

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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AKERMIN, INC.,  
Petitioner,

v.

CO<sub>2</sub> SOLUTIONS INC.,  
Patent Owner.

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Case IPR2015-00880  
Patent 8,329,458 B2

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Before MICHAEL P. TIERNEY, JON B. TORNQUIST, and  
ELIZABETH M. ROESEL, *Administrative Patent Judges*.

ROESEL, *Administrative Patent Judge*.

FINAL WRITTEN DECISION  
*35 U.S.C. § 318 and 37 C.F.R. § 42.73*

In this *inter partes* review, instituted pursuant to 35 U.S.C. § 314, Akerman, Inc. (“Petitioner”) challenges the patentability of claims 1–4, 15–19, 22–28, and 40–43 of U.S. Patent No. 8,329,458 B2 (Ex. 1001, “the ’458 patent”), owned by CO<sub>2</sub> Solutions Inc. (“Patent Owner”).

We have jurisdiction under 35 U.S.C. § 6(c). This final written decision is issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73.

For the reasons that follow, we determine that Petitioner has shown by a preponderance of the evidence that claims 1, 2, 15, 16, 22–26, and 40–43 of the ’458 patent are unpatentable, but has not shown that claims 3, 4, 17–19, 27, and 28 of the ’458 patent are unpatentable.

## I. BACKGROUND

### A. *Procedural History*

On March 20, 2015, Petitioner filed a Corrected Petition requesting *inter partes* review of claims 1–4, 15–19, 22–28, and 40–43 of the ’458 patent. Paper 5 (“Pet.”). On June 17, 2015, Patent Owner filed a Preliminary Response. Paper 9 (“Prelim. Resp.”)

On September 15, 2015, we instituted *inter partes* review of claims 1–4, 15–19, 22–28, and 40–43. Paper 10 (“Decision to Institute” or “Dec.”).

On December 15, 2015, Patent Owner filed a Patent Owner Response. Paper 14 (“PO Resp.”) On March 17, 2016, Petitioner filed a Reply To Patent Owner’s Response. Paper 17 (“Pet. Reply”).

Petitioner submitted a Declaration of Dr. Louis DeFilippi with the Petition. Ex. 1003 (“DeFilippi Decl.”). Patent Owner cross-examined Dr. DeFilippi and filed a transcript of the deposition testimony as Exhibit 2017 (“DeFilippi Dep.”). Patent Owner submitted a Declaration of Dr. Louis Fradette with the Patent Owner Response. Ex. 2004 (“Fradette

Decl.”). Petitioner cross-examined Dr. Fradette and filed a transcript of the deposition testimony as Exhibit 1027 (“Fradette Dep.”).

An oral hearing was held June 9, 2016. A transcript of the hearing was entered in the record. Paper 24 (“Tr.”).

### *B. Related Proceedings*

No proceedings involving the ’458 patent have been identified by the parties. *See* Pet. 1; Paper 7, 2. Petitioner asserts that, on March 1, 2016, Patent Owner filed and served a complaint against Petitioner for infringement of patents involving “similar subject matter” and asserts that the lawsuit, captioned *CO<sub>2</sub> Solutions Inc. v. Akermin, Inc.*, Civil Action No. 1:15-cv-01123 (D. Del.), “may be affected by a decision in this proceeding.” Paper 19, 2.

### *C. The ’458 Patent (Ex. 1001)*

The ’458 patent relates to a triphasic bioreactor and process using carbonic anhydrase for treating carbon dioxide (CO<sub>2</sub>)-containing gas for purposes of gas effluent treatment and air purification. Ex. 1001, Abstract, 1:19–23. The triphasic bioreactor comprises a reaction chamber with a liquid and biocatalysts in suspension in the liquid, for catalyzing a reaction between the gas and the liquid to obtain a treated gas and a solution containing a reaction product. *Id.* at Abstract.

Figure 1 of the ’458 patent is reproduced below:

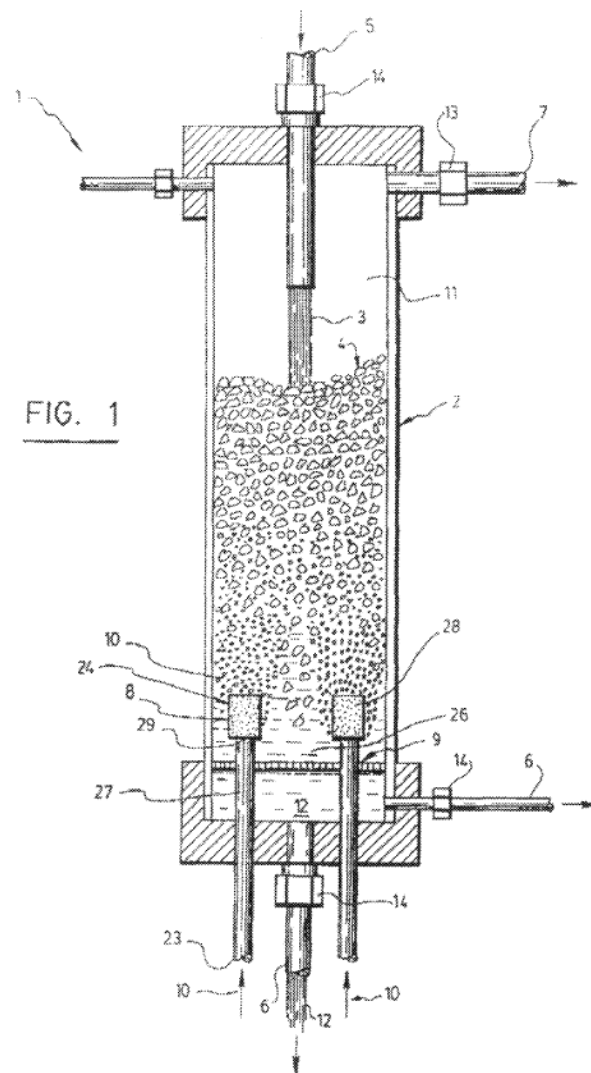


Figure 1 is a cross-sectional side view of a triphasic bioreactor. Ex. 1001, 4:66–67. The bioreactor includes reaction chamber 2 filled with biocatalysts 4 in suspension in liquid 3, and liquid inlet 5, liquid outlet 6, and gas outlet 7 in fluid communication with reaction chamber 2. *Id.* at 5:25–30. Gas 10 to be treated is bubbled via means 8 into the liquid. Biocatalysts 4 biocatalyze a reaction between the gas to be treated and the liquid to obtain treated gas 11 and solution 12 containing a reaction product. Solution 12 is released through liquid outlet 6, while retention device 9 retains the biocatalysts

within the reaction chamber. Treated gas 11 is released through gas outlet 7.  
*Id.* at 5:39–52.

The triphasic bioreactor is used for removing carbon dioxide from gas effluent 10 containing carbon dioxide. In such a case, liquid 3 is an aqueous solution, and biocatalysts 4 are preferably carbonic anhydrase enzymes, which are capable of catalyzing the conversion of dissolved carbon dioxide into an aqueous solution 12 containing hydrogen ions and bicarbonate ions.  
*Id.* at 8:30–38.

#### *D. Illustrative Claims*

Claims 1 and 25 are illustrative of the challenged claims and are reproduced below, with bold emphasis added to identify phrases that are the focus of the parties' arguments:

1. A carbonic anhydrase bioreactor for treating a CO<sub>2</sub>-containing gas, comprising:
  - a reaction chamber for receiving a liquid;
  - carbonic anhydrase provided on or in substrates that are **in suspension within the liquid** for catalyzing a reaction of CO<sub>2</sub> into bicarbonate and hydrogen ions to obtain a treated gas and an ion-rich solution, wherein the substrates comprise porous substrates and the carbonic anhydrase are **entrapped in the porous substrates**;
  - a liquid inlet in fluid communication with the reaction chamber for providing the reaction chamber with the liquid;
  - a gas inlet connected to the reaction chamber for providing the CO<sub>2</sub>-containing gas to be treated into the reaction chamber in order to contact the liquid;
  - a liquid outlet in fluid communication with the reaction chamber for releasing the ion-rich solution; and
  - a gas outlet in fluid communication with the reaction chamber to release the treated gas.
  
25. A process using carbonic anhydrase for treating a CO<sub>2</sub>-containing gas, comprising:

**suspending substrates within a liquid** provided to a reaction chamber, carbonic anhydrase being provided on or in the substrates, wherein the substrates comprise porous substrates and the carbonic anhydrase are **entrapped in the porous substrates**;

contacting the CO<sub>2</sub>-containing gas to be treated with the liquid within the reaction chamber in the presence of the carbonic anhydrase, to promote the chemical conversion of the dissolved CO<sub>2</sub> into an ion-rich solution containing hydrogen ions and bicarbonate ions and obtaining a treated gas;

releasing the ion-rich solution from the reaction chamber;  
and

releasing the treated gas from the reaction chamber.

#### *E. Petitioner's Asserted References*

Petitioner's asserted grounds of unpatentability are based on the following references:

Bonaventura et al., US 4,602,987, issued July 29, 1986  
("Bonaventura '987"), Ex. 1004;

Bonaventura et al., US 4,427,416, issued January 24, 1984  
("Bonaventura '416"), Ex. 1005;

Douglas N. Dean et al., *Batch Absorption of CO<sub>2</sub> by Free and Microencapsulated Carbonic Anhydrase*, 16 INDUS. ENG'G & CHEMISTRY FUNDAMENTALS 452–458 (1977) ("Dean"), Ex. 1006;

Rau et al., WO 00/10691, published Mar. 2, 2000 ("Rau"), Ex. 1007;

Arthur Kohl & Richard Nielsen, GAS PURIFICATION 330–414 (5<sup>th</sup> ed. 1997) ("Kohl"), Ex. 1008; and

Jovica D. Badjic & Nenad M. Kostic, *Effects of Encapsulation in Sol-Gel Silica Glass on Esterase Activity, Conformational Stability,*

*and Unfolding of Bovine Carbonic Anhydrase II*, 11 CHEMISTRY MATERIALS 3671–3679 (1999) (“Badjic”), Ex. 1009.<sup>1</sup>

*F. Instituted Grounds of Unpatentability*

*Inter partes* review was instituted based on the following five grounds of unpatentability asserted in the Petition:

1. Claims 1–3, 15, 17, 24–27, 40, 41, and 43 under 35 U.S.C. § 102(b) as anticipated by Bonaventura ’987;
2. Claims 1–3, 15–17, 24–27, and 40–43 under 35 U.S.C. § 103(a) as obvious over Bonaventura ’987 and Bonaventura ’416;
3. Claims 1, 4, 25, and 28 under 35 U.S.C. § 103(a) as obvious over Bonaventura ’987 and Badjic;
4. Claims 1, 18, and 19 under 35 U.S.C. § 103(a) as obvious over Bonaventura ’987 and Kohl; and
5. Claims 1, 2, 15, 16, 22–26, and 40–43 under 35 U.S.C. § 103(a) as obvious over Dean and Rau.

II. DISCUSSION

*A. Claim Construction*

In an *inter partes* review, claim terms in an unexpired patent are given their broadest reasonable interpretation in light of the specification of the patent in which they appear. 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2144–46 (2016). Claim terms are presumed to have their ordinary and customary meaning, as understood by one of

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<sup>1</sup> With the exception of Exhibit 1002 (the ’458 prosecution history), we cite to the Exhibits using the original page numbers, not those added by Petitioner or Patent Owner.

ordinary skill in the art in the context of the entire disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007).

“[C]laim terms need only be construed ‘to the extent necessary to resolve the controversy.’” *Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011)) (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

The parties dispute the meaning of “entrapped in” (claims 1 and 25), as well as “in suspension” (claim 1) and “suspending” (claim 25). Pet. 10–12; PO Resp. 7–13.

*entrapped in*

In the Decision to Institute, we provided a preliminary construction for the phrase “entrapped in the porous substrates” based on the record existing at that time. Dec. 8–12. Based on the current record, we provide the following analysis and construction of this term.

Petitioner argues that “entrapped in” the porous substrates should be construed to mean that “the enzyme is physically trapped within the structure of the substrate while retaining at least some of its activity.” Pet. 11.

Patent Owner does not dispute that “entrapped” requires that enzymes be physically trapped within the structure of the substrate, as set forth in Petitioner’s proposed construction. The experts agree that “entrapped” refers to retention by physical means, as opposed to a chemical bond or link. Ex. 2004 (Fradette Decl.) ¶¶ 58 (enzyme immobilization techniques are generally classified as physical or chemical), 86(b) (skilled person would not understand entrapment to include chemical bonding or linking); Ex. 2017 (DeFilippi Dep.) 39:12–40:8, 42:3–21. We determine that the experts’



agreement is not inconsistent with the intrinsic evidence. *Compare* Ex. 2004 ¶ 86(b) *and* Ex. 2017 40:2–8, *with* Ex. 1005, 5:40–43 (“oxygen carriers . . . [may be] entrapped and/or covalently linked to a polyurethane matrix or to comparable supports”). We therefore revise our preliminary construction to include a requirement that the enzyme is physically trapped within the structure of the substrate. *Cf.* Dec. 10.

Patent Owner also does not dispute that an “entrapped” enzyme retains at least some of its activity, as stated in Petitioner’s proposed construction. Retention of activity is consistent with the claims and the Specification, both of which recite that the function of the entrapped carbonic anhydrase is to catalyze and promote a reaction by which carbon dioxide (CO<sub>2</sub>) is converted into bicarbonate and hydrogen ions. Ex. 1001, 10:17–22 (claim 1), 11:40–12:3 (claim 25), 3:35–37 (summary of the invention). Accordingly, we adopt this undisputed aspect of Petitioner’s proposed construction.

The parties’ dispute focuses on whether the term “entrapped in” encompasses “encapsulation,” which is disclosed in one of Petitioner’s asserted references (Dean). Petitioner contends “entrapped” includes encapsulation, Pet. 14, while Patent Owner argues that “entrapped” excludes encapsulation, PO Resp. 10–12. To distinguish encapsulation, Patent Owner proposes that “entrapped in” be construed to require that “the enzyme molecules are free in solution, but restricted in movement within the interstitial confines of the porous substrate lattice network.” PO Resp. 13.

For the reasons discussed below, we determine that “entrapped,” as used in the ’458 patent, does not exclude encapsulation and does not require

“interstitial confines” or a “lattice network,” as set forth in Patent Owner’s proposed construction.

Our analysis begins with the claim language, which recites: “the carbonic anhydrase are entrapped in the porous substrates.” Ex. 1001, 10:21–22 (claim 1), 11:41–42 (claim 25). The claims do not describe the porous substrates as having “interstitial confines” or a “lattice network,” as set forth in Patent Owner’s proposed construction.

Patent Owner agrees that the dictionary definition of “entrap” does not exclude encapsulation. The definition of “entrap” cited by both sides is: “to capture and hold (a substance).” Ex. 2012,<sup>2</sup> 758; *see also* PO Resp. 11 (citing Ex. 2012, 758); Ex. 2004 (Fradette Decl.) ¶ 62 (quoting Ex. 2012, 758); Pet. Reply 5 (same). At the oral hearing, Patent Owner agreed that if you encapsulate an enzyme, you “capture and hold it inside the shell.” Tr. 39:4–14.

Turning next to the Specification, the term “entrapped” appears in the following three passages of the ’458 patent (with bold added for emphasis):

Most preferably, the biocatalysts are **entrapped** in porous substrates pervading the reaction chamber. Alternatively, the biocatalysts may be carried by the liquid that feeds the reaction chamber.

Ex. 1001, 4:6–9.

Biocatalysts . . . may be selected from a wide variety of biological materials including enzymes, liposomes, microorganisms, animal cells and/or plant cells and the like. Fractions, complexes or combinations thereof may also be used simultaneously. . . . For the purpose of the invention, the

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<sup>2</sup> WEBSTER’S THIRD NEW INTERNATIONAL DICTIONARY (3<sup>rd</sup> ed. 1986), Ex. 2012.

biocatalysts may also be **entrapped** in a porous substrate, for example, an insoluble gel particle such as silica, alginate, alginate/chitosane, alginate/carboxymethylcellulose, etc. For the purpose of the invention, biocatalysts may also be immobilized on solid packing in suspension in the liquid, such as enzymes covalently bound to plastic packing. Alternatively, enzymes might be in a free state, or chemically linked in an albumin or PEG network.

*Id.* at 6:13–31.

The enzyme carbonic anhydrase, which is of relatively low molecular weight (30,000 daltons), may be made to form part of a complex in order to increase its size. This, in turn, allows the use of membranes with greater porosity and enhances liquid flow rates. Different types of enzyme complexes may be formed. Among these are those using whole cells such as red blood cells. However, with red blood cells, the enzymes rapidly leak out and are lost. **Encapsulation** techniques may therefore overcome this problem. Enzymes may be immobilized on solid packing. Packing made of polymers such as nylon, polystyrene, polyurethane, polymethyl methacrylate, functionalized silica gel, etc. may be used. Enzymes may also be **entrapped** in insoluble gel particles such as silica, alginate, alginate/chitosane or alginate/carboxymethylcellulose, etc. or covalently linked or non covalently linked in a network of albumin, PEG or other molecule. Such a network constitutes a loose type network. It may appear as a cloudy suspension, “filaments” of which are often visible to the naked eye. For the purpose of the invention, alginate particles should preferably possess a diameter comprised in a range from 1 to 9 mm, and preferably, a diameter inferior to 3 mm.

*Id.* at 8:51–9:4.

These Specification passages do not explicitly define “entrapped” and do not explain how biocatalysts (enzymes) are entrapped in the porous substrates. The Specification does not describe the porous substrates as having “interstitial confines” or a “lattice network,” as set forth in Patent

Owner's proposed construction. Nor does the Specification require that the "porous substrates" be insoluble gel particles, as opposed, for example, to a semipermeable membrane or capsule.

Patent Owner relies upon the above-quoted passages from columns 6 and 8 to argue that entrapment is different from encapsulation. PO Resp. 10–11; Ex. 2004 ¶¶ 79, 80 (quoting Ex. 1001, 6:23–31 and 8:51–9:4). We are not persuaded by Patent Owner's argument.

As support for its position, Patent Owner relies on Dr. Fradette's testimony, which inserts bracketed numbers in the above-quoted passages from columns 6 and 8 to designate what he avers are "distinct ways to retain the enzyme." Ex. 2004 (Fradette Decl.) ¶¶ 79, 80. The Specification as written, however, does not include numerical designations inserted by Dr. Fradette and does not define "entrapped" as excluding encapsulation. *See In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994) ("Although an inventor is indeed free to define the specific terms used to describe his or her invention, this must be done with reasonable clarity, deliberateness, and precision.")

The above-quoted passage from column 6 does not mention encapsulation and is therefore not persuasive to show that encapsulation and entrapment are distinct forms of enzyme immobilization. The above-quoted passage from column 8 discloses that a problem associated with enzyme complexation using red blood cells may be overcome by "[e]ncapsulation techniques." Ex. 1001, 8:55–59. The passage then discusses various materials that may be used as alternatives to red blood cells. *Id.* at 8:59–66. As part of this discussion, the passage states: "[e]nzymes may also be entrapped in insoluble gel particles . . . ." *Id.* at 8:62–63. When read as a

whole, the above-quoted passage from column 8 does not suggest with “reasonable clarity, deliberateness, and precision” that entrapment and encapsulation are mutually exclusive. *In re Paulsen*, 30 F.3d at 1480. Instead, the passage may reasonably be interpreted as suggesting that encapsulation is a form of entrapment. Ex. 1001, 8:62–63 (“Enzymes **may also be entrapped . . .**”). Our interpretation is consistent with the Summary of the Invention, which uses the term “entrapped” broadly to distinguish entrapped enzymes from enzymes that are free in solution, i.e., not immobilized. *Id.* at 4:6–9.

Bonaventura ’416 and Bonaventura ’987 were both cited during prosecution of the ’458 patent. Ex. 1001, page 2 (listing cited references). Bonaventura ’987 is cited in the Specification of the ’458 patent, *id.* at 2:44, 2:53, and a divisional having the same disclosure as Bonaventura ’987 — U.S. Patent No. 4,761,209—was relied upon to reject the claims during prosecution of the ’458 patent. Ex. 1002, 51, 83. We, therefore, consider Bonaventura ’416 and Bonaventura ’987 intrinsic evidence for purposes of claim construction. *V-Formation v. Benetton Group & Rollerblade, Inc.*, 401 F.3d 1307, 1311 (Fed. Cir. 2005) (“prior art cited in a patent or cited in the prosecution history of the patent constitutes intrinsic evidence” (quoting *Kumar v. Ovonic Battery Co.*, 351 F.3d 1364, 1368 (Fed. Cir. 2003))).

Both sides rely on the following discussion of “entrapped” in Bonaventura ’416:

This invention relates to the incorporation of an oxygen carrier, which can be a biological macromolecule, into an insolubilized form, which can be a polymeric matrix. More particularly, the preferred embodiment of the invention involves a biochemical engineering technique known as **molecular entrapment**. The oxygen carrier used by man and other

mammals, as well as by most other vertebrates, is hemoglobin. By **molecular entrapment**, hemoglobin can be made insoluble and consequently more amenable for use in a recycling and regenerable system. **Optimally, entrapment is analogous to placing a cage around the biologically active material. This cage, or network, entraps the material but does not render it inactive.** The **entrapment** insolubilizes the material and renders it amenable to manipulation. The degree to which function is maintained varies greatly with the **type of entrapment process** used. In the preferred polyurethane matrices of this invention, the material retains essentially full biological activity.

Ex. 1005, 6:28–46 (emphasis added). According to Petitioner, “placing a cage around the [enzyme],” *id.* at 6:39–40, includes the use of “a synthetic or natural polymeric network or membrane” and does not exclude micro-encapsulation. Pet. 14; Ex. 1003 ¶ 20. Patent Owner, on the other hand, relies on the same language to argue that “entrapment” is different from “encapsulation, in which the enzyme is enveloped in a semipermeable membrane.” PO Resp. 12–13, 39; *see also* Ex. 1027 (Fradette Dep.) 71:17–73:7 (differentiating “entrapment” within a cage from “encapsulation” within a membrane).

Even if we interpret the term “cage” as referring to a network rather than a membrane, however, that distinction does not support Patent Owner’s proposed construction. The claims recite that carbonic anhydrase is entrapped in porous substrates, not in a cage. Ex. 1001, 10:21–22 (claim 1); 11:40–42 (claim 25). Furthermore, the discussion of a “cage” begins with the term “optimally” indicating that the analogy is exemplary rather than definitional. Ex. 1005, 6:38–41. There is also discussion of variation that depends on “the type of entrapment process used.” *Id.* at 6:43–44. Accordingly, the cited passage from Bonaventura ’416 does not persuade us

that that “entrapment” is limited to retention within the “interstitial confines” of a “lattice network,” as argued by Patent Owner.

Patent Owner argues that Bonaventura ’987 uses the terms “entrapped” and “encapsulation” separately in referring to enzyme immobilization techniques. PO Resp. 11 (citing Ex. 1004, 4:46–5:35). The cited portion of Bonaventura ’987 discusses “[v]arious techniques for the insolubilization (or immobilization) of biological materials,” Ex. 1004, 4:46–47, one of which involves “encapsulation,” *id.* at 4:62, and another of which is the method of Bonaventura ’416 involving entrapment, *id.* at 5:28–35. The cited disclosure does not, however, indicate that “entrapped,” as used in the claims of the ’458 patent, excludes encapsulation.

Patent Owner directs us to the prosecution history, where the independent claims were amended to include the “entrapped” limitation from originally-filed dependent claims 8 and 41, which the Examiner indicated were allowable. Ex. 1002, 117, 121 (independent claims amended to recite “the substrates comprise porous substrates and the carbonic anhydrase are entrapped in the porous substrates”);<sup>3</sup> Tr. 34:16–35:3 (Patent Owner’s argument regarding prosecution history). The identified portions of the prosecution history do not, however, indicate that “entrapped” is different from “encapsulation.”

The parties cite various books and articles to support their respective positions regarding the meaning of “entrapped.” Both parties rely on

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<sup>3</sup> See also *id.* at 125 (applicant remarks), 188 (Examiner’s indication of allowable subject matter), 289–90, 293–294 (originally filed claims).

Perry's<sup>4</sup> and Zaborsky.<sup>5</sup> Patent Owner additionally relies on Bickerstaff,<sup>6</sup> and Petitioner additionally relies on Roig<sup>7</sup> and Dumitriu.<sup>8</sup> PO Resp. 11–12; Pet. Reply 6–7. These references show that “entrapped” (or another form of that word) is sometimes used in a broad sense to refer to a class of physical immobilization techniques that includes encapsulation and is sometimes used in a narrower sense to refer to entrapment within a gel or polymer, which does not include encapsulation. Roig and Dumitriu, for example, each provide a tree diagram showing “entrapped” or “entrapment” as a class of immobilization techniques that includes “micro encapsulated” or “microencapsulation,” as well as “polymer entrapped” or “gel entrapment.” Ex. 1024, 181; Ex. 1028, 631. Like Roig and Dumitriu, Perry's uses the term “entrapment” first in a broad sense and then in a narrower sense. More specifically, Perry's first identifies the methods of immobilization as “adsorption, covalent bonding, or entrapment” and then provides specific examples, including gel “entrapment” and “encapsulation.” Ex. 2006, 24-21. Zaborsky uses the word “entrapped” not only with respect to

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<sup>4</sup> PERRY'S CHEMICAL ENGINEER'S HANDBOOK 23-52 to 23-55, 24-21, 24-22 (Robert H. Perry & Don W. Green eds., 7th ed. 1997), Ex. 2006.

<sup>5</sup> O. Zaborsky, IMMOBILIZED ENZYMES 83–101 (1973), Ex. 2011.

<sup>6</sup> Gordon F. Bickerstaff, *Methods in Biotechnology*, in IMMOBILIZATION OF ENZYMES AND CELLS 1–11 (1997), Ex. 2002.

<sup>7</sup> M.G. Roig, et al., *Methods for Immobilizing Enzymes*, 14 BIOCHEMICAL EDUC. 180–185 (1986), Ex. 1024.

<sup>8</sup> S. Dumitriu & E. Chornet, *Polysaccharides as Support for Enzyme and Cell Immobilization*, in POLYSACCHARIDES: STRUCTURAL DIVERSITY AND FUNCTIONAL VERSATILITY 629–748 (Severian Dumitriu, ed., 1998), Ex. 1028.



immobilization within the interstitial space of crosslinked polymers, but also with respect to immobilization within microcapsules. Ex. 2011, 83–91 (Chapter 6: “Entrapment within Crosslinked Polymers”); *id.* at 93–95 (Chapter 7: “Microencapsulation”). Figure 18, for example, shows a “microcapsule” with “entrapped enzyme molecules.” *Id.* at 93. In contrast to these references, Bickerstaff characterizes entrapment and encapsulation as separate methods of immobilization of enzymes. Ex. 2002, 2–9.

As noted above, the ’458 patent does not describe the porous substrates as having interstitial confines or a lattice network. Nor does the ’458 patent exclude a semipermeable membrane as a means for immobilizing the enzymes. *Cf.* Ex. 2002 (Bickerstaff) 9 (encapsulation is achieved by “enveloping the biological components within various forms of semipermeable membranes”). We, therefore, conclude that “entrapped,” as used in the ’458 patent, is properly construed consistent with the broader of the two meanings suggested by the extrinsic evidence.

Accordingly, based on the arguments and evidence on this record and applying the broadest reasonable interpretation,<sup>9</sup> we adopt Petitioner’s proposed construction for “entrapped”: “the enzyme is physically trapped within the structure of the substrate while retaining at least some of its activity.”

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<sup>9</sup> Neither party contends that application of the claim construction standard of *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005), would require a different construction for “entrapped.” Tr. 17:17–18:16 (Petitioner); Tr. 35:9–24 (Patent Owner).

*in suspension/suspending*

Construction of the terms “in suspension” (claim 1) and “suspending” (claim 25) is discussed below in connection with our analysis of Petitioner’s Ground 1.

*B. Asserted Grounds of Unpatentability*

*Ground 1: Anticipation by Bonaventura ’987*

Petitioner asserts that claims 1–3, 15, 17, 24–27, 40, 41, and 43 of the ’458 patent are unpatentable under 35 U.S.C. § 102(b) as anticipated by Bonaventura ’987.

*Bonaventura ’987 (Ex. 1004)*

Bonaventura ’987 discloses, in relevant part, a method and apparatus for removing carbon dioxide from a fluid using carbonic anhydrase as an enzyme catalyst. Ex. 1004, 22:55–63, 23:40–44, 25:7–20, 30:1–32:38, Figs. 5–8. The method is illustrated in Figure 5, which is reproduced below:

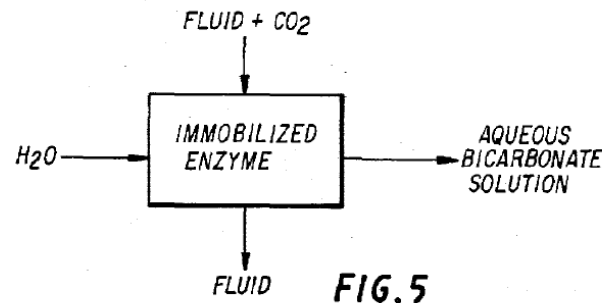


Figure 5 shows a generalized process for removing carbon dioxide from a fluid. *Id.* at 6:55–58. According to Bonaventura ’987, water and a fluid containing carbon dioxide are brought into contact with immobilized carbonic anhydrase, which results in the removal of carbon dioxide from the fluid and produces an aqueous solution of bicarbonate. *Id.* at 24:19–28, 30:1–11.

Bonaventura '987 discloses an apparatus for carrying out the carbon dioxide removal method in Figure 6, which is reproduced below:

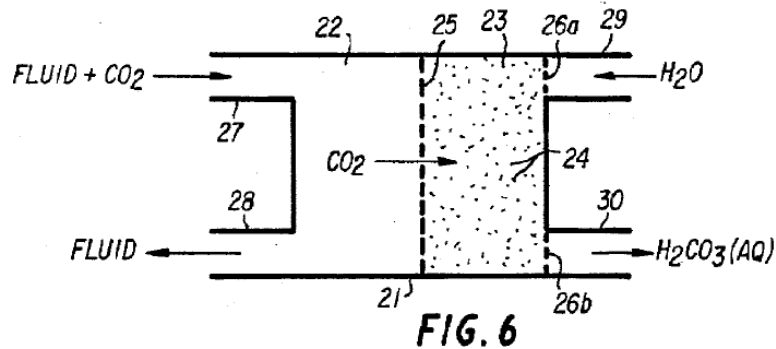


Figure 6 shows an apparatus for removing carbon dioxide from a fluid. Ex. 1004, 6:59–62. The apparatus includes: container 21, compartment 22 through which flows fluid containing carbon dioxide to be removed, compartment 23 containing immobilized enzyme 24, gas permeable membrane 25 separating compartment 22 from compartment 23, inlet 27 for fluid containing carbon dioxide, outlet 28 for fluid from which carbon dioxide has been removed, water inlet 29, and outlet 30 for aqueous carbonic acid. *Id.* at 30:15–21, 30:30–37. According to Bonaventura '987, the carbon dioxide passes from chamber 22 across gas permeable membrane 25 into chamber 23, where it is converted by immobilized enzyme 24 into carbonic acid. *Id.* at 30:37–47. Bonaventura '987 discusses ways of retaining immobilized enzyme 24 within compartment 23 as follows:

If immobilized enzyme 24 is attached to the walls of compartment 23 or if immobilized enzyme 24 is present on a solid substrate which is not capable of flowing out of compartment 24 [*sic*, 23], no further entrainment [*sic*] of the enzyme or its support material is needed. However, in the event that the support material is small (for example, gel particles capable of flowing with water) means for entrapping

the flowable substrate, shown in FIG. 6 as screens 26a and 26b, are required.

*Id.* at 30:20–30.

Bonaventura '987 discloses another embodiment of an enzyme reactor in Figure 7, which is reproduced below:

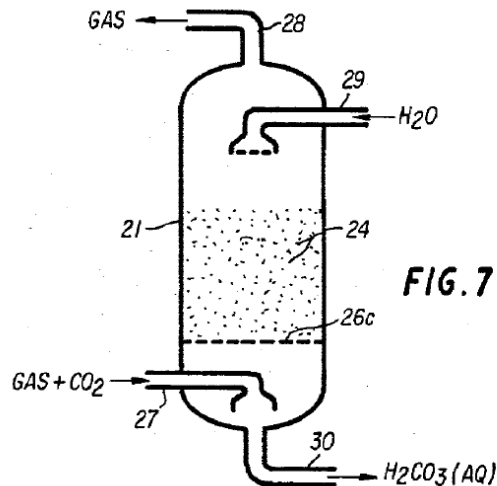


Figure 7 shows a vertical enzyme reactor for removing carbon dioxide by the countercurrent flow of water and a gas stream containing carbon dioxide. Ex. 1004, 6:63–65, 30:54–60. In the Figure 7 embodiment, gas containing carbon dioxide to be removed is injected through inlet 27 into enzyme reactor container 21 and diffuses upwardly through the reaction zone. Water is injected through inlet 29 and flows downwardly through the reaction zone. Carbon dioxide reacts with water under the influence of immobilized enzyme 24 and is converted into carbonic acid. Gas from which carbon dioxide has been removed exits the reactor through outlet 28, and a carbonic acid solution exits through outlet 30. *Id.* at 30:66–31:11. Regarding retention of immobilized enzymes 24 within reactor container 21 in the Figure 7 embodiment, Bonaventura '987 discloses:

[C]arbonic anhydrase is immobilized on a porous substrate (24). Substrate 24 is held in place by a substrate support 26c, which may be a fine screen when the support by which the enzyme is immobilized is a porous gel.

*Id.* 30:59–63.

*Claims 1–3, 15, 17, 24–27, 40, 41, and 43*

Petitioner contends that claims 1–3, 15, 17, 24–27, 40, 41, and 43 are anticipated by the Figure 6 embodiment of Bonaventura '987. Pet. 18–28; Ex. 1003 ¶¶ 77–91. Regarding the “in suspension” limitation of claim 1 and the “suspending” limitation of claim 25, Petitioner asserts that Bonaventura '987 “teaches using immobilized carbonic anhydrase in suspension” in the reactor of Figure 6. Pet. 19; *see also* Ex. 1003 (DeFilippi Decl.) ¶ 54 (same). Petitioner cites Bonaventura '987's disclosure that ““in the event that the support material is small (for example, gel particles capable of flowing with water) means for entrapping the flowable substrate, shown in FIG. 6 as screens 26a and 26b, are required.” Pet. 20 (quoting Ex. 1004, 30:26–30); *see also id.* at 21–22 (chart for claim 1); *id.* at 26 (chart for claim 25); *see also* Ex. 1003 ¶¶ 79 (p. 35—chart for claim 1), 85 (p. 44—chart for claim 25).

Patent Owner argues that Bonaventura '987 does not disclose the “in suspension” or “suspending” features of the claims. PO Resp. 26. Patent Owner provides two reasons for its assertion that Bonaventura '987 Figure 6 does not disclose immobilized enzyme suspended in a fluid. *Id.* at 21–22. First, Patent Owner contends that a person of ordinary skill in the art would understand there is not a suspension because immobilized enzyme 24 is not described as being “suspended” or “in suspension.” *Id.* at 21 (citing Ex. 2004 (Fradette Decl.) ¶ 96). Second, Patent Owner contends that Figure

6 depicts immobilized enzyme 24 “held in a matrix (i.e., a monolith), similar to the Hemosponge of the Bonaventura ’416 patent, or in a packed configuration within compartment 23.” *Id.* (citing Ex. 2004 ¶ 97); *see also id.* at 20 (discussing similarity between Figs. 6 and 7 of Bonaventura ’987 and Figs. 9–11 of Bonaventura ’416, citing Ex. 2004 ¶ 93).

Anticipation is a question of fact, *In re Hyatt*, 211 F.3d 1367, 1371–72 (Fed. Cir. 2000), and can be found only if a single prior art reference discloses every element of the challenged claim, *In re King*, 801 F.2d 1324, 1326 (Fed. Cir. 1986). It is not, however, an *ipsissimis verbis* test, i.e., identity of terminology is not required. *In re Bond*, 910 F.2d 831, 832 (Fed. Cir. 1990). The dispositive question is “whether one skilled in the art would reasonably understand or infer from [a prior art reference’s] teaching” that each claim element is disclosed by the reference. *In re Baxter Travenol Labs.*, 952 F.2d 388, 390 (Fed. Cir. 1991). Declarations, depositions, and admissions from the perspective of one of ordinary skill in the art may be useful to explain, but not to expand, the meaning of an asserted prior art reference. *Id.* To show anticipation, such testimony should “explain in detail how each claim element is disclosed in the prior art reference.” *Schumer v. Lab. Computer Sys., Inc.*, 308 F.3d 1304, 1315 (Fed. Cir. 2002).

On this record, we find that Petitioner has not shown by a preponderance of the evidence that one of ordinary skill in the art would reasonably understand or infer that Bonaventura ’987 discloses enzyme-supporting substrates “in suspension” within a liquid (claim 1) or the step of “suspending” such substrates in a liquid (claim 25).

The parties and their respective experts agree that, to be “in suspension,” the enzyme-supporting substrates must be dispersed in a liquid

and not settle out during operation of the bioreactor or process. PO Resp. 9; Rely Br. 2; Ex. 2017 (DeFilippi Dep.) 29:13–16; Ex. 1027 (Fradette Dep.) 51:4–13; Tr. 6:17–7:5 (Petitioner). The parties’ agreed construction is not inconsistent with the ’458 patent, which does not define the terms “suspension” or “suspend.” The parties’ agreed construction is consistent with the parties’ dictionary definitions of “suspension.” Ex. 1010, 1443 (Oxford Dictionary: “a mixture in which particles are dispersed throughout the bulk of a fluid”); Ex. 2013, 365 (McGraw-Hill Dictionary of Chemistry: “A mixture of fine, nonsettling particles of any solid within a liquid or gas . . .”). We, therefore, adopt the parties’ agreed construction.

The “in suspension” and “suspending” features of the challenged claims are not expressly disclosed in Bonaventura ’987. *See* Ex. 2017 (DeFilippi Dep.), 79:18–80:1 (agreeing that suspension feature is not expressly described in Bonaventura ’987). Petitioner contends, however, that immobilized enzymes 24 are taught as being “in suspension” in Bonaventura ’987 Figure 6, relying on the description of “gel particles capable of flowing with water” and a “flowable substrate,” Ex. 1004, 30:26–30, and the way that substrates 24 are depicted in Figure 6. Pet. 19–20, 21–22, 26; Pet. Reply 12, 14. On this record, we are not persuaded by Petitioner’s argument that Bonaventura ’987 discloses that substrates 24 are “in suspension” in Figure 6.

The experts provide competing interpretations of Bonaventura ’987 Figure 6. Petitioner’s expert testifies that it shows a suspension, Ex. 2017, 75:12–20, while Patent Owner’s expert testifies that it shows either a matrix or a packed column, Ex. 2004 ¶ 97. On this record, the evidence favors the interpretation of Patent Owner’s expert. As discussed below, Bonaventura

'987's disclosure of "flowable" gel particles does not distinguish between the experts' competing interpretations of Figure 6. Furthermore, although the experts agree that a source of agitation is generally required to create and maintain a suspension, neither Petitioner nor its expert persuasively identifies a source of agitation that suspends or maintains a suspension of substrates 24 in Bonaventura '987 Figure 6.

Bonaventura '987 discloses that, if substrates 24 are "gel particles capable of flowing with water," i.e., a "flowable substrate," then screens 26a and 26b are required to prevent the substrates from exiting the reactor. Ex. 1004, 30:26–30. Petitioner's expert agrees that particles in a packed column are not "in suspension," but nevertheless acknowledges that such particles may be capable of flowing and exiting the reactor. Ex. 2017, 29:2–16 ("in suspension" does not include particles in a packed reactor column); *id.* at 87:21–88:2 (screens can be used in packed columns "[t]o prevent the exiting of the packing material"). Similarly, Petitioner agrees that particles that are settled to the bottom, but are slowly flowing with the water, are not "in suspension." Tr. 26:1–15. Thus, Petitioner and its expert agree that Bonaventura '987's description of "gel particles capable of flowing with water" and a "flowable substrate," Ex. 1004, 30:26–30, is consistent with particles in a packed column. Accordingly, these descriptions are not sufficient to show that Bonaventura '987 discloses that substrates 24 are "in suspension," as opposed to in a packed column, in Figure 6.

Petitioner argues that Bonaventura '987 Figure 6 shows a suspension because it depicts particles that "flow with water" and are "distributed



throughout the liquid.” Pet. Reply 14.<sup>10</sup> Petitioner cites the deposition of Patent Owner’s expert, but the cited testimony does not support Petitioner’s argument. Dr. Fradette testified that “if [a gel particle] flows with water, you could find a configuration where it’s in suspension.” Ex. 1027 (Fradette Dep.), 120:11–17. That testimony is not sufficient to show that the reactor configuration of Figure 6 results in a suspension of gel particles. Petitioner does not persuade us that Bonaventura ’987’s depiction of substrates 24 as dots distributed throughout compartment 23 in Figure 6 would reasonably be understood by one of ordinary skill in the art as showing a suspension, as opposed to a matrix or a packed column.

Petitioner and its expert assert that whether particles will be suspended in a particular reactor depends on a number of variables, including the size and density of the particles, the liquid flow, the gas flow, and the presence or absence of a mechanical agitator. Pet. Reply 15–16; Ex. 2017, 32:17–33:2. Petitioner’s expert agreed that, in a chemical reactor involving a suspension, “[i]n general, you have a source of agitation,” such as an impeller or a flow of liquid or gas. *Id.* at 34:14–20; *see also id.* at 34:21–35:11 (agitation is not required for a colloidal suspension, but is required for a “settleable suspension”).

Petitioner does not, however, explain sufficiently how the relevant variables result in substrates 24 being “in suspension” in the reactor of

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<sup>10</sup> Petitioner’s argument is consistent with our preliminary finding that Bonaventura ’987 Figure 6 shows “enzyme-supporting substrate particles 24 dispersed throughout a fluid.” Dec. 16. On the current record, and for all the reasons stated in this final decision, that finding is not supported by a preponderance of the evidence.

Bonaventura '987 Figure 6. For example, Petitioner argues that gas bubbles or the flow of liquid through a reactor “can maintain a suspension,” Pet. Reply 16, but fails to show sufficiently that either the flow of gas or the flow of water in Bonaventura '987 Figure 6 would suspend substrate particles 24 or keep the particles in suspension. Despite agreeing that agitation is sometimes required to keep particles in suspension, Ex. 2017, 32:17–20, Dr. DeFilippi does not explain how the flow of water or gas suspends or maintains a suspension of substrates 24 in Bonaventura '987 Figure 6. Nor does Dr. DeFilippi opine that the nature of substrates 24 or other circumstances are such that agitation would not be required. Petitioner faults Patent Owner for failing to address the liquid flow and other variables. Pet. Reply 16. The burden, however, is on Petitioner, not Patent Owner, to make the requisite showing. 35 U.S.C. § 316(e); *In re Magnum Oil Tools Int'l Ltd.*, No. 2015-1300, slip op. 16–17 (Fed. Cir. July 25, 2016) (“no burden shifts from the patent challenger to the patentee” on the question of obviousness under the *Graham* factors).

Regarding whether one of ordinary skill in the art would reasonably understand or infer that immobilized enzyme particles 24 are in suspension in Bonaventura '987 Figure 6, we credit the testimony of Patent Owner's expert.<sup>11</sup> Dr. Fradette testifies that a person of ordinary skill in the art would

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<sup>11</sup> Based on his education and experience, Ex. 2004 ¶¶ 1, 3–7; Ex. 2005, we find that Dr. Fradette is qualified to testify from the perspective of one of ordinary skill in the art regarding Bonaventura '987 Figures 6 and 7. Fed. R. Evid. 702; Tr. 63:23–64:6. Petitioner argues that Dr. Fradette's testimony is not credible due to a financial interest in Patent Owner, Pet. Reply 24–25; however, Petitioner has not identified any specific and credible instance where his testimony is tainted by bias. See Tr. 64:7–18.

understand that, in the context of a triphasic chemical reactor, “maintaining a suspension of a solid dispersed in a liquid would require the input of mechanical energy (such as by using a mechanical agitator) to maintain the solid in suspension and to prevent solid particles from settling out of suspension.” Ex. 2004 ¶ 73 (citing Ex. 2014, 10-2).<sup>12</sup>

We credit Dr. Fradette’s testimony that, if there was a suspension in Bonaventura ’987 Figure 6, a person of ordinary skill in the art would expect the figure to “depict a mechanical agitator or some other mechanism for inputting mechanical energy into the system to keep the immobilized enzyme 24 in suspension.” Ex. 2004 ¶ 97. Dr. Fradette explains that, in some applications, gas bubbles may provide mechanical energy to maintain a suspension, but that in Figure 6, gas permeable membrane 25 would not permit a sufficient flow rate of gas to maintain a suspension. *Id.* Dr. Fradette’s testimony is not contradicted by Dr. DeFilippi and is consistent with Bonaventura ’987, which discloses that carbon dioxide passes across gas permeable membrane 25 before reacting with immobilized enzyme 24 in compartment 23. Ex. 1004, Fig. 6, 30:15–21, 30:37–44.

On this record, we credit Dr. Fradette’s explanation that “flowable substrate,” as disclosed in Bonaventura ’987 (Ex. 1004, 30:26–30), refers “to the use of relatively small gel particles in a packed configuration within compartment 23, or to the potential that relatively small gel particles may potentially come loose from a solid substrate.” Ex. 2004 ¶ 99. Dr. Fradette explains that, whether the flow of liquid is top-to-bottom (as shown in

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<sup>12</sup>HANDBOOK OF INDUSTRIAL MIXING 10-2 (E. Paul et al. eds., John Wiley & Sons, Inc., 2004), Ex. 2014.

Figure 6) or bottom-to-top (as suggested, Ex. 1004, 30:46–53), the particles would not be in suspension, but would instead accumulate at the outlet screen or in stagnant regions of the reactor. Ex. 2004 ¶ 99. According to Dr. Fradette, “due to the difference in density” between the immobilized enzyme particles and the water, “it’s very hard to imagine a configuration where the particles would not be either settled [to the bottom] or creamed at the top.” Ex. 1027, 125:2–13. We find that Dr. Fradette’s testimony regarding Bonaventura ’987 Figure 6 is credible and demonstrates that Petitioner fails to meet its burden to show that Bonaventura ’987 discloses the “in suspension” and “suspending” features of claims 1 and 25.

We, therefore, conclude that Petitioner has not shown by a preponderance of the evidence that claims 1–3, 15, 17, 24–27, 40, 41, and 43 are unpatentable under 35 U.S.C. § 102(b) as anticipated by Bonaventura ’987.

*Ground 2: Obviousness in view of Bonaventura ’987 and Bonaventura ’416*

Petitioner contends that claims 1–3, 15–17, 24–27, and 40–43 of the ’458 patent are unpatentable under 35 U.S.C. § 103(a) as obvious over Bonaventura ’987 and Bonaventura ’416. Pet. 29–42.

Petitioner asserts that Bonaventura ’987’s Figure 7 embodiment has all of the reactor limitations of the ’458 patent claims. Pet. 29. Petitioner acknowledges that Bonaventura ’987’s description of Figure 7 does not disclose the “in suspension” or “suspending” features of claims 1 and 25, but asserts that these features are disclosed by Bonaventura ’987’s description of Figures 6 and 8. *Id.* at 29–30. Petitioner further asserts that Bonaventura ’987 references Bonaventura ’416, which teaches using polyurethane gel

particles for enzyme immobilization. *Id.* at 30 (citing Ex. 1004, 27:35–40 and Ex. 1005, 6:25–7:55, 10:20–12:29, Figs. 1–3).

Citing the DeFilippi Declaration, Petitioner asserts that it would have been obvious to one of ordinary skill in the art to implement Bonaventura '987's Figure 7 embodiment using polyurethane gel particles, as taught by Bonaventura '416, and to use such gel particles as the porous substrate 24, as taught by Bonaventura '987 in connection with Figures 6 and 8. *Id.* at 31; Ex. 1003 ¶ 96. According to Petitioner, one of ordinary skill in the art would have been motivated to use polyurethane gel in the form of particles (as opposed to an intact mass) because particles are easier to replace in a reactor than a fixed substrate. *Id.* (citing Ex. 1018, 464–465); Ex. 1003 ¶ 97.

Patent Owner asserts that, even if combined, Bonaventura '987 and Bonaventura '416 do not disclose the “in suspension” or “suspending” features of claims 1 and 25. PO Resp. 27, 30–31. Patent Owner acknowledges that Bonaventura '416 discloses a two-phase fluidized bed reactor, *id.* at 28, which involves a suspension. Ex. 2004 (Fradette Decl.) ¶¶ 50–52 (in a fluidized bed reactor, solids are suspended (or fluidized) by a flow of liquid, gas, or both). Patent Owner asserts, however, that Bonaventura '416 does not disclose the “suspending” feature “in the context of a triphasic reactor.” PO Resp. 28.

Patent Owner accepts that a person of ordinary skill in the art would have had a reason to use Bonaventura '416's polyurethane material in the apparatus and method of Bonaventura '987. *Id.* But Patent Owner contends that neither the Petition nor the cited art suggests that a two-phase fluidized bed, as taught by Bonaventura '416, should be combined with a three-phase reactor, as taught by Bonaventura '987 Figure 7, and that any such argument

in the reply brief would be untimely. *Id.* at 28–30. Citing Dr. Fradette’s testimony, Patent Owner contends that the reactors of Bonaventura ’987 Figures 6 and 7 are not compatible with fluidized bed operation because neither is capable of delivering and distributing a sufficient gas flow to suspend the substrate 24. *Id.* at 30 (citing Ex. 2004 ¶¶ 97, 105).

The Reply Brief clarifies that Petitioner’s Ground 2 relies on the reactor of Bonaventura ’987 Figure 7 and that Bonaventura ’416 is cited “not for its reactor design, but for the immobilization substrate.” Pet. Reply 17. According to Petitioner, Patent Owner’s argument regarding sufficiency of the gas flow in Bonaventura ’987 Figure 7 is based on an incorrect assumption regarding the need for an upward flow of gas to suspend the substrates, which are less dense than water. *Id.* at 18 (citing Ex. 1027, 103:19–104:20 and Ex. 1005, 10:65–67). Petitioner argues that a downward flow of liquid can achieve a fluidized bed and that such a flow is shown in both Bonaventura ’987 Figure 7 and Figure 1 of the ’458 patent. *Id.* at 19 (citing Ex. 2007, 333).

A claim is unpatentable as obvious if the differences between the claimed subject matter and the prior art are such that the subject matter, as a whole, would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. 35 U.S.C. § 103(a). The question of obviousness is resolved on the basis of underlying factual determinations, including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of skill in the art; and (4) where in evidence, so-called secondary considerations. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

To establish unpatentability of a challenged claim based on obviousness, Petitioner must show that all limitations of the claim are taught or suggested by the prior art. *See In re Royka*, 490 F.2d 981, 985 (CCPA 1974). In addition, Petitioner must show that a person of ordinary skill in the art would have had a reason to combine the prior art teachings in the manner set forth in the challenged claim. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 427 (2007); *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, No. 2015–1693, 2016 WL 2620512, \*7 (Fed. Cir. May 9, 2016).

On this record, we determine that Petitioner has not shown by a preponderance of the evidence that the subject matter of claims 1 and 25 would have been obvious over the cited teachings of Bonaventura '987 and Bonaventura '416.

We accept Petitioner's contention—not disputed by Patent Owner—that it would have been obvious to one of ordinary skill in the art to use polyurethane gel particles, as taught by Bonaventura '416, as the enzyme-entrapping substrate in the bioreactor of Bonaventura '987 Figure 7. Pet. 30–31; PO Resp. 28–29; Ex. 1003 (DeFilippi Decl.) ¶¶ 94–98; Ex. 1004, 27:35–40 (referencing polyurethane foam of Bonaventura '416); Ex. 1005, 7:33–34 (disclosing polyurethane ground into gel particles).

Petitioner acknowledges that Bonaventura '987's description of Figure 7 does “not expressly describe” that the enzyme-supporting substrates are “in suspension within the liquid,” as recited in the challenged patent claims. Pet. 29. Petitioner argues that Bonaventura '987 describes using substrate particles in suspension in connection with Figures 6 and 8. Pet. 29–30. No citation is provided for this argument, which we interpret as referring to Bonaventura '987's description of “gel particles capable of

flowing with water” and “flowable substrate.” Ex. 1004, 30:28–30. Even if that description is interpreted as applying to the Figure 7 embodiment, however, Petitioner has not shown that it discloses or suggests that the substrates are “in suspension within the liquid.” As discussed above, Petitioner and its expert agree that Bonaventura ’987’s description of “gel particles capable of flowing with water” and “flowable substrate” is consistent with a packed column, which is not a suspension. Ex. 2017, 29:2–16, 87:21–88:2; Tr. 26:1–15.

Petitioner and its expert agree that whether particles will be suspended in a particular reactor depends on a number of variables, including the size and density of the particles, the liquid flow, the gas flow, and the presence or absence of a mechanical agitator. Pet. Reply 15–16; Ex. 2017, 32:17–33:2; 34:14–35:11. As with Bonaventura ’987 Figure 6, however, Petitioner fails to show sufficiently that the flow of liquid and gas in the reactor of Bonaventura ’987 Figure 7 would result in polyurethane gel particles being in suspension. The declaration of Dr. DeFilippi, for example, does not provide a credible or persuasive evaluation of the variables that Petitioner contends are pertinent to whether particles will be suspended. *Compare* Pet. Reply 15 *with* Ex. 1003 ¶¶ 57–59, 92–98, 100 (pp. 54–55) 108 (pp. 66–67) (addressing Bonaventura ’987 Figure 7 and obviousness).

Petitioner argues that, when polyurethane gel particles are used as the substrates in the reactor of Bonaventura ’987 Figure 7, there is a “fluidized bed” with the substrates in suspension. Pet. Reply 18–20.<sup>13</sup> Petitioner does

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<sup>13</sup> We do not view Petitioner’s reply argument as untimely because it focuses on Bonaventura ’987 Figure 7, which is the basis for Petitioner’s obviousness Ground 2. *Compare* Pet. Reply 18–20, *with* Pet. 29.



not, however, direct us to any credible testimony from its own expert as support for this argument. Instead, Petitioner cites the deposition testimony of Patent Owner's expert. Pet. Reply 18 (citing Ex. 1027, 103:19–104:20). Dr. Fradette agreed with Petitioner that the polyurethane material disclosed in Bonaventura '416 and Bonaventura '987 is less dense than water. Ex. 1027, 103:19–104:20; *see also* Ex. 1004, 28:63–65 (density of polyurethane foam); Ex. 1005, 10:65–67 (same). But Dr. Fradette also testified that the low density of this material makes it “very difficult to disperse” in a liquid phase. Ex. 1027, 104:21–105:2. Petitioner does not show sufficiently how the flow of liquid and/or gas in Bonaventura '987 Figure 7 would result in a suspension of low density polyurethane gel particles.

Although not explicitly stated in the Reply Brief, Petitioner's fluidized bed theory presumes that polyurethane substrate particles would float in the reactor configuration shown in Bonaventura '987 Figure 7. Pet. Reply 18–19. That theory is not persuasively supported by Bonaventura '987 or the expert testimony regarding the Figure 7 embodiment. Bonaventura '987 discloses that, in Figure 7, substrate 24 is held in place by substrate support 26c, which may be a fine screen. Ex. 1004, 30:60–63; *see* Ex. 2004 ¶ 101. As Dr. Fradette explained, this description means that the substrate is sitting on support 26c and is not in suspension. Ex. 1027, 128:15–24. Bonaventura '987 discloses that gas diffuses upwardly through the reaction zone, and water flows downwardly through the reaction zone, including through substrate support 26c. Ex. 1004, 30:68–31:2, 31:5–11; *see* Ex. 2004 ¶ 102. On this record, the evidence is not sufficient to show that water accumulates

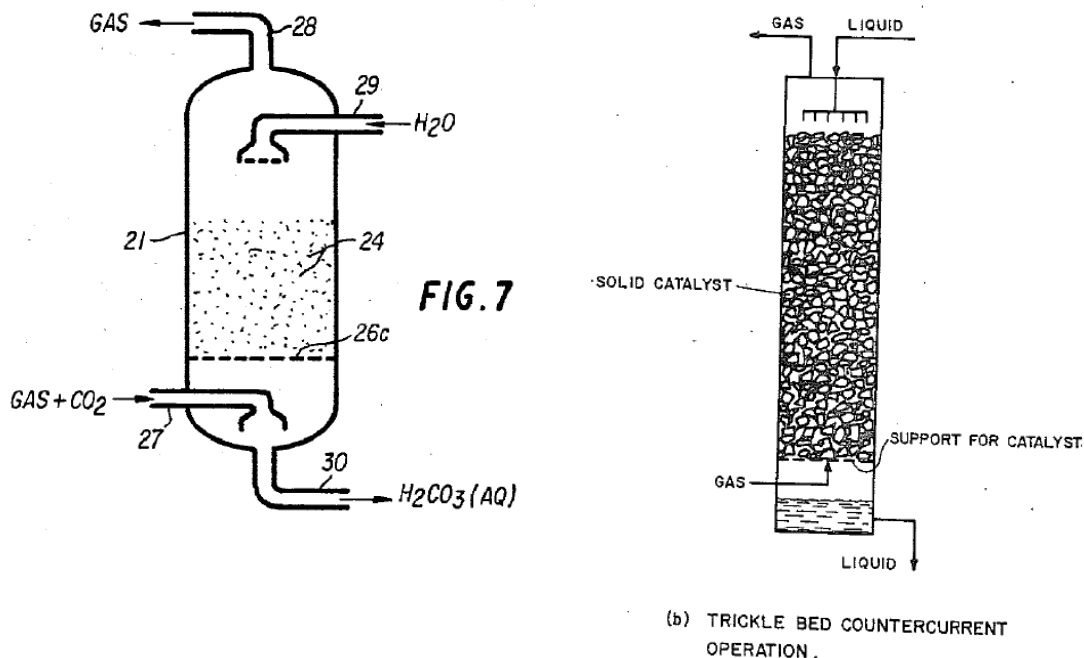
above substrate support 26c or causes substrates 24 to float, as would be required by Petitioner's fluidized bed theory.

Petitioner argues that Bonaventura '987 Figure 7 is the same or similar to Figure 1 of the '458 patent. Pet. Reply 19. We are not persuaded by Petitioner's comparison. *See In re Geisler*, 116 F.3d 1465, 1471 (Fed. Cir. 1997) (attorney argument cannot take the place of evidence). The evidence, including declaration testimony, reveals important differences between the figures. Figure 1 of the '458 patent shows a reaction chamber being filled with liquid. Ex. 1001, 5:34–35 (“liquid inlet (5) is for receiving the liquid (3) and filling the reaction chamber (2)”); Ex. 1003 (DeFilippi Decl.) ¶ 28. Bonaventura '987 Figure 7, on the other hand, does not show water filling the reaction chamber, and substrate 24 is shown sitting on support grid 26c, through which water flows. Ex. 2004 ¶¶ 101–102; Ex. 1027, 128:3–24. In view of these differences, we are not persuaded by Petitioner's argument that Bonaventura '987 Figure 7 is the same or similar to Figure 1 of the '458 patent.

Regarding whether Bonaventura '416 and Bonaventura '987 teach or suggest that enzyme-supporting substrates (gel particles) are suspended in liquid in the reactor of Bonaventura '987 Figure 7, we credit the testimony of Patent Owner's expert. Dr. Fradette testifies that Figure 7 does not depict a reactor in which the substrates are in suspension within a liquid, but instead depicts immobilized enzyme in a sponge-like matrix or in a packed configuration, similar to the fixed bed reactor in Ramachandran Figure

1.1(b). Ex. 2004 ¶¶ 47, 104 (citing Ex. 2007, 6, Fig. 1.1(b)).<sup>14</sup>

Dr. Fradette's testimony is supported by the following side-by-side comparison of Bonaventura '987 Figure 7 and Ramachandran Figure 1.1(b):



Ex. 1004, Fig. 7; Ex. 2007, Fig. 1.1(b). The left-hand figure shows a reactor for removing carbon dioxide from a gas stream (Bonaventura '987 Figure 7), and the right-hand figure shows a fixed bed reactor having a downward flow of liquid and a countercurrent upflow of gas (Ramachandran Figure 1.1(b)). Ex. 1004, 6:59–62; Ex. 2007, 5–6. Both figures show liquid entering the reactor from the top, gas entering the reactor from the bottom, and solid catalyst particles on a catalyst support between the gas and liquid inlets. Ex. 1004, 30:60–63 (“Substrate 24 is held in place by a substrate support 26c, which may be a fine screen when the support by which the enzyme is immobilized is a porous gel.”)

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<sup>14</sup> P.A. Ramachandran and R.V. Chaudhari, *THREE-PHASE CATALYTIC REACTORS* (1983), Ex. 2007.

Significantly, in both Bonaventura '987 Figure 7 and Ramachandran Figure 1.1(b), the catalyst support is shown as having a series of perforations through which liquid can flow downwardly and gas can flow upwardly. *See* Ex. 2004 ¶ 45 (discussing perforated catalyst support in fixed bed reactors, citing Ex. 2007, Fig. 1.1). Neither figure shows gas being bubbled into a liquid. Bonaventura '987 Figure 7 shows no liquid level, and Ramachandran Figure 1.1(b) shows liquid at the bottom of the reactor below the gas inlet. Petitioner submits no reply declaration or other evidence to counter Dr. Fradette's testimony that Bonaventura '987 Figure 7 is similar to the fixed bed reactor in Ramachandran Figure 1.1(b).

On this record, we credit Dr. Fradette's testimony that Bonaventura '987 Figure 7 is not compatible with a fluidized bed reactor. Ex. 2004 ¶ 105. According to Dr. Fradette, a person of ordinary skill would understand that, in Figure 7, there would not be sufficient gas flow to suspend the immobilized enzyme 24, and there is no input of mechanical energy necessary to keep the immobilized enzyme 24 in suspension. *Id.* Dr. Fradette's testimony is consistent with Bonaventura '987, which discloses that, in Figure 7, "there is no pressure differential between th[e] gas stream and the pressure on the water stream" and "[t]he gas and carbon dioxide [injected through inlet 27] diffuse upwardly through the reaction zone." Ex. 1004, 30:56–57, 30:66–31:1; *see also* Ex. 2004 ¶ 105 (relying on Bonaventura '987's description of upward diffusion of gas to support his opinion).

Petitioner presents no persuasive argument that it would have been obvious to modify either the reactor of Bonaventura '987 Figure 7 or its operation such that the substrates are "in suspension." Nor does Petitioner

articulate or provide supporting evidence for a reason that would have prompted a person of ordinary skill in the art to modify either of the bioreactor embodiments of Bonaventura '987 such that the enzyme-supporting substrates would be in suspension in a liquid. *KSR*, 550 U.S. at 418 (it is “important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does”).

We, therefore, conclude that Petitioner has not shown by a preponderance of the evidence that claims 1–3, 15–17, 24–27, and 40–43 are unpatentable under 35 U.S.C. § 103 as obvious over Bonaventura '987 and Bonaventura '416.

*Grounds 3 and 4: Obviousness in view of  
Bonaventura '987 and either Badjic or Kohl*

Petitioner's Ground 3 asserts that claims 1, 4, 25, and 28 are unpatentable under 35 U.S.C. § 103(a) as obvious over Bonaventura '987 and Badjic. Pet. 42–45. Petitioner's Ground 4 asserts that claims 1, 18, and 19 are unpatentable under 35 U.S.C. § 103(a) as obvious over Bonaventura '987 and Kohl. *Id.* at 45–47. Claims 4, 18, and 19 depend from claim 1, and claim 28 depends from claim 25.

Petitioner does not rely on either Badjic or Kohl to teach the “in suspension” or “suspending” limitations of independent claims 1 and 25. *See* Pet. 42–47. Accordingly, we determine that Petitioner's arguments and evidence in support of Grounds 3 and 4 do not remedy the deficiencies in Bonaventura '987, as discussed above.

We, therefore, conclude that Petitioner has not shown by a preponderance of the evidence that claims 1, 4, 25, and 28 are unpatentable

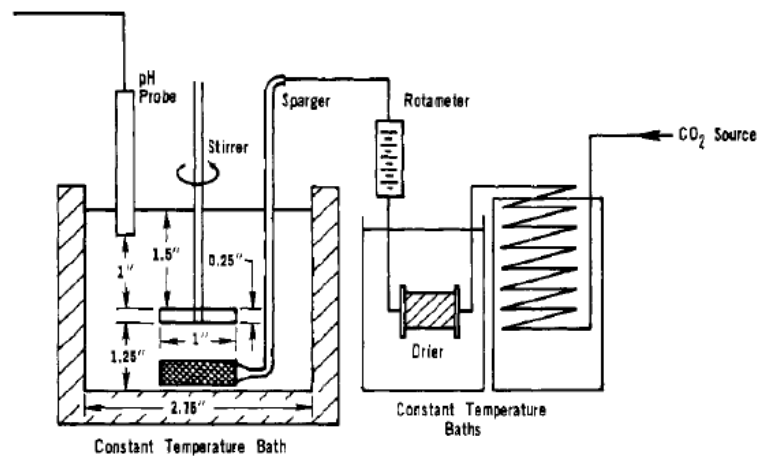
under 35 U.S.C. § 103(a) as obvious over Bonaventura '987 and Badjic. We further conclude that Petitioner has not shown that claims 1, 18, and 19 are unpatentable under 35 U.S.C. § 103(a) as obvious over Bonaventura '987 and Kohl.

*Ground 5: Obviousness in view of Dean and Rau*

Petitioner asserts that claims 1, 2, 15, 16, 22–26, and 40–43 are unpatentable under 35 U.S.C. § 103 as obvious over Dean and Rau.

*Dean (Ex. 1006)*

Dean discloses a study of rates of carbon dioxide absorption in solutions containing carbonic anhydrase using a slurry reactor. Ex. 1006, Abstract. Figure 1 of Dean is reproduced below:



**Figure 1.** Experimental apparatus (not drawn to scale).

Ex. 1006, 454. Figure 1 shows the experimental apparatus used in Dean's study, including a beaker containing a solution, a gas sparger for introducing carbon dioxide gas into the solution, and a stirrer. *Id.* Dean discloses carbon dioxide absorption rate measurements in three buffered solutions: (1) a solution containing no enzyme, (2) a solution of carbonic anhydrase, and

(3) a solution of cellulose nitrate microcapsules containing carbonic anhydrase. *Id.*

*Rau (Ex. 1007)*

Rau discloses a method and apparatus to extract and sequester carbon dioxide from a stream or volume of gas. Ex. 1007, Abstract. Petitioner cites Rau's Figure 3, which is reproduced below:

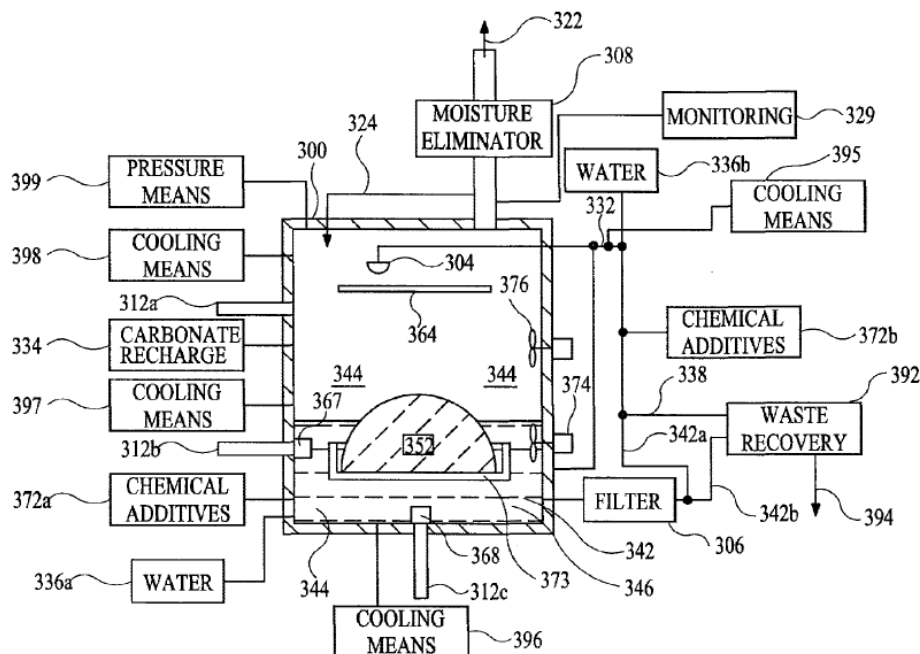


Figure 3 shows an apparatus that extracts and sequesters carbon dioxide from a gas stream, including reactor vessel 300, CO<sub>2</sub>-containing gas streams 312a, 312b, and 312c, CO<sub>2</sub>-depleted gas stream 322, water sources 336a and 336b, and recirculation and waste streams 342a and 342b. Ex. 1007, 5:5–15, 15:11–16:10. In Rau Figure 3, carbon dioxide is hydrated to form carbonic acid 344, which reacts with metal carbonate 352 (held in liquid-porous/gas permeable container 373) to form metal ion/bicarbonate solution 346. *Id.* at 15:15–18, 15:22, 15:33–34; *see id.* at 6:32–7:13. According to Rau, chemical additives 372a and 372b, such as carbonic anhydrase, may be

added to the reactor to enhance carbonic acid formation. *Id.* at 15:30–33; *see id.* at 13:25–27, 14:3–4.

*Claims 1, 2, 22–26, 40, and 43*

Petitioner asserts that Dean discloses a bioreactor and process in which carbonic anhydrase is entrapped in cellulose nitrate microcapsules in suspension in a liquid. Pet. 48. According to Petitioner, Dean’s apparatus lacks only the liquid inlet and the liquid outlet of claim 1. *Id.* at 50.

Petitioner asserts that Rau’s reactor includes all of the reactor limitations of the challenged claims, *id.* at 49, including the liquid inlet and the liquid outlet missing from Dean, *id.* at 50. Regarding a motivation for combining the teachings of Dean and Rau, Petitioner relies on Dr. DeFilippi’s testimony that it would have been necessary to add a liquid inlet and a liquid outlet—as disclosed in Rau—to the reactor of Dean to convert it from a laboratory-scale batch reactor to a pilot plant or commercial-scale continuous reactor. Pet. 50–52; Ex. 1003 ¶¶ 130–136.

Patent Owner argues that Dean does not disclose or suggest that carbonic anhydrase could or should be entrapped, instead of encapsulated, and that the “entrapped” feature of the claims is not disclosed by either Dean or Rau. PO Resp. 35–41.<sup>15</sup> Patent Owner further argues that a person of ordinary skill in the art would have had no reasonable expectation of success in combining Dean and Rau because the mere addition of a liquid inlet and outlet to the reactor of Dean would result in flushing the microencapsulated enzyme from the reaction volume. *Id.* at 41–42; Ex. 2004 ¶ 167. Patent

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<sup>15</sup> Patent Owner acknowledges that the Board’s decision regarding Petitioner’s Ground 5 “will likely turn on how it construes the term entrapped.” Tr. 30:8–9.



Owner contends that any reply argument regarding obviousness of combining Dean with other features of Rau, such as recirculation of liquid and recovery of immobilized enzyme, would be untimely. *Id.* at 42–43.

On this record, we find that Petitioner has shown by a preponderance of the evidence that the combination of Dean and Rau discloses all limitations of claims 1, 2, 22–26, 40, and 43. As support for this finding, we rely on the claim charts provided by Petitioner and Dr. DeFilippi, which identify particular disclosures from Dean and/or Rau for each limitation of claims 1, 2, 22–26, 40, and 43. Pet. 52–60; Ex. 1003 ¶¶ 139, 140, 144–149 and 153.<sup>16</sup>

Regarding the “in suspension” and “suspending” limitations of claims 1 and 25, our finding is supported by Dr. DeFilippi’s testimony that the cellulose nitrate microcapsules, as disclosed in Dean, “were distributed within the reactor and stirred at 840 rpm using a submerged stirrer” and therefore “would have been in suspension in the aqueous liquid.” Ex. 1003 ¶ 67 (citing Ex. 1006, 454). Our finding is further supported by Dean’s characterization of the disclosed apparatus as a “slurry reactor,” Ex. 1006, Abstract, and Dr. DeFilippi’s testimony that “[s]lurry reactors suspend substrates in a fluid.” Ex. 1003 ¶ 147.

Regarding the limitation, “the carbonic anhydrase are entrapped in the porous substrates,” we construe “entrapped in” to mean “the enzyme is physically trapped within the structure of the substrate while retaining at

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<sup>16</sup> Based on his education and experience, Ex. 1003 ¶¶ 1–2; Ex. 1013, we find that Dr. DeFilippi is qualified to testify from the perspective of one of ordinary skill in the art regarding Dean and Rau and reasons for combining their disclosures. Fed. R. Evid. 702.

least some of its activity.” See pages 8–17, *supra*. Under this construction, Patent Owner does not dispute, and we find by a preponderance of the evidence, that Dean discloses carbonic anhydrase “entrapped in” porous substrates. See Ex. 2004 (Fradette Decl.) ¶ 81 (agreeing that Petitioner’s construction of “entrapped in” “necessarily encompasses ‘encapsulation’”).

The parties’ experts agree that Dean discloses carbonic anhydrase in porous substrates, namely cellulose nitrate microcapsules. Ex. 1006, Abstract (“carbonic anhydrase microencapsulated in cellulose nitrate microcapsules”); Ex. 1003 (DeFilippi Decl.) ¶¶ 67 (“[C]ellulose nitrate is a porous material . . . .” (citing Ex. 1006, 457)), 139 (p. 87, “The membrane is porous . . . .” (citing Ex. 1015,<sup>17</sup> 618)); Ex. 2004 (Fradette Decl.) ¶ 164 (“Dean’s encapsulating cellulose nitrate shell is semi-permeable . . . .”).

We find that carbonic anhydrase is physically trapped within the structure of Dean’s cellulose nitrate microcapsules. Our finding is supported by Dr. Fradette’s testimony that, in the method of forming cellulose nitrate microcapsules according to Dean and Paine, a semi-permeable membrane is formed around the enzyme, whereby the enzyme is prevented from passing through the membrane (i.e., the enzyme is insolubilized), but reactants and products are permitted to pass through the membrane. Ex. 2004 ¶¶ 126, 164. We also find that carbonic anhydrase retains at least some of its activity while within Dean’s cellulose nitrate microcapsules. Our finding is supported by Dean, which analyzes the rate at which carbonic anhydrase

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<sup>17</sup> M.A. Paine & R.G. Carbonell, *Immobilization of  $\beta$ -Galactosidase in Collodion Microcapsules*, 17 BIOTECHNOLOGY AND BIOENGINEERING 617–619 (1975) (“Paine”), Ex. 1015. Dean references Paine as disclosing the procedure for preparing cellulose nitrate microcapsules. Ex. 1006, 454.

catalyzes the absorption of CO<sub>2</sub>, when the enzyme is microencapsulated in cellulose nitrate microcapsules. Ex. 1006, Abstract, 454; *see also id.* at 458 (discussing “the very fast rate of the enzymatic reaction” with microencapsulated enzyme); *see also* Ex. 1003 (DeFilippi Decl.) ¶ 64; Ex. 2004 (Fradette Decl.) ¶¶ 124, 127.

Our finding that carbonic anhydrase is “entrapped” in Dean’s cellulose nitrate microcapsules is further supported by Exhibit 1029,<sup>18</sup> which summarizes Dean’s disclosure, using the word “entrapped” to describe the microencapsulated enzyme:

Dean et al. studied the batch absorp[t]ion of carbon dioxide by free and microencapsulated carbonic anhydrase. The process was described by a pseudo-steady-state model which enabled to determine the mass-transfer coefficients and the effectiveness factor for the *entrapped enzyme*.

Ex. 1029, 290 (emphasis added).

On this record, we also find that Petitioner has shown by a preponderance of the evidence that a person of ordinary skill in the art would have had a reason to combine the cited disclosures of Dean and Rau and, in making that combination, would have had a reasonable expectation of success in achieving the claimed subject matter. Our finding is supported by Dr. DeFilippi’s testimony that one skilled in the art would have been motivated to add a liquid inlet and liquid outlet, as disclosed in Rau, to the reactor of Dean, in order to convert it from a laboratory scale batch reactor to a pilot plant or commercial scale continuous reactor. Ex. 1003 ¶¶ 131–

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<sup>18</sup> F. Cioci and R. Lavecchia, *Enzyme-Loaded Liposomes as Microreactors*, in HANDBOOK OF NONMEDICAL APPLICATIONS OF LIPOSOMES: FROM DESIGN TO MICROREACTORS, Vol. III, 287–316 (Yechezkel Barenholz and Danilo D. Lasic eds., 1996), Ex. 1029.

132. Our finding is further supported by Dr. DeFilippi's testimony that a continuous reactor and process would have been advantageous because Dean's enzyme-catalyzed carbon dioxide absorption reaction is reversible, which necessitates the continuous addition of reactants (water) and removal of products (bicarbonate-rich solution) from the reactor in order to drive the reaction forward. *Id.* ¶¶ 133–34; *see also* Ex. 1006, 454 (discussing kinetics of the “forward and reverse enzymatic reactions”). Still further support is provided by Dr. DeFilippi's observation that a continuous process would be required to implement carbon dioxide capture on a commercial scale. Ex. 1003 ¶ 135; *see also* Ex. 1027 (Fradette Dep.) 159:21–160:12 (chemical engineers are trained to favor the continuous reactor over batch processes).

We are not persuaded by Patent Owner's argument regarding a lack of reasonable expectation of success. PO Resp. 41–43; Ex. 2004 ¶ 167. We find that a person of ordinary skill in the art would have had a reasonable expectation of success of maintaining the carbonic anhydrase-containing cellulose nitrate microcapsules within the reaction volume by using a filter or other similar means to either retain or recover the entrapped enzymes. Our finding is supported by Dr. DeFilippi's testimony: “In order to recover the substrates, the filter must necessarily have pores smaller than the diameter of the substrates.” Ex. 1003 ¶ 141; *see also* Ex. 2006 (Perry's) 24–22 (“Particles with immobilized enzymes are sometimes added to a reactor and recovered later by filtration . . .”).

Our finding is further supported by the testimony of both sides' experts that techniques were known in the art for separating suspended particles from dissolved solutes. Ex. 1003 ¶ 142; Ex. 1027 (Fradette Dep.)

183:18–185:15; *see also* Ex. 1020,<sup>19</sup> 188 (Figure 4.24 depicting an enzyme filtration membrane used to retain entrapped enzyme in a reactor); Ex. 1011,<sup>20</sup> 3 (microfiltration disclosed as useful for retaining suspended particles and separating them from dissolved solutes). In our view, Patent Owner’s argument that one of ordinary skill in the art would “merely add” an inlet and outlet to Dean’s reactor, without also adding a filter or other similar means to retain or recover the entrapped enzymes, PO Resp. 41–42, underestimates the level of ordinary skill in the art, as reflected by the expert testimony and cited references. We also find that Petitioner’s reply arguments are not untimely. *Compare* Pet. Reply 23–24, *with* Pet. 55, 59.

*Claims 15, 16, 41, and 42*

Claim 15 depends from claim 1 and recites that the bioreactor includes “a filter having pores with a smaller diameter than a diameter of the suspended substrates for separating the substrates from the ion-rich solution.” Ex. 1001 11:1–4. Claim 41 depends ultimately from claim 25, and recites that “the substrates are separated from the ion-rich solution by filtration.” *Id.* at 12:37–38. Dependent claims 16 and 42 depend from claims 15 and 41, respectively, and recite “ultrafiltration or microfiltration.” *Id.* at 11:5–7, 12:39–40.

Petitioner contends that the additional limitations of claims 15 and 41 would have been obvious in view of Rau’s disclosure of “a solid/liquid separation means, such as a filter” for preventing entrainment of large

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<sup>19</sup> James E. Bailey & David F. Ollis, *BIOCHEMICAL ENGINEERING FUNDAMENTALS* (1977) (“Bailey”), Ex. 1020.

<sup>20</sup> Munir Cheryan, *ULTRAFILTRATION AND MICROFILTRATION HANDBOOK* (1998) (“Cheryan”), Ex. 1011.

particulate carbonate in the recirculation and waste streams 342a and 342b. Pet. 55, 59 (citing Ex. 1007, Fig. 3, 16:2–4); Ex. 1003 ¶¶ 141, 149, 150. Petitioner further contends ultrafiltration or microfiltration were well-known filtration techniques and would have been obvious to use for separating or retaining suspended particles. Pet. 55, 59; Ex. 1003 ¶¶ 142–43, 151–52.

Patent Owner argues that there is no reason to incorporate Rau’s filter into Dean’s reaction system, and no reason is provided by Petitioner or Dr. DeFilippi. PO Resp. 44. According to Patent Owner, preventing entrainment of large particulate carbonate “is the only disclosed purpose of Rau’s filter” and “[a]bsent the addition of the particulate carbonate to Dean’s reaction system,” which is not proposed by the Petition, “the skilled person would have no reason to add Rau’s filter to Dean’s reaction system.” *Id.* at 44–46; Ex. 2004 ¶ 171.

On this record, we find that Petitioner has shown by a preponderance of the evidence that a person of ordinary skill in the art would have had a reason to combine a filter, such as that disclosed by Rau, with a bioreactor that utilizes entrapped carbonic anhydrase, as disclosed by Dean. Our finding is supported by the same evidence discussed above in connection with claims 1, 2, 22–26, 40, and 43. *See* pages 42–43, *supra*. This evidence shows that, in converting Dean’s laboratory scale batch reactor into a pilot plant or commercial scale continuous reactor, a person of ordinary skill in the art would have had a reason to add a filter: namely, in order to retain or recover the entrapped enzymes. Ex. 1003 ¶¶ 141–42; Ex. 2006 (Perry’s) 24–22; Ex. 1027 (Fradette Dep.) 183:18–185:15; Ex. 1020 (Bailey), 176, 188; Ex. 1011 (Cheryan), 3.

We also find that Petitioner has shown by a preponderance of the evidence that it would have been obvious to employ ultrafiltration or microfiltration as the filtration technique. Our finding is supported by evidence showing ultrafiltration and microfiltration were known in the art for the same purpose as recited in the claims—separating suspended particles from a solution. Ex. 1003 ¶¶ 142–43, 151–52; Ex. 1011 (Cheryan) 3 (Table 1.1), 6; Ex. 1020 (Bailey), 176, 188. This same evidence also shows that the combination of ultrafiltration or microfiltration with a bioreactor as taught by Dean modified by Rau reflects a combination of known elements, for their known purpose, to achieve a predictable result. Ex. 1003 ¶ 136; *KSR*, 550 U.S. at 416.

We, therefore, conclude that Petitioner has shown that claims 1, 2, 15, 16, 22–26, and 40–43 are unpatentable under 35 U.S.C. § 103 as obvious over Dean and Rau.

### III. CONCLUSION

1. Petitioner has not demonstrated by a preponderance of the evidence that claims 1–3, 15, 17, 24–27, 40, 41, and 43 are unpatentable under 35 U.S.C. § 102(b) as anticipated by Bonaventura '987;

2. Petitioner has not demonstrated by a preponderance of the evidence that claims 1–3, 15–17, 24–27, and 40–43 are unpatentable under 35 U.S.C. § 103(a) as obvious over Bonaventura '987 and Bonaventura '416;

3. Petitioner has not demonstrated by a preponderance of the evidence that claims 1, 4, 25, and 28 are unpatentable under 35 U.S.C. § 103(a) as obvious over Bonaventura '987 and Badjic;

4. Petitioner has not demonstrated by a preponderance of the evidence that claims 1, 18, and 19 are unpatentable under 35 U.S.C. § 103(a) as obvious over Bonaventura '987 and Kohl; and

5. Petitioner has demonstrated by a preponderance of the evidence that claims 1, 2, 15, 16, 22–26, and 40–43 are unpatentable under 35 U.S.C. § 103(a) as obvious over Dean and Rau.

#### IV. ORDER

Accordingly, in consideration of the foregoing, it is hereby:

ORDERED that claims 1, 2, 15, 16, 22–26, and 40–43 of the '458 patent are held unpatentable under 35 U.S.C. § 103(a); and

FURTHER ORDERED that claims 3, 4, 17–19, 27, and 28 of the '458 patent have not been shown by a preponderance of the evidence to be unpatentable; and

FURTHER ORDERED that, because this is a final written decision, any party to the proceeding seeking judicial review of the decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.



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Patent 8,329,458 B2

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