

Filed on behalf of Cytonome/ST, LLC.

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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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NANOCELLECT BIOMEDICAL, INC.,  
Petitioner

v.

CYTONOME/ST, LLC,  
Patent Owner

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Case IPR2020-00550  
Patent 9,011,797

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**CYTONOME/ST, LLC'S PRELIMINARY RESPONSE**

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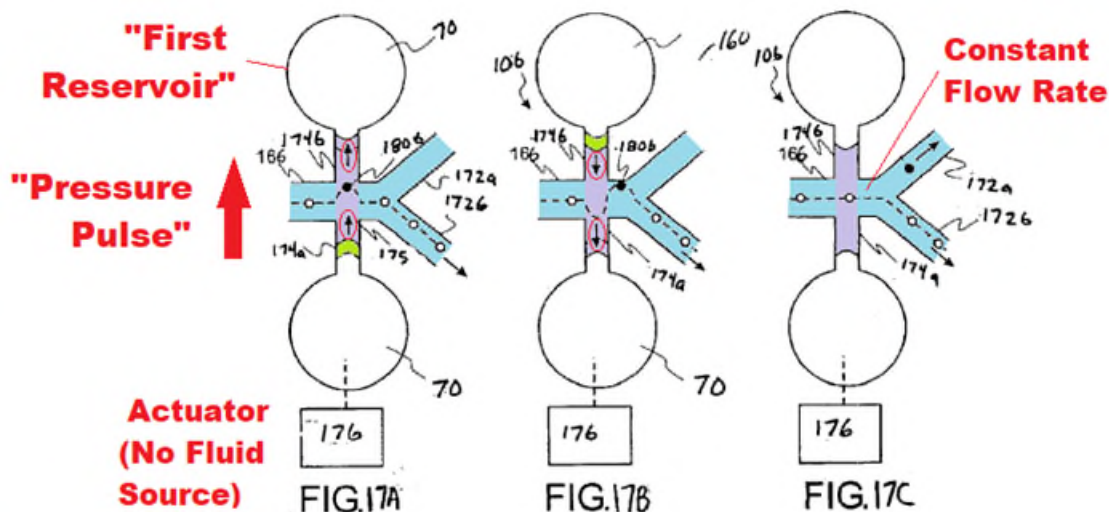
## I. INTRODUCTION

Pursuant to 35 U.S.C. §313, Patent Owner Cytonome/ST, LLC (“Cytonome”) submits this Patent Owner Preliminary Response to NanoCollect Biomedical, Inc.’s (“Petitioner”) Petition for *inter partes* review (“IPR”) of claims 1, 2, 5, 13, 16, 18, and 19 of U.S. Patent No. 9,011,797 (EX1001, “the ’797 Patent”). Cytonome requests that the Board deny institution because (1) the factors the Board considers for discretionary denial under 35 U.S.C. §314(a) weigh heavily against institution, (2) Petitioner fails to offer constructions for key claim terms at issue as required under the rules, and (3) Petitioner fails to show a reasonable likelihood of success on any of its Grounds.

Every factor provided in the precedential *Apple Inc. v. Fintiv, Inc.* order favors denying institution based on the “advanced state” of the related district court litigation between Cytonome and Petitioner, namely: (1) no stay has been granted in the litigation; (2) trial is set to occur four months before a final written decision; (3) the parties and court are deeply invested in the litigation (a factor exacerbated by Petitioner’s delay tactics here); (4) the same prior art and claims are at issue; (5) the parties are identical; and (6) the merits of the Petition are exceptionally weak. Moreover, Petitioner’s lack of candor and its gamesmanship with respect to its conflicting claim construction positions across the two forums are “other considerations” that strongly favor denial.

The Board should also deny institution under 37 C.F.R. §§42.104(b)(3)–(4), which requires petitioners to offer affirmative constructions for terms it should know would be at issue in the IPR. For example, Petitioner knows the term “reservoir” would be at issue because it argued in district court that the term is a means-plus-function limitation, yet it argues here that no construction is needed. The Board has explained that taking such “conflicting positions” with respect to a claim term triggers the obligation to offer an affirmative construction in the Petition.

Finally, Petitioner fails to establish a reasonable likelihood of success for any of its Grounds. Petitioner’s primary asserted references describe fundamentally different principles of operation from the claimed invention that lack key claim elements. The claimed methods and devices operate by deflecting a selected particle by momentarily shifting a constant volume of fluid without increasing or accelerating flow in the system. As illustrated below, this momentary shift is made possible by “propagating a pressure pulse across the microfluidic flow channel in a crosswise direction” and “dampening or absorbing the pressure pulse using a first reservoir”:

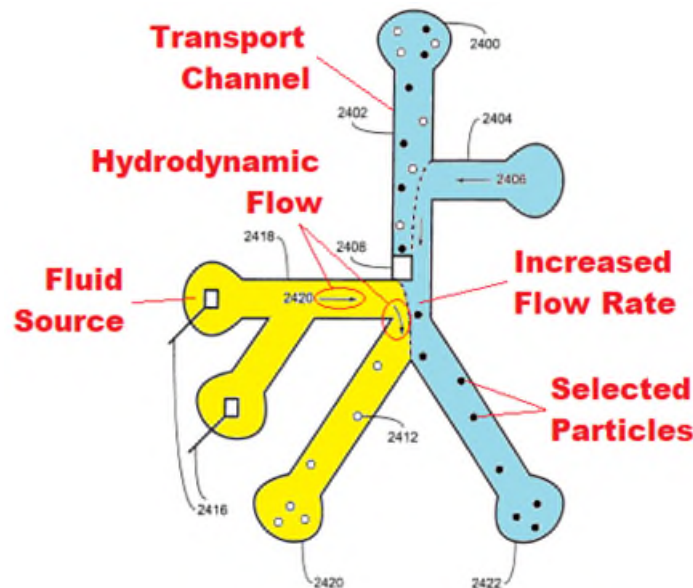


EX1001, Figs. 17A–17C (annotated). When a selected particle enters the region between the actuator and “first reservoir,” the actuator propagates a pressure pulse across the main transport channel, causing the volume of fluid within that narrow region to shift up into the first reservoir. As shown in Figure 17B, immediately after deflection, *the same volume of fluid* returns to the actuator side, ready for the next sort. The device is thus in its original state immediately after a sort, and the flow rate through the transport channel never changes.

To operate according to those principles, cooperation between the claimed “first reservoir” and “pressure pulse” is necessary—and critical to the invention. Indeed, these terms are central to the claim construction disputes in district court, and ultimately to the validity of the challenged claims. Because the reservoir “dampen[s] or absorb[s]” the pressure pulse, its impact is limited in both space and time—namely, to the narrow region between the actuator and reservoir and to the brief moment when a selected particle is in that region. This prevents the pressure

pulse from propagating throughout the channels and inadvertently deflecting non-selected particles or otherwise disrupting the flow of particles in the system.

In stark contrast, Petitioner's asserted principal reference operates on a completely different principle and employs neither a "pressure pulse" nor a "reservoir" that absorbs it. As illustrated below, Wada teaches a flow-based sorting operation that sorts particles by adding fluid to increase "hydrodynamic flow" that is not absorbed by a reservoir and never retreats back into the side channel:



EX1006, Fig. 24 (annotated); EX2001 ¶128. This hydrodynamic flow—which Petitioner identifies as the "pressure pulse"—is clearly shown entering the transport channel and turning downstream before exiting the device altogether. It is not a pressure pulse, it never crosses the channel, and there is no opposed reservoir to absorb it.

Petitioner fails to provide a reason why a POSA would have modified Wada to deviate from this flow-based operation at all, much less in a way that achieves the claimed invention. Indeed—as explained by Patent Owner’s expert in his declaration accompanying this Preliminary Response—no such reason existed because changing Wada from employing a flow-based device that adds fluid to the system to a device that dispatches a pressure pulse across a transport channel into a reservoir (without adding fluid) would fundamentally change Wada’s basic principle of operation.

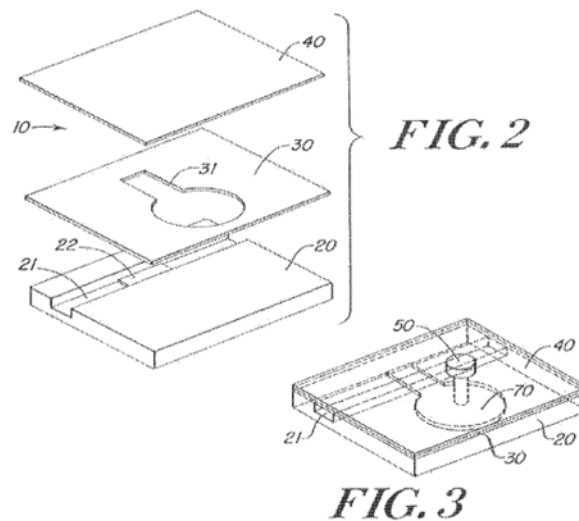
Petitioner’s other base reference, Marcus (EX1005), provides almost no information on its particle sorting apparatus, but what little information is given confirms that Marcus fails to employ the claimed pressure pulse and reservoir. Rather, Marcus teaches sorting by actuating opposed “control ports”—one actuated when a “Type A” particle is sensed, and the other actuated when a “Type B” particle is sensed. Such a technique—activating *both* ports to deflect particles—teaches away from using one of the ports to dispatch a cross-channel pressure pulse and the other as a passive reservoir for dampening or absorbing that pressure pulse.

## **II. BACKGROUND**

### **A. The ’797 Patent**

The ’797 Patent—titled “Microfluidic System Including a Bubble Valve for Regulating Fluid Flow Through a Microchannel”—issued on April 21, 2015 and

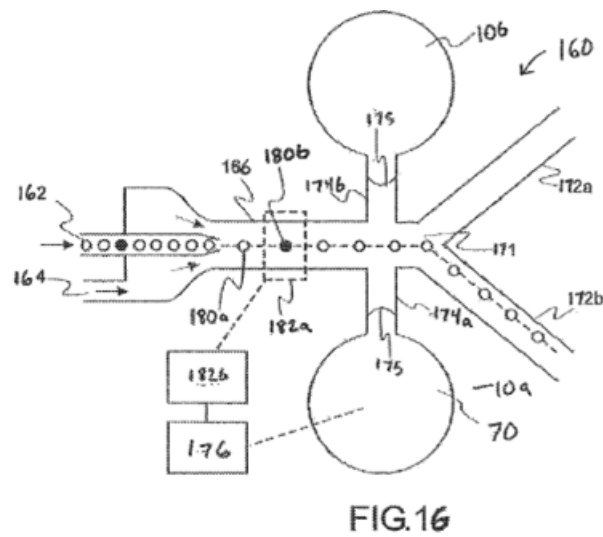
claims priority to a provisional application filed April 17, 2002. EX1001. The disclosure is generally directed to controlling fluid flow—with or without particles—in microfluidic devices using a “bubble valve,” which is preferably a gas-filled reservoir that creates an air/fluid meniscus which, upon actuation, pushes the meniscus into a transport channel to vary the flow of liquid. *Id.* at 2:59–3:6, Figs. 2–5C. Figures 2 and 3 show one configuration of a “bubble valve,” including an actuator (50) and actuating reservoir/chamber (70):



In another configuration, the bubble valve applies pressure from above the transport channel, which can block fluid flow *completely*. *Id.* at 8:37–9:31, Figs. 6–9. And in another configuration, the meniscus is retained within a side channel, which is useful for fluid switching. *Id.* at 10:56–11:8, Fig. 13B.

The challenged claims are drawn specifically to the use of such bubble valves in microfluidic particle sorting devices, to which part of the specification is

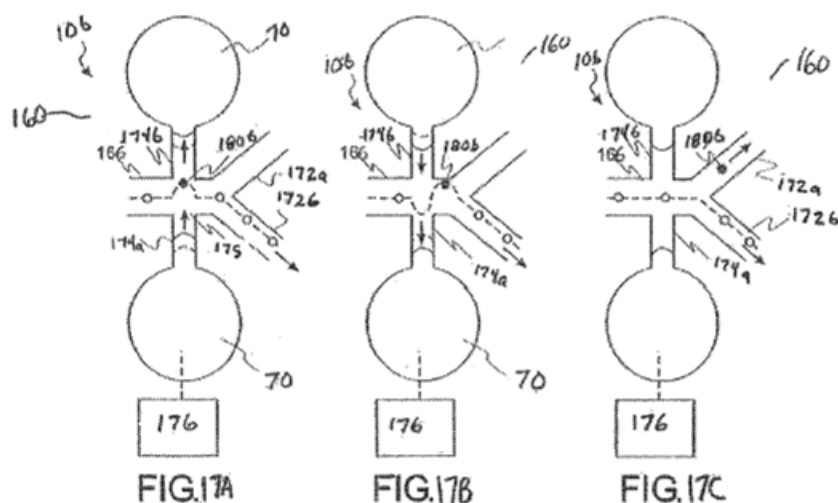
devoted. The disclosed embodiments flow a sample of particles in a “microfluidic flow channel” (i.e., a main transport channel), employ a first bubble valve as an actuator to “propagate[e] a pressure pulse” to sort one or more particles, and further include a second bubble valve as a “first reservoir” for dampening or absorbing that pressure pulse. *Id.* at 13:41–51. The challenged claims are therefore best understood with reference to the sorting device depicted in Figures 16–17C and described at 11:35–12:65. Figure 16 is below:



This actuator and “first reservoir” cooperate by, respectively, generating and absorbing the pressure pulse, and by deflecting the particles without increasing the flow of fluid into collection wells. *See, e.g., id.* at 4:31–41, 12:13–22.

The “pressure pulse” generated by the actuator and the “first reservoir” that absorbs it are central to the invention. The actuator “var[ies] the volume of the reservoir to increase an internal pressure of the reservoir to vary the flow of liquid

through the channel.” *Id.* at 3:55–59. The resultant pressure pulse is a “transient pressure variation” (*id.* at 12:13–15) that “momentarily causes a flow disturbance in the duct to deflect the flow therein” (*id.* at 11:58–62). More specifically, the pressure pulse deflects a particle by shifting a volume of fluid between the actuator and the “first reservoir” (Figure 17A), with the same volume of fluid returning to its original position after deflection (Figures 17B–17C):



*See id.* at 12:23–65. Because the volume of fluid displaced in the actuator side channel is equal to the volume of fluid increased in the first reservoir side channel, the sorting operation produces no change in flow rate through the transport channel. EX2001 ¶¶39–49.

The patent further discloses that the “actuator” can be a reservoir/chamber with—preferably—a movable membrane and a piezoelectric transducer mounted thereon. *Id.* at 7:17–20, 8:61–62, 11:58–12:15. The claimed “first reservoir” for dampening or absorbing the pressure pulse is described as “[t]he second side



passage 174b and the second bubble valve 10b” in Figures 16–17C, and is depicted as a reservoir/chamber comparable to the one associated with the actuator. *Id.* at 12:15–18. The patent explains that the first reservoir can be “a chamber having a resilient wall or contains a compressible fluid such as a gas,” which “allow[s] the flow of liquid from the measurement duct into the second side passage 174b.” *Id.* at 12:18–22. And the first reservoir is sized and configured to “absorb the transient pressure variations in the measurement duct 166 induced via the actuator 176.” *Id.* at 12:15–18.

## **B. Challenged Claims of the '797 Patent**

Petitioner challenges claims 1, 2, 5, 13, 16, 18, and 19, among which claims 1 and 5 are independent. Claim 1 is below:

1. A method for facilitating analysis or processing of a sample, the method comprising:  
flowing a sample through a microfluidic flow channel formed in a substrate;  
propagating a pressure pulse across the microfluidic flow channel in a crosswise direction; and  
dampening or absorbing the pressure pulse using a first reservoir in fluid communication with the microfluidic flow channel, wherein the pressure pulse is used to sort one or more particles suspended within the sample.

Independent claim 5 is essentially a microfluidic device that can be used to employ the method of claim 1.

### **C. The Related District Court Litigation**

On February 12, 2019, Cytonome filed suit in the District of Delaware alleging that Petitioner infringed seven Cytonome patents, including the '797 Patent. EX1044. On May 8, 2019, the court entered a scheduling order that set a trial date of April 26, 2021 (EX2003 at 9; EX2004–2005), which is four months before a final written decision is expected here.

The litigation is at an advanced state—particularly so with respect to claim construction. After reviewing the briefings (EX2006) and holding a *Markman* hearing (EX2015), the Court issued its *Markman* rulings (EX2012, EX2028). The court specifically ruled on several terms at issue here—namely, “reservoir” and “pressure pulse.” EX2012 at 5–7.<sup>1</sup>

Significantly, although Petitioner disclosed only Cytonome’s district-court constructions and briefings to the Board, Petitioner initially identified “reservoir” and “pressure pulse” for construction on October 11, 2019. EX2016 at 3–4. Then,

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<sup>1</sup> This Paper uses page numbers from the exhibit stamp, not from the original document.

on October 25, Petitioner proposed much narrower constructions for those terms than the interpretations it applies here. EX2017 at 3, 5, 10. The parties’ competing positions on those terms are:

Term	Cytonome’s Constructions	Petitioner’s Constructions
“pressure pulse” (EX2006 at 22–23)	Plain and ordinary meaning	“a unidirectional flow to the [microchannel/supply duct]”
“dampening or absorbing the pressure pulse using [a/the] first reservoir” (EX2006 at 79; <i>see also id.</i> at 59–60)	A reservoir is “a physical structure that contains fluid.” Otherwise, the plain and ordinary meaning should be applied.	Indefinite or “to meaningfully dissipate or to receive the unidirectional flow to the microchannel without recoil or echo using [a/the] first reservoir”

Though not disclosed in the Petition, the litigation is at an advanced state in many other respects, including the validity issues raised in the Petition. Petitioner served invalidity contentions, accompanied by detailed element-by-element claim charts, on September 20, 2019. EX2007–2008. Petitioner’s contentions relied on substantially the same prior art as here—including Wada, Marcus, and Anderson, and “background” references such as Zöld, Glaettli, and Chou. EX2007 at 10–33, 37. The claim charts specifically asserted Wada and Marcus against the challenged claims, including relying on Wada Figures 22–24 for the “pressure pulse” and “first reservoir” limitations. EX2008 at 26–33, 53–56.

Finally, discovery in the litigation has been underway since May 22, 2019. EX2003 at 1. And the parties’ technical expert witnesses are currently developing their reports (including on validity issues), which are due on August 3, 2020 (EX2004 at 2, EX2005)—over a month before an institution decision is due here.

### **III. THE BOARD SHOULD USE ITS DISCRETION TO DECLINE INSTITUTION UNDER 35 U.S.C. §314(a)**

The Board should deny institution under 35 U.S.C. §314(a) because the parties are engaged in related district court litigation that has reached an “advanced state.”<sup>2</sup> Indeed, every factor the Board considers for determining whether to deny institution on this basis favors denial. “[O]ther considerations”—such as Petitioner’s lack of candor and its gamesmanship with respect to claim construction—also heavily favor denial.

#### **A. Legal Standards**

The Board regularly exercises its discretion to deny institution under 35 U.S.C. §314(a) when related district court litigation has reached an “advanced state” that would render IPR inefficient. *Apple Inc. v. Fintiv, Inc.*, IPR2020-00019,

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<sup>2</sup> Cytonome seeks discretionary denial of the six related Petitions on substantially similar grounds as here. *See* IPR2020-00545, IPR2020-00546, IPR2020-00547, IPR2020-00548, IPR2020-00549, and IPR2020-00551.

Paper 11 (PTAB Mar. 20, 2020) (precedential) (collecting cases). In *Apple's* precedential order, the Board outlined six factors for making this determination:

1. whether the court granted a stay or evidence exists that one may be granted if a proceeding is instituted;
2. proximity of the court's trial date to the Board's projected statutory deadline for a final written decision;
3. investment in the parallel proceeding by the court and the parties;
4. overlap between issues raised in the petition and in the parallel proceeding;
5. whether the petitioner and the defendant in the parallel proceeding are the same party; and
6. other circumstances that impact the Board's exercise of discretion, including the merits.

*Id.* at 5–6. The Board also takes into account any “other considerations” that warrant denial. *Id.* at 16.

**B. Every *Apple* Factor Favors Denying Institution Based on the “Advanced State” of the Related District Court Litigation**

The first factor in *Apple*—regarding whether a motion to stay has been either granted or denied without prejudice pending an institution decision—cannot weigh against denial because Petitioner has not sought a stay. *Apple*, IPR2020-00019, Paper 11 at 6–9. And in light of the factors below demonstrating the advanced

stage of the litigation and Petitioner’s intentionally-delayed filing, one should not be granted if IPR is instituted.

The second *Apple* factor—which asks whether the trial date is near the projected date for the final written decision—favors denial here because trial is set to occur four months *before* a final written decision is expected. *Id.* at 2–3, 10. This Preliminary Response is due on June 5, 2020, three months after the March 5 Notice (Paper 5) granting a filing date. 37 C.F.R. §42.107(b). The institution deadline is three months later on September 5, 2020. 35 U.S.C. §314(b). And because it must issue within one year of institution, the projected date for a final written decision is September 5, 2021. 35 U.S.C. §316(a)(11). Trial is set to begin over four months earlier on April 26, 2021. EX2003 at 9.

The third factor—which relates to “the amount and type of work already completed in the parallel litigation by the court and the parties at the time of the institution decision”—heavily favors denial. *Apple*, IPR2020-00019, Paper 11 at 9–12. In particular, the parties and court have performed considerable work related to claim construction. After reviewing briefings, expert declarations, and intrinsic evidence (EX2006, EX2019), and following a *Markman* hearing (EX2015), the court issued claim construction rulings. (EX2012, EX2028). The court specifically ruled on the critical term at issue here—“pressure pulse” (EX2012 at 6–7)—after assessing supplemental evidence and briefings on those terms (EX2024–2027).

Moreover, Petitioner has already served voluminous invalidity contentions, including detailed claim charts asserting the same primary prior art (Wada and Marcus) asserted here. EX2008 at 2–90, 133–186. And expert witness reports are due by August 3, 2020 (EX2004 at 2)—before the institution decision is expected. The Board and parties should not have to (and likely cannot) duplicate these substantial efforts.

Still under the third factor, the Board further considers whether and why the petitioner waited until the litigation “has progressed significantly before filing a petition at the Office.” *Apple*, IPR2020-00019, Paper 11 at 11–12. Petitioner here indeed waited until the day before the statutory deadline of February 13, 2020 before filing. 35 U.S.C. §315(b); Pet. 3, 83. The only plausible reason for this delay was to wait for Cytonome’s final claim construction brief (and related expert declaration) that was due two weeks earlier on January 31 (EX2003 at 6) so that Petitioner could exploit Cytonome’s arguments, which it did (*see* Pet. 9–11, EX1042–1043). Petitioner intentionally delayed in order to adopt an overall strategy of employing broader claim interpretations here than in district court—with part of that strategy being the use of Cytonome’s broader interpretations. *Id.*; *infra* Part III.C.

Petitioner’s suggestion that it was instead waiting for Cytonome to “identif[y] the claims in dispute” in district court is misleading. *See* Pet. 6. To be

sure, Cytonome voluntarily withdrew some of its asserted claims in November 2019 in an effort to streamline the litigation. But Petitioner fails to reveal that Cytonome had already identified all of “the claims in dispute” three months earlier when it served infringement contentions. EX2021. And on September 20—*based on those identified claims*—Petitioner served Cytonome with extensive invalidity contentions. EX2007–2008. Those contentions asserted and analyzed the same Wada reference asserted here against every challenged claim. EX2007 at 40–41; *see also, e.g.*, EX2008 at 2–90 (charting Wada and Marcus against claim 1), 133–86 (claim 5). So by September 20, 2019, Petitioner knew of the trial date (EX2003 at 9), the asserted claims, and its own detailed analysis of the primary reference asserted here. Thus it had everything it needed to work diligently to ensure that a final written decision would occur before trial. *See Apple*, IPR2020-00019, Paper 11 at 11–12, n. 22. There was no need to wait on Cytonome.

Moreover, because Petitioner waited *another* three months after Cytonome reduced the number of asserted claims in district court, it tries to justify its February filing by suggesting that ongoing settlement discussions suddenly reached an “impasse” at that time. Pet. 5–7. Petitioner cites no evidence to support that story, and settlement discussions were not at an impasse. In fact, the day after the Petition



was filed, the parties requested court-supervised mediation.<sup>3</sup>

As to the fourth *Apple* factor, there is substantial overlap between issues raised in the petition and the related litigation. *Apple*, IPR2020-00019, Paper 11 at 12–13. Petitioner asserts two primary references (Wada and Marcus) against the challenged claims. And as explained above, Petitioner asserted the exact same reference against the challenged claims in its invalidity contentions in district court. *See, e.g.*, EX2008 at 2–90. Moreover, the court has already ruled on claim constructions at issue here. EX2012 at 5–7.

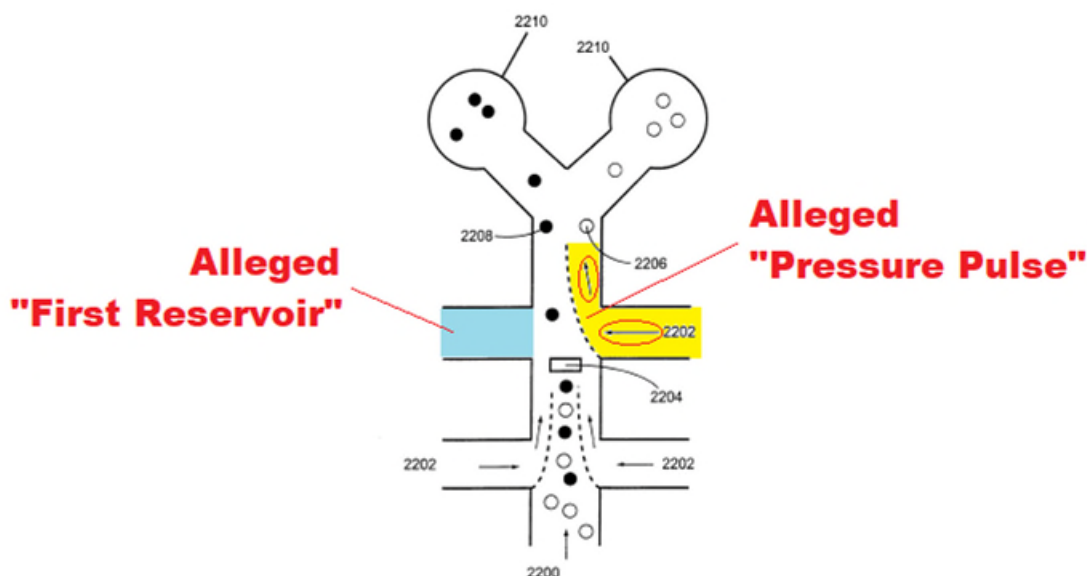
The fifth factor weighs in favor of denial because there is no dispute that Petitioner here is also the defendant in the related litigation. Pet. 3–7; *Apple*, IPR2020-00019, Paper 11 at 13–14.

Finally, under the sixth factor, the Board should consider “all the relevant circumstances in the case, including the merits.” *Apple*, IPR2020-00019, Paper 11 at 14–16. *Apple* explains that this “is not to suggest that a full merits analysis is necessary,” but that “there may be strengths or weaknesses” worth considering. *Id.*

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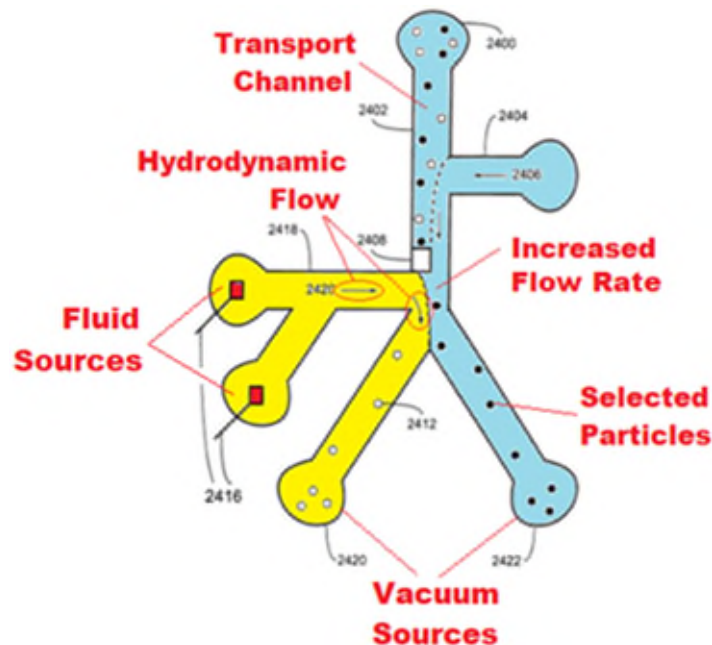
<sup>3</sup> The Court obliged the request (EX2020, EX2022), and the parties cooperated in making the settlement discussions fruitful (EX2009–2010) until the Court canceled the mediation on June 1, 2020.

Petitioner's arguments regarding "pressure pulse" and the "reservoir" for dampening or absorbing that pressure pulse are worth considering. *See infra* Part VIII. For example, Petitioner identifies Wada's introducing of "hydrodynamic flow" in Figure 22 as the claimed "propagating a pressure pulse across the microfluidic flow channel in a crosswise direction" and a side channel as the claimed "reservoir" used for "dampening or absorbing the pressure pulse." Pet. 23–31, 36–37. But this alleged "pressure pulse" clearly does not even *reach* the alleged "first reservoir," much less be dampened or absorbed by it:



EX1006, Fig. 22 (annotated); EX2001 ¶118.

The other sorting embodiments that Petitioner relies on, Figures 23–24, fare no better. Indeed, Figure 24 depicts the same half-channel hydrodynamic flow and *does not even depict an opposed side channel* to serve as the alleged "first reservoir":



EX1006, Fig. 24 (annotated); Pet. 23–31, 36–37. Accordingly, factor six—as well as all the other *Apple* factors—weigh against institution.

**C. Petitioner’s Lack of Candor and its Gamesmanship Are “Other Considerations” That Strongly Favor Denial**

The Board also considers any “[o]ther facts and circumstances” that warrant denial. *Apple*, IPR2020-00019, Paper 11 at 16. Here, the Board should strongly consider Petitioner’s lack of candor and its gamesmanship related to its conflicting claim construction positions across forums.<sup>4</sup>

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<sup>4</sup> Following the filing of the Petition, the court issued its claim construction rulings. EX2012; EX2028. Specifically, the court rejected both parties’ proposals for “reservoir.” *Id.* at 5–6. These rulings do not diminish Petitioner’s lack of candor

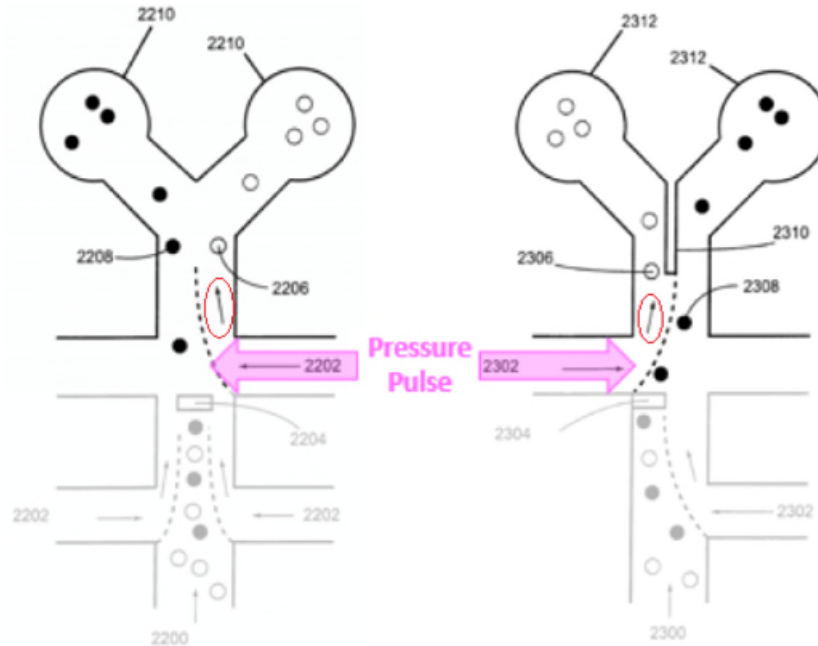
In denying institution under §314(a), the Board has considered petitioners’ “lack of candor” stemming from a failure to disclose even “*seemingly* inconsistent claim construction positions” from district court. *Facebook, Inc. v. Sound View Innovations, LLC*, IPR2017-00998, Paper 13 at 16–18 (PTAB Sep. 5, 2017) (emphasis added). In *Facebook*, the petitioner asserted that a term was “means-plus-function” in district court but failed to disclose that position to the Board. *Id.* Instead, the petitioner contended that no terms required construction and that “no claim construction ruling . . . has occurred.” *Id.* at 8, 17. In denying institution, the Board explained that the petitioner’s failure to inform the Board of its district-court construction—“le[aving] it to Patent Owner to advise [the Board] of Petitioner’s differing claim construction arguments”—was “troubling” because it “raise[d] the specter of lack of candor.” *Id.* at 17–18.

Petitioner here engages in the same tactic. As in *Facebook*, Petitioner here contends that no “express claim constructions are required” (Pet. 10) and withholds its narrow district-court constructions that are inconsistent with its arguments here, leaving it to Cytonome to disclose those constructions. EX2017 (Petitioner’s claim

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and gamesmanship *at the time of filing*. Indeed, Petitioner indicated that it might appeal certain rulings. EX2026 at 4, n.3; EX2023.

construction positions disclosed on October 25, 2019), EX2018 (Petitioner’s responsive claim construction brief of January 10, 2020) (later reproduced and filed in Joint Claim Construction Brief (EX2006)). For example, in district court, Petitioner contends that “pressure pulse” means “a unidirectional flow to the [microchannel/supply duct].” EX2006 at 22–24 (arguing that this is the “only understanding”); EX2017 at 5. Here, however, Petitioner argues that Wada’s *multidirectional* flow (depicted in yellow) is the claimed pressure pulse:



Pet. 24 (red circle by Cytonome; other annotations by Petitioner). As shown by the arrows, Wada’s flow indisputably travels in at least *two* directions—exiting the side channel and turning upward into the transport channel. Arguing that this is a “pressure pulse” directly conflicts with Petitioner’s position that the “only understanding” of “pressure pulse” is that it is a “*unidirectional* flow.”

Petitioner takes another conflicting position with respect to the functionality of the “first reservoir.” In district court, Petitioner contends that “dampening or absorbing the pressure pulse using a first reservoir” means “to meaningfully dissipate or to receive the unidirectional flow to the microchannel without recoil or echo using a first reservoir.” EX2006 at 59–60. As shown in the figures above, Petitioner’s alleged “pressure pulse” is a “hydrodynamic flow” that *never even reaches* an opposed reservoir—thus it certainly is not “meaningfully dissipated” or “received without recoil or echo” by one.

Furthermore, Petitioner demonstrates more than a mere “specter” of lack of candor because, unlike *Facebook*, there is no plausible justification for Petitioner’s failure to disclose its district-court constructions and related briefings. In *Facebook*, the petitioner implied that neither party’s claim construction positions from district court were relevant because they had not yet been ruled on. *Facebook, LLC*, IPR2017-00998, Paper 13 at 16–18. There is no such implication here. Petitioner deliberately attached *Cytonome*’s claim construction briefings to the Petition (EX1042–1043, EX1045), provided *Cytonome*’s briefings to its expert (EX1002 ¶¶41–46), and then used *Cytonome*’s claim interpretations where—and only where—Petitioner deemed it advantageous to do so in the Petition (Pet. 10–11, 29, 37, 62). Petitioner’s withholding of *its own* constructions from the Board was deliberate.

Moreover, denial is warranted because Petitioner concealed its district-court constructions specifically so that it could employ meanings so-called “ordinary and customary” meanings that are much broader than the non-infringement-based constructions it seeks in district court. *See* Pet. 9–11. This type of gamesmanship is improper because it violates the well-settled principle that “claims are construed the same way for both invalidity and infringement.” *Eaton Corp. v. Rockwell Int’l Corp.*, 323 F.3d 1332, 1343 (Fed. Cir. 2003). Indeed, seeking one set of constructions favoring non-infringement in district court and a second set of constructions that favor invalidity in IPR proceedings invites the exact “troubling” inconsistency that the Patent Office sought to avoid when it harmonized its claim construction standard with district courts. *Changes to the Claim Construction Standard*, 83 Fed. Reg. 51,340 at 51,342–43 (Oct. 11, 2018) (Final Rule).

#### **IV. THE PETITION SHOULD BE DENIED FOR FAILING TO COMPLY WITH 37 C.F.R. §§42.104(b)(3)–(4)**

For every challenged claim, petitioners must identify “[h]ow the challenged claim is to be construed.” 37 C.F.R. §42.104(b)(3). Section 42.104(b)(4) further requires petitioners to explain “[h]ow the construed claim is unpatentable.” Under these rules, the Board denies institution when petitioners fail to offer and apply constructions for terms they “should have known” would be at issue.

*Orthopediatrics Corp. v. K2M, Inc.*, IPR2018-01548, Paper 9, 12 (PTAB March 1, 2019).

Denial is warranted here under 37 C.F.R. §§42.104(b)(3)–(4) for the same reasons as *Orthopediatrics*, where the petitioner failed to offer a construction for terms it “should have known” would be at issue. Like the petitioner there—who asserted that no “specific claim term . . . requires construction” and “that every claim term should be given its ‘broadest reasonable construction in light of the specification’” (*id.* at 9)—Petitioner here contends that no “express claim constructions are required” and that it simply applies “ordinary and customary” meanings (Pet. 9–11). Petitioner here also suggests that there are no terms “at issue” by asserting that its invalidity analysis “is consistent with the claim construction positions that Cytonome has offered in district court.” *Id.*; *Orthopediatrics*, IPR2018-01548, Paper 9 at 7–9 (asserting that the “petition [wa]s based on the claim constructions urged by Patent Owner in the related district court litigation”).

But Petitioner should have known that “pressure pulse” would be at issue because—like the *Orthopediatrics* petitioner—it took “conflicting positions between [the IPR] and the related district court litigation” as to those terms. *Orthopediatrics*, IPR2018-01548, Paper 9 at 12. As explained *supra* Parts III.C, Petitioner applies a much broader construction here than in district court when it identifies Wada’s multidirectional “hydrodynamic flow” and side channel as the claimed “pressure pulse” and “first reservoir.” Petitioner also should have known



those terms would be at issue because they “go to the heart” of Petitioner’s patentability arguments, as demonstrated *infra* Part VIII. *See Infinera Corp. v. Core Optical Techs., LLC*, IPR2018-01259, Paper 9, 13 (PTAB January 14, 2019). Petitioner’s failure to offer a construction therefore warrants denial under §§42.104(b)(3)–(4). *Orthopediatrics*, IPR2018-01548, Paper 9 at 10–12.

Finally, Petitioner’s statement that it “applies the prior art to the claims using this [ordinary and customary] standard” cannot alone satisfy §§42.104(b)(3)–(4). Pet. 9. Disputed terms are to be “construed” even when their “ordinary and customary” meanings apply. *Wavetronix v. EIS Elec. Integrated Sys.*, 573 F.3d 1343, 1355 (Fed. Cir. 2009) (emphasis added).

## **V. PERSON OF ORDINARY SKILL IN THE ART**

Petitioner proposes defining a person of skill in the art (POSA) as someone with “a bachelor’s or master’s degree in the field of bioengineering, mechanical engineering, chemical engineering, or analytical chemistry; or a bachelor’s or master’s degree in a related field and at least three years of experience in designing or developing microfluidic systems.” Pet. 12. Solely for purposes of this Paper, Cytonome applies Petitioner’s proposal, while reserving the right to dispute it later.

## **VI. CLAIM CONSTRUCTION**

Cytonome requests that the Board construe the “pressure pulse” and “first reservoir” terms as follows.

**A. “pressure pulse” (claims 1, 2, 5, 13, 16, 18, and 19)**

The district court rejected Petitioner’s proposed construction of “pressure pulse”—namely, “a unidirectional flow to the [microchannel/supply duct]”—and will apply the term’s “plain and ordinary meaning.” EX2012 at 6–7. Here, the Board should also apply the plain and ordinary meaning, which is “a transient increase in pressure.” Moreover, in light of surrounding claim language, the Board should find that the claimed “pressure pulse” must be “propagate[ed] . . . across the microfluidic flow channel in a crosswise direction” and be “dampen[ed] or absorb[ed]” by a “first reservoir” (claim 1). *See also* claim 5 (reciting a “a first reservoir . . . adapted for dampening or absorbing a pressure pulse propagated across the width of the flow channel”).

Petitioner employs part of its incorrect district-court construction here to try to capture flow-based devices like Wada that add “flow” into and down a transport channel. *See* Pet. 23–31, 36–37. Specifically, Petitioner asserts in district court that “pressure pulse” is “a unidirectional flow to the [microchannel/supply duct].” EX2006 at 22–23. Petitioner conceals this construction here because of the overly-narrow “unidirectional” limitation, but it continues to suggest that any “flow” is necessarily a “pressure pulse.” That suggestion is technically inaccurate (EX2001 ¶¶50–55) and plainly at odds with the plain language of the claims. In claim 1, Petitioner fails to take into account that the claims themselves expressly require

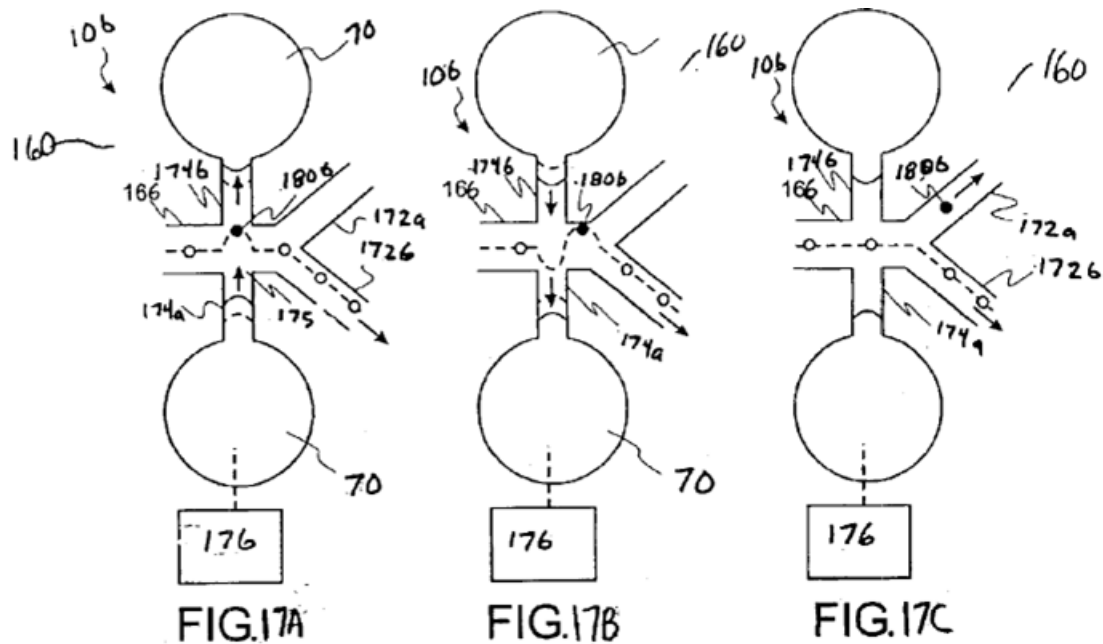
that the “pressure pulse” be “propagate[ed] . . . across the microfluidic flow channel in a crosswise direction,” and be “dampen[ed] or absorb[ed]” by a “reservoir.” Similarly, in claim 5, Petitioner fails to appreciate that the “pressure pulse” must be “propagated across the width of the flow channel” to be “dampen[ed] or absorb[ed]” by a “reservoir.”

To resolve the issues raised in the Petition, the Board should construe “pressure pulse” as “a transient increase in pressure.” Moreover, in the context of the remainder of the claim, the pressure pulse must travel across the microfluidic channel to a reservoir.

Unlike the express language requiring the claimed “pressure pulse” to cross the channel to an opposed reservoir, there is no language indicating that “flow” is inherent to the “pressure pulse,” as Petitioner’s construction in district court (and arguments here) suggest. In fact, when the claims use the word “flow,” they expressly refer to flow through the main “microfluidic flow channel” for conveying/transporting the particles—not to a pressure pulse delivered by an actuator. *See, e.g.*, EX1001, claim 1 (referring to “flowing a sample through a microfluidic flow channel”); *see also* claims 2, 18.

The specification further explains that the claimed “pressure pulse” is a “transient pressure variation” and a “sudden pressure increase,” and it never suggests that it is a “flow” in the way prior art such as Wada uses the term. *Id.* at

12:13–32. The description of the sorting embodiments depicted in Figures 17A–17C explains that “the *pressure* within the reservoir of the first bubble valve 10a is *increased*,” which in turn “caus[es] a *transient* discharge of liquid” from the actuator to the opposed reservoir, as indicated by the arrows in Figure 17A below:



*Id.* at 12:23–47 (emphases added). The patent further explains that the same volume of discharged liquid *immediately* returns back to the actuator side channel in the “relief phase,” as depicted in Figure 17B. *Id.* at 12:48–65. The “pressure pulse” does not “flow” through the transport channel. Wada’s “hydrodynamic flow” cited by Petitioner is very different, as it turns and flows downstream through the transport channel instead of shifting back-and-forth between reservoirs. See EX1006 at 19:23–23:18.

The prosecution history further confirms that a “pressure pulse” is a transient increase in pressure. In distinguishing a “Dunaway” reference during prosecution of an earlier/related patent,<sup>5</sup> the applicants explained that Dunaway “does not create a pressure variation or *pressure pulse, which are transient increases in pressure*, but rather a pressure differential *condition* between two openings.” EX2011 at 43 (first emphasis added); *see also* EX2013 at 319–321 (distinguishing Zöld and Glaettli during prosecution of another earlier/related patent because they rely on neither positive nor transient/momentary pressure variations).

**B. “dampening or absorbing the pressure pulse using [a/the] first reservoir” (claims 1, 5, and 18)**

The district court declined to construe “reservoir” and instead will apply its “plain and ordinary meaning.” EX2012 at 5–6. The Board likewise need not construe the term. But in light of Petitioner’s arguments, the Board should confirm that the prior art must disclose the “functional” language associated with “first reservoir,” namely that it must be for “dampening or absorbing the pressure pulse” that was propagated across the flow channel (*see* claims 1 and 5).

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<sup>5</sup> *See NTP, Inc. v. Research In Motion, Ltd.*, 418 F.3d 1282, 1293 (Fed. Cir. 2005) (construing common terms the same across related patents).

Although Petitioner ostensibly applies Cytonome’s district-court construction of “reservoir,” its arguments here largely ignore that the claimed “first reservoir” must be configured to “dampen[] or absorb[]” the cross-channel “pressure pulse.” *See K-2 Corp. v. Salomon S.A.*, 191 F.3d 1356, 1363 (Fed. Cir. 1999) (holding that “functional” language is limiting when it “tells us something about the [claim’s] structural requirements”). Petitioner does not dispute that the “dampening or absorbing” language is limiting.<sup>6</sup> Indeed, that language provides key details about the structure of the “reservoir,” such as having the proper geometry and/or “resilient properties” to absorb or dampen a pressure pulse. *See* EX1001 at 12:18–32; EX2001 ¶¶56–59. Petitioner, however, repeatedly suggests that the “first reservoir” is *any* side channel, even if it does not absorb or dampen. Pet. 27–31, 36–37. Petitioner’s annotations to Figures 22–23 of Wada are demonstrative:

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<sup>6</sup> Petitioner does not dispute that any of the functional language in the challenged claims is limiting, and the Board should interpret all functional language as limiting.

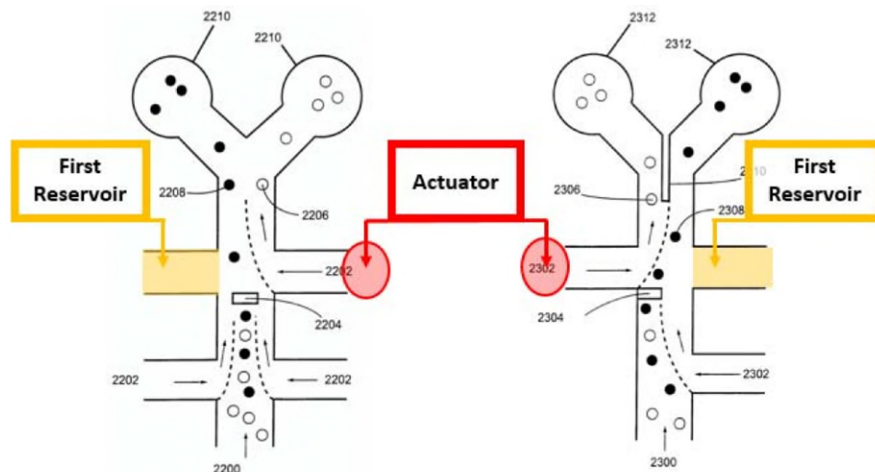


Fig. 22

Fig. 23

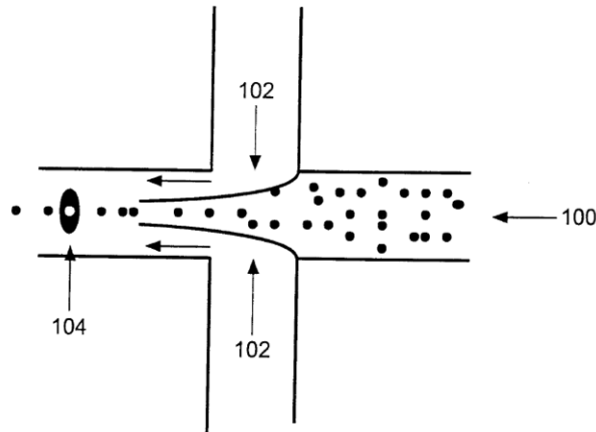
Pet. 31. The side channels Petitioner identifies as “First Reservoir” cannot “absorb” or “dampen” anything—they are structurally and functionally identical to Wada’s alleged “Actuator” side channels and are likewise configured to *introduce* fluid. EX1006 at 19:23–20:14; EX2001 ¶¶94–99, 120, 130–35.

Accordingly, for these proceedings, it is sufficient for the Board to decide that a channel/port configured to introduce fluid is not the claimed “first reservoir.”

## VII. OVERVIEW OF THE PRIOR ART

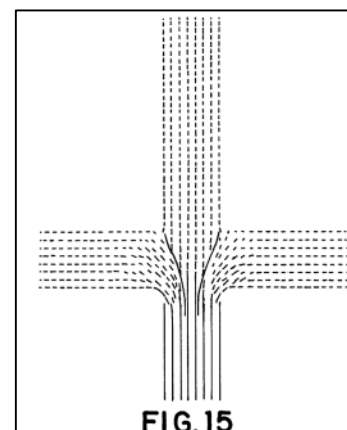
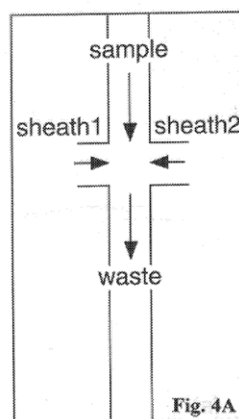
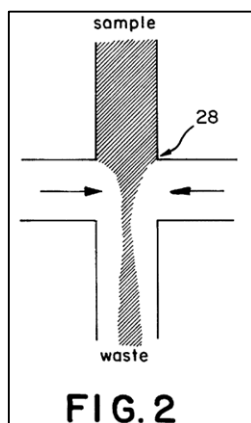
### A. Wada

Wada (EX1006) initially discloses devices for “focusing” particles in a transport channel using “hydrodynamic flow.” As shown in Figure 1A, particles are focused to flow past a detector (104) by introducing fluid from two side channels (102) that enters the transport channel and continues to flow downstream:



EX1006 at 9:2–5, 13:11–14:2; *see also* 4:11–14.

Citing U.S. Patent No. 5,858,187 (“Ramsey”), Wada describes focusing by inducing flow from side channel(s) through “electodynamic[] . . . and/or other fluid movement methods,” including “Joule heating.” *Id.* at 12:7–13. And Ramsey (EX2014) indeed describes such focusing, wherein fluid flows from side channels into and down a transport channel by “electrodynamics” (or “electrokinetics”) by applying a voltage differential between “sheath” fluid sources and the waste reservoir at the end of the transport channel. EX2014 at 3:61–4:40. Below are figures depicting Ramsey’s “electrodynamic focusing”:



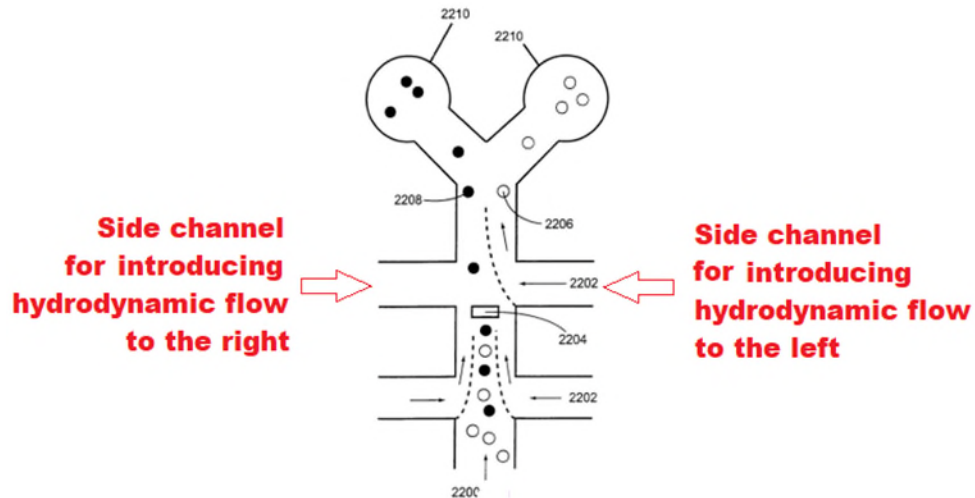


After discussing focusing by using “hydrodynamic flow,” Wada describes using this same hydrodynamic flow principle to *sort* particles after they are properly focused—namely, by increasing flow from a side channel to add net flow to the transport channel, which in turn directs selected particles into an outlet. *Id.* at 17:10–24:12. Wada discloses such sorting embodiments solely with reference to Figures 22–24. *Id.*

More specifically, Wada describes a “sorting function” that uses “electrokinetics” to “nudge” selected particles across the width of the transport channel. *Id.* at 18:26–19:13. Wada again cites Ramsey for this technique, thus teaching the use of electrokinetically-induced flow from side channels for sorting. *Id.* at 18:31–19:9. Referencing Figure 22, Wada describes this sorting technique as introducing “hydrodynamic flow”:

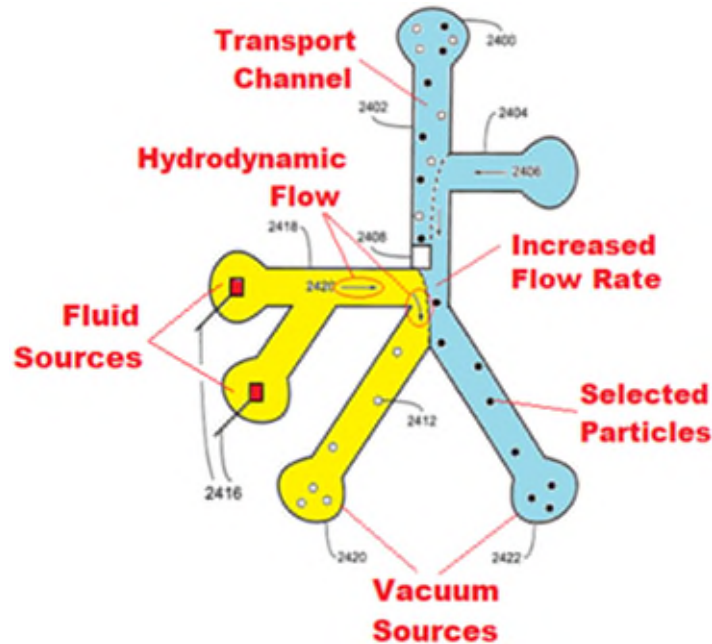
A second set of opposing microchannels is typically located downstream from detector **2204** for introducing at least one hydrodynamic flow **2202** so as to direct selected cells **2208** (e.g., fluorescently-labeled cells) and non-selected cells **2206** into in this case, one of two microchannels, each terminating in particular collection wells **2210**.

EX1006 at 19:29–20:2. Figure 22 (annotated) is reproduced below:



EX2001 ¶97. Wada describes Figure 23, a slightly modified version of Figure 22, in nearly identical terms. *Id.* at 20:8–13.

Wada then provides an extensive discussion of using “heating elements” to induce flow similar to the electrokinetic-based technique discussed above. *Id.* at 20:15–24:12. Wada explains that such heating elements are disposed in “wells” (fluid sources containing liquids/gels) connected to side channels, which induce “hydrodynamic flow,” as depicted in Figure 24 below (annotated):

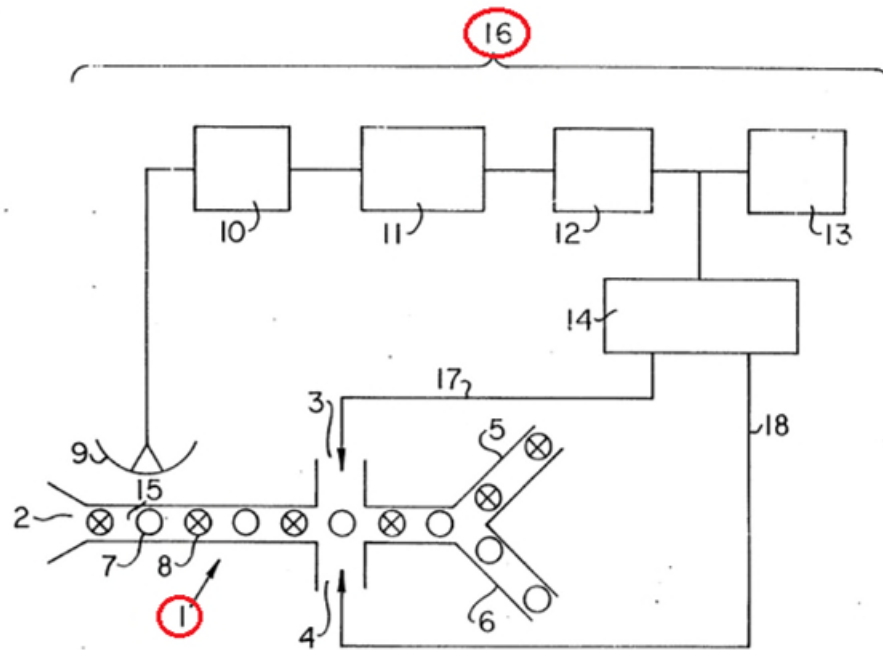


Wada explains that heat from “Joule heating electrodes 2416 raises the temperature of, e.g., a buffer or gel disposed within branched particle sorting microchannel 2418” to “induce or increase flow of the buffer or gel from branched particle sorting microchannel 2418,” which “thus deflects or redirects the flow of selected particle 2410 into selected particle collection well.” *Id.* at 23:7–16. Wada also teaches that the induced flow into the transport channel can be further aided by “vacuum source(s) that are typically operably connected to . . . particle collection well 2420 and/or selected particle collection well 2422.” *Id.*

In short, Wada teaches various techniques for sorting, but all of them rely on the same basic principle of inducing “hydrodynamic flow” to increase the net flow of fluid in the transport channel. EX2001 ¶¶87–89, 104.

## B. Marcus

Marcus (EX1005) discloses a “fluidic sorting device” comprising a “machine vision apparatus” (“MVA”) for particle analysis and a “fluidic logic element” to sort particles based on that analysis (EX1005 at 3:28–4:3)—depicted as items 16 and 1 in Marcus’s sole Figure 1:



Most of Marcus’s very short disclosure describes the MVA. The MVA generates a signal according to a visually distinct characteristic that is detected by a camera (9, 10) and analyzed by an “image interpretation device” (11). *Id.* at 3:38–41. That device sends a signal to a “decision control device” (12) and “fluidic controller device” (14) based on a detected particle characteristic. *Id.* at 3:43–46. The fluidic controller issues a signal to generic “control ports” 3 and 4, causing the particles to sort into branched outlets 5 and 6. *Id.* at 3:43–48.

Marcus provides almost no information on the sorting apparatus or its operation. In the Background of the Invention, Marcus simply describes a “conventional” and generic “fluidic logic element”:

The fluidic logic element comprises one input port, two control ports and two output ports. This fluidic logic element is, as stated above, conventional and may be produced using conventional micromachining technology or any other conventional means.

*Id.* at 2:15–31; *see also id.* at 2:7–13 (explaining that the invention “makes use of two conventional components,” namely “a fluidic sorting device and a machine vision apparatus”). The sorting apparatus is further described as “commercially available.” *Id.* at 3:9–12. And the text regarding the operation of the “control ports” explains that *both* are actuated to “separate out” particles by type:

This distinction [between particles] is then transmitted to a control decision device 12 which signals a fluidic controller device 14 to instruct control ports A and B, 4 and 3 respectively, to separate out said particles 7 and 8.

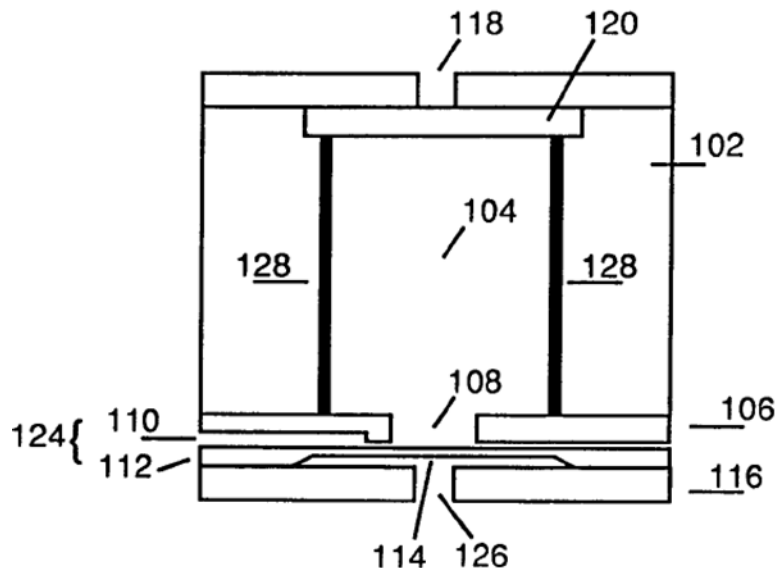
*Id.* at 3:57–62; *see also id.* at 3:43–48 (describing two signal “leads,” one for each control port, to instruct each port on how to sort particles).

In sum, while generic “control ports” 3 and 4 are depicted as side channels intersecting the main flow channel, there is no description of actual side channels or components connected to such channels. And the limited disclosure on

Marcus's sorting operation indicates that both control ports are actuated to effect sorting. Neither is described as a passive component that cooperates with the other, and neither is described as configured for, or capable of, applying or absorbing a "pressure pulse." See EX2001 ¶¶152–59.

### C. Anderson

Anderson (EX1012) discloses a diagnostic device in which nucleic acid samples are transported between chambers for "carrying out a variety of preparative and analytical operations" on the samples, including "manipulation, identification and/or sequencing of nucleic acid samples." EX1012 at 3:11–14, 69:30–34, Figs. 5a–5b. The device includes two or more "reaction chambers" and "fluid channels" connecting the various chambers. *Id.* at 32:24–33:4. A representative reaction chamber is shown in Figure 2b:



The reaction chambers “perform a number of varied functions, e.g., as storage chambers, incubation chambers, mixing chambers and the like.” *Id.* at 33:4–7.

Anderson discloses fabrication techniques for its “reaction chambers” and various techniques for transporting nucleic acid samples between them, including: diaphragm pump and valve combination (*id.* at 45:3–46:22); “pressure differentials” set up with vacuum sources, “positive displacement pump[s],” and the like (*id.* at 46:23–52:15); electrohydrodynamic pumps (*id.* at 63:33–64:32); and an assortment of “microvalves” placed between chambers to control flow of the sample (*id.* at 65:33–67:6).

Anderson’s disclosure regarding actuators and pumps solely addresses delivering/transporting samples from one chamber to another. Throughout the disclosure, Anderson states that its device functions to “deliver the sample” between chambers (*id.* at 51:11–13), or “push a sample through the device” (*id.* at 51:31–33), or is used for the “transport” of fluid samples between chambers of the device (46:23–27; 44:15–20). In other words, Anderson’s chambers are used exclusively as containers—either source or destination—for the sample of interest. *See* EX2001 ¶¶ 79–86.

#### **VIII. PETITIONER FAILS TO SHOW A REASONABLE LIKELIHOOD THAT ANY OF THE CHALLENGED CLAIMS ARE OBVIOUS**

The Board should deny institution under 35 U.S.C. §314(a) because Petitioner fails to show that there is a reasonable likelihood that it will prevail on

any of its stated grounds. For each Ground, Petitioner fails to explain how the prior art discloses—or why and how references would be combined to disclose—each limitation of each challenged claim.

#### **A. Legal Standards**

Petitioner bears the burden of showing that there is a “reasonable likelihood” that it will prevail as to at least one challenged claim. 35 U.S.C. §314(a). Under 35 U.S.C. §312(a)(3), the Petition must “identif[y] . . . with particularity . . . the grounds on which the challenge to each claim is based.” And Petitioner has the burden of proof to establish that it is entitled to the requested relief. 37 C.F.R. §42.20(c). Accordingly, the Board “address[es] only the basis, rationale, and reasoning put forth by the Petitioner in the Petition, and resolve[s] all vagueness and ambiguity . . . against Petitioners.” *Hopkins Mfg. Corp. v. Cequent Performance Prods., Inc.*, IPR2015-00616, Paper 9, 7 (PTAB Aug. 17, 2015) (denying institution).

For obviousness, Petitioner must show that “all claimed limitations are disclosed in the prior art.” *PAR Pharm. v. TWI Pharms.*, 773 F.3d 1186, 1194 (Fed. Cir. 2014). But a patent is not proved obvious merely by showing that each limitation was in the prior art. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007). Rather, patent challengers must provide a “reason to combine the teaching of the prior art references to achieve the claimed invention.” *PAR Pharm.*, 773



F.3d at 1193. This reason to combine must be supported by evidence, not conclusory statements. *KSR*, 550 U.S. at 418.

Moreover, there is likely no such reason to combine if the proposed combination requires “a change in the basic principles under which the [base reference] was designed to operate” or “require[s] a substantial reconstruction and redesign” of the reference. *In re Ratti*, 270 F.2d 810, 813 (C.C.P.A. 1959). In *Ratti*, the patent-at-issue claimed devices for “sealing the space between a bore in a housing and a . . . shaft centrally located in the bore.” *Id.* at 810–11. The claims required a seal made of a “resilient material” that employed “spring fingers to exert a[n] [outward] force on the resilient material” for “maintain[ing] a snug engagement between the . . . resilient member and the inner surface of the bore.” *Id.* The asserted reference, “Chinnery,” also endeavored to engage a “resilient” sealing member with a bore, but it did so without “spring fingers.” *Id.* at 811–13. Instead, Chinnery employed an “interference press fit” that caused the resilient material to “stiffen” between the shaft and the bore—with such “stiffening” precluding the need (and ability) to employ “spring fingers.” *Id.* The Court explained that this “interference press fit” was “alone relied on to keep the seal tight” in Chinnery. *Id.* Accordingly, the combination of a reference employing “spring fingers” with Chinnery was “not a proper ground for rejection” because it would require a “change in the basic principles under which [Chinnery] was

designed to operate” and “would require a substantial reconstruction and redesign.”

*Id.*

Courts and the Board have relied on *Ratti* to reject combinations that change a base reference’s “principle of operation.” For example, in *Plas-Pak Industries v. Sulzer Mixpac AG*, the Federal Circuit relied on *Ratti* to affirm the Board’s non-obviousness decision when a proposed combination would have changed “Fukuta” from a paint mixing system that *prevents* backflow to one that *employs* backflow because such change would “fundamentally alter Fukuta’s ‘principle of operation.’” 600 F. App’x 755, 758–59 (Fed. Cir. 2015) (non-precedential). And in *R.J. Reynolds Vapor Co. v. Fontem Holdings I B.V.*, the Board rejected a proposed combination that would have changed a flow device from (a) one using “capillary infiltration” to transport fluid *with* “airflow to atomize liquid” to (b) one using a “porous wick” to transport fluid *without* using airflow to atomize liquid. IPR2016-01692, Paper 45, 24–25 (PTAB Mar. 2, 2018). The Board held that the “teachings of the references are not sufficient to render the claims obvious” because combining them “would change the principle of operation of the prior art.”

*Id.*

Indeed, the Board regularly rejects combinations and modifications on this basis, including when denying institution. *See, e.g., Microsoft Corp. v. Koninklijke Philips N.V.*, IPR2018-00185, Paper 7, 12 (PTAB May 22, 2018) (denying

institution; *Apple Inc. v. Papst Licensing GMBH & Co. KG*, IPR2016-01842, Paper 35, 55–58 (PTAB Apr. 26, 2018); *Fisher & Paykel Healthcare Ltd. v. Resmed Ltd.*, IPR2017-00059, Paper 27, 45 (PTAB Mar. 7, 2018).

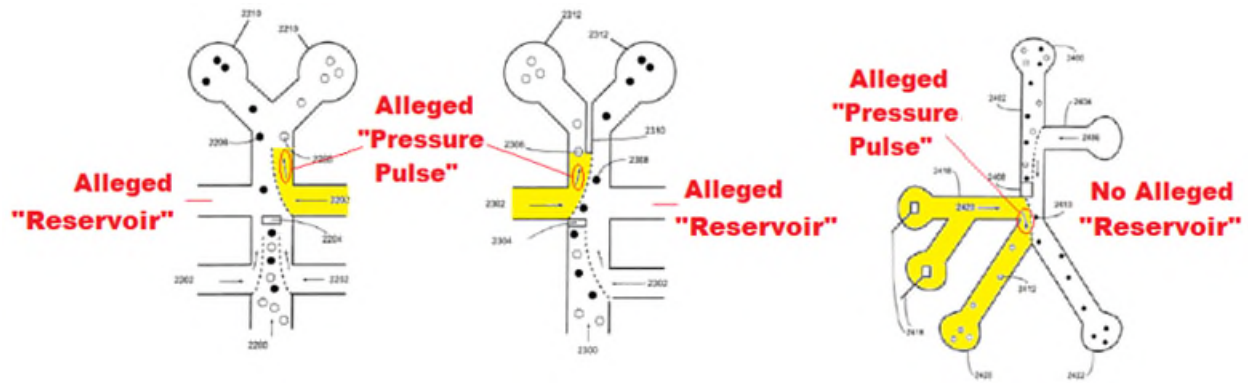
**B. Ground 1 — Petitioner Fails to Show That Wada Renders Obvious Claims 1, 2, 5, 13, 16, 18, and 19**

Wada discloses neither a “pressure pulse” nor a “reservoir” for “dampening or absorbing” that pressure pulse as claimed in independent claims 1 and 15. Instead, Wada discloses only: (1) deflecting particles with a “hydrodynamic flow” that is not a pressure pulse, and (2) side channels that *introduce* this “hydrodynamic flow” and thus are not “reservoir[s]” that “dampen[] or absorb[]” the alleged pressure pulse. There was no reason to modify Wada to include these limitations because doing so would fundamentally change Wada from (a) a flow-based device that adds fluid to the system to sort particles to (b) a pressure-based device that delivers a pressure pulse into a reservoir (without adding fluid) to sort particles.

***1. Petitioner fails to show that Wada discloses the claimed “pressure pulse” (all challenged claims)***

Wada fails to disclose the claimed “pressure pulse” in claims 1 and 5 because the claims expressly require that the “pressure pulse” be “propagate[ed] . . . across the microfluidic flow channel” and be “dampen[ed] or absorb[ed]” by a “first reservoir.” As is readily apparent in Wada’s Figures 22–24, the

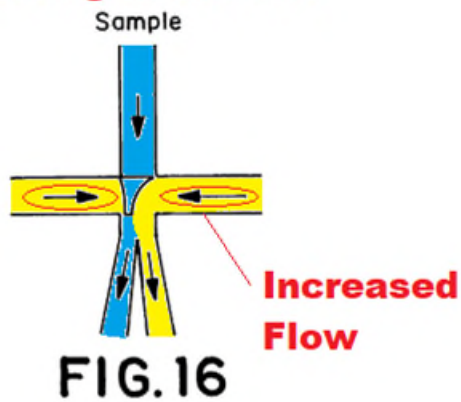
“hydrodynamic flow” that Petitioner identifies as the “pressure pulse” fails to even *reach* any alleged “reservoir,” much less be absorbed or dampened by one:



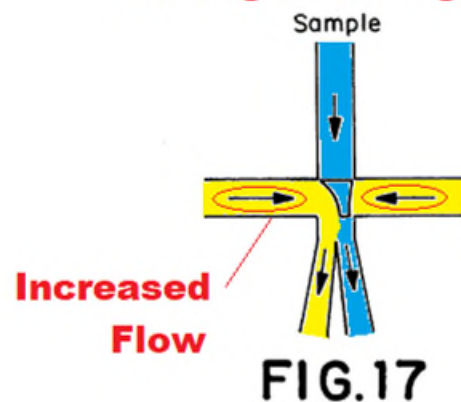
Instead, the alleged pressure pulse enters the transport channel and immediately turns downstream. EX2001 ¶¶117–19.

In any event, Wada’s “hydrodynamic flow” is not a “pressure pulse” in the first place. Wada’s “hydrodynamic flow” is a continuous flow of fluid that is increased/accelerated when a selected particle is detected, not a “pressure pulse” that simply disrupts the flow in the channel without adding fluid. EX2001 ¶¶73, 100, 119–23. Unlike the invention—whose sorting operation does not add fluid at all—Wada requires fluid sources to continuously supply fluid to (and out of) the side channels. *Id.* Wada’s reliance on Ramsey to teach the sorting operation employed in Figures 22–23 is instructive, as Ramsey clearly teaches continuously introducing flow from both side channels to sort particles:

**Sorting to the left**

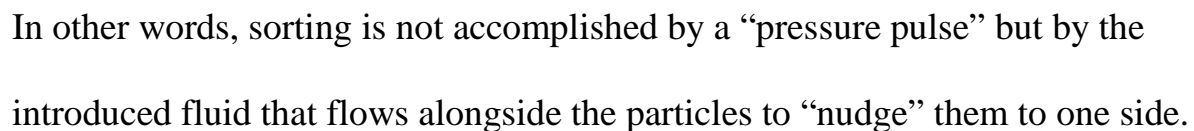
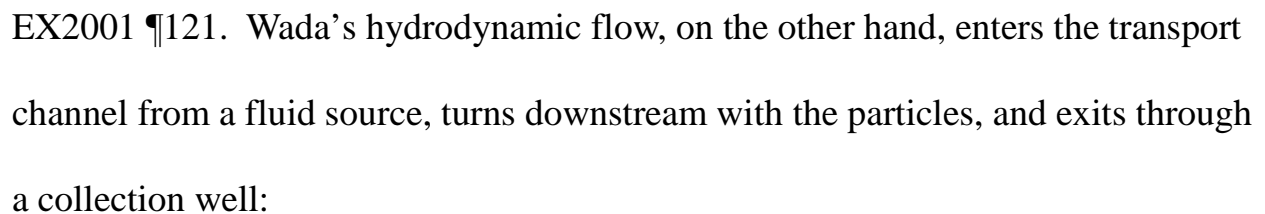


**Sorting to the right**



EX2014, Figs. 16, 17 (annotated), 7:24–50. As shown by the encircled arrows, sorting is achieved by modulating the relative amounts of this continuous flow from each side channel. *See id.*; EX2001 ¶120.

Even if Wada’s side channels were not continuously flowing, “hydrodynamic flow” would still not be a pressure pulse. As demonstrated below, a pressure pulse is a *momentary* disturbance that deflects a single particle without varying flow rate in the device. Due to being absorbed by the first reservoir, the pressure pulse (and resultant disturbance) does not even *exist* after the moment when the particle is deflected:



EX2001 ¶¶122–23; *see also id.* ¶¶94–95.

In short, Wada’s hydrodynamic flow-based sorting operation fails to employ a “pressure pulse” as claimed. Petitioner and its expert repeatedly refer to Wada’s “hydrodynamic flow” as the pressure pulse, but they fail to identify, much less reconcile, the stark difference between Wada’s devices and the pressure pulse-based devices/methods of the challenged claims. *See, e.g.*, Pet. 23–27, 29–30, 37; EX1002 ¶¶124–28, 133.

Moreover, although *no* flow-based devices employ a pressure pulse because they operate by increasing flow through the transport channel (EX2001 ¶¶65–78), Wada’s specific techniques for increasing flow—namely, electrokinetics and Joule heating—further illustrate that Wada’s sorting devices fail to employ a “pressure pulse.” Indeed, those techniques avoid relying on pressure altogether.

As Dr. Arnold explains, electrokinetics (i.e., “electroosmotic flow”) “allows for pulse-free voltage-controlled fluid delivery with no moving parts, no valves, and no pumps” by applying an electric field along a microfluidic channel that contains a thin layer of ionically-charged fluid. EX2001 ¶¶63–64, 74. When charged, that layer of fluid moves under the influence of the field and essentially “drag[s] the rest of the fluid along” without increasing pressure. *Id.* In devices employing this technique (such as Wada), “[n]o pressure is generated within the channel by the force generating the electroosmotic flow in open channels and no

additional applied pressure is required to accomplish fluid motion.” *Id.*; *see also id.* ¶74.

Similarly, Joule heating induces flow without applying pressure by relying instead on the “the inverse relationship between temperature and viscosity.” *Id.* ¶¶106–08, 114 (quoting EX1006 at 20:15). As Dr. Arnold explains, viscosity is essentially the “thickness” of a fluid, and “as the fluid temperature increases, the viscosity decreases, and fluid flow rate increases.” *Id.* ¶¶108–10 (citing “Poiseuille’s” fluid-flow equation). In Wada Figure 24, the heated fluid exiting the side channel will flow adjacent to the sample and “the reduced viscosity will result in an increased flow rate . . . even though there is no change whatsoever in the applied pressures on the channels.” *Id.*

Dr. Arnold further explains that Dr. Weigl was incorrect to suggest that there would be a sudden pressure change in the device of Figure 24. *Id.* ¶111. Because “Wada describes heating a localized volume of liquid, the pressure would need to be generated by the expansion of the liquid within the channels.” *Id.* Dr. Arnold then uses the channel dimensions provided in Wada and the typical “Thermal Coefficient of Expansion” for liquids to conclude that “the miniscule fluid expansion” in Wada “would not generate enough volume change to significantly affect the pressure in the microfluidic channel, certainly not enough to deflect a particle as required for sorting.” *Id.*



In fact, to effect pressure-based sorting via heating, Wada's devices would need to generate vapor or gas specifically to increase pressure. EX2001 ¶¶112–13. Both Wada and the '797 Patent teach away from such a heating technique. *Id.* Wada teaches that liquid/gel fluid flow—not air bubbles—should be used to sort particles. *Id.* Generating vapor or gas would impede such an operation. *Id.* The '797 Patent explains that heating-based systems that generate a “gas bubble” present “a number of disadvantages,” including “the required power to operate the valve,” the “disastrous effects on . . . biochemical substances” caused by heating, and “the complexity” and “high costs” of the heater's circuitry. EX1001 at 2:36–53; EX2001 ¶113.

Electrokinetics and Joule heating are the only two techniques for introducing/increasing flow that Wada discusses with any detail, but Wada does make a brief reference to “other alternative techniques for inducing the flow of focusing fluids to sort particles,” including “pressure, hydrostatic, wicking, capillary, and other forces.” Pet. 26–27 (citing EX1006 at 19:9–13); *see also* Pet. 24 (referring to “pressure-based flow”). The word “pressure” is misleading here. As Dr. Arnold explains, using “pressure” to “*induc[e] the flow of focusing fluid to sort particles*” is referring to the same flow-based principle discussed throughout Wada. EX2001 ¶102. (emphasis added). In such systems, flow from the side channels is modulated by varying the pressure applied *at the fluid source* (not at

the particles or in the transport channel) so as to vary the amount of fluid flowing around the particles. *Id.* Fundamentally, this is no different from the principle described in Ramsey above. *Id.* Indeed, pressure-based pumps “were not known to be suitable for sorting operations at all,” (*id.*), much less to perform the specific pressure-pulse/absorption technique as claimed.

Finally, Wada’s brief mentions of other “fluidic direction components,” such as a “pressure source” or “pressure based-flow, electrokinetic flow, or other mechanisms or combinations of mechanisms,” also do not disclose the claimed “pressure pulse.” *See* Pet. 23–27, 48–50. These other components are mentioned entirely outside of Wada’s sorting section and are expressly directed at establishing flow through the “first microchannel”—i.e., the transport channel—not sorting the particles therein. EX2001 ¶142; EX1006 at 3:22–4:5, 42:8–43:14. To the extent Petitioner is arguing that it would have been obvious to somehow incorporate such “fluid direction components” into Wada’s side channels and reconfigure them to apply a “pressure pulse” across a channel to sort particles, Petitioner fails to make the requisite showing. The entire sorting section of Wada emphasizes sorting by introducing “hydrodynamic flow” as described in Figures 22–24. EX1006 at 17:10–24:12. Brief, non-detailed statements aimed at establishing flow in the transport channel cannot undermine and contradict Wada’s extensive and detailed teaching about its fundamental sorting operation.

a) *Background References*

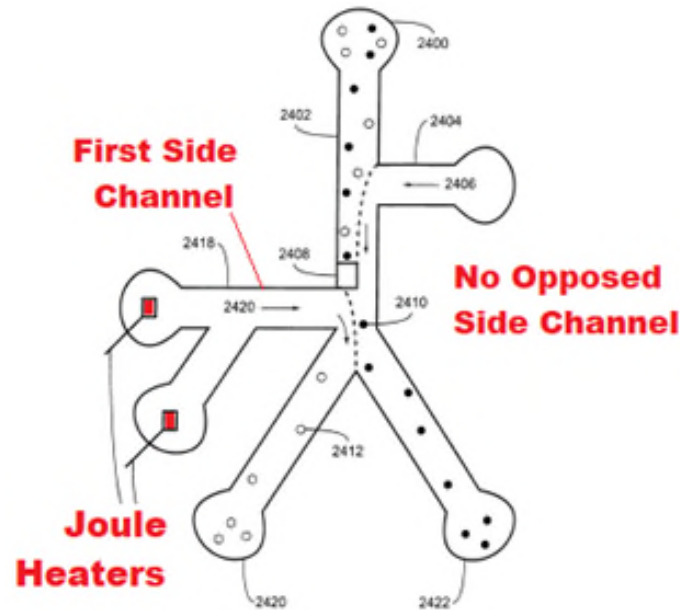
Implicitly acknowledging Wada's lack of a "pressure pulse," Petitioner string-cites a number of "background references" cited in Dr. Weigl's declaration to suggest that "propagating a pressure pulse across a microfluidic flow channel was well-known in the art." Pet. 27, 54. These references should not be considered at all because they were not included in Petitioner's stated Grounds and because Petitioner is improperly incorporating-by-reference Dr. Weigl's conclusory observations on these references. 37 C.F.R. §42.6(a)(3); 35 U.S.C. §312(a)(3); *Boehringer Ingelheim Int'l GmbH v. Genentech, Inc.*, IPR2015-00415, Paper 13, 5, n. 1, 11 (PTAB July 17, 2015) ("Our analysis of the challenged claims is limited to the specific combinations of references that Petitioner identified in the grounds set forth in the Petition.").

In any event, the cited references disclose neither the claimed cross-channel "pressure pulse" to sort particles nor an opposed "reservoir" to absorb one. Deshpande (EX1018) and Dubrow (EX1032) disclose electrokinetic flow-based devices that are not materially different from Wada. *See, e.g.*, EX1018 at 341–42 (Deshpande explaining that he is "specifically focusing on one component—the electrokinetic injector"); EX2001 ¶¶173–77. Zöld (EX1007) is another flow-based device that modulates flow in side channels using a gas-bubble—similar to the technique disparaged in the '797 Patent. EX2001 ¶¶178–81. Neukermans

(EX1020), Williams (1023), and Zeng (1022) are completely irrelevant because they have nothing to do with particle sorting, much less applying a “pressure pulse” to sort a particle. EX2001 ¶¶183–85. Similar to Anderson, they disclose only devices for establishing and regulating flow through a transport channel. *Id.* Chapman (EX1014) discusses two commercial sorters. One increases flow in a transport channel by regulating flow at an *outlet*—there is no “pressure pulse” applied to a particle. EX2001 ¶191. The other does not move particles at all—it moves a collection tube so as to “catch” selected particles. *Id.* Finally, Glaettli (EX1016) is a device from the 1970s that attempts to suck particles out of a channel using pulleys and a piston attached to an extraction tube. EX2001 ¶¶192–93. It specifically deals with problems caused by “cavitation” due to accelerating large volumes of fluid—an issue irrelevant to microfluidic devices by the time of the invention. *Id.*

**2. *Petitioner fails to show that Wada discloses the claimed “reservoir” that dampens or absorbs the “pressure pulse” (all challenged claims)***

Because the claimed “pressure pulse” is not disclosed in Wada, there is no “reservoir” for “dampening or absorbing” that pressure pulse as required in claims 1 and 5. Figure 24 of Wada is particularly informative. It conspicuously lacks *any* structure on the opposite side of the transport channel from the first side channel:

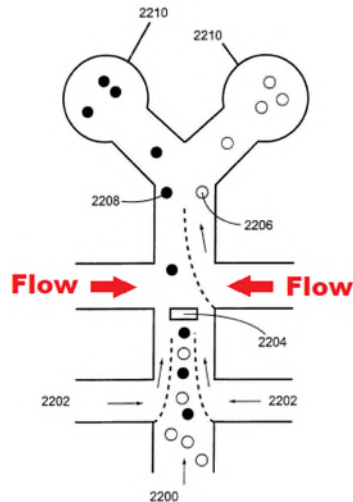


EX1006, Fig. 24 (annotated). Petitioner never explains *why* Figure 24 fails to include side channels like those in Figures 22–23—the components that form the basis of its “first reservoir” argument. *See* Pet. 27–31, 36–37 (arguing only that “Wada’s teaching of opposing microchannel structures is not limited to Figures 22–23, but applies equally to Figure 24.”).

Figure 24 and its accompanying text in fact *teach away* from using a reservoir to dampen or absorb any pressure or fluid dispensed from the side channel by teaching that the hydrodynamic flow emanating from that channel can be *increased* by using multiple Joule heaters. EX1006 at 23:1–3; EX2001 ¶¶127–129. By failing to employ an opposed side channel despite including multiple Joule heaters, Figure 24 suggests that whatever benefit is gained from the increased flow would be diminished by an opposed side channel. *Id.* Similarly, Wada’s

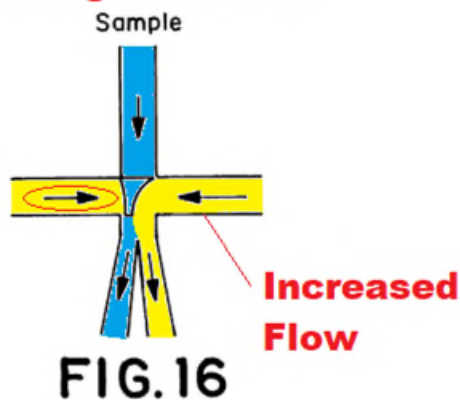
additional emphasis on enhancing the hydrodynamic flow of fluid into and down the transport channel by the addition of “vacuum sources” in the collection wells (EX1006 at 23:10–14) further teaches away from the use of any “reservoir” or other structure to dampen/absorb pressure or fluid. EX2001 ¶130. The vacuum sources make Wada’s sorting operation abundantly clear—induce a hydrodynamic flow that flows into the collection wells alongside the particles, not across the channel. *Id.* (drawing same conclusion for electrokinetic systems such as Wada that apply a voltage between the side channel and the collection well).

Petitioner maintains that a POSA would modify Figures 22 and 23 by adding the claimed reservoir to one of the side channels, yet offers no explanation or reconciliation of the counter-teaching of Figure 24. *See* Pet. 27–31, 36–37. In any event, Figures 22 and 23 also fail to disclose the claimed reservoir. Regarding Wada’s “opposing microchannels,” they do not “dampen” or “absorb” anything—they are described as useful solely for introducing “hydrodynamic flow.” EX2001 ¶¶131–35. Wada explains that, in Figure 22, “[a] second set of opposing microchannels is typically located downstream from detector 2204 *for introducing* at least one *hydrodynamic flow* 2202 so as to direct selected cells 2208 . . . [into] collection wells 2210.” *Id.* at 19:29–20:2 (emphasis added); *see also id.* at 20:8–13 (similar description for Figure 23). In other words, when two downstream side channels are employed, both are used to introduce flow, as illustrated below:

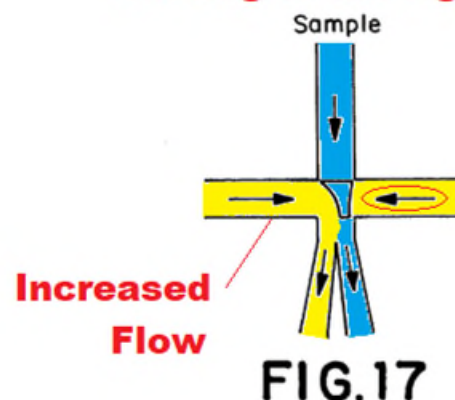


*Id.*, Fig. 22 (annotated); EX2001 ¶130. This is entirely consistent with Wada’s reliance on Ramsey to teach the sorting operation of Figures 22–23, wherein one of the two side channels *increases* flow, but fluid from the opposed side channel nonetheless continues flowing into the transport channel:

**Sorting to the left**



**Sorting to the right**



EX2014, Figs. 16, 17 (annotated), 7:24–50. In other words, fluid is never received by either side channel. EX2001 ¶¶134–35.

Petitioner characterizes Wada’s opposed side channel as “non-actuated” and “aligned” with the actuated side channel, and concludes that it therefore constitutes

the claimed “reservoir” or, alternatively, that a POSA would simply know to attach a dampening or absorbing “reservoir.” Pet. 27–31, 37. No such teaching or suggestion is found in Wada. EX2001 ¶¶59, 97, 127–28. Instead, Wada’s second opposed side channel is *optional* and for the expressly-stated purpose of also “introducing” an additional “hydrodynamic flow.” EX1006 at 19:29–20:2, 20:8–13. Petitioner’s expert acknowledges as much by describing Wada’s opposed channels as “individually actuate[d].” EX1002 ¶141; *see also id.* ¶¶125, 143–49.

Petitioner attempts to buttress its absorption “first reservoir” argument by noting that Wada’s side channel may comprise a “well” or “other cavity.” Pet. 28, 38 (citing EX1006 at 20:23–25, 23:19–26). But the specific support given for that proposition is that Wada’s “Joule heating” electrodes may be positioned in such a well or cavity. *Id.* These Joule heaters are employed *solely* to induce hydrodynamic flow out of a side channel, so that disclosure fails to teach anything about a structure or function for any other purpose. EX2001 ¶¶76, 98–99, 128–29. Wada certainly never explains that the Joule heating wells dampen or absorb a pressure pulse or fluid.

Petitioner also cites—without explanation—Wada’s reference to “chambers” that may be included in its devices. Pet. 28, 38, 40 (citing EX1006 at 37:29–32, 38:11–17, 39:19–33). Each of the statements from Petitioner’s citations is extracted from the section of Wada on “Assay Devices,” and they amount to



nothing more than generic statements about manufacturing microfluidic devices in general. *See, e.g.*, EX1006 at 39:19–33 (explaining that “channels and/or chambers of the microfluidic devices are typically fabricated into the upper surface of the bottom substrate”). None specifically apply to modifications to Figures 22–24 or otherwise provide any teaching or suggestion of a “reservoir” that could dampen or absorb a pressure pulse as claimed. EX2001 ¶136.

a) *Background References*

Similar to the “pressure pule” limitation, Petitioner string-cites several background references to account for Wada’s failure to disclose a dampening or absorbing “reservoir” and suggests (with little explanation) that such reservoirs were simply known in the art. Pet. 31. The Board should not consider these references at all because they were not in the stated Grounds and were improperly incorporated-by-reference (along with Dr. Weigl’s conclusory observations on them). 37 C.F.R. §42.6(a)(3); 35 U.S.C. §312(a)(3); *Boehringer*, IPR2015-00415, Paper 13 at 5, n. 1, 11.

In any event, the “compliance devices” Dr. Weigl cites such as from Zengerle (EX1033) and Veenstra (EX1035) deal only with adding “pressure smoothing elements” along a transport channel to address vibrations that emanate from fluid supply pumps. As Dr. Arnold explains, these components were addressing problems with fluid delivery and did not involve absorbing a pressure

pulse delivered across a channel to deflect particles. EX2001 ¶¶186–89. Similarly, the “dampers” referenced in Chou (EX1035) are located *upstream* of any sorting mechanism to “eliminate[] the fluid oscillations” in the transport channel. EX1034 at 39:25–33, 43:8–48:19, Fig. 30A. Again, they had nothing to do with receiving, dampening, or absorbing a pressure pulse delivered across a channel to sort particles. EX2001 ¶¶186–89. Finally, the “flow-based” and other sorting devices cited by Dr. Weigl also fail to disclose a “reservoir” for absorbing or dampening a pressure pulse; indeed, they fail to disclose the claimed “pressure pulse” at all. EX2001 ¶¶172–81, 190–93.

**3. *Petitioner fails to show that a POSA had reason to modify Wada to achieve the claimed invention***

To the extent the Board finds that Petitioner adequately identified the claimed “pressure pulse” and “first reservoir” in the prior art, Petitioner nonetheless fails to provide the requisite “reason to combine” because it fails to explain *why* a POSA would have combined the elements as claimed. *See* 35 U.S.C. §312(a)(3); *PAR Pharm.*, 773 F.3d at 1193. Petitioner merely cites to Wada’s boilerplate language about “various combinations” (Pet. 19) commonly placed at the end of specifications. *Cf. D Three Enters., LLC v. SunModo Corp.*, 890 F.3d 1042, 1050–51 (Fed. Cir. 2018) (explaining that the “boilerplate language at the end of [an application] is not sufficient to show adequate disclosure” of claimed combinations). This alone cannot provide a basis for “picking and

choosing” from among various components, especially ones having nothing to do with Wada’s sorting operation. Selectively choosing components and contending they would be employed in the base reference to achieve the claimed invention—without explaining why that would be done—is classic hindsight reconstruction of the invention that is prohibited in obviousness analyses. *In re NTP, Inc.*, 654 F.3d 1279, 1299 (Fed. Cir. 2011).

Indeed, a POSA would not have had reason to modify Wada to achieve the invention because doing so would require changing Wada’s “principle of operation” from hydrodynamic flow-based sorting to pressure pulse-based sorting. *Ratti*, 270 F.2d at 813. Wada’s disclosure is limited solely to sorting by introducing flow into the transport channel (from a source) to increase flow so as to nudge particles against the opposite wall, whereby that flow travels downstream into a collection well. EX2001 ¶¶88–113, 138. This flow-based operating principle was central to Wada’s invention and described extensively and in great detail in the disclosure. EX1006 at 17:10–24:12. And it is a completely different sorting principle from shifting *a set volume of fluid* between an actuator and a first reservoir—specifically so as to not increase flow rate—using a pressure pulse. EX2001 ¶¶137–38, *see also id.* ¶¶39–49. Petitioner fails to identify any “benefits from the proposed modification” to overcome this destruction of Wada’s sorting principle. *See Fisher*, IPR2017-00059, Paper 27 at 45 (“[T]he evidence showing

that such a modification would destroy Ogden’s principle of operation outweighs the relatively unsupported evidence of benefits from the proposed modification.”).

Moreover, modifying Wada’s sorting mechanisms to achieve the invention would require “substantial reconstruction,” further nullifying any alleged reason to combine. *See Ratti*, 270 F.2d at 813. In Figures 22–23, one of the side channels would need to be reconfigured to deliver a cross-channel pressure pulse from an actuated reservoir instead of flow from a fluid source. EX2001 ¶139 And the opposed side channel would need to be completely redesigned from a structure that *introduces* flow to a reservoir that dampens or absorbs that pressure pulse. *Id.* Figure 24, which is solely a Joule heating embodiment, would need to be completely overhauled to add an entirely new “reservoir” structure—where no structure currently exists. *Id.* ¶140. And the multi-channel heating structure would need to be reconfigured to deliver a cross-channel pulse to that new reservoir instead of delivering a heated fluid into and down the transport channel. *Id.* The vacuum sources at the collection wells that draw the hydrodynamic flow into the collections wells would also need to be eliminated. *Id.* Such substantial reconstruction would not have been obvious without the benefit of the ’797 Patent.

In sum, Wada discloses neither the claimed “pressure pulse” that propagates across a channel nor the absorbing or dampening of that pressure pulse by a “reservoir.” Petitioner does not articulate any reason why a POSA would

reconfigure Wada to incorporate those features, and indeed POSAs had no such reason. Petitioner's picking-and-choosing of elements, attaching them to Wada's figures, and endowing them with the claimed functions is classic hindsight analysis.

**C. Ground 2 — Petitioner Fails to Show That Wada in View of Anderson Renders Obvious Claims 1, 2, 5, 13, 16, 18, and 19**

Petitioner fails to show a reasonable likelihood of success as to Ground 2 because it fails to show why and how Wada and Anderson would be combined to achieve the claimed inventions. In particular, Anderson fails to disclose the limitations missing from Wada as explained in Part VIII.B—which is hereby incorporated by reference—and Petitioner also fails to explain why the two references would be combined in the first place. Moreover, because independent claims 1 and 5 are not anticipated or rendered obvious, whether Anderson provides evidence of limitations added in the dependent claims is of no moment.

**1. *Petitioner fails to show that Wada and Anderson disclose the claimed “pressure pulse” and “first reservoir” (all challenged claims)***

As explained in Part VIII.B, Wada fails to disclose the claimed “pressure pulse” or “first reservoir” that dampens or absorbs it. Anderson also fails to disclose any component that can deliver, dampen, or absorb the claimed pressure pulse. The actuators and pumps in Anderson are “micropumps” that apply *constant* pressure—not pulses—to flow a sample through a transport channel.

EX2001 ¶¶144–46, 162; *see* Part VII.C. Anderson actually teaches away from using its pumps to “propagate[]” a “pressure pulse” because the goal of microfluidic supply pumps is to provide a smooth, constant flow—not to pulsate. *Id.* Similarly, because Anderson’s pumps *deliver* flow, they do not “dampen or absorb” anything—and thus suffer from the same deficiency as Wada’s side channels. EX2001 ¶¶79–86, 146.

To the extent Petitioner is arguing that Anderson’s non-pulsating pumps *would* achieve the claimed functions—e.g., propagating and dampening or absorbing a pressure pulse to “sort one or more particles”—*if* they were somehow attached to Wada’s side channels, that would be improper “hindsight” reconstruction of the claims. *NTP*, 654 F.3d at 1299. Petitioner identifies nothing in Anderson that suggests its pumps were “reservoirs” that performed (or were suitable for) the claimed sorting functions. It simply improperly endows Anderson’s pumps with those functions based on the teachings of the ’797 Patent.

**2. *Petitioner fails to show that a POSA had reason to combine Wada and Anderson to achieve the claimed invention (all challenged claims)***

Petitioner fails to provide *any* reason to combine Wada and Anderson, much less to achieve the claimed invention. Petitioner’s “rationale to combine” argument hinges on two lines from Wada stating that “[e]xamples of microfabricated pumps have been widely described in the art. *See, e.g.,* published

[I]nternational Application No. WO 97/02357.” Pet. 48–50 (citing EX1006 at 43:13–14). To be sure, the Application cited in Wada is the “Anderson” reference, but what Petitioner fails to explain is that Anderson’s “microfabricated pumps” are not for sorting (or generating cross-channel pulses) but for establishing a continuous (longitudinal) flow through the transport channel. The paragraph citing Anderson—which is completely outside of Wada’s sorting disclosure in a section titled “Assay Devices”—makes that clear. Although Petitioner cites only the final two lines, the remainder of the paragraph solely describes applying pressure or a vacuum at the end(s) of a main transport channel specifically for “*forcing the cell suspension through the analysis channel.*” EX1006 at 42:31–43:9 (emphasis added); *see* EX2001 ¶144.

Wada’s citation to Anderson for the sole purpose of pumping fluids through a main transport channel is consistent with Anderson’s disclosure. As explained *supra* Part VII.C, Anderson is directed to pumping and transporting fluids and samples from chamber-to-chamber through a transport channel—it has nothing to do with generating, dampening, or absorbing cross-channel pressure pulses. EX2001 ¶146. Accordingly, POSAs would not find Wada’s citation to Anderson at all relevant to Wada’s (or any) sorting operation. EX2001 ¶¶79–86, 144–46.

Moreover, Petitioner fails to offer any reason why POSAs would need to look to references such as Anderson in the first place to accomplish sorting in light

of Wada's extensive disclosure on sorting. For example, Petitioner identifies no benefit to somehow incorporating Anderson's micropumps in place of the Joule heaters and electrokinetic components already described and cited in Wada to accomplish sorting. EX1006 at 17:10–24:12. Petitioner simply argues that “Anderson's microfabricated pumps were *capable of* generating pressure-based fluid flow” and would have been “*useful* as fluid pressure force modulator[s].” Pet. 50 (emphasis added). But Wada's techniques are already described as capable and useful for sorting. EX2001 ¶¶145, 150. Anderson's pumps were not needed. In any event, even if there were a reason to replace Wada's sorting components with the various pumping mechanisms in Anderson, such reason would be nullified because doing so in a way that achieves the claimed invention would necessarily require changing Wada's principle of operation. *See supra* Part VIII.B.3; EX2001 ¶151.

Finally, Petitioner cites a number of other passages from Wada (*see* Pet. 48–52) that likewise are either (1) directed at the main flow through a transport channel, or (2) address Wada's Joule heating and electrokinetic techniques and thus provide no reason to combine references. For example, Wada at 3:23–25 refers to “methods of providing substantially uniform flow velocity to particles flowing in [the] first microchannel,” which is the transport channel. And Wada at 6:30–7:29, 19:9–13, and 26:26–27:2 specifically address using heating elements or other



hydrodynamic flow-based techniques, which are completely different from the claimed invention. Indeed, as described *supra* Parts VII.A and VIII.BVIII.B.1, such sorting techniques do not rely on pressure variations at all. *See* EX2001 ¶¶160-61.

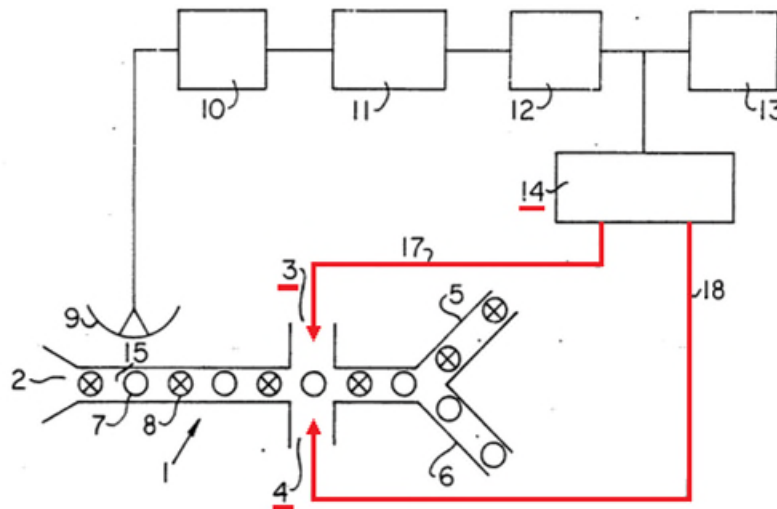
**D. Ground 3 — Petitioner Fails to Show That Marcus in View of Anderson Renders Obvious Claims 1, 2, 5, 13, 16, 18, and 19**

Marcus and Anderson fail to disclose the “pressure pulse” and “first reservoir” limitations recited in independent claims 1 and 5. Marcus’s very limited disclosure describes only dual-actuated control ports to sort particles, which *teaches away* from using the ports to dispatch a pressure pulse and as a “first reservoir” to dampen or absorb it. Anderson does not supply the missing limitations or reasons to combine because it discloses fluid supply pumps that only deliver a sample through a transport channel. Instead of providing a reason to modify or combine these references, Petitioner simply picks-and-chooses elements from the prior art, grafts them onto Marcus for no reason, and assigns functions to them based on the teachings of the ’797 Patent. Such hindsight analysis cannot demonstrate obviousness.

***1. Petitioner fails to show that Marcus and Anderson disclose the claimed “pressure pulse” (all challenged claims)***

Neither Marcus nor Anderson discloses the claimed “pressure pulse” that propagates across a channel as recited in claims 1 and 5. EX2001 ¶¶160–61.

Marcus provides no specifics on its “sorting apparatus,” explaining only that it is comprised of “conventional and commercially available components” and uses controller 14 to instruct “control ports 4 and 3” on how to sort particles, as depicted generically in Figure 1 (annotated):



*See* EX1005 at 3:9–12, 3:57–62; *supra* Part VII.B. Marcus provides no other details, and it certainly never describes employing a “pressure pulse” for sorting. EX2001 ¶¶152–59. Petitioner acknowledges this deficiency when it argues that “a POSA would have recognized the utility of using known actuators (e.g., thermopneumatic or piezoelectric micropumps) to generate a pressure pulse to sort individual particles.” Pet. 53.

But Anderson cannot supply that missing limitation because it fails to disclose anything that “propagate[es] a pressure pulse across [a] microfluidic flow channel” for sorting as claimed. Anderson cannot supply that missing limitation because it fails to disclose any component that “propagate[s]” a pressure pulse

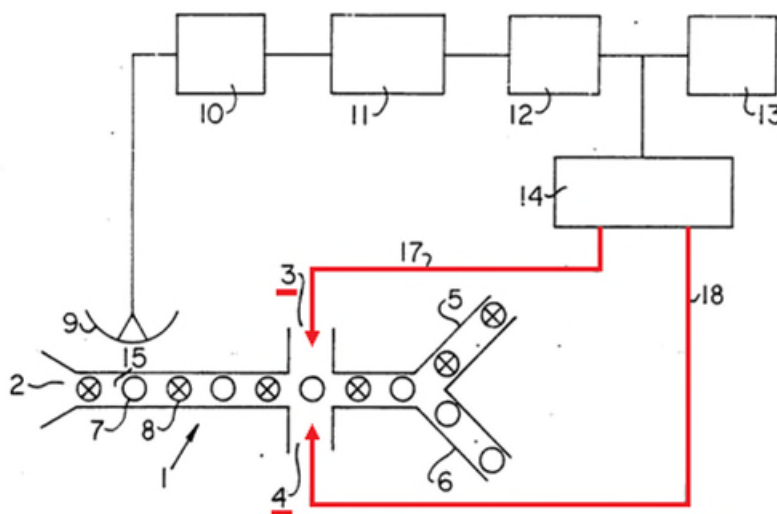
“across the flow channel.” As explained *supra* Part VIII.C.1, Anderson actually teaches away from using its pumps (cited at Pet. 59) to employ a “pressure pulse” because the goal of Anderson was to provide a smooth, constant flow with its pumps—*not* to pulsate. EX2001 ¶164. Indeed, Anderson never discusses using its pumps for *any* sorting application. EX2001 ¶¶ 79–86, , 160–64.

To the extent Petitioner is arguing that Anderson’s non-pulsing pumps *would* “propagate[e] a pressure pulse across the microfluidic flow channel in a crosswise direction” to “sort or one more particles suspended in a sample” *if* the pumps were somehow attached to Marcus’s control ports, that would be hindsight reconstruction of the claims. Petitioner identifies nothing in Anderson that suggests its pumps performed (or were suitable for) those claimed functions and is simply endowing Anderson’s pumps with those functions based on the teachings of the ’797 Patent. *See NTP*, 654 F.3d at 1299.

Furthermore, Petitioner attempts to buttress its arguments by incorporating-by-reference background art and Dr. Weigl’s conclusory observations on them. *See* Pet. 54. For the reasons provided *supra* Part VIII.B.1.a), the references should not be considered at all, and they fail to disclose or render obvious the claimed “pressure pulse.”

2. *Petitioner fails to show that Marcus and Anderson disclose the claimed “first reservoir” that dampens or absorbs the “pressure pulse” (all challenged claims)*

Because neither Marcus nor Anderson discloses a “pressure pulse” as claimed, there is no “reservoir” for dampening or absorbing it. Marcus in fact teaches away from using a reservoir to dampen or absorb a cross-channel pressure pulse by explaining that *both* control ports 3 and 4 are actuated by “decision device 12 which signals a fluidic controller device 14 to *instruct control ports A and B, 4 and 3 respectively, to separate out said particles 7 and 8.*” EX1005 at 3:57–61 (emphasis added). This actuation of both control ports is illustrated clearly in Figure 1:



EX1005, Fig. 1 (annotated); EX2001 ¶¶152, 165–66.

Petitioner acknowledges that both control ports in Marcus are “trigger[ed]” (Pet. 57–58) but makes the same deficient argument it makes for Wada, namely that one of the two opposed control ports must dampen or absorb the pressure

pulse simply because a control port is “disposed opposite the actuated” port (*see* Pet. 60). In other words, Petitioner’s argument is based solely on the control ports’ “symmetrical geometry”—the ability to dampen or absorb is assumed. But the mere fact that two control ports are opposite one another does not mean one of them “dampen[s] or absorb[s]” fluid or pressure. EX2001 ¶167; *supra* Part VIII.B.2. Anderson does not address this deficiency in Marcus, as Anderson’s pumps only supply fluid flow—they do not dampen or absorb anything. EX2001 ¶¶81–83, 170. Petitioner once again endows structures with the claimed functions based on hindsight.

Petitioner acknowledges that Marcus and Anderson fail to disclose the claimed “first reservoir” when it again improperly string-cites “background” references and Dr. Weigl’s assertions that a dampening or absorbing reservoir was “well-reported.” *See* Pet. 62. For the reasons provided *supra* Part VIII.B.2.a), those references and Dr. Weigl’s assertions should not be considered at all, and they fail to disclose or render obvious the claimed “first reservoir.”

**3. *Petitioner fails to show that a POSA had reason to combine Marcus and Anderson to achieve the claimed invention***

Even if the Board finds that Petitioner adequately identified the claimed “pressure pulse” or “first reservoir” in Marcus and Anderson, Petitioner’s “rationale to combine” argument (Pet. 53–54) would be deficient because it is not backed by any evidence. *See* 35 U.S.C. §312(a)(3); *PAR Pharm.*, 773 F.3d at 1193.

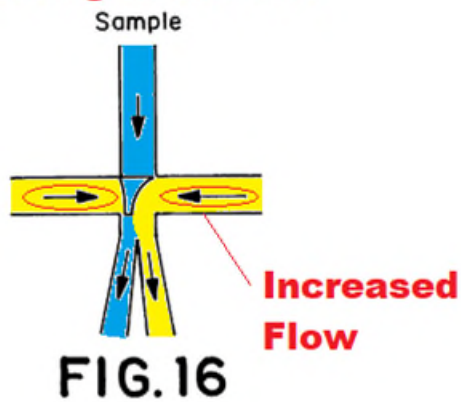
Petitioner merely refers to Marcus’s statement that it uses “conventional” components (Pet. 53–64.)—conspicuously omitting that Marcus also states the components were “commercially available” (EX1005 at 3:9–11). Petitioner offers *no* evidence that the components were indeed “conventional and commercially available.”

In any event, there was no reason to combine components from the prior art and arrange them as claimed. Marcus’s generic “control ports” are not described as having any particular structure or function, other than they somehow cause the particles to be sorted into the respective collection wells. EX1005 at 3:57–61; EX2001 ¶168. In particular, they are not described as cooperating with each other at all, much less to propagate and absorb or dampen a “pressure pulse,” as the claimed reservoirs are required to do. Accordingly, POSAs would not have looked to prior art such as Anderson for a component to perform the claimed “pressure pulse” and the “reservoir” for dampening or absorbing it because Marcus provides no reason for POSAs to seek such cooperative components. EX2001 ¶¶168–69. Indeed, as explained above, Marcus’s dual-actuating apparatus would *teach away* from doing so. *Id.* Anderson likewise fails to provide any such reason because, with respect to the actuators and pumps relied on by Petitioner, Anderson is geared solely toward fluid delivery through a transport channel, not sorting or propagating a pressure pulse, as explained *supra* Parts VII.B, VIII.D.1. *See also* EX2001 ¶170.

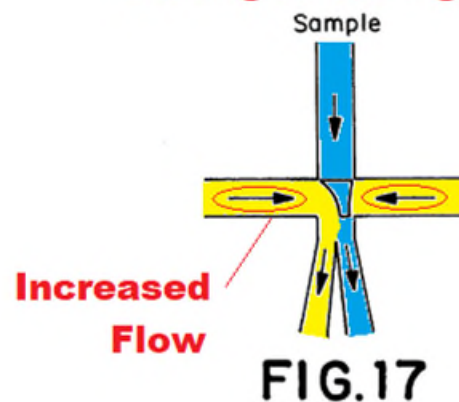
Tacitly acknowledging the lack of any reason within the asserted references to employ a “pressure pulse” and “first reservoir” in Marcus to yield the claimed invention, Petitioner argues that POSAs would have, on their own, “recognized how to implement conventional fluidic sorting components to achieve the functionality described in Marcus” and “would have recognized the utility of using known actuators . . . to generate a pressure pulse to sort individual particles.” Pet. at 53. The only “functionality described in Marcus,” however, is “sorting.” Marcus says nothing about generating a pressure pulse to sort particles, or about dampening or absorbing such a pressure pulse with a reservoir. Petitioner necessarily endows a POSA with the knowledge that the objective is to perform those claimed functions. A proper obviousness analysis requires POSAs to seek suitable components from other prior art *without* that knowledge.

Here, POSAs without knowledge of the invention would have most naturally looked to the flow-based devices like Ramsey for suitable mechanisms for Marcus’s “control ports.” EX2001 ¶171. Marcus’s dual-actuating opposed control ports are similar in appearance and function to Ramsey’s technique, wherein *both* side channels introduce fluid, with one channel’s flow increased to accomplish sorting:

**Sorting to the left**



**Sorting to the right**



EX2001 ¶¶71–75, 171; EX2014, Figs. 16, 17 (annotated), 7:24–50. Additionally, as Dr. Arnold explains, such techniques were indeed conventional at the time of the invention. *Id.* (citing EX1018).

In sum, Marcus and Anderson fail to disclose the claimed actuator, pressure pulse, and “first reservoir.” Petitioner does not specify *why* a POSA would incorporate such components into Marcus, and POSAs had no such reason. Petitioner’s picking-and-choosing of elements and their functions is an improper hindsight analysis.

## **IX. CONCLUSION**

Institution should be denied for the above reasons.



Dated: June 4, 2020

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**CERTIFICATE OF SERVICE**

The undersigned hereby certifies that a copy of the foregoing Cytonome/ST, LLC's Preliminary Response was served on counsel of record on June 4, 2020 by filing this document through the End-to-End System, as well as delivering a copy via electronic mail to counsel of record for the Petitioner at the following addresses:

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**CERTIFICATE OF COMPLIANCE PURSUANT TO 37 C.F.R. §42.24**

This paper complies with the type-volume limitation of 37 C.F.R. § 42.24.  
The paper contains 13,809 words, excluding the parts of the paper exempted by  
§42.24(a).

This paper also complies with the typeface requirements of 37 C.F.R.  
§ 42.6(a)(ii) and the type style requirements of § 42.6(a)(iii)&(iv).

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