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Butamax(TM) Advanced Biofuels LLC v. Gevo, Inc. (Fed. Cir. February 18, 2014)

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February 26, 2014

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Background

- Butamax owns U.S. 7,851,188 and U.S. 7,993,889.
- Butamax was formed in 2009 as a joint venture between Du Pont and BP Biofuels North America LLC.
- Gevo was incorporated in 2005 as Methanotech, Inc.

Butamax™

A joint venture between BP and DuPont

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Background

- 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.
- The ‘889 Patent is a divisional of the ‘188 Patent. The ‘889 Patent focuses on a method of producing isobutanol from a recombinant yeast microorganism.

Claim 1 of the ‘188 Patent

- 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.

Claim 1 of the ‘188 Patent

- Focused on acetohydroxy acid isomeroreductase (or KARI)
- KARI assists reactions by rearranging a reagent and also by reducing the rearranged molecule.
- To accomplish the reduction, KARI needs a cofactor as an electron source.
- Two examples of cofactors are NADH and NADPH.

Claim 1 of the ‘188 Patent

- The ‘188 Patent defines KARI as “an enzyme that catalyzes the conversion of acetolactate to 2-3-dihydroxyisovalerate using NADPH…as an electron donor. Preferred acetohydroxy acid isomeroreductases are known by the EC number 1.1.1.86…” (col. 7, lines 35-47).

Claim 1 of the ‘889 Patent

- 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.

Claim 1 of the ‘889 Patent

- Also focused on KARI.
- The ‘889 Patent provides the same definition of KARI as the ‘188 Patent, but claim 1 does not refer to any EC classification number.

Background

- January 14, 2011 – Butamax sues Gevo
- September 22, 2011 – Butamax moves for preliminary injunction

- The district court construed the KARI limitation as “an enzyme that is solely NADPH-dependent.”
- Since Gevo uses NADH as a cofactor, the motion was denied.

Background

- The Federal Circuit affirmed the denial of the preliminary injunction.
- However, the Federal Circuit also noted that the district court's claim construction was "very questionable" and asked the district court to reconsider at the *Markman* hearing.

Markman Hearing

- The District Court construed KARI to mean “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.”

Background

- Butamax appeals the Delaware District Court's judgment of:
  - Claim construction and denial of Butamax's motion for summary judgment of literal infringement
  - Grant of Gevo's motion for summary judgment of noninfringement
  - Grant of Gevo's motion for summary judgment of invalidity of claims 12-13 of the '889 Patent for lack of written description
  - Judgment of invalidity of claims 12-13 of the '889 Patent for lack of enablement.

Spoiler

- Reversed-in-part, Vacated-in-part, and Remanded
  - District Court erred in claim construction so denial of Butamax's motion for summary judgment of literal infringement is vacated
  - Grant of Gevo's motion for summary judgment of noninfringement is vacated
  - Grant of Gevo's motion for summary judgment of invalidity for lack of written description is reversed due to genuine issues of material fact
  - Judgment of invalidity for lack of enablement is reversed due to scrivener's error

Claim Construction

- The primary dispute is whether the claimed KARI must be NADPH-dependent.
- The District Court determined that the claimed KARI must be NADPH-dependent.
- Butamax argues that KARI's plain meaning refers to an enzyme catalyzing the acetolactate to 2,3-dihydroxyisovalerate conversion. Butamax did not relinquish this claim scope in the specification or during prosecution.

Claim Construction

- 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.

Claim Construction

- The Federal Circuit will construe the term “KARI” by looking at:
  - KARI’s ordinary meaning
  - The specification and claims
    - Patentee’s definition of KARI
    - Reference to EC Number 1.1.1.86 in claim 1
    - Preferred embodiments and dependent claims
  - Prosecution history
  - Extrinsic evidence

Claim Construction – KARI's Ordinary Meaning

- Does the plain meaning of KARI indicate that the enzyme is NADPH-dependent?
- Federal Circuit states there is nothing on the record to indicate that one of ordinary skill in the art in 2005 understood the plain meaning to be limited to NADPH as a cofactor.
- Gevo conceded this but asserted that Butamax limited the definition of KARI to be NADPH-dependent.

Claim Construction – Patentee's Definition

- The Patentees explicitly defined KARI in the specification.
- However, does this definition clearly express an intent to redefine KARI in a way that differs from the plain and ordinary meaning?
- Gevo asserts that the phrase "using NADPH…as an electron donor" is a clear expression of intent to exclude KARI that are not NADPH-dependent.

Claim Construction – Patentee's Definition

- Butamax argues that the fact that an enzyme can catalyze the conversion of acetolactate to 2,3-dihydroxyisovalerate "using NADPH" does not indicate that the enzyme cannot also use other cofactors such as NADH.

Claim Construction – Patentee's Definition

- Gevo then argues that Butamax's interpretation eliminates an aspect of the patentee's definition because all KARI are capable of using NADPH as a cofactor.
- Thus, the recitation of "using NADPH" is unnecessary unless it was meant to limit KARI.

Claim Construction – Patentee's Definition

- The Federal Circuit agrees with Butamax.

Claim Construction – Patentee's Definition

- Gevo also argues that the specifications describe other enzymes that use NAD^+, NADH, or NADPH.
- Thus, patentees knew how to describe enzymes that used cofactors other than NADPH but chose to define KARI as using only NADPH.

Claim Construction – Patentee's Definition

- Butamax argues that the standard assay for KARI is the Arfin-Umbarger assay, which "uses" NADPH to measure KARI activity.
- The definition also matches the description of the enzyme in EC number 1.1.1.86, which notes the use of $NADP^+$ but not NAD^+ or NADH.
- In contrast, the other enzymes have multiple EC numbers for different cofactors and/or have multiple different assays using different cofactors.

Claim Construction – Patentee's Definition

- The Federal Circuit agrees with Butamax.

Claim Construction – EC Number 1.1.1.86

- Claim 1 of the ‘188 Patent explicitly refers to EC number 1.1.1.86.
- EC number 1.1.1.86 notes the use of $NADP^+$ but not NAD^+ or NADH.
- As such, Gevo argues that one of ordinary skill in the art understood KARI having EC number 1.1.1.86 to be NADPH-dependent.

Claim Construction – EC Number 1.1.1.86

- EC nomenclature was drafted to categorize naturally-occurring enzymes and are generally not created for modified forms that might rely on different cofactors.
- The EC number 1.1.1.86 entry contains a link to the BRENDA database, which contains a reference to a mutated KARI enzyme that can use NADH as a substitute for NADPH.

Claim Construction – EC Number 1.1.1.86

- Butamax also noted that Gevo described its own mutant enzymes by reference to EC number 1.1.1.86.
- Gevo admitted that EC number 1.1.1.86 would have been the best way they knew how to describe its own enzyme, which is not NADPH-dependent.
- Thus, the Federal Circuit concluded that the reference to EC number 1.1.1.86 was not a clear intent to define KARI as being NADPH-dependent.

Claim Construction – Preferred Embodiments

- The patents specifically list *Methanococcus maripaludis* in the specification and a dependent claim.
- This organism is not NADPH-dependent.
- The Federal Circuit concluded that it normally does not interpret claim terms in a way that excludes embodiments disclosed in the specification.

Claim Construction – Prosecution History

- During prosecution, the USPTO rejected claim 1 of the ‘188 Patent for lack of enablement and lack of written description.
- In response, Butamax amended claim 1 to include the EC numbers.
- In view of the amendment, the USPTO withdrew the lack of written description rejection but maintained the lack of enablement rejection.
- After Butamax argued against the rejection, the rejection was withdrawn.

Claim Construction – Prosecution History

- In the ‘889 Patent, the USPTO rejected the claims for lack of enablement.
- Butamax amended the claims to name the enzymes used in each step without referring to any EC numbers.
- Butamax also specifically named *Methanococcus maripaludis* KARI as an example, which uses NADH.
- The Federal Circuit concluded that the prosecution history did not limit the definition of KARI.

Claim Construction – Extrinsic Evidence

- Gevo relies on another Butamax application, 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.”
- Gevo asserts that this application demonstrates that Butamax recognized that the earlier filed patents did not encompass KARI that use NADH.
- The Federal Circuit concluded that this evidence does not clearly express an intent at the time of the invention to redefine KARI to use one cofactor over another.

Claim Construction

- Federal Circuit defines the term KARI 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.”

Infringement

- Remanded in view of the new claim construction

Improper Dependent Claims

- Neither the Federal Circuit nor the parties addressed the fact that claim 12 of the ‘889 Patent appears to be improper under 35 U.S.C. 112, fourth paragraph.

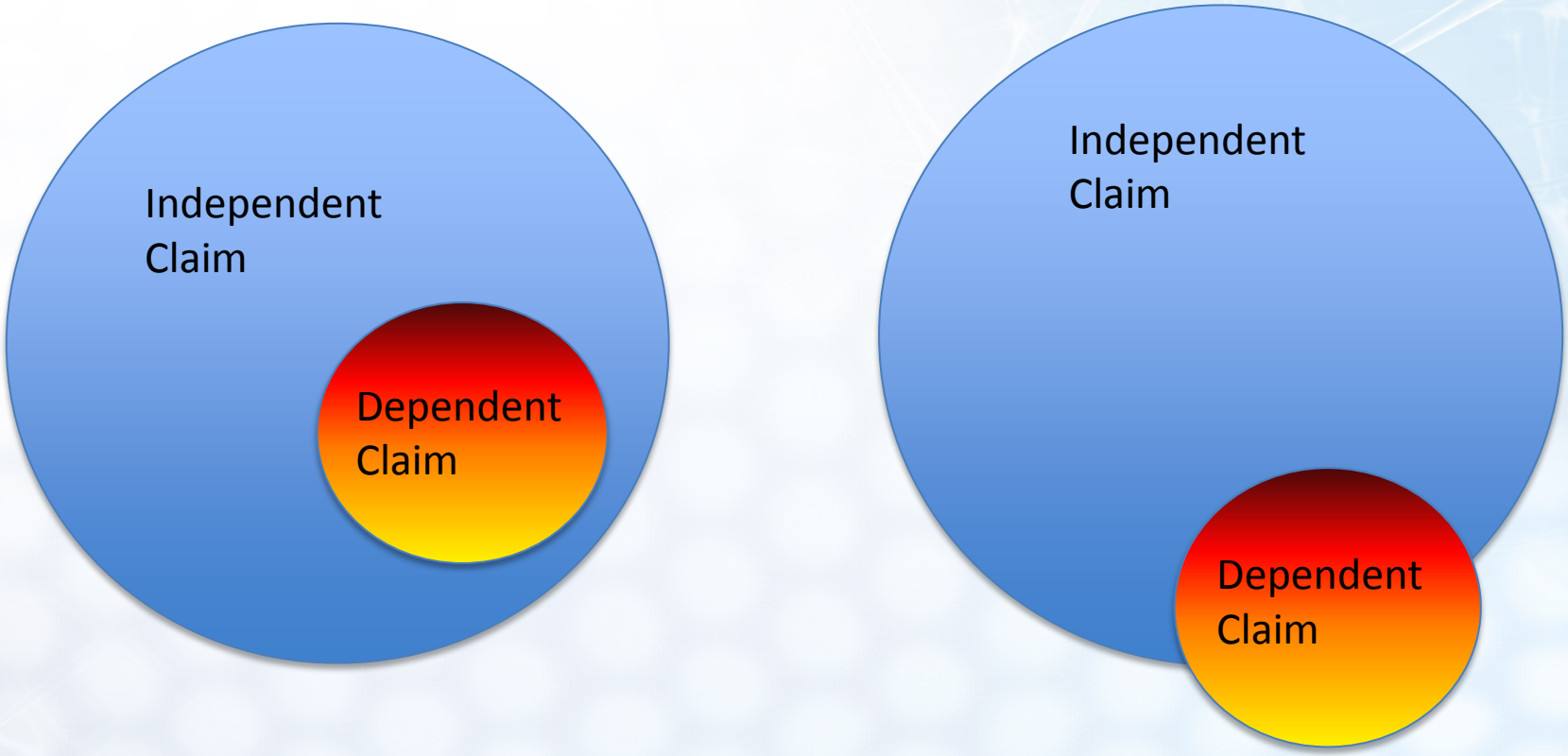
Improper Dependent Claims

- Claim 1 of the ‘889 Patent recites, “A method for producing isobutanol….”
- Claim 12 of the ‘889 Patent recites, “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.”

35 U.S.C. 112, fourth paragraph

- Subject to the following paragraph, a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.

35 U.S.C. 112, fourth paragraph



35 U.S.C. 112, fourth paragraph

- Does composition claim 12 incorporate all of the limitations of method claim 1?
- Should the claim be considered invalid as set forth in *Pfizer, Inc. v. Ranbaxy Laboratories, Ltd.*, 457 F.3d 1284 (Fed. Cir. 2006)?

Pfizer v. Ranbaxy

- Claim 1 of U.S. 5,273,995 recites atorvastatin acid, atorvastatin lactone, or pharmaceutically acceptable salts thereof.
- Claim 2 depends from claim 1 and only recites atorvastatin acid.
- Claim 6 recites, “The hemicalcium salt of the compound of claim 2.”
- Claim 2 does not include the pharmaceutically acceptable salts of atorvastatin acid.

Pfizer v. Ranbaxy

- The Federal Circuit concluded that it would not rewrite claims to preserve validity, and as such, claim 6 is invalid under 35 U.S.C. 112, fourth paragraph.

Practice Points

- Confirm with the client whether definitions and examples are accurate.
- Try to be consistent with terms for all applications.
- Be aware of issues under 35 U.S.C. 112, fourth paragraph.

Questions?

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