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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BUTAMAX™ ADVANCED BIOFUELS LLC,
Petitioner,

v.

GEVO, INC.,
Patent Owner.

Case IPR2013-00539
Patent 8,273,565 B2

Before RAMA G. ELLURU, CHRISTOPHER L. CRUMBLEY, and KERRY BEGLEY, *Administrative Patent Judges.*

BEGLEY, *Administrative Patent Judge.*

FINAL WRITTEN DECISION
35 U.S.C. § 318(a) and 37 C.F.R. § 42.73

Butamax™ Advanced Biofuels LLC ("Petitioner") filed a Petition requesting *inter partes* review of claims 1–19 of U.S. Patent No. 8,273,565 B2 (Ex. 1001, "the '565 patent"). Paper 4 ("Pet."). Pursuant to 35 U.S.C. § 314(a), we determined the Petition showed a reasonable likelihood that Petitioner would prevail in establishing the unpatentability of claims 1–9 and 11–19 of the '565 patent, and instituted an *inter partes* review of these

claims on certain asserted grounds of unpatentability. Paper 9 ("Inst. Dec."). We, however, did not institute review of claim 10 of the '565 patent, because we determined the Petition did not show a reasonable likelihood that Petitioner would prevail in establishing the claim to be unpatentable. *Id.* at 27–29.

Patent Owner Gevo, Inc. ("Patent Owner") then filed a Patent Owner Response. Paper 19 ("PO Resp."). Petitioner filed a Reply to Patent Owner's Response. Paper 21 ("Reply").

An oral hearing was held on October 28, 2014, pursuant to a request by Petitioner. Paper 32 ("Tr."); Petitioner Butamax's Request for Oral Argument (Paper 23); Order – Trial Hearing (Paper 24), at 1. During the oral hearing, Petitioner presented argument; Patent Owner rested on its arguments in the Patent Owner Response. Tr. 40:3–13; *see id.* at 39:7–42:18; Order – Conduct of the Proceeding (Paper 25).

We issue this Final Written Decision pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. For the reasons that follow, we determine Petitioner has shown by a preponderance of the evidence that claims 1–9 and 11–19 of the '565 patent are unpatentable.

I. BACKGROUND

A. THE '565 PATENT

The '565 patent, titled "Methods of Increasing Dihydroxy Acid Dehydratase Activity to Improve Production of Fuels, Chemicals, and Amino Acids," is directed to recombinant yeast microorganisms with increased activity of dihydroxy acid dehydratase ("DHAD"). Ex. 1001, [57], 1:29–2:25. DHAD is an enzyme that catalyzes steps in various biosynthetic pathways that produce metabolites, such as isobutanol, a

common fuel additive. *Id.* at [57], 1:46–66, Fig. 1. Increased DHAD activity is favorable for producing these metabolites. *Id.* at 1:65–2:20, 24:31–33. The patent also discloses methods of producing such metabolites by cultivating the disclosed recombinant microorganisms in a culture medium containing a carbon source feedstock. *Id.* at [57], 8:55–63.

The specification of the '565 patent discloses recombinant microorganisms with increased DHAD activity resulting from alterations in the regulation, expression, or activity of either or both the *GRX3* and *GRX4* genes, which encode the proteins monothiol glutaredoxin-3 ("Grx3") and monothiol glutaredoxin-4 ("Grx4"), respectively. *Id.* at 24:36–50; *see id.* at 23:30–57, 24:1–30. For example, in one embodiment, the Grx3 protein, the Grx4 protein, or both the Grx3 and Grx4 proteins are "deleted or attenuated." *Id.* at 24:9–11. The specification also discloses recombinant microorganisms with improved DHAD activity resulting from overexpression of either or both the transcriptional activator genes *AFT1* and *AFT2*, which encode activator of ferrous transport ("Aft") proteins, Aft1 and Aft2, respectively. *Id.* at 2:9–25, 4:14–26, 15:49–54. The DHAD in these embodiments may be localized in either the cytosol or the mitochondria of the microorganisms. *Id.* at 3:30–46, 16:33–34, 24:36–45. Further, the recombinant microorganisms may be one of various disclosed yeast genera and species, including *Saccharomyces cerevisiae*. *See id.* at 7:49–8:54.

B. Illustrative Claim

Claim 1, the only independent claim of the '565 patent, is illustrative of the challenged claims:

> 1. A recombinant yeast microorganism comprising a recombinantly overexpressed polynucleotide encoding a dihydroxy acid dehydratase (DHAD),

> wherein said recombinant yeast microorganism is engineered to comprise at least one inactivated monothiol glutaredoxin selected from the group consisting of monothiol glutaredoxin-3 (GRX3) and monothiol glutaredoxin-4 (GRX4),
>
> and wherein said inactivated monothiol glutaredoxin results from the deletion of one or more nucleotides of an endogenous gene encoding said monothiol glutaredoxin, the insertion of one or more nucleotides into an endogenous gene encoding said monothiol glutaredoxin, or combinations thereof.

Id. at 91:15–26 (line breaks added).

C. Instituted Grounds of Unpatentability

We instituted *inter partes* review of the '565 patent on the following grounds of unpatentability asserted in the Petition. Inst. Dec. 29.

Claim[s]	Basis	Reference[s]
1–4, 6–8, and 11–19	§ 102(e)	Flint
1–4, 6–8, 11, 13, 14, and 16–19	§ 103(a)	Anthony, Puig, and Ojeda
5	§ 103(a)	Anthony, Puig, Ojeda, and Li
9	§ 103(a)	Anthony, Puig, Ojeda, and van Maris

These instituted grounds rely on the following prior art references:

Anthony	US 2010/0081179 A1	Apr. 1, 2010	Ex. 1005
Li	US 2009/0163376 A1	June 25, 2009	Ex. 1015
Flint	WO 2011/103300 A2	Aug. 25, 2011	Ex. 1003

Antonius J. A. van Maris et al., *Directed Evolution of Pyruvate Decarboxylase-Negative* Saccharomyces cerevisiae, *Yielding a C_2-Independent, Glucose-Tolerant, and Pyruvate-Hyperproducing Yeast*, 70 Applied & Envtl. Microbiology 159 (2004). (Ex. 1008, "van Maris.")

Sergi Puig et al., *Coordinated Remodeling of Cellular Metabolism During Iron Deficiency Through Targeted mRNA Degradation*, 120 Cell 99 (2005). (Ex. 1006, "Puig.")

Luis Ojeda et al., *Role of Glutaredoxin-3 and Glutaredoxin-4 in the Iron Regulation of the Aft1 Transcriptional Activator in* Saccharomyces cerevisiae, 281 J. BIOLOGICAL CHEMISTRY 17661 (2006). (Ex. 1007, "Ojeda.")

II. ANALYSIS

A. LEVEL OF ORDINARY SKILL IN THE ART

We begin our analysis by addressing the level of ordinary skill in the art, which is relevant to the governing standards we apply in the remainder of our analysis. Petitioner proposes a standard for one of ordinary skill in the art. Pet. 6; *see* Ex. 1002 (Decl. of Dennis J. Thiele, Ph.D.) ¶ 17. Patent Owner has not contested this proposal or proffered an alternative standard. We adopt Petitioner's proposed standard and, therefore, determine that one of ordinary skill in the art would have had either: (1) "a Ph.D. in the life sciences or a similar related discipline, and . . . familiarity, training, and experience in molecular biology, microbial genetics and/or microbial metabolism," or (2) "a scientific background such as a Bachelor's degree in the life sciences (e.g., biology, microbiology, molecular biology or biochemistry) or a similar related discipline, and . . . substantial familiarity, training, and experience in molecular biology, microbial genetics and/or microbial metabolism." Pet. 6; *see* Ex. 1002 ¶ 17.

B. CLAIM INTERPRETATION

We next address the meaning of the claims. The Board interprets claims using the "broadest reasonable construction in light of the specification of the patent in which [they] appear[]." 37 C.F.R. § 42.100(b); *see In re Cuozzo Speed Techs., LLC*, No. 2014-1301, 2015 WL 448667, at *5–*8 (Fed. Cir. Feb. 4, 2015). We presume a claim term carries its "ordinary and customary meaning," which is "the meaning that the term

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