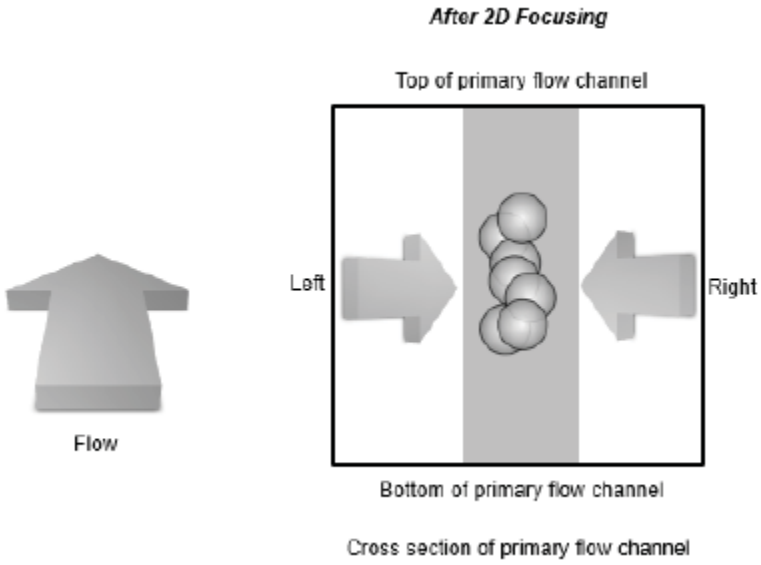
*3. Dependent Claims 2–8 and 10–20*

Because dependent claims 2–8 and 10–16, which depend respectively from independent claims 1 and 9, include the same corresponding subject matter and recite the same specific limitations, we address these dependent claims together.

*Claims 2 and 10*

Claims 2 and 10 recite "wherein adjusting the sample in at least the first direction and adjusting the sample in at least the second direction includes *aligning* the sample." Ex. 1001, 11:11–13, 12:4–6 (emphasis added). Based in part on the parties' agreement, we determined that "aligning" means "to move into a line." Section II.D.

Petitioner argues that Wada "describes this alignment in the context of alignment in two different directions." Pet. 55. Relying on support from its declarant, Dr. Di Carlo, Petitioner reproduces the following diagram and explains that "[f]or example, the sheath fluid pinches the sample fluid into a narrower stream, aligning both the sample and the particles within the sample:




Pet. 56 (citing Ex. 1003 ¶ 198). According to Petitioner, the figure above, illustrates that "a microfluidic system that focuses cells and other particles within a sample into a desired region within the flow channel would have been understood by a skilled person to be aligning the sample within the flow channel." *Id.* (citing Ex. 1003 ¶ 199).

Patent Owner argues that Wada fails to disclose "a second adjustment region that aligns the sample and/or particles within the sample" as required by the claims. PO Resp. 44. Patent Owner points out that in our Decision on Institution, we were not convinced that Wada's disclosure of different directional alignment of a sample fluid met the limitation that such alignment occur in distinct upstream and downstream adjustment regions in the flow channel, as called for in claims 2 and 10. Here, based on the evidence developed in the complete proceeding and the proper claim construction, we remain unpersuaded that Wada discloses alignment, i.e. moving sample particles into a line in the secondary adjustment region downstream from the primary adjustment region.

We find Patent Owner's position and evidence to be the most compelling, namely that in Wada at the second intersection, shown for example in Petitioner's annotated Figure 23 (green highlighted area), above, "the particles and sample are knocked out of "alignment" for the same reasons they are knocked out of focus." PO Resp. 45 (citing Ex. 2002 ¶ 19). Indeed, Patent Owner's evidence and argument is consistent with Dr. Di Carlo's testimony that "[a] microfluidic system that focuses a sample containing cells and other particles within a sample into a line within the flow channel would have been understood by a skilled person to be aligning the sample within the flow channel." Ex. 1003 ¶ 199.

Because Wada discloses sorting the particles, which removes the particles from alignment at the second intersection in Wada, we are persuaded that Wada does not disclose the limitation of "adjusting the sample in at least the second direction includes aligning the sample," as called for in claims 2 and 10. Wada, therefore, does not anticipate claims 2 and 10.

*Claims 3 and 11*

Claims 3 and 11 depend from claims 2 and 10 respectively, and both recite "wherein aligning the sample includes aligning one or more particles in the sample." Ex. 1001, 11:14–15, 12:7–8. For the same reasons discussed above, namely that Wada does not disclose alignment of the sample or the particles within the sample at the second intersection, claims 3 and 4 are also not anticipated by Wada.

*Claims 4 and 12*

Claims 4 and 12 depend directly from independent claims 1 and 9 respectively, and recite "wherein adjusting the sample in at least the first

direction and adjusting the sample in at least the second direction includes adjusting a spatial characteristic of one or more particles in the sample." Ex. 1001, 11:16–19, 12:9–12. Based in part on the parties' agreement, we determined that "a spatial characteristic" means changing "the position in space." Pet. 32; PO Resp. 38.

Petitioner argues that Figure 23 of Wada discloses positioning particles in alignment to pass through detector 2304 and then separating into separate collection wells 2312, so that "the location in the channel of a plurality of particles in each of the two groups relative to the flow channel becomes more regular as the particles travel through the adjustment regions." Pet. 59 (citing Ex. 1003 ¶ 205).

Patent Owner does not present substantive arguments with respect to claims 4 and 12. *See* PO Resp. 39–60.

As discussed above, our review of the complete record of this case reveals that Wada initially adjusts and aligns, as we have construed these terms, so that the sample particles pass detector 2304, and then, at the second intersection "direct[s] selected cells **2308** (e.g., fluorescently-labeled cells) and non-selected cells **2306** to . . . one of two microchannels, each terminating in particular collection wells **2312.**" Ex. 1006, 13:27–31. Claims 4 and 12, consistent with their respective independent claims 1 and 9, recite the limitation that "adjusting the sample . . . includes adjusting a spatial characteristic." Based on the correct claim constructions, we understand, as set forth previously, that "adjusting" means "moved," or "moving," and that adjusting "a spatial characteristic" means changing, or moving, "the position in space." We are persuaded that Wada discloses these limitations, even at the second intersection where the sample particles

are directed out of alignment and sorted into separate wells, it is reasonable to recognize that the sample particles are moving and changing their position in space as they are sorted into the collection wells.

We find that Petitioner has shown by a preponderance of the evidence that Wada discloses "adjusting the sample . . . includes adjusting a spatial characteristic" as recited in claims 4 and 12. On the complete record now before us, we determine, therefore, that claims 4 and 12 are anticipated by Wada.

*Claims 5 and 13*

Claims 5 and 13 depend directly from claims 1 and 9 respectively, and recite the additional limitation "wherein adjusting the sample in at least the first direction and adjusting the sample in at least the second direction increases a spatial uniformity of a plurality of particles relative to the flow channel." Ex. 1001, 11:20–23, 12:13–17. We determined, in part based on the parties agreement, that "increas[ing] a spatial uniformity . . . relative to the flow channel" means "increasing the similarity of the position in space of the object of the phrase (particles) relative to the flow channel." Pet. 32; PO Resp. 35.

We find Patent Owner's position and evidence to be the most compelling, namely that in Wada at the second intersection, shown for example in Petitioner's annotated Figure 23 (green highlighted area. p. 26) above, in sorting the sample particles, "the particles and sample are knocked out of "alignment" for the same reasons they are knocked out of focus." PO Resp. 45 (citing Ex. 2002 ¶ 19). Because Wada discloses sorting the particles, which directs the particles out of alignment at the second intersection in Wada, we find that Wada does not disclose "*increasing the*

*similarity* of the position in space of the object of the particles relative to the flow channel" as the proper claim construction requires. *See* Section II.F. Wada, therefore, does not anticipate claims 5 and 13.

*Claims 6 and 14*

Claims 6 and 14 depend directly from claims 1 and 9 respectively, and recite the limitation "wherein adjusting the sample in at least the first direction and adjusting the sample in at least the second direction includes focusing the sample." Ex. 1001, 11:24–26, 12:18–20. We determined that "focusing" requires "sheath fluid exerting a force on the particles, which narrows and aligns the particle stream in a desired direction relative to the boundaries of the channel, while achieving or maintaining laminar flow." Section II.C.

As discussed above, our review of Wada is most consistent with that of Patent Owner, namely that in Wada at the second intersection, shown for example in annotated Figure 23 (green highlighted area, p. 26) above, in sorting the sample particles, "the particles and sample are knocked out of 'alignment' for the same reasons they are knocked out of focus." PO Resp. 45 (citing Ex. 2002 ¶ 19). Because Wada discloses sorting the particles, which directs the particles out of alignment at the second intersection in Wada, we find that Wada does not disclose "focusing" at both first and second intersections.

Because we determined that "focusing" requires, "sheath fluid exerting a force on the particles, which narrows and aligns the particle stream in a desired direction relative to the boundaries of the channel . . ." we are not persuaded that Petitioner has proved by a preponderance of the evidence that Wada's directing of particles out of alignment and into

different collection wells is commensurate with "focusing" as properly construed. On the complete record before us, Wada does not anticipate claims 5 and 13.

*Claims 7 and 15*

Claims 7 and 15 depend from claims 6 and 14 respectively, and recite the further limitation "wherein focusing the sample includes focusing the sample in a first axis and subsequently focusing the sample in a second axis." Ex. 1001, 11:27–29, 12:21–23. Claims 7 and 15 are not anticipated by Wada for the same reasons as claims 6 and 14, namely that Wada fails to disclose "focusing" and alignment of the sample particle stream at Wada's second intersection.

*Claims 8 and 16*

Claims 8 and 16 depend directly from independent claims 1 and 9, and recite the further limitation "wherein adjusting the sample in at least the first direction and adjusting the sample in at least the second direction includes orienting the sample." Ex. 1001, 11:30–32, 12:24–26. On the complete record now before us, we determined that "orienting" correctly means "moving the object of the phrase (the sample) into a specified position." Section II.E.

Petitioner argues that Wada discloses positioning, and thus "orienting," the sample in the first intersection for passing the detector and also "orienting" the sample in the second intersection so that certain particles are directed to the appropriate collection wells. Pet. 65–66 (citing Ex. 1003 ¶ 227). Relying on its same arguments for a narrow interpretation of "adjusting," Patent Owner argues that Wada fails to disclose "orienting" the

sample "for the same reasons it fails to 'move [the sample] into proper position for use.'" PO Resp. 58.

As discussed above, we determined in our claim construction that the plain and ordinary meaning of "adjusting," means, "to move," and "orienting" means "moving the object of the phrase (the sample) into a specified position." *See* Section II.C. Even considering Patent Owner's description of Wada, that the downstream channel "***disrupts*** the sample core by sorting," it is reasonable to understand that the sample cells, as they are sorted, are still being moved into a specified position, i.e., "oriented," into separate collection wells. *See* PO Resp. 40. In light of our claim construction and our analysis based on Wada's disclosure we do not agree with Patent Owner's argument that there is a material difference between sorting sample particles as disclosed by Wada, and either "adjusting" or "orienting" the sample as called for in claims 8 and 16.

We find that Petitioner has shown by a preponderance of the evidence that Wada discloses "adjusting the sample . . . includes orienting the sample" as recited in claims 8 and 16. Therefore, on the complete record now before us, we determine that claims 8 and 16 are anticipated by Wada.

*Claims 17 and 19*

Claims 17 and 19 depend from claim 1 and claim 9 respectively, and include the further limitation of "a sample inlet." Ex. 1001, 12:27–31, 36–39. Claim 17, for example, adds the limitation of "a sample inlet intersecting the primary flow channel . . . for injecting the one or more particles into the suspension medium." *Id.* at 12:27–31.

We need not determine whether claims 17 and 19 are anticipated by Wada, because, as discussed below, we find that Petitioner has shown by a

preponderance of the evidence that claims 17 and 19 would have been obvious over Wada and Micronics.

*Claims 18 and 20*

Claims 18 and 20 depend directly from claims 1 and 9 respective, and similarly recite the limitation "wherein adjusting the sample in at least the first direction and adjusting the sample in at least the second direction *includes positioning* the one or more particles within the primary flow channel." Ex. 1001 12:32–35, 40–44 (emphasis added). Based in part upon the parties' agreement, we determined that "positioning" means, "moving the object of the phrase (particles) 'to a particular place.'"

Petitioner argues that at the second intersection "the system in Figure 23, for example, adjusts the position of the particles in the sample first to the left, and then to the right, of the flow channel." Pet. 68. Petitioner argues that "positioning particles in a sample within the flow channel was one of the known practical applications of these microfluidic systems." *Id.*

Patent Owner argues further that "Wada fails to disclose moving particles to a 'particular place' for the same reasons its fails to 'move [the sample] into proper position for use.'"[7] *Id.*

As discussed above, we determined in our claim construction that the plain and ordinary meaning of "adjusting," means, "to move," and "positioning" means "moving the sample particles to a particular place." *See* Section II.F. Even allowing for Patent Owner's description of Wada, that the downstream intersection "***disrupts*** the sample core by sorting," we

[7] Patent Owner also argues that our claim construction is incorrect. PO Resp. 59. Patent Owner, however, fails to offer any different construction, and we are thus not persuaded to change our construction, particularly one that both parties find acceptable.

find that the sample cells, as they are sorted, are still being moved, and positioned, within the primary flow channel, and then sorted into separate collection wells. *See* PO Resp. 40. Neither claim 18 nor claim 20 recites "positioning" the particle sample in any specific place, other than "within the primary flow channel" as recited in the claims. For instance, the claims do not recite "positioning the one or more particles by aligning the particles within the primary flow channel." Thus, at the second intersection, "directing" the sample particles into separate collection wells, as Wada describes, is therefore commensurate with the scope of "positioning the one or more particles within the primary flow channel," as called for in claims 18 and 20. In light of our claim construction and our analysis based on Wada's disclosure we do not agree with Patent Owner's argument that there is a material difference between "sorting" sample particles as disclosed by Wada, and either "adjusting" or "positioning" the sample as called for in claims 18 and 20.

We find that Petitioner has shown by a preponderance of the evidence that Wada discloses "adjusting the sample . . . includes positioning the one or more particles within the primary flow channel." as recited in claims 18 and 20. On the complete record now before us, we determine, therefore, that claims 8 and 16 are anticipated by Wada.

*D. Claims 1–20 Obviousness over Wada and Micronics 2001*

Petitioner contends that claims 1–20 would have been obvious based on the combination of Wada and Micronics 2001, and Patent Owner disputes that contention. Pet. 69–74; Prelim. Resp. 60–65. We do not address the issue of whether claims 1, 4, 8, 9, 10, 12, 16, 18, and 20 are obvious, as we determined above that these claims are anticipated by Wada.

*1. Micronics 2001*

Micronics 2001 describes an integrated microfluidic design, modeling, and rapid prototyping process that "allows the rapid and low-cost manufacturing of both simple and complex 3-dimensional microfluidic flow structures." Ex. 1017, 267. Micronics 2001 describes that "Lab-on-a-chip companies have developed technologies that work very well for highly predictable and homogenous samples," but analysis of clinical samples such as whole blood presented additional complexities that remained a challenge. *Id.* To address the shortcomings of then-extant technologies, Micronics 2001 describes a microfluidic circuit built of several layers, each of which can be manufactured easily and inexpensively. *See id.* ("[t]hese disposables are typically credit-card sized, and most structural elements on these cards have dimensions ranging from about 100 micrometers to a few millimeters."). *Id.*

Micronics 2001 explains further that

> microfluidic circuits comprise laminates built of several layers of individually cut or stamped fluidic circuits. While each layer can be manufactured very easily and inexpensively, the lamination process yields complex 3-dimensional microfluidic structures. This allows the design, for example, of 3-dimensional hydrodynamic focusing channels for cell analysis.

*Id.* Figure 1 from Micronics 2001 is reproduced below.

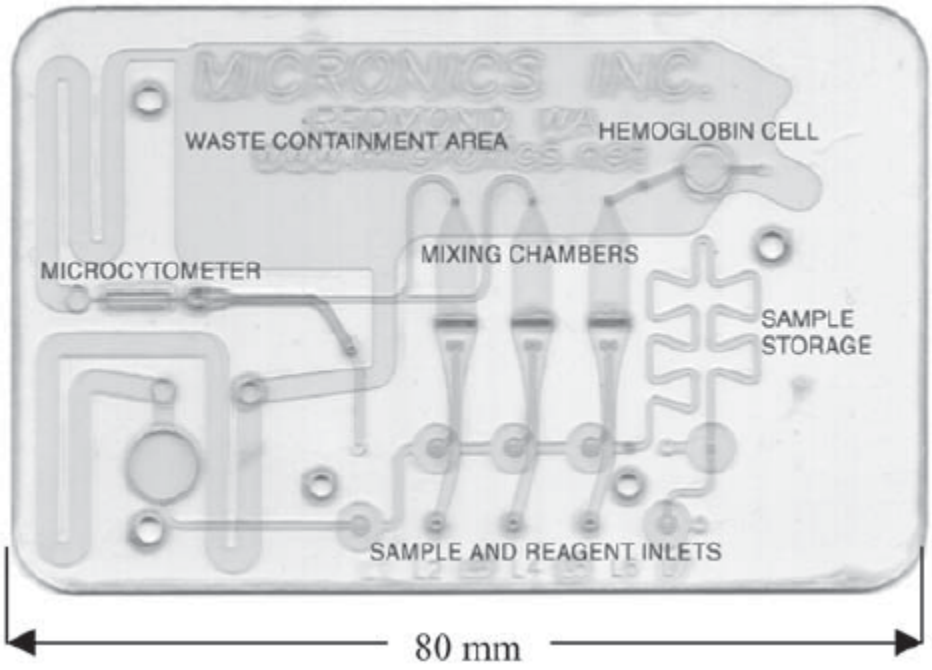



Figure 1, from Micronics 2001, above, details a disposable laminated flow structure having a fluidic circuit including sample and reagent inlets.

*2. Petitioner's Obviousness Arguments*

*Claims 2, 3, 5–7, 10, 11, 13–15, 17, and 19*

Petitioner argues that defining microfluidic flow in a system or method as recited in the '161 patent, including sample particle adjustments such as "aligning," "focusing," and "increas[ing] a spatial uniformity," even if not expressly described in Wada, do not make the claims patentable. Pet. 69–70. Petitioner argues that the resulting hydrodynamic flow in such systems was well-known to those of ordinary skill in the art to "predictably yield successful, functional microfluidic systems for focusing particles in a sample." *Id.* at 74. Petitioner argues further, that "a person of ordinary skill in the art "would have been able to achieve any of these types of adjustments through the routine selection of design choices and configurations of the

microfluidic systems described in Wada" and "the guidance in Micronics 2001." Pet. 70 (citing Ex. 1003 ¶ 236).

Petitioner's declarant, Dr. Di Carlo, supports this position, testifying that "Wada expressly explains that microfluidic hydrodynamic focusing would be 'highly effective' in such settings. Ex. 1003 ¶ 241. According to Dr. Di Carlo, "[a] skilled person would therefore understand that each of the adjustments claimed in the '161 Patent could be employed in the microfluidic systems disclosed in Wada." Ex. 1003 ¶ 241.

Petitioner's arguments with respect to obviousness do not specifically address any claim or express limitation recited in any of claims 1–20.

Patent Owner argues that "Petitioner has not pointed to any prior art disclosing a second set of inlets for adjusting a sample," and that "the sorting mechanism does not adjust the sample or perform any of the other claimed 'adjustments' in the dependent claims." PO Resp. 61. Patent Owner argues that Petitioner has failed to show how Micronics 2001 addresses either of these specific deficiencies and, that it is not sufficient for purposes of obviousness that Petitioner simply assert "'a skilled person would have known to consider alterations to' the structures in Wada 'so as to achieve any particular type of adjustment.'" *Id.* citing Pet. 73.

Although Patent Owner argues that Petitioner has not provided sufficient reasoning to combine Wada and Micronics 2001, we disagree. *See* PO Resp. 62. Petitioner explained that prior to the filing of the application that became the '161 patent, a person of ordinary skill in the art would have been familiar with devices, systems, and methods such as described in Wada, "for using microfluidic hydrodynamic focusing techniques in flow cytometry systems, namely, to cause any of a variety of types of movements

of a sample or particles in a sheath flow to position the particles for accurate detection by a flow cytometer." Pet 70 (citing Ex. 1003 ¶ 237). According to Petitioner's declarant, Dr. Di Carlo, Micronics 2001 shows that a person of ordinary skill in the art would have known how to design a microfluidic system to adjust a sample, (a) "hydrodynamically focused into a single stream of cells for individual interrogation by a downstream sensor;" and to (b) "quickly produce microfluidic-based designs . . . using commercially available software and fabrication techniques." Ex. 1003 ¶ 243. A person of ordinary skill in the art would have combined Micronics 2001's rapid design and prototyping fabrication techniques to produce systems such as those taught by Wada, Dr. Di Carlo testifies, because "new microfluidic systems—including those producing each of the adjustments discussed above—could be conceptualized, designed, and prototyped using commercially available software, and then tested in a laboratory, in about a day." *Id.* ¶ 244 (citing Ex. 1017, Fig. 2, Abstract). We find that, on the complete record now before us, Petitioner provides sufficient reasoning supported by evidentiary underpinnings for combining the specific fabrication and design techniques in Micronics 2001, with Wada's microfluidic systems.

*Claim 2, 3, 10, and 11*

In the case of claims 2 and 10, which depend directly from claims 1 and 9, what Petitioner has not provided, however, is sufficient evidence that the even with the combination of Wada, and Micronics 2001 fabrication techniques, a person of ordinary skill in the art would have achieved the specifically claimed invention in claims 2 and 10. Claims 2 and 10 recite the system limitation "wherein adjusting the sample in at least the first direction and adjusting the sample in at least the second direction includes aligning

the sample." The "aligning" limitation is not simply a first and second alignment, it builds on the underlying limitations in the independent claims requiring that, "aligning the sample" must occur in the "a secondary adjustment region downstream of the primary [adjustment] region."

Neither Petitioner, nor Dr. Di Carlo, have adequately explained why a person of ordinary skill in the art would have been motivated to meet the requirement of "aligning the sample," as the proper claim construction requires, in both a primary upstream adjustment region *and* a downstream second adjustment region. *See Unigene Labs., Inc. v. Apotex, Inc.*, 655 F.3d 1352, 1360 (Fed. Cir. 2011), ("[O]bviousness requires the additional showing that a person of ordinary skill at the time of the invention would have selected and combined those prior art elements in the normal course of research and development to yield the claimed invention."). Petitioner argues that a person of ordinary skill in the art "would have understood that any of these adjustments could be achieved readily by simply configuring the microfluidic systems disclosed in Wada." Pet. 72 (citing Ex. 1003 ¶ 241). This argument fails to provide a reason that a person of ordinary skill would have configured Wada's system to have a second downstream adjustment region where the particle sample would be aligned, as opposed to sorted. Dr. Di Carlo similarly fails to provide persuasive testimony explaining why a person of skill in the art would have been motivated to design the configuration of a second downstream adjustment region that also aligns the particle sample. For example, Dr. Di Carlo points to Micronics 2001, and testifies that "Micronics had commercially developed complete, integrated microfluidic devices that used hydrodynamic focusing in two directions to analyze cells in a flow cytometer." Ex. 1003 ¶ 241. Neither

Petitioner nor Dr. Di Carlo point to any design or structure in Micronics 2001 that shows a second downstream region aligning a particle sample.

Not only is this limitation apparently absent from either of the references, but the mere fact that Micronics discloses an integrated microfluidic device for focusing a particle sample, and a way of rapidly fabricating such a device, does not explain sufficiently *why* a person of ordinary skill in the art would have modified Wada, or any of the designs in Micronics 2001, and provided a second downstream adjustment region for aligning the particle sample. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 401, (2007) (noting that the Federal Circuit has consistently explained that "it can be important to identify a reason that would have prompted a person of ordinary skill in the art to combine the elements as the new invention does."). Here, we are apprised of neither the elements in the prior art, nor a reason as to why a person of ordinary skill in the art would have configured a microfluidic system with "a secondary adjustment region downstream" where "adjusting the sample in at least the second direction includes aligning the sample" as called for in claims 2 and 10. It is not enough to show that a person of ordinary skill in the art could have combined the prior art without explaining why the combination would have resulted in the claimed invention. *See PersonalWeb Techs., LLC v. Apple, Inc.*, 848 F.3d 987, 993–94 (Fed. Cir. 2017) (finding that a skilled artisan would have understood that prior art could be combined insufficient; "it does not imply a motivation to pick out those two references and combine them to arrive at the claimed invention").

"In an [inter partes review], the petitioner has the burden from the onset to show with particularity why the patent it challenges is

unpatentable." *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016). This burden never shifts to Patent Owner. *Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015). Petitioner has not provided persuasive reasoning supported by evidentiary underpinnings explaining why a person of ordinary skill in the art would have accomplished the claimed invention in view of Wada either alone, or in combination with Micronics. Therefore, on the complete record now before us, Petitioner has not shown by a preponderance of the evidence that claims 2 and 10 are obvious in view of Wada and Micronics.

Claims 3 and 11 depend directly from claim 2 and 10, and thus Petitioner's obviousness challenge against these claims is insufficient for the same reasons discussed above.

*Claims 5 and 13*

Claims 5 and 13 depend directly from claims 1 and 9 respectively, and recite the limitation "wherein adjusting the sample in at least the first direction and adjusting the sample in at least the second direction increases a spatial uniformity of a plurality of particles relative to the flow channel." Ex. 1001, 11:20–23, 12:13–16. We determined, in part based on the parties' agreement, that "increas[ing] a spatial uniformity . . . relative to the flow channel" means "increasing the similarity of the position in space of the object of the phrase (particles) relative to the flow channel." Pet. 32; PO Resp. 35.

Petitioner does not address, specifically, claims 5 and 13 in terms of obviousness. Petitioner argues in general that a person of ordinary skill in the art would have understood "increas[ing] a spatial uniformity" of samples or particles in a sheath flow for detection by a flow cytometer could be

accomplished "through the routine selection of design choices and configurations of the microfluidic systems described in Wada, particularly when Wada is considered in view of the guidance in Micronics 2001." Pet. 70 (citing Ex. 1003 ¶¶ 236–237).

Petitioner's argument fails, again, to provide adequate reasoning supported by sufficient evidentiary underpinnings that a person of ordinary skill would have configured Wada's system to have a second downstream adjustment region where "increas[ing] a spatial uniformity . . . relative to the flow channel" occurs, as opposed to the particle sample being sorted. Dr. Di Carlo also fails to provide persuasive testimony explaining why a person of skill in the art would have been motivated to design the configuration of a second downstream adjustment region that "increases a spatial uniformity" of samples or particles in a sheath flow. For example, Dr. Di Carlo points to Micronics, and testifies that "Micronics had commercially developed complete, integrated microfluidic devices that used hydrodynamic focusing in two directions to analyze cells in a flow cytometer." Ex. 1003 ¶ 242 (citing Ex. 1017, Figs. 5, 6, 8). Neither Petitioner nor Dr. Di Carlo point to any design or structure in Micronics that shows a second downstream region increasing a spatial uniformity of a particle sample relative to the flow channel, as recited in claims 5 and 13. Dr. Di Carlo's testimony that the design, fabrication and testing of microfluidic systems would have been viewed by a person of ordinary skill in the art as "routine," and "manufactured very easily," does not persuade us that it would have been obvious to configure a microfluidic system as recited in claims 5 and 13. Ex. 1003 ¶ 245. Perhaps it would have been easy to *fabricate* such a design, but that does not tell us why a person of ordinary skill in the art would have

been motivated to configure the sheath flow microchannels and inlets in the manner claimed.

Petitioner has not provided persuasive reasoning supported by evidentiary underpinnings explaining why a person of ordinary skill in the art would have accomplished the claimed invention in view of Wada either alone, or in combination with Micronics. Therefore, on the complete record now before us, Petitioner has not shown by a preponderance of the evidence that claims 5 and 13 are obvious in view of Wada and Micronics.

*Claims 6, 7, 14, and 15*

Claims 6 and 14 depend directly from claims 1 and 9 respectively, and recite the limitation "wherein adjusting the sample in at least the first direction and adjusting the sample in at least the second direction includes focusing the sample." Ex. 1001, 11:24–26, 12:18–20. We determined above that "focusing" means "sheath fluid exerting a force on the particles, which narrows and aligns the particle stream in a desired direction relative to the boundaries of the channel, while achieving or maintaining laminar flow." Section II.C.

Petitioner does not address, specifically, claims 6 and 14 in terms of obviousness. Petitioner argues in general that a person of ordinary skill in the art would have understood that "focusing" of samples or particles in a sheath flow for detection by a flow cytometer could be accomplished "through the routine selection of design choices and configurations of the microfluidic systems described in Wada, particularly when Wada is considered in view of the guidance in Micronics 2001." Pet. 70 (citing Ex. 1003 ¶¶ 236–237).

Similar to claims 5 and 13, Petitioner's argument fails to provide a reason supported by sufficient evidentiary underpinnings that a person of ordinary skill would have configured Wada's system to have a second downstream adjustment region that "includes focusing the sample," as opposed to the particle sample being sorted. The simple fact that Wada could be modified does not satisfy the requirements for a finding of obviousness. *In re Laskowski*, 871 F.2d 115, 117 (Fed. Cir. 1989); *In re* Mills, 916 F.2d 680,682 (Fed. Cir. 1990). Dr. Di Carlo fails to provide persuasive testimony explaining why a person of skill in the art would have been motivated to design the configuration of a second downstream adjustment region that "includes focusing the sample" or particles in a sheath flow. For example, Dr. Di Carlo testifies that "Micronics had commercially developed complete, integrated microfluidic devices that used hydrodynamic focusing in two directions to analyze cells in a flow cytometer." Ex. 1003 ¶ 242 (citing Ex. 1017, Figs. 5, 6, 8). Neither Petitioner nor Dr. Di Carlo point to any design or structure in Micronics that shows a second downstream region that includes "focusing" a particle sample as recited in claims 6 and 14. Dr. Di Carlo's testimony that the design, fabrication and testing of microfluidic systems would have been viewed by a person of ordinary skill in the art as "routine," and "manufactured very easily," does not persuade us that it would have been obvious to configure a microfluidic system as recited in claims 6 and 14. Ex. 1003 ¶ 245. Perhaps it would have been easy to *fabricate* such a design, but that does not explain sufficiently why a person of ordinary skill in the art would have been motivated to configure the sheath flow microchannels and

inlets in the manner claimed, so that "adjusting the sample in at least the second direction includes focusing the sample." Ex. 1001, 11:25–26.

Petitioner has not provided persuasive reasoning supported by evidentiary underpinnings explaining why a person of ordinary skill in the art would have accomplished the claimed invention in view of Wada either alone, or in combination with Micronics. Patent Owner's position on claims 6 and 14 is persuasive, that simply asserting the requisite elements are known in the prior art, without sufficient explanation and credible testimony as to the motivations to modify the prior art does not provide the necessary articulated reasoning and sufficient evidentiary underpinnings to support a finding of obviousness. PO Resp. 61–63. We are not persuaded that Petitioner has shown by a preponderance of the evidence that claims 6 and 14 are obvious in view of Wada and Micronics.

Claims 7 and 15 depend directly from claim 6 and 14, and thus Petitioner's obviousness challenge against these claims is insufficient for the same reasons discussed above.

*Claims 17 and 19*

Claims 17 and 19 depend from claim 1 and claim 9 respectively, and include the further limitation of "a sample inlet." Ex. 1001, 12:27–31, 36–39. Claim 17, for example, adds the limitation of "a sample inlet intersecting the primary flow channel . . . for injecting the one or more particles into the suspension medium." *Id.* at 12:27–31.

Initially, under the auspices of anticipation, Petitioner argues that Wada's Figure 23 show "particles are injected through an inlet upstream of the sheath fluid inlets." Pet. 66 (citing Ex. 1006, Fig. 23). Patent Owner disagrees, and argues that Petitioner fails to "explain how Wada discloses

any sample inlets, much less one intersecting a primary flow channel." PO Resp. 59. Patent Owner contends, specifically, that "Figure 23's various microchannels that (as shown below) do not depict where the particles originate, much less whether they enter the system via inlets." *Id.* at 60. These arguments are presented by the parties most clearly with respect to anticipation, neither party argues these claims with any particularity in the context of obviousness. Pet. 69–74; PO Resp. 61–65. In light of Petitioner's obviousness challenge to claims 17 and 19, we now address the arguments of both parties in the context of obviousness.

We acknowledge Patent Owner's argument, namely that Petitioner's explanation of "sample inlets" is lacking in precise details as to its location, and what structure in Wada's Figure 23 is "a sample inlet." Observing Figure 23, Wada discloses a primary sample flow channel in which the sample particles are shown flowing into the first intersection, although Wada does not expressly call out, or describe, "a sample inlet." Even though there is no specific "sample inlet" structure illustrated in Figure 23, what we cannot ignore, particularly in the context of obviousness, is the express written description and other disclosure in both Wada and Micronics 2001 of sample inlets to a primary flow channel for injecting sample particles into a microfluidic device. Wada, for example, describes structural formations including "apertures, holes, or ports" on a planar surface of a substrate as part of a microfluidic device where "[i]n the completed device, these holes function as reservoirs for facilitating fluid or material introduction into the channels." Ex. 1006, 26:13–14, 29–31. Also, in Micronics, we observe that Figure 1 clearly specifies "sample and reagent inlets" on the top layer of a microfluidic cartridge. Ex. 1017, 268. In light of this express disclosure in

Wada and Micronics 2001, for claims 17 and 19, we give weight to Dr. Di Carlo's testimony that for, "a sample inlet," it is not a significant leap that a person of ordinary skill in the art "would have looked to Micronics 2001 for guidance in creating such a system." Ex. 1003 ¶ 242.

For claims 17 and 19, we find that Petitioner has provided the necessary reasoning and evidentiary underpinnings showing that even if not anticipated by Wada, a person of ordinary skill in the art would have understood, from either Wada's description or Micronics' express disclosure, that in a microfluidic system, a sample inlet would intersect a primary flow channel "upstream" of the first and second adjustment regions. *See KSR*, 550 U.S. at 420 ("any need or problem known in the field . . . and addressed by the patent can provide a reason for combining the elements in the manner claimed"). Therefore, on the complete record now before us, we are persuaded that Petitioner has shown by a preponderance of the evidence that claims 17 and 19 are obvious in view of Wada and Micronics.

*E. Patent Owner's Motion to Exclude*

Patent Owner timely objected to Petitioner's reliance on Exhibits 1025, 1026, 1027 and portions of Exhibit 2004 in support of Petitioner's asserted claim construction and filed a Motion to Exclude these exhibits. Papers 32, 38. We do not rely on Exhibits 1025, 1026, or 1027, or on any of the disputed portions of Ex. 2004 that are re-direct examination of Dr. Di Carlo by Petitioner's counsel to which Patent Owner objects. Accordingly, Patent Owner's Motion to Exclude as to Exhibits 1025, 1026, 1027, and 2004 is *dismissed* as moot.

## IV. SUMMARY

Petitioner has proved by a preponderance of the evidence that claims 1, 4, 8, 9, 12, 16, 18, and 20 are anticipated by Wada.

Petitioner has proved by a preponderance of the evidence that claims 17 and 19 would have been obvious in view of Wada and Micronics 2001.

Petitioner has not proved by a preponderance of the evidence that claims 2, 3, 5–7, 10, 11, and 13–15 are anticipated by Wada or would have been obvious in view of Wada and Micronics.

## V. ORDER

For the reasons given, it is

ORDERED, based on a preponderance of the evidence that claims 1, 4, 8, 9, 12, and 16–20 are unpatentable;

FURTHER ORDERED, that Patent Owner's Motion to Exclude is *dismissed*; and

FURTHER ORDERED, because this is a final written decision, the parties to this proceeding seeking judicial review of our Decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

For PETITIONER:

Jeffrey P. Kushan
Paul J. Zegger
Fitz Collings
SIDLEY AUSTIN LLP
jkushan@sidley.com
pzegger@sidley.com
fcollings@sidley.com

For PATENT OWNER:

Kirt O'Neill
Daniel L. Moffett
George A. L. Rosbrook
Dorian Ojemen
AKIN GUMP STRAUSS HAUER & FELD LLP
koneill@akingump.com
dmoffett@akingump.com
arosbrook@akingump.com
dojemen@akingump.com