NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

QIAGEN NORTH AMERICAN HOLDINGS, INC.,
NEUMODX MOLECULAR, INC.,
Appellants

v.

HANDYLAB, INC.,
Appellee

2020-2249, 2020-2250, 2020-2273, 2020-2276

Appeals from the United States Patent and Trademark Office, Patent Trial and Appeal Board in Nos. IPR2019-00488, IPR2019-00490, IPR2019-01493, IPR2019-01494.

Decided: October 29, 2021

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Before TARANTO, CLEVENGER, and CHEN, *Circuit Judges*.

CLEVENGER, *Circuit Judge*.

Qiagen North American Holdings, Inc. ("Qiagen Holdings") and NeuMoDx Molecular, Inc. ("NeuMoDx") (collectively, "Qiagen") appeal from the Final Written Decisions of the Patent Trial and Appeal Board ("Board") holding that the challenged claims of U.S. Patent No. 7,998,708 ("the '708 Patent") and U.S. Patent No. 8,323,900 ("the '900 Patent") would have been non-obvious. *See Qiagen N. Am. Holdings, Inc. v. HandyLab, Inc.*, No. IPR2019-00488 (P.T.A.B. July 14, 2020); *NeuMoDx Molecular, Inc. v. HandyLab, Inc.*, No. IPR2019-01493 (P.T.A.B. July 14, 2020); *Qiagen N. Am. Holdings, Inc. v. HandyLab, Inc.*, No. IPR2019-00490 (P.T.A.B. July 14, 2020); *NeuMoDx Molecular, Inc. v. HandyLab, Inc.*, No. IPR2019-01494 (P.T.A.B. July 14, 2020). This appeal focuses specifically on the challenged independent claims of the two patents. For the reasons set forth below, we *affirm*.

BACKGROUND

I

HandyLab, Inc. ("HandyLab") owns the '708 and '900 Patents, which are both entitled "Microfluidic System for Amplifying and Detecting Polynucleotides in Parallel." The '900 Patent is a continuation of the '708 Patent, and the two share a common specification. Both relate to microfluidic devices for detection of nucleotides in biological

samples. '708 Patent Abstract.[1] These microfluidic devices "carry out PCR on nucleotides of interest within microfluidic channels, and detect those nucleotides." *Id*. col. 2 ll. 10–14. The PCR reactions, which occur on a microfluidic cartridge, can be performed on a plurality of samples, as the microfluidic cartridge "has a plurality of PCR reaction chambers configured to permit thermal cycling of the plurality of samples independently of one another." *Id*. col. 2 ll. 28–30; *see also id*. Abstract.

Independent Claim 1 of the '708 Patent is representative and is 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
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> 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.

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[1] Citations to the common specification are to the '708 Patent.

'708 Patent col. 46 ll. 5–22. The independent claims of the '900 Patent track those of the '708 Patent, with the main difference being that the former recites "a plurality of multi-lane microfluidic cartridges" and "a plurality of receiving bays." '900 Patent col. 46 ll. 4–20.

The cartridge used in these devices is a "multi-lane microfluidic cartridge," which contains multiple sample lanes and "is configured to accept a number of samples in series or in parallel, simultaneously or consecutively." '708 Patent col. 13 ll. 21–23; *see also id*. col. 13 ll. 34–36. The specification sets forth the structure of the sample lane:

> 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.

Id. col. 12 l. 66–col. 13 l. 4.

The main prior art reference at issue here is U.S. Patent No. 6,509,186 to Quanbo Zou, et al. ("Zou I"), which discloses "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." Zou I Abstract. Specifically, Zou I discloses a standalone "multi-chamber thermal cycler chip," where each chamber is thermally isolated. *Id*. col. 8 ll. 46–63; *see also id*. col. 2 ll. 49–60. In one embodiment, "unprocessed fluid is stored in common reservoir 7 and is directed to chamber 11 through fluid-bearing channel 31." *Id*. col. 4 ll. 30–32.

II

Qiagen Holdings and NeuMoDx each filed petitions for *inter partes* review of claims 1–33 of the '708 Patent and claims 1–22 of the '900 Patent, asserting that the

challenged claims of the '708 and '900 Patents are unpatentable for obviousness. The Board instituted review and consolidated the IPRs by patent.[2] Relevant to this appeal, Qiagen argued that the challenged independent claims of the '708 Patent would have been obvious in view of Zou I and U.S. Patent Publication No. 2004/0037739 A1 to Michael McNeely, et al. ("McNeely") or U.S. Patent Publication No. 2004/0151629 to Grant Pease, et al. ("Pease") and that the challenged independent claims of the '900 Patent would have been obvious in view of Zou I and McNeely or U.S. Patent Publication No. 2002/0055,167 to Farzad Pourahmadi, et al. ("Pourahmadi"). The parties' arguments, and the Board's Final Written Decision, largely track across the two consolidated IPRs, so we discuss them together below.

In its Final Written Decision for IPR2019-00488, the Board construed the claim term "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." J.A. 17.[3] Turning to the merits of Qiagen's obviousness argument, the Board then determined that Qiagen failed to demonstrate by a preponderance of the evidence that the challenged independent claims were obvious over the combination of Zou I and McNeely, Pease, or Pourahmadi. J.A. 39–40, 83.

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[2] IPR2019-01493 was consolidated with IPR2019-00488, and IPR2019-01494 was consolidated with IPR2019-00490.

[3] In its Final Written Decision for IPR2019-00490, the Board likewise construed the term "multi-lane microfluidic cartridges" to mean "microfluidic cartridges each comprising a plurality of sample lanes with separate sample inlets and microfluidic networks." J.A. 59.

The Board had two independent bases for its conclusion. First, it concluded that "Zou I does not teach a multi-lane microfluidic unit under the proper claim construction" because the reference taught "that all of the lanes are associated with a single sample inlet, namely, common reservoir 7." J.A. 28, 70. The Board further concluded that this deficiency in Zou I was not remedied by any of the other three references. J.A. 32, 75. Second, the Board held that Qiagen failed to demonstrate that a POSA would have been motivated to combine the prior art references with a reasonable expectation of success in doing so. J.A. 39, 83. In particular, the Board noted that Qiagen's Petitions offered only a single conclusory statement regarding the POSA's alleged reasonable expectation of success and that Qiagen's expert offered only conclusory statements on this issue. J.A. 36, 38, 80, 82. In contrast, the Board viewed HandyLab's evidence, including the testimony of its expert, as credibly demonstrating that the development of microfluidic PCR devices was "a very complex endeavor that presented challenges" on numerous fronts. J.A. 37, 81. The Board also declined to consider Qiagen's Exhibit 1030 because "Petitioner did not submit [it] with the Petition." J.A. 37, 80. This appeal followed.

DISCUSSION

Qiagen challenges three aspects of the Board's decision: (1) the Board's construction of "multi-lane microfluidic cartridge," (2) the Board's determination that Zou I failed to disclose a "multi-lane" microfluidic cartridge, and (3) the Board's determination that Qiagen failed to demonstrate motivation to combine with a reasonable expectation of success. We have jurisdiction to decide the appeal under 28 U.S.C. § 1295(a)(4)(A).

Our analysis begins with the Board's decision on reasonable expectation of success. For the reasons below, we find that substantial evidence supports the Board's finding

of no reasonable expectation of success, and thus we affirm without reaching the other issues raised on appeal.

I

Because Qiagen contends that the Board erred in declining to consider Exhibit 1030, our review of the Board's finding of no reasonable expectation of success begins with the scope of the evidence considered by the Board.

We review the Board's evidentiary rulings for abuse of discretion, *VidStream LLC v. Twitter, Inc.*, 981 F.3d 1060, 1064 (Fed. Cir. 2020), and we disagree with Qiagen that the Board abused its discretion in declining to consider Exhibit 1030. Per the standard, we only disturb the Board's evidentiary rulings if the Board's decision: "(1) is clearly unreasonable, arbitrary, or fanciful; (2) is based on an erroneous conclusion of law; (3) rests on clearly erroneous fact findings; or (4) follows from a record that contains no evidence on which the Board could rationally base its decision." *Id.* (quoting *Shu-Hui Chen v. Bouchard*, 347 F.3d 1299, 1307 (Fed. Cir. 2003)).

The statutes and regulations governing IPRs set forth the required contents of petition-stage filings and of reply-stage filings:

> *First*, they generally require a petitioner to provide in the petition itself an understandable explanation of the element-by-element specifics of its unpatentability contentions, identifying supporting parts of the relied-on prior art. *Second*, reinforcing that requirement for what must be in the petition is a regulatory limit on permissible reply material.

AMC Multi-Cinema, Inc. v. Fall Line Pats., LLC, No. 2021-1051, 2021 WL 4470062, at *5 (Fed. Cir. Sept. 30, 2021) (internal citations omitted; emphasis in original).

Relevant here, a petition must set forth "the evidence that supports the grounds for the challenge to each claim,

including" copies of "printed publications that the petitioner relies upon in support of the petition." 35 U.S.C. § 312(a)(3); *see also* 37 C.F.R. § 42.22(a)(2) (requiring "[a] full statement of the reasons for the relief requested, including a detailed explanation of the significance of the evidence including material facts, and the governing law, rules, and precedent"); 37 C.F.R. § 42.104(b)(5) (stating that a petition must set forth "[t]he exhibit number of the supporting evidence relied upon to support the challenge and the relevance of the evidence to the challenge raised, including identifying specific portions of the evidence that support the challenge").

Qiagen could have submitted Exhibit 1030 in its Petitions to support its contention that a skilled artisan would have had "a high expectation of success" in combining the PCR unit of Zou I with "a conventional integrated machine," but it did not. J.A. 435–36. As Qiagen tacitly acknowledged, its Petitions did not address the general state of the art of the relevant field. *See* J.A. 4962 (Qiagen Reply, stating that "[t]he Petition did not need to address in granular detail each purported general 'challenge' in the field"); J.A. 4998 (same). In this case, the Board acted within its discretion in disregarding Exhibit 1030, and we see no reason to overturn its decision. *See Henny Penny Corp. v. Frymaster LLC*, 938 F.3d 1324, 1330 (Fed. Cir. 2019) ("Because of the expedited nature of IPR proceedings, '[i]t is of the utmost importance that petitioners in the IPR proceedings adhere to the requirement that the initial petition identify with particularity the evidence that supports the grounds for the challenge to each claim.'" (quoting *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1369 (Fed. Cir. 2016))); *see also* USPTO, *PTAB Consolidated Patent Trial Practice Guide* (Nov. 21, 2019), *available at* https://www.uspto.gov/sites/default/files/documents/tpgnov.pdf, at 73 ("Petitioner may not submit new evidence or argument in reply that it could have presented earlier, e.g.[,] to make out a prima facie case of

unpatentability."); *id*. at 74 ("While replies and sur-replies can help crystalize issues for decision, a reply or sur-reply that raises a new issue or belatedly presents evidence may not be considered.").

Qiagen contends that Exhibit 1030 constitutes permissible reply evidence and that the Board abused its discretion by excluding it. We disagree that the Board erred. Qiagen did not use Exhibit 1030, as it claims, to rebut a general argument from HandyLab "that interfacing microfluidic chips with cartridges was unpredictable"; rather, the portion of HandyLab's Response Qiagen sought to rebut was specific to McNeely and Pease. *See* J.A. 4962–63 (Qiagen Reply); J.A. 2263–64 (HandyLab Response). In particular, HandyLab argued that neither McNeely nor Pease suggest that the disclosed cartridges can accommodate a PCR chip and, further, that Qiagen "d[id] not identify a general teaching from either reference that would have applied to Zou I's chip." J.A. 2263–64 (HandyLab Response). In its Reply, Qiagen specifically discussed McNeely and Pease, then cited new evidence (Exhibit 1030) to argue much more broadly that "using a microfluidic PCR chip like Zou I with a cartridge was routine and predictable by March 2006." J.A. 4963 (Qiagen Reply). But "[a] reply may only respond to arguments raised in the corresponding opposition, patent owner preliminary response, patent owner response, or decision on institution." 37 C.F.R. § 42.23.

We have "applied those rules [governing filing content in IPRs] in a number of decisions that restrict use of certain reply material in forming the record." *AMC*, 2021 WL 4470062, at *6 (collecting cases); *see also Wasica Fin. GmbH v. Cont'l Auto. Sys., Inc.*, 853 F.3d 1272, 1285–87 (Fed. Cir. 2017) (affirming Board's ruling that an obviousness challenge was "insufficiently precise and underdeveloped" where the petitioner "did not make out its obviousness case in its petition," which "offered only a conclusory and sweeping allegation," while the reply argued

that a relevant artisan would have looked to a different passage and would have modified the prior art). The Board reasonably concluded that this case presents no exception. This is not an instance where the later-submitted material (Exhibit 1030) can be tied to a non-conclusory assertion in the original Petition: As noted above, Exhibit 1030 was only submitted with Qiagen's Reply, not with the original Petition, and Qiagen's Petition did not include any argument or evidence that using a microfluidic PCR chip with a cartridge was routine and predictable as of the priority date. *Cf. AMC*, 2021 WL 4470062, at *6 ("[W]e have made clear that if the petition asserts that a claim requirement is met, provides a reason that the assertion is true, and cites evidentiary support for that reason, then reply material that fairly adds confirmation that the initially presented material does in fact support the assertion is not prohibited new material, but a proper part of the record." (collecting cases)).

Because the Board did not abuse its discretion by excluding Exhibit 1030, our analysis on reasonable expectation of success centers on the evidence considered by the Board—primarily, the testimony of the parties' experts.

II

Whether a skilled artisan would have had a reasonable expectation of success in combining the prior art is a question of fact that we review for substantial evidence. *Intelligent Bio-Sys.*, 821 F.3d at 1366. A factual finding is supported by substantial evidence "if a reasonable mind might accept the evidence as sufficient to support the finding." *HP Inc. v. MPHJ Tech. Invs., LLC*, 817 F.3d 1339, 1343–44 (Fed. Cir. 2016) (citing *Consol. Edison Co. v. NLRB*, 305 U.S. 197, 229 (1938)).

The Board concluded, after "[h]aving considered the complete trial record," that Qiagen "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 NcNeely or Pease" or Pourahmadi. J.A. 35, 79. In arriving at its conclusion, the Board reviewed the parties' submissions as well as testimony by their experts. The Board found that Qiagen's Petitions contained only "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'" or Pourahmadi, "'with a high expectation of success.'" J.A. 36, 80; *see also* J.A. 435–36 (Qiagen Petition). The Board further found the declaration of Qiagen's expert, Dr. Bruce Gale, to be "similarly conclusory as to how Zou I and McNeely or Pease" or Pourahmadi "could be combined" and that it "does not elaborate on reasonable expectation of success." J.A. 36, 80; *see also* J.A. 558–65 (Gale Decl., ¶¶ 117–27). Substantial evidence supports these findings.

Moreover, the Board agreed with HandyLab 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." J.A. 37, 81. In arriving at this conclusion, the Board expressly credited the declaration of HandyLab's expert, Dr. Allen Northrup, in which Dr. Northrup "provide[d] factual support . . . with reference to numerous contemporaneous publications in the field." J.A. 37; *see also* J.A. 81. Indeed, Dr. Northrup discussed in detail the "host of specific technical difficulties" presented by the development of microfluidic PCR devices, including the particular challenges identified above. J.A. 3499–505 (Northrup Decl., ¶¶ 33–42); J.A. 3790–98 (Northrup Decl., ¶¶ 771–86). In contrast, the Board viewed Dr. Gale's testimony that a skilled artisan would expect to combine Zou I's unit "virtually unaltered" into a cartridge system "to be

conclusory and not supported by the evidence of record." J.A. 38, 82. The Board further noted that this testimony was "inconsistent" with other portions of Dr. Gale's testimony. J.A. 38–39, 82. Qiagen provides no basis for overruling the Board's credibility determinations, and, based on the record before us, substantial evidence supports the Board's conclusion regarding the complexity and challenges in developing microfluidic PCR devices.

Qiagen argues that the Board's findings with respect to the challenges presented by "contamination" and "design and configuration of a microfluidic network" are predicated on the Board's reading of Zou I, which is in turn predicated on the Board's construction of "multi-lane microfluidic cartridge," with which Qiagen disagrees. Even if we were to agree with Qiagen on these two points, they are insufficient to overcome the substantial evidence standard in light of the evidence considered by the Board—including evidence regarding the challenges of providing uniform heating, detecting small volumes of products, and interfacing the reaction instrument with control machinery. J.A. 3499–501, 3503–05, 3790–98 (Northrup Decl., ¶¶ 34–36, 39–42, 771–86). Further, some of this evidence was unrefuted; the Board additionally found that Dr. Gale "d[id] not address the evidence supporting Dr. Northrup's testimony regarding the complexities of connecting PCR microfluidic chips to heat sources or detection mechanisms." J.A. 39; *see also* J.A. 83.

CONCLUSION

For the reasons stated above, we affirm the Board's conclusion that Qiagen failed to demonstrate by a preponderance of the evidence that the challenged independent claims of the '708 and '900 Patents are unpatentable for obviousness in view of Zou I and McNeely, Pease, or Pourahmadi.

AFFIRMED