NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

CORNELL RESEARCH FOUNDATION, INC.,
Appellant

v.

KATHERINE K. VIDAL, UNDER SECRETARY OF COMMERCE FOR INTELLECTUAL PROPERTY AND DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE,
Intervenor

2020-2334, 2020-2335, 2020-2337, 2020-2338, 2020-2339, 2020-2340

Appeals from the United States Patent and Trademark Office, Patent Trial and Appeal Board in Nos. IPR2019-00577, IPR2019-00578, IPR2019-00579, IPR2019-00580, IPR2019-00581, IPR2019-00582.

Decided: May 24, 2022

JULIE S. GOLDEMBERG, Morgan, Lewis & Bockius LLP, Philadelphia, PA, argued for appellant. Also represented by ROBERT CHRISTIAN BERTIN, ROBERT JOHN SMYTH, Washington, DC; AJIT VAIDYA, Kenealy Vaidya LLP, Washington, DC.

MAUREEN DONOVAN QUELER, Office of the Solicitor, United States Patent and Trademark Office, Alexandria, VA, argued for intervenor. Also represented by MICHAEL S. FORMAN, THOMAS W. KRAUSE, AMY J. NELSON, FARHEENA YASMEEN RASHEED.

Before PROST, REYNA, and TARANTO, *Circuit Judges*.

PROST, *Circuit Judge*.

Cornell Research Foundation, Inc. ("Cornell") appeals from six inter partes reviews ("IPR"), each regarding a different Cornell patent, in which the Patent Trial and Appeal Board ("Board") concluded that the challenged claims were unpatentable as anticipated or obvious. *E.g.*, *Associated British Foods PLC v. Cornell Rsch. Found., Inc.*, No. IPR2019-00577, Paper 117 (P.T.A.B. July 23, 2020) ("*Final Written Decision*"). Because substantial evidence supports the Board's determinations that the claims were obvious, we affirm.

BACKGROUND

I

The patents at issue relate to phytases in livestock feed. Phytases are enzymes that help certain animals absorb phosphate, an important nutrient. Skilled artisans can produce phytase enzymes by taking a phytase gene from one organism and incorporating it into a host; the host then replicates and expresses the phytase protein, which can then be added to the feed.

U.S. Patent No. 8,993,300 ("the '300 patent"), representative in this appeal, describes a heterologous method of producing phytase: it uses a phytase gene derived from *Escherichia coli*, a species of bacteria, and a fungal host. There are different strains of *E. coli*, and different strains express different phytases. Two are relevant here: *E. coli*

appA phytase and *E. coli* B phytase. There are also a variety of fungal species. As is relevant here, the fungal kingdom includes yeast, of which *Saccharomyces cerevisiae* and *Pichia pastoris* are species.

Independent claim 1 and dependent claims 10–12 of the '300 patent are representative for the purposes of this consolidated appeal. They recite:

> 1. A method of producing a phytase in fungal cells, the method comprising:
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> providing a polynucleotide encoding an *Escherichia coli* phytase;
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> expressing the polynucleotide in the fungal cells; and
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> isolating the expressed *Escherichia coli* phytase wherein the *Escherichia coli* phytase catalyzes the release of phosphate from phytate.
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> 10. The method of claim 1 wherein the *Escherichia coli* phytase has an optimum activity at a temperature range of 57 degrees C. to 65 degrees C.
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> 11. The method of claim 1 wherein the *Escherichia coli* phytase retains at least 40% of its activity after heating the phytase for 15 minutes at 80 degrees C.
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> 12. The method of claim 1 wherein the *Escherichia coli* phytase retains at least 60% of its activity after heating the phytase for 15 minutes at 60 degrees C.

Dependent claims 10–12 add so-called "thermostability limitations" to the phytases produced by the heterologous method described in independent claim 1.

II

We recount only the relevant procedural history below. Associated British Foods PLC ("ABF") filed six IPR petitions, each challenging a different Cornell patent. The Board instituted review for all six and found all challenged claims unpatentable.

ABF asserted two varieties of prior-art combinations in its petitions—those involving Kretz[1] and those not involving Kretz. The Kretz-based challenges apply only to the '300 patent. But the parties agree that all six Board decisions "stand and fall" with the Board's non-Kretz obviousness analysis for the '300 patent. Reply Br. 26–27. We accordingly focus our discussion on the Board's Final Written Decision for the '300 patent.

Beginning with the non-Kretz grounds, ABF asserted that all challenged claims of the '300 patent would have been obvious over two combinations: (1) Dassa,[2] Greiner,[3] and Cheng[4] and (2) Dassa, Greiner, Romanos,[5] and Van Gorcom[6] (collectively, "the Dassa/Greiner

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[1] U.S. Patent No. 5,876,997 ("Kretz").

[2] Janie Dassa, Christian Marck, & Paul L. Boquet, *The Complete Nucleotide Sequence of the* Escherichia coli *Gene* appA *Reveals Significant Homology Between pH 2.5 Acid Phosphatase and Glucose-1-Phosphatase*, 172 J. BACTERIOLOGY 5497 (1990) ("Dassa").

[3] R. Greiner, U. Konietzny, & Kl.-D. Jany, *Purification and Characterization of Two Phytases from* Escherichia coli, 303 ARCHIVES BIOCHEMISTRY & BIOPHYSICS 107 (1993) ("Greiner").

[4] U.S. Patent No. 5,985,605 ("Cheng").

[5] Michael A. Romanos, Carol A. Scorer, & Jeffrey J. Clare, *Foreign Gene Expression in Yeast: A Review*, 8 YEAST 423 (1992) ("Romanos").

[6] U.S. Patent No. 5,436,156 ("Van Gorcom").

combinations"). ABF argued that the thermostability claims of the '300 patent would have been obvious for two independent reasons: (1) they were inherent properties of the Dassa/Greiner combinations, and (2) they were disclosed by Olsen.[7] In its Final Written Decision, the Board concluded that there was a motivation to combine and reasonable expectation of success for the Dassa/Greiner combinations and that the thermostability dependent claims of the '300 patent were obvious due to inherency. *See Final Written Decision*, at 127–31, 141, 172–73.

For the Kretz-based invalidity arguments, ABF asserted that Kretz (1) anticipated certain challenged claims of the '300 patent as § 102(e) prior art[8] and (2) rendered all challenged claims obvious in combination with other references. *See id.* at 10–11. The Board determined that Cornell failed to antedate Kretz, *id.* at 34, and that Kretz anticipated certain claims and rendered obvious the rest in light of those other references, *see id.* at 172–73.

Cornell appeals from all six final written decisions in this consolidated appeal. The Patent and Trademark Office Director intervened to defend the Board's decisions after ABF filed a notice of non-participation. We have jurisdiction under 28 U.S.C. § 1295(a)(4)(A).

DISCUSSION

Cornell asserts primarily that three Board conclusions lack substantial evidence: (1) that there was a motivation to combine and reasonable expectation of success for the Dassa/Greiner combinations; (2) that the thermostability properties of the phytases produced by the claimed heterologous method are inherent; and (3) that Cornell failed to

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[7] Ole Olsen & Karl Kristian Thomsen, *Improvement of Bacterial* ß*-Glucanase Thermostability by Glycosylation*, 137 J. GEN. MICROBIOLOGY 579 (1991) ("Olsen").

[8] 35 U.S.C. § 102(e) (2010).

antedate Kretz. We affirm the Board on the first two issues and accordingly do not reach the third.

I

Putting aside the thermostability limitations of the '300 patent's dependent claims (discussed below), Cornell does not dispute that the Dassa/Greiner combinations disclose all limitations of the relevant claims. Cornell disputes only the Board's findings of motivation to combine and reasonable expectation of success for an *E. coli* phytase with a fungal host. Those are both fact questions that we review for substantial evidence, which is "such relevant evidence as a reasonable mind might accept as adequate to support a conclusion." *In re Mouttet*, 686 F.3d 1322, 1331 (Fed. Cir. 2012); *PAR Pharm., Inc. v. TWI Pharms., Inc.*, 773 F.3d 1186, 1196 (Fed. Cir. 2014).

In finding a motivation to combine, the Board credited ABF's expert testimony that *P. pastoris* yeast was known to "produce high yields of heterologous protein [e.g., bacterial protein] and, thus, reduce industrial costs—an important factor in producing phytases for livestock feed" on an industrial level. *Final Written Decision*, at 128. The Board found this to be "persuasive evidence setting forth reasons why [a] skilled artisan would have been motivated to express an *E. coli* appA [enzyme] in a fungal cell." *Id.* This constitutes substantial evidence for a motivation to combine. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 420 (2007) ("[A]ny need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.").

Cornell's two main arguments to the contrary are unpersuasive. First, Cornell asserts that the Board's motivation-to-combine conclusion is contrary to ABF's expert

testimony that the Wodzinski reference[9] taught away from using a bacterial phytase in animal feed. We note that Wodzinski is not a part of the Dassa/Greiner combinations; additionally, the Board did not make any determination as to whether Wodzinski does or does not teach away. *Final Written Decision*, at 84. And even if the Board concluded that Wodzinski's suggestions about bacterial phytases in animal feed, generally, were outweighed by the rest of the record evidence about producing *E. coli* appA phytase via a fungal host for use in animal feed, specifically, we would see no error. *See In re Young*, 927 F.2d 588, 591 (Fed. Cir. 1991).

Second, Cornell contends that the art suggested that pairing a bacterial phytase with a bacterial host was more advantageous than pairing such a phytase with a fungal host. Even if that's true, as the Board correctly noted, "the law 'does not require that the motivation be the best option, only that it be a suitable option.'" *Final Written Decision*, at 81–82 (emphasis omitted in original) (quoting *PAR Pharm.*, 773 F.3d at 1197–98).

Cornell's challenge to the substantial evidence of the Board's reasonable-expectation-of-success finding is similarly flawed. Cornell asserts a skilled artisan would have "had no reason to expect 'that expressing the *E. coli* phytase in a fungal host would have produced an active enzyme'" due to increased glycosylation, as its expert testified. Appellant's Br. 33 (quoting J.A. 4084–89). Cornell's expert provided two examples of unsuccessful heterologous systems "where one of ordinary skill . . . may have attributed the lack of enzyme activity to glycosylation." *Final Written Decision*, at 90. But the Board was free to weigh ABF's expert testimony more heavily, and that's what it did. The Board credited ABF's expert testimony providing "nine or ten" contrary examples of systems that

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[9] *See* J.A. 22462–63; *see also* J.A. 15187–89.

produced active bacterial enzymes in yeast hosts. *Id.* at 90–91. In addition, the Board pointed to Cornell's expert testimony that, "in the majority of cases[,] glycosylation did not have an effect on the activity of the enzyme." *Id.* at 91–92.

We accordingly affirm the Board's determination that there was a motivation to combine and reasonable expectation of success for the Dassa/Greiner combinations.[10]

II

Cornell also challenges the Board's finding that the thermostability limitations in the '300 patent's dependent claims are inherent results of the Dassa/Greiner combinations. Whether prior art inherently discloses a claim limitation is a question of fact that we review for substantial evidence. *PAR Pharm.*, 773 F.3d at 1194.

The Board found the thermostability limitations inherent to a heterologous system expressing the Dassa/Greiner *E. coli* appA phytase in a fungal host disclosed by Cheng, Romanos, or Van Gorcom, including *P. pastoris* and *S. cerevisiae*. The Board cited Cornell's expert testimony, ABF's expert testimony, the '300 patent, and prosecution history as support. *Final Written Decision*, at 78–79. Indeed, the Board credited Cornell's expert, who confirmed that "express[ing] the *same enzyme* in the *same host* under the *same conditions*" produces "inherent results," like thermostability characteristics. J.A. 7694–95 (emphasis added); *Final Written Decision*, at 78 (citing J.A. 7695). This constitutes substantial evidence supporting the Board's determination.

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[10] We are not persuaded by Cornell's contention that the Board's analysis of the non-Kretz combinations is infected by analysis of Kretz.

Cornell's two arguments to the contrary are not persuasive. First, Cornell faults the Board for citing no data outside of the '300 patent to support its inherency finding. But the Board permissibly cited the '300 patent's disclosure that an *E. coli* appA phytase expressed in a *P. pastoris* host has optimum activity at 60 degrees Celsius as well as the patent's teaching that an *E. coli* appA phytase expressed in a *S. cerevisiae* host retained 69 percent of its activity after heating it for 15 minutes at 80 degrees Celsius. *Final Written Decision*, at 78–79; *see Hospira, Inc. v. Fresenius Kabi USA, LLC*, 946 F.3d 1322, 1329–30 (Fed. Cir. 2020). That data is consistent with the thermostability limitations of claims 10–12. Although it may be possible that the conditions of the Dassa/Greiner combinations were not the same as those described in the '300 patent, Cornell did not make that argument and offered no evidence to that effect. Oral Arg. at 26:27–27:10, No. 20-2334, https://oralarguments.cafc.uscourts.gov/default.aspx?fl=20-2334_05032022.mp3.

Second, Cornell asserts that the Board's inherency finding for the Dassa/Greiner combinations is at odds with its finding of no inherency with respect to Kretz as anticipatory art. Cornell argues that this is especially concerning because the standard for inherency under § 103 is higher than that under § 102. In this case, we find no error. The Board explained that it did not find the thermostability limitations inherent under Kretz because ABF was relying on Kretz's teachings using the *E. coli* B phytase whereas the thermostability data from the '300 patent resulted from using the *E. coli* appA phytase. *Final Written Decision*, at 58. This is consistent with the Board's reliance on Cornell's expert testimony that the same enzyme is needed for the thermostability characteristics of an enzyme produced by a particular enzyme-host combination to be inherent.

We thus also affirm the Board's inherency finding as supported by substantial evidence. Since that resolves this

appeal as to all patents and all claims, we do not reach Cornell's other arguments, including those about antedating Kretz.

CONCLUSION

We have considered the parties' remaining arguments but find them unpersuasive. For the foregoing reasons, we affirm the Board's obviousness conclusions.

AFFIRMED

COSTS

Costs to Intervenor.