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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte CHANDRA M. VALMIKINATHAN,
NIKHIL NIRAJ GHEEWALA, BRENT DONALD YOUNG, and
THOMAS WAYNE GILBERT[1]

Appeal 2020-001646
Application 14/860,781
Technology Center 1600

Before JEFFREY N. FREDMAN, DEBORAH KATZ, and
JOHN G. NEW, *Administrative Patent Judges*.

NEW, *Administrative Patent Judge*.

DECISION ON APPEAL

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[1] We use the word "Appellant" to refer to "applicant" as defined in 37 C.F.R. § 1.42. Appellant identifies ACell, Inc. as the real party-in-interest. App. Br. 3.

SUMMARY

Appellant files this appeal under 35 U.S.C. § 134(a) from the Examiner's Final Rejection of claims 1, 4–8, 10, and 17–20. Specifically, claims 1, 4–8, 10, and 17–20 stand rejected as unpatentable under 35 U.S.C. § 103 as being obvious over the combination of Badylak et al. (US 2008/0260831 A1, October 23, 2008) ("Badylak"), Patel et al. (US 2014/0271472 A1, September 18, 2014) ("Patel"), and Malaviya et al. (US 8,025,896 B2, September 27, 2011) ("Malaviya").

The Examiner also rejected claim 17 under 35 U.S.C. § 112(b) as being indefinite.

We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

NATURE OF THE CLAIMED INVENTION

Appellant's claimed invention is directed to a method for making a medical foam device from an extracellular matrix ("ECM") material. Abstr.

REPRESENTATIVE CLAIM

Claim 1 is representative of the claims on appeal and recites:

1. A method for making a medical foam device, comprising:

(a) solubilizing dehydrated extracellular matrix material obtained from a mammalian tissue in a solution with a pH less than 4.0 or a pH greater than 9.0 in the absence of an enzyme;

(b) blending said acidified (pH<4) or basic (pH>9) solubilized extracellular matrix material in an industrial blender at speeds in the range of about 500 RPM to about 2500 RPM to form a foamy extracellular matrix material slurry;

(c) adding one or more minerals during step (b)

> (d) mixing said foamy extracellular matrix material slurry in a buffering solution to neutralize said foamy extracellular matrix material slurry with added minerals to a pH of about 7;
>
> (e) introducing said neutralized foamy extracellular matrix material slurry of step (d) into a mold;
>
> (f) lyophilizing said neutralized molded foamy extracellular matrix material slurry in pre-cooled lyophilizer shelves; followed by;
>
> (g) introducing ice crystals into said lyophilized molded extracellular matrix material of step (f) at a temperature range between 0°C to -40°C for periods of time ranging between 0 minutes to 240 minutes; and,
>
> (h) sublimating said ice crystals introduced in step (g) at a vacuum pressure in the range of 60–120mmHg to produce said medical foam device.

App. Br. 17–18.

ISSUES AND ANALYSIS

We agree with, and expressly adopt, the Examiner's findings, reasoning, and conclusion that the claims are obvious and indefinite (with respect to claim 17). We address below the arguments raised by Appellant.

A. Rejection of the claims over Badylak, Patel, and Malaviya

Issue 1

Appellant argues that the Examiner erred in finding that the combined prior art teaches the claimed method in the claimed order of steps to make a medical foam device. *See* App. Br. 9–10, 15.

Analysis

The Examiner finds that Badylak teaches a method of preparing an ECM-derived gel including the steps of: (1) solubilizing dehydrated mammalian ECM by digesting with an enzyme in an acidic solution having a pH between 2 and 4; (2) blending the acidified ECM mixture; (3) neutralizing the ECM mixture with a buffer to form a pre-gel; (4) placing the pre-gel in a suitable mold; and (5) gelling the mixture. Final Act. 4–5. The Examiner acknowledges that Badylak does not teach: (1) solubilizing ECM in the absence of an enzyme (in claimed step (a)); (2) adding one or more minerals (claimed step (c)); and (3) the lyophilizing process (claimed steps (f)–(h)). *Id.* at 6.

The Examiner finds that Patel teaches a method of preparing an ECM-derived foam including the steps of: (1) solubilizing dehydrated mammalian ECM by digesting in an acidic solution; (2) foaming the ECM gel mixture with mechanical techniques, e.g., aerating; (3) neutralizing the acidic ECM mixture; (4) casting the foamed ECM material into a mold; and (5) lyophilizing the foamed ECM gel material to form a porous medical device. Final Act. 6–8. The Examiner finds that Patel teaches solubilizing ECM in an acid in the absence of an enzyme, resulting in a neutralized non-toxic material that is free of digestive enzyme. *Id.* at 6. The Examiner finds that Patel teaches adding bioactive agents to the mixture before forming the gel. *Id.* at 8.

The Examiner finds that Malaviya teaches a method of preparing ECM foams by: (1) preparing a slurry of ECM material; (2) placing the slurry in a container; and (3) lyophilizing the slurry. Final Act. 8–9. The Examiner finds that Malaviya teaches adding biocompatible inorganic

materials including calcium or phosphate salts to the ECM material at the time of manufacture, prior to forming the ECM foam. *Id.* at 9. The Examiner further finds that Malaviya teaches detailed parameters for lyophilizing, including: (1) pre-freezing a container to -20°C; (2) lyophilizing ECM material at a temperature of -13°C for 8 hours; and (3) sublimating ice crystals under vacuum and low temperatures. *Id.* at 8–9.

The Examiner therefore concludes that it would have been obvious to a person of ordinary skill in the art to prepare an ECM foam by digesting ECM in an acid in the absence of a digestive enzyme, foaming the ECM mixture in a blender, adding a mineral, neutralizing the mixture, adding the mixture to a mold, and lyophilizing the mixture under the claimed conditions. Final Act. 9. The Examiner arrives at this conclusion because all the references teach methods for preparing ECM-derived medical devices including the claimed steps limited by result-effective parameters, e.g., digesting in acid, blending, and lyophilizing. *Id.* at 9–10.

Appellant argues that Badylak's method is "fundamentally different" from the claimed method because Badylak "is entirely about methods of making gels." App. Br. 6 (emphasis in original). Appellant argues that Badylak's blending step does not form a foamy ECM material slurry, and Badylak's method does not end with lyophilizing the mixture to form a foam. *Id.* at 8. Likewise, Appellant argues that Patel teaches forming a gel by alkaline treatment at elevated temperature, as opposed to blending solubilized ECM material at speeds sufficient to form a foamy ECM slurry. *Id.* at 11. Appellant argues that the Examiner "randomly" chooses from "different sections of Patel referring to various forms of ECM materials, including particulate, expanded, gel, dried and foam shapes." *Id.* Appellant

further argues that neither Badylak, Patel, nor Malaviya teach the order of steps in the claimed method because the references fail to disclose all of the ordered steps. *Id.* at 9–10, 15.

We are not persuaded by Appellant's argument. We begin with Appellant's arguments against the references individually rather than the combination. "Non-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references." *In re Merck & Co*., 800 F.2d 1091, 1097 (Fed. Cir. 1986). Patel teaches that ECM gels, such as those taught by Badylak, can be expanded into foamed forms, e.g., foamy slurries, by mechanical techniques, e.g., aeration, alkaline treatment, or heat treatment. Patel ¶¶ 39, 42, 47, 71. Patel expressly teaches that acid digestion is an alternative to enzyme digestion, resulting in a non-toxic preparation free of digestive enzyme. *Id.* ¶ 31. Patel further teaches adding bioadditives before, during, or after forming the gel, casting the foamed gel into a mold, and lyophilizing material to form a foamed device. *Id.* ¶¶ 37, 71. Although the Examiner picks and chooses from Patel's different teachings, such picking and choosing is entirely proper in the making of a § 103, obviousness rejection. *In re Arkley*, 455 F.2d 586, 587 (C.C.P.A. 1972).

With respect to the claimed order of steps, we agree with the Examiner that the claimed order, including the step of adding minerals to the mixture after blending but before neutralizing the mixture, would have been obvious to a person of ordinary skill in the art. *See* Final Act. 9. Patel teaches that the bioactive materials may be added throughout the gel-forming process. Patel ¶ 37. Specifically, Patel teaches "incorporating the additional component(s) into an aqueous, ungelled composition of the ECM

hydrolysate *before*, during (e.g. with) or after addition of the neutralization agent." *Id.* Similarly, Malaviya teaches incorporating biocompatible inorganic materials, e.g., minerals, "prior to the formation of the ECM foam." Malaviya col. 12, ll. 14–16. We therefore find that the prior art collectively suggests "doing the thing that appellant has done in this case" and conclude that the claims would have been obvious absent evidence of new or unexpected results due to the claimed order of steps. *See In re Burhans*, 154 F.2d 690, 692 (C.C.P.A. 1946). Appellant provides no evidence that the order of steps, particularly the sequence of "(c) adding one or more mineral during step (b)," provides new or unexpected results over the prior art that teaches the addition of the mineral, but does not specify at which step the addition occurs.

Issue 2

Appellant argues that a person of ordinary skill in the art would not have been motivated to combine the references because the combination would render Badylak inoperable for its intended use. *See* App. Br. 12–14.

Analysis

Appellant argues that "adding the steps of aerating and lyophilizing to the method of making the gel of Badylak are inappropriate modifications for an obviousness inquiry because the modifications render the gel of Badylak inoperable for its intended purpose." App. Br. 12. Specifically, Appellant argues that modifying Badylak's gel by aerating and lyophilizing according to Patel would change Badylak's flowable gel into a porous solid

structure. *Id.* at 13. Appellant contends that the change would frustrate Badylak's intended purpose of using a gel to infiltrate a porous scaffold thereby permitting tissue in-growth. *Id.* at 14.

We are not persuaded by Appellant's argument. Badylak, Patel, and Malaviya concern reactions for processing ECM materials to form medical devices. *See supra.* The references further recognize that the reaction conditions can be varied to produce different final products. *See* Patel ¶¶ 39, 43, 47. Although Badylak teaches the benefits of gel formulations, Patel and Malaviya teach the desirable properties of ECM-derived foams. For example, Patel teaches that "[t]he more foamy and porous structure of an expanded ECM … can allow the material to be cast or otherwise prepared into a variety of sponge or foam shapes for use in the preparation of medical materials and devices." *Id.* ¶ 47. Malaviya teaches that "ECM foams … provide a relatively large surface area of naturally occurring ECM … [that] can be advantageous in providing a relatively large surface area to which … biocompatible inorganic materials can be affixed pre-implantation." Malaviya 11:42–49. Appellant adduces no evidence, nor can we discern any, to support the premise that the cited prior art teaches or suggests that the proposed modification of converting a gel to a foam would result in an inoperable *process*, or a foam with undesirable properties. Accordingly, a person of ordinary skill in the art would have been motivated to pursue the desirable properties of ECM foams taught by Patel and Malaviya, even at the expense of the benefits of ECM gels taught by Badylak. *See In re Urbanski*, 809 F.3d 1237, 1243 (Fed. Cir. 2016).

Issue 3

Appellant argues that the Examiner erred in finding that the combined prior art teaches blending in an industrial blend at speeds in the range of 500 RPM to about 2500 RPM to form a foamy ECM material slurry. *See* App. Br. 8–9.

Analysis

Appellant argues that "Badylak's blending is an action associated with solubilizing for a period of 12–48 hours." App. Br. 8. Appellant contrasts the claimed step (b) which "is performed 'at speeds in the range of about 500 RPM to about 2500 RPM to form a foamy extracellular matrix material slurry.'" *Id.* Appellant further argues that Patel requires neutralizing an ECM hydrolysate prior to aerating to form a foam, and thus "Patel at least does not teach or suggest blending solubilized ECM material at speeds sufficient to form a foamy ECM material slurry as recited in step (b)." *Id.* at 11.

The Examiner responds that Badylak teaches solubilizing ECM by blending and Patel teaches foaming ECM material by mechanically aerating. Ans. 6. The Examiner finds that "[o]ne having ordinary skill in the art at the time of filing would have recognized that the foamed ECM gel material would form a slurry comprising bubbles and particulate ECM material." *Id.* With respect to the blending speed, the Examiner finds that Appellant has not established that the claimed range is critical by showing that the claimed speed provides unexpected results over the prior art. *Id.*

We are not persuaded by Appellant's arguments. The combination of Badylak and Patel teaches that blending an ECM digestion mixture may

result in a foamy mixture. *See* Patel ¶ 39. Accordingly, the blending speed is a result-effective variable that can be varied to adjust the ECM foam's properties in a predictable manner. *See Urbanski*, 809 F.3d at 1242. Our reviewing court has explained that:

> The law is replete with cases in which the difference between the claimed invention and the prior art is some range or other variable within the claims. These cases have consistently held that in such a situation, the applicant must show that the particular range is *critical*, generally by showing that the claimed range achieves unexpected results relative to the prior art range.

In re Woodruff, 919 F. 2d 1575, 1578, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). Appellant has not submitted any evidence showing that the claimed range achieves unexpected results relative to the prior art. Accordingly, we are not persuaded that the Examiner erred.

We consequently affirm the Examiner's rejection of the claims.

B. Rejection of claim 17 as indefinite

The Examiner finds that claim 17 recites a broad limitation together with a narrow limitation that falls within the broad limitation. Final Act. 3. Specifically, the Examiner finds claims 17 recites a genus, *viz.*, "calcium and phosphate salts," and species within the genus, *viz.*, "calcium nitrate and tricalcium phosphate." *Id.* A claim that recites both a broad limitation and a narrow limitation within the broad limitation is indefinite under 35 U.S.C. § 112(b) because the boundaries of the claim are not discernible. *See* MPEP § 2173.05(c).

Appellant does not address the indefiniteness rejection in the Appeal Brief. *See generally* App. Br. We consequently summarily affirm this

rejection. *See* 37 C.F.R. § 41.37(c)(iv) ("[A]ny arguments or authorities not included in the appeal brief will be refused consideration by the Board for purposes of the present appeal").

CONCLUSION

The Examiner's rejection of claims 1, 4–8, 10, and 17–20 as unpatentable under 35 U.S.C. § 103 is affirmed.

The Examiner's rejection of claim 17 as unpatentable under 35 U.S.C. § 112(b) is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1).

AFFIRMED

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
1, 4–8, 10, 17–20	103	Badylak, Patel, Malaviya	1, 4–8, 10, 17–20	
17	112(b)	Indefiniteness	17	
Overall Outcome			1, 4–8, 10, 17–20	