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Paper 32
Entered: April 21, 2016

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BIO-RAD LABORATORIES, INC.,
Petitioner,

v.

CALIFORNIA INSTITUTE OF TECHNOLOGY and
FLUIDIGM CORPORATION,
Patent Owner.

Case IPR2015-00009
Patent 7,294,503 B2

Before GRACE KARAFFA OBERMANN, DONNA M. PRAISS, and KRISTINA M. KALAN, *Administrative Patent Judges.*

PRAISS, *Administrative Patent Judge.*

FINAL WRITTEN DECISION
35 U.S.C. § 318(a) and 37 C.F.R. § 42.73

Bio-Rad Laboratories, Inc. ("Petitioner") filed a Petition to institute an *inter partes* review of claims 1, 2, 5–15, 18, 19, 30–35, 39–43, 46, 47, and 49–51 of U.S. Patent No. 7,294,503 B2 (Ex. 1001, "the '503 patent") pursuant to 35 U.S.C. §§ 311–319, relying on the Declaration of Dr. Shelley Anna (Ex. 1002, the "Anna Declaration"). Paper 1 ("Pet."). The Board granted the Petition and instituted trial for claims 1, 2, 5–11, 18, 19, 30, 31, 46, 47, and 49–51. Paper 16 ("Dec. on Inst."). Trial was instituted on the following grounds:

(1) Claims 1, 2, 5–11, 18, 19, 30, 31, 46, 47, and 49–51 as obvious over Stewart II[1] and Burns;[2]

(2) Claims 49 and 51 as obvious over Stewart II, Burns, and Kobayashi;[3] and

(3) Claims 18, 19, 46, and 47 as obvious over Stewart II, Burns, and Chou.[4]

During trial, Patent Owner, California Institute of Technology and its exclusive licensee Fluidigm Corporation (collectively, "Patent Owner"), filed a Patent Owner Response relying on the Declaration of Dr. Todd Squires (Ex. 2019, the "Squires Declaration"). Paper 21 ("PO Resp."). Petitioner filed a Reply to Patent Owner's Response. Paper 23 ("Pet.

[1] WO 84/02000, published May 24, 1984 (Ex. 1004).
[2] WO 98/22625, published May 28, 1998 (Ex. 1005).
[3] Kobayashi, et al., *Production and Characterization of Monodispersed Oil-in-Water Microspheres Using Microchannels*, Food Sci. Technol. Res. 5(4), 350–55 (1999) (Ex. 1012).
[4] Chou, et al., *Microfabricated Devices for Sizing DNA and Sorting Cells*, Proceedings of the SPIE, Vol. 3258, 181–87 (1998) (Ex. 1006).

Reply"). An unopposed Motion to Seal Exhibits 2003–2008 was filed by Fluidigm Corporation. Paper 11.

A consolidated oral hearing was held on January 5, 2016, with concurrently-filed *inter partes* review proceeding IPR2015-00010 involving U.S. Patent No. 8,252,539, which issued from a continuation of the '503 patent. A transcript of the hearing is included in the record. Paper 30 ("Tr.").

We have jurisdiction under 35 U.S.C. § 6(c). This final written decision is issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73.

For the reasons that follow, we determine that Petitioner has met its burden to prove by a preponderance of the evidence that claims 1, 2, 5–15, 18, 19, 30–35, 39–43, 46, 47, and 49–51 of the '503 patent are unpatentable.

I. BACKGROUND

A. The '503 Patent (Ex. 1001)

The '503 patent, titled "Microfabricated Crossflow Devices and Methods," is directed to a microfluidic device for analyzing and/or sorting biological materials. Ex. 1001, Abstr. The device comprises a main channel, through which a fluid incompatible with the biological material flows, an inlet region in communication with the main channel, and a droplet extrusion region, through which droplets of solution containing the biological material are deposited into the main channel. *Id*. The droplet extrusion region is "a junction between an inlet region and the main channel" that "permits the introduction of a pressurized fluid to the main channel at an angle perpendicular to the flow of fluid in the main channel." *Id*. at 13:28–32. Figures 16A and 16B are reproduced below.

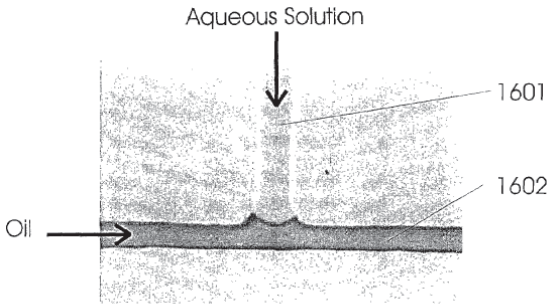

FIG. 16A

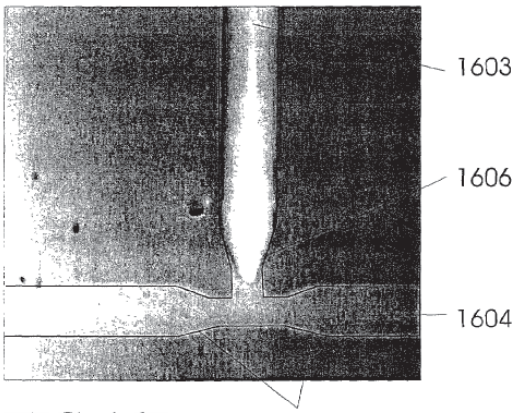

FIG. 16B

Figures 16A and 16B are exemplary architectures for droplet extrusion regions in the microfabricated device. *Id*. at 7:60–61. The channels are microfabricated, such as by etching a silicon chip. *Id*. at 17:29–33. Channels that are rounded and have a diameter between about 2 and 100 microns are preferred for particles or molecules that are in droplets within the main channel flow. *Id*. at 18:25–31. At these dimensions, the droplets "tend to conform to the size and shape of the channels, while maintaining their respective volumes." *Id*. at 18:41–43. "[T]he size and frequency of droplets formed in a main channel of such devices may be precisely controlled by modifying the relative pressure of the incompatible fluids (e.g., water and oil) in the device." *Id*. at 55:62–66. Modifying the relative pressures produces water droplets in the oil stream "such that the water enter[s] the droplet extrusion region, shearing off into discrete droplets." *Id.* at 56:52–56.

B. Illustrative Claim

Claims 1, 46, 49, and 50 are the independent claims at issue. Claim 1 is illustrative:

> 1. A microfluidic product comprising:
>
> (a) a main channel with a diameter of between about 2 and 100 microns or cross-sectional dimensions in the range of 1 to 100 microns in fluidic communication with a source of extrusion fluid passing therethrough;
>
> (b) a second microfluidic channel, wherein said channel has a diameter in the range of 2 to 100 microns or cross-sectional dimensions in the range of 1 to 100 microns and is in fluidic communication with a source of sample fluid, and said sample fluid is immiscible with the extrusion fluid; and
>
> (c) said second microfluidic channel having at least one inlet region in communication with the main channel in a droplet extrusion region, the inlet region having a particle containing sample fluid immiscible with the extrusion fluid passing therethrough and constructed and arranged so that droplets of the sample fluid are sheared into the main channel at the extrusion region resulting in discrete sample fluid droplets containing particles in the extrusion fluid stream.

Ex. 1001, 62:19–38. Claim 46 recites "a source of particle containing sample fluid" and "the main channel resides in a layer of elastomeric material." *Id*. at 64:56–57, 64:63–64. Claim 49 recites "wherein when the extrusion fluid is flowed through the first channel at a first pressure and the sample fluid is flowed through the second channel at a second pressure lower than the first pressure, monodisperse droplets of aqueous solution are formed at the junction." *Id*. at 66:1–5. Claim 50 recites "an output channel in communication with the junction." *Id*. at 66:16.

C. Claim Interpretation

In an *inter partes* review, claim terms in an unexpired patent are interpreted according to their "broadest reasonable construction in light of the specification of the patent in which [they] appear[]." 37 C.F.R.

§ 42.100(b). Under that standard, claim terms are given their ordinary and customary meaning, as would be understood by one of ordinary skill in the art in the context of the entire disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Also, care is exercised to avoid reading a particular embodiment appearing in the written description into the claim if the claim language is broader than the embodiment. *See In re Van Geuns*, 988 F.2d 1181, 1184 (Fed. Cir. 1993) ("limitations are not to be read into the claims from the specification").

In our Decision on Institution, we interpreted two claim terms of the '503 patent as shown below:

Table 1

Term	Construction
sheared	severed or broken off
monodisperse sample fluid droplets	dispersed droplets of sample fluid of substantially uniform size

Dec. on Inst. 6–7. The parties do not challenge our claim constructions. Consequently, for purposes of this Final Written Decision, we adopt the constructions as stated in Table 1 in accordance with the analysis set forth in our Decision on Institution. *Id*.

II. ANALYSIS

We turn now to the patentability of the claims. To prevail in its challenges to the patentability of the claims, Petitioner must establish facts supporting its challenges by a preponderance of the evidence. 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d). As noted above, there are three grounds of unpatentability under 35 U.S.C. § 103(a) involved in this *inter partes* review

proceeding: (1) claims 1, 2, 5–11, 18, 19, 30, 31, 46, 47, and 49–51 as obvious over Stewart II and Burns; (2) claims 49 and 51 as obvious over Stewart II, Burns, and Kobayashi; and (3) claims 18, 19, 46, and 47 as obvious over Stewart II, Burns, and Chou.

We consider the respective positions of the parties in light of the record before us.

A. Principles of Law

A claim is unpatentable under § 103(a) if the differences between the claimed subject matter and the prior art are such that the subject matter, as a whole, would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations, including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of skill in the art; and (4) where in evidence, so-called secondary conditions. *See Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966). We also recognize that prior art references must be "considered together with the knowledge of one of ordinary skill in the pertinent art." *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994) (citing *In re Samour*, 571 F.2d 559, 562 (CCPA 1978)).

B. Level of Skill in the Art

In determining the level of skill in the art, various factors may be considered, including "type of problems encountered in the art; prior art solutions to those problems; rapidity with which innovations are made;

sophistication of the technology; and educational level of active workers in the field." *In re GPAC, Inc*., 57 F.3d 1573, 1579 (Fed. Cir. 1995) (citing *Custom Accessories, Inc. v. Jeffrey-Allan Indus., Inc.*, 807 F.2d 955, 962 (Fed. Cir. 1986)). There is evidence in the record before us that reflects the knowledge level of a person with ordinary skill in the art. Petitioner's Declarant, Dr. Anna, attests that a person with ordinary skill in the art would "hav[e] at least the equivalent of a Bachelor's degree in engineering, physics, or chemistry and two years of academic, research, or industry experience related to fluid mechanics, fluid dynamics, or microfluidics." Ex. 1002 ¶ 29. Patent Owner does not dispute Dr. Anna's assessment of the level of ordinary skill. PO Resp. 3. Thus, we adopt Petitioner's Declarant's attestation as to the level of skill in the art.

C. Overview of Stewart II

Stewart II describes a method and apparatus "particularly suited to the manipulation of microscopic quantities of reactant with volumes of less than 10 nanolitres . . . ." Ex. 1004, 3. The reactants used in the system "can be liquids" which "will be supported, defined and moved by another, immiscible liquid, referred to hereafter as the carrier phase." *Id*. at 4. Figure 1, below, depicts two conduits for carrying out the method of producing droplets of reactants as taught by Stewart II.

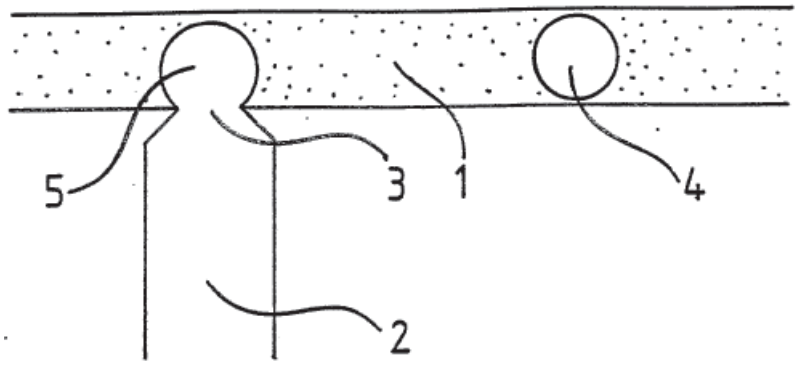

Figure 1.

Figure 1 illustrates one method of separating droplets of a predetermined volume from a larger reservoir of reactant. *Id.* The stippled areas indicate carrier phase (1) in one of the conduits. *Id.* at 2. The droplet volume shown as (5) is pushed or sucked out of small opening (3) before separation of the reactant from the side arm (2) into the carrier phase. A flow of carrier phase separates the droplet and carries it down the conduit. *Id*. at 4. The dimensions of the conduits are described by Stewart II as follows: "All conduits should have diameters approximately the same as the droplets to be used in them." *Id*. at 5. The apparatus may be constructed by etching, molding, or machining "indentations or channels of the appropriate configuration in the surface of a plate, and [clamping or holding] this plate against another, producing closed ducts or conduits." *Id*. at 7. Suggested materials for the plate include glass, Teflon, metal, polyvinylchloride, and polypropylene with one of the plates being preferably transparent to allow "visual inspection of the procedures." *Id*.

Stewart II discloses three methods for determining the volume of the droplet produced. *Id*. at 4–5. The second method, quoted below, uses two currents to generate droplets of reactant in the apparatus described above:

> If large numbers of droplets are required, a continuous flow of carrier phase flows down the conduit. When reactant is simultaneously passed through the opening 3 a series of droplets will be formed, each broken off just before it spans the conduit. The exact size of the droplets thus produced will depend on the magnitudes of the two currents.

Id. at 4–5. The droplets may contain micro-organisms. *Id*. at 7.

D. Overview of Burns

Burns relates to microfabricated substrates and methods for amplifying and detecting nucleic acids. Ex. 1005, Abstract. Micromachined structures for use with nanoliter volumes, called "microdevices," are preferred. *Id*. at 5:4–5. Materials such as silicon, quartz, and glass are preferred because they can be manipulated to define channels, such as by etching. *Id*. at 6:23–28. One or more channels in the substrate connect the components, are preferably in liquid communication, and the channels configured in microns accommodate "microdroplets." *Id.* at 7:9–14. Illustrative size ranges for the channels are 0.5 to 50 μm in depth and 20 to 1000 μm in width and, for the microdroplets, are "approximately 0.01 and 100 nanoliters (more typically between ten and fifty)." *Id*. at 7:15–19. Figure 3B, below, is an embodiment of the device.

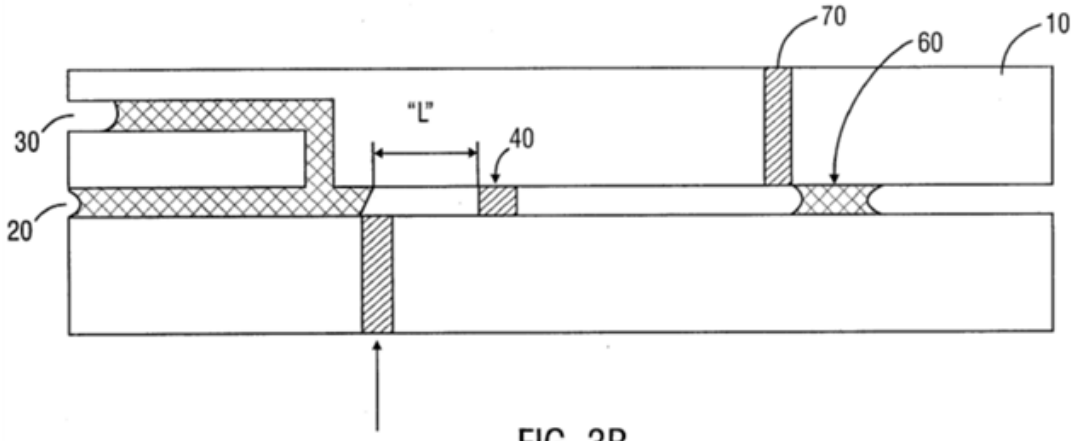

FIG. 3B

Figure 3B shows "a schematic of . . . a device (10) to split a nanoliter-volume liquid sample and move it using external air." *Id*. at 50:17–18. Gas is injected (lower arrow) "to split a microdroplet of length 'L'." *Id*. at 50:24–27. "[L]iquid . . . placed at the inlet (20) is drawn in by surface forces." *Id*. at 50:17–29. "[O]verflow ports (30) may be blocked or may be loaded with excess water to increase the resistance to flow." *Id*. at 50:28–29. "[A] hydrophobic gas vent (70) further down the channel . . . can stop the liquid microdroplet (60) after moving beyond the vent (70)." *Id*. at 51:1–3.

E. Obviousness over Stewart II and Burns Independent Claims 1, 46, 49, 51

Claim 1 recites "a main channel with a diameter of between about 2 and 100 microns or cross-sectional dimensions in the range of 1 to 100 microns." Ex. 1001, 62:20–22. Claim 1 also recites "a second microfluidic channel" with the same dimensions. *Id.* at 62:24–27. Petitioner argues that the claimed dimensions for the microfluidic product's channels are not patentably distinct from Stewart II's device because the claimed device would not perform differently from the prior art device. Pet. at 19–20 (citing *Gardner v. TEC Syst., Inc.*, 725 F.2d 1338 (Fed. Cir. 1984)). Petitioner provides the Anna Declaration as support for its contention that the forces governing the behavior of fluid in a channel with Stewart II's calculated dimension of 267 microns in diameter are the same as those governing the behavior of a fluid "in an otherwise similar channel with a diameter of 100 microns." *Id*. at 20; Ex. 1002 ¶¶ 49–50. The basis for Dr. Anna's opinion is that the relative magnitudes of the capillary forces, viscous forces, and

inertia governing droplet formation or breakup are similar in sub-millimeter devices. Ex. 1002 ¶ 50.

Petitioner also asserts that "these particular dimensions are obvious in light of Burns." Pet. 19. According to Petitioner, "Burns specifically recites that 'illustrative ranges for channels [for microfluidic devices] may be between 0.5 and 50/μm in depth (preferably between 5 and 20 μm) and between 20 and 1000/μm in width (preferably 500/μm).'" *Id*. at 20 (citing Ex. 1005, 7:16–19). Petitioner's rationale for combining Stewart II and Burns is based on the teaching in Stewart II to use channel sizes less than 10 nanoliters in volume, which Dr. Anna calculates to be a 267 micron diameter. *Id*. at 8 (citing Ex. 1002 ¶¶ 41–42), 20. As discussed above, Petitioner argues that "the forces governing the behavior of fluid in a channel with a diameter of 267 microns, as disclosed in Stewart II, would be the same as those governing the behavior of fluid in an otherwise similar channel with a diameter of 100 microns." *Id*. at 20 (citing Ex. 1002 ¶¶ 49–50). Therefore, one of ordinary skill in the art, in determining an appropriate channel size for the Stewart II device, would have included the channel dimensions described by Burns and would have understood the use of channel sizes in the range of 1–100 microns both (1) was technically possible and (2) could have been predictably and effectively used in a droplet-creating device as taught by Stewart II. *Id*. at 20–21.

Claim 1 further requires that the second microfluidic channel have "at least one inlet region in communication with the main channel" and that the inlet region be "constructed and arranged so that droplets of the sample fluid are sheared into the main channel". Ex. 1001, 62:30–36. Petitioner asserts that Stewart II discloses "a droplet-creating device" in which channel sizes

of 1–100 microns could be effectively and predictably used in view of Burns. Pet. 21 (citing Ex. 1002 ¶ 66).

Petitioner also asserts that Burns and Stewart II disclose properties of the fluids recited in claims 1 (particle containing sample fluid), 46 (particle containing sample fluid), 49 (first pressure and second pressure), and 51 (first pressure and second pressure), even though these limitations should not be given patentable weight. *Id*. at 22–25. Likewise, Petitioner argues that the "monodisperse droplets" recited in claims 49 and 51 are merely properties of the sample and extrusion fluids, but, nevertheless, obvious from the teaching in Stewart II that large numbers of droplets can be formed from passing reactant into a continuous flow of carrier, that the conduits have diameters approximately the same as the droplets to be used in them, and that optimization to produce monodisperse droplets with regular periodicity in Stewart II's device would have been within the level of ordinary skill in the art. *Id*. at 26 (citing Ex. 1004, 5; Ex. 1002 ¶¶ 34, 76–79). According to Dr. Anna, one of ordinary skill in the art would have known how to optimize Stewart II's device by varying the pressures of the carrier phase and reactant to form monodisperse droplets. Ex. 1002 ¶¶ 77–78 (providing Kawakatsu[5] (Ex. 1011) and Kobayashi (Ex. 1012) as examples of monodisperse droplets being achieved by optimizing devices without undue experimentation).

Petitioner also argues that the recitations in claims 49 and 51 of "a diameter less than 60 microns" for the droplet size are merely properties of

[5] Kawakatsu *et al*., *Effect of Microchannel Structure on Droplet Size During Crossflow Microchannel Emulsification*, J. Surfactants and Detergents, Vol. 3, No. 3 (July 2000).

the fluids, which nevertheless would have been obvious over Stewart II's teaching of droplet diameters in view of Burns's teaching of microdevice diameters. *See id*. at 27–28. The additional requirement of claim 46 that the main channel reside in a layer of elastomeric material would have been an obvious substitution of materials in view of Stewart II's disclosure of channels residing in a polymer block that is adjacent to one or more substrates, according to Petitioner. *Id*. at 32 (citing Ex. 1004, 7, 8; Ex. 1002 ¶¶ 83–85).

Patent Owner contends that the Anna Declaration should be given little weight because Dr. Anna has taken inconsistent positions and her explanations are not credible. PO Resp. 4–9. Dr. Anna testified at deposition that "Thorsen [a named inventor on the '503 patent and author of a 2001 article (Ex. 2017)] was the first to publish generating droplets at a microfluidic T-junction." PO Resp. 6–8 (citing Ex. 2018, 62:8–63:21). According to Patent Owner, Dr. Anna's deposition testimony is consistent with statements attributed to her in a 2007 journal article (Ex. 2016), that Patent Owner quotes as follows:

> 3.2 Droplet breakup in cross-flowing streams
>
> One of the most common microfluidic methods of generating droplets uses cross-flowing continuous and dispersed phase streams. In microfluidics, this is typically implemented using T-shaped microchannel junctions, depicted schematically in figure 1(b). Droplet formation in a T-shaped device was first reported by Thorsen et al [53], who used pressure controlled flow in microchannels 35μm wide and 6.5μm deep to generate droplets of water in a variety of different oils.

Id. at 5 (quoting Ex. 2016, R322). Patent Owner contends the statements in the article "were made well after the work of Stewart and Burns had published" and independent of this proceeding, but are inconsistent with her

positions regarding Stewart II, Burns, and the ’503 patent in this proceeding. *Id*. at 5–6.

Patent Owner contends that Dr. Anna’s explanation that Stewart II “would not have been considered part of the popular microfluidics field that we think of that I was referring to in this review article” is inconsistent with her declaration statement that “Stewart II falls squarely within the definition of microfluidics.” *Id.* at 7–8 (quoting Ex. 2018, 62:8–63:21, citing Ex. 1002 ¶ 42). Patent Owner also contends that the 2007 article contains no qualifiers to support Dr. Anna’s testimony that the article pertained to a particular time period. *Id*. at 8.

Patent Owner further contends that Dr. Anna’s Declaration should be given little weight because she “was unable to answer basic questions about the understanding a person of ordinary skill in the art would have regarding the disclosure of the prior art.” *Id*. at 9–10. Patent Owner specifically asserts a “lack of ability to answer question[s] on how . . . a reduction in channel [size] would affect the operation of the Stewart II device” and on the “cost of materials as those relate to the materials disclosed in Stewart II.” *Id*. at 11. Patent Owner further asserts that “Dr. Anna was asked if Kobayashi forms droplets using a cross-flow” and was unable to answer the question other than by reading from her declaration statement. *Id*. at 12–13.

Patent Owner also asserts that the combination of Burns with Stewart II is improper because (1) Burns teaches away from Stewart II and (2) the combination is unpredictable and lacks a reasonable chance of success. *Id*. at 28–42. Patent Owner argues that “having the ‘microdroplet’ remain in contact with the channel walls is expressly discouraged by Stewart II” because Stewart II maintains a film of the continuous phase around the

reactant to reduce or eliminate contamination of the reactant while Burns's channels contact the dispersed phase and, therefore, are incompatible with forming a spherical droplet. Patent Owner also argues that the smaller dimensions of Burns's channels "would increase the possibility of an obstruction, protrusion, or imperfection on the wall from contacting the dispersed phase." *Id*. at 28–31, 37 (citing Ex. 2019 ¶¶ 39–42).

Regarding predictability, Patent Owner contends that has not been demonstrated because Dr. Anna's declaration states that the teachings of the references are compatible with each other, not that their combination yields a predictable result. *Id*. at 32–33. Additionally, Dr. Anna's deposition testimony regarding needing more factors in order to predict how changing one variable would affect Stewart II's system evidences unpredictability, according to Patent Owner. *Id*. at 33 (citing Ex. 2018, 110:12–13, 111:17–19, 112:10–12, 114:3–8). Patent Owner asserts that "the factors involved in droplet formation are numerous and complex," would not have been known well enough to predictably be manipulated at the time of the invention of the '503 patent, and the prior art does not "provide[] guidance on what combinations would succeed." *Id*. at 33–36 (citing Ex. 2019 ¶¶ 23–27, 29, 30, 37, 38). Patent Owner also asserts that "implausible and inconsistent statements within Stewart II" would "cause skepticism" about successful droplet formation and evidence unreliability of the Stewart II disclosure. *Id.* at 38–40. Specifically, Patent Owner asserts that Stewart II's claim that the T-junction can generate droplets at volumes from more than 1 liter to less than 10 nL is "impossible under any reasonable operating parameters." *Id*. at 38 (citing Ex. 2019 ¶ 35). Patent Owner also asserts that Stewart II's disclosure of generating a large amount of droplets using a continuous flow

of carrier phase is inconsistent with both the statement that "the present invention does not operate a continuous stream" and Stewart II's method of combining droplets for chemical reactions "using a sequence of distinct and discrete steps." *Id*. at 38–39 (citing Ex. 2019 ¶¶ 47–48). Patent Owner further argues that the second channel or side arm of Stewart II would not necessarily have the same dimension as the main channel because the side arm does not also contain droplets. *Id*. at 45–47.

Patent Owner presents generally the same arguments regarding the patentability of independent claims 1, 46, 49, and 51, but presents additional arguments directed to the elastomeric material required by claim 46 and the monodispersity required by claims 49 and 51. Patent Owner contends that "the Petition does not provide any rationale [] why one of ordinary skill in the art would use an elastomer in light of the teachings of Stewart II alone. Nor does the Petition allege that Burns cures this deficiency." *Id*. at 50. Patent Owner also contends that "there is a structural element in the claims that must be constructed to form monodisperse droplets having a diameter of less than 60 microns" as specified in claim 51. *Id*. at 53. Patent Owner asserts that this is not disclosed in Stewart II and that Dr. Anna's assertion that monodispersity can be achieved in a microfluidic channel by optimizing pressure is not supported by Kobayashi. *Id.* at 54–57.

Dependent Claims 2, 5–11, 18, 19, 30, 31, 47, and 50

Claims 2, 5, and 7 depend from claim 1 and require that the extrusion fluid is a non-polar solvent, the sample solution is aqueous, and the particles are biological material, respectively. Ex. 1001, 62:30–40, 62:46–47, 62:51–52. Claim 6 further defines the aqueous solution of claim 5. *Id*. at 62:48–

50. Claims 8–11 further define the biological material of claim 7. *Id*. at 62:53–63. Claims 30 and 31 depend from claim 1 and further define the extrusion fluid in terms of its refractive index. *Id*. at 63:49–53. Petitioner argues that the dependent claims are obvious over Stewart II and Burns because the fluids and properties of the fluids do not distinguish the claimed apparatus patentably over the prior art. Pet. 28, 30 (citing *id*. at 8–9). Nevertheless, Petitioner argues that the use of a TE buffer (Tris-HCl and EDTA) in a sample solution and the modification of the sample concentration as taught by Burns makes obvious the buffer composition of claim 6, and the selection of a viral particle as the biological material meets the requirements of claims 8, 9, and 11. *Id*. at 28–31.

Regarding the elastomeric material recited in claims 18, 19, and 47, as discussed with respect to claim 46 above, Petitioner argues the limitations would be an obvious substitution of materials in view of Stewart II's disclosure of channels residing in a polymer block that is adjacent to one or more substrates. *Id*. at 32 (citing Ex. 1004, 7, 8; Ex. 1002 ¶¶ 83–85).

Patent Owner does not separately argue the patentability of dependent claims 2, 5–11, 30, and 31. Regarding the elastomeric material of claims 18, 19, and 47, Patent Owner argues that the Petition lacks a rationale for the substitution, and that the deficiency of Stewart II is not cured by Burns. PO Resp. 50.

Discussion

At the outset, we note that Patent Owner contends that the testimony of Dr. Anna should be given little weight, but does not seek to exclude the Anna Declaration. Patent Owner does not challenge Dr. Anna's

qualifications as an expert in the field of microfluidics. Tr. 28:16–18. Instead, Patent Owner argues that the credibility of her statements regarding Stewart II is diminished by her cross-examination at deposition on the subject of (a) her paper, independent of this proceeding, that acknowledges the Thorsen 2001 Article and (b) hypotheticals concerning the Stewart II device presented at deposition. PO Resp. 4–14.

Patent Owner essentially contends that Dr. Anna's deposition and declaration statements in this proceeding concerning Stewart II are inconsistent with statements in her earlier publication indicating that the named inventors on the '503 patent were the first to report droplet formation in a T-shaped device. Dr. Anna explained she was unaware of Stewart II at the time of her publication and that, even in view of Stewart II, her published statements about the Thorsen 2001 Article being the first to report on microdroplet formation in a T-shaped device would still be accurate, because Stewart II was not part of the body of work reported in the academic literature. Ex. 2018, 31:9–11, 59:21–60:3, 61:2–12, 63:11–21. The veracity of Dr. Anna's explanation is supported by Patent Owner's expert, Dr. Squires, who testified at deposition that he does not typically include patents in his own academic review papers and did not cite the patent literature in his own papers on the subject of microfluidics. Ex. 1020, 31:5–9, 37:19–38:21, 40:20–41:17. Dr. Anna's deposition testimony, in fact, clarifies any apparent inconsistency between her declaration and the Thorson 2001 Article. Accordingly, we are not persuaded that Dr. Anna's testimony should be given diminished weight in light of her prior statements about the Thorson 2001 Article.

Regarding hypothetical modifications to the Stewart II device that Dr. Anna allegedly could not answer during deposition, Patent Owner asserts Dr. Anna was "asked to discuss the effect that reducing the channel size would have on Stewart II's device." PO Resp. 10–11 (citing Ex. 2018, 113:4–115:5, 109:24–110:13). Patent Owner's questions, however, were hypotheticals concerning contamination or pressure, which, Dr. Anna testified, required additional information about the nature of the contamination. Ex. 2018, 113:4–6, 113:11–14, 114:9–12. Patent Owner further asserts that Dr. Anna was not able to explain "how one of ordinary skill in the art would understand the dimensions and operation of SII's device in light of the disclosure it works at both 10nl and 1L volumes." PO Resp. 10 (citing Ex. 2018, 107:21–109:16). That assertion is unpersuasive, because the questions presented to Dr. Anna were directed to the forces that govern droplet formation at 10nl and 1L; Dr. Anna testified that the relevant forces were the same, specifically, viscous forces, capillary forces, and inertia. Ex. 2018, 107:21–108:2, 108:10–19.

Patent Owner further asserts that Dr. Anna's credibility is undermined by her inability to opine on "low material costs" mentioned in Chou or whether "Kobayashi forms droplets using a cross-flow." PO Resp. 11–13 (citing Ex. 2018, 142:18–145:6, 137:2–140:4). The cost of materials asked about at deposition, however, went beyond the scope of Dr. Anna's declaration, as Dr. Anna's declaration does not address relative material costs. Dr. Anna did opine at deposition that materials mentioned in Stewart II may be cheaper than those in Chou depending on additional factors. Ex. 2018, 142:18–145:6. As to Kobayashi, Dr. Anna testified that "Kobayashi uses microchannels with pressure-driven flow to form

monodisperse droplets, as does Stewart" (Ex. 2018, 140:22–24) and "[w]hether a pressure-driven flow is the same as a cross-flow depends on the context." Ex. 2018, 139, 17–19. We do not find Dr. Anna's deposition testimony to undermine the credibility of her declaration in this proceeding because the questions asked of the witness were fairly answered. Therefore, after considering arguments and evidence by both Petitioner and Patent Owner, we are not persuaded that Dr. Anna's testimony is entitled to little or no weight.

Regarding Petitioner's prior art challenges, there is no dispute that the 10 nanoliter volume disclosed in Stewart II translates to a 267 micron diameter in the size of a spherical droplet in the channel. Ex. 1002 ¶ 42; Ex. 1020, 149:15–150:10. There also is no dispute that Stewart II discloses a microfluidic device having two channels arranged so that droplets of a sample fluid in the second channel are capable of being sheared into the main channel containing an extrusion fluid. Ex. 1002 ¶¶ 45–48, 50–57; Ex. 1020, 163:17–168:16. The key issue is whether the disclosure in Burns of a particular channel size (between 5 and 20 microns in depth) and a specific material (elastomeric) for microfluidic devices is properly combined with the disclosures of Stewart II.

We are persuaded that Petitioner meets its burden of showing that the selection of known channel sizes for microfluidic devices as disclosed in Burns would have been obvious as a predictable variation in the same field because the dimensions of Burns are less than 267 microns as directed by Stewart II. *KSR,* 550 U.S. at 417. The combination is supported by the Anna Declaration. Dr. Anna testified that the fluid behavior in the Stewart II device would be "substantially the same" in a device having the dimensions

disclosed by Burns. Ex. 1002 ¶ 50 ("fluid behavior (including flow characteristics, fluid forces, etc.) would be substantially the same in devices designed for droplets of less than 267 microns as they would be in devices designed for droplets of less than 100 microns."). Dr. Squires's testimony that the combination of Burns with Stewart II would have been unpredictable with no reasonable expectation of success due to multiple factors affecting droplet formation is not supported by the record. *See* Ex. 2019 ¶¶ 23–27, 29, 30, 37, 38. Dr. Squires's opinion is based on Stewart II being unbelievable because it does not disclose operating data. *Id*. at ¶¶ 29–30. Referring to Burns, Dr. Squires further states "[n]or does the mere fact that channels with dimensions smaller than 100 microns could be fabricated at the time of invention provide a basis for one of ordinary skill in the art to believe that Stewart II's device would operate as described by Stewart II when using channels with dimensions of 100 microns or less." *Id*. at ¶ 37. The formation of microdroplets, however, is disclosed in both Stewart II and Burns. Stewart II discloses droplet formation in a microfluidic device at dimensions less than 267 microns in diameter. Ex. 1004, 3–4. Burns discloses droplet formation in a microfluidic device at the claimed dimensions. Ex. 1005, 7. While multiple factors may affect droplet formation, the formation of droplets in devices having a channel that is less than 267 microns in diameter (Stewart II) or in the claimed range (Burns) is supported by the evidence.

Dr. Squires's testimony regarding the combination of Stewart II and Burns is based also on his assertion that the 10nL size disclosed in Stewart II would not be accepted by one of ordinary skill in the art at the time of the invention because "the upper bound volume in Stewart II is so implausible."

Ex. 2019 ¶ 36. However, Dr. Squires admitted at deposition that it was "physically possible" to make one liter droplets using Stewart II's device under low gravity and pressure conditions, such as in outer space. Ex. 1020, 176:21–177:6. Stewart II states that some types of chemical analysis or synthesis can be conducted in its device in space. Ex. 1004, 8 ("It could also be used for chemical analysis or synthesis in outer space, in conditions of very low gravity and pressure."). Stewart II also discloses a continuous flow embodiment having two currents that form a series of droplets when a reactant passes through an opening such that each droplet is "broken off just before it spans the conduit" and that "[a]ll conduits should have diameters approximately the same as the droplets." *Id*. at 4, 5. In a determination of obviousness, a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill in the art. *Merck & Co. v. Biocraft Labs.*, 874 F.2d 804, 807 (Fed. Cir. 1989) ("That the [prior art] patent discloses a multitude of effective combinations does not render any particular formulation less obvious.").

Dr. Squires asserts that "one of ordinary skill in the art would have to perform his or her own independent experimentation and research to determine what operating parameters could be combined to form a droplet using the T-junction geometry disclosed by Stewart II." Ex. 2019 ¶ 30. Such experimentation has not been shown on this record to be undue experimentation. In addition to the formation of microdroplets in the devices of Stewart II and Burns, the evidence shows, as Dr. Squires concedes, that for given materials, dimensions, and geometries, it would be a matter of "simple optimization" to adjust pressure to form droplets and is relatively easy to do. Ex. 1020, 134:12–135:5. Therefore, in view of the

totality of the evidence in the record, we credit Dr. Anna's testimony on the combination of Stewart II and Burns to arrive at the microfluidic product as claimed in claim 1.

We are not persuaded that Burns teaches away from the asserted combination as argued by Patent Owner. *See* PO Resp. 28. "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994). According to Patent Owner, the operation of Burns's system, showing a droplet in contact with a channel wall, is incompatible with Stewart II in two ways: (1) Stewart II requires a continuous phase between the channel and the dispersed phase to reduce contamination by the reactants in the dispersed phase, and (2) Stewart II requires droplets to be spherical. PO Resp. 29–30. These distinctions between the two references do not amount to discouraging one skilled in the art from the path leading to the claimed invention. Both Burns and Stewart II address contamination of the walls and disclose ways in which to reduce contamination, including making the walls smooth and washing them. Ex. 1005, 108; Ex. 1004, 2, 7. The common objective of Burns and Stewart II would have provided a further reason to combine their disclosures, rather than discouraging the combination. In addition, the evidence does not support a particular droplet geometry being critical to the microfluidic device of Stewart II as asserted by Patent Owner. *See* PO Resp. 30. Dr. Squires testified that the droplets shown in Figure 1 of Stewart could have alternate shapes. Ex. 1020, 143:11–13.

Regarding claims 18, 19, 46, and 47, Patent Owner also argues that the Petition lacks a rationale for the substitution of elastomeric material for the polymeric material in the device of Stewart II and that the Petition does not argue the deficiency of Stewart II is cured by Burns. PO Resp. 48–50. The Petition states that "Stewart discloses a number of alternative polymers in which channels can be formed, and polymers include numerous elastomeric materials." Pet. 32 (citing Ex. 1002 ¶¶ 83–85). Petitioner argues that the substitution of an elastomeric material would have been prima facie obvious because it was known to be a suitable substitute for other polymers in the field of microfluidics. *Id*. at 32–33 (citing Ex. 1002 ¶ 85). According to Dr. Anna, such a substitution would have been technically simple and would have yielded predictable results. Ex. 1002 ¶ 85. Dr. Anna's testimony on the subject is not refuted. Dr. Squires's assertion that swelling of the elastomeric material may occur in the presence of "certain fluids" is not applicable to the combination of Stewart II and Burns because Stewart II uses mineral oil as the carrier phase, which is the same carrier phase fluid taught in the '503 patent. Ex. 2019 ¶¶ 54–57; Ex. 1004, 4; Ex. 1001, 4:39–43. Based on the full trial record, the substitution of an elastomeric material for the polymeric material in the device of Stewart II would have been obvious as a predictable variation in the field of microfluidic devices, and, therefore, Petitioner has met its burden in showing that claims 18, 19, 46, and 47 would have been obvious over the combination of Stewart II and Burns. *See KSR*, 550 U.S. at 417 ("If a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability.").

Regarding the obviousness challenge as to claims 2, 5, 7, 10, 30, and 31, based on the combination of Stewart II and Burns, these claims all depend directly or indirectly from claim 1 and recite limitations of the properties of the sample and/or extrusion fluids. Ex. 1001, 62:39–63:53. The Petition explicitly challenges claim 1 as obvious over the combination of Stewart II and Burns and sets forth Petitioner's obviousness grounds with respect to each of the limitations recited in claim 1, including the limitations that refer to properties of the fluid. Pet. 19–23. The Petition also argues that the properties of the fluids do not impart patentable weight to the claims, referencing Section VI.A.1.i. on pages 8–9 of the Petition, where this argument is first expressed in connection with the challenge based on anticipation by Stewart II. *Id*. at 22; *see also id*. at 23, 26, 28, 30. Petitioner's argument that the presence and properties of the sample and extrusion fluids do not confer patentable weight to the claims identifies all the claims to which this argument applies, namely, claims 1, 2, 5–11, 30, 31, 46, 49, and 41 [sic 51]. We agree with Petitioner that properties of the fluids flowing through the claimed device impart no patentable weight to dependent claims 2, 5, 7, 30, and 31. *Catalina Marketing Int'l., Inc. v. Coolsavings.com, Inc*., 289 F.3d 801, 809 (Fed. Cir. 2002) ("the patentability of apparatus or composition claims depends on the claimed structure, not on the use or purpose of the structure") (citing *In re Gardiner*, 171 F.3d 313, 315–16 (CCPA 1948)).

In addition to the contentions above, Patent Owner argues that objective indicia (secondary considerations) establish non-obviousness of the claimed subject matter. PO Resp. 15–16. We analyze Patent Owner's proffered evidence in this regard in Section II.H. below.

F. Obviousness over Stewart II, Burns, and Kobayashi

Petitioner asserts that if the combination of Stewart II and Burns would not have rendered obvious the production of monodisperse droplets, as required by claims 49 and 51, then the combination in further view of Kobayashi would have rendered obvious the claimed microfluidic product. Pet. 36–37. According to Petitioner, Kobayashi discloses forming monodisperse oil-in-water emulsions in microchannels by adjusting parameters such as pressure and concentration of surfactant. *Id*. (citing Ex. 1012; Ex. 1002 ¶¶ 97–99). Petitioner argues that Kobayashi evidences the desire to achieve monodispersity of droplets in the microfluidic field and that monodispersity can be achieved through optimization of a microfluidic device. *Id*.

Patent Owner contends that Kobayashi creates droplets without requiring a junction of channels and that the "size of droplets was independent of adjustment of pressure beyond the pressure needed to create a microsphere in the first place." PO Resp. 57–58 (citing Ex. 1012, 353). Because the manner in which droplets are formed in Kobayashi is different from Stewart II, Patent Owner contends that "one of ordinary skill in the art would not have considered [Kobayashi's] method of forming monodisperse microspheres to be helpful in modifying Stewart II to form monodisperse droplets." *Id*. at 58 (citing Ex. 2019 ¶ 59). Because size is not adjusted by pressure beyond a certain point and only 10% of the channels produce microspheres, Patent Owner contends that generating monodisperse microspheres using Kobayashi's system is neither routine optimization nor simple. *Id*. at 58 (citing Ex. 2019 ¶¶ 60–62).

We are persuaded that monodispersity of the droplets formed in a microfluidic device is a property of the fluids contained in the device rather than an element of the claimed structure of two channels with a junction, as evidenced by Kobayashi itself. *See* Ex. 1020, 61:5–8 (Dr. Squires testified that Kobayashi forms monodispersed oil-in-water droplets using microchannels). Additionally, we find that Petitioner has met its burden to show that it would have been within the skill of one of ordinary skill in the art to optimize pressure and surface tension in order to form monodisperse droplets. Ex. 1002 ¶ 77; Ex. 1012, 352. The difficulties noted by Kobayashi, and argued by Patent Owner, were at higher surfactant concentration, but at less than 0.5 percent weight; Dr. Squires testified that Kobayashi's "monodispersity was high." Ex. 1020, 83:2–84:11. Therefore, Petitioner has shown that monodispersity of droplets in microfluidic channels as required by claims 49 and 51 was known and subject to pressure and surface tension conditions.

G. Obviousness over Stewart II, Burns, Chou

Petitioner challenges claims 18, 19, 46, and 47 as obvious over the combination of Stewart II, Burns, and Chou. Petitioner asserts that Chou "specifically teaches forming channels in an elastomeric material adjacent to a substrate layer," with citations to the claim chart. Pet. 38. Petitioner further asserts that it would have been obvious to substitute the elastomeric material of Chou for the polymeric material taught by Stewart II because it would have been technically simple and would have yielded predictable results. *Id*. (citing Ex. 1002 ¶¶ 100, 101). The Anna Declaration supports the known use of elastomeric materials in microfluidic devices, the ease of substituting the material of Chou in the device of Stewart II, and the benefit

of low material costs and an easy one-step process when silicone elastomer is used to form the channel. Ex. 1002 ¶¶ 100, 101.

Patent Owner contends that if the elastomer in Chou is not cheaper than the polymeric material in Stewart II, then there is no reason for the asserted substitution. PO Resp. 51. Patent Owner further argues that such substitution would not produce predictable results because the elastomer in Chou "could swell and prevent [] formation of droplets in a variety of non-aqueous fluids." *Id*. (citing Ex. 2019 ¶ 57). We are not persuaded by Patent Owner's argument because there is no evidence in the record that the carrier fluid of Stewart II would have been incompatible with the elastomer of Chou. The carrier fluid of Stewart II is the same carrier fluid used in the '503 patent. Ex. 1004, 4; Ex. 1001, 4:39–43.

We are persuaded that a known elastomeric polymer used to form a channel in a microfluidic device would have been an obvious substitution of material in Stewart II, and that the obviousness of interchanging them does not depend on a price differential. *See KSR*, 550 U.S. at 417. Stewart II teaches polymeric material generally with its recitation of an expansive list of alternative polymers "Kel-F . . . polyvinylchloride, polypropylene etc." as the material in which a channel may be produced to form a conduit against a second plate. Ex. 1004, 7. Chou's disclosure of silicone elastomer to form microfluidic channels supports Stewart II's broad teaching of useful polymeric materials. Ex. 1002 ¶¶ 83–85, 100; Pet. 32–33, and 37–38.

H. Objective Indicia of Non-Obviousness

In addition to the contentions above, Patent Owner argues that objective indicia, including industry praise (PO Resp. 16–25) and long-felt but unmet need (*id*. at 25–28) is probative evidence showing the inventions

of the claims at issue are non-obvious. *Id*. at 16. In support, Patent Owner relies on the Squires Declaration (Ex. 2019), the Anna Declaration (Ex. 1002), the Anna 2007 Article (Ex. 2016), and other evidence (Exs. 1007, 2018, 2021–25, 2027.

Industry Praise

Patent Owner contends that "the Thorsen 2001 Article is substantially similar to Example 12 in the '503 patent" and provides a chart setting forth how the Thorsen 2001 Article (Ex. 2017) discloses the elements of claim 1. PO Resp. 20–23. Patent Owner also sets forth how researchers in the field, including Dr. Anna, praised the Thorsen 2001 Article as (1) first reporting "droplet formation in a T-shaped device" (Ex. 2016), (2) "first introduc[ing microfluidic T-junction geometry] for the controlled formation of water-in-oil dispersions" (Ex. 2022), (3) "first incorporate[ing T-junction geometry] into a microfluidic chip" (Ex. 2023), (4) "first[] consider[ing] droplet formation within a T-junction microchannel" (Ex. 2024), and (5) "first report[ing] "[d]roplet formation in a T-shaped device" (Ex. 2025). PO Resp. 16–19. It is not sufficient, however, that a product or its use merely falls within the scope of a claim in order for objective evidence of nonobviousness tied to that product to be given substantial weight. There must also be a causal relationship, termed a "nexus," between the evidence and the claimed invention. *Merck & Co., Inc. v. Teva Pharm. USA, Inc*., 395 F.3d 1364, 1376 (Fed. Cir. 2005). Nexus must exist in relation to all types of objective evidence of nonobviousness. *See In re GPAC, Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995) (generally); *Ormco Corp. v. Align Tech., Inc.*, 463 F.3d 1299, 1312 (Fed. Cir. 2006) (long-felt but unmet need); *Muniauction, Inc. v. Thomson Corp*., 532 F.3d 1318, 1328 (Fed. Cir. 2008)

(praise). A showing of sufficient nexus is required in order to establish that the evidence relied upon traces its basis to a novel element in the claim, not to something in the prior art. *Institut Pasteur & Universite Pierre Et Marie Curie v. Focarino*, 738 F.3d 1337, 1347 (Fed. Cir. 2013). Objective evidence that results from something that is not "both claimed and novel in the claim" lacks a nexus to the merits of the invention. *In re Kao*, 639 F.3d 1057, 1068 (Fed. Cir. 2011). Thus, establishing nexus involves a showing that novel elements in the claim, not prior-art elements, account for the objective evidence of nonobviousness. *Id*. The stronger the showing of nexus, the more weight will be accorded the objective evidence of nonobviousness. *See GPAC*, 57 F.3d at 1580 ("To the extent that the patentee demonstrates the required nexus, his objective evidence of nonobviousness will be accorded more or less weight."); *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc*., 776 F.2d 281, 306 (Fed. Cir. 1985) ("The objective evidence of secondary considerations may in any given case be entitled to more or less weight, depending upon its nature and its relationship to the merits of the invention.").

As noted, the objective evidence cited by Patent Owner requires a nexus with the claimed subject matter. Patent Owner's evidence of praise relies, however, on Thorsen being first to report on a T-shaped junction geometry for a microfluidic device to produce droplets and, more generally, to "landmark work" in droplet based microfluidics, not any specific praise for the device itself even if encompassed by claim 1. *See* PO Resp. 17–19; Ex. 2016, R322; Ex. 2021, 25; Ex. 2022, 142–44; Ex. 2023, 438; Ex. 2024, 712; Ex. 2025, 2036. As discussed above, T-shaped junctions were known in the art for use in microfluidic devices as early as 1984. Ex. 1004, Fig. 1.

Consequently, it cannot be used to tie the objective evidence of praise to the claimed subject matter. Thus, even if being recognized as first to report in the academic literature on a particular microfluidic structure constitutes praise for the device, we are not persuaded that Patent Owner establishes sufficient nexus in relation to the microfluidic device being praised versus what is "both claimed and novel in the claim." *Kao*, 639 F.3d at 1068. Accordingly, we are not persuaded by Patent Owner's contentions in relation to praise in the industry.

Long-Felt but Unmet Need

Patent Owner also contends that long-felt need is established by the length of time between Stewart II's disclosure of a T-junction structure in 1984, Manz's disclosure of capillary tubing having internal diameters between 0.9 μm and 24 μm in 1990, and the earliest priority date of the '503 patent in November 8, 2000. PO Resp. 25–28 (citing *Leo Pharmaceutical Prods., Ltd. v. Rea*, 726 F.3d 1346, 1357–59 (Fed. Cir. 2013)).

Patent Owner's evidence of a long-felt but unmet need is premised on the prior art T-junction structure to form droplets of Stewart II not meeting the need for miniaturization of microfluidic devices. *See* PO Resp. 25–26. When asked about direct evidence of long-felt need at oral hearing, Patent Owner answered, "Dr. Anna's statement that Stewart II professed a desire to reduce the size of his device." Tr. 54:1–3. Patent Owner essentially takes Petitioner's reason to combine references and characterizes it as a "desire" or "need" rather than a direction to use devices that are smaller than 267 microns in size. Patent Owner then measures the length of time between Stewart II's publication in 1984 and the November 8, 2000 filing date of the '503 patent to argue an analogous situation to the finding of long-felt need in

Leo Pharma. PO Resp. 26–27. The problem with this argument is that Stewart II does not evidence difficulty in constructing a T-junction microfluidic device in dimensions below 267 microns. Rather, Stewart II discloses "the manipulation of microscopic quantities of reactant with volumes of less than 10 nanolitres," which the parties do not dispute translates to droplets of less than 267 microns and channels of less than 267 microns in diameter. Ex. 1004, 3; Ex. 1002 ¶¶ 42, 44 ("Because Stewart II expressly states that it is suited for volumes of less than 10 nanoliters, or less than 267 microns, Stewart II expressly relates to smaller droplets as well . . . ."); Ex. 1020, 149:19–150:10, 158:2–9 (When Stewart II says "ten nanoliters or less" and spherical droplets are involved, this translates into a channel width of "267 microns or less."). Therefore, we are not persuaded that the evidence on the complete record establishes a long-felt, unmet need for microfluidic channels in the claimed range of 2 to 100 microns.

We also are not persuaded that the time gap drawn between Stewart II's 1984 publication and the '503 patent priority date is sufficient to establish long-felt need in view of the fourteen year gap in *Leo Pharma,* 726 F.3d at 1359. PO Resp. 27–28. *Leo Pharma* involved "the need for a single formulation to treat psoriasis" where benefits of the separate components, vitamin D and corticosteroids, were known from the cited prior art references twenty-two years and fourteen years before the filing of the patent at issue. *Leo Pharma,* 726 F.3d at 1359. The factual background of *Leo Pharma* includes evidence that "several medical research articles . . . discourag[ed] the combination of a vitamin D analog with a corticosteroid because of the stability problems of vitamin D analogs at lower pHs." *Id*. at 1353. There was also a finding that the cited prior art formulations were not

storage stable and the problem of storage stability was not recognized. *Id*. at 1354, 1357. Thus, *Leo Pharma* included circumstances that are not present here, not just the mere passage of time. *See Nike, Inc. v. Adidas AG*, 812 F.3d 1326, 1338 (Fed. Cir. 2016) (the decision in *Leo Pharma* "hinged on the fact that nothing in the cited prior art appreciated the problem the invention recognized and then solved" not merely the passage of time); *Iron Grip Barbell Co., Inc. v. USA Sports, Inc*., 392 F.3d 1317, 1325 (Fed. Cir. 2004) ("the mere passage of time without the claimed invention is not evidence of nonobviousness."). Even if the time span between cited prior art and the priority date of a patent were sufficient to establish long-felt need, Patent Owner has not addressed the Burns reference, published two years prior to the '503 patent priority date and relied upon by Petitioner in each of its obviousness challenges. Ex. 1005. The evidence is insufficient to establish that any long-felt need was solved by the invention of the '503 patent, as opposed to the prior art techniques reflected in Burns. Consequently, we are not persuaded by Patent Owner's contentions with respect to long-felt need.

I. Conclusion

After considering Petitioner's and Patent Owner's positions, as well as their supporting evidence, we determine the preponderance of the evidence demonstrates that (1) claims 1, 2, 5–11, 18, 19, 30, 31, 46, 47, and 49–51 of the '503 patent would have been obvious over Stewart II and Burns; (2) claims 49 and 51 would have been obvious over Stewart II, Burns, and Kobayashi; and (3) claims 18, 19, 46, and 47 would have been obvious over Stewart II, Burns, and Chou for the reasons provided by Petitioner. *See* Pet.

19–33, 36–60; Pet. Reply 1–25. Patent Owner's objective evidence is not sufficient to overcome the strong showing of obviousness in this case.

J. Motion to Seal

Fluidigm Corporation's Motion to Seal Exhibits 2003–2008 (Paper 11) is unopposed and is granted. There is an expectation that information will be made public where the information is identified in a final written decision, and that confidential information that is subject to a protective order ordinarily becomes public 45 days after final judgment in a trial, unless a motion to expunge is granted. 37 C.F.R. § 42.56; Office Patent Trial Practice Guide, 77 Fed. Reg. 48,756, 48,761 (Aug. 14, 2012). In rendering this Final Written Decision, it was not necessary to identify, nor discuss in detail, any confidential information because it was not relied upon by the parties in their trial briefing. However, a party who is dissatisfied with this Final Written Decision may appeal the Decision pursuant to 35 U.S.C. § 141(c), and has 63 days after the date of this Decision to file a notice of appeal. 37 C.F.R. § 90.3(a). Thus, it remains necessary to maintain the record, as is, until resolution of an appeal, if any. In view of the foregoing, the confidential documents filed in the instant proceeding will remain under seal, at least until the time period for filing a notice of appeal has expired or, if an appeal is taken, the appeal process has concluded. The record for the instant proceeding will be preserved in its entirety, and the confidential documents will not be expunged or made public, pending appeal. Notwithstanding 37 C.F.R. § 42.56 and the Office Patent Trial Practice Guide, neither a motion to expunge confidential documents nor a motion to maintain these documents under seal is necessary or authorized at this time. *See* 37 C.F.R. § 42.5(b).

This is a final written decision of the Board under 35 U.S.C. § 318(a). Parties to the proceeding seeking judicial review of this decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

III. ORDER

Accordingly, it is hereby:

ORDERED that, as set forth in Section II.I above, claims 1, 2, 5–11, 18, 19, 30, 31, 46, 47, and 49–51 of the '503 patent have been shown to be unpatentable.

FURTHER ORDERED that the Motion to Seal Exhibits 2003–2008 (Paper 11) is *granted*.

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

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