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Paper 8
Entered: July 16, 2019

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

QIAGEN NORTH AMERICAN HOLDINGS, INC.,
Petitioner,

v.

HANDYLAB, INC.,
Patent Owner.

Case IPR2019-00490
Patent 8,323,900 B2

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

HEANEY, *Administrative Patent Judge.*

DECISION
Institution of *Inter Partes* Review
35 U.S.C. § 314(a)

I. INTRODUCTION

QIAGEN North American Holdings, Inc. ("Petitioner") filed a Petition to institute an *inter partes* review of claims 1–22 of U.S. Patent No. 8,323,900 B2 ("the '900 patent," Ex. 1003). Paper 1 ("Pet."). HandyLab, Inc. ("Patent Owner") filed a Preliminary Response. Paper 5 ("Prelim. Resp.").

Institution of an *inter partes* review is authorized by statute when "the information presented in the petition . . . and any response . . . shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314; *see* 37 C.F.R. § 42.4. Upon consideration of the Petition, the Preliminary Response, and the evidence of record, we determine that Petitioner has established a reasonable likelihood of prevailing with respect to the unpatentability of at least 1 claim of the '900 patent. Accordingly, we institute an *inter partes* review of claims 1–22 of the '900 patent.

A. Related Proceedings

Petitioner indicates that there are no related matters. Pet. 1. Patent Owner identifies *QIAGEN North American Holdings, Inc. v. HandyLab, Inc.*, Case IPR2019-00488, which concerns U.S. Patent No. 7,998,708 ("the '708 patent"), as a related matter. Paper 3, 1.[1] We issue our decision instituting trial in IPR2019-00488 concurrently with this decision.

B. The '900 Patent

The '900 patent, titled "Microfluidic System for Amplifying and Detecting Polynucleotides in Parallel," is directed to "a system and related

[1] Petitioner indicates that the '900 patent issued from the same application as the '708 patent. Pet. 7.

methods for amplifying, and carrying out diagnostic analyses on, polynucleotides (e.g., a DNA, RNA, mRNA, or rRNA) from biological samples." Ex. 1003, 4:4–7. 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 4:14–20. The system optionally "can display the results on a graphical user interface." *Id.* at 4:20–21.

The '900 patent's Figure 1 is reproduced below.

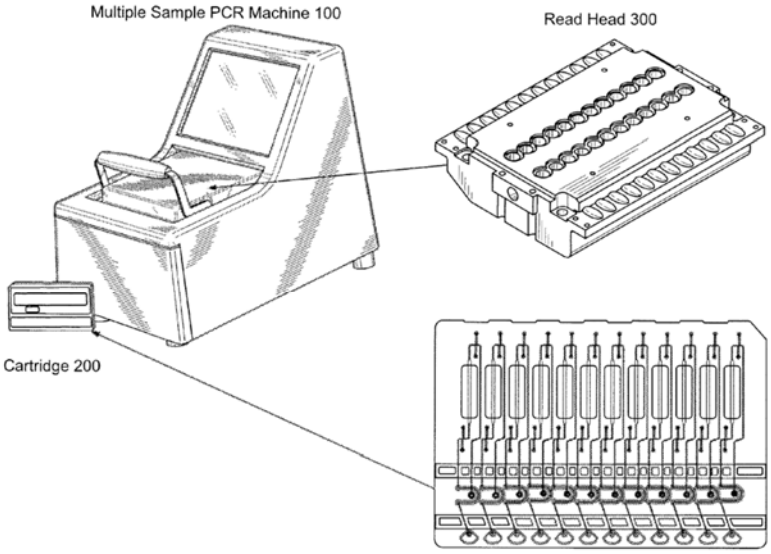

FIG. 1

Figure 1 is "a perspective view of an exemplary apparatus 100" described by the '900 patent. *Id.* at 4:33–34. Apparatus 100 includes read head 300 "that contains detection apparatus for reading signals from cartridge 200." *Id.* at 4:38–39. Apparatus 100 "is able to carry out real-time PCR on a number of samples in cartridge 200 simultaneously." *Id.* at 4:43–45. Cartridge 200

contains multiple sample lanes, and the '900 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 4:40–41, 4:45–46.

The '900 patent's Figure 3 is reproduced below.

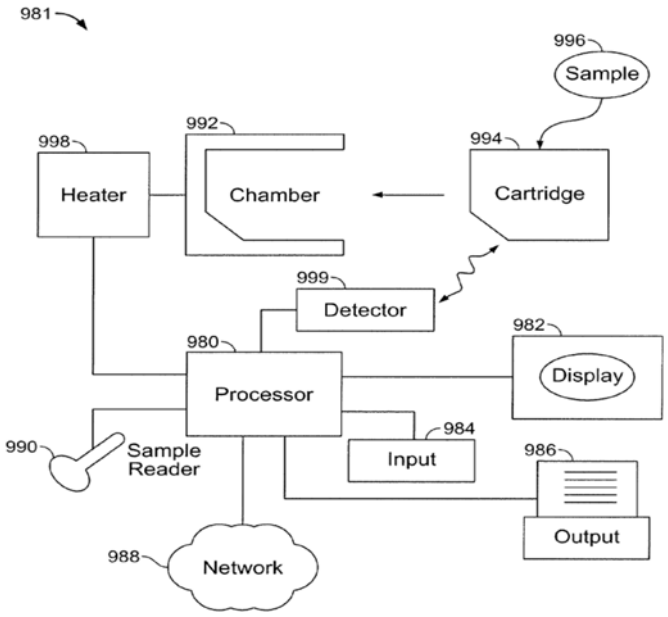

FIG. 3

Figure 3 is a "schematic overview of a system 981 for carrying out the analyses described" in the '900 patent. *Id.* at 4:59–62. 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 4:67–5:3. 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 5:5–19, 6:6–7.

System 981 "is configured to operate in conjunction with a complementary cartridge 994, such as a microfluidic cartridge." *Id.* at 6:8–10. 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 6:12–17. 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 6:18–19, 6:39–43.

Processor 980 "is also configured to receive signals from and control a detector 999 configured to detect a polynucleotide sample in one or more individual sample lanes, separately or simultaneously." *Id.* at 7:36–39. 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 7:45–50.

The '900 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 8:1–4. According to the '900 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 8:9–15.

C. Challenged Claims

Petitioner challenges claims 1–22 ("the challenged claims") of the '900 patent. Claims 1, 7, and 20 are independent. Claim 1 is representative and is reproduced below.

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

Ex. 1003, 46:4–20.

D. The Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–22 of the '900 patent on the following grounds:

Reference(s)	Basis	Challenged Claim(s)
Zou I[2] and McNeely[3] or Pourahmadi[4]	§ 103	1–8, 12, 14, 15, 17, 19–22
Zou I, McNeely or Pourahmadi, and Zou II[5]	§ 103	9–11, 13
Zou I, McNeely or Pourahmadi, and Chow[6]	§ 103	18
Zou I, McNeely or Pourahmadi, and Duong[7]	§ 103	16

Petitioner relies on the Declaration of Bruce K. Gale, Ph.D. ("Gale Declaration," Ex. 1001) in support of its contentions. Patent Owner relies on the Declaration of Michael G. Mauk, Ph.D. ("Mauk Declaration," Ex. 2005) in support of its Preliminary Response.

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. 7. Patent Owner does not dispute Petitioner's proposed definition at this stage of the proceeding. Prelim.

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[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 2002/0055167 A1, published May 9, 2002 (Ex. 1015).
[5] U.S. Patent No. 6,762,049 B2, issued July 13, 2004 (Ex. 1011).
[6] U.S. Patent No. 5,955,028, issued Sept. 21, 1999 (Ex. 1014).
[7] WO 01/54813 A2, published Aug. 2, 2001 (Ex. 1013).

Resp. 4. Accordingly, for purposes of this Decision, we adopt Petitioner's assessment of the level of ordinary skill in the art, 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. 2011).

B. Claim Interpretation

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)).

Petitioner proposes a construction for the term "contact heat source" in dependent claims 8–13. Pet. 6–7. Patent Owner responds that construction of "contact heat source" is not necessary at this stage of the proceeding. Prelim. Resp. 4. Based on the record before us, for purposes of

this Decision, we determine that no claim term requires explicit construction.

C. Obviousness over Zou I and Pourahmadi

Petitioner contends that the combined teachings of Zou I and Pourahmadi teach or suggest each limitation of claims 1–8, 12, 14, 15, 17, and 19–22. Pet. 33–40. 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, multiple microfluidic cartridges, and a plurality of receiving bays each configured to receive one of the cartridges, were standard features of integrated machines used for performing biochemical reactions such as PCR." *Id.* at 26 (citing Ex. 1001 ¶¶ 116, 313–315, 319–321). Petitioner also 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 Pourahmadi, with a reasonable expectation of success. *Id.* at 27–32.

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 each 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.

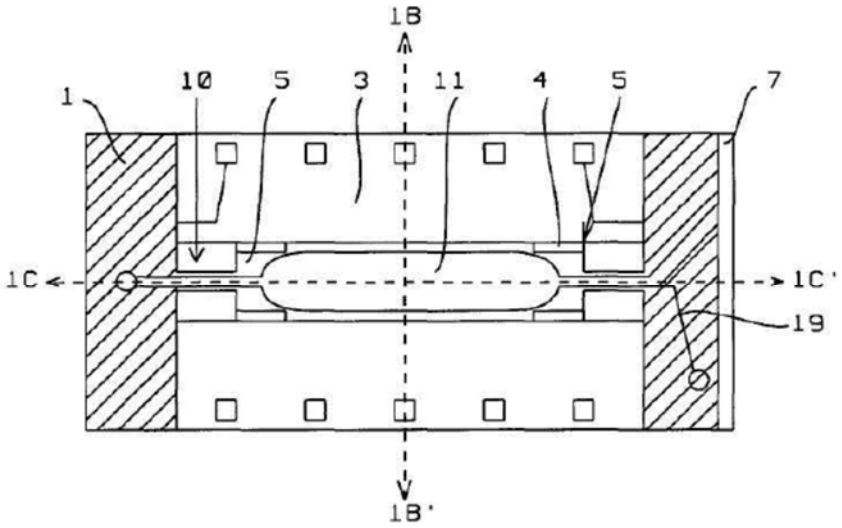

FIG. 1A

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 chamber 11 through silicon beams 10. *Id.* at 4:28–30. Unprocessed fluid is stored in common reservoir 7, and then directed to chamber 11 through fluid bearing channel 31. *Id.* at 4:31–33.

Figure 4 of Zou I is reproduced below.

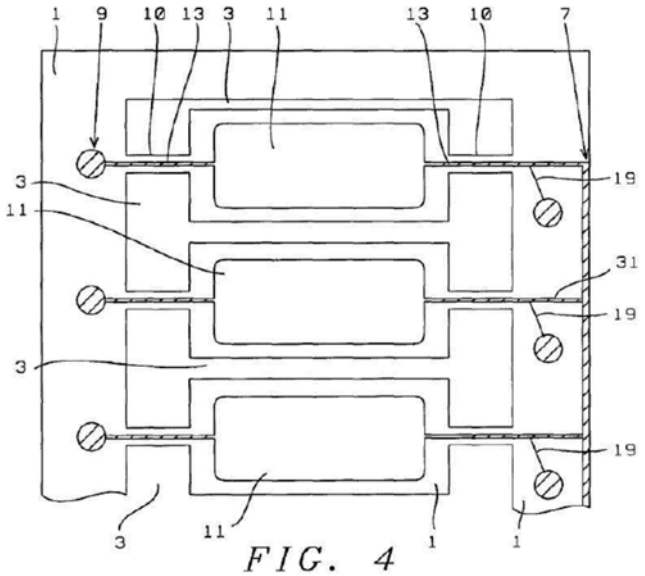

FIG. 4

Figure 4 depicts "an example of several chambers integrated to form a single multi-sample recycling unit." *Id.* at 5:4–6. Individual 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 Pourahmadi

Pourahmadi describes an instrument with multiple microfluidic cartridges for performing various operations, such as PCR, on a fluid sample. Ex. 1010 ¶¶ 21, 43, 48. Pourahmadi teaches that the instrument may include a processor for controlling the operation of each cartridge, and that the processor is connected to various sensors in the cartridge, such as temperature sensors. *Id.* ¶ 64. The processor is programmed to receive and record temperature data, and provides thermal control of the sample to achieve the desired temperature for a particular stage of reaction. *Id.* ¶ 125, 129. Alternatively, thermal control may be achieved by transferring the

sample among different reaction regions having different, constant temperatures. *Id.* ¶ 125. The processor "will typically include programming for instructing the delivery of appropriate current for raising and lowering the temperature" of cartridge regions in order to carry out "predetermined time/temperature profiles, e.g., thermal cycling for PCR, and the like." *Id.* ¶ 129. Pourahmadi further teaches

> In addition to sensors for monitoring temperature, the cartridge may contain sensors to monitor the progress of one or more of the operations of the device. For example, optical sensors and pressure sensors may be incorporated into one or more regions to monitor the progress of the various reactions, or within flow channels to monitor the progress of fluids or detect characteristics of the fluids ….

Id. ¶ 130.

Figure 2 of Pourahmadi is reproduced below.

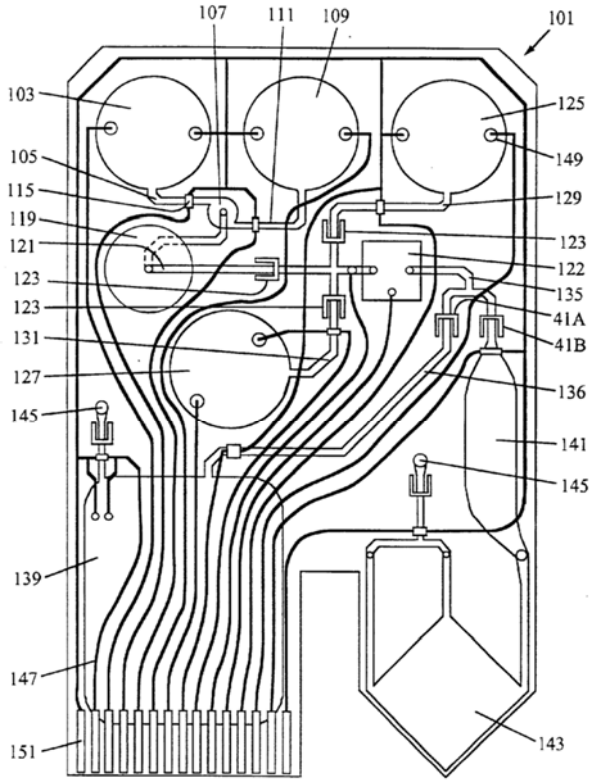

FIG. 2

Figure 2 depicts an example of a cartridge according to an embodiment of Pourahmadi. *Id.* ¶ 48. The cartridge is designed to process a fluid sample and amplify nucleic acids, such as by PCR, and includes a sample flow path extending from inlet port 103 through reagent mixing chamber 107 and lysing chamber 119. *Id.* ¶¶ 48–49. The sample flow path also includes flow-through component 122 which Pourahmadi describes as a microfabricated chip comprising an array of columns for capturing analyte as the sample flows through the chip. *Id.* ¶ 50. Following capture in the flow-through component, the analyte is released into elution fluid that flows through reagent chamber 141 which contains PCR reagents, and then flows into reaction chamber 143 for PCR amplification. *Id.* ¶¶ 53–54.

3. Claims 1–8, 12, 14, 15, 17, and 19–22

Independent claims 1, 7, and 20 recite, among other elements, that the heat source "maintain[s] a substantially uniform temperature throughout the PCR reaction zone during each cycle." Ex. 1003, 46:11–15, 55–57, 48:25–27. Petitioner contends that Zou I meets this limitation because it "teaches the importance of achieving temperature uniformity inside each reaction chamber when conducting PCR," and also that the heat source thermal cycles the PCR reaction zone to carry out PCR on a polynucleotide-containing sample in the PCR reaction zone. Pet. 37 (citing Ex. 1001 ¶¶ 345–347; Ex. 1008, Abstract, 1:18–31, 2:50–54, 61–62, 4:8–11, 8:25–35). Petitioner further argues that a person of ordinary skill in the art "would have been motivated to maintain a substantially uniform temperature throughout the PCR reaction zone during each cycle," because it was known that those conditions "increased efficacy and accuracy of the PCR process." *Id.* (citing Ex. 1001 ¶ 348; Ex. 1011, 5:2–4; Ex. 1016, 13:39–44, 14:1–9).

Patent Owner responds that Zou I does not disclose this limitation, but merely indicates testing for temperature uniformity at a single static temperature. Prelim. Resp. 29 (citing Ex. 1008, 8:25–30). Patent Owner further argues that Petitioner fails to explain how a person of ordinary skill in the art would have modified Zou I in order to maintain a substantially uniform temperature during each cycle. *Id.* at 30.

We are persuaded, based on the record before us, that Petitioner has established sufficiently at this stage of the proceeding that a person of ordinary skill in the art would have been motivated to maintain a substantially uniform temperature throughout Zou I's PCR reaction zone during each cycle. We find unpersuasive Patent Owner's argument that Petitioner "concocts its own rationale, absent in any prior art teaching" (Prelim. Resp. 30), to satisfy this claim limitation. As discussed above, Petitioner relies on Zou I as teaching the importance of achieving temperature uniformity inside a PCR reaction chamber, and further relies on additional references (Exs. 1011 and 1016) as demonstrating that the desirability of achieving thermal uniformity during temperature cycling in PCR was known. Patent Owner does not address these references, and the record before us indicates that they support Petitioner's assertion. Further, to the extent Patent Owner asserts that a person of ordinary skill in the art would have been unable to achieve temperature uniformity during each cycle, in view of Zou I's teaching of the desirability of temperature uniformity in a single cycle, at this stage of the proceeding, we must view disputed facts in a light most favorable to Petitioner. 37 C.F.R. § 42.108(c). We will resolve the dispute, if necessary, after consideration of the full trial record.

Claims 1 and 7 further recite "a processor coupled to the detector and the heat sources, configured to control heating of one or more PCR reaction zones by the heat sources." Ex. 1003, 46:18–20. Petitioner contends that Pourahmadi discloses this element because "Pourahmadi's instrument 211 may include a processor 'for controlling the operation of the cartridge 101,'" "the processor controls heat sources to supply the heat for the thermal cycling required for PCR reactions" and "[t]he processor is also connected to various 'sensors' contained in the system, such as the optical detectors." Pet. 39–40 (citing Ex. 1001 ¶ 353; Ex. 1015 ¶¶ 21, 64, 123, 125, 129–131). Petitioner further argues that even if Pourahmadi does not expressly disclose that the processor controlling the heat sources is also coupled to the detector, a person of ordinary skill would have been motived to incorporate this feature, because

> coupling a processor to both a detector and the heat sources was a known feature and would have predictably provided the benefits of (i) allowing a user to access information from both the heat sources and detector using the same interface, and (ii) allow feedback between the detected assay response and control of the heat sources.

Id. at 40 (citing Ex. 1001 ¶ 355; Ex. 1021 ¶¶ 15, 19).

Patent Owner responds that Pourahmadi does not disclose that its processor is coupled to an optical sensor incorporated in the cartridge, for control of heating in its single reaction chamber. Prelim. Resp. 41. Patent Owner further asserts that Pourahmadi does not disclose how to control or monitor real-time detection of reactions anywhere in the cartridge, much less in the reaction chamber. *Id.*

We are persuaded, based on the record before us, that Petitioner has shown sufficiently at this stage of the proceeding that a person of ordinary skill would have been motivated to combine the teachings of Zou I and Pourahmadi to arrive at the processor limitation. Zou I supports Petitioner's assertion that it teaches a processor configured to control heating of one or more PCR reaction zones in a microfluidic unit (Ex. 1008, 7:63–8:17, 8:45–63), and Pourahmadi teaches processor control of heaters for thermal cycling in PCR reactions. Ex. 1015 ¶¶ 123–131. Although Petitioner acknowledges that Pourahmadi does not expressly disclose that the processor controlling the heat sources is also coupled to a detector configured to detect the presence of an amplification product, Petitioner provides a rationale, with evidentiary support, for why a person of ordinary skill in the art would have incorporated this feature. Pet. 40 (citing Ex. 1021 ¶¶ 15, 19). We have considered Patent Owner's arguments and do not find them persuasive on this record, because they do not address Petitioner's evidence (Ex. 1021) that coupling a processor to both a detector and to heat sources was a known feature. Further, Patent Owner's argument that Pourahmadi does not describe how to monitor real-time detection of reactions is contrary to Pourahmadi's disclosure, which teaches, for example "detection of fluid presence (by detecting changes in optical transmittance), and … monitoring of chemical reactions …." Ex. 1015 ¶ 118.

Petitioner also contends that a person of ordinary skill in the art would have been motivated to combine the multiplexing PCR unit of Zou I with a conventional integrated machine such as in Pourahmadi, with an expectation of success, at least because: (1) Zou I "teaches combining its microfluidic chip into existing machines suitable for performing biochemical reactions,"

and Pourahmadi's machine is "similar to the 'macro thermal cycler' or 'total analysis' systems that Zou I suggested;" (2) the combination would have predictably provided the ability to process large numbers of PCR samples simultaneously in a short time, which Zou I expressly identifies; (3) the combination would have predictably improved the versatility of the machine by allowing processing PCR samples to be performed asynchronously; (4) the combination "would have provided the known benefit of integrating detection with the amplification reaction process," which "would have predictably allowed real-time detection of amplification" and "could be used to improve the quality and accuracy of PCR amplification;" (5) "the combination, and in particular the cartridges of . . . Pourahmadi, would have predictably provided the necessary interfacing with the outside world;" (6) "the combination would have predictably improved reproducibility, reliability, and safety;" and (7) modifying Zou I to be operated by a standard machine such as disclosed by Pourahmadi would have been no more than applying known techniques to yield predictable results." *Id.* at 28–32.

Patent Owner responds that Petitioner does not establish that a person of ordinary skill would have been motivated to combine Zou I with Pourahmadi and have a reasonable expectation of success in doing so. Prelim. Resp. 46–61. Patent Owner argues that "[t]echnical constraints inherent in [Zou I's] thermal cycler would have dissuaded a person of ordinary skill from modifying [Zou I's] system to perform optical detection of an amplification product within [Zou I's] chambers." *Id.* at 46. In that regard, Patent Owner argues that Zou I's thermal cycler is made of a silicon substrate, which "is not transparent, often limiting the application of real-time optical detection to the PCR microfluidic devices." *Id.* at 47 (emphasis

omitted) (quoting Ex. 2002, 247). Patent Owner also argues that a person of ordinary skill would have recognized that the glass top sheet applied over Zou I's silicon chambers creates "substantial impediments to optical detection of an amplification product in" Zou I's chambers. *Id.* (citing Ex. 2005 ¶¶ 42–43). According to Patent Owner, "Petitioner glosses over the practical impediments" the combination of Zou I and Pourahmadi "would face, and never addresses the ways in which silicon would optically interfere with efforts to detect an amplification product within" Zou I's chambers. *Id.* at 49. Patent Owner further argues that Petitioner never proposes experimental designs to address these impediments, and therefore fails to explain with particularity its grounds for obviousness. *Id.* (citing 35 U.S.C. § 312(a)(3)). Patent Owner also argues that Petitioner fails to consider the effect Zou I's glass top sheet would have in creating optical cross-talk between reaction chambers, and does not explain how Zou I could be combined with a multi-chamber detector. *Id.* at 50–51.

Patent Owner further argues that a person of ordinary skill in the art would have been dissuaded "from modifying Zou I's thermal cycler to attempt to detect an amplification product in chamber of Zou's thermal cycler" (*id.* at 53 (citing Ex. 2005 ¶ 59)) because Zou I teaches that physical volume of its reaction chamber should be "kept to a minimum" and it was known that reducing fluid volume in the chamber would reduce emission signal levels. *Id.* at 51–52 (citing Ex. 1008, 5:18–21). Patent Owner relies on an additional reference, Zou's Article (Ex. 2001),[8] as disclosing the experimental set up, and specifically the chamber dimensions, used in Zou I.

[8] Quanbo Zou et al., *"A Micromachined Integratable Thermal Reactor,"* International Electron Devices Meeting Technical Digest (2001) (Ex. 2001).

Id. at 52 (citing Ex. 2001, 16.5.2); *see also* Prelim. Resp. 8–10). Patent Owner further relies on the '900 patent specification to argue that an amplification signal from a chamber of Zou I's dimensions would be faint, and thus "would exacerbate the issue of an already weak emission signal due to light absorption by the silicon substrate." *Id.* at 52–53 (citing Ex. 1003, 37:9–11, 40–42, 62–65).

We have considered these arguments raised by Patent Owner, and do not find them to be persuasive on this record. For example, Patent Owner argues that the size of Zou I's reaction chamber would have dissuaded a person of ordinary skill from modifying Zou I because the amplification signal from such a small chamber would be too weak. We understand Petitioner, however, to be relying on Pourahmadi as teaching optical detection of the amplification signal. *See* Pet. 38–39. Thus, Patent Owner's argument based solely on Zou I's amplification signal, without consideration of the capability of Pourahmadi's optical detector, does not fully respond to Petitioner's challenge. Although Patent Owner does raise issues that will benefit from further development during trial, we are persuaded based on the current record that Petitioner has established a reasonable likelihood of prevailing in showing obviousness of the challenged claims.

Patent Owner further responds to each of the seven reasons that Petitioner argues would have led a person of ordinary skill to combine Zou I with Pourahmadi. *Id.* at 54–61. For example, Patent Owner argues that each of Petitioner's asserted second and third reasons to combine Zou I with Pourahmadi (i.e., providing the ability to process large numbers of samples simultaneously, or asynchronously) "fails to address the practical realities associated with the proposed combinations" because Zou I's thermal cycler

"is not a 'multi-sample PCR unit' at all, because a **single fluidic sample** is introduced into the Zou thermal cycler and then directed to each chamber 11 through a fluid-bearing channel 31." *Id.* at 56 (citing Ex. 1008, 4:3–6, 31–33; Fig. 4). As another example, Patent Owner argues that Petitioner's contention that the combination of Zou I and Pourahmadi would have provided the known benefit of integrating detection with the amplification process "presupposes that a POSA may have attempted any detection, much less real-time detection, of an amplification product in [Zou I's] reaction chambers" and a person of ordinary skill would not have been motivated to use Pourahmadi's detector because its detector is associated with a single reaction chamber in a cartridge. *Id.* at 56–57.

We have considered these and other arguments raised by Patent Owner, but do not consider Patent Owner's arguments on the whole to be persuasive on this record. For example, Patent Owner's argument against combining Zou I and Pourahmadi does not acknowledge that Zou I also expressly states "The invention describes a thermal cycler which permits simultaneous treatment of multiple individual samples in independent thermal protocols …." Ex. 1008, Abstract. Further, Patent Owner does not explain its assertion that a person of ordinary skill would not combine Pourahmadi's detector with Zou I, simply because Pourahmadi has a single reaction chamber. Thus, we are persuaded, based on the current record, that Petitioner has established a reasonable likelihood of prevailing on its assertion that the challenged claims would have been obvious over the combined teachings of Zou I and Pourahmadi. The parties will have the opportunity to further develop these facts and arguments during trial, and the Board will evaluate the fully-developed record at the close of the evidence.

In particular, we encourage the parties to address, in subsequent briefing, Patent Owner's assertions that a POSA would not have had a reasonable expectation of success in achieving the claimed invention by combining the disclosures of Zou I and Pourahmadi.

4. Claims 9–11, 13, 16, and 18

Petitioner contends that dependent claims 9–11, 13, 16, and 18 would have been obvious over different combinations of Zou I, Pourahmadi, McNeely, Zou II, Chow, and Duong, as set forth above in Section I.D. Patent Owner does not offer any arguments with respect to the portions of the cited references that purportedly teach the limitations of these dependent claims. Having found that Petitioner has established a reasonable likelihood of prevailing with respect to claims 1–8, 12, 14, 15, 17, and 19–22 of the '900 patent, we also institute review with respect to challenged dependent claims 9–11, 13, 16, and 18. *See* United States Patent and Trademark Office, *Guidance on the Impact of SAS on AIA Trial Proceedings*, Patent Trial and Appeal Board (April 26, 2018) ("As required by *SAS*, the PTAB will institute as to all claims or none.") ("SAS Guidance").

D. Obviousness over Zou I and McNeely

Petitioner contends that the combined teachings of Zou I and McNeely teach or suggest each limitation of claims 1–8, 12, 14, 15, 17, and 19–22. Pet. 33–40. This ground relies on the same arguments as to Zou I as discussed above in Section II.C.3. *Id.* Petitioner also relies on the same arguments as to why a person of ordinary skill in the art would have been motivated to combine the references with a high expectation of success. Pet. 26–33. Patent Owner disputes the sufficiency of Petitioner's

allegations. Prelim. Resp. 24–61. A detailed analysis of this ground is not necessary at this time, and for purposes of this Decision, we do not address in detail Patent Owner's arguments regarding McNeely's disclosure or the sufficiency of Petitioner's allegations regarding motivation to combine Zou I and McNeely. *See* SAS Guidance. This does not constitute, however, a determination regarding the persuasiveness of Patent Owner's arguments in this regard. In particular, we encourage the parties to address, in subsequent briefing, Patent Owner's assertions that McNeely does not disclose the detector limitation recited in claims 1 and 7.

III. CONCLUSION

Based on the arguments in the Petition and Preliminary Response, and the evidence of record, we determine that Petitioner has demonstrated a reasonable likelihood that it will prevail on its challenge to at least one of the claims of the '900 patent.

Although we exercise our discretion and institute review, we remind the parties that we have not yet made a final determination as to the patentability of any of the challenged claims.

IV. ORDER

In consideration of the foregoing, it is hereby

ORDERED that, pursuant to 35 U.S.C. § 314(a), an *inter partes* review is hereby instituted as to claims 1–22 of the '900 patent with respect to the grounds set forth in the Petition; and

FURTHER ORDERED that, pursuant to 35 U.S.C. § 315(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial commencing on the entry date of this Decision.

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