NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

UNIVERSITY OF MARYLAND BIOTECHNOLOGY INSTITUTE,
Appellant

v.

PRESENS PRECISION SENSING GMBH,
Cross-Appellant

2016-2745, 2017-1057

Appeals from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. 95/000,615.

Decided: November 3, 2017

RENE A. VAZQUEZ, Sinergia Technology Law Group, PLLC, Leesburg, VA, argued for appellant.

MICHAEL STEVEN CULVER, Millen, White, Zelano & Branigan PC, Arlington, VA, argued for cross-appellant.

Before LOURIE, O'MALLEY, and TARANTO, *Circuit Judges*.

LOURIE, *Circuit Judge*.

The University of Maryland Biotechnology Institute ("Maryland") appeals from the *inter partes* reexamination decision of the United States Patent and Trademark Office ("PTO") Patent Trial and Appeal Board ("the Board") affirming the examiner's rejection of claims 1, 3–6, 9–11, 13–16, 19, and 20 ("the claims") of U.S. Patent 6,673,532 ("'532 patent") as obvious under 35 U.S.C. § 103 (2006).[1] *Presens Precision Sensing GmbH v. Univ. of Md. Biotechnology Inst.*, No. 2015-006297, 2015 WL 9581532 (P.T.A.B. Dec. 29, 2015) ("*Decision*"), *reh'g denied*, (P.T.A.B. July 29, 2016). Because the Board did not err in holding the claims invalid as obvious, we *affirm*.

BACKGROUND

Maryland owns the '532 patent, which covers methods of measuring parameters in cell culture. Cell culture is a widely used technique to cultivate cells *in vitro*. Parameters such as glucose, pH, and carbon dioxide and oxygen levels affect the viability of cell cultures. Consequently, monitoring such parameters is important in optimizing cell culture conditions. *See, e.g.*, '532 patent col. 1 ll. 47–64.

The '532 patent discloses an optical method of monitoring various cell culture parameters. The method implements four key components: (1) a cultivation vessel; (2) a sensor; (3) an excitation source; and (4) a detector. *Id.* col. 5 ll. 1–5. Cells are grown in a cultivation vessel that includes sensors which selectively bind to certain analytes. The sensors are light-sensitive, so when an

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[1] Because the application of the '532 patent was filed before March 16, 2013, the pre-Leahy-Smith America Invents Act version of § 103 applies. *See* Pub L. No. 112-29, 125 Stat. 284 (2011); 35 U.S.C. § 103 (2006).

excitation source such as a light-emitting diode ("LED") shines on the sensors, the sensors emit light corresponding to the concentration of the relevant analytes. Detectors such as photomultiplier tubes then measure the light emitted by the sensors. *Id.* col. 4 l. 57–col. 5 l. 10.

Appellee Presens Precision Sensing ("Presens") petitioned for *inter partes* reexamination of the '532 patent, which the PTO granted. Claim 1 of the '532 patent, as amended during reexamination, is representative and reads as follows:

> 1. A method of measuring at least two cultivation parameters in a cell culture, comprising:
>
> (a) providing a cultivation vessel, wherein the cultivation vessel comprises, walls that define a single continuous volume or a non-planar surface that defines a single continuous volume, and at least two types of optical chemical sensors positioned within the single continuous volume;
>
> (b) placing a continuous culture medium within the single continuous volume of the cultivation vessel such that the continuous culture medium is in contact with at least one of the walls that define the single continuous volume of the cultivation vessel or the non-planar surface that defines the single continuous volume of the cultivation vessel, wherein the optical chemical sensors are positioned such that they are in contact with the continuous culture medium;
>
> (c) establishing a cell culture in the continuous culture medium;
>
> (d) exciting the optical chemical sensors to generate emission and/or light absorption, wherein the optical chemical sensors are excited using at least one excitation source per optical chemical sensor;

> (e) detecting the emission and/or absorption generated by the at least two optical chemical sensors in (d) by at least one detector for each type of optical chemical sensor used; and
>
> (f) analyzing the detected emission and/or absorption detected in (c) to assess the at least two cultivation parameters measured.

J.A. 646–47, 1005.

The examiner rejected the claims as, *inter alia*, obvious over Shabbir B. Bambot et al., *Potential Applications of Lifetime-Based, Phase-Modulation Fluorimetry in Bioprocess and Clinical Monitoring*, 13 Trends in Biotechnology 106 (1995) ("Bambot"), and Bernhard H. Weigl et al., *Optical Triple Sensor for Measuring pH, Oxygen and Carbon Dioxide*, 32 J. Biotechnology 127 (1994) ("Weigl").

Bambot described optical methods of measuring analytes such as glucose, pH, and oxygen and carbon dioxide levels in bioreactors. The methods implemented the same set of components as the '532 patent. Various cultivation vessels housed sensors excitable by several types of excitation sources, and the sensors' emissions could be measured by several different detectors.

Similarly, Weigl described a triple sensor device for measuring pH, oxygen, and carbon dioxide in a cultivation vessel. However, in Weigl the sensors were located in individual flow-through units outside the cultivation vessel. Each unit had a dedicated excitation source and detector. Given the teachings of Bambot and Weigl in combination, the examiner concluded that the claims of the '532 patent would have been obvious over the references at the time the invention was made.

The Board affirmed the examiner's obviousness rejection. The Board agreed that Bambot taught placing sensors inside a cultivation vessel, and also disclosed

multiple types of sensors, detectors, and excitation sources. Furthermore, the Board found that Weigl taught monitoring multiple parameters using a separate detector and excitation source for each type of sensor. Consequently, the Board concluded that "it would have been obvious to arrange more than one sensor inside a cultivation vessel and [use] the light excitation and detection means described in Bambot for each one." *Decision*, 2015 WL 9581532, at *13.

Maryland appealed, and we have jurisdiction under 28 U.S.C. § 1295(a)(4)(A).

DISCUSSION

Our review of a Board decision is limited. *In re Baxter Int'l, Inc.* 678 F.3d 1357, 1361 (Fed. Cir. 2012). We review the Board's legal determinations *de novo*, *In re Elsner*, 381 F.3d 1125, 1127 (Fed. Cir. 2004), but we review the Board's factual findings underlying those determinations for substantial evidence, *In re Gartside*, 203 F.3d 1305, 1316 (Fed. Cir. 2000). A finding is supported by substantial evidence if a reasonable mind might accept the evidence as adequate to support the finding. *Consol. Edison Co. v. NLRB*, 305 U.S. 197, 229 (1938).

The legal conclusion of obviousness turns on the familiar *Graham* factors, including the teachings of the prior art and the differences between those teachings and the claimed invention. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966). In assessing obviousness, we must "look with care at a patent application that claims as innovation the combination of two known devices according to their established functions." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007). However, we also exercise caution before holding a claimed invention obvious when combining references would violate the principle of operation of the modified reference. *See In re Mouttet*, 686 F.3d 1322, 1332 (Fed. Cir. 2012) (discussing *In re Ratti*, 270 F.2d 810, 813 (CCPA 1959)). This is

because a person of ordinary skill generally would not be motivated to modify a reference by contradicting its basic teachings, *see id.*, or by making it "inoperable for its intended purpose," *In re Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984).

Maryland argues that because Weigl's sensors are positioned outside the cultivation vessel, Weigl cannot be modified in view of Bambot without "completely chang[ing] the fundamental principle of operation of Weigl." Appellant's Br. 20. When such a modification of a reference is necessary, Maryland contends, it does not support a determination of obviousness under *Ratti*, 270 F.2d at 813.

Presens responds that Maryland misinterprets the Board's reliance on Weigl. According to Presens, the Board did not conclude that claim 1 was obvious by modifying the configuration of Weigl's sensors; rather, the Board, citing the examiner's finding, relied on Weigl for measuring multiple parameters and using a separate detector and excitation source for each sensor. Presens argues that the Board's obviousness holding was based on Bambot's sensor configuration, not Weigl's, so Maryland's application of *Ratti* is misplaced.

We agree with Presens that Maryland misapplies *Ratti*. A person of ordinary skill is "not an automaton," *KSR*, 550 U.S. at 421, limited to physically combining references, *see Mouttet*, 686 F.3d at 1332 (citing *In re Etter*, 756 F.2d 852, 859 (Fed. Cir. 1985) (en banc)). Even assuming that extra-vessel sensors are a "basic principle" of Weigl, *Ratti*, 270 F.2d at 813, that principle is independent of Weigl's pertinence to the Board's obviousness determination. The Board found that Weigl taught measuring multiple parameters and using a separate detector and excitation source for each sensor. Substantial evidence supports that finding. Figure 1 of Weigl depicts a separate detector and excitation source for each

sensor membrane. J.A. 366. Weigl described each flow-through unit as "independent," *id.*, and implemented different types of excitation sources and detectors for different sensors, J.A. 367, 369.

The Board's findings regarding Weigl are consistent with Bambot's principle of operation, as substantial evidence also supports the Board's findings that Bambot taught intra-vessel sensors in addition to multiple types of sensors, detectors, and excitation sources, and that Bambot suggested measuring multiple analytes in cultivation vessels. For example, Bambot disclosed oxygen sensors embedded within cultivation vessels, J.A. 130, and stated that the oxygen sensors "performed satisfactorily in a bioreactor environment," J.A. 128–29. Bambot also described other optical sensors for pH, carbon dioxide, and glucose, multiple types of excitation sources such as blue LEDs and red laser diodes, and multiple detectors such as photomultiplier tubes and semiconductor detectors. J.A. 127–30. In its conclusion, Bambot indicated that measurement of "oxygen (and other analytes)" in cultivation vessels was feasible, J.A. 132, and proposed a separate "multianalyte sensing system," J.A. 131.

Unlike in *Ratti*, we cannot say here that the "suggested combination of references would require a substantial reconstruction and redesign of the elements shown" in Bambot, or a "change in [its] basic principles." 270 F.2d at 813. Rather, Bambot and Weigl taught every element of the claimed invention and the combination of the references accords with their teachings. "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR*, 550 U.S. at 416. That is the case here. Consequently, the Board did not err in concluding that combining Bambot with Weigl rendered the claims obvious, regardless of Weigl's extra-vessel sensors.

Maryland also argues that Weigl teaches away from the claimed invention because: (1) Weigl's carbon dioxide sensor is unstable; (2) each of Weigl's flow-through units has only one sensor, not multiple sensors; (3) Weigl's various outlets are inconsistent with the claimed invention's "continuous volume" limitation; and (4) Weigl's device is "invasive" because it requires extra-vessel sensors.

Presens responds that Maryland's teaching away arguments are not supported by the references' teachings or improperly attempt to distinguish Weigl from technical features not in the claims.

We agree with Presens that Maryland's teaching away arguments do not demonstrate Board error. Like its argument based on the positioning of Weigl's sensors, Maryland's teaching away arguments narrowly focus on Weigl's physical arrangement. But "mere disclosure of alternative designs does not teach away." *In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004). Rather, teaching away requires "clear discouragement" from implementing a technical feature. *In re Ethicon, Inc.*, 844 F.3d 1344, 1351 (Fed. Cir. 2017).

Maryland directs us to no such discouragement. Substantial evidence supports the Board's finding that a person of ordinary skill would not be limited to Weigl's unstable carbon dioxide sensor, but would instead look to Bambot's alternative carbon dioxide sensor. The same is true regarding Weigl's flow-through units, outlets, and alleged invasiveness, as the Board's finding that Bambot taught cultivation vessels with sensors embedded inside, which did not require flow-through units or outlets, is supported by substantial evidence. *See supra* at 7. While Weigl did adopt an "alternative design[]" to Bambot, *Fulton*, 391 F.3d at 1201, it did not provide "clear discouragement" from monitoring carbon dioxide with a stable

sensor or from using intra-vessel sensors, *Ethicon*, 844 F.3d at 1344.

We have considered Maryland's remaining arguments and find them unpersuasive.

CONCLUSION

Because the Board did not err in concluding that the combination of Bambot and Weigl renders the claims of the '532 patent obvious, we *affirm*. As such, we do not reach Presens's conditional cross-appeal.

AFFIRMED