United States Court of Appeals for the Federal Circuit

BUTAMAX(TM) ADVANCED BIOFUELS LLC,
Plaintiff-Appellant,

v.

GEVO, INC.,
Defendant- Appellee.

2013-1342

Appeal from the United States District Court for the District of Delaware in No. 11-CV-0054, Judge Sue L. Robinson.

Decided: February 18, 2014

LEORA BEN-AMI, Kirkland & Ellis, LLP, of New York, New York, argued for plaintiff-appellant. With her on the brief were THOMAS F. FLEMING, CHRISTOPHER T. JAGOE, and PETER B. SILVERMAN.

MICHELLE S. RHYU, Cooley, LLP, of Palo Alto, California, argued for defendant-appellee. With her on the brief were STEPHEN C. NEAL, BENJAMIN G. DAMSTEDT, DANIEL J. KNAUSS, of Palo Alto, California; and JAMES P. BROGAN, of Broomfield, Colorado.

Before RADER, *Chief Judge,* LINN, and WALLACH, *Circuit Judges.*

LINN, *Circuit Judge.*

Butamax™ Advanced Biofuels LLC ("Butamax") owns U.S. Pat. No. 7,851,188 ("'188 patent") and No. 7,993,889 ("'889 patent") (collectively, the "patents-in-suit") and appeals a final judgment entered against it following the district court's 1) claim construction and denial of Butamax's motion for summary judgment of literal infringement of the asserted claims of the '188 and '889 patents by Gevo, Inc. ("Gevo"), 2) grant of Gevo's motion for summary judgment of noninfringement under the doctrine of equivalents of the asserted claims of the '188 and '889 patents, 3) grant of Gevo's motion for summary judgment of invalidity of claims 12 and 13 of the '889 patent for lack of written description, and 4) judgment of invalidity of claims 12 and 13 of the '889 patent for lack of enablement. Opinion, *Butamax™ Advanced Biofuels LLC v. Gevo, Inc.*, No. 11-54-SLR, 2013 WL 3914467 (D. Del. March 19, 2013) ("*Opinion*"). Because the district court erred in its claim construction, this court vacates the district court's denial of Butamax's motion for summary judgment of infringement and its grant of Gevo's motion of noninfringement under the doctrine of equivalents. Because the district court failed to recognize the existence of genuine issues of material fact on Gevo's motion for summary judgment of invalidity as to claims 12 and 13 of the '889 patent, this court reverses the district court's grant of that motion. Finally, this court reverses the grant of summary judgment of invalidity for lack of enablement because that judgment appears to have been a scrivener's error.

I. BACKGROUND

A. The '188 Patent

The '188 patent covers a recombinant microbial host cell that uses a particular biosynthetic pathway to produce isobutanol, which is useful as a fuel or fuel additive. *Opinion* at *3. The claimed biosynthetic pathway comprises essentially five steps. *See* '188 Patent fig. 1.

Claim 1 of the '188 patent recites the first four steps:

> 1. A recombinant microbial host cell comprising heterologous DNA molecules encoding polypeptides that catalyze substrate to product conversions for each step below:
>
> i) pyruvate to acetolactate;
>
> ii) acetolactate to 2,3-dihydroxyisovalerate;
>
> iii) 2,3-dihydroxyisovalerate to α-ketoisovalerate; and
>
> iv) α-ketoisovalerate to isobutyraldehyde;
>
> wherein said microbial host cell produces isobutanol; and wherein
>
> a) the polypeptide that catalyzes a substrate to product conversion of pyruvate to acetolactate is acetolactate synthase having the EC number 2.2.1.6;
>
> b) the polypeptide that catalyzes a substrate to product conversion of acetolactate to 2,3-dihydroxyisovalerate is *acetohydroxy acid isomeroreductase* having the EC number 1.1.1.86;
>
> c) the polypeptide that catalyzes a substrate to product conversion of 2,3-dihydroxyisovalerate to α-ketoisovalerate is acetohydroxy acid dehydratase having the EC number 4.2.1.9;

> d) the polypeptide that catalyzes a substrate to product conversion of α-ketoisovalerate to isobutyraldehyde is branched-chain α-keto acid decarboxylase having the EC number 4.1.1.72.

'188 Patent col. 335 ll. 21–44 (emphasis added). In the fifth step, isobutyraldehyde is converted into isobutanol. *See* '188 Patent col. 336 ll. 43–48 (dependent claim 18, reciting a method for producing isobutanol from the recombinant microbial host cell of claim 1).

Claim 15 depends from claim 1 and recites "[a] host cell according to claim 1 wherein the acetohydroxy acid isomeroreductase has an amino acid sequence selected from the group consisting of SEQ ID NO:43, SEQ ID NO:181, SEQ ID NO:183, and SEQ ID NO:185." '188 Patent col. 336 ll. 33–36. SEQ ID NO:183 is a sequence of *Methanococcus*.

This appeal primarily concerns step (ii): the conversion of acetolactate ("AL") to 2,3-dihydroxyisovalerate ("DHIV"), catalyzed by the polypeptide enzyme acetohydroxy acid isomeroreductase (also known as keto-acid reductoisomerase, or "KARI") "having the EC number 1.1.1.86." KARI assists reactions by rearranging (i.e., isomerizing) a reagent and also by "reducing" (the process of adding electrons) this rearranged molecule. To accomplish the reduction, KARI needs a source for the added electrons. This electron source is known as the "cofactor" or "coenzyme." Two such cofactors are NADH (nicotinamide adenine dinucleotide + hydrogen) and NADPH (nicotinamide adenine dinucleotide phosphate + hydrogen).

The '188 patent's specification provides "definitions . . . to be used for the interpretation of the claims," including a definition of KARI:

> an enzyme that catalyzes the conversion of acetolactate to 2,3-dihydroxyisovalerate using NADPH

> (reduced nicotinamide adenine dinucleotide phosphate) as an electron donor. Preferred acetohydroxy acid isomeroreductases are known by the EC number 1.1.1.86 and sequences are available from a vast array of microorganisms, including but not limited to . . . *Methanococcus maripaludis* . . . .

'188 Patent col. 7 ll. 35–47.

EC number 1.1.1.86, referenced in both this definition and claim 1, is an Enzyme Commission number for an enzyme known by the names KARI, "acetohydroxy acid isomeroreductase," and several other names. The EC enzyme classification system was developed in the 1950s to standardize enzyme nomenclature. *Opinion* at *15. Notably, Rule 18 of the EC system states that "[f]or oxidoreductases using NAD^+ or $NADP^+$ [the oxidized states of NADH and NADPH, respectively], the coenzyme should always be named as the acceptor" unless a certain exception applies, which is irrelevant here. *Id.* However, it also appears common to assign different EC numbers to the same enzyme, where the difference between the numbers is the identity of the cofactor named. *Id.* at 15 n.8. EC number 1.1.1.86 names only $NADP^+$ as an acceptor, and neither party calls attention to another EC number for KARI naming any other cofactor as an acceptor.

Butamax alleges that Gevo infringes claim 1 of the '188 patent and claims 2–4, 13–15, 17, and 36 dependent therefrom, as well as claim 18 and claims 19–25, and 34–35 dependent therefrom.

B. The '889 Patent

The '889 patent issued from a divisional of the application from which the '188 patent issued. The patents' specifications largely are identical, each for example including the KARI definition quoted above. *See* '889

Patent col. 7 ll. 8–20. The '889 patent focuses on a method of producing isobutanol from a recombinant yeast microorganism that expresses the five-step biosynthetic pathway described above.

Claim 1 of the '889 patent states:

> 1. A method for producing isobutanol comprising;
>
> a. providing a fermentation media comprising carbon substrate; and
>
> b. contacting said media with a recombinant yeast microorganism expressing an engineered isobutanol biosynthetic pathway wherein said pathway comprises the following substrate to product conversions;
>
> i. pyruvate to acetolactate (pathway step a);
>
> ii. acetolactate to 2,3-dihydroxyisovalerate (pathway step b);
>
> iii. 2,3-dihydroxyisovalerate to α-ketoisovalerate (pathway step c);
>
> iv. α-ketoisovalerate to isobutyraldehyde (pathway step d); and
>
> v. isobutyraldehyde to isobutanol (pathway step e);
>
> and wherein
>
> a) the substrate to product conversion of step (i) is performed by an acetolactate synthase enzyme;
>
> b) the substrate to product conversion of step (ii) is performed by an acetohydroxy acid isomeroreductase enzyme;

> c) the substrate to product conversion of step (iii) is performed by an acetohydroxy acid dehydratase enzyme;
>
> d) the substrate to product conversion of step (iv) is performed by a decarboxylase enzyme; and
>
> e) the substrate to product conversion of step (v) is performed by an alcohol dehydrogenase enzyme;
>
> whereby isobutanol is produced.

'889 Patent col. 325 ll. 14–43. As with the '188 patent, the primary issue with the '889 patent on appeal involves step (ii): the conversion of AL to DHIV using acetohydroxy acid isomeroreductase enzyme, i.e., KARI. Unlike claim 1 of the '188 patent, claim 1 of the '889 patent does not refer to any EC classification number.

Butamax alleges that Gevo has infringed claim 1 of the '889 patent and claims 2–14 and 16–19 dependent therefrom.

C. The Parties and Previous Proceedings

Butamax was formed in 2009 as a joint venture between E.I. du Pont de Nemours and Co. ("Du Pont") and BP Biofuels North America LLC. The applications that led to the patents-in-suit are part of Du Pont's previous research and development into isobutanol production. The patents-in-suit have been assigned to Butamax.

Gevo was incorporated in 2005 as Methanotech, Inc. and likewise pursues isobutanol production. Gevo uses mutant KARI enzymes that when using NADH as a cofactor exhibit significantly lower K_m (Michaelis-Menten constant) for the AL-to-DHIV conversion than when using NADPH as a cofactor. This indicates that the reaction rate with Gevo's mutant enzymes is much faster with NADH than with NADPH.

On January 14, 2011, Butamax sued Gevo in the district court and on September 22, 2011, moved for a preliminary injunction predicated on the '889 patent. The district court construed the KARI term as "an enzyme that is solely NADPH-dependent" and denied the motion. *Butamax(TM) Advanced Biofuels LLC v. Gevo, Inc.*, 486 F. App'x 883 (Fed. Cir. 2012). This court affirmed the denial of the preliminary injunction. *Id.* However, this court noted that the district court's construction of the KARI term was "very questionable" and asked the district court "to reconsider its construction when it holds the *Markman* hearing." *Id.*

At the *Markman* hearing, the district court construed the term as "an enzyme known by the EC number 1.1.1.86 that catalyzes the conversion of acetolactate to 2,3-dihydroxyisovalerate and is NADPH-dependent." *Opinion* at *21. Additionally, adopting Butamax's proposed construction, the district court construed the '889 patent's term "pathway step (a); . . . pathway step (b); . . . pathway step (c); . . . pathway step (d); . . . pathway step (e)" to mean "the pathway steps a-e are contiguous steps such that the product of step a is the substrate for step b; the product of step b is the substrate for step c; etc." *Id.* at *22.

At the district court, Butamax moved for summary judgment of infringement of the patents-in-suit and for a judgment of no invalidity of the '889 patent. *Opinion* at *2. Gevo moved for summary judgment of invalidity and non-infringement. *Id.* In a memorandum opinion, the district court denied Butamax's motion for summary judgment of infringement. The district court granted Gevo's motion for summary judgment of noninfringement as it related to the doctrine of equivalents, but otherwise denied the motion. Each of Butamax's motion of no invalidity and Gevo's motion for invalidity was granted by the district court with respect to some claims and denied with respect to others. Relevant to this appeal, the dis-

trict court granted Gevo's invalidity motion and denied Butamax's motion of no invalidity with respect to claims 12 and 13 of the '889 patent, finding the claims lacking in written description support. *Opinion* at *52–53. The district court issued an order reflecting the memorandum opinion and also holding claims 12 and 13 the '889 patent invalid for lack of enablement, a ground not raised in the motions of the parties.

Butamax appeals the claim construction of the KARI term, the denial of Butamax's motion for summary judgment of literal infringement, the grant of Gevo's motion for summary judgment of noninfringement under the doctrine of equivalents, the grant of Gevo's motion for summary judgment of invalidity of claims 12 and 13 of the '889 patent for inadequate written description, and the order also holding those same claims invalid for lack of enablement. This court has jurisdiction under 28 U.S.C. § 1295(a)(1).

II. DISCUSSION

A. Standards of Review

"We review claim construction de novo." *Thorner v. Sony Computer Entm't Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012).

Summary judgment is granted "if the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). "This court reviews the district court's grant or denial of summary judgment under the law of the regional circuit." *Lexion Med., LLC v. Northgate Techs., Inc.,* 641 F.3d 1352, 1358 (Fed. Cir. 2011). The Third Circuit "review[s] an order granting summary judgment de novo, applying the same standard used by the District Court." *Azur v. Chase Bank, USA, Nat'l Ass'n,* 601 F.3d 212, 216 (3d Cir. 2010) (quotation omitted).

"[A] determination of infringement, both literal and under the doctrine of equivalents, is a question of fact." *Lockheed Martin Corp. v. Space Sys./Loral, Inc.*, 324 F.3d 1308, 1318 (Fed. Cir. 2003). "Summary judgment on the issue of infringement is proper when no reasonable jury could find that every limitation recited in a properly construed claim either is or is not found in the accused device either literally or under the doctrine of equivalents." *PC Connector Solutions LLC v. SmartDisk Corp.*, 406 F.3d 1359, 1364 (Fed. Cir. 2005).

B. Claim Construction

The primary dispute between the parties concerns whether the claimed KARI must be "NADPH-dependent." The district court considered the patents' specifications, prosecution histories, and the extrinsic evidence such as expert testimony and the EC enzyme classification system and other enzyme databases. It concluded that in the "state of the art," the "KARI enzyme known by the EC number 1.1.1.86 was generally understood to be NADPH-dependent." *Opinion* at *20. This decision is premised in large part on the district court's conclusion that the patentees acted as their own lexicographers in defining KARI by reference to EC number 1.1.1.86 and the enzyme's "use" of NADPH rather than use of NADH or both NADPH and NADH. *Id.* at *19–20. The district court therefore construed the KARI term as "an enzyme known by the EC number 1.1.1.86 that catalyzes the conversion of acetolactate to 2,3-dihydroxyisovalerate and is NADPH-dependent." *Id.* at *21.

Butamax argues that the district court erred because KARI's plain meaning merely refers to an enzyme catalyzing the AL to DHIV conversion and because the patentees did not expressly relinquish any of that claim scope in the specification or the prosecution history. Butamax contends that the patentees in defining KARI did not clearly express an intent to redefine KARI to be NADPH-

dependent. In support, Butamax points to the other claims, the embodiments provided in the specifications, and extrinsic evidence including contemporary scientific literature, a database referenced in EC number 1.1.1.86, and Gevo's use of EC number 1.1.1.86 to describe its own enzymes.

Gevo disagrees, arguing that the district court construed the term correctly. Gevo contends that the specifications' definition of KARI demonstrates that the patentees did clearly express an intent to specify KARI as NADPH-dependent, and points to other aspects of the specifications as well as the prosecution histories in support. Gevo further contends that extrinsic evidence, such as EC number 1.1.1.86 and its references, the EC rules, and Butamax's internal documents and subsequent patent applications indicate that the claimed KARI must be NADPH-dependent.

Generally, claim terms are:

> given their ordinary and customary meaning as understood by a person of ordinary skill in the art when read in the context of the specification and prosecution history. There are only two exceptions to this general rule: 1) when a patentee sets out a definition and acts as his own lexicographer, or 2) when the patentee disavows the full scope of a claim term either in the specification or during prosecution.

Thorner, 669 F.3d at 1365 (citation omitted). "To act as its own lexicographer, a patentee must 'clearly set forth a definition of the disputed claim term' other than its plain and ordinary meaning." *Id.* at 1365 (quoting *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002)). "It is not enough for a patentee to simply disclose a single embodiment or use a word in the same manner in all embodiments, the patentee must 'clearly express an intent' to redefine the term." *Id.* (citing *Helmsderfer v.*

Bobrick Washroom Equip., Inc., 527 F.3d 1379, 1381 (Fed. Cir. 2008)).

i. KARI's Ordinary Meaning

The initial inquiry is whether the plain meaning of KARI indicates that the enzyme is NADPH-dependent. While the district court found that "the scientific references almost exclusively characterize KARI enzymes as NADPH-dependent," *Opinion* at *19, there is nothing in the record to indicate that persons of ordinary skill in the art in 2005 understood the plain meaning to be limited to dependence on NADPH as a cofactor. Gevo conceded as much at the district court, acknowledging that under KARI's plain meaning, the enzyme converts AL to DHIV "using NADH or NADPH as a cofactor." *See* Joint Appendix ("J.A.") 10240.

We agree that the plain meaning of KARI itself imposes no limitation on the cofactor or source of electrons for the AL to DHIV conversion. The question then becomes whether the asserted claims are limited, as Gevo contends, to the use of NADPH only based principally on the "explicit definition" set forth in the patents-in-suit. *See* J.A. 10241.

ii. The Specifications and Claims

a. The Patentees' Definition of KARI

The patents provide definitions of several terms, noting that "[t]he following definitions and abbreviations are to be used for the interpretation of the claims and specification." '188 Patent col. 7 ll. 12–14.[1] As described above, the patents subsequently define KARI as:

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[1] Because the specifications of the patents-in-suit largely are identical, the court for brevity will cite only to the '188 patent.

> an enzyme that catalyzes the conversion of acetolactate to 2,3-dihydroxyisovalerate using NADPH (reduced nicotinamide adenine dinucleotide phosphate) as an electron donor. Preferred acetohydroxy acid isomeroreductases are known by the EC number 1.1.1.86 and sequences are available from a vast array of microorganisms, including but not limited to . . . *Methanococcus maripaludis* . . . .

'188 Patent col. 7 ll. 35–47.

It cannot be disputed that the patentees offered a definition of KARI. It is disputed, however, whether this definition "clearly expresses an intent" to redefine KARI in a way that differs from the plain and ordinary meaning identified above and, if so, the extent of any such difference. Gevo contends that the phrase "using NADPH . . . as an electron donor" is a clear expression of the patentees' intent to exclude KARI that are not "NADPH-dependent."

Butamax disagrees and asserts that the fact that an enzyme can catalyze the conversion of AL to DHIV "using NADPH" does not, on its own, indicate that the enzyme cannot *also* use other cofactors, such as NADH, to catalyze that conversion.

Gevo argues that Butamax's interpretation reads out an important aspect of the patentees' definition of KARI because all KARI are capable of using NADPH as a cofactor. Thus, Gevo argues it would have been completely unnecessary for the patents to have referred to "using NADPH" in the first instance. Gevo also argues that the phrase "using NADPH" must be understood in light of other aspects of the specifications. Gevo first contends that the specifications use the term "use(s) NADPH" interchangeably with the phrase "NADPH-dependent." Gevo points to this passage:

> [A]lcohol dehydrogenase VI (ADH6) and Ypr1p . . . use NADPH as electron donor. An NADPH-dependent reductase, YqhD, . . . has also been recently identified in *E. coli* . . . .

'188 Patent col. 12 ll. 50–60. The patents further describe ADH6 as "NADPH-dependent cinnamyl alcohol dehydrogenase." *Id.* at col. 4 ll. 60–62. However, "[i]t is not enough for a patentee to simply disclose a single embodiment or use a word in the same manner in all embodiments." *Thorner*, 669 F.3d at 1365.

We agree with Butamax and find no reason to constrict the phrase "using NADPH" to mean "only use NADPH" or "NADPH-dependent." We also disagree with Gevo's argument that such an interpretation reads out an important part of the patentees' definition. The patents' definition at least excludes as-yet-undiscovered KARI enzymes that could catalyze the conversion of AL to DHIV without using NADPH at all. Moreover, the description of specific types of KARI as NADPH-dependent does not clearly express an intent to redefine all KARI "using NADPH" as KARI that must be NADPH-dependent.

Next, Gevo points to the patents' descriptions of other enzymes that use or utilize either NAD^+ or "NADH . . . and/or NADPH" as an electron donor. *Id.* at col. 8 ll. 14–16, 25–29. Gevo contends that the patentees knew how to describe enzymes that used NADH or both NADH and NADPH and that the patentees instead chose to define KARI as using only NADPH.

Butamax counters that the patents' descriptions of other enzymes "using" or "utilizing" various cofactors merely is a reference to particular EC numbers or the assays for the enzymes in question. For example, Butamax contends that the standard assay for KARI is the Arfin-Umbarger assay, which "uses" NADPH to measure KARI activity by monitoring the consumption of NADPH in the presence of acetolactate and the enzyme in ques-

tion. Appellant's Br. 14. The patents' Example 2 expressly teaches to measure KARI activity "using the method described by Arfin and Umbarger," '188 Patent col. 33 ll. 45–47. Example 10 teaches using the same method. *Id.* at col. 39 ll. 4–5. Butamax also argues that the patents' reference to "using NADPH" merely matches the description of the enzyme in EC number 1.1.1.86, which notes the use of $NADP^+$ but is silent as to NAD^+ or NADH. Butamax notes that the other enzymes in question from the specifications have multiple EC numbers—each referring to NADH, NADPH, or both NADH and NADPH—and/or have multiple different assays for their identification—each assay using a different cofactor. Thus, Butamax argues that the patentees merely referred the other cofactors where appropriate. Appellant's Br. 45.

We agree with Butamax that the references to other enzymes as either using NAD^+ or using NADH and/or NADPH do not imply that the patentees intended to limit KARI's use of NADH. The patentees' description of KARI merely corresponds with the Arfin-Umbarger assay and the description of KARI in EC Number 1.1.1.86.

b. Reference to EC Number 1.1.1.86 in Claim 1

The '188 patent's claim 1 explicitly states that the enzyme in question is "acetohydroxy acid isomeroreductase having the EC number 1.1.1.86." '188 Patent col. 335 ll. 33–36. As described above, EC number 1.1.1.86 identifies $NADP^+$ as the cofactor, but does not itself mention NAD^+ or NADH. *See* Appellee's Br. 45. The EC rules provide that for an enzyme "using" both NADH and NADPH, the entry should "always" name both cofactors. Gevo contends that this confirms that a person of ordinary skill in the art understood KARI having EC number 1.1.1.86 to be NADPH-dependent.

It must first be appreciated that the EC nomenclature was drafted to categorize naturally-occurring enzymes and that new EC numbers generally are not created for

modified forms of enzymes that might rely on different cofactors. *See* J.A. 17810–11. The nomenclature is also not necessarily complete. In 2005, for example, it was known that some KARI, such as KARI from at least some species of *Methanococcus*, can use either cofactor effectively. Significantly, *Methanococcus* was explicitly recited in Butamax's own definition as a preferred KARI and recited in dependent claim 15. '188 Patent col. 7 ll. 40–47.

Butamax points to additional evidence showing persons of skill in the art would have understood that EC number 1.1.1.86 enzymes need not be NADPH-dependent. The EC number 1.1.1.86 entry contains a link to the BRENDA database (Braunchschweig Enzyme Database), which contains a reference to a mutated KARI enzyme in which NADH "can substitute for NADPH." Appellant's Br. 16. The district court discounted this lone reference because it was the only reference out of many indicating that NADH could be substituted and because the specific enzyme in question was a "quadruplet mutant." *Opinion* at *19–20.

However, even a single reference to mutant KARI under EC number 1.1.1.86 is particularly important here because the accused enzymes also are mutants. Butamax points to evidence that Gevo in approximately 2008—prior to the litigation—described its own mutant enzymes by reference to EC number 1.1.1.86. *See, e.g.,* Appellant's Br. 25; J.A. 9804. And of course Gevo contends that its enzymes are not NADPH-dependent. Though this evidence identified by Butamax did not exist until years after the patents-in-suits were filed in 2005, the BRENDA entry for EC number 1.1.1.86 referred to a mutant KARI that was not NADPH-dependent and was known prior to 2005, and Gevo years later indicated that EC number 1.1.1.86 still "would have been the best way [they] knew how" to describe its own mutant enzyme. Appellant's Br. 25 (citing testimony of Gevo's former Executive Vice President of Technology). *See e.g., ASM Am., Inc. v.*

Genus, Inc., 401 F.3d 1340, 1347 (Fed. Cir. 2005) (concluding that extrinsic evidence that post-dated the patent filing date nonetheless was helpful in determining how a person of ordinary skill in the art would have understood the claim term at the time it was filed).

For the foregoing reasons, the Court cannot conclude that the reference to EC number 1.1.1.86 is an expression of a clear intent to redefine KARI to be NADPH-dependent.

c. Preferred Embodiments and Dependent Claims

Other aspects of the patents raise further doubt of any express intent to redefine KARI in the limited way adopted by the district court. As above, the patents specifically list "*Methanococcus maripaludis* . . . SEQ ID NO: 183" as a source organism for the preferred KARI. '188 patent at col. 7 ll. 35–47. Moreover, dependent claim 15 of the '188 patent claims that KARI. '188 Patent col. 336 ll. 33–36. Butamax contends that it would be wrong to conclude that KARI from this organism are NADPH-dependent, pointing to evidence that at least some *Methanococcus* KARI are "able to utilize NADH as well as NADPH" and have "broad specificity for NADPH and NADH." Further, Butamax notes that "NADH supported 60% of the methanococcal activity obtained with NADPH." *See* R. Xing & W. Whitman, Characterization of Enzymes of the Branched-Chain Amino Acid Biosynthetic Pathway in Methanococcus spp, 173(6) J. Bacteriology 2086–92 (1991) ("Xing").

The district court discounted Xing because it provided no references or data to support these findings. *Opinion* at *19 (noting that Xing "included a single conclusory sentence with no data or other literature references to support it"). However, Xing's accuracy is not in dispute. Indeed, Gevo's 2007 Pat. App. No. 61/016,483 cites to Xing for this very proposition. Gevo does note that the patents identify the KARI of *Methanococcus maripaludis* while

Xing examined the KARI of *Methanococcus aeolicus*, a different species of *Methanococcus*. However, there is no genuine dispute that *Methanococcus maripaludis* exhibits similar characteristics. *See* Appellant's Reply Br. 9.

The district court's claim construction, without justification, excludes a preferred embodiment, which in this case also is the subject of dependent claim 15, and this court "normally do[es] not interpret claim terms in a way that excludes embodiments disclosed in the specification." *Oatey Co. v. IPS Corp.*, 514 F.3d 1271, 1276 (Fed. Cir. 2008).

iii. Prosecution History

Gevo also contends that the prosecution history evinces an express intent to redefine KARI to be NADPH-dependent. The Patent Office separately rejected Butamax's claims for lack of enablement and for lack of written description, and Gevo contends that the patentees' responses demonstrated that the claimed KARI are NADPH-dependent.

In the application leading to the '188 patent, the Patent Office rejected for inadequate written description a then-pending claim which stated:

> A recombinant microbial host cell comprising at least one DNA molecule encoding a polypeptide that catalyzes a substrate to product conversion selected from the group consisting of:
>
> i) pyruvate to acetolactate (pathway step a)
>
> ii) acetolactate to 2,3-dihydroxyisQvalerate (pathway step b)
>
> iii) 2,3-dihydroxyisovalerate to a-ketoisovalerate (pathway step c)
>
> iv) a-ketoisovalerate to isobutyraldehyde, (pathway step d), and

> v) isobutyraldehyde to isobutanol; (pathway step e)
>
> wherein the at least one DNA molecule is heterologous to said microbial host cell and wherein said microbial host cell produces isobutanol.

J.A. 6906. The Patent Office concluded that "[o]ne skilled in the art would require additional guidance, such as information regarding the specific identity and structure of the polypeptides that catalyze[]" the conversions in the claim. J.A. 6927. The patentees responded, amending the claim to refer to the EC numbers of the various enzymes, submitting a copy of the EC nomenclature rules, and pointing to the specific examples of the enzymes in the specification (including SEQ ID No: 183—*Methanococcus maripaludis*—as an example of KARI). J.A. 7095. The Patent Office concluded that this sufficiently described the claimed inventions but concluded that the claim lacked enablement for its full scope. J.A. 7117. The patentees disagreed, contending that the EC numbers, together with the level of ordinary skill in the art (including knowledge reflected in the BRENDA database) did enable skilled artisans to identify appropriate enzymes, and the examiner eventually withdrew the rejection. J.A. 7209, 7251.

In the application leading to the '889 patent, a then-pending claim similarly was rejected for lack of enablement. J.A. 7572–73. The patentees again amended, this time naming the enzymes used in each claimed step without referring to any EC numbers. J.A. 7585. The patentees argued that "[t]he specific enzymes that catalyze the steps of the pathway recited in the claims are described in the application in an abundance of detail," and went on to discuss Table 2 as a particular example. J.A. 7583.

In the prosecution history, the patentees defended their claims by referring the Patent Office to the EC

numbers and the examples of the enzymes provided in the specifications. For the reasons stated above, these references do not clearly express an intent by the patentees to redefine KARI to be NADPH-dependent. Indeed, the patentees specifically named *Methanococcus maripaludis* KARI as an example during the prosecution history, a KARI that appears to "use" NADH.

Accordingly, the court does not consider the prosecution history to warrant any limitation of the claimed KARI as being NADPH-dependent.

iv. Extrinsic Evidence

Gevo also relies on extrinsic evidence to support its arguments. EC number 1.1.1.86 was discussed above. Gevo further points to Butamax's internal documents and subsequent patent applications. For example, based on its research, Butamax filed a patent application in 2008 which stated that "discovery of a KARI enzyme that can use NADH as a cofactor as opposed to NADPH would be an advance in the art." J.A. 8794. Gevo contends that this application and the related evidence demonstrate that Butamax itself recognized that the earlier-filed patents-in-suit did not encompass KARI that use NADH.

However, as discussed above, the ordinary meaning of KARI is not cofactor dependent, and this subsequent extrinsic evidence does not clearly express an intent *at the time of the invention* to redefine KARI to use one cofactor over another. The subsequent discovery of the beneficial results obtained by the use of NADH does not support the conclusion that it was understood to be excluded as a cofactor at the time the patents-in-suit were filed.

v. Claim Construction

For all of the foregoing reasons, the term "acetohydroxy acid reductoisomerase" is construed as "an enzyme, whether naturally occurring or otherwise, known by the

EC number 1.1.1.86 that catalyzes the conversion of acetolactate to 2,3-dihydroxyisovalerate."

C. Infringement

Butamax contends that this court, under the more accurate claim construction, should reverse the district court's ruling that denied Butamax's motion for summary judgment of literal infringement. Gevo disagrees, contending that 1) there remains a dispute concerning the "contiguous" pathway term and 2) there remains a dispute as to the accused enzymes' "use" of NADPH.

The continuous pathway term relates only to the '889 patent and does not present a genuine issue of material fact on this record. Butamax provided expert testimony, and Gevo failed to present any contention, interrogatory, or expert testimony challenging Butamax's contention that the limitation was met.

As to the dispute over whether Gevo's enzymes use detectable levels of NADPH, Gevo argues on appeal that there is a distinction between *in vivo* and *in vitro* use that gives rise to a genuine issue of material dispute. However, Gevo does not appear to have argued at any point before the district court that the construction of KARI requires focusing on use of a specific cofactor *in vivo* as opposed to *in vitro*. This court declines to consider what appears to be a new claim construction argument raised for the first time on appeal.

Gevo further contends that Butamax's *in vitro* testing of Gevo's enzymes, showing them to use NADPH, may be unreliable. Appellee's Br. 61. Gevo's argument however, is not that the results of the testing were inaccurate, but rather that a person of ordinary skill in the art would not draw the same conclusions from the experiments as the conclusions drawn by Butamax's expert. Whether Gevo's arguments create a genuine issue of material fact under

the claim construction set forth in this opinion is best left to the district court on remand.

The court accordingly vacates the district court's denial of Butamax's motion for summary judgment of infringement of claims 1, 2–4, 13–15, 17–25, and 34–36 of the '188 patent and claims 1, 2–14, and 16–19 of the '889 patent and directs the district court to reconsider the question under this court's new claim construction.

D. Invalidity

i. Written Description of Claims 12 and 13 of the '889 Patent

Claim 12 of the '889 patent states:

> 12. The recombinant yeast microorganism of claim 1 wherein the said microorganism further comprises inactivated genes thereby reducing yield loss from competing pathways for carbon flow.

Claim 13 of the '889 patent states:

> 13. The recombinant yeast microorganism of claim 12, wherein said inactivated genes reduce pyruvate decarboxylase activity.

The district court found that both claims were inadequately described and thus invalid because the specification does not sufficiently describe how to inactivate genes to disable the competing synthetic pathway.

> When determining whether a specification contains adequate written description, one must make an "objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art." [Citation.] Because the specification is viewed from the perspective of one of skill, in some circumstances, a patentee may rely on information that is "well-known in

> the art" for purposes of meeting the written description requirement.

Boston Scientific Corp. v. Johnson & Johnson, 647 F.3d 1353, 1366 (Fed. Cir. 2011) (citation omitted).

The district court concluded that while the patent's specification "may be interpreted as identifying both the [ ] problem and the solution, it does not even begin to describe how to put into practice the solution." *Opinion* at *52. Butamax disagrees, but its evidence in support of its arguments is weak. First, Butamax contends that the patent does teach how to deactivate the pathway in question. In support, Butamax cites to multiple aspects of the specification, but each describes only a desire to deactivate the genes rather than how to actually do it. *See, e.g.,* '889 Patent col. 1 ll. 63–65 ("[t]here is a *need* . . . for an environmentally responsible, cost-effective process for the production of isobutanol as a single product"), col. 16 ll. 55–57 ("[t]he microbial host *has to be* manipulated in order to inactivate competing pathways for carbon flow by deleting various genes"), col. 12 ll. 12–17 ("[t]o prevent misdirection of pyruvate away from isobutanol production, a decarboxylase with decreased affinity for pyruvate *is desired*") (all emphasis added).

Next, Butamax contends that irrespective of what is explicitly taught in the specification itself, it was well-known in the art how to deactivate the genes that express the pathway. Butamax points to the testimony of Gevo's own experts, Dr. Stephanopolous and Dr. Kirsch, contending that they agreed that it was "conventional" in 2005 to deactivate the pathway. However, the expert testimony on which Butamax relies merely agrees that, in light of the specification, it would have been understood that such deactivation was desirable. *See, e.g.,* Appellant's Br. 68 (Dr. Stephanopolous agreeing that "the concept" of deactivating the pathway was conventional by 2005, that it was "nothing new" to "want to get rid of competing path-

ways," that the patents "tell you [you] want to delete" the competing pathway, and that the patent "tells you you're knocking out" that pathway); s*ee also, e.g.,* Appellant's Br. 69 (Dr. Kirsch agreeing that the patents teach that "you *want* to knock out" the competing pathway) (emphasis added).

Butamax also relies on extrinsic evidence purportedly teaching how to deactivate the pathway. Butamax submitted the declaration of Alexander M. Klibanov, who opined that it would have been well-known to a person of ordinary skill in the art how to deactivate the genes, citing to seven references that purportedly describe organisms with reduced or inactivated pyruvate decarboxylase activity. Appellant's Br. 67; J.A. 3141. The district court does not appear to have addressed Mr. Klibanov's testimony or six of the references he cited. The seventh reference, Dickinson, was addressed by the district court, which agreed that Dickinson discloses yeast with deactivated genes associated with pyruvate decarboxylase activity as described in claim 13. *Opinion* at *53. However, the district court concluded that Dickinson was not appropriately incorporated by reference into the '889 patent for this point and even if it had been, that Dickinson effectively teaches away from claim 13 because in deactivating those genes responsible for expressing the pathway, isobutanol production was "virtually abolished." *Id.*

Notwithstanding the shortcomings of the foregoing, Butamax has identified sufficient evidence that at least creates a genuine dispute of material fact. Gevo makes much of the fact that Dickinson, though cited in the '889 patent, was not cited in connection with the deactivation of this pathway and was not incorporated by reference into the patent. Nonetheless, Dickinson's teachings still reflect what was known in the art. *See Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1368 (Fed. Cir. 2006) (holding that where "accessible literature sources clearly

provided" a description of the teachings at issue, the written description requirement does not require their incorporation by reference). Dickinson does show that persons of ordinary skill in the art could deactivate the pathway in question, and though it appears that according to Dickinson the claimed invention would not have worked particularly well (isobutanol production would be "virtually abolished"), the evidence at least creates a genuine dispute as to whether a person of ordinary skill in the art would have understood the patentees to have possessed the invention on some level (isobutanol production would not necessarily have been completely abolished). Further, Mr. Klibanov opined that deactivation of the genes associated with the pathway was well-known in the art, and cited Dickinson as well as six other references in support. Gevo's experts disagree with Mr. Klibanov and his interpretation of these references, but this merely indicates the existence of a genuine dispute of material fact.

Though not addressed by the district court, Gevo raises an argument that there can be no genuine dispute of material fact because a subsequent Butamax patent application demonstrates conclusively that the '889 patent lacks an adequate written description of these claims. Butamax filed a continuation-in-part of the applications leading to the '188 and '889 patents, this time providing additional detail on the deactivation of certain genes. *See* U.S. Pat. App. No. 12/966,333. The Patent Office concluded that the '889 patent was not—on its own—invalidating prior art to this application because the '889 patent "do[es] not teach the disruption of endogenous pyruvate decarboxylase genes." J.A. 17353. However, the issue here is not just whether the '889 patent itself teaches the disruption such that the patent itself would be invalidating prior art on that point. There is a genuine dispute with respect to whether in 2005 it was generally well-known in the art how to deactivate the genetic path-

way such that a person of ordinary skill in the art reading the '889 patent would understand the patentees to have possessed the invention claimed in claims 12 and 13.

For these reasons, the district court's grant of Gevo's motion for summary judgment of invalidity of claims 12 and 13 for lack of adequate written description is reversed.

ii. Enablement of the '889 Patent's Claims 12 and 13

In its order, the district court summarily concluded that claims 12 and 13 were invalid for lack of enablement. However, its memorandum opinion does not reflect that judgment, nor did Gevo move for invalidity of those claims on this basis. On appeal, Gevo does not defend the judgment. It thus appears that the judgment was a scrivener's error, and this court reverses the judgment that the claims are invalid for lack of enablement.

III. CONCLUSION

For the forgoing reasons, this court vacates the district court's denial of Butamax's motion for summary judgment of literal infringement of the asserted claims of the '188 and '889 patents and remands the question of infringement to the district court for reconsideration under the claim construction set forth herein. Further, this court likewise vacates and remands the district court's grant of Gevo's motion for summary judgment of noninfringement under the doctrine of equivalents. The court further reverses the district court's grant of Gevo's motion for summary judgment of invalidity for lack of written description of claims 12 and 13 of the '889 patent and the district court's order that those same claims are invalid for lack of enablement.

REVERSED-IN-PART, VACATED-IN-PART, AND REMANDED

IV. COSTS

Costs are awarded to Butamax.