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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

RTI SURGICAL, INC.,
Petitioner,

v.

LIFENET HEALTH,
Patent Owner.

Case IPR2019-00572
Patent 9,579,420 B2

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

HOSKINS, *Administrative Patent Judge*.

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

I. INTRODUCTION

RTI Surgical, Inc. ("Petitioner") has filed a Petition (Paper 2, "Pet.") pursuant to 35 U.S.C. §§ 311–319 to institute an *inter partes* review of claims 1–18, 20–22, and 24–36 of U.S. Patent No. 9,579,420 B2 ("the '420 patent").

LifeNet Health ("Patent Owner") has filed a Preliminary Response (Paper 9, "Prelim. Resp.").

Applying the standard set forth in 35 U.S.C. § 314(a), which requires demonstration of a reasonable likelihood that Petitioner would prevail with respect to at least one challenged claim, we institute, on behalf of the Director (37 C.F.R. § 42.4(a)), an *inter partes* review to determine whether Petitioner demonstrates by a preponderance of the evidence that claims 1–18, 20–22, and 24–36 of the '420 patent are unpatentable.

II. BACKGROUND

A. Real Parties in Interest and Related Proceedings

Petitioner identifies itself as the real party-in-interest. Pet. 3. Patent Owner identifies itself as the real party-in-interest. Paper 4, 1.

The parties identify two litigations as related to this proceeding. The first is *LifeNet Health v. LifeCell Corp.*, Case No. 2:13-CV-00486 (E.D. Va.), which led to a Federal Circuit decision reported at 837 F.3d 1316 (Fed. Cir. 2016) (hereafter "the LifeCell Litigation"). Pet. 9 n.2, 10 n.3, 13–16; Paper 4, 1. The second is *LifeNet Health v. RTI Surgical, Inc.*, Case No. 1:18-CV-00146 (N.D. Fla.), which was filed in June 2018 and remains pending. Pet. 3; Paper 4, 1. Our review of the District Court's docket in the second litigation indicates it has been stayed.

There are two related IPR proceedings filed on the same day as the present proceeding, challenging related patents to the ’420 patent. Paper 4, 1. The first is IPR2019-00571, challenging U.S. Patent No. 6,569,200 B2 (“the ’200 patent”), which shares a common parent application with the ’420 patent. The second is IPR2019-00573, challenging U.S. Patent No. 9,585,986 B2, which is a continuation of the ’420 patent.

Another related proceeding is IPR 2015-01888 (“the ’1888 IPR”), challenging U.S. Patent No. 9,125,971 B2 (“the ’971 patent”), which is a continuation of the ’420 patent.

B. The ’420 Patent

The ’420 patent discloses a plasticized soft tissue graft product. Ex. 1002, Title, Abstract. A plasticizer replaces water in the molecular structure of the soft tissue matrix, which beneficially dehydrates the graft without increasing the brittleness of the graft, and results in the graft having properties similar to those of normal hydrated tissue. *Id.* at Abstract, 1:15–33, 4:36–39. Such properties may include that the plasticized graft maintains the native orientation of collagen fibers present in the un-plasticized soft tissue graft. *Id.* at 1:49–2:4 (discussing bone grafts); *id.* at 3:15–18 & 3:28–30 (discussing soft tissue grafts). The plasticized graft, further, may be placed directly into a human patient without significant preparation in the operating room, such as rehydration of the graft. *Id.* at Abstract, 1:15–33, 4:36–39, 4:43–45, 5:28–34, 5:43–46. The plasticizer may include glycerol. *Id.* at 5:28–32, 7:52–53, 10:32–34, 25:6–7 (claim 10).

C. The Challenged Claims

The ’420 patent contains thirty-six claims. Ex. 1002, 24:35–26:44. Petitioner challenges claims 1–18, 20–22, and 24–36, including five independent claims 1–3, 15, and 16. *Id.*; Pet. 5. Claim 1 illustratively recites:

> 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,
>
> wherein said cleaned soft tissue graft comprise collagen fibers and the native orientation of the collagen fibers is maintained in said plasticized soft tissue graft.

Ex. 1002, 24:35–41.

Claims 2 and 3 are substantially similar to claim 1, except they differ in describing how the one or more plasticizers are maintained within the graft. *Id.* at 24:42–54. Specifically, claim 2 specifies the “graft is impregnated with” the plasticizer(s), and claim 3 specifies the “graft compris[es]” the plasticizer(s). *Id.* at 24:44–45, 24:50–51.

Claim 15 is identical to claim 3, except claim 15 specifies that the graft is “load-bearing.” *Id.* at 25:22–27.

Claim 16 recites a method for producing a plasticized soft tissue graft, including “impregnating” a cleaned graft with one or more plasticizers, and maintaining the native orientation of collagen fibers within the plasticized graft. *Id.* at 25:28–36.

D. Asserted Grounds of Unpatentability

Petitioner presents the following five challenges to the '420 patent in this proceeding. *See* Pet. 5.

Statutory Basis	Reference(s)	Claim(s) Challenged
§ 102	Walker[1]	1–3, 5, 8, 10, 13–18, 20, 21, 24–28, 30, and 33–35
§ 103	Walker	1–3, 5, 7–11, 13–18, 20–22, 24–31, and 33–35[2]
§ 102	Livesey[3]	1–3, 6, 8, 9, 11–14, 16–18, 24, 25, 28, 29, 31, 32, and 34–36
§ 103	Livesey	1–3, 6, 8, 9, 11–14, 16–18, 24, 25, 28, 29, 31, 32, and 34–36[4]
§ 103	Walker or Livesey, in view of Werner[5]	4

III. ANALYSIS

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. 9, *with* Prelim. Resp. 15. Consistent with

[1] Ex. 1005, Int'l App. Pub. No. WO 98/07452, pub. Feb. 26, 1998.

[2] As discussed below, there is some confusion in the Petition as to whether claims 3, 9, 11, 15, 29, and 31 are part of this ground. *See* Pet. 5, 38–42.

[3] Ex. 1004, U.S. Patent No. 5,336,616, iss. Aug. 9, 1994.

[4] As discussed below, there is some confusion in the Petition as to whether claim 3 is part of this ground. *See* Pet. 5, 59–61.

[5] Ex. 1006, U.S. Patent No. 4,357,274, iss. Nov. 2, 1982.

those proposals, we determine 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 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

We interpret the claims of the '420 patent "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)." Changes to the Claim Construction Standard for Interpreting Claims in Trial Proceedings Before the Patent Trial and Appeal Board, 83 Fed. Reg. 51,340, 51,358 (Oct. 11, 2018) (to be codified at 37 C.F.R. § 42.100(b)). This "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).

1. Plasticized Soft Tissue Graft

Each of the challenged independent claims is directed to a "plasticized soft tissue graft" comprising "one or more plasticizers."

Petitioner contends a "plasticized soft tissue graft" should be construed as:

> 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.

Pet. 13, 14–15. The Preliminary Response agrees with this construction. Prelim. Resp. 19.

On the present record, we adopt the agreed-upon construction of "plasticized soft tissue graft," as set forth above. This construction is identical to the construction of the same term in the '200 patent adopted by the District Court in the LifeCell Litigation. *See* Ex. 1019, 7–9, 14; Ex. 2001, 2–3. LifeCell challenged certain aspects of the construction on appeal, but the Federal Circuit did not disturb the District Court's construction. *See* Ex. 2002, 10–11 (837 F.3d at 1327–28).

2. Rehydration of Graft

Although not presented as a claim construction issue *per se*, Patent Owner seeks to distinguish both Walker and Livesey from the '420 patent claims on the basis that Walker and Livesey require rehydration after the graft is (allegedly) plasticized. Prelim. Resp. 3, 4–6, 21–25, 32. In Patent Owner's view, the need for rehydration is inconsistent with plasticization of

the graft, because rehydration indicates the alleged plasticizer does not replace loosely bound waters of hydration in the tissue such that the mechanical properties of the graft are similar to those of normal hydrated tissue. *Id.*

One problem with Patent Owner's contention, based on the present record, is that it misconstrues the scope of the independent claims. There is nothing in the plain language of claims 1–3, 15, and 16, or in the agreed-upon construction of "plasticized" (*see supra* Section III.B.1), that precludes hydration of the graft after plasticization. Indeed, claim 4 of the '420 patent recites: "The plasticized soft tissue graft of any one of claim 1, 2, or 3, wherein said plasticized soft tissue graft is suitable for *direct* transplant into a human *without rehydration*." Ex. 1002, 24:55–57 (emphases added). Claim differentiation thus suggests the parent claims 1, 2, and 3 are open to rehydration, so that dependent claim 4 properly "specif[ies] a further limitation of the subject matter claimed." 35 U.S.C. § 112, ¶ 4; *Phillips*, 415 F.3d at 1314–15 ("[T]he presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim.").

The '420 patent specification, further, reflects that plasticization of a graft is not inconsistent with later rehydration of the graft. To be sure, the '420 patent indicates it is "advantageous" to avoid the need for rehydration of the graft, especially in the operating room immediately prior to implanting the graft in a patient. *See* Ex. 1002, 4:23–28, 4:43–45, 5:23–34, 11:62–12:3. However, the '420 patent also indicates that "hydrating a dehydrated plasticized graft" may be beneficial, and during such hydration the plasticizer "may optionally be not replaced by water or may optionally

be partially or fully replaced by water." *Id.* at 8:7–13; *see also id.* at 4:55–57, 7:46–50, 8:37–40 (the plasticizer of a plasticized soft tissue product "can be readily removed prior to implantation," for example when the plasticizer is toxic). The '420 patent further suggests that plasticization of a graft may, in some cases, be followed by a further dehydration step, suggesting that the plasticization does not *fully* replace loosely bound waters of hydration in the tissue. *Id.* at 11:43–12:3. Thus, when read as a whole, the '420 patent reflects that it is preferable but not necessary to avoid the need for rehydrating a plasticized graft before implantation into a patient. Reading the independent claims to preclude rehydration following plasticization would improperly incorporate a limitation into the claims from a preferred embodiment of the specification. *See Cisco Systems, Inc. v. TQ Delta, LLC*, 928 F.3d 1359, 1363–64 (Fed. Cir. 2019) ("[W]ithout any clear indication otherwise in the specification, synchronization is not restricted to the 'advantageous' clock-based preferred embodiment as described in the specification.") (citing *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 913 (Fed. Cir. 2004), as "explaining that 'it is improper to read limitations from a preferred embodiment described in the specification — even if it is the only embodiment — into the claims absent a clear indication in the intrinsic record that the patentee intended the claims to be so limited'").

Also, so far as we can tell from the present record, this specific issue was not litigated in the LifeCell Litigation. *See* Ex. 1019 (District Court opinion and order on claim construction); Ex. 2001 (District Court opinion and order on LifeCell's Motion for New Trial or JMOL); Ex. 2002 (Federal Circuit decision on appeal).

For the foregoing reasons, we determine independent claims 1–3, 15, and 16 of the ’420 patent do not preclude rehydration after plasticization. Dependent claim 4 does preclude rehydration after plasticization.

3. Other Claim Terms

Petitioner proposes constructions for various other claim terms, including “cleaned” (claims 1–3, 15, and 16), “the native orientation of the collagen fibers is maintained” (claims 1–3, 15, and 16), “internal matrix” (claim 1), and “mechanical properties approximating mechanical properties of natural soft tissue” (claim 14). Pet. 12, 13, 15–16. The Preliminary Response agrees with Petitioner’s proposals in some respects, and disagrees in other respects. Prelim. Resp. 17, 18–19, 20. Based on the present record, we conclude no explicit claim construction of these terms or any other term is needed to decide whether to institute review of the ’420 patent. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co. Ltd.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (per curiam) (claim terms need to be construed “only to the extent necessary to resolve the controversy” (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999))).

C. Anticipation by Walker

Petitioner asserts claims 1–3, 5, 8, 10, 13–18, 20, 21, 24–28, 30, and 33–35 of the ’420 patent are unpatentable under 35 U.S.C. § 102 as anticipated by Walker. Pet. 5, 21–38.

Given the arguments and evidence of record, Petitioner has demonstrated a reasonable likelihood of prevailing on its assertions at least as to claim 1, which is representative as to the objections raised in the Preliminary Response. We begin our analysis with a brief summary of the

law of anticipation, then we summarize the Walker disclosure, and finally we address Petitioner's and Patent Owner's contentions as to anticipation by Walker.

1. Law of Anticipation

A patent claim is unpatentable as anticipated under 35 U.S.C. § 102 "if each and every limitation is found either expressly or inherently in a single prior art reference." *WhitServe, LLC v. Computer Packages, Inc.*, 694 F.3d 10, 21 (Fed. Cir. 2012) (quoting *Celeritas Techs., Ltd. v. Rockwell Int'l Corp.*, 150 F.3d 1354, 1361 (Fed. Cir. 1998)).

2. Walker Disclosure

Walker discloses a method of sterilizing a soft tissue graft, such as vascular tissue, for implantation into a human body. Ex. 1005, 1 (Abstract), 3:3–9.[6] Sterilization of the graft is preferably achieved by treating the graft with ethylene oxide (EtO), but this treatment presents certain challenges. *Id.* at 4:2–12. To help alleviate those challenges, Walker proposes to incubate the graft in a substance such as glycerol, before sterilization with EtO. *Id.* at 4:14–5:27. Walker refers to this pre-sterilization treatment with glycerol as "[p]lasticization" of the graft. *Id.* at 7:4–21, 8:16–18, 8:26–28. Walker discloses that the glycerol plasticization maintains certain "physical characteristics" of the soft tissue graft, such as its "flexibility" and the "structure of cells or extracellular material such as collagen, particularly the microstructure of collagen." *Id.* at 4:23–27, 6:20–22. The glycerol

[6] Citations herein to Walker (Exhibit 1005) refer to the page numbering added to the bottom of each page by Petitioner.

plasticization also "can suitably replace at least some of the water contained in the" soft tissue graft. *Id.* at 6:20–27.

3. Claim 1

Petitioner provides detailed arguments and evidence, including the Declaration of Dr. David McQuillan (Ex. 1034), in support of contending claim 1 is unpatentable as anticipated by Walker. Pet. 21–27; Ex. 1034 ¶¶ 82–89, 187–192.

a) "A plasticized soft tissue graft suitable for transplantation into a human"

Petitioner contends Walker discloses a plasticized soft tissue graft suitable for transplantation into a human. Pet. 21–22, 25; Ex. 1034 ¶¶ 82–83, 188. In support, Petitioner cites Walker's "material for implantation into a human or animal body" (Ex. 1005, 4:15–16), which may be "biological material, such as vascular tissue" (*id.* at 6:17–18), as corresponding to the claimed soft tissue graft. Pet. 21, 25 (further citing Ex. 1005, 3:3–4); Ex. 1034 ¶ 188. Petitioner contends Walker's graft is "plasticized" as recited in claim 1, because Walker discloses incubating the graft in a solution containing glycerol, which is a plasticizer, thereby "resulting in the incorporation of the plasticizer within the" graft. Pet. 21–22 (citing Ex. 1005, 5:23–24, 17:16–18); Ex. 1034 ¶¶ 85–86, 190. According to Petitioner, Walker discloses that the plasticized graft substantially retains certain physical characteristics of the unplasticized graft, such as flexibility, holding of sutures, and maximum loading. Pet. 22, 25 (citing Ex. 1005, 6:20–24, 9:31–16:31, 21:9–12); Ex. 1034 ¶¶ 88–89, 188.

Patent Owner contends Walker's biological material is not "plasticized," even though the material is incubated in a solution containing a glycerol plasticizer, because Walker indicates that water must be reintroduced into the material following the incubation step in order for the material to feel "softer and more natural." Prelim. 21–25 (citing Ex. 1005, 5, 7, 9, 10, 17–27); Ex. 1005, 26:13–35. Based on the alleged need to reintroduce water following incubation, Patent Owner contends Walker's incubation *does not* result in the glycerol *replacing* waters of hydration in Walker's biological material such that the mechanical properties of the tissue are similar to those of normal hydrated tissue, as required by the agreed-upon claim construction of a "plasticized" graft. Prelim. Resp. 21–25; *see supra* Section III.B.1 (claim construction).

Patent Owner particularly cites Walker's disclosure that "[i]ncreasing periods of *rehydration improved the appearance* of 50–70% glycerol samples," and such samples "felt softer and more natural." Ex. 1005, 26:26–28 (emphases added); Prelim. Resp. 22. Similarly: "*Humidification* had much the same effect on pericardium samples, at 50–60% glycerol these *felt more like their natural counterparts*," and samples treated in 50% glycerol with "*humidification* . . . felt *more natural than any others*." Ex. 1005, 26:31–35 (emphases added); Prelim. Resp. 23, 25. Patent Owner also cites Walker's disclosure that "the treated material may be *humidified* to *reduce the need for or extent of rehydration* prior to implantation." Ex. 1005, 5:25–27 (emphasis added); Prelim. Resp. 22. Finally, Patent Owner dismisses the test results reported at pages 11–16 of Walker, because in those tests "[a]ll samples were rehydrated, as before, prior to testing." Ex. 1005, 10:14–15; Prelim. Resp. 23.

Patent Owner's arguments are not persuasive, on the present record, for at least two reasons. First, claim 1 does not preclude rehydration of the graft after plasticization of the graft. *See supra* Section III.B.2 (claim construction). Thus, even if Walker does require rehydration of the graft after plasticization, that requirement does not distinguish Walker from the scope of claim 1.

Second, it is not clear, from the present record, that Walker requires rehydration in order for Walker's grafts to have mechanical properties similar to those of normal hydrated tissue. Walker describes its glycerol plasticization as a process in which "[t]he physical characteristics of the material . . . may be maintained," such as "flexibility, and/or structure of cells." Ex. 1005, 4:23–27, 6:20–24. Walker, further, specifically describes post-plasticization humidification as being an "optional[]" step, which "may . . . reduce the need for or extent of rehydration prior to implantation." *Id.* at 5:2–15, 5:25–27. These disclosures suggest rehydration may not be required for Walker's grafts to have mechanical properties similar to those of normal hydrated tissue. Indeed, Dr. McQuillan testifies that Walker's plasticization replaces free and loosely bound water within the internal matrix of the graft with glycerol, which maintains the graft's flexibility and cellular structure, and "the tissue need not (but may) be rehydrated prior to implantation." Ex. 1034 ¶¶ 85–86, 88–89, 188, 190.

In the face of those disclosures, and testimony from Dr. McQuillan, Patent Owner offers only attorney argument that Walker requires rehydration to have mechanical properties similar to those of normal hydrated tissue. It appears to be true, as Patent Owner contends, that many of Walker's testing results were achieved after rehydrating the tested

samples. *See* Ex. 1005, 9:32–34, 10:14–15, 18:7–11. Nonetheless, reading the Walker disclosure as a whole, on the present record, we are not persuaded by Patent Owner's attorney argument that Walker requires rehydration in order for Walker's grafts to have mechanical properties similar to those of normal hydrated tissue.

For example, 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 '420 patent, would not yield the same results, i.e., a plasticized soft tissue graft that has mechanical properties similar to 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))).

Walker's discussions of graft rehydration do not persuade us otherwise, because they do 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 '420 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 ’420 patent.

We determine the present record sufficiently supports Petitioner’s contentions in the foregoing regards to justify institution of review.

b) “a cleaned soft tissue graft”

Petitioner contends Walker discloses cleaning its graft, by storing it in ethanol. Pet. 22, 26 (citing Ex. 1005, 9:19–20, 17:3–5). Petitioner asserts a person of ordinary skill in the art “would have recognized that storing the biological tissue in ethanol would at least partially remove potentially harmful immunogenic cellular components.” *Id.* at 22; Ex. 1034 ¶¶ 84, 189. Patent Owner does not dispute these contentions at the present time. We determine the present record sufficiently supports Petitioner’s contentions in this regard to justify institution of review.

c) a “soft tissue graft having an internal matrix” with “one or more plasticizers contained in said internal matrix”

Petitioner contends Walker’s graft has an internal matrix containing the glycerol plasticizer, as a result of Walker’s incubating the graft in a glycerol solution. Pet. 22–23, 26 (citing Ex. 1005, 4:30–34, 5:23–24, 6:29–31, 7:11–13, 17:16–17, 21:9–12, 22:7–8); Ex. 1034 ¶¶ 85–86, 190. To the extent Patent Owner opposes this contention at the present time (*see* Prelim. Resp. 20–25), Patent Owner’s arguments are considered above, and are unpersuasive on the present record. We determine the present record sufficiently supports Petitioner’s contentions in this regard to justify institution of review.

d) "wherein said cleaned soft tissue graft comprise collagen fibers and the native orientation of the collagen fibers is maintained in said plasticized soft tissue graft"

Petitioner contends Walker's biological material comprises collagen fibers. Pet. 23, 26 (citing Ex. 1005, 4:23–27); Ex. 1034 ¶¶ 85, 191–192. According to Petitioner, Walker discloses that the native orientation of the collagen fibers is maintained during plasticization of the biological material with glycerol. Pet. 23–24, 27 (citing Ex. 1005, 4:16–27, 6:20–24, 10:25–32, 11:1–16:31, 21:9–15); Ex. 1034 ¶¶ 191–192. For example, Walker indicates that its glycerol plasticization maintains "flexibility" and "the structure of cells or extracellular material such as collagen, particularly the microstructure of collagen." Ex. 1005, 4:23–27, 6:20–22.

The Preliminary Response states that Walker does not teach maintaining the native orientation of collagen fibers in Walker's biological material. Prelim. Resp. 21. However, that conclusion is not accompanied by any discussion of the Walker disclosures cited in the Petition, or of Dr. McQuillan's testimony, concerning collagen structure. *Id.* at 21–25. Thus, on the present record, Patent Owner's position is not persuasive.

We determine the present record sufficiently supports Petitioner's contentions in the foregoing regards to justify institution of review.

e) Conclusion Regarding Claim 1

Based on the foregoing arguments and evidence, Petitioner has shown sufficiently that Walker discloses each and every limitation of claim 1 to demonstrate a reasonable likelihood of prevailing on the challenge to claim 1 as anticipated by Walker. We, therefore, institute a review of this challenge.

4. Claims 2, 3, 5, 8, 10, 13–18, 20, 21, 24–28, 30, and 33–35

Petitioner provides detailed arguments and evidence, including the McQuillan Declaration, in support of contending claims 2, 3, 5, 8, 10, 13–18, 20, 21, 24–28, 30, and 33–35 are unpatentable as anticipated by Walker. *See* Pet. 28–38; Ex. 1034 ¶¶ 82–89, 193–235. The Preliminary Response does not address any of these claims separately from arguments concerning claim 1, which we have already considered above. *See* Prelim. Resp. 20–25. Thus, in light of our consideration of Patent Owner's arguments above, as well as Petitioner's arguments, Petitioner has shown a reasonable likelihood of success on the challenge to these claims as anticipated by Walker. *See Guidance on the Impact of* SAS *on AIA Trial Proceedings* (Apr. 26, 2018), https://www.uspto.gov/patents-application-process/patent-trial-and-appeal-board/trials/guidance-impact-sas-aia-trial ("*SAS Guidance*") ("As required by [*SAS Institute Inc. v. Iancu*, 138 S. Ct. 1348 (2018)], the PTAB will institute as to all claims or none," and "[a]t this time, if the PTAB institutes a trial, the PTAB will institute on all challenges raised in the petition.").

D. Obviousness over Walker

Petitioner asserts claims 1–3, 5, 7–11, 13–18, 20–22, 24–31, and 33–35 of the '420 patent are unpatentable under 35 U.S.C. § 103 as having been obvious over Walker. Pet. 5, 38–42.

Given the arguments and evidence of record, Petitioner has demonstrated a reasonable likelihood of prevailing on its assertions. We begin our analysis with a brief summary of the law of obviousness, then we

address Petitioner's and Patent Owner's contentions as to obviousness over Walker.

1. Law of Obviousness

A patent claim is unpatentable under 35 U.S.C. § 103 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. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). 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 ordinary skill in the art; and (4) objective evidence of nonobviousness, if made available in the record. *See Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

2. Claims 1, 2, and 16

Petitioner provides detailed arguments and evidence, including the McQuillan Declaration, in support of contending independent claims 1, 2, and 16 are unpatentable as having been obvious over Walker. Pet. 38–40. Petitioner presents this obviousness ground based on Walker, as an alternative to the anticipation ground based on Walker, in the event it is found Walker does not disclose "one or more plasticizers [are] contained in said internal matrix" as recited in claim 1, or "the soft tissue graft is 'impregnated with said one or more plasticizers'" as recited in claims 2 and 16. *Id.* at 39. In that event, Petitioner contends a person of ordinary skill in the art "would have understood from Walker that small chemical

compounds, such as those disclosed in Walker, act by replacing free and loosely bound water within the tissue thereby incorporating themselves within the internal matrix." *Id.* at 39–40 (citing Ex. 1034 ¶¶ 85–86, 88, 236–237). Further according to Petitioner, a person of ordinary skill in the art "would have recognized that such penetration of the plasticizer in the soft tissue graft would have yielded the predictable result of a soft tissue graft where the plasticizer is contained in the internal matrix and that the plasticizers impregnate the soft tissue graft." *Id.* at 39–40 (citing Ex. 1034 ¶¶ 85–86, 88, 236–237).

Patent Owner contends Petitioner cannot establish a rationale for the proposed obviousness, because Walker teaches away from plasticization of its grafts in that "Walker teaches the need for *rehydration* prior to implantation." Prelim. Resp. 26–27 (emphasis added). Patent Owner particularly contends "Walker teaches that without rehydration, humidification, or both, its grafts do not feel like normal, hydrated tissue." *Id.* at 27 (citing Ex. 1005, 26). Patent Owner's view is that Walker's need for rehydration would have led a person of ordinary skill in the art "in a direction entirely different from the claimed plasticized soft tissue grafts of the '420 patent, which do not require any rehydration prior to use." *Id.* (citing Ex. 1002, 9:21–30).

Patent Owner's contentions are not persuasive, on the present record, for reasons articulated above. *See supra* Section III.C.3.a. That is, Patent Owner relies on unclaimed limitations, and Patent Owner does not persuasively establish that Walker requires rehydration in order for Walker's grafts to have mechanical properties similar to those of normal hydrated tissue. *See id.*

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). Based on the foregoing arguments and evidence, Petitioner has demonstrated a reasonable likelihood of prevailing on the challenge to claims 1, 2, and 16 as unpatentable for having been obvious over Walker. *See also SAS Guidance*, *supra*. Thus, we institute a review of this challenge to these claims.

3. Claims 3 and 15

There is some confusion in the Petition as to whether independent claims 3 and 15 are part of the Walker obviousness ground. *Compare* Pet. 5 & 38–39 (including claim 3), *with id.* at 39–40 (not including claim 3). Neither of these claims includes the "internal matrix" or the "impregnated" limitations addressed by the obviousness analysis at pages 38–40 of the Petition. *See* Ex. 1002, 24:50–51, 25:22–23 (claims 3 and 15 pertinently recite a "soft tissue graft comprising one or more plasticizers"). The Preliminary Response does not address either claim 3 or claim 15 separately from arguments concerning claim 1, which we have already considered above. *See* Prelim. Resp. 26–27. In light of our consideration of Patent Owner's arguments above as well as Petitioner's arguments, and in light of the *SAS Guidance*, *supra*, we institute a review of this challenge to these claims.

4. Claims 5, 7–11, 13, 14, 17, 18, 20–22, 24–31, and 33–35

There is some confusion in the Petition as to whether dependent claims 9, 11, 29, and 31 are part of the Walker obviousness ground. *Compare* Pet. 5 (not including claims), *with id.* at 38–42 (including claims). The Preliminary Response does not address any of dependent claims 5, 7–11, 13, 14, 17, 18, 20–22, 24–31, and 33–35 separately from arguments concerning their respective independent claims, which we have already considered above. *See* Prelim. Resp. 26–27. In light of our consideration of Patent Owner's arguments above as well as Petitioner's arguments, and in light of the *SAS Guidance*, *supra*, we institute a review of this challenge to these claims.

E. Anticipation by Livesey

Petitioner asserts claims 1–3, 6, 8, 9, 11–14, 16–18, 24, 25, 28, 29, 31, 32, and 34–36 of the '420 patent are unpatentable under 35 U.S.C. § 102 as anticipated by Livesey. Pet. 5, 42–59.

Given the arguments and evidence of record, Petitioner has demonstrated a reasonable likelihood of prevailing on its assertions at least as to claim 1, which is representative as to the objections raised in the Preliminary Response. We first summarize the Livesey disclosure, then we address Petitioner's and Patent Owner's contentions as to anticipation by Livesey.

1. Livesey Disclosure

Livesey discloses a method for processing and preserving collagen-based biological tissues for transplantation. Ex. 1004, Abstract. The method includes several successive treatment steps, including:

(1) applying a processing solution to remove cells; (2) applying a cryoprotectant solution; (3) freezing; (4) drying; (5) storing; and (6) rehydrating. *Id.* at Abstract, 4:19–43.

In step (1), the biological tissue is incubated in a processing solution to remove viable antigenic cells, without damaging the basement membrane complex or the structural integrity of the collagen matrix. *Id.* at 5:1–14. In this way, the biological tissue "is devoid of certain viable cells which normally express major histocompatibility complex antigenic determinants and other antigens which would be recognized as foreign by the recipient." *Id.* at 1:21–26.

In step (2), the biological tissue is incubated in a cryopreservation solution to minimize ice crystal damage during freezing step (3), and minimize structural damage during drying step (4). *Id.* at 3:35–38, 5:15–24, 11:9–23. Glyercol is disclosed as a suitable cryoprotectant. *Id.* at 11:49–60.

After freezing step (3) and drying step (4), in step (5) the biological tissue is stored for extended periods of time under ambient conditions. *Id.* at 5:45–55, 6:1–11. In step (6), the biological tissue is rehydrated prior to the tissue being transplanted into a human patient. *Id.* at 6:12–29.

2. Claim 1

Petitioner provides detailed arguments and evidence, including the McQuillan Declaration, in support of contending claim 1 is unpatentable as anticipated by Livesey. Pet. 42–49; Ex. 1034 ¶¶ 58–81, 246–251.

a) "A plasticized soft tissue graft suitable for transplantation into a human"

Petitioner contends Livesey discloses a plasticized soft tissue graft suitable for transplantation into a human. Pet. 42–43, 46; Ex. 1034 ¶¶ 58–59, 247. In support, Petitioner cites Livesey's "collagen-based biological tissues for transplantation" (Ex. 1004, 4:39–42) as corresponding to the claimed soft tissue graft. Pet. 42–43, 46 (further citing Ex. 1004, 1:17–21); Ex. 1034 ¶¶ 58–59, 247. Petitioner contends Livesey's graft is "plasticized" as recited in claim 1, because Livesey discloses incubating the biological tissue in a cryosolution "for a time long enough to obtain complete penetration of the cryoprotectants into the tissue." Pet. 43, 44, 47 (citing Ex. 1004, 12:31–39); Ex. 1034 ¶¶ 62–64, 247. According to Petitioner, Livesey's cryoprotectants are "plasticizers" as described in the '420 patent, because "[s]everal examples of plasticizer components given in the ['420 patent match the non-exclusive examples of cryoprotectant listed in Livesey." Pet. 44, 47–48 (citing Ex. 1004, 5:15–24, 11:17–23, 11:49–55, 24:10–19, and Ex. 1002, 7:52–61); Ex. 1034 ¶¶ 62–64, 247. Petitioner further asserts Livesey discloses that the plasticized biological tissue remains structurally intact with normal collagen banding, and with the collagen bundles preserved, versus the unplasticized biological tissue. Pet. 43, 46 (citing Ex. 1004, 5:1–14, 25:12–17); Ex. 1034 ¶¶ 65, 247.

Patent Owner contends Livesey's biological tissue is not "plasticized," even though the tissue is incubated in a solution containing cryoprotectants that include one or more plasticizers, because Livesey indicates the incubation is "*followed by freezing, drying, storage, and rehydration.*" Prelim Resp. 27–28 (quoting Ex. 1004, Abstract) (emphasis

added by Patent Owner). Patent Owner contends such processing is "exactly the type of [freeze-drying and rehydration] processing that [Patent Owner's] inventors sought to avoid." *Id.* at 28–29, 30 (citing Ex. 1002, 3:49–66, 5:28–34).

In particular, Patent Owner contends it is Livesey's freeze-drying step that removes water from the biological tissue, rather than the pre-freeze-drying cryoprotectant plasticizer replacing waters of hydration in the biological tissue such that the mechanical properties of the tissue are similar to those of normal hydrated tissue, as required by the agreed-upon claim construction of a "plasticized" tissue graft. Prelim. Resp. 30–32 (citing Ex. 1004, 17:26–30, 17:49–51, 18:32–35, 21:45–50); *see supra* Section III.B.1 (claim construction). According to Patent Owner, "Livesey teaches that the graft must be rehydrated prior to implantation," which "involves re-introducing the free and loosely bound waters back into the tissue." Prelim. Resp. 32. Thus, in Patent Owner's view, Livesey's description of its biological tissue as being similar to normal tissue does not demonstrate that Livesey's graft is plasticized. *Id.* Patent Owner additionally relies on the Federal Circuit's statement, during the LifeCell Litigation, that the "plasticized" tissue grafts of the '200 patent claims avoid various problems because "[t]he tissue is preserved not by freeze-drying but by replacing the tissue's water with biocompatible plasticizers." *Id.* at 6 (quoting Ex. 2002, 5 (837 F.3d at 1320)).

Patent Owner's arguments are not persuasive, on the present record, for at least two reasons. First, claim 1 does not preclude freeze-drying or rehydration of the graft after plasticization of the graft. *See, e.g.*, *supra* Section III.B.2 (claim construction). Indeed, the '420 patent discloses

processes that involve freeze-drying. *See* Ex. 1002, 10:24–40. We appreciate that the Federal Circuit has characterized the '200 patent claims, which are similar to the '420 patent claims at issue here, as requiring tissue preservation "not by freeze-drying but by replacing the tissue's water with biocompatible plasticizers." Ex. 2002, 5 (837 F.3d at 1320). However, the Federal Circuit decision did not discuss any intrinsic or extrinsic evidence that would indicate the '200 patent claims preclude *first* "plasticizing" the graft, pursuant to the construction the Federal Circuit applied there and we apply here, *and then* freeze-drying the graft. *Id.* at 4–5 (837 F.3d at 1319–20). Thus, even if Livesey does require freeze-drying and/or rehydration of the graft after plasticization, that requirement does not distinguish Livesey from the scope of claim 1.

Second, it is not clear, from the present record, that Livesey's freeze-drying step is necessarily inconsistent with Petitioner's contention that Livesey's pre-freeze-drying cryoprotectant incubation results in plasticization of the graft. As described in Livesey, the cryoprotectant incubation is designed "to minimize ice crystal damage to the structural matrix that could occur during freezing." Ex. 1004, 5:15–19, 11:17–19, 11:27–48, 14:36–38. Incubation of the graft in the cryopreservation solution results in "complete penetration" of the cryoprotectant compounds, such as glycerol, into the graft, which "exert[s] colligative action within the cells" of the graft. *Id.* at 12:31–39, 14:47–54, 15:11–30.

Further, similar to both Walker and the '420 patent itself, Livesey discloses "incubat[ing]" soft tissue samples in glycerol. *See* Ex. 1004, 5:27, 11:17–18, 11:49–51, 12:31–33. Glycerol is the same material disclosed by both Walker and the '420 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 being similar to those of natural tissue.

According to Dr. McQuillan, a person of ordinary skill would have understood from Livesey's disclosure "that glycerol or other small cryoprotectants replace free or loosely bound water in the internal matrix and preserve the structural integrity of the tissue," and "the cryopreservation method taught by Livesey was the same as the plasticization method" disclosed in the '420 patent. Ex. 1034 ¶¶ 62, 64, 247, 249. We do not agree with Patent Owner's contention that Dr. McQuillan's testimony "merely parrots the attorney arguments made in the Petition" and makes "conclusory assertions." Prelim. Resp. 14. Instead, the McQuillan Declaration summarizes the disclosures in Livesey that lead him to reach his conclusions. Ex. 1034 ¶¶ 62, 64, 247, 249. Dr. McQuillan's testimony linking Livesey's disclosures to the claimed invention stands unrebutted in the evidence presently of record.

In the face of Livesey's disclosures, and testimony from Dr. McQuillan, Patent Owner offers only attorney argument that Livesey's freeze-drying step is necessarily inconsistent with Petitioner's contention that Livesey's pre-freeze-drying cryoprotectant incubation results in

plasticization of the graft.[7] Based on the present record as a whole, we are not persuaded by Patent Owner's attorney argument on this issue. For example, the Federal Circuit considered only whether Werner (not Livesey) discloses a "plasticized" graft, and freeze-drying did not play any part in the Federal Circuit's consideration of Werner's disclosure in that regard. *See* Ex. 2002, 11–12 (837 F.3d at 1328–29).

We determine the present record sufficiently supports Petitioner's contentions in the foregoing regards to justify institution of review.

b) "a cleaned soft tissue graft"

Petitioner contends Livesey discloses cleaning its biological tissue, because the tissue is "decellularized by treatment with a 0.5% sodium dodecyl sulfate solution for 1 hour on a rotator at 40±5 RPM." Pet. 43, 47 (citing Ex. 1004, 1:21–26, 5:1–6, 23:62–67); Ex. 1034 ¶¶ 61, 248. Petitioner asserts a person of ordinary skill in the art "would have recognized that treatment under those conditions would cause cellular elements to be at least partially, if not substantially, removed, resulting in a cleaned graft." Pet. 43; Ex. 1034 ¶¶ 61, 248. Patent Owner does not dispute these contentions at the present time. We determine the present record sufficiently supports Petitioner's contentions in this regard to justify institution of review.

[7] 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. 30 n.11. Although we find that to be noteworthy, at least at this stage of the proceeding, we do not discern sufficient differences between Livesey's incubation-in-glycerol process and that of Walker and/or the '420 patent that would explain how or why the glycerol in Livesey fails to replace water molecules in tissue when tissue is incubated in glycerol.

c) a "soft tissue graft having an internal matrix" with "one or more plasticizers contained in said internal matrix"

Petitioner contends Livesey's biological tissue has an internal matrix containing the plasticizer. Pet. 44, 47–48 (citing Ex. 1004, 5:15–24, 11:17–23, 11:49–55, 12:33–37, 24:10–19); Ex. 1034 ¶¶ 62–64, 249. To the extent Patent Owner opposes this contention at the present time (*see* Prelim. Resp. 27–32), Patent Owner's arguments are considered above, and are unpersuasive on the present record. We determine the present record sufficiently supports Petitioner's contentions in this regard to justify institution of review.

d) "wherein said cleaned soft tissue graft comprise collagen fibers and the native orientation of the collagen fibers is maintained in said plasticized soft tissue graft"

Petitioner contends Livesey's biological tissue comprises collagen fibers. Pet. 44–45, 49 (citing Ex. 1004, 5:1–14, 25:12–17); Ex. 1034 ¶¶ 65, 250. According to Petitioner, Livesey discloses that the native orientation of the collagen fibers is maintained during plasticization of the biological tissue. Pet. 45, 49 (citing Ex. 1004, 5:1–14, 25:12–17); Ex. 1034 ¶¶ 65, 251.

Patent Owner contends: "*Because Livesey's graft is not plasticized* . . . it also cannot be a plasticized soft tissue graft where the native orientation of the collagen fibers is maintained." Prelim. Resp. 32 (emphasis added). This is a re-packaging of Patent Owner's argument that Livesey does not disclose a "plasticized" graft, which we have already addressed above.

Patent Owner also argues Livesey's freeze-drying process does not maintain the native orientation of collagen fibers, as required by claim 1. *See* Prelim. Resp. 10–13. Indeed, it was on this basis that the Examiner

allowed the ’420 patent during prosecution. *Id.*; Ex. 1024, 3–5 (Examiner rejecting claims as anticipated by or unpatentable over Livesey); Ex. 1025, 7–9 (Patent Owner’s argument in opposition to the rejections); Ex. 1026, 2 (Examiner’s reasons for allowance).

However, Livesey discloses that “the end product” of its tissue processing (that is, after cryopreservation, freezing, drying, storing, and rehydrating), in at least one example, was “structurally intact with normal collagen banding.” Ex. 1004, 25:14–17; *see* Pet. 45, 49 (citing Ex. 1004, 25:12–17). Livesey also indicates its pre-freeze-drying cryopreservation process “attempts to cool and store biological samples without causing structural and functional damage.” Ex. 1004, 14:59–63; *see* Pet. 65 (citing Ex. 1004, 14:59–63). Dr. McQuillan relies on those and other Livesey disclosures in support of his testimony that “the process disclosed in Livesey teaches that . . . the native orientation of the collagen fibers . . . [is] maintained.” Pet. 45, 65–66 (citing Ex. 1034 ¶¶ 65–73, 78–81, 251); Ex. 1034 ¶¶ 65, 67, 71–73. The Examiner did not expressly consider, on the record, these specific Livesey disclosures during prosecution of the ’420 patent. *See* Ex. 1024, 3 (pertinently discussing only Ex. 1004, 5:1–6, 7:36–51); Ex. 1025, 7–9 (same); Ex. 1026, 2 (same).

We determine the present record sufficiently supports Petitioner’s contentions in the foregoing regards to justify institution of review.

e) Conclusion Regarding Claim 1

Based on the foregoing arguments and evidence, Petitioner has shown sufficiently that Livesey discloses each and every limitation of claim 1 to demonstrate a reasonable likelihood of prevailing on the challenge to claim 1

as anticipated by Livesey. We, therefore, institute a review of this challenge.

3. Claims 2, 3, 6, 8, 9, 11–14, 16–18, 24, 25, 28, 29, 31, 32, and 34–36

Petitioner provides detailed arguments and evidence, including the McQuillan Declaration, in support of contending claims 2, 3, 6, 8, 9, 11–14, 16–18, 24, 25, 28, 29, 31, 32, and 34–36 are unpatentable as anticipated by Livesey. *See* Pet. 50–59; Ex. 1034 ¶¶ 58–81, 252–288. The Preliminary Response does not address any of these claims separately from arguments concerning claim 1, which we have already considered above. *See* Prelim. Resp. 27–32. Thus, in light of our consideration of Patent Owner's arguments above as well as Petitioner's arguments, and in light of the *SAS Guidance*, *supra*, we institute a review of this challenge to these claims.

F. Obviousness over Livesey

Petitioner asserts claims 1–3, 6, 8, 9, 11–14, 16–18, 24, 25, 28, 29, 31, 32, and 34–36 of the '420 patent are unpatentable under 35 U.S.C. § 103 as having been obvious over Livesey. Pet. 5, 59–61. Given the arguments and evidence of record, Petitioner has demonstrated a reasonable likelihood of prevailing on its assertions, for the following reasons.

1. Claims 1, 2, and 16

Petitioner provides detailed arguments and evidence, including the McQuillan Declaration, in support of contending independent claims 1, 2, and 16 are unpatentable as having been obvious over Livesey. Pet. 59–61. Petitioner presents this obviousness ground based on Livesey, as an alternative to the anticipation ground based on Livesey, in the event it is

found Livesey does not disclose "one or more plasticizers [are] contained in said internal matrix" as recited in claim 1, or "the soft tissue graft is 'impregnated with said one or more plasticizers'" as recited in claims 2 and 16. *Id.* at 59–60. In that event, Petitioner contends a person of ordinary skill in the art "would have understood from Livesey that small chemical compounds, such as the cryoprotectants disclosed in Livesey, act by replacing free and loosely bound water within the tissue thereby incorporating themselves within the internal matrix." *Id.* at 60 (citing Ex. 1034 ¶¶ 62–64, 289–290). Further according to Petitioner, a person of ordinary skill in the art "would have recognized that such penetration would have yielded the desirable and predictable result of a soft tissue graft having the plasticizer is contained in the internal matrix and impregnates the soft tissue graft." *Id.* at 60–61 (citing Ex. 1034 ¶¶ 62–64, 289–290).

Patent Owner contends Petitioner's case for obviousness "ignores the explicit teaching of Livesey, that it is the drying process, not the treatment with cryoprotectant that removes the 'free or unbound water' and the 'structurally bound water' from the tissue." Prelim. Resp. 33 (citing Ex. 1004, 21:47–50). Patent Owner further asserts Livesey teaches away from plasticization of its grafts because Livesey "requires treatment with a cryoprotectant solution[,] freeze-drying, and rehydration," which "is inapposite to" the claimed plasticization, which avoids damage caused by freeze-drying and avoids the need for rehydration. *Id.*

Patent Owner's contentions are not persuasive, on the present record, for reasons articulated above. *See supra* Section III.E.2. That is, Patent Owner relies on unclaimed limitations, and further Patent Owner does not

persuasively establish that Livesey's cryopreservation step does not plasticize the graft. *See id.*

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). Based on the foregoing arguments and evidence, Petitioner has demonstrated a reasonable likelihood of prevailing on the challenge to claims 1, 2, and 16 as unpatentable for having been obvious over Livesey. *See also SAS Guidance*, *supra*. Thus, we institute a review of this challenge to these claims.

2. Claim 3

There is some confusion in the Petition as to whether independent claim 3 is part of the Livesey obviousness ground. *Compare* Pet. 5 & 59–60 (including claim 3), *with id.* at 60–61 (not including claim 3). Claim 3 does not include the "internal matrix" or the "impregnated" limitations addressed by the obviousness analysis at pages 59–61 of the Petition. *See* Ex. 1002, 24:51 (claim 3 pertinently recites a "soft tissue graft comprising one or more plasticizers"). The Preliminary Response does not address claim 3 separately from arguments concerning claim 1, which we have already considered above. *See* Prelim. Resp. 33–34. In light of our consideration of Patent Owner's arguments above as well as Petitioner's arguments, and in light of the *SAS Guidance*, *supra*, we institute a review of this challenge to claim 3.

3. Claims 6, 8, 9, 11–14, 17, 18, 24, 25, 28, 29, 31, 32, and 34–36

The Preliminary Response does not address any of dependent claims 6, 8, 9, 11–14, 17, 18, 24, 25, 28, 29, 31, 32, and 34–36 separately from arguments concerning their respective independent claims, which we have already considered above. *See* Prelim. Resp. 33–34. In light of our consideration of Patent Owner's arguments above as well as Petitioner's arguments, and in light of the *SAS Guidance*, *supra*, we institute a review of this challenge to these claims.

G. Obviousness over Walker and Werner, or over Livesey and Werner

Petitioner asserts claim 4 of the '420 patent is unpatentable under 35 U.S.C. § 103 as having been obvious over Walker and Werner, or over Livesey and Werner. Pet. 5, 61–63. Given the arguments and evidence of record, Petitioner has demonstrated a reasonable likelihood of prevailing on its assertions, for the following reasons.

Claim 4 recites: "The plasticized soft tissue graft of any one of claim 1, 2, or 3, wherein said plasticized soft tissue graft is suitable for direct transplant into a human without rehydration." Ex. 1002, 24:55–57.

Petitioner provides detailed arguments and evidence, including the McQuillan Declaration, in support of contending claim 4 would have been obvious. Pet. 61–63; Ex. 1034 ¶¶ 291–297. According to Petitioner, Walker and Livesey independently anticipate parent claims 1, 2, and 3. Pet. 61, 63; Ex. 1034 ¶¶ 293, 296. Petitioner cites Werner as disclosing a tissue graft suitable for direct transplant into a human without rehydration, as recited in claim 4. Pet. 61 (citing Ex. 1006, Abstract, 2:37–41); Ex. 1034 ¶¶ 294, 297.

Petitioner contends a person of ordinary skill in the art would have recognized that adapting "Werner's teaching of the use of glycerol for use in" either Walker or Livesey would advantageously provide that "no rehydration of the tissue product is necessary before implantation." Pet. 61–62 (citing Ex. 1034 ¶¶ 174–175, 292–293, 295–296). In Petitioner's view, a person of ordinary skill in the art "would have been motivated to simplify the steps for the processing of a soft tissue graft both during preparation and at the time of implantation and would have explored avenues" that would not require rehydration before implantation. *Id.* at 62 (citing Ex. 1034 ¶¶ 176–180, 292–293, 295–296).

Patent Owner contends none of Walker, Livesey, and Werner discloses a plasticized graft. Prelim. Resp. 34–35. Patent Owner also asserts "both Walker and Livesey explicitly teach needing to rehydrate the grafts in order for them to appear more natural and ready to implant," and Werner does not cure this deficiency as to claim 4 because "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," as required by the agreed-upon claim construction of a "plasticized" tissue graft. *Id.*; *see supra* Section III.B.1 (claim construction). In particular, Patent Owner contends Werner increases the tensile strength of the transplanted tissue. Prelim. Resp. 34–35 (citing Ex. 1006, Fig., 1:50–68, 3:5–25).

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 '420 patent, it is unclear why the grafts of Walker and Livesey would require rehydration but the graft of the '420 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. 35. 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.").

Based on the foregoing arguments and evidence, Petitioner has demonstrated a reasonable likelihood of prevailing on the challenge to claim 4 as unpatentable for having been obvious over Walker and Werner, or over Livesey and Werner. *See also SAS Guidance*, *supra*. Thus, we institute a review of these challenges to claim 4.

H. 35 U.S.C. § 325(d) Discretion

Pursuant to 35 U.S.C. § 325(d), when determining whether to institute an *inter partes* review, we "*may* take into account whether, and reject the petition . . . because, *the same or substantially the same prior art or arguments* previously were presented to the Office." 35 U.S.C. § 325(d) (emphases added). In deciding whether to reject a petition on this basis, the Board typically weighs several non-exclusive factors, such as:

(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) (precedential)).

Patent Owner urges us to deny the Petition under § 325(d) on the basis that the Petition presents the same or substantially the same prior art or arguments previously presented to the Office during prosecution of the '420 patent. Prelim. Resp. 1–3, 6–15. Petitioner requested, and was granted, authorization to file a Reply to the Preliminary Response to address § 325(d). *See* Paper 14; Paper 16 ("Reply"). Patent Owner was granted authorization to file a Sur-Reply to the Reply. *See* Paper 14; Paper 19 ("Sur-Reply").

We consider the parties' § 325(d) arguments in connection with the grounds presented by the present Petition, divided into two groups. The first group is anticipation by Walker, obviousness over Walker, and obviousness

over Walker and Werner ("the Walker Grounds"). The second group is anticipation by Livesey, obviousness over Livesey, and obviousness over Livesey and Werner ("the Livesey Grounds").

1. The Walker Grounds

As to the Walker Grounds, Patent Owner asserts the Petition attacks claimed subject matter already vetted against Walker and Werner during prosecution of the '420 patent. Prelim. Resp. 6. For example, Walker and Werner were both considered by the Examiner during the '420 patent prosecution. *Id.* at 8–9. The Examiner also considered the '1888 IPR Petition, which challenged certain '971 patent claims as being unpatentable in part over Walker. *Id.* at 9, 11 (citing Ex. 2006, "at Ground 3"; Ex. 2007, 8); Sur-Reply 7–9 (citing Ex. 2006, 53–54). The Examiner further considered several items from the LifeCell Litigation concerning Werner and the '200 patent. Prelim. Resp. 2–3, 6, 7–8, 11 (citing Ex. 2001, 28–38; Ex. 2002, 6, 11–12; Ex. 2010, 22; Ex. 2011, 12). Patent Owner finally points out that the Examiner, having considered the foregoing items, did not cite Walker to reject any claims, and withdrew a rejection based on unpatentability over Livesey and Werner. *Id.* at 2–3, 8–9 (citing Ex. 2007, 2–5); Sur-Reply 1–2.

Petitioner replies that Walker was considered but not substantively discussed during prosecution of the '420 patent, and every other § 325(d) factor weighs against denying institution here. Pet. 66; Reply 7–9. For example, neither the '1888 IPR nor the LifeCell Litigation involved allegations of anticipation by Walker, or obviousness over Walker, or obviousness over Walker and Werner. Reply 3–5, 7–9. Petitioner further

asserts that any overlap between the ’1888 IPR Petition concerning the ’971 patent, and the present Petition concerning the ’420 patent, supports institution because the Board instituted review in the ’1888 IPR which led to an adverse judgment against Patent Owner. *Id.* at 4–5, 8–9 (citing Exs. 1036, 1037).

Upon consideration of the foregoing, we are not persuaded that we should exercise our discretion under § 325(d) to deny the Petition as to the Walker Grounds. 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 ’420 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. 1002, at 2–7.

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. For example, there is no evidentiary support for Patent Owner’s oft-repeated contention that the ’420 patent prosecution establishes Walker fails to disclose a “plasticized” graft. The Examiner cited Werner as disclosing plasticizer solutions containing claimed ranges of plasticizer and solvent. Ex. 1024, 4–5. The present Petition, however, cites Werner as disclosing a tissue graft suitable for direct transplant into a human without rehydration. Pet. 61. So, there is no overlap as to Werner.

As to the citation of certain LifeCell Litigation materials to the Examiner during prosecution of the ’420 patent, Walker was not even

mentioned in the Federal Circuit decision (Ex. 2002) or in the District Court decision (Ex. 2001). Therefore, the LifeCell Litigation has no relevance to the present challenges based on anticipation by or obviousness over Walker. Further, while the Federal Circuit and the District Court both discussed Werner at length, the issue presented was whether substantial evidence supported a jury finding that Werner does not disclose a "plasticized" graft, not whether Werner discloses a graft suitable for direct transplant into a human without rehydration as Petitioner contends here. Ex. 2002, 11–12 (837 F.3d at 1328–29); Ex. 2001, 28–31, 35–38. So, there is no overlap as to Werner.

Thus, most or all of the *Becton* factors weigh against exercising our discretion to deny the Petition under § 325(d) as to the Walker Grounds. 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, Paper 14, at 35–36 (PTAB Jan. 17, 2019); *see also, e.g.*, *Shenzhen Zhiyi Tech. Co. v. iRobot Corp.*, Case IPR2017-02137, Paper 9, at 9–10 (PTAB Apr. 2, 2018) (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 institution as to the Walker Grounds pursuant to § 325(d).

2. The Livesey Grounds

As to the Livesey Grounds, Patent Owner asserts the Petition attacks claimed subject matter already vetted against Livesey and Werner during

prosecution of the '420 patent. Prelim. Resp. 6. For example, Livesey and Werner were both considered by the Examiner during the '420 patent prosecution. *Id.* at 8–9. The Examiner also considered the '1888 IPR Petition, which challenged certain '971 patent claims as being unpatentable over Livesey. Prelim. Resp. 11; Sur-Reply 8–9, 10. The Examiner further considered several items from the LifeCell Litigation concerning Livesey, Werner, and the '200 patent. Prelim. Resp. 2–3, 6, 7–8, 11. Patent Owner finally points out that the Examiner, having considered the foregoing items, withdrew claim rejections based on anticipation by Livesey and on unpatentability over Livesey and Werner. *Id.* at 2–3, 8, 11.

Because we have determined that denial under § 325(d) is not warranted as to at least the Walker 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*, 138 S. Ct. at 1359–60, and the *SAS Guidance*, *supra*), even were we to find Patent Owner's § 325(d) arguments persuasive as to the Livesey Grounds, we would not deny institution of the entire Petition on that basis.[8] Thus, we

[8] Patent Owner cites *Chevron Oronite Co. LLC v. Infieum USA LP*, Case IPR2018-00923 (PTAB Nov. 7, 2018) (Paper 9) (informative), as "denying institution on all claims when the petitioner's arguments and proofs were deficient with respect to a subset of claims." Prelim. Resp. 7. In *Chevron*, Paper 9, at 11, the Board concluded the petitioner had "demonstrate[d], at most, a reasonable likelihood of prevailing with respect to two dependent claims out of a total of twenty challenged claims." By contrast, here the Walker Grounds encompass thirty claims, and the Livesey Grounds encompass twenty-three claims. Thus, the Walker Grounds are not the tail wagging the dog, as was the case in *Chevron*.

decline to provide a detailed analysis of § 325(d) as to the Livesey Grounds. We briefly observe that *Becton* factors (a)–(d) provide at least some support for Patent Owner's position, but that factors (e) and (f) provide significant support for Petitioner's position that institution should not be denied under § 325(d). *See* Pet. 63–66.

As a final observation, we note that Patent Owner places significant emphasis on the LifeCell Litigation, in which a jury determined that LifeCell failed to establish the invalidity of asserted '971 patent claims by clear and convincing evidence, and the Federal Circuit affirmed. *See* Exs. 2001 & 2002; *see also* Prelim. Resp. 1. Although we have considered the LifeCell Litigation in deciding whether to institute *inter partes* review of the '420 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." Sur-Reply 4; *see also id.* at 6. Thus, to the extent 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 all of the foregoing reasons, we decline to exercise our discretion under 35 U.S.C. § 325(d) to deny institution of the present Petition.

IV. CONCLUSION

For the above reasons, we determine the information presented in the record establishes there is a reasonable likelihood that Petitioner would

prevail with respect to at least one claim of the ’420 patent challenged in the Petition. We further decline to exercise our discretion to deny institution under § 325(d). Accordingly, we institute an *inter partes* review. 35 U.S.C. § 314(a). At this preliminary stage, the Board has not made a final determination with respect to the patentability of the challenged claims or any underlying factual or legal issue. The Board’s final determination will be based on the record as developed during the *inter partes* review.

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 314(a), *inter partes* review of claims 1–18, 20–22, and 24–36 of the ’420 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, *inter partes* review of claims 1–18, 20–22, and 24–36 of the ’420 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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