Trials@uspto.gov
571-272-7822

Paper 52
Date: July 14, 2020

1030UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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QIAGEN NORTH AMERICAN HOLDINGS, INC.,
Petitioner,

v.

HANDYLAB, INC.,
Patent Owner.

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IPR2019-00488[1]
Patent 7,998,708 B2

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Before JO-ANNE M. KOKOSKI, CHRISTOPHER G. PAULRAJ, and JULIA HEANEY, *Administrative Patent Judges.*

KOKOSKI, *Administrative Patent Judge*.

JUDGMENT
Final Written Decision
Determining No Challenged Claims Unpatentable
*35 U.S.C. § 318(a)*
Dismissing Patent Owner's Motion to Exclude
*37 C.F.R. § 42.64(c)*

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[1] IPR2019-01493 has been joined with this proceeding.

# I. INTRODUCTION

We have jurisdiction to conduct this *inter partes* review under 35 U.S.C. § 6, and this Final Written Decision is issued pursuant to 35 U.S.C. § 318(a). For the reasons that follow, we determine that QIAGEN North American Holdings, Inc. ("Petitioner") has not shown by a preponderance of the evidence that claims 1–33 of U.S. Patent No. 7,998,708 B2 ("the '708 patent," Ex. 1002) are unpatentable.

## *A. Procedural History*

Petitioner filed a Petition ("Pet.") to institute an *inter partes* review of claims 1–33 of the '708 patent. Paper 1. HandyLab, Inc. ("Patent Owner") filed a Preliminary Response. Paper 5. Pursuant to 35 U.S.C. § 314(a), we instituted an *inter partes* review of claims 1–33 on all grounds advanced in the Petition. Paper 8 ("Dec. on Inst." or "Institution Decision"), 7, 20.

After institution of trial, Patent Owner filed a Patent Owner Response ("PO Resp.," Paper 24), Petitioner filed a Reply ("Pet. Reply," Paper 31), and Patent Owner filed a Sur-Reply ("PO Sur-Reply," Paper 43). Patent Owner filed a Motion to Exclude Exhibits 1030 and 1032. Paper 44. Petitioner filed an Opposition (Paper 46), and Patent Owner filed a Reply (Paper 47).

Patent Owner also filed a Motion to Strike certain portions of Petitioner's Reply. Paper 38. Petitioner filed an Opposition. Paper 39. We granted Patent Owner's Motion to Strike in part, striking the arguments in Section II.B.ii from Petitioner's Reply. Paper 42, 6–8, 13. We did not consider those arguments in the course of preparing this Final Written Decision.

An oral hearing was held on April 21, 2020, and a transcript is included in the record. Paper 51.

*B. Related Proceedings*

Petitioner indicates that there are no related matters. Pet. 1. Patent Owner identifies *QIAGEN North American Holdings, Inc. v. HandyLab, Inc.*, IPR2019-00490, concerning U.S. Patent No. 8,323,900 (which is a continuation of the '708 patent) as a related matter. Paper 3, 1.

*C. The '708 Patent*

The '708 patent, titled "Microfluidic System for Amplifying and Detecting Polynucleotides in Parallel," is directed to "a system and related methods for amplifying, and carrying out diagnostic analyses on, polynucleotides (e.g., a DNA, RNA, mRNA, or rRNA) from biological samples." Ex. 1002, code (54), 3:64–67. The claimed system "includes a disposable microfluidic cartridge containing multiple sample lanes in parallel and a reusable instrument platform (a PCR analyzer apparatus) that can actuate on-cartridge operations" and "can detect (e.g., by fluorescence detection) and analyze the products of the PCR amplification in each of the lanes separately, in all simultaneously, or in groups simultaneously." *Id.* at 4:7–13. The system optionally "can display the results on a graphical user interface." *Id.* at 4:13–15.

The '708 patent's Figure 1 is reproduced below.

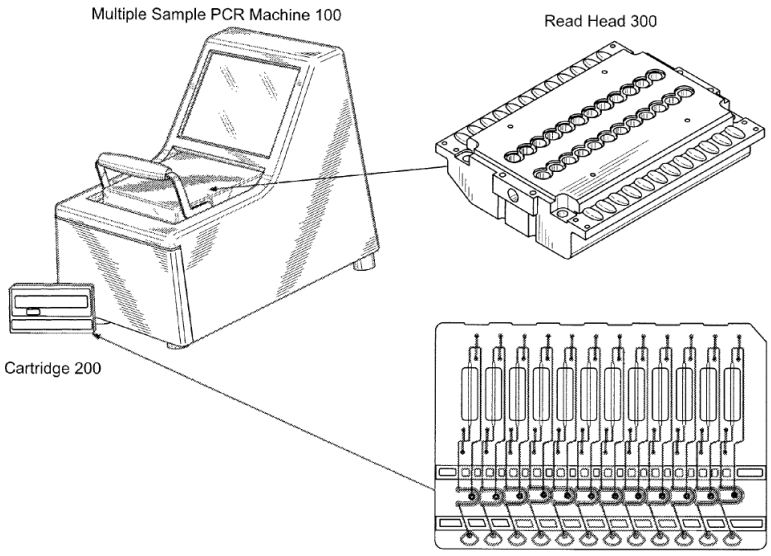



FIG. 1

Figure 1 is "a perspective view of an exemplary apparatus 100" described by the '708 patent. *Id.* at 4:33–34. Apparatus 100 includes read head 300 "that contains detection apparatus for reading signals from cartridge 200." *Id.* at 4:35–37. Apparatus 100 "is able to carry out real-time PCR on a number of samples in cartridge 200 simultaneously." *Id.* at 4:38–40. Cartridge 200 contains multiple sample lanes, and the '708 patent explains that "[p]referably the number of samples is 12 samples, as illustrated with exemplary cartridge 200," although other numbers of samples can be present. *Id.* at 4:34–35, 4:40–43.

The '708 patent's Figure 3 is reproduced below.

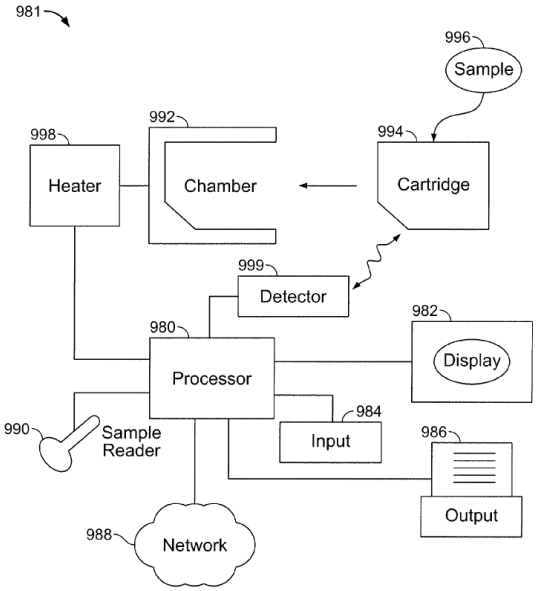



FIG. 3

Figure 3 is a "schematic overview of a system 981 for carrying out the analyses described" in the '708 patent. *Id.* at 4:54–55. Processor 980 "is configured to control functions of various components of the system," such as receiving data about a sample to be analyzed from sample reader 990, "which may be a barcode reader, an optical character reader, or an RFID scanner (radio frequency tag reader)." *Id.* at 4:59–65. Processor 980 can also be configured to accept user instructions from input 984, to communicate with optional display 982, to transmit analysis results to an output device, and to control various aspects of sample diagnostics. *Id.* at 4:67–5:19, 6:1–3.

System 981 "is configured to operate in conjunction with a complementary cartridge 994, such as a microfluidic cartridge." *Id.* at 6:3–5. Cartridge 994 is itself configured "to receive one or more samples 996 containing one or more polynucleotides in a form suitable for amplification and diagnostic analysis," and "has dedicated regions within which

amplification, such as by PCR, of the polynucleotides is carried out when the cartridge is situated in the apparatus." *Id.* at 6:5–11. Receiving bay 992 is "configured to selectively receive the cartridge," and "is in communication with a heater unit 998 that itself is controlled by processor 980 in such a way that specific regions of the cartridge, such as individual sample lanes, are independently and selectively heated at specific times during amplification and analysis." *Id.* at 6:12–13, 6:33–37.

Processor 980 "is also configured to receive signals from and control a detector 999 configured to detect a polynucleotide in a sample in one or more individual sample lanes, separately or simultaneously." *Id.* at 7:31–34. Detector 999 can be "an optical detector that includes a light source that selectively emits light in an absorption band of a fluorescent dye, and a light detector that selectively detects light in an emission band of the fluorescent dye, wherein the fluorescent dye corresponds to a fluorescent polynucleotide probe." *Id.* at 7:41–46.

The '708 patent explains that system 981 "is configured so that a cartridge with capacity to receive multiple samples can be acted upon by the system to analyze multiple samples—or subsets thereof—simultaneously, or to analyze the samples consecutively." *Id.* at 7:64–67. According to the '708 patent, this system is self-contained and therefore "is advantageous at least because it does not require locations within the system suitably configured for storage of reagents," and does not "require inlet or outlet ports that are configured to receive reagents from, e.g., externally stored containers such as bottles, canisters, or reservoirs." *Id.* at 8:4–11.

Claims 1 and 33 are the only independent claims, and are reproduced below.

> 1. An apparatus, comprising:
>
> a multi-lane microfluidic cartridge, each lane comprising a PCR reaction zone;
>
> a receiving bay configured to receive the microfluidic cartridge;
>
> each PCR reaction zone comprising a separately controllable heat source thermally coupled thereto, wherein the heat source maintains a substantially uniform temperature throughout the PCR reaction zone and thermal cycles the PCR reaction zone to carry out PCR on a polynucleotide-containing sample in the PCR reaction zone;
>
> a detector configured to detect the presence of an amplification product in the respective PCR reaction zone; and
>
> a processor coupled to the detector and the heat source, configured to control heating of one or more PCR reaction zones by the heat sources.

Ex. 1002, 46:5–22.

> 33. A method of carrying out PCR on a plurality of samples, the method comprising:
>
> introducing the plurality of samples into a multi-lane microfluidic cartridge, wherein each lane comprises a PCR reaction zone configure to permit thermal cycling of a sample independently of the other samples;
>
> moving the plurality of samples into the respective plurality of PCR reaction zones; and
>
> amplifying polynucleotides contained with the plurality of samples in the PCR reaction zones while thermal cycling the PCR reaction zones, at least one PCR reaction zone separately thermally controllable from another PCR reaction zone.

*Id.* at 48:28–40.

*D. Prior Art and Asserted Grounds*

Petitioner asserts that claims 1–33 of the '708 patent are unpatentable on the following grounds:

| References | 35 U.S.C. § | Claim(s) Challenged |
|---|---|---|
| Zou I[2], McNeely[3] or Pease[4] | 103 | 1–6, 9, 10, 18–20, 23–25, 28, 30–33 |
| Zou I, McNeely or Pease, Hsieh[5] | 103 | 7, 8 |
| Zou I, McNeely or Pease, Zou II[6] | 103 | 11–17 |
| Zou I, McNeely | 103 | 21, 22 |
| Zou I, McNeely or Pease, Duong[7] | 103 | 26, 27 |
| Zou I, McNeely or Pease, Chow[8] | 103 | 29 |

Petitioner relies on the Declaration of Bruce K. Gale, Ph.D. ("First Gale Declaration," Ex. 1001) and the Second Declaration of Bruce K. Gale, Ph.D. ("Second Gale Declaration," Ex. 1026) (collectively, "Gale Declarations"). Patent Owner relies on the Declaration of Allen Northrup, Ph.D. ("Northrup Declaration," Ex. 2036).

[2] U.S. Patent No. 6,509,186 B1, issued Jan. 21, 2003 (Ex. 1008).
[3] U.S. Patent App. Pub. No. US 2004/0037739 A1, published Feb. 26, 2004 (Ex. 1009).
[4] U.S. Patent App. Pub. No. US 2004/0151629 A1, published Aug. 5, 2004 (Ex. 1010).
[5] U.S. Patent No. 7,122,799 B2, issued Oct. 17, 2006 (Ex. 1012).
[6] U.S. Patent No. 6,762,049 B2, issued July 13, 2004 (Ex. 1011).
[7] WO 01/54813 A2, published Aug. 2, 2001 (Ex. 1013).
[8] U.S. Patent No. 5,955,028, issued Sept. 21, 1999 (Ex. 1014).

## II. ANALYSIS

### *A. Level of Ordinary Skill in the Art*

Petitioner contends that a person having ordinary skill in the art ("POSA") would have had "a degree in Mechanical Engineering, Bioengineering, or a similar field, and three years of experience with microfluidic devices or systems relating to biochemical reactions/analysis, such as PCR," or "an advanced degree in a similar field with at least one year of related experience." Pet. 5. Patent Owner argues that Petitioner's proposed definition "is not narrowly drawn to experience in 'microfluidic systems that carry out PCR,'" and contends that a POSA "would have had a degree in Mechanical Engineering, Bioengineering, or a similar field, and three years of experience with microfluidic devices that carry out PCR, or would have an advanced degree in a similar field with at least one year of related experience." PO Resp. 9 (citing Ex. 2036 ¶¶ 25–26). Patent Owner's declarant Dr. Northrup states that, although he disagrees with Petitioner's proposed definition of a POSA, his "opinions would not change under" that definition. Ex. 2036 ¶ 28.

We agree with the parties that a POSA would have had an engineering background and experience with microfluidic devices, which is consistent with the level of ordinary skill in the art at the time of the invention as reflected in the prior art in this proceeding. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that specific findings regarding ordinary skill level are not required "where the prior art itself reflects an appropriate level and a need for testimony is not shown" (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 163 (Fed. Cir. 1985))). Our determination regarding the patentability of the challenged claims does not turn on the differences between Petitioner's and Patent

Owner's definitions, and we note that our conclusions would be the same under either assessment.

*B. Claim Construction*

For petitions such as this one, filed after November 13, 2018, we apply the same claim construction standard "used in the federal courts, in other words, the claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. [§] 282(b), which is articulated in" *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (en banc). 83 Fed. Reg. 51,340, 51,343 (Oct. 11, 2018). Under the *Phillips* standard, the "words of a claim 'are generally given their ordinary and customary meaning,'" which is "the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Phillips*, 415 F.3d at 1312–13. Only those terms in controversy need to be construed, and only to the extent necessary to resolve the controversy. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) ("[W]e need only construe terms 'that are in controversy, and only to the extent necessary to resolve the controversy.'") (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

In its Petition, Petitioner proposes a construction for the term "contact heat source" in dependent claims 10–17. Pet. 4–5. Patent Owner proposes a construction for the term "multi-lane microfluidic cartridge" in independent claims 1 and 33. PO Resp. 11–15. For purposes of the Institution Decision, we determined that no term required explicit construction. Dec. on Inst. 9. Based on our review of the complete record and the claim construction arguments raised by the parties, for purposes of this Final Written Decision

we determine it is necessary to expressly construe "multi-lane microfluidic cartridge."

Patent Owner proposes that we construe "multi-lane microfluidic cartridge" to mean "a microfluidic cartridge comprising a plurality of sample lanes with separate sample inlets and microfluidic networks." PO Resp. 11 (citing Ex. 2036 ¶¶ 51–58). In support of its construction, Patent Owner contends that "the specification makes clear that the claimed '***multi***-lane microfluidic cartridge' has a plurality of samples lanes," and "defines that, in the context of the '708 patented invention, a 'sample lane' or 'lane' has certain specific characteristics," such as a sample inlet and certain microfluidic components. *Id.* at 11–12 (citing Ex. 1002, 12:66–13:15, 13:24–36; Ex. 2036 ¶¶ 53–54). Patent Owner further contends that the specification states that the sample inlet and the microfluidic network are separate from one another and unique to each lane. *Id.* at 12 (citing Ex. 1002, 12:64–65, 13:34–36, 14:64–67). According to Patent Owner, the disclosures in the specification "confirm the basic design of the '708 patented invention: the disclosed cartridge has ***separate*** sample lanes that can process multiple ***different*** samples independently." *Id.* at 13 (citing Ex. 1002, 13:21–23, 13:38–42).

Petitioner argues in its Reply that the claims "do not recite a 'sample inlet' associated with each lane, much less a '*separate* sample inlet,'" and, therefore, "'[m]ulti-lane microfluidic cartridge' should be given its ordinary meaning," which is "a cartridge with multiple microfluidic channels." Pet. Reply 2 (citing Ex. 1026 ¶¶ 10, 12–13). Petitioner also argues that Patent Owner's construction improperly relies on the specification's use of the term "sample lane" to import a separate sample inlet into the claims, because "the claims say 'lane,' not 'sample lane,'" and also "say what each

'lane' must include: 'each lane comprising a PCR reaction zone.'" *Id.* at 2–3 (citing Ex. 1002, claims 1 and 33; Ex. 1026 ¶¶ 13–14). Petitioner further contends that the "claims should not be limited to the embodiments in the specification," and, "[h]ere[,] the specification confirms that the disclosed cartridges are only 'exemplary' and that the purported invention includes '[o]ther configurations of inlets though not explicitly described or depicted.'" *Id.* at 3 (citing Ex. 1002, 2:55–56, 13:5–6, 17:15–20, 17:65–67). Petitioner also contends that Patent Owner added the term "multi-lane" to the claims during prosecution to distinguish over a prior art reference, and in doing so "expressly equat[ed] 'lane' to 'flow channel,'" which is "more evidence that the term 'lane' is used according to its ordinary meaning." *Id.* at 3–4 (citing Ex. 1005, 7–8; Ex. 1026 ¶ 21).

We have considered, but are not persuaded by, Petitioner's claim arguments regarding the construction of the term "multi-lane microfluidic cartridge." The claim language requires that "each lane" of the multi-lane microfluidic cartridge comprises a separately controllable PCR reaction zone. While this much is apparent from the plain language of the claims, the issue is what constitutes a "lane." For guidance, we turn to the specification. *See Phillips*, 415 F.3d at 1315 (the specification is "the single best guide to the meaning of a disputed term") (citing *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996).

As an initial matter, we are not persuaded by Petitioner's implicit argument that, as used in the '708 patent specification, a "lane" is something different from a "sample lane." *See* Pet. Reply 2–3. The specification consistently uses the terms "lane" and "sample lane" interchangeably to refer to the structure in which the polynucleotide analysis occurs. For example, the specification explains that "[o]ne aspect of the present

technology relates to a microfluidic cartridge having two or more *sample lanes* arranged so that analyses can be carried out in two or more of *the lanes* in parallel, for example simultaneously, and wherein each lane is independently associated with a given sample." Ex. 1002, 12:61–65 (emphasis added); *see also id.* at 4:7–14 (describing the apparatus as including "a disposable microfluidic cartridge containing multiple sample lanes in parallel" with an instrument platform that can analyze the PCR amplification products "in each of the lanes" separately or simultaneously), 13:34–42 ("The multi-lane cartridge comprises at least a first sample lane having a first microfluidic network and a second lane having a second microfluidic network . . ."), 13:55–61 (describing a microfluidic cartridge containing "twelve independent sample lanes" in which "each lane" is "configured to carry out amplification"). Petitioner does not direct us to, nor do we discern, anything in the specification that indicates that a "lane" is something different than a "sample lane." *See Phillips*, 415 F.3d at 1313 ("[T]he person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification.").

We also agree with Patent Owner that the specification defines the structure of the sample lane. PO Resp. 12. The specification states:

> A sample lane is an independently controllable set of elements by which a sample can be analyzed, according to methods described herein as well as others known in the art. A sample lane comprises at least a sample inlet, and a microfluidic network having one or more microfluidic components as further described herein.

Ex. 1002, 12:66–13:4. The embodiments described in the specification include sample inlets associated with each of the sample lanes. *See, e.g., id.*

at 14:34–45, Figs. 10A, 10B (describing an exemplary microfluidic cartridge depicted in Figures 10A and 10B as showing "[m]ore than one inlet 202 . . . wherein one inlet operates in conjunction with a single sample lane"), 17:55–60, Fig. 13 (describing and depicting a 48-sample cartridge with separate inlets 602 for each sample lane). In contrast, when describing other elements (such as inlet ports and valves) that may be included in a sample lane, the specification clearly conveys that these other elements are optional. *Id.* at 13:5–12 ("In various embodiments, a sample lane *can include* a sample inlet port or valve, and a microfluidic network that comprises, in fluidic communication one or more components selected from the group consisting of" certain specified valves, vents, pumps, and chambers. (emphasis added)).

That each sample lane must be associated with a separate, dedicated inlet is further supported by the '708 patent specification's teaching that

> [a] multi-lane cartridge is configured to accept a number of samples in series or in parallel, simultaneously or consecutively, in particular in embodiments [of] 12 samples, wherein the samples include at least a first sample and a second sample, wherein the first sample and the second sample each contain one or more polynucleotides in a form suitable for amplification. The polynucleotides in question may be the same as, or different from one another, in different samples and hence in different lanes of the cartridge.

Ex. 1002, 13:21–29; *see also id.* at 13:38–42 ("[T]he first microfluidic network is configured to amplify polynucleotides in the first sample, and . . . the second microfluidic network is configured to amplify polynucleotides in the second sample."). The '708 patent specification further teaches that the "sample inlets of adjacent lanes are reasonably spaced apart from one another to prevent any contamination of one sample inlet from another

sample when a user introduces a sample into any one cartridge," and describes an embodiment where "the sample inlets are configured so as to prevent inadvertent introduction of sample into a given lane after sample has already been introduced into that lane." *Id.* at 14:64–15:3.

Taken as a whole, these disclosures indicate that the multi-lane microfluidic cartridge claimed in the '708 patent is capable of analyzing a distinct sample in each lane, such that multiple different samples can be processed in the cartridge at the same time. This is achieved by associating a separate sample inlet with each sample lane.

Moreover, Petitioner's proposed construction merges the meaning of "channel" with "sample lane" or "lane" as those terms are used in the '708 patent. As Patent Owner notes, in the '708 patent specification, the terms "channel" and "sample lane" or "lane" are not used interchangeably, and instead refer to separate structures. PO Sur-Reply 3. In particular, the '708 patent specification teaches that a channel is an element of a microfluidic network, which in turn is an element of the sample lane. *See* Ex. 1002, 18:55–57 ("Channels of a microfluidic network in a lane of [a] cartridge typically have at least one sub-millimeter cross-sectional dimension."); *see also id.* at 14:48–52 ("Also shown [in Figs. 10A and 10B] is an ultrafast PCR reactor 210, which, as further described herein, is a microfluidic channel in a given sample lane that is long enough to permit PCR to amplify polynucleotides present in a sample.").

Finally, Petitioner's argument that Patent Owner equated "lane" and "flow channel" to overcome prior art during prosecution of the '708 patent is not persuasive. Petitioner directs us to an amendment in which the applicants added the phrase "multi-lane" to modify "microfluidic cartridge"

in the pending claims in response to a rejection over a reference called Wilding. Ex. 1005, 2–5. In that amendment, the applicants argued:

> The amplification device disclosed in Wilding is a single lane (flow channel) amplification device for conducting PCR. *See, e.g., Wilding*, paragraph [0039] and Figures 2 and 5. Thus, Wilding fails to disclose a "multi-lane microfluidic cartridge, each lane comprising a PCR reaction zone" as required by Claim 1. Furthermore, Wilding teaches a PCR reaction chamber with multiple sections, and if the two chambers are interpreted to be the same reaction zone, the device fails to satisfy the claim limitations that "the heat source maintains substantially uniform temperature throughout the PCR reaction zone" and that it "thermal cycles the PCR reaction zone."

*Id.* at 7.

The Federal Circuit has cautioned that "prosecution history comments cannot trump the plain language of the claims and the direct teaching of the specification." *Telecordia Techs., Inc. v. Cisco Sys., Inc.*, 612 F.3d 1365, 1375 (Fed. Cir. 2010) (citation omitted). As set forth above, the direct teaching of the specification here establishes that "lane" and "channel" refer to different structures. On its face, the applicants appear to use the phrase "single lane (flow channel)" only to characterize the device used in Wilding, which is consistent with Patent Owner's representation that the applicants were "simply using the terminology that Wilding itself uses ('flow channel') as short-hand for discussing the relevant features of the Wilding reference." PO Sur-Reply 3–4.[9] Furthermore, the applicants did not distinguish Wilding on the basis that a lane and a flow channel are actually the same structures, but instead argued that the *number* of such lanes or flow channels in the Wilding device did not satisfy the claim requirement of a "multi-lane

[9] A complete copy of the prosecution history, including Wilding, is not of record in this proceeding.

microfluidic cartridge." Accordingly, we find that, on this record, the applicants' remarks regarding Wilding are insufficient to overcome the direct teaching of the '708 patent, namely, that a "lane" and a "channel" are different structures.

In view of the foregoing, we construe the phrase "multi-lane microfluidic cartridge" to mean "a microfluidic cartridge comprising a plurality of sample lanes, each sample lane comprising a separate sample inlet and microfluidic network." The express language of the claims further requires that each lane also comprise a PCR reaction zone. Ex. 1002, 46:6–7 ("a multi-lane microfluidic cartridge, each lane comprising a PCR reaction zone"), 48:30–32 ("a multi-lane microfluidic cartridge, wherein each lane comprises a PCR reaction zone").

*C. Claims 1–6, 9, 10, 18–20, 23–25, 28, and 30–33*

Petitioner asserts that claims 1–6, 9, 10, 18–20, 23–25, 28, and 30–33 would have been obvious over the combined teachings of Zou I and McNeely or Pease, and relies on the Gale Declarations to support its assertions. Pet. 28–63; Pet. Reply 4–27. Patent Owner disagrees with Petitioner's assertions, and relies on the Northrup Declaration. PO Resp. 29–76; PO Sur-Reply 1–31.

*1. Overview of Zou I*

Zou I is directed to "a thermal cycler which permits simultaneous treatment of multiple individual samples in independent thermal protocols, so as to implement large numbers of DNA experiments simultaneously in a short time." Ex. 1008, at [57]. Zou I explains that "[t]he basic principle that governs the present invention is that the thermally conductive cycler chamber is thermally isolated from its surroundings except for one or more heat transfer members through which all heat that flows in and out of the

chamber passes," and "by placing at least one heating element in each transfer area, heat lost from the chamber can be continuously and precisely replaced, as needed." *Id.* at 3:55–62. Zou I teaches that "[t]his is achieved by placing, within the chamber, at least one temperature sensor per heating element and locating this sensor close to the heating elements," and, further, that the chamber can be rapidly cooled "by connecting the heat transfer areas to a heat sink through a high thermal conductance path." *Id.* at 3:62–67.

Figure 1a of Zou I is reproduced below.

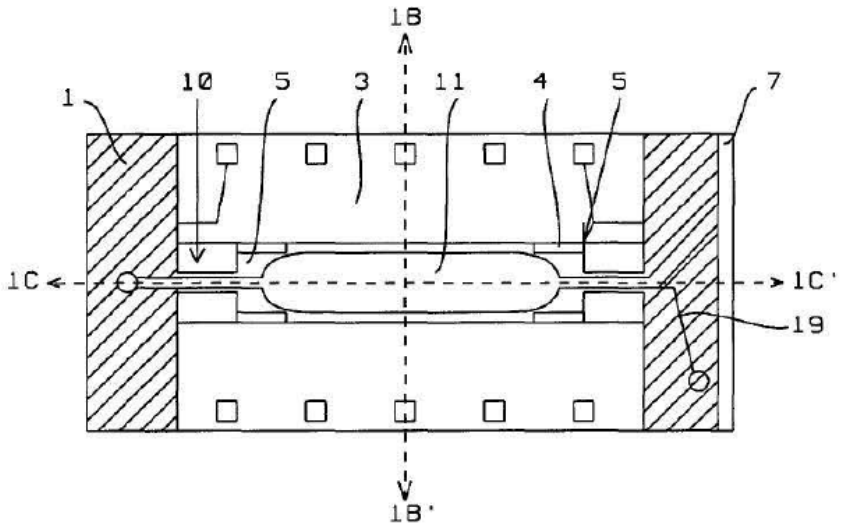



*FIG. 1A*

Figure 1a is a "plan view of a first embodiment of the invention" described in Zou I. *Id.* at 3:14–15. Chamber 11 "is connected at both ends to silicon frame 1 through monocrystalline silicon beams 10," with heaters 5 "at each end inside the heat transfer areas." *Id.* at 4:19–22. Each chamber also "contains at least one heat temperature sensor 4 for each heating element 5." *Id.* at 4:24–27. "Fluid bearing channels dispense fluid into and remove fluid from the chamber 11" through silicon beams 10. *Id.* at 4:28–30.

"[U]nprocessed fluid is stored in common reservoir 7, and is directed to chamber 11 through fluid bearing channel 31." *Id.* at 4:31–33.

Figure 4 of Zou I is reproduced below.

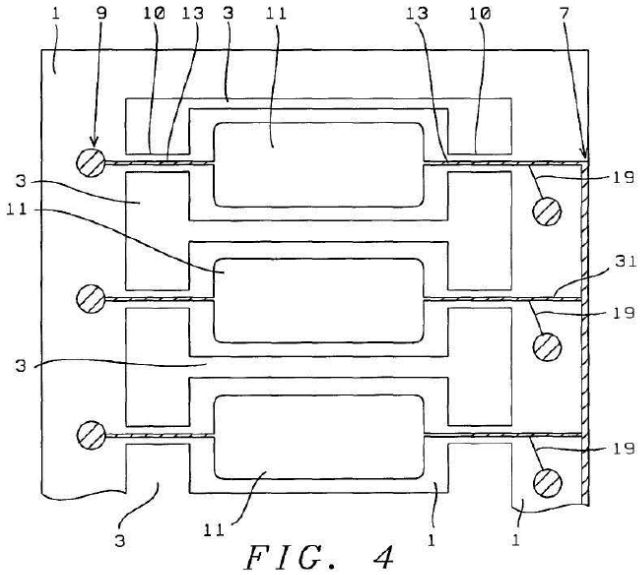



FIG. 4

Figure 4 depicts "an example of several chambers integrated to form a single multi-sample recycling unit." *Id.* at 5:4–6. "[I]ndividual chambers 11 are positioned inside the interior open area of silicon frame 1 and are connected to it through silicon beams 10," and, "except for these beams, the chamber is always thermally isolated from the frame by open space 3." *Id.* at 5:6–11.

*2. Overview of McNeely*

McNeely is directed to devices for processing microarray slides used in detection reactions involving biomolecules. Ex. 1009 ¶ 2. In particular, McNeely states that "the invention relates to a novel device for interfacing with a microarray slide to provide for the controlled delivery of fluids to selected regions of the slide surface as well as an instrument for performing simultaneous processing of a plurality of microarray slides," each of which is used in combination with an interface device. *Id.* McNeely teaches that the "microarray interface device can be connected to a substrate bearing a

microarray of spots made up of DNA, RNA, oligonucleotides, proteins, or other biomolecules," and "is adapted to for interfacing with glass microscope slides and similar planar substrates." *Id.* ¶ 17. "The interface device provides for the delivery of sample, reagents, rinses, and so forth, to selected portions of the array in a controlled manner." *Id.* According to McNeely, "[o]ne of the advantages of the inventive system is that it can be configured for use in processing a single slide, or it can be multiplexed to handle the processing of multiple slides." *Id.* ¶ 139.

Figure 1 of McNeely is reproduced below.

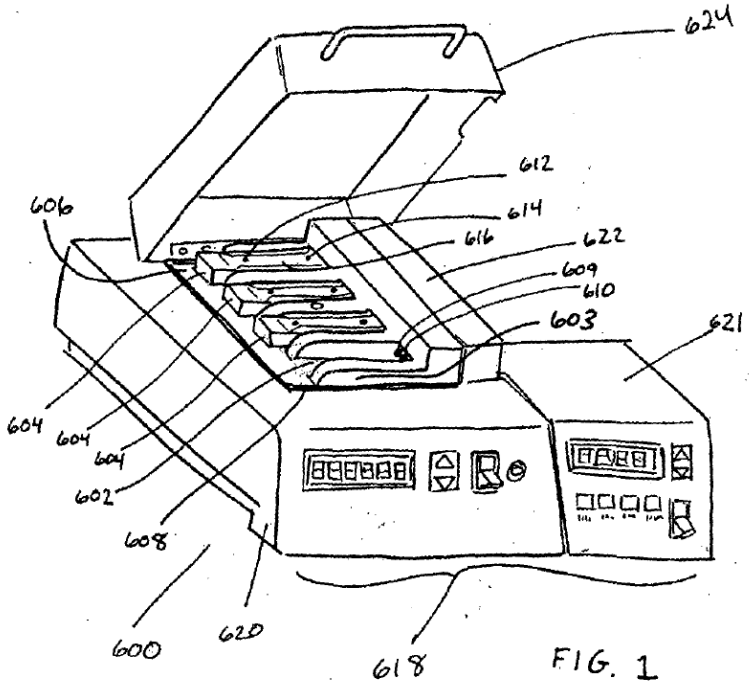



FIG. 1

Figure 1 "is a perspective view of an exemplary embodiment of a slide processing device" described by McNeely. *Id.* ¶ 35. Instrument 600 includes multiple bays 602, each of which is adapted to receive reaction device 604. *Id.* ¶ 82. Reaction device 604 "is made up of a microarray slide in combination with a microarray interface device." *Id.* "Bays 602 are

located in base 603 on heat block 606," and bays 602 and base 603 "are in thermal communication with heat block 606." *Id.* Sample, reagent, and wash liquids are introduced into each reaction device 604 via inlet hole 612, and air or liquid exits reaction device 604 through outlet hole 614. *Id.* "Inlet hole 612 and outlet hole 614 are formed in interface device 616, and are in fluid communication with a reaction chamber on the surface of the microarray slide." *Id.* Instrument 600 may "also include opaque lid 624 to keep the microarray slides from being exposed to light." *Id.* Lid 624 may also provide thermal insulation. *Id.*

McNeely Figures 5 and 6 are reproduced below.

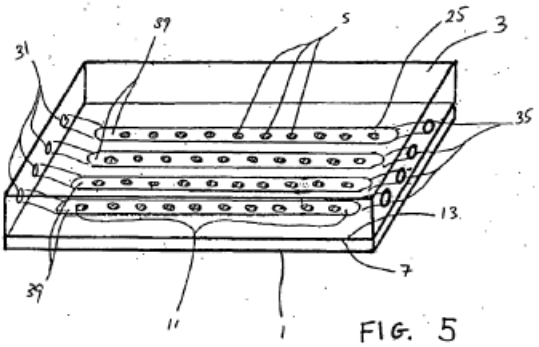



FIG. 5

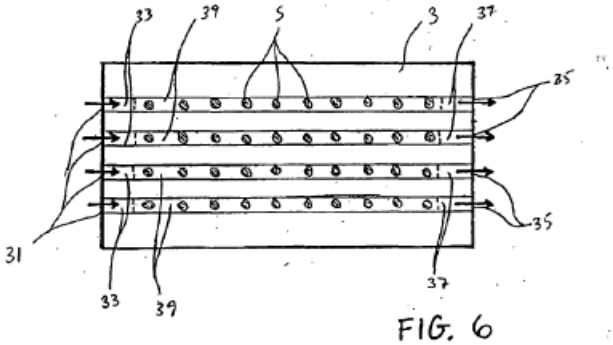



FIG. 6

Figure 5 is a perspective view of an interface device and microarray structure described by McNeely, and Figure 6 is a top view of the microarray structure depicted in Figure 5. *Id.* ¶¶ 39–40. In Figure 5, closed interface channels 39 are formed "when interface surface 13 is pressed

against surface 7 of microarray slide 1" and "grooves 25 are closed or covered by surface 7." *Id.* ¶ 95. Each interface channel 39 contains column 11 of spots 5. *Id.* "Interface inlets 31 and interface outlets 35 in interface device 3 provide access to interface channels 39." *Id.* The top view of interface device 3 shown in Figure 6 shows "spots 5 on microarray slide 1, interface channels 39, inlet channels 33, outlet channels 37, interface inlets 31, and interface outlets 35." *Id.* ¶ 96. In this embodiment, fluid samples may enter interface inlets 31, travel through interface channels 39 and over spots 5, and exit the interface device through interface outlets 35. *Id.*

McNeely teaches that the embodiment shown in Figures 5 and 6 "permits column 11 of spots 5 to be accessed individually," and "[c]ontinuous flow of samples, reagents, or other reactants may be provided to each column of spots." *Id.* ¶ 97. "Inlet channels 33 and outlet channels 37 may be closed channels formed in the interior of interface device 3," and "[i]t would also be possible to form inlet channels 33 and outlet channels 37 as open grooves in interface surface 13 of interface device 3, continuous with grooves 25, which would similarly form closed channels when interface device 3 was sealed to microarray slide 1." *Id.* McNeely further teaches that the interface device may include various types of sensors, including "optical sensors for real time detection of reactions occurring in the interface device." *Id.* ¶ 138. The interface device may also include "heating elements or other mechanism for regulating reaction conditions," and that such "heating elements may be used to perform thermo-cycling during PCR." *Id.*

*3. Overview of Pease*

Pease describes systems, including methods and apparatus, "for microfluidic processing of samples using a microfluidic device having an array of thin-film electronic devices." Ex. 1010 ¶ 35. Pease teaches that

"the array may include an arrangement of thermal control devices and associated thermal control features that enables independent temperature control of closely spaced regions of fluid disposed adjacent the array." *Id.* ¶ 40. Pease also teaches that thermal control zones "are isolated so that each zone may be adjusted independently to a different temperature," and "may correspond to regions under different fluid chambers and/or to different regions under one fluid chamber." *Id.* ¶ 48.

Pease describes an embodiment of a microfluidic system "for processing and analysis of samples, particularly samples containing nucleic acids." *Id.* ¶ 71. The system includes a control apparatus and an integrated cartridge that is configured to be electrically coupled to the control apparatus. *Id.* Figure 15 of Pease is reproduced below.

Fig. 15

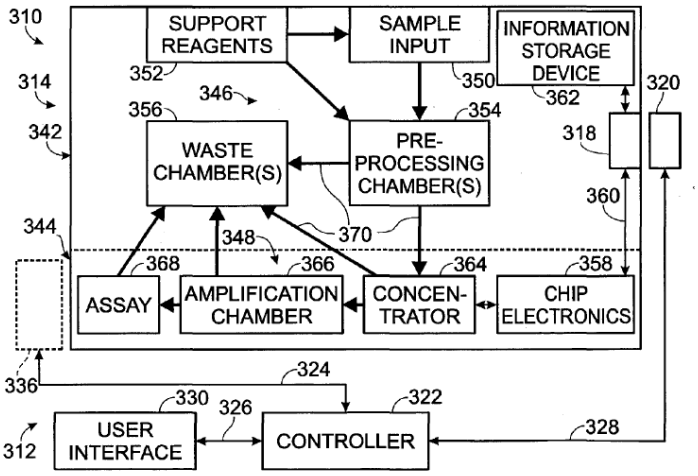



Figure 15 is a schematic view of the cartridge and control apparatus, "illustrating movement of fluid, sample, electricity, digital information, and detected signals" in one of Pease's embodiments. *Id.* ¶ 19. In order to control processing in the cartridge, "[c]ontrol apparatus 312 is configured to send and receive control signals to cartridge 314." *Id.* ¶ 72. Cartridge 314 can include detection electronics, which allows control apparatus 312 to

receive signals from cartridge 314 that are utilized to determine the assay result. *Id.* Additionally, control apparatus 312 "may include one or more optical, mechanical, and/or fluid interfaces with cartridge 314." *Id.* ¶ 76. For example, optical interface 336 may send light to and/or receive light from cartridge 314, and "may act as a detection mechanism having one or more emitters and detectors to receive optical information from" cartridge 314. *Id.*

"Assay portion 344 is configured for further processing of nucleic acid in fluid network 348 after nucleic acid isolation in fluid-handling portion 342," and "relies on electronics or electronic circuitry 358, which may include thin-film electronic devices to facilitate controlled processing of [the] nucleic acids." *Id.* ¶ 84. Amplification chamber 366 may be used to copy one or more target nucleic acids from among the concentrated nucleic acids, using an amplification reaction. *Id.* ¶ 90. Pease explains that "amplification may involve thermal cycling (for example, polymerase chain reaction (PCR) or ligase chain reaction (LCR))." *Id.* Optical interface 366 "may measure sample processing at any suitable position of assay portion 344," and "may include separate emitter-detector pairs for monitoring amplification of nucleic acids in amplification chamber 366, and for detecting binding and/or position of amplified nucleic acids after processing in assay chamber 368." *Id.* ¶ 92.

*4. Analysis*

Petitioner contends that "Zou I discloses much of the purported invention," and that "[t]he remaining elements, such as a detector, a processor coupled to the detector, and a receiving bay configured to receive a microfluidic cartridge, were standard features of integrated machines used for performing biochemical reactions such as PCR." Pet. 28 (citing

Ex. 1001 ¶¶ 49, 52–58, 115, 116). Petitioner contends that "[s]uch apparatuses were common by March of 2006," and that McNeely and Pease "disclosed two such machines." *Id.* Petitioner further contends that "a POSA would have been motivated to combine the multiplexing PCR unit of Zou I with a conventional integrated machine such as in McNeely or Pease, with a high expectation of success," and provides a number of reasons why a POSA would have been motivated to do so. *Id.* at 28–33.

Patent Owner argues in response that Zou I does not disclose a "multi-lane microfluidic cartridge, each lane comprising a PCR reaction zone." PO Resp. 30–35. Patent Owner also argues that "Petitioner fails to show a motivation to combine the references to teach or suggest" a "cartridge," "receiving bay," or "detector configured to detect the presence of an amplification product in the respective PCR reaction zone" as recited in claim 1, and that Petitioner does not explain "why or how the teachings [of the prior art] would have or could have been successfully combined." *Id.* at 38–55. We address these arguments in turn below.

*a) multi-lane microfluidic cartridge, each lane comprising a PCR reaction zone*

Each of the challenged claims requires a "multi-lane microfluidic cartridge, each lane comprising a PCR reaction zone" (Ex. 1002, 46:1–48:40), which we interpret to mean "a microfluidic cartridge comprising a plurality of sample lanes, each sample lane comprising a separate sample inlet and microfluidic network" and a PCR reaction zone (*see supra* § II.B). Petitioner contends that "Zou I discloses a multi-lane microfluidic unit" wherein "[e]ach lane includes an inlet, a PCR reaction chamber 11, and an exit reservoir 9." Pet. 34 (citing Ex. 1008, 4:28–5:21, Figs. 3 and 4; Ex. 1001 ¶ 129). Petitioner contends that "Zou I further teaches that PCR

can be carried out in each chamber 11." *Id.* (citing Ex. 1008, Abstract, 1:12–20, 2:49–54, 5:51–55, 8:30–35; Ex. 1001 ¶ 130).

Petitioner uses an annotated version of Zou I's Figure 4, shown below, to depict its contentions:

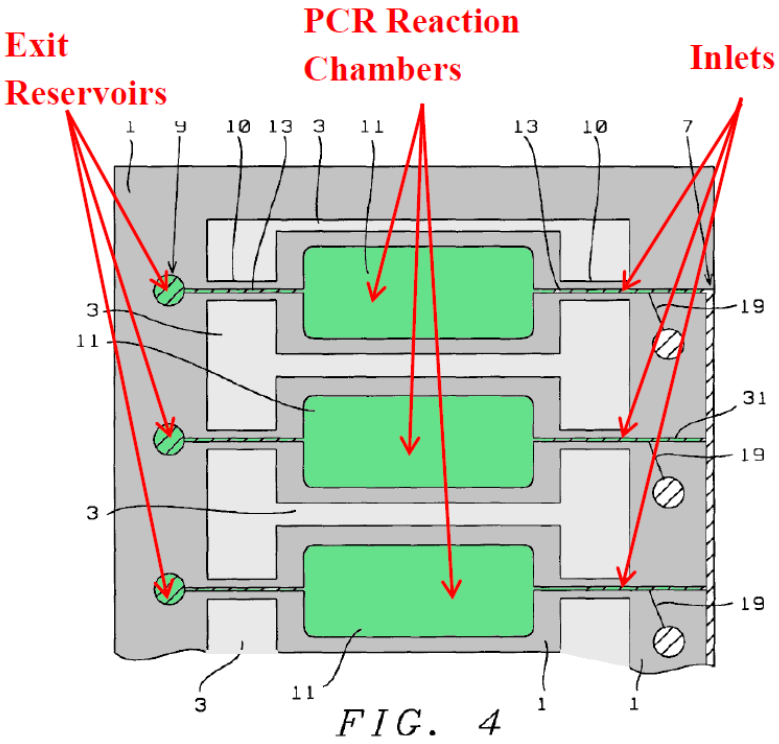



FIG. 4

*Id.* (citing Ex. 1001 ¶ 130). Figure 4 depicts "several chambers integrated to form a single multi-sample recycling unit" (Ex. 1008, 5:4–6), with Petitioner's annotations in the form of green shading to delineate the claimed PCR reaction zone, and arrows pointing to the features Petitioner contends comprise each lane of the claimed "multi-lane microfluidic cartridge," namely, the PCR reaction chambers, inlets, and exit reservoirs. Pet. 34.

Petitioner further contends that, "[t]o the extent that Zou I doesn't expressly disclose a cartridge, each of McNeely and Pease does." Pet. 35; *see also* Pet. Reply 8 n. 5 (Stating that "Zou I *could* be considered a cartridge itself" without explaining how or why, but that "Pease and

McNeely disclose cartridges." (emphasis added)). According to Petitioner, "McNeely discloses a multilane microfluidic cartridge that can be used to perform PCR on samples in the cartridge, with inlets and outlets for each lane" (Pet. 35 (citing Ex. 1009 ¶¶ 96, 97, 138, Figs. 5, 6; Ex. 1001 ¶ 131)), and "Pease also discloses a multilane microfluidic cartridge that can be used to perform PCR on samples in a cartridge, with plural separate fluid channels and chambers" (*id.* (citing Ex. 1010, Abstract et. seq.; Ex. 1001 ¶ 132)).

In response, Patent Owner argues that "Zou I does not disclose multiple separate microfluidic networks, but a single microfluidic network." PO Resp. 32 (emphasis omitted). In particular, Patent Owner argues that "Zou I has a single 'common reservoir 7' that directs fluid to individual chambers (11) through single channel (31)." *Id.* (emphasis omitted).

Patent Owner further argues that "Zou I does not disclose multiple lanes with separate inlets, but instead multiple chambers that share a single inlet." PO Resp. 33 (emphasis omitted). Patent Owner argues that reservoir 7 shown in Zou I's Figure 4 is "the inlet for all three chambers, as fluid is dispensed from that reservoir into each chamber." *Id.* at 34. Patent Owner also argues that "Petitioner offers no explanation or justification for why it identifies multiple inlets to chambers 11," when Zou I uses the term "inlet" to refer to "reservoir 7." *Id.* at 35 (citing Ex. 1008, 4:36, 6:12–15). According to Patent Owner, "an 'inlet' is a common term in both the '708 patent and Zou I, and would have been understood to refer to a location where sample is input." *Id.* (citing Ex. 2036 ¶ 173).

Petitioner argues in its Reply that "Zou I describes element 7 as 'inlet fluid source reservoir 7,'" and a "POSA would understand reservoir 7 is the source of the fluid for the inlets, not the inlet itself." Pet. Reply 5 (citing

Ex. 1008, 4:4; Ex. 1026 ¶ 25) (emphasis omitted). Patent Owner contends in its Sur-Reply that "Petitioners' so-called 'inlets' (valve 8 and channel 31) are within the chip in Zou I," and, "[c]onversely, a sample inlet in the '708 patent is 'a location where the sample is input into the cartridge.'" PO Sur-Reply 8 (citing Ex. 1008, 4:1–6, Figs. 3 & 4; Ex. 2036 ¶¶ 376–378; Ex. 1027, 156:2–9; Ex. 1002, 14:64–67) (emphasis omitted).

We have considered the arguments and evidence of record and determine that Zou I does not teach a multi-lane microfluidic unit under the proper claim construction. In particular, we find that Zou I does not teach a plurality of sample lanes wherein each sample lane comprises a separate sample inlet. We agree with Patent Owner that Zou I teaches that all of the lanes are associated with a single sample inlet, namely, common reservoir 7. PO Resp. 32–35; PO Sur-Reply 7–10. Patent Owner's annotated version of Figure 4 of Zou I is shown below:

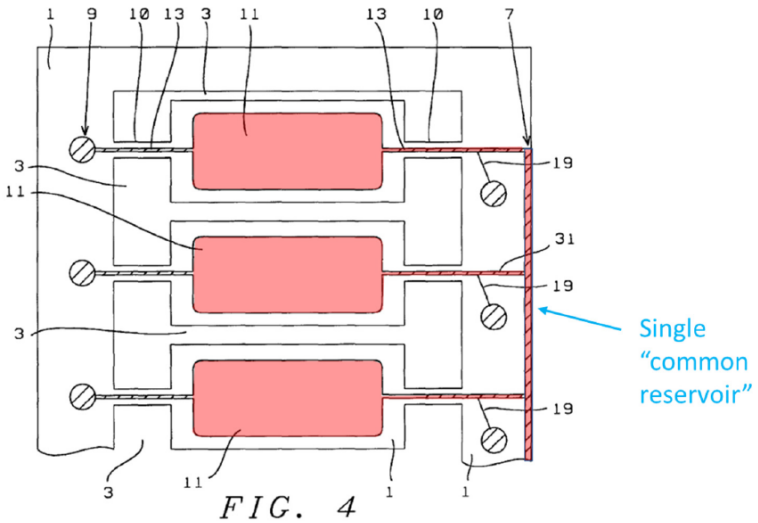



FIG. 4

PO Resp. 33 (citing Ex. 1008, Fig. 4, 4:30–33). Patent Owner annotates the "several chambers integrated to form a single multi-sample recycling unit" shown in Zou I's Figure 4 above by using red shading to show that "the PCR

reaction zones (chambers 11) and the common reservoir are in fluid communication with one another as a single fluidic network." *Id.* (citing Ex. 1008, 4:1–6).

Patent Owner's annotated Figure 4 is consistent with the teachings of Zou I. Zou I teaches "a fully integrated fluid dispensing and retrieval system" that "allows multiple chambers to share both a common heat sink as well as an inlet fluid source reservoir with both fluid flow and temperature being separately and independently controllable." Ex. 1008, 4:1–6. Zou I further teaches that "unprocessed fluid is stored in common reservoir 7 and is directed to chamber 11 through fluid-bearing channel 31," and that pressure valves 8 (not shown) "are placed at both ends of the chamber" in order to "prevent unintended entry of fluid into the chamber." *Id.* at 4:30–35, 4:43–45. We credit Dr. Northrup's testimony that

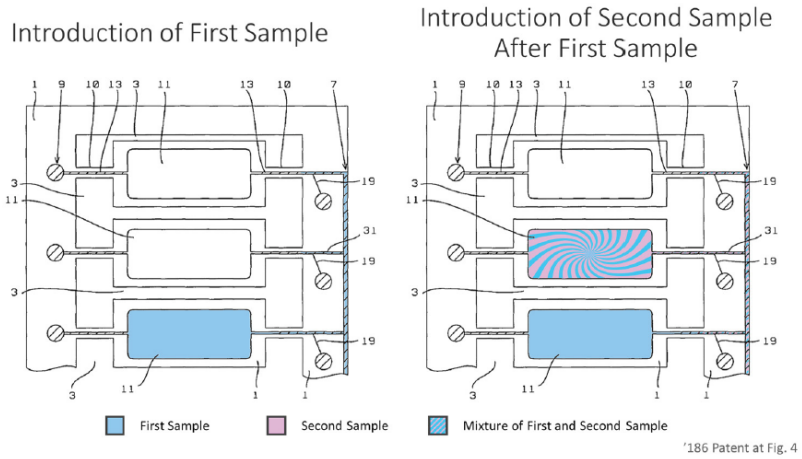
> [a]n "inlet" is a common term used in the '708 patent, Zou I, and understood in the art to refer to a location where sample is input. In Zou I, as the Zou I authors expressly stated, the "inlet" is a common reservoir that dispenses fluid to multiple chambers; Zou I Figure 4 does not include multiple inlets, each of which is associated with a separate lane.

Ex. 2036 ¶ 101 (emphasis omitted).

Moreover, Petitioner does not direct us to, nor do we discern, any teaching in Zou I that its microfluidic unit is capable of analyzing a distinct sample in each lane, such that multiple different samples can be processed in the cartridge at the same time. In that regard, we also credit Dr. Northrup's testimony that

> Zou I could not effectively function to analyze multiple separate samples independently. When a nucleic acid sample passes through a channel or container, it will contaminate that receptacle by leaving some nucleic acid behind. As illustrated in the further annotated Figure 4 of Zou [I] below, any second sample (pink)

> that passed through the common reservoir 7 of Figure 4 would be contaminated by the residue left by a first sample (blue), resulting in a mixture of both samples.




> A POSA would have understood that such cross-contamination would render the Figure 4 device unreliable, if not inoperable for its purpose.

*Id.* ¶¶ 104–105 (citing Ex. 1008, Figure 4 (depicting "several chambers integrated to form a single multi-sample recycling unit")).

We note that, in its Reply, Petitioner argues that "Zou I's Figure 5 shows an embodiment with at least four physically distinct fluid input locations." Pet. Reply 5–6 (citing Ex. 1008, Figure 4; Ex. 2012, 185:18–186:3; Ex. 1026 ¶ 28). In support of this argument, Dr. Gale testifies that

> [b]ased on the layout of the reaction chambers in Fig. 5 of Zou I and the layout of each reaction chamber from Fig. 4 of Zou I, there would be a maximum of 24 reaction chambers connected to one fluid reservoir if the reaction chambers were mirrored across the fluid reservoir, leading to a minimum of 4 physically distinct input ports.

Ex. 1026 ¶ 28. This argument is unpersuasive. Zou I does not discuss Figure 5 other than to say it "shows a full population of cycling chambers covering an entire wafer," and that it "shows how the sub-structure shown in FIG. 4 appears when full wafer 66 of silicon has been used to form multiple

chambers." Ex. 1008, 3:24–25, 5:11–13. In light of these limited disclosures in Zou I, Dr. Gale does not sufficiently explain why or how Zou I's Figure 5 discloses separate sample inlets for each sample lane, or that each sample lane in Figure 5 is associated with a separate sample inlet, as required by the claims of the '708 patent.

Petitioner also argues in its Reply that "it would have been obvious to modify Zou I's Figure 4" to have "physically distinct exterior sample input locations." Pet. Reply 7. In support of this argument, Dr. Gale testifies that drilling access holes in the glass cover of Zou I's microfluidic chip would have been "a common technique by March 2006," and "it would have been trivial for a POSA to drill individual ports through the glass cover of Zou I in order to provide physically distinct ports into each of Zou I's microfluidic lanes." Ex. 1026 ¶ 30. Neither Petitioner nor Dr. Gale sufficiently explain, however, why a POSA would have been motivated to make this modification, or how this modification would affect how Zou I's microfluidic chip functions. For example, neither Petitioner nor Dr. Gale address how such access holes would interact, if at all, with Zou I's common reservoir. *See* PO Sur-Reply 10 (citing Ex. 1008, 4:1–11, 4:30–32; Ex. 2036 ¶¶ 101–105; PO Resp. 32–33).

In an obviousness analysis, a sufficient reason must be shown as to why a POSA would have thought of combining or modifying the prior art to achieve the patented invention. *See Innogenetics, N.V. v. Abbott Labs.*, 512 F.3d 1363, 1374 (Fed. Cir. 2008). Here, Petitioner offers only the general proposition that drilling access holes into the glass cover of Zou I's microfluidic chip was a "common technique," but this does not provide a reason why a POSA would have been motivated to modify Zou I's microfluidic chip. Pet. Reply 7. Petitioner's argument and Dr. Gale's

testimony with respect to the modification of Zou I leaves an analytical gap that does not apprise us of why a POSA would have modified Zou I with access holes that would operate as separate sample inlets for each sample lane as required by the claims of the '708 patent.

Here, Petitioner attempts to imbue a POSA with the knowledge of the claimed invention, when no prior art reference, references of record, or other evidence conveys or suggests that knowledge. Petitioner's argument that a POSA would have modified Zou I in this way appears to be premised on Petitioner's knowledge of the '708 patent disclosure. This is improper hindsight reasoning. Petitioner needed to explain what would have led a POSA at the time of the invention to consider modifying Zou I to include a separate sample inlet with each sample lane. Petitioner failed to provide such an explanation. *See W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1553 (Fed. Cir. 1983) (In an obviousness analysis, we must "cast the mind back to the time the invention was made" and "occupy the mind of one skilled in the art who is presented only with the references, and who is normally guided by the then-accepted wisdom in the art.").

For these reasons, after considering Petitioner's and Patent Owner's positions, as well as their supporting evidence, we are not persuaded that Petitioner has demonstrated that Zou I teaches or suggests a multi-lane microfluidic unit. Petitioner does not rely on McNeely or Pease to remedy this deficiency in Zou I. Accordingly, we find that Petitioner has not established that the combined teachings of Zou I and McNeely or Pease teaches a "multi-lane microfluidic cartridge, each lane comprising a PCR reaction zone" as required by the challenged claims.

*b) Motivation to Combine*

Petitioner contends that a POSA "would have been motivated to combine the multiplexing PCR unit of Zou I with a conventional integrated machine such as in McNeely or Pease," with a reasonable expectation of success. Pet. 28–33. Petitioner characterizes Zou I as teaching a microfluidic PCR "unit," or "chip," but not a cartridge. *See, e.g.*, Pet. 29 ("Zou I suggests that its chip may be 'used in current macro thermal cycler machines'"), 34 ("Zou I discloses a multi-lane microfluidic unit"); Pet. Reply 11 ("a multi-lane microfluidic unit or chip like Zou I"), 13 ("use [Zou I's] chip with 'current macro thermal cycler machines'"), 15 ("Zou I's fully functional multi-lane microfluidic unit, virtually unaltered"). Thus, Petitioner does not dispute Patent Owner's assertion that Zou I discloses "a 'thermal cycler chip,' not a 'cartridge' – nor does it contain any reference to a cartridge." PO Sur-Reply 6 (citing Ex. 1008, 7:51–62, 8:45–63; PO Resp. 15–16, 30–31; Ex. 2036 ¶¶ 97–100, 165–166).

As to the cartridge requirement of the challenged claims, Petitioner relies on McNeely and Pease as teaching a cartridge as part of a "conventional integrated machine." Pet. 28–29. Specifically, Petitioner argues that "McNeely discloses a multilane microfluidic cartridge that can be used to perform PCR on samples in the cartridge" (*id.* at 35 (citing Ex. 1009 ¶¶ 96, 97, 138, Figs. 5, 6; Ex. 1001 ¶¶ 79–80, 131)), and that "Pease also discloses a multilane microfluidic cartridge that can be used to perform PCR on samples in a cartridge, with plural separate fluid channels and chambers" (*id.* (citing Ex. 1010, Abstract *et. seq.*; Ex. 1001 ¶ 132)). Petitioner argues that "a POSA would have been motivated to combine the multiplexing PCR unit of Zou I with a conventional integrated machine as in McNeely or Pease, with a high expectation of success," because: (1) Zou I

"teaches combining its microfluidic unit into existing machines suitable for performing biochemical reactions" (*id.* at 29 (citing Ex. 1001 ¶¶ 36–46, 118–121)); (2) "the combination would have provided the known benefit of integrating detection with the amplification reaction process" (*id.* at 29–30 (citing Ex. 1001 ¶¶ 50–53, 122); (3) the combination "would have predictably provided the necessary interfacing with the outside world" (*id.* at 30–31 (citing Ex. 1001 ¶¶ 123–124)); (4) "the combination would have predictably improved reproducibility, reliability, and safety" (*id.* at 31–32 (citing Ex. 1001 ¶¶ 125–126)); and (5) "combining Zou I to be operated by a standard machine such as disclosed by McNeely or Pease would have been no more than applying known techniques to yield predictable results" (*id.* at 32–33 (citing Ex. 1001 ¶¶ 88, 127)).

In its Reply, Petitioner further argues that a POSA would have had a reasonable expectation of success in combining the teachings of Zou I and McNeely or Pease because the level of ordinary skill in the art was high, the art was relatively advanced, and "[t]he combinations are straightforward – Zou I's fully functional multi-lane microfluidic unit, virtually unaltered and maintaining its 'basic principles of operation,' with Pease or McNeely's cartridge-based systems." Pet. Reply 15. Petitioner also argues that "using a microfluidic PCR chip like Zou I with a cartridge was routine and predictable by March 2006." *Id.* at 16 (citing Ex. 1026 ¶ 66; Ex. 1030, 846–847).

Patent Owner responds that Petitioner's arguments regarding motivation and reasonable expectation of success are conclusory and contradicted by the record evidence. PO Sur-Reply 17. Patent Owner asserts that "[t]he state of the art was early and aspirational" (*id.* (citing Ex. 2036 ¶¶ 25–42; Ex. 2018, 2121)), neither McNeely nor Pease teach how

to interface a generic chip with a cartridge, and "both experts agree that the proposed combinations would 'have to be designed' to 'match each other,' including design of 'the right interfaces,' 'heat sinks' and other components" (*id.* at 18 (citing Ex. 2068, 149:4–150:13; Ex. 2057, 170; Ex. 2002, 245–248, 259–261; Ex. 2058, 536; Ex. 2036 ¶ 99)). Patent Owner further asserts that "skilled artisans reported challenges in seeking to interface a PCR chip within a cartridge" with regard to placement of heaters and temperature uniformity. *Id.* (citing Ex. 1030, 845; Ex. 2002, 252; Ex. 2001, 16.5.1; Ex. 2023, 346–353). Patent Owner also argues that specific features of Zou I's chip do not support a motivation to combine, namely, the fragility of the monocrystalline silicon beams that connect each of Zou I's PCR reaction chambers to the frame. PO Resp. 41–42 (citing Ex. 1008, 4:17–21, Figs. 1B, 4; Ex. 2012, 44:18–22; Ex. 2036 ¶¶ 499–500); PO Sur-Reply 18–19 (citing Ex. 1031, 421–422; Ex. 2068, 180:19–181:10, 182:3–19, 284:18–286:22).

Having considered the complete trial record, we determine that Petitioner has failed to sufficiently demonstrate that the combination of Zou I and McNeely or Pease teaches multi-lane microfluidic cartridges, because Petitioner has failed to establish by a preponderance of the evidence that a POSA would reasonably have expected to be successful in combining Zou I's microfluidic chip with a cartridge as taught by McNeely or Pease. In order to demonstrate that the challenged claims are obvious, a petitioner must demonstrate "that a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so." *ActiveVideo Networks, Inc. v. Verizon Commc'ns, Inc.*, 694 F.3d 1312, 1327 (Fed. Cir. 2012) (quoting *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1361 (Fed. Cir. 2007)). A petitioner must

articulate "[1] how specific references could be combined, [2] which combination(s) of elements in specific references would yield a predictable result, or [3] how any specific combination would operate or read on the asserted claims." *Id.* at 1327–28.

Focusing on the parties' arguments pertaining to how Zou I and McNeely or Pease could be combined, which combination of elements in the references would yield a predictable result, and how the combination would operate or read on the challenged claims, we determine that the evidence on this record is not sufficient to show that a POSA could have had a reasonable expectation of success in attempting to combine the teachings of Zou I with McNeely or Pease. Although the Petition sets forth various rationales for why a person of ordinary skill would have had reason to combine the teachings of Zou I and McNeely or Pease, the rationales are general in nature and do not address any specific modification to either of the references. Pet. 28–33. The Petition includes a single reference to reasonable expectation of success, in a conclusory statement that "a POSA would have been motivated to combine the multiplexing PCR unit of Zou I with a conventional integrated machine such as in McNeely or Pease, with a high expectation of success." *Id.* at 28–29. The First Gale Declaration is similarly conclusory as to how Zou I and McNeely or Pease could be combined and does not elaborate on reasonable expectation of success. *See* Ex. 1001 ¶¶ 116–127. Such conclusory assertions, lacking factual substantiation, are insufficient for evaluating reasonable expectation of success as part of an obviousness determination. *Wasica Fin. GmbH v. Cont'l Auto. Sys., Inc.,* 853 F.3d 1272, 1286 (Fed. Cir. 2017).

As discussed above, Petitioner in its Reply argues that Pease teaches "a microfluidic 'chip' with multiple chambers for performing PCR, used in

cartridge 314," and that "McNeely shows various options combining its 'interface device' with a glass slide to create a cartridge 604." Pet. Reply 16 (citing Ex. 1010 ¶ 78; Ex. 1009, ¶¶ 82, 126–129,Figs. 2, 23–24, 30, 32; Ex. 1026 ¶ 65). Petitioner's assertion that "using a microfluidic PCR chip like Zou I as a cartridge was routine and predictable by March 2006," however, is based on Exhibit 1030, which Petitioner did not submit with the Petition. *Id.* (citing Ex. 1026 ¶ 66; Ex. 1030, 846–847).

Moreover, we find persuasive Patent Owner's argument that the development of microfluidic PCR devices was not routine and predictable by March 2006, but rather a very complex endeavor that presented challenges with regard to uniform heating, detection of small volume reactions, contamination, design and configuration of a microfluidic network, and functionally interfacing the reaction instrument with control machinery. PO Resp. 4–6, 50–55. Dr. Northrup provides factual support for Patent Owner's arguments, with reference to numerous contemporaneous publications in the field (*see, e.g.*, Ex. 2036 ¶¶ 29–47, 771–786; Exs. 2001, 2002, 2023, 2026, 2032, 2033), and persuasively explains that "[w]here PCR microfluidic devices are designed as chips, connecting these chips to heat sources or detection mechanisms, can be a complex task, particularly in view of the need to ensure that other functionalities (e.g. uniform temperature, optical detection, multiple reaction chambers, etc.) are not adversely affected." Ex. 2036 ¶ 39. Therefore, we credit Dr. Northrup's testimony that, in light of the state of the art in March 2006, a POSA would not reasonably have expected a combination of Zou I and McNeely or Pease to be successful, because of the particular challenges listed above. Ex. 2036 ¶¶ 771–786. Dr. Gale's testimony that interfacing a PCR chip with a cartridge, such as Zou I with McNeely and Pease, would require that they be

designed to match with each other, also supports that conclusion. Ex. 2068, 149:4–150:13.

Dr. Northrup also credibly explains why Zou I's teaching relating to integration into a micro total analysis system does not support the combination of Zou I's unit with the integrated machines described in McNeely and Pease. Ex. 2036 ¶¶ 507–511. In particular, Dr. Northrup explains that Zou I does not describe integrating its chip into a "total-analysis" cartridge-based system as asserted by Petitioner, but rather describes the possibility of integrating Zou I's PCR unit into a total analysis system on a single chip, i.e. combining Zou I's chip with another chip capable of providing other functionalities. *Id.* Additional evidence corroborates Dr. Northrup's opinion, which is unrebutted on this point. Ex. 2001.

Furthermore, we disagree with Petitioner's assertions that combining Zou I and McNeely or Pease to arrive at the claimed invention would have been "straightforward," and that "each of Zou I, Pease, and McNeely already disclosed functional cartridge devices for performing PCR" (Pet. Reply 15–17), because Dr. Northrup's credible testimony and the evidence of record contradicts those assertions as discussed above. We also find that Dr. Gale's opinions in the Second Gale Declaration that "a POSA would expect to be able to combine Zou I's microfluidic unit, virtually unaltered and including its thermally-isolated chamber structure" into a cartridge system (Ex. 1026 ¶¶ 67, 70) to be conclusory and not supported by the evidence of record. In particular, we note that Dr. Gale's statement that "Zou I's unit is more or less a cartridge itself" and "all that would be required to combine into Pease or McNeely would be potentially the addition of a basic cartridge housing" is unsupported by sufficient analysis or objective evidence. *Id.* ¶ 70. It is

also inconsistent with Dr. Gale's testimony that a POSA would have combined "Zou I's multi-sample PCR unit with a cartridge configured for an integrated machine," and his consistent usage of "unit" or "chip" (instead of "cartridge") to describe Zou I's device. Ex. 1001 ¶ 133; *see also id.* ¶¶ 76 ("Zou I further provides examples of a multi-lane microfluidic unit for conducting PCR on multiple samples."), 123 ("the cartridges of McNeely or Pease, would have predictably provided beneficial interfacing of the microfluidic chip of Zou I with the outside world"); 129 ("Zou I discloses a multi-lane microfluidic unit"); 137 ("Zou I discloses a unit with multiple PCR reaction zones 11"); Ex. 1026 ¶ 66 ("using a microfluidic PCR chip like Zou I with cartridge-based machines was routine and predictable by March 2006"). Furthermore, Dr. Gale does not address the evidence supporting Dr. Northrup's testimony regarding the complexity of connecting PCR microfluidic chips to heat sources or detection mechanisms discussed above. Thus, we would remain unpersuaded that Petitioner met its evidentiary burden of providing sufficient evidence to support its proposed combination even if the evidence and arguments from Petitioner's Reply had been set forth properly in the Petition.

Accordingly, after considering Petitioner's and Patent Owner's positions, as well as their supporting evidence, we are not persuaded that Petitioner has demonstrated that a POSA would have been motivated to combine the teachings of Zou I with McNeely or Pease as Petitioner contends, with a reasonable expectation of success in doing so.

*c) Conclusion*

For the foregoing reasons, we conclude that Petitioner has not demonstrated by a preponderance of the evidence that claims 1–6, 9, 10, 18–

20, 23–25, 28, 30–33 of the '708 patent would have been obvious over the combined teachings of Zou I and McNeely or Pease.[10]

*D. Claims 7, 8, 11–17, 21, 22, 26, 27, and 29*

Petitioner argues that: (1) claims 7 and 8 would have been obvious over the combined teachings of Zou I, McNeely or Pease, and Hsieh; (2) claims 11–17 would have been obvious over the combined teachings of Zou I, McNeely or and Zou II; (3) claims 21 and 22 would have been obvious over the combined teachings of Zou I and McNeely; (4) claims 26 and 27 would have been obvious over the combined teachings of Zou I , McNeely or Pease, and Duong; and (5) claim 29 would have been obvious over the combined teachings of Zou I, McNeely or Pease, and Chow. Pet. 3–4, 63–86. Each of claims 7, 8, 11–17, 21, 22, 26, 27, and 29 depend, directly or indirectly, from independent claim 1, and, therefore, require a "multi-lane microfluidic cartridge." Ex. 1002, 46:44–53, 46:60–47:21, 47:31–35, 48:6–11, 48:17–20. Thus, for the same reasons given above with respect to Petitioner's challenge of claim 1, we also conclude that Petitioner has not demonstrated by a preponderance of the evidence that 7, 8, 11–17, 21, 22, 26, 27, and 29 would have been obvious over the asserted prior art.

## III. PATENT OWNER'S MOTION TO EXCLUDE

Patent Owner moves to exclude Exhibits 1030 and 1032. Paper 44. We do not reach the merits of Patent Owner's Motion to Exclude because

[10] Patent Owner argues that objective indicia (namely, commercial success) support the nonobviousness of the challenged claims. PO Resp. 74–77. Because we find that Petitioner has not demonstrated that the claims would have been obvious over the asserted prior art, we need not address Patent Owner's evidence regarding objective indicia of nonobviousness.

our Decision does not rely on Exhibits 1030 and 1032. Accordingly, we dismiss Petitioner's Motion to Exclude as moot.

## IV. CONCLUSION

For the reasons given, we are not persuaded that Petitioner has shown by a preponderance of the evidence that claims 1–33 of the '708 patent would have been unpatentable based on the challenges presented in the Petition.

In summary:

| Claims | 35 U.S.C. § | Reference(s)/Basis | Claims Shown Unpatentable | Claims Not shown Unpatentable |
|---|---|---|---|---|
| 1–6, 9, 10, 18–20, 23–25, 28, 30–33 | 103 | Zou I, McNeely or Pease | | 1–6, 9, 10, 18–20, 23–25, 28, 30–33 |
| 7, 8 | 103 | Zou I, McNeely or Pease, Hsieh | | 7, 8 |
| 11–17 | 103 | Zou I, McNeely or Pease, Zou II | | 11–17 |
| 21, 22 | 103 | Zou I, McNeely | | 21, 22 |
| 26, 27 | 103 | Zou I, McNeely or Pease, Duong | | 26, 27 |
| 29 | 103 | Zou I, McNeely or Pease, Chow | | 29 |
| **Overall Outcome** | | | | 1–33 |

## V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that Petitioner has not shown by a preponderance of the evidence that claims 1–33 of the '708 patent are unpatentable;

FURTHER ORDERED that Patent Owner's Motion to Exclude (Paper 44) is *dismissed*; and

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

FOR PETITIONER:

Gary Speier
J. Derek Vandenburgh
Jonathan D. Carpenter
CARLSON, CASPERS, VANDENBURGH & LINDQUIST
gspeier@carlsoncaspers.com
dvandenburgh@carlsoncaspers.com
jcarpenter@carlsoncaspers.com

FOR PATENT OWNER:

Heather M. Petruzzi
Barish Ozdamar, Ph.D.
Christopher M. Cherry
WILMER CUTLER PICKERING HALE AND DORR LLP
Heather.Petruzzi@wilmerhale.com
Barish.Ozdamar@wilmerhale.com
Chris.Cherry@wilmerhale.com

Kerry S. Taylor
Maria V. Stout
Benjamin B. Anger
KNOBBBE, MARTENS, OLSON & BEAR, LLP
2kst@knobbe.com
2mvs@knobbe.com
2bba@knobbe.com