NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

QUEST DIAGNOSTICS INVESTMENTS LLC,
Appellant

v.

ANDREW HIRSHFELD, PERFORMING THE FUNCTIONS AND DUTIES OF THE UNDER SECRETARY OF COMMERCE FOR INTELLECTUAL PROPERTY AND DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE,
Intervenor

2021-1115

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. IPR2019-00738.

Decided: December 27, 2021

THOMAS H. WINTNER, Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, MA, for appellant. Also represented by PETER CUOMO; ADAM GAHTAN, Fenwick & West LLP, New York, NY.

ROBERT MCBRIDE, Office of the Solicitor, United States Patent and Trademark Office, Alexandria, VA, for intervenor. Also represented by THOMAS W. KRAUSE, FARHEENA YASMEEN RASHEED, MEREDITH HOPE SCHOENFELD.

Before MOORE, *Chief Judge*, CLEVENGER and CHEN, *Circuit Judges*.

CHEN, *Circuit Judge*.

Quest Diagnostics Investments LLC (Quest) appeals a decision of the Patent Trial and Appeal Board (Board) in IPR2019-00738 finding claims 1, 2, and 4–14 of U.S. Patent No. 8,409,862 (the '862 patent) unpatentable as either anticipated under 35 U.S.C. § 102 or obvious under 35 U.S.C. § 103. For the reasons stated herein, we *affirm*.

BACKGROUND

Quest owns the '862 patent, which claims priority to September 8, 2003 and is directed to using mass spectrometry to detect low levels of testosterone in female humans. *See, e.g.*, '862 patent col. 1 ll. 49–59, col. 5 ll. 50–65, claim 1. The '862 patent explains that "[t]estosterone levels are much lower in females compared to males" and "[t]he clinical manifestations of excess testosterone in females include infertility, hirsutism, amenorrhea, and obesity." *Id.* col. 1 ll. 49–59. The '862 patent further explains that testosterone can be purified prior to mass spectrometry, which can improve the limit of detection (i.e., the lowest amount of testosterone the method can detect). *See, e.g.*, *id.* col. 3 ll. 7–21. Accordingly, the '862 patent claims methods for "determining the amount of testosterone in a sample" where a user purifies the testosterone prior to mass spectrometry. *Id.* at claim 1. However, the '862 patent explicitly excludes derivatization of testosterone before mass

spectrometry, the lack of which Quest argues offers improvements in ease of use.[1] *See id.*

Claims 8 and 9, relevant here, depend upon claim 1 and further require "wherein the method is capable of detecting testosterone at concentrations of less than 5 ng/dL in the sample" and "less than 1 ng/dL in the sample," respectively. *Id.* at claims 8–9.

On February 25, 2019, Laboratory Corporation of America Holdings (LabCorp) petitioned for *inter partes* review of claims 1, 2, and 4–14 of the '862 patent. J.A. 79, 152. Relevant to this appeal, LabCorp asserted that claims 8 and 9 would have been obvious in view of Clarke,[2] or alternatively would have been obvious in view of Clarke in combination with Draisci.[3]

Clarke is an abstract found on a compact disc (CD) from the 49th annual conference of the American Society for Mass Spectrometry (ASMS) held in May 2001. J.A. 1356–57. Clarke details a method for detecting low levels of testosterone and describes a method similar to the '862 patent—wherein testosterone is purified before mass spectrometry. *Lab'y Corp. of Am. Holdings v. Quest*

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[1] Quest explains that derivatization of testosterone is one method to improve detection of testosterone using mass spectrometry. *See* Appellant's Br. at 6–7. However, Quest contends that the derivatization process can be laborious and time consuming. *See id.*

[2] Clarke, et al., *Determination of Suppressed Testosterone Levels in Human Serum by LC-MS/MS*, Proceedings of the 49th ASMS Conference on Mass Spectrometry and Allied Topics, Chicago, Illinois, May 27–31, 2001.

[3] Draisci, et al., *Quantitation of anabolic hormones and their metabolites in bovine serum and urine by liquid chromatography-tandem mass spectrometry*, 870 J. CHROMATOGRAPHY A, 511–22 (2000).

Diagnostics Invs. LLC, 2020 WL 5224211, at *6–7 (P.T.A.B. Sept. 1, 2020). Clarke claims to detect testosterone down to 50 pg/mL—equivalent to 5 ng/dL.

C

On September 1, 2020, the Board issued its Final Written Decision finding that claims 1, 2, and 4–14 would have been unpatentable as either obvious or anticipated. *See id.* at *1. Two of the Board's findings are challenged here—first, that Clarke was valid prior art as a printed publication and, second, that claims 8 and 9 would have been obvious in light of Clarke or Clarke in combination with Draisci.

As to whether Clarke is a printed publication, the Board found Clarke was publicly available and therefore a prior art printed publication. Specifically, the Board recognized that the ASMS sent a CD containing Clarke to thousands of ASMS members, and that the CD was available in the University of Wisconsin-Madison library before the priority date of the '862 patent. *See id.* at *8–10. Further, the Board noted that although Clarke appeared alongside approximately 1,600 other abstracts, the CD permitted users to search the abstracts using selected keywords. *See id.* at *10. Given the dissemination, accessibility, and searchability of the CD, the Board found Clarke to be prior art. *Id.*

As to claims 8 and 9, the Board concluded it would have been obvious to reach detection limits below 5 ng/dL and 1 ng/dL based on the teachings of Clarke or Clarke with Draisci. The Board found that a skilled artisan would have been motivated to achieve a lower level of detection and have reached these levels by optimizing several experimental parameters, specifically by "increasing the volume of the sample" and "modernizing the equipment." *Id.* at *19–20.

DISCUSSION

On appeal, Quest makes two arguments.[4] First, that the Board erred in finding Clarke was publicly available and thus the Board's unpatentability determination as to all challenged claims must be reversed. Second, that the Board erred in holding that claims 8 and 9 would have been obvious over Clarke and/or Clarke in view of Draisci. We address each in turn.

A

Quest argues that Clarke was not a printed publication because it was not publicly accessible. *See* Appellant's Br. at 40–55. "Whether a reference qualifies as a 'printed publication' . . . is a legal conclusion based on underlying factual findings." *Jazz Pharms., Inc. v. Amneal Pharms., LLC*, 895 F.3d 1347, 1356 (Fed. Cir. 2018). We review the Board's legal determinations *de novo* and the underlying factual findings for substantial evidence. *Id.* at 1355.

The Board found that the ASMS widely disseminated the CD containing Clarke and that the CD was available in a university library. *See Lab'y*, 2020 WL 5224211, at *7–10. Quest largely ignores the ASMS's public dissemination and instead highlights that Clarke was a single abstract out of approximately 1,600, all with minimal indexing. *See* Appellant's Br. at 43–45. Quest contends that this makes Clarke an obscure, inaccessible reference. We disagree.

As this court has recognized, "the breadth of the dissemination [] to persons of ordinary skill is significant," and "[w]hether the disseminated material is addressed to

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[4] Initially, Quest also argued for reversal on the basis of unconstitutionality of *inter partes* review under the Appointments Clause. *See* Appellant's Br. at 56–57. However, Quest has since abandoned this argument. *See* ECF No. 30.

or of interest to persons of ordinary skill is also relevant to the public accessibility inquiry." *Jazz Pharms.*, 895 F.3d at 1357–58. Here, although Clarke was surrounded by hundreds of other abstracts, the ASMS distributed the CD to the *specific people* most motivated to search the CD and find Clarke, a fact Quest does not dispute.

Moreover, the CD permitted keyword searching. While the CD did not allow users to search the word "testosterone," the CD permitted several mass spectrometry-related keywords. *Lab'y*, 2020 WL 5224211, at *10; *see also* J.A. 1347–55 (listing search terms). Quest objects that LabCorp did not identify the *specific* keywords the Board ultimately relied on and presented no evidence that such keywords could meaningfully narrow the abstracts. Appellant's Br. at 48–54. Nonetheless, given the wide dissemination of the CD, we are unpersuaded that any identified limitations in searchability require finding Clarke inaccessible. As this court has already held, "a printed publication need not be easily searchable after publication if it was sufficiently disseminated at the time of its publication." *Suffolk Techs., LLC v. AOL Inc.*, 752 F.3d 1358, 1365 (Fed. Cir. 2014).

Accordingly, we conclude that substantial evidence supports the Board's finding that Clarke was publicly available and thus prior art.

B

Quest also argues that the Board erred by holding that claims 8 and 9 would have been obvious in light of Clarke or Clarke in combination with Draisci.[5] "Whether a claimed invention is unpatentable as obvious under § 103 is a question of law based on underlying findings of fact."

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[5] Quest made no separate argument as to the patentability of claims 1, 2, 4–7, and 10–14 other than Clarke not being prior art.

In re Gartside, 203 F.3d 1305, 1316 (Fed. Cir. 2000). We review the legal conclusion of obviousness *de novo* and the factual determinations for substantial evidence. *See id*.

As an initial matter, the parties dispute which precise framework the Board applied in finding claims 8 and 9 obvious—either the "routine optimization" analysis or the "obvious-to-try" analysis. *See* Appellant's Br. at 20–25. Regardless of this distinction, the Board articulated a clear motivation to modify and a clear reasonable expectation of success, *see Lab'y*, 2020 WL 5224211, at *18–20, findings that we conclude are supported by substantial evidence.

Specifically, Quest argues that there was no motivation to modify Clarke to increase sensitivity, that there was no reasonable expectation of success in doing so, and that there was a documented failure of others. *See* Appellant's Br. at 26–40.

We find that substantial evidence supports the Board's conclusion that there was a motivation to improve the sensitivity of methods measuring testosterone. The Board relied on LabCorp's expert testimony, as well as the scientific papers underlying that expert testimony to conclude that "measuring low testosterone levels are known to be clinically relevant." *Lab'y*, 2020 WL 5224211, at *18–19 (citing, for example, J.A. 1228–29). Although Quest argues that 5 ng/dL and 1 ng/dL of testosterone are below the "'clinically relevant' range of testosterone," we are unpersuaded this discourages developing more sensitive methods. Appellant's Br. at 26. In sum, we find that the Board had substantial evidence to find a motivation to modify Clarke to reach 5 ng/dL and 1 ng/dL detection limits.

Turning to reasonable expectation of success, the Board recognized a number of parameters a skilled artisan could modify to reach 5 ng/dL or 1 ng/dL detection. *Lab'y*, 2020 WL 5224211, at *18–19. The Board focused on "increasing sample volume" as a likely starting point. *Id.* at *19. Neither party disputes that increasing sample volume

would increase level of detection, and experts for both parties agreed. *Id.* at *20, *24; *see also* J.A. 702 (LabCorp's expert stating that "one of skill in the art would have routinely identified the suitable volume to optimize sensitivity"), 2467 (Quest's expert recognizing that increasing sample volume "would increase the signal"). While Quest contends that an increased sample volume would decrease resolution, the claims at issue are silent as to resolution—instead, the claims only refer to being "capable of detecting." '862 patent at claims 1, 8, 9. Therefore, and particularly when coupled with the Board's consideration of other parameters, we are persuaded that substantial evidence supports the Board's finding that a skilled artisan would have had a reasonable expectation of success of achieving a lower level of detection.

Lastly, we are unpersuaded by Quest's argument that the alleged failure of others establishes nonobviousness. Quest points to a paper by Kushnir, et al.[6] Quest argues that the paper demonstrates a failure of others to reach detection levels of 5 ng/dL or 1 ng/dL without derivatizing testosterone. Appellant's Br. at 33–40. However, the Board explicitly considered Kushnir and found that the conditions were different and not indicative of failure to achieve the relevant detection levels. *Lab'y*, 2020 WL 5224211, at *17, * 20. In particular, the Board noted differences in equipment and "sample preparation methods." *Id.* Given the deferential standard of review, as well as the differences in Kushnir's detection method relative to the claims at issue, we decline to say that the Board erred in determining that Kushnir fails to establish nonobviousness.

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[6] Kushnir, et al., Performance characteristics of a novel tandem mass spectrometry assay for serum testosterone, 52(1) CLIN. CHEM. 120–28 (2006).

In sum, we find that substantial evidence supports the facts underlying the Board's conclusion that claims 8 and 9 would have been obvious in light of Clarke. Because we affirm the Board's obviousness determination on Clarke alone, we need not reach the combination of Clarke and Draisci.

CONCLUSION

For the reasons set forth above, we *affirm* the Board's decision finding claims 1, 2, and 4–14 of the '862 patent unpatentable as either obvious or anticipated.

AFFIRMED