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Paper 20
Entered: August 12, 2019

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

RTI SURGICAL, INC.,
Petitioner,

v.

LIFENET HEALTH,
Patent Owner.

Case IPR2019-00573
Patent 9,585,986 B2

Before GEORGE R. HOSKINS, TIMOTHY J. GOODSON, and CHRISTOPHER C. KENNEDY, *Administrative Patent Judges*.

KENNEDY, *Administrative Patent Judge*.

DECISION
Granting Institution of *Inter Partes* Review
35 U.S.C. § 314

I. INTRODUCTION

Petitioner RTI Surgical, Inc., filed a Petition for *inter partes* review of claims 1–27 of U.S. Patent No. 9,585,986 B2 (Ex. 1003). Paper 2 ("Pet."). Patent Owner LifeNet Health filed a Preliminary Response. Paper 9. With our authorization, Petitioner filed a Reply (Paper 16), and Patent Owner filed a Surreply (Paper 19).

Pursuant to 35 U.S.C. § 314 and 37 C.F.R. § 42.4(a), the Board has authority to determine whether to institute *inter partes* review. *Inter partes* review may not be instituted unless "there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a). A decision to institute under § 314 must institute on all claims challenged in the petition. *SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348, 1359–60 (2018).

For the reasons set forth below, we institute *inter partes* review of claims 1–27.

A. RELATED MATTERS

Petitioner identifies the following related matter: *LifeNet Health v. RTI Surgical, Inc.*, No. 3:18-cv-817 (M.D. Fla.), filed June 25, 2018. Pet. 3–4. That case was transferred to another judicial district and is now captioned as *LifeNet Health v. RTI Surgical, Inc.*, No. 1:18-cv-00146-MW-GRJ (N.D. Fla.). Paper 3 at 1.

We also note that a related patent, U.S. Patent No. 6,569,200, was involved in *LifeNet Health v. LifeCell Corp.*, No. 2:13-cv-486 (E.D. Va.) ("LifeCell litigation"). In that case, a jury determined that the defendant failed to establish the invalidity of the asserted claims by clear and convincing evidence, and the Federal Circuit affirmed. *See LifeNet Health*

v. LifeCell Corp., 837 F.3d 1316 (Fed. Cir. 2016) (Ex. 2002); *see also* Paper 3 at 1.

Additionally, we note that the '200 patent is the subject of IPR2019-00571, and that another related patent, U.S. Patent No. 9,579,420, is the subject of IPR2019-00572. *See* Paper 3 at 1.

B. THE '986 PATENT

The '986 patent relates to plasticized tissue grafts. *E.g.*, Ex. 1003 at [54] (title), claim 1. The '986 patent discloses that "[s]oft tissue products are typically provided as fresh-frozen or freeze-dried," which "causes [such] grafts to be brittle and typically causes shrinkage where the shrinkage is often not uniform, thereby causing graft failure." *Id.* at 3:46–51, 57–61. The '986 patent further discloses that "solvent preservation . . . can cause irreversible denaturation of proteins, and solubilization of solvent soluble components, including for example, lipids." *Id.* at 3:60–63. According to the '986 patent, typical methods of preparing tissue grafts "necessitate[] a rehydration step . . . for implantation." *Id.* at 3:63–66.

The '986 patent discloses the use of a "plasticizer," such as glycerol, in the preparation of tissue grafts. *E.g.*, *id.* at [57] (abstract), 5:33–35. The plasticizer is said to "replace[] water in the molecular structure of the bone or soft tissue matrix . . . allowing for dehydration of the tissue, yet not resulting in an increase in brittleness of the plasticized product, and resulting in compressive and/or tensile properties similar to those of normal hydrated bone." *Id.* at [57] (abstract). The '986 patent teaches that a benefit of its plasticized tissue graft is that rehydration "prior to clinical implantation" is not required, and "the dehydrated bone or soft tissue plasticized product can

be placed directly into an implant site without significant preparation in the operating room." *Id.*

C. ILLUSTRATIVE CLAIM

Claim 1, reproduced below, is illustrative of the challenged claims.

> 1. A plasticized soft tissue graft suitable for transplantation into a human, comprising:
>
> a cleaned soft tissue graft having an internal matrix; and
>
> one or more plasticizers contained in said internal matrix, said one or more plasticizers not being removed from said internal matrix prior to packaging,
>
> wherein said plasticized soft tissue graft does not require refrigeration or freezing for storage,
>
> wherein the plasticized soft tissue graft has mechanical properties approximating mechanical properties of natural soft tissue.

D. PRIOR ART RELIED UPON

Petitioner relies on the following references, as well as the Declaration of David McQuillan, Ph.D. (Ex. 1034).

Reference	Patent/Pub. No.	Date	Exhibit
Livesey	US 5,336,616	Aug. 9, 1994	1004
Walker	WO 98/07452	Feb. 26, 1998	1005
Werner	US 4,357,274	Nov. 2, 1982	1006

E. ASSERTED GROUNDS OF UNPATENTABILITY

Petitioner contends that the challenged claims are unpatentable based on the following six grounds.

Reference(s)	Basis[1]	Claim(s) Challenged
Walker	§ 102(b)	11, 12
Walker	§ 103(a)	1–3, 5[2], 9, 11–15, and 23–25
Livesey	§ 102(b)	1–6, 9–20, 23, 24
Livesey	§ 103(a)	1–6, 9–20, 23, 24
Walker and Livesey	§ 103(a)	1–10, 13–25, 27
Walker, Livesey, and Werner	§ 103(a)	26

Pet. 5.

II. DISCUSSION

A. LEVEL OF ORDINARY SKILL IN THE ART

The parties provide very similar proposals for the level of ordinary skill in the art. *Compare* Pet. 8–9, *with* Prelim. Resp. 15. Consistent with those proposals, we determine that the level of ordinary skill in the art is (1) a master's degree in biology, chemistry, physiology, biochemistry, biomaterials engineering, biomedical engineering, or a related field, and approximately three years of research or work experience related to preparing and/or processing tissue for transplantation into humans, or (2) a

[1] The relevant sections of the Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112–29, took effect on March 16, 2013. Because the earliest effective filing date of the '986 patent is before March 16, 2013, we apply the pre-AIA statutory framework.

[2] Petitioner's "Identification of Challenge" and section headers fail to list claim 5 as subject to this proposed ground of unpatentability. *See* Pet. 5, 30. Petitioner's analysis, however, directly asserts that claim 5 would have been obvious over Walker. *See id.* at 34–35. Accordingly, we understand claim 5 to be part of this proposed ground.

bachelor's degree in biology, chemistry, physiology, biochemistry, biomaterials engineering, biomedical engineering, or a related field, and approximately five years of research or work experience related to preparing and/or processing tissue for transplantation into humans. That level of ordinary skill in the art is consistent with the prior art of record. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001); *In re GPAC Inc.*, 57 F.3d 1573, 1579 (Fed. Cir. 1995); *In re Oelrich*, 579 F.2d 86, 91 (CCPA 1978).

B. CLAIM CONSTRUCTION

"In an *inter partes* review proceeding, a claim of a patent . . . shall be construed using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. 282(b)." *See* Changes to the Claim Construction Standard for Interpreting Claims in Trial Proceedings Before the Patent Trial and Appeal Board, 83 Fed. Reg. 51,340 (Oct. 11, 2018) (codified at 37 C.F.R. § 42.100(b) (2019)) (amending 37 C.F.R. § 42.100(b) effective November 13, 2018). That standard "includ[es] construing the claim in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent." *Id.*; *see also Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005).

We discuss two terms below. No other claim term needs to be expressly construed to reach a decision on institution. *See Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) (claim terms need only be construed "to the extent necessary to resolve the controversy"); *see also Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d

1013, 1017 (Fed. Cir. 2017) (applying *Vivid Techs.* in the context of an *inter partes* review).

1. "plasticized soft tissue graft"

The parties agree that the term "plasticized soft tissue graft" should be construed as follows:

> a load-bearing and/or non-load-bearing soft tissue product, including skin, pericardium, dura mater, fascia lata, and a variety of ligaments and tendons composed of an internal matrix where free and loosely bound waters of hydration in the tissue have been replaced with one or more plasticizers without altering the orientation of the collagen fibers, such that the mechanical properties, including the material, physical and use properties, of the tissue product are similar to those of normal hydrated tissue.

See Pet. 12–13; Prelim. Resp. 19. That is the construction adopted by the district court in the LifeCell litigation involving the related '200 patent, and the Federal Circuit declined to modify that construction on appeal. Ex. 2002 at 10–11.

Because that construction appears to be consistent with the evidence of record, *e.g.*, Ex. 1003 at 7:37–41, 8:16–25, 9:28–32, we accept the parties' agreed construction of the term "plasticized soft tissue graft."

2. "cleaned"

The parties agree that, in the LifeCell litigation, the district court construed the term "cleaned" as "a process during which cellular elements and small molecular weight solutes are removed." Pet. 12; Prelim. Resp. 18. The parties dispute whether that construction encompasses partial removal of cellular elements and small molecular weight solutes. Pet. 12 ("A POSITA would have understood that the cleaning process . . . only partially removes cellular elements from the soft tissue."); Prelim. Resp. 18–19

("Petitioner's attempt to read in additional limitations from the examples in the specification is improper and should be rejected.").

The parties' briefing of this issue is limited. Petitioner does not explain what specific modification, if any, it is proposing to the construction adopted by the district court in the LifeCell litigation. *See* Pet. 12. Meanwhile, Patent Owner's discussion does not cite any portion of the '986 patent or its prosecution history to support Patent Owner's apparent position that cleaning must remove all cellular elements and small molecular weight solutes. *See* Prelim. Resp. 18–19. Additionally, Patent Owner's criticism that Petitioner is improperly importing limitations from the specification appears inapt because Petitioner is arguing for a broader understanding of the claim term, not a narrower one.

The plain language of the district court construction quoted by the parties appears to encompass partial removal of cellular elements and small molecular weight solutes. Additionally, the specification of the '986 patent discloses that, even when tissue has been "cleaned," it can nevertheless be "further cleaned," indicating that "cleaned" tissue retains at least some elements that could be "further cleaned" if desired. *See* Ex. 1003 at 10:7–15 ("The *cleaned* bone *can then be further cleaned*" to "dislodg[e] residual bone marrow materials . . . ." (emphasis added)).

At this stage of the proceeding, we agree with Petitioner that the term "cleaned" as it appears in, e.g., the term "cleaned soft tissue graft" (claim 1), encompasses soft tissue grafts in which some but not necessarily all cellular elements and small molecular weight solutes have been removed. We encourage the parties to develop this issue further if they believe it would be helpful to the resolution of the issues presented in this case.

C. PRINCIPLES OF LAW

Anticipation under 35 U.S.C. § 102 requires "the presence in a single prior art disclosure of all elements of a claimed invention arranged as in the claim." *Therasense, Inc. v. Becton, Dickinson & Co.*, 593 F.3d 1325, 1332 (Fed. Cir. 2010) (internal quotation marks omitted); *see also Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008).

"Section 103(a) forbids issuance of a patent when the differences between the subject matter sought to be patented 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." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007) (internal quotation marks omitted). Obviousness under § 103 is resolved based on 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 ordinary skill in the art; and (4) objective evidence of nonobviousness, i.e., secondary considerations. *See Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

D. ANTICIPATION BY WALKER

Petitioner asserts that claims 11 and 12 are anticipated by Walker. Pet. 19–30. For reasons set forth below, we determine that Petitioner's arguments and evidence fail to establish a reasonable likelihood that Petitioner will prevail with respect to this proposed ground of unpatentability.

1. Walker (Ex. 1005)

Walker discloses "[a] method of sterilising material . . . for implantation into a human or animal body" in which the material is treated with "a substance . . . selected so as to maintain certain physical characteristics of the material such as flexibility and/or structure of cells or extra cellular material." Ex. 1005 at 1 (Abstract).[3] "Suitable substances include . . . glycerol." *Id.* Walker teaches that its method "can be used on gra[ft]s for implantation or on biological material such as vascular tissue etc. and has the advantage that the substance does not react with water and so the material can be treated in solution without drying out or becoming brittle." *Id.*

Walker's method includes, *inter alia*, storing the material in an ethanol solution, treating with glycerol, and treating with ethylene oxide to sterilize. *E.g.*, *id.* at 4:2–3, 5:17–20. Walker discloses that the "pre-sterilising treatment," which may include treatment with glycerol, "enables the material substantially to retain certain physical characteristics, such as flexibility, and can suitably replace at least some of the water contained in the material." *Id.* at 6:20–24.

2. Analysis

Claims 11 and 12 require, *inter alia*, that cellular elements are "substantially" removed from the soft tissue. Petitioner's analysis of that requirement is as follows: "A POSITA would have recognized that storing the biological tissue in ethanol would *at least partially, if not substantially*,

[3] Page number pincites to Walker are to the stamp added by Petitioner to the lower right corner of each page of Walker.

remove cellular components from the soft tissue." Pet. 21 (claim 11 analysis, citing Ex. 1034 ¶¶ 84, 303) (emphasis added), Pet. 23 (claim chart), Pet. 25 (claim 12 analysis, citing Ex. 1034 ¶¶ 84, 308). The argument in the Petition, at best, suggests that storage in ethanol accomplishes "partial" removal and might accomplish "substantial" removal. *E.g.*, Pet. 21.

Turning to paragraphs 84, 303, and 308 of the McQuillan Declaration, cited by Petitioner, Dr. McQuillan states that "storage of the tissue in ethanol . . . would *at least partially remove* potentially adverse immunogenic cellular components from the tissue by solubilizing the lipid cell membrane." Ex. 1034 ¶ 84 (emphasis added); *see also* Ex. 1034 ¶ 303 (similar), ¶ 308 (similar).

Patent Owner argues that Petitioner's assertion that ethanol would "at least partially remove" cellular elements, even if true, fails to establish that cellular elements would be "substantially removed" as required by claims 11 and 12. Prelim. Resp. 25–27. Patent Owner also argues that Walker's disclosure that the "structure of cells" in Walker's material is "maintain[ed]" indicates that Walker's treatment with ethanol does not substantially remove cellular elements. *Id.* at 26. Patent Owner also argues that the purpose of substantial removal of cellular elements is to avoid "inflammatory and immune system reactions in the recipient." *Id.* at 26–27. Patent Owner suggests that Walker's treatment with ethylene oxide for purposes of sterilization would be unnecessary if Walker's treatment with ethanol substantially removed cellular elements. *Id.* ("Walker's sterilization process is necessary because Walker teaches keeping the cellular elements that cause the inflammatory response, rather than their removal.").

Petitioner's arguments and evidence fail to establish a reasonable likelihood that Petitioner will prevail as to this proposed ground. In particular, as set forth above, neither the relevant portions of the Petition nor the cited paragraphs of the McQuillan Declaration include an affirmative assertion that treatment of soft tissue with ethanol as disclosed by Walker will substantially remove cellular elements as required by claims 11 and 12. Nor do the relevant portions of the Petition or the cited paragraphs of the McQuillan Declaration explain how the alleged "partial" removal of cellular elements falls within the scope of the claimed "substantial[]" removal of cellular elements. In that regard, we observe that the relevant portions of the Petition and the cited paragraphs of the McQuillan Declaration also fail to address (1) Walker's disclosure that the "structure of cells" is maintained, (2) why sterilization with ethylene oxide is necessary in Walker if Walker's ethanol treatment substantially removes cellular elements.

On this record, we are not persuaded that the Petition establishes a reasonable likelihood that Petitioner would prevail as to this proposed ground of unpatentability.

E. OBVIOUSNESS OVER WALKER

Petitioner asserts that claims 1–3, 5, 9, 11–15, and 23–25 would have been obvious in view of Walker. Pet. 30–36. As to claims 11 and 12, Petitioner fails to establish a reasonable likelihood of prevailing for reasons set forth above. For reasons set forth below, however, we determine that Petitioner's arguments and evidence establish a reasonable likelihood that Petitioner will prevail as to claims 1–3, 5, 9, 13–15, and 23–25, which do not recite "substantially" removing cellular elements.

The preamble[4] of claim 1 recites "[a] plasticized soft tissue graft suitable for transplantation into a human." Petitioner argues that Walker's disclosure of treating tissue with glycerol, one of the principal plasticizers disclosed by the '986 patent, would yield "a plasticized soft tissue graft" within the scope of claim 1. Pet. 19–24, 30–31. Patent Owner disputes that. *E.g.*, Prelim. Resp. 20–25. As explained in detail below, we do not find Patent Owner's argument to be persuasive at this stage of the proceeding. For purposes of institution, Petitioner has adequately shown that Walker discloses this limitation for the reasons stated in the Petition, *see* Pet. 19–24, 30–31, and elaborated upon below.

Claim 1 further recites "a cleaned soft tissue graft having an internal matrix." Petitioner argues that Walker's treatment with ethanol would at least partially remove cellular elements from Walker's tissue, and that Walker's tissue has an internal matrix that would contain glycerol in view of Walker's disclosure of treating tissue with glycerol. Pet. 19–21. At this stage of the proceeding, we do not discern Patent Owner to argue that Walker fails to disclose "a cleaned soft tissue graft having an internal matrix." *See* Prelim. Resp. 27–29. For purposes of institution, Petitioner has adequately shown that Walker discloses this limitation for the reasons stated in the Petition. *See* Pet. 19–21.

Claim 1 further recites "one or more plasticizers contained in said internal matrix, said one or more plasticizers not being removed from said

[4] The general rule is that a preamble is not limiting. *See Allen Eng'g Corp. v. Bartell Indus., Inc.*, 299 F.3d 1336, 1346 (Fed. Cir. 2002) ("Generally, the preamble does not limit the claims."). In the Petition, Petitioner addresses the preamble and does not assert that it is not limiting. Pet. 19. For purposes of this Decision, we assume that the preamble is limiting.

internal matrix prior to packaging." As noted above, Petitioner argues that Walker's tissue has an internal matrix that would contain the plasticizer glycerol in view of Walker's disclosure of treating tissue with glycerol, and Petitioner argues that Walker's disclosure of packaging the glycerol-treated tissue samples prior to sterilization, with optional drainage to remove excess glycerol, indicates that Walker's plasticizer is not removed prior to packaging. Pet. 26, 31. Beyond arguing that Walker does not teach a plasticized soft tissue graft, which we discuss below, Patent Owner does not specifically address these limitations. For purposes of institution, Petitioner has adequately shown that Walker discloses these limitations for the reasons stated in the Petition. *See* Pet. 26, 31.

Claim 1 further recites "wherein said plasticized soft tissue graft does not require refrigeration or freezing for storage." Petitioner argues that a person of ordinary skill in the art would have understood that Walker's soft tissue grafts do not require "any special conditions for storage" because there is "[n]othing in Walker" indicating that any special storage conditions are required. Pet. 32–33. Petitioner also argues, with citations to Dr. McQuillan's declaration, that a person of ordinary skill in the art would have understood that Walker's method of glycerol treatment yields "dried/dehydrated" grafts that "d[o] not require special conditions for storage" and "could be stored at room temperature." *Id.* At this stage of the proceeding, Patent Owner does not argue that a person of ordinary skill in the art would have understood Walker's grafts to require refrigerated storage. For purposes of institution, Petitioner has adequately shown that Walker teaches or suggests this limitation for reasons stated in the Petition. *See* Pet. 32–33.

Claim 1 further recites "wherein the plasticized soft tissue graft has mechanical properties approximating mechanical properties of natural soft tissue." Petitioner argues that Walker's disclosure that glycerol treatment results in the maintenance of tissue flexibility and the microstructure of collagen in the material, along with disclosures concerning physical properties, shrinkage, and swelling, indicate that Walker's method produces tissue grafts that have mechanical properties approximating mechanical properties of natural soft tissue. Pet. 21–22. Patent Owner argues that Walker does not teach a plasticized soft tissue graft, and Patent Owner suggests that Walker's disclosure of rehydration indicates that Walker's tissue grafts do not have mechanical properties that approximate those of natural soft tissue. Prelim. Resp. 23–25. As set forth below, we find those arguments to be unpersuasive at this stage of the proceeding. For purposes of institution, Petitioner has adequately shown that Walker discloses this limitation for reasons set forth in the Petition, *see* Pet. 21–22, and elaborated upon below.

We turn now to Patent Owner's arguments. Patent Owner's principal argument is that Walker does not teach a plasticized soft tissue graft because Walker's glycerol allegedly does not replace the free and loosely bound waters of hydration in the tissue, as required by the parties' agreed construction of the term "plasticized soft tissue graft," which we have adopted. Prelim. Resp. 20–25, 28.

That argument does not persuade us that the Petition's analysis fails to meet the threshold for institution of trial. The '986 patent discloses "[i]ncubating" tissue in a plasticizer composition; i.e., "soaking the graft in the composition." Ex. 1003 at 6:59–63. The '986 patent discloses that

"[m]ethods of incubation include for example: soaking and mild agitation." *Id.* at 19:9–10. The '986 patent teaches that plasticizers, including glycerol, "can easily displace/replace water at the molecular level." *Id.* at 7:42–45. These descriptions in the '986 patent indicate that replacement of water in the tissue with glycerol is the natural result of soaking tissue in a glycerol composition.

Walker teaches an incubation method that appears to be the same in relevant respects. Walker teaches incubation, "preferably with agitation," of the tissue in a glycerol composition. Ex. 1005 at 5:17–24, 7:7–13. Walker explicitly states that its methods result in "plasticized" tissues. *E.g.*, *id.* at 9:22–23.

At this stage of the proceeding, Patent Owner has not persuasively explained why Walker, which subjects essentially the same ingredients and materials to essentially the same soaking/agitating process as disclosed by the '986 patent, would not yield the same results, i.e., a plasticized soft tissue graft that has mechanical properties approximating those of natural soft tissue. *See Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, 970 (Fed. Cir. 2001) ("A reference includes an inherent characteristic if that characteristic is the 'natural result' flowing from the reference's explicitly explicated limitations." (quoting *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1290 (Fed. Cir. 1991))).

That Walker discusses rehydration of its tissue grafts, *see* Prelim. Resp. 21–25, does not persuade us otherwise, because that does not explain why subjecting the same materials to the same process would yield a different result in Walker, particularly given that Walker expressly describes its tissues as "plasticized." Patent Owner does not persuasively identify a

difference between its materials or incubation process and those of Walker that would cause differences in the resulting soft tissue graft, or that would make rehydration essential in Walker but unnecessary using the invention claimed in the ’986 patent. Nor does Patent Owner offer a persuasive explanation as to the meaning of the term “plasticized” in Walker, to the extent that Patent Owner’s argument implicitly requires that the meaning of that term in Walker is different from its meaning in the ’986 patent. We also observe that none of the claims subject to Petitioner’s Ground 2 prohibit rehydration. To the extent that rehydration of Walker’s tissues would result in Walker’s glycerol molecules being replaced by water molecules, it would appear that Walker’s tissues, at least prior to being rehydrated, remain relevant to the obviousness of the challenged claims.

Finally, we observe that, although Walker indicates differences in certain tissue samples depending on whether humidification was present, Prelim. Resp. 23–24 (citing Ex. 1005 at 24), claim 1 requires only that the mechanical properties of the graft “approximat[e]” the mechanical properties of natural soft tissue; not that the mechanical properties are identical. As explained above, at this stage of the proceeding it is unclear how or why Walker’s tissue grafts, subjected to the same materials (i.e., glycerol) and processes (i.e., incubation/agitation) as disclosed in the ’986 patent, would be materially different from the claimed tissue grafts.

Thus, for reasons set forth above, we determine that Petitioner’s arguments and evidence establish a reasonable likelihood that Petitioner will prevail with respect to claim 1.

Petitioner provides a detailed explanation of its challenge to claims 2, 3, 5, 9, 13–15, and 23–25. Pet. 19–36. At this stage of the proceeding,

Patent Owner has not raised distinct arguments concerning those claims. *See* Prelim. Resp. 27–29. We have reviewed Petitioner's arguments and evidence, and we determine that Petitioner has demonstrated a reasonable likelihood of prevailing in its challenge to those claims for the reasons stated in the Petition. *See* Pet. 19–36.

F. ANTICIPATION BY LIVESEY

Petitioner asserts that claims 1–6, 9–20, 23, and 24 are anticipated by Livesey. Pet. 36–56. For reasons set forth below, we determine that Petitioner's arguments and evidence establish a reasonable likelihood that Petitioner will prevail with respect to this proposed ground of unpatentability.

1. Livesey (Ex. 1004)

Livesey discloses methods for processing and preserving tissue matrixes for transplantation in which tissues are treated "with a processing solution to remove cells" and then treated with a cryoprotectant solution (which may comprise glycerol) before freezing, drying, storage, and rehydration. Ex. 1004 at [57] (abstract), 11:49–51. Livesey discloses that its methods allow biological samples to be cooled and stored "without causing structural and functional damage." *Id.* at 14:59–63.

2. Analysis

Petitioner provides a detailed explanation of its challenge to claim 1 as anticipated by Livesey. *See* Pet. 36–43. Livesey's disclosure has many similarities to that of Walker, and Petitioner's analysis of Livesey is similar to Petitioner's analysis of Walker. *See id.* We have reviewed Petitioner's arguments and evidence, and we determine that Petitioner has demonstrated

a reasonable likelihood of prevailing in its challenge to claim 1 for reasons set forth in the Petition, *see* Pet. 36–43, and elaborated upon below.

Patent Owner argues that Livesey does not teach a plasticized soft tissue graft with mechanical properties approximating those of natural tissue. Prelim. Resp. 31–35. In particular, Patent Owner focuses on Livesey's disclosures of freeze-drying and rehydration prior to implantation. *See id.*

Patent Owner's arguments do not persuade us that the Petition's analysis fails to meet the threshold for institution of trial. Similar to both Walker and the '986 patent itself, Livesey discloses "incubat[ing]" soft tissue samples in glycerol, which Livesey describes as a cryoprotectant. *E.g.*, Ex. 1004 at 5:27, 11:17–18, 11:49–51, 12:31–33. Notwithstanding Livesey's description of glycerol as a "cryoprotectant" rather than as a "plasticizer," glycerol is the same material disclosed by both Walker and the '986 patent as resulting in tissue plasticization when tissue is soaked in the composition. As above with respect to our discussion of Walker, it is unclear how or why subjecting the same materials (e.g., soft tissue) to the same composition (glycerol) as part of the same process (i.e., incubation/soaking) would not result in the same product, i.e., glycerol replacing the free and loosely bound waters of hydration in Livesey's tissue to produce a plasticized soft tissue graft with mechanical properties approximating those of natural tissue.[5] Dr. McQuillan states that it would.

[5] We are aware of Patent Owner's assertion that the patentee of the Livesey reference argued during prosecution of a related application that Livesey "describes drying of acellular tissue matrices, not water replacement." Prelim. Resp. 32 n.12. Although we find that to be noteworthy, at least at this stage of the proceeding, we do not discern sufficient differences

Ex. 1034 ¶¶ 17, 25, 62, 65–81, 333. Patent Owner has not yet filed an expert declaration in this proceeding.

The fact that Livesey describes freeze-drying and rehydration prior to implantation does not persuade us, at this stage of the proceeding, that Livesey's tissue falls beyond the scope of claim 1. *See* Prelim. Resp. 32–34. None of the claims subject to this proposed ground of unpatentability prohibit freeze-drying or rehydration. As Petitioner explains, the '986 patent itself discloses processes that involve freeze-drying. *E.g.*, Pet. 67 (citing Ex. 1003 at 10:26–42). In any event, even were we to conclude that the challenged claims preclude freeze-drying and/or rehydration, Livesey's tissue is treated with glycerol after it is cleaned but prior to freeze-drying and/or rehydration. *E.g.*, Livesey at [57] (abstract). It appears that the tissue graft prior to freeze-drying and/or rehydration is relevant to the patentability of the challenged claims.

On the record presently before us, we determine that Petitioner's arguments and evidence establish a reasonable likelihood that Petitioner will prevail with respect to claim 1.

Petitioner provides a detailed explanation of its challenge to claims 2–6, 9–20, 23, and 24. Pet. 44–56. At this stage of the proceeding, Patent Owner has not raised distinct arguments concerning those claims. *See* Prelim. Resp. 30–35. We have reviewed Petitioner's arguments and evidence, and we determine that Petitioner has demonstrated a reasonable

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between Livesey's incubation-in-glycerol process and that of Walker and/or the '986 patent that would explain how or why the glycerol in Livesey fails to replace water molecules in tissue when tissue is incubated in glycerol.

likelihood of prevailing in its challenge to those claims for the reasons stated in the Petition. *See* Pet. 44–56.

G. OBVIOUSNESS OVER LIVESEY

Petitioner asserts that claims 1–6, 9–20, 23, and 24 would have been obvious in view of Livesey. Pet. 56–57. Petitioner relies on Petitioner's analysis of anticipation of the same claims by Livesey discussed above, and further asserts that if "Livesey does not explicitly disclose that the plasticizer is contained in the internal matrix or that the plasticizer impregnates the soft tissue graft, a POSITA in February 1998 would have understood from Livesey that small chemical compounds, such as the cryoprotectants in Livesey, act by replacing free and loosely bound water within the tissue thereby incorporating themselves within the internal matrix." *Id.*

Patent Owner does not raise distinct arguments beyond those discussed above. Prelim. Resp. 35–36.

Although Petitioner's analysis appears to be more relevant to inherent anticipation than to obviousness, in a case such as this involving a single reference obviousness ground as an alternative to an anticipation ground that we have found reasonably likely to prevail, the principle that "anticipation is the epitome of obviousness" would appear to be relevant. *See Realtime Data, LLC v. Iancu*, 912 F.3d 1368, 1372–74 (Fed. Cir. 2019). On the record before us, we determine that Petitioner's arguments and evidence establish a reasonable likelihood that Petitioner will prevail with respect to this proposed ground of unpatentability.

H. OBVIOUSNESS OVER WALKER AND LIVESEY

Petitioner asserts that claims 1–10, 13–25, and 27 would have been obvious in view of Walker and Livesey. Pet. 57–62. We determine that Petitioner's arguments and evidence establish a reasonable likelihood that Petitioner will prevail with respect to this proposed ground of unpatentability.

Petitioner relies on Walker largely as set forth above and further argues that, to the extent that Walker does not disclose certain claim limitations, a person of ordinary skill in the art would have been motivated to combine Walker with Livesey to achieve those limitations. Pet. 57–62. We have reviewed Petitioner's arguments and evidence, and we determine that Petitioner has demonstrated a reasonable likelihood of prevailing in its challenge for reasons set forth in the Petition. *See id.*

Patent Owner argues only that "neither Livesey nor Walker teaches a plasticized soft tissue graft." Prelim. Resp. 36. At this stage of the proceeding, that argument does not persuade us that the Petition's analysis fails to meet the threshold for institution of trial for reasons set forth above with respect to the proposed grounds of unpatentability based on Walker and Livesey individually.

I. OBVIOUSNESS OVER WALKER, LIVESEY, AND WERNER

Petitioner asserts that claim 26 would have been obvious in view of Walker, Livesey, and Werner. Pet. 62–63. Claim 26 depends indirectly from claim 13 and requires, *inter alia*, "surgically implanting the plasticized soft tissue graft into a patient *without rehydration*" (emphasis added). For reasons set forth below, we determine that Petitioner's arguments and

evidence establish a reasonable likelihood that Petitioner will prevail with respect to this proposed ground of unpatentability.

1. Werner (Ex. 1006)

Werner discloses methods of manufacturing "sclera protein transplants." Ex. 1006 at [57] (abstract). In particular, Werner discloses a method in which tissue such as "raw dura matter from humans" is treated with H_2O_2, degreased, rinsed, treated with a glycerin[6] solution, and then dried. *Id.* at 2:21–29. Werner discloses that the "glycerin impregnates the transplant by a diffusion process." *Id.* at 2:5–6. Werner discloses that its "product is soft and no rehydration is necessary prior to its use." *Id.* at 2:39–40.

2. Analysis

Petitioner relies on Walker and Livesey largely as set forth above and further argues that, to the extent that neither Walker nor Livesey discloses implantation without rehydration, Werner teaches a similar tissue product treated with glycerol that does not require rehydration before implantation. Pet. 62. Petitioner argues that, due to the similarities of Walker, Livesey, and Werner, a person of ordinary skill in the art would have recognized in view of Werner "that no rehydration of the tissue product [of Walker or Livesey] is necessary before implantation and would have had a reasonable expectation of success in that adaptation." *Id.* Petitioner argues that such a modification would "simpl[if]y the processing of the soft tissue graft during implantation" and "would achieve the known advantage of allowing for

[6] The words "glycerin" and "glycerol" refer to the same compound. *E.g.*, Ex. 1034 ¶ 37; Ex. 1003 at 5:35 (referring to "glycerol (glycerin USP)").

direct implantation of the plasticized soft tissue graft instead of requiring rehydration before implantation." *Id.* at 63. Dr. McQuillan states that Werner's process of treating tissue with H_2O_2, degreasing, and rinsing is a cleaning process that removes cellular elements from tissue. Ex. 1034 ¶ 92.

We find Petitioner's arguments and evidence to be adequate to meet the threshold for institution of trial.

Patent Owner argues that "neither Walker nor Livesey teach a 'plasticized soft tissue graft,'" and that "both Walker and Livesey explicitly teach needing to rehydrate the grafts." Prelim. Resp. 37. Patent Owner also argues that "Werner does not remedy the deficient teaching of Livesey or Walker," and that "Werner makes clear that the mechanical properties of the tissue are intentionally affected—such that they do not approximate the mechanical properties of natural soft tissue." *Id.*

Patent Owner's arguments do not persuade us that the Petition's analysis fails to meet the threshold for institution of trial. Even assuming that Walker and Livesey indicate a preference for rehydration, that does not meaningfully address Petitioner's assertion that, in view of Werner, a person of ordinary skill in the art would have reconsidered whether rehydration is necessary in Walker and/or Livesey. Additionally, as set forth above, given the similarities of the processes of both Walker and Livesey to the process disclosed by the '986 patent, it is unclear why the grafts of Walker and Livesey would require rehydration but the graft of the '986 patent would not.

As to Patent Owner's argument concerning the mechanical properties of Werner's tissue, Patent Owner acknowledges that Werner's results involved "hard cerebral meninges" tissue. Prelim. Resp. 37–38. Patent Owner does not allege that a person of ordinary skill in the art would have

expected the same results in the different types of tissue disclosed by Livesey and Walker. *Id.*; *cf. In re Keller*, 642 F.2d 413, 426 (CCPA 1981) ("[O]ne cannot show non-obviousness by attacking references individually where, as here, the rejections are based on combinations of references.").

On the record before us, we determine that Petitioner's arguments and evidence establish a reasonable likelihood that Petitioner will prevail with respect to this proposed ground of unpatentability.

J. 35 U.S.C. § 325(d)

Patent Owner argues that we should exercise our discretion to deny the Petition under 35 U.S.C. § 325(d). Prelim. Resp. 6–15. Patent Owner explains that Livesey and Werner were the basis for rejections issued during prosecution of the application that led to the '986 patent. *Id.* Patent Owner points out that Walker was a prior art reference used in an IPR petition that challenged the claims of a related patent,[7] and that "[d]uring prosecution of the '986 patent, LifeNet submitted a copy of [that] IPR petition and the Examiner acknowledged consideration." *Id.* at 8–9.

Institution of *inter partes* review is discretionary. *See* 35 U.S.C. § 314(a); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2140 (2016) (the AIA does not impose a "mandate to institute review"). Our discretion is guided by 35 U.S.C. § 325(d), which provides, in relevant part:

> MULTIPLE PROCEEDINGS -- . . . In determining whether to institute or order a proceeding under this chapter, chapter 30, or

[7] U.S. Patent No. 9,125,971. The IPR petition challenging the '971 patent is in the record as Exhibit 2006 and was later assigned the following case number: Case IPR2015-01888. In that IPR, the Board instituted trial and then terminated the proceeding when Patent Owner requested adverse judgment. *See* Ex. 1036 (institution decision); Ex. 1037 (termination order).

> chapter 31, the Director may take into account whether, and reject the petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office.

We may consider multiple factors when determining whether to exercise our discretion not to institute under § 325(d), including:

> (a) the similarities and material differences between the asserted art and the prior art involved during examination; (b) the cumulative nature of the asserted art and the prior art evaluated during examination; (c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection; (d) the extent of the overlap between the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art; (e) whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the asserted prior art; and (f) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of the prior art or arguments.

Becton, Dickinson & Co. v. B. Braun Melsungen AG, Case IPR2017-01586, Paper 8 at 17–18 (PTAB Dec. 15, 2017) (informative).

In this case, we are not persuaded that we should exercise our discretion under § 325(d) to deny the Petition. Although we recognize that citation to the Examiner of an IPR petition providing a detailed description of a particular prior art reference may provide a more compelling scenario under § 325(d) than the mere listing of a reference on a lengthy IDS, the ’986 patent includes a list of references cited to the Examiner that spans several pages and includes dozens of citations to documents from related court and Patent Office proceedings. *See* Ex. 1003 at 2–6. There is no dispute that the Examiner did not issue a rejection on the basis of Walker or otherwise substantively address Walker, and Patent Owner does not allege

that Walker is cumulative of references substantively addressed during prosecution. Thus, most or all of the *Becton* factors weigh against exercising our discretion to deny the Petition under § 325(d) as to the grounds based on Walker. The Board has frequently held that a reference that "was neither applied against the claims nor discussed by the Examiner" does not weigh in favor of exercising the Board's discretion under § 325(d) to deny a petition. *E.g.*, *Zip-Top LLC v. Stasher, Inc.*, Case IPR2018-01216, slip op. at 35–36 (PTAB Jan. 17, 2019) (Paper 14); *see also*, *e.g.*, *Shenzhen Zhiyi Tech. Co. v. iRobot Corp.*, Case IPR2017-02137, slip op. at 9–10 (PTAB Apr. 2, 2018) (Paper 9) (declining to exercise discretion under § 325(d) to deny petition when the reference was merely cited in a Notice of References Cited). Accordingly, we decline to deny the grounds based on Walker pursuant to § 325(d).

Because we have determined that denial under § 325(d) is not warranted as to at least those asserted grounds, and because a decision to institute is "a simple yes-or-no institution choice respecting a petition, embracing all challenges included in the petition," *PGS Geophysical AS v. Iancu*, 891 F.3d 1354, 1360 & n.2 (Fed. Cir. 2018) (citing *SAS Inst. Inc. v. Iancu*, 138 S. Ct. 1348, 1359–60 (2018) and corresponding USPTO Guidance (Apr. 26, 2018), https://www.uspto.gov/patents-application-process/patent-trial-and-appeal-board/trials/guidance-impact-sas-aia-trial), even were we to find Patent Owner's § 325(d) arguments persuasive as to the grounds based on Livesey and Werner, we would not deny institution of the entire Petition on that basis. Thus, we decline to provide a detailed analysis of § 325(d) as to Livesey and Werner. We briefly observe that *Becton* factors (a)–(d) provide at least some support for Patent Owner's

position, but factors (e) and (f) provide significant support for Petitioner's position that institution should not be denied under § 325(d). *See* Pet. 63–69.

As a final observation, we note that Patent Owner places significant emphasis on the LifeCell litigation, in which a jury determined that the defendant failed to establish the invalidity of the asserted claims by clear and convincing evidence, and the Federal Circuit affirmed. *See* Ex. 2002; *see also* Prelim. Resp. 1. Section 325(d) concerns art and arguments that "previously were presented to the Office." Thus, beyond the litigation materials considered by the Office, the LifeCell litigation is not directly relevant to § 325(d). In any event, we have considered the LifeCell litigation in deciding whether to institute *inter partes* review of the '986 patent. Petitioner was not a party to the LifeCell litigation, and that case involved a different (but related) patent. Additionally, by Patent Owner's own characterization of the invalidity theories at issue in the LifeCell litigation, "LifeCell did not even attempt to argue that Livesey taught a plasticized soft tissue graft, and instead relied upon Livesey only for its teaching of cleaning." Surreply 4; *see also* Surreply 6. Thus, to the extent that Livesey and Werner were at issue in the LifeCell litigation, the invalidity theories involving those references were materially different from the theories of unpatentability presented by the Petitioner in this case.

For reasons set forth above, we are not persuaded that we should exercise our discretion under § 325(d) to deny the Petition.

III. CONCLUSION

We determine that Petitioner has demonstrated a reasonable likelihood of prevailing in showing the unpatentability of at least one claim of the '986 patent. At this preliminary stage of the proceeding, we have not made a final determination with respect to the resolution of any factual or legal issue.

IV. ORDER

It is hereby:

ORDERED that, pursuant to 35 U.S.C. § 314(a), *inter partes* review of claims 1–27 of the '986 patent is instituted with respect to all grounds set forth in the Petition; and

FURTHER ORDERED that, pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4(b), *inter partes* review of claims 1–27 of the '986 patent shall commence on the entry date of this Order, and notice is hereby given of the institution of *inter partes* review.

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