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Paper 74
Date: August 4, 2020

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

RTI SURGICAL, INC.,
Petitioner,

v.

LIFENET HEALTH,
Patent Owner.

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*.

JUDGMENT
Final Written Decision
Determining Some Challenged Claims Unpatentable
Denying Petitioner's Motion to Exclude
Dismissing Patent Owner's Motion to Exclude
35 U.S.C. § 318(a)

I. INTRODUCTION

RTI Surgical, Inc. ("Petitioner") 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") filed a Preliminary Response (Paper 9, "Prelim. Resp."). We instituted a trial to determine whether claims 1–18, 20–22, and 24–36 are unpatentable, on all challenges presented in the Petition. Paper 20 ("Institution Decision" or "Inst. Dec."), 2, 5, 43.

Patent Owner then filed a Patent Owner Response (Papers 32 & 34, "PO Resp.") to the Petition. Petitioner filed a Reply (Paper 43, "Pet. Reply") to the Patent Owner Response. Patent Owner filed a Sur-reply (Papers 55 & 56, "Sur-reply") to Petitioner's Reply. An oral hearing was held, for which the transcript was entered into the record (Paper 73, "Tr.").

Petitioner filed a Motion to Exclude Evidence (Paper 63). Patent Owner filed an Opposition (Paper 65) to Petitioner's Motion. Petitioner filed a Reply (Paper 69) to Patent Owner's Opposition. For reasons provided below, we deny Petitioner's Motion.

Patent Owner filed a Motion to Exclude Evidence (Paper 62). Petitioner filed an Opposition (Paper 66) to Patent Owner's Motion. Patent Owner filed a Reply (Paper 68) to Petitioner's Opposition. For reasons provided below, we dismiss Patent Owner's Motion as moot.

We have jurisdiction under 35 U.S.C. § 6(b)(4) and § 318(a). Petitioner bears the burden of proving unpatentability of the challenged claims, and the burden of persuasion never shifts to Patent Owner. *Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir.

2015). To prevail, Petitioner must prove unpatentability by a preponderance of the evidence. *See* 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d). This Decision is a final written decision under 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73 as to the patentability of claims 1–18, 20–22, and 24–36 of the '420 patent.

For the reasons discussed below, we determine Petitioner has shown by a preponderance of the evidence that claims 1–3, 5–18, 20–22, and 24–36 of the '420 patent are unpatentable, but Petitioner has not shown by a preponderance of the evidence that claim 4 is unpatentable.

Several materials in the record have been filed in two versions: a redacted version that is publicly accessible, and a non-redacted version that is viewable only by the parties and the Board. In this Decision, we cite to the non-redacted versions. The public versions are identical, except for the blacked out redactions.

As set forth in our Order concluding this Decision, we are initially issuing this Decision under seal, and granting the parties an opportunity to file a motion seeking to keep this Decision or portions thereof under seal. Any such motion must be filed within 10 days of the entry of the Decision.

II. BACKGROUND

A. Real Parties-in-Interest

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

B. Related Matters

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.) (hereafter "LifeCell Litigation"). Pet. 9 n.2, 10 n.3, 13–16; Paper 4, 1. In

that case, Patent Owner accused LifeCell of infringing U.S. Patent No. 6,569,200 B2 ("the '200 patent"), which shares a common parent application with the '420 patent. *See* Ex. 2001. After a two-week trial, a jury found the accused products infringed the '200 patent and the defendant failed to establish the invalidity of the asserted claims, and awarded approximately $35 million in damages. *See id*. at 5–6. The district court denied the defendant's post-trial motions, and the Federal Circuit affirmed. *See id*. at 1; *LifeNet Health v. LifeCell Corp.*, 837 F.3d 1316, 1319 (Fed. Cir. 2016) (Ex. 2002, 4). Though two of the Petition's three cited references were asserted by LifeCell for its invalidity case in the LifeCell Litigation, the grounds presented in the present Petition were not considered during the trial or appeal of the LifeCell Litigation. *See* Inst. Dec. 37–42; Ex. 2001, 28–31, 35–38; *LifeNet v. LifeCell*, 837 F.3d at 1328–29 (Ex. 2002, 11–12).

The second litigation 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 until early September 2020.

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 the '200 patent. The second is IPR2019-00573, challenging U.S. Patent No. 9,585,986 B2, which is a continuation of the '420 patent.

C. 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 tissue without increasing the brittleness of the plasticized graft, and results in the plasticized 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 tissue. *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).

D. 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.

E. Asserted Grounds of Unpatentability

Petitioner presents the following six grounds challenging the '420 patent claims in this proceeding. *See* Pet. 5.

Claim(s) Challenged	**35 U.S.C. §[1]**	**Reference(s)**
1–3, 5, 8, 10, 13–18, 20, 21, 24–28, 30, 33–35	102(b)	Walker[2]
1–3, 5, 7–11, 13–18, 20–22, 24–31, 33–35	103(a)	Walker
1–3, 6, 8, 9, 11–14, 16–18, 24, 25, 28, 29, 31, 32, 34–36	102(b)	Livesey[3]

[1] The Leahy-Smith America Invents Act ("AIA") included revisions to 35 U.S.C. §§ 102, 103 that became effective on March 16, 2013. Because the '420 patent issued from an application filed before March 16, 2013, we apply the pre-AIA versions of the statutory bases for unpatentability.

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

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

Claim(s) Challenged	35 U.S.C. §[1]	Reference(s)
1–3, 6, 8, 9, 11–14, 16–18, 24, 25, 28, 29, 31, 32, 34–36	103(a)	Livesey
4	103(a)	Walker or Livesey, and Werner[4]

F. Testimonial Evidence

The parties have provided witness testimony. The table below lists the witnesses, their roles in this proceeding, and the exhibits in which their testimony is presented:

Witness	Role	Exhibits
David McQuillan, Ph.D.	Petitioner's technical expert[5]	Ex. 1034 (declaration of Jan. 28, 2019); Ex. 2015 (transcript of deposition of Oct. 8, 2019); Ex. 1045 (declaration of Feb. 11, 2020); Ex. 1059 (declaration of Mar. 10, 2020).
David L. Kaplan, Ph.D.	Patent Owner's technical expert[6]	Ex. 1018 (declaration of June 24, 2014);

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

[5] *See* Ex. 1034 ¶ 1 ("I have been retained as an expert witness to offer technical opinions on behalf of RTI Surgical, Inc. . . . .").

[6] *See* Ex. 2016 ¶ 1 ("I have been retained as an expert witness on behalf of Patent Owner . . . ."); *id.* ¶ 11 ("Based upon my education, experience, and qualifications, I consider myself to be an expert in the fields of biomaterials, biopolymers, tissue engineering, and regenerative medicine, including the

Witness	Role	Exhibits
		Exs. 2016 & 2136 (declaration of Nov. 11, 2019); Ex. 1057 (declaration of Dec. 4, 2019); Ex. 1046 (transcript of deposition of Jan. 10, 2020).
Arun Sharma	Patent Owner's commercial success expert[7]	Exs. 2125 & 2137 (declaration of Nov. 12, 2019); Ex. 1044 (declaration of Dec. 6, 2019); Ex. 1056 (transcript of deposition of Jan. 24, 2020).

III. MOTIONS TO EXCLUDE

A. Petitioner's Motion to Exclude

Petitioner moves to exclude several documents from the LifeCell Litigation, as well as the testimony of Patent Owner's experts based on those documents. *See* Paper 63. Specifically, Petitioner moves to exclude Exhibit 2049, which is a lengthy excerpt of the trial transcript from the LifeCell Litigation, and Exhibits 2053, 2056–2063, 2065, and 2069, which are documents from the LifeCell Litigation relating to product sales information or market analysis. *Id.* at 3–6. Petitioner argues that both the transcript and documents are inadmissible hearsay under Federal Rule of Evidence 802, and that the documents are inadmissible under Federal Rule

processing and use of bone and soft-tissue for transplantation into humans.").

[7] *See* Ex. 2125 ¶¶ 4–5 ("I have been retained by counsel for LifeNet to evaluate whether soft tissue grafts with [Ready to Use] features made possible by the challenged claims have been commercially successful.").

of Evidence 901 for lack of authentication. *Id.* at 3–8. Petitioner further argues that Exhibits 2016 and 2125, setting forth Patent Owner's experts' testimony relying on the transcript and documents from the LifeCell Litigation, "simply add[] another layer of inadmissible hearsay" and that Patent Owner has not shown that experts would reasonably rely on documents like these in forming opinions. *Id.* at 9–11; Paper 69, 4–5.

Patent Owner opposes the motion, arguing that experts in Dr. Kaplan's and Mr. Sharma's fields would reasonably rely on sworn testimony and admitted trial exhibits relating to product information, sales and revenue data, and internal business planning documents in forming opinions regarding the secondary considerations topics on which they testify. *See* Paper 65, 4–6. Patent Owner further argues that Federal Rule of Evidence 703 allows admission of facts or data underlying an expert's opinion even if they would otherwise be inadmissible, and that the transcript and documents from the LifeCell Litigation should be admitted so the Board can fully consider the opinions of Dr. Kaplan and Mr. Sharma. *Id.* at 7–8.

Federal Rule of Evidence 703 provides that an expert may base an opinion on facts or data that is not admissible "[i]f experts in the particular field would reasonably rely on those kinds of facts or data in forming an opinion on the subject." Fed. R. Evid. 703. We are persuaded by Patent Owner's argument that experts in Dr. Kaplan's and Mr. Sharma's fields would reasonably rely on the kinds of facts and data in the LifeCell Litigation transcript and documents in forming opinions on the subjects about which they testify. *See* Paper 65, 6. Further, Rule 703 provides that "if the facts or data would otherwise be inadmissible, the proponent of the opinion may disclose them to the jury only if their probative value in helping

the jury evaluate the opinion substantially outweighs their prejudicial effect." Fed. R. Evid. 703. The Board has repeatedly applied Rule 703 to deny motions to exclude materials underlying expert opinions, reasoning that the benefit to the Board of assessing the underlying support for the expert testimony outweighs any prejudicial effect. *See, e.g.*, *Argentum Pharms. LLC v. Research Corp. Techs., Inc.*, IPR2016-00204, Paper 85, 48 (PTAB Mar. 22, 2017) ("[T]he probative value of reviewing the documents substantially assisted our evaluation of Patent Owner's contentions regarding skepticism."); *LG Chem, Ltd. v. Celgard, LLC*, IPR2014-00692, Paper 76, 44–45 (PTAB Oct. 5, 2015) ("[W]e find that these exhibits have substantial probative value in helping us to evaluate Dr. White's opinion.").[8] We follow that same course here, based on our determination that the value of reviewing the transcript and documents from the LifeCell Litigation in assessing the weight to be given to Patent Owner's experts' testimony substantially outweighs any prejudicial effect.

For the foregoing reasons, we deny Petitioner's motion to exclude.

[8] One panel determined Rule 703's restriction on disclosure of otherwise inadmissible facts or data to the factfinder is inapplicable in Board proceedings. *See Nestle Healthcare Nutrition, Inc. v. Steuben Foods, Inc.*, IPR2015-00249, Paper 76, 13–14 (PTAB June 2, 2016) ("Our determination is not made by a jury, so this caveat does not apply. *See* 37 C.F.R. § 42.62(b) (portions of the Federal Rules of Evidence relating to juries do not apply)."). Because we find that the test is met here — i.e., the probative value of the underlying exhibits outweighs their prejudicial effect — it is unnecessary for us to determine whether Rule 703's restriction on disclosure applies in Board proceedings.

B. Patent Owner's Motion to Exclude

Patent Owner moves to exclude Exhibit 1048 as lacking authentication and because a certified translation of the entire document has not been provided. *See* Paper 62, 1. Because we do not rely on Exhibit 1048 in this Decision, we dismiss as moot Patent Owner's motion to exclude.

IV. ANALYSIS

A. Level of Ordinary Skill in the Art

At the institution stage of this proceeding, the parties provided very similar proposals for the level of ordinary skill in the art. *See* Inst. Dec. 5–6. Consistent with those proposals, we preliminarily determined the level of ordinary skill in the art to be (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. *Id.*

During the instituted trial, neither party further addressed the level of ordinary skill in the art. Based on the entire evidence presented in the proceeding, we maintain the foregoing description of the level of ordinary skill, which 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)." 37 C.F.R. § 42.100(b) (2019).[9] 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) (en banc).

1. "plasticized"

Each of the independent claims is directed to a "plasticized soft tissue graft" comprising "one or more plasticizers." Ex. 1002, 24:35–38 (claim 1), 24:42–45 (claim 2), 24:50–51 (claim 3), 25:21–23 (claim 15), 25:28–31 (claim 16).

Petitioner contends a "plasticized" graft should be construed as a graft that is:

> 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. 14–15 (emphasis omitted). Patent Owner agrees. PO Resp. 13–14.

We adopt the agreed-upon construction of a "plasticized" graft, as set forth above. This construction is identical to the construction of the same

[9] The Petition in this case was filed on January 29, 2019. *See* Paper 3, 1. Moreover, the *Phillips* standard applies in this proceeding for the additional reason that the '420 patent is expired. *See* Prelim. Resp. 16 n.5.

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 LifeNet v. LifeCell*, 837 F.3d at 1327–28 (Ex. 2002, 10–11).

2. "cleaned"

Each of the independent claims requires a "cleaned" graft. Ex. 1002, 24:37 (claim 1), 24:43 (claim 2), 24:50–51 (claim 3), 25:22 (claim 15), 25:30 (claim 16).

a) Background

The term "cleaned" was construed by the district court in the LifeCell Litigation. Specifically, the district court adopted Patent Owner's proposed construction of "a process during which cellular elements and small molecular weight solutes are removed." Ex. 1019, 9–10, 14. The Federal Circuit did not review the district court's construction of that term in the appeal of the LifeCell Litigation. *See* Ex. 2002; *see also* Tr. 69:12–17 (Patent Owner's counsel stating Federal Circuit did not address the construction of "cleaned"). The district court's construction sets the stage for the claim construction dispute in this proceeding, as the parties' arguments seek to clarify or build upon that construction.

b) Summary of the Parties' Contentions

Patent Owner argues "'cleaned' does not require all of the cellular elements and small molecular weight solutes to have been removed . . . but with a caveat." PO Resp. 14–15. According to Patent Owner, an ordinarily

skilled artisan "would understand that a 'cleaned' soft tissue graft must have enough cellular elements and small molecular weight solutes removed to avoid transmission of disease and rejection of the tissue by the patient's body." *Id.* (citing Ex. 2016 ¶ 63). Patent Owner asserts "[t]he processes to create a 'cleaned' graft in the '420 patent are conventional, known in the art, and described in several cited patents and publications." *Id.* at 16 (citing Ex. 2016 ¶¶ 64–72; Ex. 1002, 6:40–43, 9:34–10:13, 10:24–25, 11:18–32, 22:60–65; 23:47–62). Those processes, Patent Owner contends, remove enough cellular elements to reduce the potential for transmission of infective agents. *Id.*

Petitioner responds that Patent Owner's construction limits "cleaned" to fully cleaned, in contradiction of the Specification's teaching that cleaned tissue can still be further cleaned. Pet. Reply 3 (citing Ex. 1002, 10:5–13, 11:2–5; Ex. 1045 ¶¶ 21, 26). Petitioner further argues Patent Owner's construction conflates cleaning, which is intended to reduce the likelihood of rejection by the patient, with sterilization, which prevents disease transmission, and which is separately recited in dependent claim 8 of the '420 patent. *Id.* at 3–4 (citing Ex. 1045 ¶¶ 27, 62). Petitioner's proposed construction is the one adopted by the district court in the LifeCell Litigation. Pet. 13; Tr. 7:8–11.

In its Sur-Reply, Patent Owner argues that Petitioner's expert, Dr. McQuillan, agrees that an ordinarily skilled artisan would understand a cleaned graft to be one that has been subjected to a process to prevent adverse immunogenic responses. Sur-reply 3 (citing Ex. 1034 ¶¶ 22–23). Patent Owner also disputes the distinction Petitioner draws between cleaning and sterilization, arguing that this position "contradicts the '420 patent

specification and the disclosures incorporated [therein] that disclose the use of conventional methods to remove cellular elements from tissue in order to prevent disease transmission." *Id.* at 3–4 (citing Ex. 2016 ¶¶ 65–70; Ex. 1002, 9:36–64, 10:47–52; Ex. 2044, 3:21–37).

c) Analysis

In considering the parties' dispute over this term's meaning, we look first to the language of the claims. *See Phillips*, 415 F.3d at 1314 ("Quite apart from the written description and the prosecution history, the claims themselves provide substantial guidance as to the meaning of particular claim terms.").

The language of the '420 patent's independent claims themselves, which simply recite that the soft tissue graft is "cleaned," is broad and generic. Dependent claim 13 adds the limitation that "said plasticized soft tissue graft is essentially free from cellular elements." Ex. 1002, 25:15–17; *see also Phillips*, 415 F.3d at 1314 ("Differences among claims can also be a useful guide in understanding the meaning of particular claim terms."). In assessing this claim language, we also consider how it compares to the language of claims in related patents. *See Trustees of Columbia University v. Symantec Corp.*, 811 F.3d 1359, 1369 (Fed. Cir. 2016) ("We have previously held that where multiple patents 'derive from the same parent application and share many common terms, we must interpret the claims consistently across all asserted patents.'"). In the related '986 patent, some claims use the "cleaned" term but claim 12 recites "substantially removing cellular elements from soft tissue." Ex. 1003, 25:35–36. The language of these claims shows that when the patentee wished to be specific about the

amount of cellular material that must be removed, it knew how to do so. Here, for the independent claims in the '420 patent, the patentee instead chose the broad term "cleaned."

The genericness of the term "cleaned" in the independent claims of the '420 patent, in comparison to the specificity of the language used in dependent claim 13 and the claims of related patents, tends to support an interpretation that the term does not require any particular amount of cellular material to be removed. *See Intellectual Ventures I LLC v. T-Mobile USA, Inc.*, 902 F.3d 1372, 1378 (Fed. Cir. 2018) ("Since '[i]t is the claims that define the metes and bounds of the patentee's invention,' '[t]he patentee is free to choose a broad term and expect to obtain the full scope of its plain and ordinary meaning unless the patentee explicitly . . . disavows its full scope.") (quoting *Thorner v. Sony Comput. Entm't Am. LLC*, 669 F.3d 1362, 1367 (Fed. Cir. 2012)).

Turning to the Specification, the '420 patent is generic and open-ended regarding cleaning, relying on background knowledge and citation to other prior art references for its disclosure of cleaning processes. For example, the '420 patent defines "cleaned bone graft" as "a bone graft that has been processed using means know[n] in the art, to remove bone marrow elements." Ex. 1002, 6:40–43; *see also id.* at 9:36–38 ("Bone processing and cleaning procedures suitable for use with the present invention include known processes . . . ."). Likewise, the '420 patent explains that "[b]one and soft tissue grafts can be cleaned and processed using conventional methods." *Id.* at 10:24–25; *see also id.* at 11:19–21 ("For example, tissue can be processed and cleaned according to any method including known methods . . . ."). In the '420 patent's two examples relating

to soft tissue grafts, cleaning is achieved by placing a prepared graft "in a basin containing a 1:100 dilution of Allowash™ Solution or other surfactant(s) for at least 15 minutes." *Id.* at 23:2–5, 23:55–57. Thus, we agree with Patent Owner's frank acknowledgement that the cleaning methods described in the '420 patent are "conventional." PO Resp. 16; Sur-reply 4.

The parties and their experts disagree on the degree of cellular element removal that is achieved by the cleaning techniques described in the '420 patent Specification. *See, e.g.*, PO Resp. 15 n.3 (citing Ex. 1034 ¶ 35) (disputing Dr. McQuillan's statement that the cleaning methods described in the '420 patent would provide only some cleaning of the tissue); Ex. 2016 ¶ 71 n.5 ("I disagree with Dr. McQuillan's characterization that the cleaning methods, including the Allowash™ treatment, described in the subject patents would provide only 'some cleaning of the tissue.' Allowash™ is known to be effective in removing cellular elements and small molecular weight solvents to render the tissue safe for implantation.") (citations omitted); Ex. 1045 ¶ 25 ("Dr. Kaplan ignores that the Allowash technique that is marketed as readying a soft tissue graft for implantation is much more involved than the bath/rinse disclosed at Examples 9 and 10 of the LifeNet patents."). We need not resolve this dispute because the Specification only describes these techniques as potential methods of cleaning and does not specify any cellular removal result that must be obtained before a tissue is adequately cleaned. In other words, regardless of the level of cellular material that the cleaning processes referenced in the Specification were capable of removing under certain protocols, the Specification never indicates that those results are critical to achieve a "cleaned" graft. Instead,

the Specification simply lists multiple known ways that a graft can be cleaned.

For similar reasons, we need not resolve the parties' dispute over the purported distinction between cleaning and sterilization. Even accepting Patent Owner's argument that an important purpose of cleaning a tissue graft is to prevent disease transmission, the Specification does not purport to set any particular standard of efficacy for a "cleaned" graft toward that goal. Patent Owner's proposed construction requires that a soft tissue graft does not qualify as "cleaned" unless disease transmission and rejection of the tissue by the patient's body have been prevented. PO Resp. 15. But Patent Owner does not point us to, and we do not find, any portion of the Specification supporting that these criteria must be met for a "cleaned" graft.

We recognize the Specification includes a description that "[a]fter the sterile water wash[,] the tissue (for example bone tissue) is cleaned of virtually all cellular elements (for example, bone marrow) present in the tissue and the cleaned tissue can be further processed . . . ." Ex. 1002, 11:22–25. However, that description does not purport to define "cleaned" but simply describes one "example." *Id.* at 11:19. Indeed, Patent Owner has expressly stated that "'cleaned' does not require all of the cellular elements and small molecular weight solutes to have been removed . . . ."
PO Resp. 14–15.

We have also considered the extrinsic evidence the parties have presented. *See Phillips*, 415 F.3d at 1317 ("[W]hile extrinsic evidence can shed useful light on the relevant art, we have explained that it is less significant than the intrinsic record in determining the legally operative meaning of claim language.") (internal citations and quotations omitted).

The testimony of Dr. Kaplan, Patent Owner's expert, indicates that an advantage or goal of the known cleaning techniques is to "reduc[e] the potential for transmission of disease" or remove elements "that can potentially transmit disease or cause an immune reaction in the recipient." Ex. 2016 ¶¶ 68, 70. Patent Owner also points to Dr. McQuillan's testimony that prior art cleaning techniques "reduced the risk for adverse immunogenic responses" and "reduce[d] the risk of an adverse reaction in the transplant recipient." Ex. 1034 ¶¶ 23–24. Patent Owner's reliance on these aspects of Dr. Kaplan's and Dr. McQuillan's testimony substitutes the goal of reducing the potential for adverse outcomes with a guarantee of avoiding them.

Indeed, it is unclear what quantity or percentage of cellular elements and small molecular weight solutes would need to be removed to avoid transmission of disease and rejection of the tissue by the patient's body, and neither Patent Owner nor Dr. Kaplan attempts to draw that line. *See* PO Resp. 15 ("No matter the precise number of cellular elements and small molecular weight solutes removed, a POSA would understand that a 'cleaned' soft tissue graft must have enough . . . removed to avoid transmission of disease and rejection of the tissue by the patient's body."). Consequently, the extrinsic evidence of record does not persuade us that ordinarily skilled artisans would consider a tissue to be "cleaned" only if the potential for adverse results has been eliminated.

Based on the foregoing, we adopt the district court's construction of "cleaned" to mean "a process during which cellular elements and small molecular weight solutes are removed." We further determine that this term does not specify any particular amount of cellular elements and small molecular weight solutes that must be removed.

3. "the native orientation of the collagen fibers is maintained"

Each of the independent claims requires that "the native orientation of the collagen fibers is maintained" in the plasticized graft. Ex. 1002, 24:39–41 (claim 1), 24:46–49 (claim 2), 24:52–54 (claim 3), 25:23–26 (claim 15), 25:31–36 (claim 16).

In the Petition, Petitioner contends this limitation requires that "the orientation of the collagen fibers is not altered" by plasticization of the graft. Pet. 15–16 (citing Ex. 1002, 7:34–39; Ex. 1034 ¶¶ 56–57).

Patent Owner responds that this limitation "should be construed to mean 'the orientation of the collagen fibers is not altered such that the collagen fibers remain in their native orientation.'" PO Resp. 17. Patent Owner opposes the construction set forth in the Petition as "improperly read[ing] out the requirement that the 'native orientation' — not just any orientation — 'is maintained.'" *Id.*; Ex. 2016 ¶ 76.

Petitioner replies that this limitation "simply can be construed as 'the native orientation of the collagen fibers is not altered.'" Pet. Reply 5 n.1 (emphasis by Petitioner). Petitioner argues this would overcome Patent Owner's criticism of Petitioner's original construction, and avoids Patent Owner's lengthy, two-part construction. *Id.*

Thus, the parties agree the native orientation of the collagen fibers is "maintained" when the native orientation is "not altered" by the plasticization process. We concur. *See, e.g.*, Ex. 1002, 7:34–39. We therefore adopt this construction.

4. "impregnated" or "impregnating"

Independent claim 2 recites that the "soft tissue graft is *impregnated* with" a plasticizer, and independent claim 16 recites "*impregnating*" a graft with a plasticizer. Ex. 1002, 24:44–45 (claim 2), 25:30–31 (claim 16) (emphases added).

Patent Owner contends the terms "impregnated" and "impregnating" "should be construed . . . to mean 'filling or filled.'" PO Resp. 18; Ex. 2016 ¶ 75. This construction is identical to the construction of the same terms in the '200 patent adopted by the district court in the LifeCell Litigation. *See* Ex. 1019, 11–13, 14; Ex. 2001, 3. The meaning of "impregnated" and "impregnated" was not addressed by the Federal Circuit decision on appeal in the LifeCell Litigation. *See generally* Ex. 2002.

Petitioner replies that these terms do not require *completely* filling, as may be suggested by Patent Owner's arguments applying the claims to the prior art. Pet. Reply 4–5. Patent Owner confirms its agreement that impregnating does not require completely filling. Sur-reply 4.

We determine the '420 patent defines "impregnating" to mean "any processing conditions which result in filling the matrix of a bone graft with a plasticizer composition." Ex. 1002, 6:64–67. Based on the express definition in the patent and the parties' agreement, we construe "impregnated" and "impregnating" to mean "filled."

5. Other Claim Terms

Petitioner proposes constructions for various other claim terms, including "internal matrix" (claim 1), "plasticizer" (claims 1, 2, 3, 15, and 16), "soft tissue graft" (claims 1, 2, 3, 15, and 16), and "mechanical

properties approximating mechanical properties of natural soft tissue" (claim 14). Pet. 12–13, 15. Patent Owner also addresses some of these terms. PO Resp. 17–18. We conclude no explicit claim construction of these terms or any further term is needed to resolve the patentability issues presented in this proceeding. *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. We determine Petitioner has demonstrated, by a preponderance of the evidence, that each of these claims except for claim 13 is anticipated by Walker. 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 claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros., Inc. v. Union Oil Co.*, 814 F.2d 628, 631 (Fed. Cir. 1987). Moreover, "[b]ecause the hallmark of anticipation is prior invention, the prior art reference — in order to anticipate under 35 U.S.C. § 102 — must not only disclose all elements of the claim within the four

corners of the document, but must also disclose those elements 'arranged as in the claim.'" *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008). Whether a reference anticipates is assessed from the perspective of an ordinarily skilled artisan. *See Dayco Prods., Inc. v. Total Containment, Inc.*, 329 F.3d 1358, 1368 (Fed. Cir. 2003) ("[T]he dispositive question regarding anticipation [i]s whether one skilled in the art would reasonably understand or infer from the [prior art reference's] teaching that every claim element was disclosed in that single reference.").

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, Abstract, 3:3–8.[10] According to Walker, biologic vascular grafts advantageously remain open in the recipient's body, but disadvantageously lack stability in the longer term and can illicit immune responses in the recipient's body. *Id.* at 3:8–12. "Current approaches to countering instability and antigenicity *in situ* include treating the graft with a cross-linking agent . . . or inducing cross-linking in the graft by other means such as dye-mediated photo-oxidation." *Id.* at 3:12–16. "Dye-mediated photo-oxidation is preferred," because this leads to a cross-linked graft that "has physical characteristics which are closer to the natural tissue," as well as "low immunogenicity." *Id.* at 3:16–19.

However, unlike cross-linking with a cross-linking agent, cross-linking with dye-mediated photo-oxidation does not sterilize the graft,

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

so an additional sterilization step is necessary. *Id.* at 3:24–4:2. This sterilization is preferably achieved by treating the graft with ethylene oxide (EtO), but this 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 plasticization also "can suitably replace at least some of the water contained in the" graft. *Id.* at 6:20–27.

3. Claim 1

Petitioner provides arguments and evidence, including the testimony of Dr. McQuillan, in support of contending claim 1 is unpatentable as anticipated by Walker. Pet. 21–27; Ex. 1034 ¶¶ 82–89, 187–192. Patent Owner provides arguments and evidence, including the testimony of Dr. Kaplan, in opposition. PO Resp. 18–29; Ex. 2016 ¶¶ 77–84, 182–196.

a) Undisputed Limitations

The only disputed aspects of Petitioner's anticipation challenge to claim 1 based on Walker are the "plasticized" and "cleaned" limitations. "The Board is 'not required to address undisputed matters' or arguments about limitations with which it was never presented." *LG Elecs., Inc. v. Conversant Wireless Licensing S.A.R.L.*, 759 F. App'x 917, 925 (Fed. Cir.

2019) (quoting *In re Nuvasive, Inc.*, 841 F.3d 966, 974 (Fed. Cir. 2016)).[11] Nevertheless, to provide a complete record, we briefly summarize our findings regarding the uncontested limitations.

The preamble recites "[a] plasticized soft tissue graft suitable for transplantation into a human." The "plasticized" term, which is also recited in the body of claim 1, is disputed and is separately discussed below. *See infra* § IV.C.3(b). Patent Owner presents no argument to show that the remaining aspects of the preamble are limiting, stating that we need not determine whether the preamble is limiting because it does not resolve the disputed issues. *See* PO Resp. 14. Although Petitioner argues that the preamble is presumptively non-limiting and that Patent Owner has failed to show otherwise, Pet. Reply 13–14, Petitioner's arguments account for the possibility that the preamble is limiting. *See* Pet. 21–22; Pet. Reply 14. We are persuaded by Petitioner's argument that, to the extent the entire preamble is limiting, Walker discloses a graft suitable for transplantation into a human. *See* Pet. 21–22; Ex. 1034 ¶¶ 97, 188. Walker describes "a method of sterili[z]ing material for implantation into a human or animal body." Ex. 1005, 4:14–16; *see also id.* at Abstract; *id.* at 6:17–18; *id.* at 21:17–31 (describing an example using tissue samples of bovine pericardium).

Claim 1 further recites "a cleaned soft tissue graft having an internal matrix." The "cleaned" aspect of this limitation is disputed and is discussed below. *See infra* § IV.C.3(c). As to a soft tissue graft having an internal

[11] *See also Papst Licensing GmbH & Co. v. Samsung Elecs. Am.*, 924 F.3d 1243, 1250 (Fed. Cir. 2019) (holding that patentee forfeited argument for patentability because it did not present it to the Board); *Bradium Techs. LLC v. Iancu*, 923 F.3d 1032, 1048 (Fed. Cir. 2019) (explaining that arguments not presented to the Board are waived).

matrix, we find Petitioner has shown Walker teaches those features. *See* Pet. 22–23; Ex. 1034 ¶¶ 98–99, 189–190. Walker describes making a graft from vascular tissue. Ex. 1005, 6:17–18.

Next, claim 1 recites "one or more plasticizers contained in said internal matrix." We find Petitioner has shown the internal matrix of Walker's tissue would contain the plasticizer glycerol in view of Walker's disclosure of treating tissue with glycerol for sixteen hours or more, as well as Walker's teaching that glycerol keeps the dimensions stable during processing. *See* Pet. 22–23, 26; Ex. 1005, 4:33, 5:23–24, 7:11–14, 21:9–12; Ex. 1034 ¶¶ 99, 190.

Finally, claim 1 recites "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." As construed above, this limitation requires that the native orientation of the collagen fibers is not altered by the plasticization process. *See supra* Section IV.B.3.

We are persuaded by Petitioner's argument that Walker's grafts comprise collagen fibers, which Patent Owner does not dispute. *See* Pet. 23, 26; Ex. 1005, 4:23–27; Ex. 1034 ¶¶ 88, 191. Petitioner further argues Walker discloses that the native orientation of the collagen fibers is not altered during treatment of the graft with glycerol. Pet. 19–20, 23–24, 27; Ex. 1034 ¶¶ 88–89, 192. To the extent Patent Owner disputes this contention, Patent Owner's opposition relies entirely on the same arguments against Walker disclosing a "plasticized" graft, on the basis that Walker does not establish its glycerol treatment leads to a graft having similar mechanical properties to normal hydrated tissue. *See* PO Resp. 19–25. Those

arguments are not persuasive, for the reasons addressed below in Section IV.C.3(b).

b) "plasticized"

As discussed above in Section IV.B.1, the construction of the "plasticized" term we have adopted is that the graft is "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." Patent Owner's arguments focus on the final clause of the construction — i.e., that the mechanical properties of the graft are similar to those of normal hydrated tissue. *See* PO Resp. 19–25.

Looking first at the undisputed water replacement and collagen preservation aspects of the construction, we find Petitioner has shown Walker discloses a soft tissue graft in which a plasticizer has replaced waters of hydration in the internal matrix of the tissue without altering the orientation of the collagen fibers. *See* Pet. 21–23, 25–27; Pet. Reply 7–12. Walker's process is carried out on "material . . . for implantation into a human or animal body" such as vascular tissue. Ex. 1005, Abstract; *see also id.* at 6:17–18; *id.* at 21:17–32 (describing an example using tissue samples of bovine pericardium).

Walker describes treating the graft with a substance, preferably glycerol, and then sterilizing. Ex. 1005, 6:4–11; *see also id.* at 5:17–20 (explaining that the substance in which the graft is treated "may be

water-soluble sugars such as sorbitol or glycerol" and "[s]uitable solutions range from 5% to 100%, usually in 50% ethanol or in water"). "The pre-sterili[z]ing treatment 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. Walker also describes that "[t]he physical characteristics of the material which may be maintained by treatment with the substance include flexibility, and/or structure of cells or extracellular material such as collagen, particularly the microstructure of collagen." *Id.* at 4:23–27.

Walker repeatedly refers to the step of soaking a tissue graft in glycerol as plasticization. *Id.* at 7:4, 8:27, 9:21, 17:12–18, 21:17–26, 22:3–11. For instance, Walker's Example 1 is titled "Plasticization of material with glycerol in preparation for EtO sterili[z]ation." *Id.* at 7:4–5. In that example, tissue samples are incubated in glycerol "for around 16 hours or more." *Id.* at 7:7–14. We credit Dr. McQuillan's testimony that an ordinarily skilled artisan "would have understood from Walker that the glycerol replaces free and loosely bound water within the internal matrix of the material." Ex. 1034 ¶ 85; *see also id.* ¶ 86 (testifying an ordinarily skilled artisan "would have understood from Walker that treatment of a soft tissue with glycerol would result in the substance penetrating the tissue and remaining in the internal matrix of the tissue"). Patent Owner does not dispute that Walker's glycerol incubation process will result in the glycerol replacing free and loosely bound waters of hydration in the tissue.[12]

[12] Patent Owner provides a detailed background discussion concerning waters of hydration in tissue. *See* PO Resp. 4–8; Ex. 2016 ¶¶ 34–42. But,

PO Resp. 18–29; *see, e.g.*, Ex. 1005, 6:20–24 (stating glycerol "can suitably replace at least some of the water contained in the material").

Turning to the disputed aspects of whether Walker's grafts are "plasticized" as construed above, we find Walker discloses that the mechanical properties, including the material, physical, and use properties, of its plasticized graft are similar to those of normal hydrated tissue. Walker's Abstract explains that the substance (e.g., glycerol) with which the graft is treated is "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, Abstract. Walker repeatedly states that the glycerol treatment allows the material to maintain certain physical characteristics, such as flexibility, cell structure, and collagen microstructure. *See id.* at 4:23–27, 6:6–8, 6:20–24. Walker also reports that because "glycerol keeps the dimensions of the grafts stable there would be little dimensional change during processing, therefore limiting concern over shrinkage or swelling on implantation." *Id.* at 21:9–12. We credit Dr. McQuillan's testimony that an ordinarily skilled artisan "would have understood that Walker teaches that the treated material maintains the structure of natural soft tissue." Ex. 1034 ¶ 88.

In addition, Walker discloses the results of testing conducted to compare a treated graft to natural tissue. Ex. 1005, 9–16. Specifically, bovine artery samples were plasticized in 50% glycerol and 50% ethanol,

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Patent Owner does not apply this background discussion to Walker as a basis for distinguishing Walker from claim 1 of the '420 patent, apart from an argument concerning cross-linking which we address below. *See* PO Resp. 4–8, 18–29.

and some of the samples were then sterilized. *Id.* at 9:17–29. The samples were rehydrated and subjected to a suture pull-out test to determine the load that was required to pull the suture out of the sample. *Id.* at 9:31–10:11. Separately, samples were rehydrated and subjected to tensile loading to determine the load and maximum stress required to pull the sample apart. *Id.* at 10:13–23. Walker includes tables showing the results of these tests, in which "[e]ach sample is compared to an untreated natural sample, which is the partner of the treated sample." *Id.* at 10:25–29. Walker reports that "[t]he results show that the physical properties of treated bovine arteries are unaffected by the plasticization and sterilization processes." *Id.* at 10:29–32. We credit Dr. McQuillan's testimony that this disclosure of testing results in Walker "demonstrates that the treated material is able to maintain physical characteristics" such that an ordinarily skilled artisan "would have understood that Walker's method produces a treated material that maintains the mechanical properties of natural material." Ex. 1034 ¶ 89.

We also credit Dr. McQuillan's testimony that an ordinarily skilled artisan "would have recognized that Walker's method of impregnation of the soft tissue by glycerol is equivalent to the method of plasticization described in the LifeNet patents." *Id.* ¶ 86; *see also* Pet. 19 ("Like the plasticization method disclosed in the 420 patent, Walker discloses the incorporation of glycerol . . . into the internal matrix of the material."); Pet. Reply 7–8 (arguing "Walker teaches the same preservation process disclosed in the challenged patent"). As just summarized, Walker describes plasticization treatments in which the soft tissue graft is incubated in a solution of glycerol and ethanol for sixteen hours or more. *See, e.g.*, Ex. 1005, 5:17–25, 7:7–14,

9:20–22. The '420 patent similarly describes plasticizing by soaking the graft in a solution of glycerol and alcohol.

Specifically, the '420 patent lists a large number of examples of suitable plasticizers, one of which is "glycerol (glycerin USP)," and explains that "[t]he plasticizer can be introduced into the bone or soft tissue matrix at any number of steps in the processing procedures and at a variety of concentrations with and without the use of permeation enhancers." Ex. 1002, 8:44–58, 9:16–20. In the section titled "Plasticization," the '420 patent explains that "bone or soft tissue cleaned and processed by conventional methods, may be plasticized by processing with the plasticizer composition containing one or more plasticizers, including for example glycerin USP, in a solvent by for example drawing the plasticizer composition into the bone" and "[s]uitable solvents include for example, 70% isopropyl alcohol." *Id.* at 10:21, 10:51–57. "The isopropyl alcohol facilitates penetration of the glycerol into the tissue by acting as a permeation enhancer and the glycerol more readily penetrates the tissue due to the reduced surface tension of the alcoholic solution." *Id.* at 10:65–11:2.

The two examples in the '420 patent relating to processing of soft tissue grafts (as opposed to bone grafts, which are the subject of Examples 1–8, *see id.* at 12:56–22:55) also describe soaking the graft in a solution of glycerin and alcohol. *See id.* at 23:13–30, 23:65–24:16. In Example 9, describing processing of fascia lata, the '420 patent discloses plasticizing by placing a cleaned and rinsed graft "in the basin containing U.S.P. grade 70% isopropyl alcohol containing 30% glycerin USP for 2–5 minutes." *Id.* at 23:13–16. The graft is "then placed into the basin containing the antibiotic solution in 30% glycerin USP for at least

15 minutes." *Id.* at 23:19–21. Example 10 describes plasticizing a pericardium sample using a very similar process. *Id.* at 23:65–24:16.

We asked Patent Owner at the hearing what steps the '200 patent (which contains substantially the same disclosure as the '420 patent) teaches are necessary to achieve a plasticized soft tissue graft beyond soaking in glycerol, and Patent Owner did not point us to any differences in the process, arguing instead that the limitation "might not require a specific process, but it does require a specific outcome." *See* Tr. 54:21–56:9. But if there are no material differences between the plasticization techniques taught in Walker compared to the '420 patent, it stands to reason that the outcome of a plasticized soft tissue would also be the same. Our questions about the similarity of Walker's plasticization process to the techniques described in the '420 patent have been apparent since institution, and Patent Owner has not persuasively identified any material differences. *See* Inst. Dec. 15–16. The similarity of Walker's plasticization process to that of the '420 patent further supports that Walker's treated graft would have mechanical properties similar to natural tissue, just as in the '420 patent.

We have considered Patent Owner's counter-arguments on this limitation but we do not find them persuasive. *See* PO Resp. 19–25; Sur-reply 5–10. Patent Owner argues Walker's tissue graft is cross-linked, and a cross-linked graft cannot have mechanical properties similar to those of normal hydrated tissue as required by the agreed construction of a plasticized soft tissue graft. PO Resp. 19–20 (citing Ex. 2016 ¶¶ 93–96, 182–185). According to Patent Owner, with supporting testimony from Dr. Kaplan, the cross-linking in Walker alters the structure of the internal matrix and makes the material properties of the resulting tissue dissimilar to

normal hydrated tissue. *Id.* at 20–21 (citing Ex. 2016 ¶¶ 94–96, 183–185). Cross-linking also makes the tissue stiffer and more durable than normal hydrated tissue. *Id.* at 21 (citing Ex. 2016 ¶¶ 184–185).

These arguments are premised on cross-linking being an essential precursor to each of Walker's tissue treatment processes. PO Resp. 19–21; *see also* Sur-reply 5 ("Every process of Walker *starts* with cross-linked tissue."). However, we agree with Petitioner that Walker is not limited to cross-linked grafts. *See* Pet. Reply 6; *see also* Ex. 1045 ¶ 10 (Dr. McQuillan testifying that "the bulk of Walker's disclosure . . . is directed to the treatment of non-cross-linked soft tissue grafts").

Patent Owner's argument, and Dr. Kaplan's testimony, that cross-linking is part of every tissue treatment process in Walker, is based on Walker's background discussion in the first two pages of its disclosure. *See* PO Resp. 18–19; Sur-reply 5; Ex. 2016 ¶¶ 77–84; Tr. 59:22–60:9. In that background, Walker describes that cross-linking is a current approach to countering drawbacks of biologic vascular grafts. Ex. 1005, 3:8–16. Of the options for cross-linking, dye-mediated photo-oxidation is preferred, but dye-mediated photo-oxidation does not sterilize the graft. *See id.* at 3:16–4:2. "The current preferred sterili[z]ation method is treatment with ethylene oxide (EtO)," but "EtO cannot be directly applied to a graft held in aqueous solution . . . since EtO reacts with water." *Id.* at 4:2–6. "Equally, the graft cannot simply be allowed to dry out to allow the application of EtO, since it would become brittle and could not be used without extensive re-hydration, and would be susceptible to damage." *Id.* at 4:8–12.

In our view, this background discussion in Walker illustrates one context in which the methods described in the remaining thirty pages of

disclosure are useful, but Walker does not limit the described methods to that particular context. Patent Owner does not point to, and we do not find, any indication in Walker that its treatment processes are inappropriate for grafts that have not been cross-linked, or that the benefits Walker describes for its methods would not obtain for non-cross-linked grafts.

Instead, Walker describes its invention in terms that are much broader than the particular context that led to Walker developing its glycerol incubation process. Walker describes its invention as "a method of sterili[z]ing *material* for implantation into a human or animal body," without indicating that the material is cross-linked material. *Id.* at 4:14–21 (emphasis added), 4:36–5:15, 6:17–18, 6:33–36. Also, Walker refers generically to utilizing a "sterili[z]ing agent," without limiting the scope of its disclosure to the EtO sterilizing agent which led to the development of Walker's glycerol incubation process. *Id.* at 4:14–21, 4:31–32, 4:36–5:15. These expansive descriptions of Walker's invention belie Patent Owner's contention that Walker's disclosure is limited to treating cross-linked tissue material.

Indeed, Walker's sole reference to cross-linking after its background discussion tends to support that the remaining disclosure is not limited to cross-linking. In Example 4, Walker discloses that "Bovine Carotid and Thoracic arteries (fixed by dye-mediated photo-oxidation) were stored in 20% or 50% ethanol at 2–8ºC." *Id.* at 17:3–5. Walker's disclosure that the samples in this example were fixed by dye-mediated photo-oxidation, which Walker describes in its background as the preferred method for cross-linking (*see id.* at 3:16–17), is a strong indication that the other examples and processes described in Walker are not limited to cross-linking. *See* Ex. 1045

¶ 9 (Dr. McQuillan testifying an ordinarily skilled artisan "would readily have understood that only Example 4 reports treatment of a cross-linked tissue graft"). This conclusion is bolstered by the evidence of record indicating that cross-linking of tissue is an *artificial* process, applied to natural tissue with the specific intent of modifying one or more properties of the natural tissue. *See, e.g.*, PO Resp. 9–11; Ex. 2016 ¶¶ 46–51; Sur-reply 6–7.

Patent Owner argues that the fact "[t]hat Walker's Example 4 specifies the exact method of cross-linking (dye mediated photooxidation) does not change that the other Example grafts are also cross-linked, but their particular methods of cross-linking are not important enough for Walker to specify them." Sur-reply 5. Yet Patent Owner does not provide a persuasive explanation why only a single example within Walker would have specified dye-mediated photo-oxidation if Walker's entire disclosure were limited to a problem encountered in the context of dye-mediated photo-oxidation. *See* Tr. 61:7–62:6.

Walker's description of Example 3 also supports that cross-linking is not carried out for each of Walker's grafts. Example 3 reports the results of suture pull-out and stress testing of bovine artery samples. *See* Ex. 1005, 9:17–10:23. In introducing the results, Walker explains that "[e]ach sample is compared to an untreated natural sample, which is the partner of the treated sample." *Id.* at 10:27–29. Patent Owner argues that the "partner of the treated sample" is made by simply cutting a sample in half before the treatment, and using one half as a control, while the other is further processed. *See* Tr. 62:12–23. Thus, according to Patent Owner's argument, the "natural" tissue results reported in Example 3 are for grafts that have

been cross-linked. PO Resp. 22 ("Walker compares un-treated *cross-linked* tissue to treated (with glycerol and then sterilized by EtO), but still *cross-linked*, tissue."); *see also* Ex. 2016 ¶¶ 98, 187 (Dr. Kaplan testifying the same).

We are not persuaded by this interpretation because it contradicts Walker's description, which expressly differentiates "natural" tissue from "cross-linked" tissue. Specifically, Walker indicates tissue that is cross-linked using dye-mediated photo-oxidation is preferred over other cross-linking methods because this produces grafts having "physical characteristics which are *closer to the natural tissue*." Ex. 1005, 3:12–19 (emphasis added). Also, as Petitioner points out, understanding "natural" tissue to refer to cross-linked tissue is inconsistent with Dr. Kaplan's testimony that the properties of "natural tissue" are different than tissue in which "artificial cross-links have been added." Ex. 2016 ¶ 94; Pet. Reply 11. We find more credible Petitioner's argument and Dr. McQuillan's testimony that Walker's Example 3 reports results for untreated, natural, non-cross-linked tissue. Pet. Reply 10; Ex. 1045 ¶ 17 ("There is no indication anywhere in Walker that when Walker sets forth data for 'natural' tissue that such tissue has been cross-linked such that it contains additional artificial cross-links."). Thus, based on Patent Owner's own understanding of how the "partner" for the treated sample is made, Example 3 supports that none of the grafts tested for that example are cross-linked.

Accordingly, we are not persuaded by Patent Owner's argument that an ordinarily skilled artisan would understand Walker to presuppose cross-linking for all grafts in its disclosure.

In its Sur-reply, Patent Owner argues that "[e]very one of Walker's grafts that was tested for tissue properties required some form of rehydration," which shows that Walker's grafts are cross-linked, as a plasticized soft tissue graft "does not require rehydration because it will have properties similar to normal hydrated tissue, with or without rehydration." Sur-reply 5–6. This argument overstates Walker's disclosure insofar as Patent Owner does not show that each of Examples 1 and 3–5 "required" rehydration. Indeed, Walker describes the step of humidifying the treated and sterilized graft as optional. Ex. 1005, 5:14. In effect, Patent Owner's argument treats claim 1 as if it required that the graft is not rehydrated, but that limitation is not included in claim 1 and is separately recited in dependent claim 4. *See infra* § IV.G.

Patent Owner further argues Walker's disclosure regarding treated samples maintaining tissue properties is unreliable because that disclosure is based on a comparison of untreated cross-linked tissue to treated cross-linked tissue. PO Resp. 22–23 (citing Ex. 2016 ¶¶ 187–188). This argument is premised on Patent Owner's assertion that Walker is limited to cross-linked grafts. As just discussed, we are not persuaded that Walker is so limited. Patent Owner's argument runs counter to the description in the reference itself, which states that the treated samples are being "compared to an untreated natural sample." Ex. 1005, 3:12–19, 10:27–28.

Patent Owner additionally argues Walker does not disclose that the material, physical, and use properties of the treated tissue are similar to normal hydrated tissue. PO Resp. 23–25; Sur-reply 7–10. Here, Patent Owner and Dr. Kaplan address a graft's material, physical, and use properties separately. *See* Ex. 2016 ¶¶ 93–96 (setting forth Dr. Kaplan's

definitions of how the three properties are different). Patent Owner notes that Walker's suture pullout test shows average pullout of 10.86 N for "natural" and 8.07 N for "treated" tissue. PO Resp. 24 (citing Ex. 1005, 9). According to Patent Owner, the only conclusion to be drawn from Walker's test data "is that Walker's . . . treated tissue has 'mechanical properties' that are quite *dissimilar* to those of normal hydrated tissue." *Id.* at 25 (citing Ex. 2016 ¶¶ 188–190). Patent Owner also argues that "the variance in [Walker's] data is too great to draw any statistically significant conclusion from it." *Id.* (citing Ex. 2016 ¶ 190); Sur-reply 9–10.

These arguments are not persuasive because they ask us to disregard the conclusions that the reference itself draws from its data, such as that "[t]he results show that the physical properties of treated bovine arteries are unaffected by the plasticization and sterilization processes." Ex. 1005, 10:29–32. Moreover, Patent Owner's statistical and quantitative criticisms of Walker's data are incongruous with the agreed construction, which simply requires properties "***similar to*** those of normal hydrated tissue." Patent Owner's arguments largely reduce to establishing there are ***differences*** between natural tissue and tissue treated with Walker's glycerol incubation process, and thus overlook the breadth imparted to claim 1 by the term "similar to" in the claim construction. Patent Owner has not provided a clear and persuasive explanation of what degree of similarity is needed. *See* Tr. 42:12–44:20. The descriptions in Walker, already discussed above, support that the material, physical, and use properties of Walker's treated tissue are similar to those of normal hydrated tissue because the glycerol treatment allows that graft to maintain flexibility, cellular structure, and collagen microstructure, and limits dimensional change, which alleviates

concern over shrinkage or swelling on implantation. *See* Ex. 1005, Abstract, 4:23–27, 6:6–8, 6:20–24, 21:9–12.

For these reasons, we find Walker discloses a "plasticized" graft under the construction we have adopted.

c) "cleaned"

As discussed above in Section IV.B.2, we construe "cleaned" as "a process during which cellular elements and small molecular weight solutes are removed."

We find Petitioner has shown Walker discloses cleaning under that construction. *See* Pet. 22, 26; Pet. Reply 12–13. Petitioner contends Walker discloses cleaning because it describes storing the graft in ethanol before the glycerol treatment. *See* Pet. 22; Pet. Reply 12–13. The portions of Walker identified by Petitioner support that contention. Walker's Example 3 explains that "samples of Bovine carotid and thoracic arteries were transferred to 50% ethanol" before samples were plasticized in a solution of 50% glycerol in 50% ethanol. Ex. 1005, 9:19–22. Walker's Example 4 explains that "Bovine Carotid and Thoracic arteries (fixed by dye-mediated photo-oxidation) were stored in 20% or 50% ethanol at 2–8ºC" before plasticization in glycerol solutions. *Id.* at 17:3–8. We credit Dr. McQuillan's testimony that an ordinarily skilled artisan "would have understood that storage of the tissue in ethanol as described in Walker would at least partially remove potentially adverse immunogenic cellular components from the tissue by solubilizing the lipid cell membrane." Ex. 1034 ¶ 84.

We have considered Patent Owner's arguments regarding this limitation but we do not find them persuasive. *See* PO Resp. 26–27; Sur-reply 10–12. Patent Owner argues Walker traps cellular elements and small molecular weight solutes rather than removing them because that is what cross-linking does. PO Resp. 26 (citing Ex. 2016 ¶ 192). But as discussed above, we are not persuaded that cross-linking is a prerequisite for the graft processing techniques Walker teaches.

Patent Owner further argues Walker's pre-glycerol storage in ethanol does not meet the "cleaned" element because it "would not remove enough cellular elements and small molecular weight solutes to avoid transmission of disease and rejection of the tissue by the patient's body." PO Resp. 26–27 (citing Ex. 2016 ¶ 193). This argument is based on Patent Owner's proposed construction of "cleaned," which we have not adopted for the reasons explained above in Section IV.B.2.

Patent Owner also argues Petitioner's understanding of Walker "sets up a paradox that relates to three requirements of the challenged claims." PO Resp. 28–29. Namely, if Walker is not cross-linked so that it can be a "plasticized" graft, then Walker does not disclose a cleaning step to remove the cellular elements that would transmit disease and cause rejection by the patient's body, which means it is not "suitable for transplantation into a human." *Id*. This argument relies on "suitable for transplantation into a human" as a limitation, and as Petitioner points out, Patent Owner has not shown why that preamble language should be treated as limiting. Pet. Reply 13–14; PO Resp. 14. Further, the argument essentially contradicts Walker itself, which states that its graft is "for implantation into a human or animal body." Ex. 1005, Abstract, 4:14–16, 6:33–36, 33:3–4.

For these reasons, we find Walker discloses a "cleaned" graft under the construction we have adopted.

d) Conclusion Regarding Claim 1

For the reasons discussed above, we determine Petitioner has demonstrated by a preponderance of the evidence that Walker anticipates claim 1.

4. Claims 2 and 16

Independent claim 2 recites many of the same limitations as claim 1, except claim 2 recites the graft is "impregnated with" a plasticizer. Ex. 1002, at 24:42–49. Independent claim 16 recites a method for producing a plasticized soft tissue graft, and includes many of the same limitations as claim 1, except claim 16 includes "impregnating" the graft with a plasticizer. *Id.* at 25:28–36.

For its argument that Walker teaches a graft impregnated with one or more plasticizers, Petitioner relies on its arguments for claim 1 that Walker discloses one or more plasticizers contained in the internal matrix. *See* Pet. 28 (claim 2), 33–34 (claim 16). Patent Owner argues that "[b]ecause Walker's graft is cross-linked, a plasticizer could not penetrate the internal matrix such that it is 'impregnating' the tissue graft with plasticizer." PO Resp. 29 (citing Ex. 2016 ¶ 195); *see also* Sur-reply 12 ("The tissue of Walker cannot be impregnated because the cross-links prevent plasticizer from filling the graft."). At the hearing, Patent Owner agreed that its arguments regarding "impregnated" rise or fall with its arguments regarding cross-linking in connection with the "plasticized" graft limitation of claim 1. *See* Tr. 75:7–21. For the reasons discussed above in Section IV.C.3(b), we

are not persuaded by Patent Owner's arguments regarding cross-linking and we find Petitioner has shown Walker describes a "plasticized" graft.

After considering the evidence and arguments of record, we find Petitioner has shown Walker discloses each limitation in claims 2 and 16. *See* Pet. 28, 33–34. Apart from the "impregnated" limitation, Patent Owner does not present any argument for claims 2 and 16 separate from its arguments regarding claim 1, which we have already discussed above. We determine Petitioner has demonstrated by a preponderance of the evidence that Walker anticipates claim 2 and 16.

5. Claim 13

Claim 13 recites: "The plasticized soft tissue graft of any one of claim 1, 2, or 3, wherein said plasticized soft tissue graft is essentially free from cellular elements." Ex. 1002, 25:15–17.

Petitioner contends Walker's storage of a graft in ethanol prior to incubating the graft in glycerol not only "cleans" the graft as required by claims 1, 2, and 3, but also makes the graft "essentially free from cellular elements" as required by claim 13. Pet. 30 (citing Ex. 1005, 9:19–20, 17:3–5); Pet. Reply 12–13. This contention is supported by testimony from Dr. McQuillan. Ex. 1034 ¶¶ 84, 209, 234; Ex. 1045 ¶¶ 22–24.

Patent Owner responds that "Walker does not disclose a graft that is 'essentially free from cellular elements.'" PO Resp. 26–27 & n.6; Sur-reply 10–12. This contention is supported by testimony from Dr. Kaplan. Ex. 2016 ¶ 193 & n.8.

We determine the evidence fails to establish that Walker's storage of its grafts in ethanol is sufficient to make the graft essentially free from

cellular elements. We, first, agree with Patent Owner's contention that this limitation of claim 13 is "stricter," requiring "a higher level of proof," than the cleaning recited in the parent claims. Tr. 64:15–65:2. That is, a graft may be cleaned, yet not be cleaned enough to make the graft essentially free from cellular elements. Claim 13 thus narrows the scope of its parent claims by setting forth a relatively high standard of cleaning that must be accomplished.

The Walker disclosures cited by Petitioner do not establish that Walker's storage of grafts in ethanol makes the grafts essentially free from cellular elements. Instead, they indicate simply that the grafts are "transferred to 50% ethanol" for an unspecified period of time under unspecified conditions (Ex. 1005, 9:19–20), or are "stored in 20% or 50% ethanol at 2–8°C" for an unspecified period of time (*id.* at 17:3–5). We credit Dr. Kaplan's testimony that these disclosures do not provide sufficient detail to conclude that the storage in ethanol makes the grafts essentially free from cellular elements. *See* Ex. 2016 ¶ 193 & n.8.

Dr. McQuillan's initial declaration testimony fails to account for the difference in scope between claim 13 and its parent claims. Ex. 1034 ¶¶ 84, 209, 234. He testifies that Walker's pre-plasticization storage in ethanol will "at least partially remove potentially adverse immunologic cellular components by solubilizing the lipid cell membrane." *Id.* But, partial removal of only some cellular elements falls well short of claim 13's requirement to make the graft essentially free of cellular elements.

Petitioner attempts to cure this deficiency with Dr. McQuillan's reply testimony. Ex. 1045 ¶¶ 22–24. There, Dr. McQuillan combines Walker's Examples 1 and 3 as teaching "a soft tissue graft may be stored in ethanol or

plasticized in a bath of 50% glycerol and 50% ethanol for 16 hours." *Id.* ¶ 22 (citing Ex. 1005, 7:7–13, 8:26–28, 9:19–22). Dr. McQuillan concludes that, "[t]aking into account that the ethanol bath is 16 hours or more," an ordinarily skilled artisan "would have understood that substantially all native cells present in the soft tissue graft will have had their cell membranes solubilized and substantially all of that loose cellular content is rinsed away, resulting in a graft that is essentially free from cellular elements." *Id.* Dr. McQuillan additionally testifies that Examples 9 and 10 of the '420 patent "teach a similar type of . . . cleaning" as is disclosed in Walker, such that an ordinarily skilled artisan "would recognize that the Walker ethanol bath and the Allowash bath of the ['420 patent] are equivalent in their ability to clean a soft tissue graft." *Id.* ¶¶ 23–24.

Patent Owner objects to Dr. McQuillan's combining of Walker's Examples 1 and 3, asserting "*none* of the examples of Walker treats the tissue to an ethanol bath for 16 hours" and "Walker never discloses how long it stores the graft in ethanol." Sur-reply 10–11. Patent Owner also argues the Allowash used in Examples 9 and 10 of the '420 patent does not contain ethanol, and the Examples include additional cleaning steps, so the Examples are dissimilar to Walker's ethanol cleaning. *Id.* at 11 (citing Ex. 1002, 5:62–6:3, 23:2–12, 23:55–62).

Upon review of the foregoing, we conclude Walker's disclosure is too sparse, and Dr. McQuillan's reply testimony is too conclusory, for his opinions on this point to be persuasive. The claimed requirement for a graft that is "essentially free from cellular elements" sets a high standard of cleaning that must be met. Even if Walker discloses plasticizing a graft in a solution containing up to 50% ethanol for 16 hours as Dr. McQuillan

testifies (*see, e.g.*, Ex. 1005, 17:12–18), Dr. McQuillan's stated opinion that this process will make the graft essentially free from cellular elements is not corroborated by cited evidence. *See* Ex. 1045 ¶ 22. His opinion, further, is unaccompanied by a persuasive explanation as to *why* he believes Walker's process will satisfy the requirement of claim 13. *See id.* We understand that storing a graft in an ethanol solution will remove cellular elements from the graft, and that under some conditions (time, temperature, agitation, etc.) this storage might be sufficient to make the graft essentially free from cellular elements. Nonetheless, the evidence and Dr. McQuillan's testimony do not persuade us that Walker's storage conditions achieve the claimed result. We therefore give this testimony little weight. *See In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1368 (Fed. Cir. 2004) ("[T]he Board is entitled to weigh the declarations and conclude that the lack of factual corroboration warrants discounting the opinions expressed in the declarations."); *Skky, Inc. v. MindGeek, s.a.r.l.*, 859 F.3d 1014, 2022 (Fed. Cir. 2017) ("[T]he Board was not required to credit [appellant]'s expert evidence simply because [appellant] offered it.").

We agree with Patent Owner that Examples 9 and 10 of the '420 patent do not aid Petitioner. Those Examples disclose cleaning grafts in Allowash™, whereas Walker discloses cleaning grafts in ethanol, and the evidence does not establish that Allowash™ includes ethanol or a functional equivalent. *See* Ex. 1002, 5:62–6:3 (defining "Allowash™ Solution"); *id.* at 23:2–5, 23:55–58 (indicating Examples 9 and 10 clean grafts in Allowash™ Solution). Given the different cleaning solutions utilized, we are not persuaded by Dr. McQuillan's unexplained conclusion that these respective processes "are not materially different." Ex. 1045 ¶ 24. Just as

important, the '420 patent does not disclose that the Allowash™ cleaning of Examples 9 and 10 makes the grafts essentially free from cellular elements. *See* Ex. 1002, 23:2–5, 23:55–58. Therefore, any similarity in the respective cleaning processes has not been established to be relevant to the cleaning standard set by claim 13.

For the foregoing reasons, we conclude Petitioner has not demonstrated by a preponderance of the evidence that Walker anticipates claim 13.

6. Claim 34

Claim 34 recites: "The method of claim 16, further comprising: producing said cleaned soft tissue graft by removing cellular elements." Ex. 1002, 26:36–38.

Petitioner contends Walker's storage of a graft in ethanol prior to incubating the graft in glycerol satisfies the requirement of claim 34. Pet. 30. Patent Owner responds that Walker "does not disclose 'producing said cleaned soft tissue graft by removing cellular elements.'" PO Resp. 26–27.

We find Walker's storage of its grafts in ethanol is sufficient to remove cellular elements. The "removing cellular elements" requirement of claim 34 is not materially different from our construction of "cleaned" in parent claim 16 as "a process during which cellular elements . . . are removed." *See supra* Section IV.B.2. Thus, for the reasons provided above in Section IV.C.3(c), we conclude Petitioner has demonstrated by a preponderance of the evidence that Walker anticipates claim 34.

7. Claims 3, 5, 8, 10, 14, 15, 17, 18, 20, 21, 24–28, 30, 33, and 35

Petitioner identifies disclosure in Walker that discloses each limitation in claims 3, 5, 8, 10, 14, 15, 17, 18, 20, 21, 24–28, 30, 33, and 35. *See* Pet. 28–32, 35–38. Patent Owner does not present any argument for these claims other than what we have already considered with respect to claim 1. *See LG Elecs.,* 759 F. App'x at 925 ("The Board is 'not required to address undisputed matters' or arguments about limitations with which it was never presented."); *Papst*, 924 F.3d at 1250; *Bradium*, 923 F.3d at 1048. After considering the evidence and arguments of record, we determine Petitioner has demonstrated by a preponderance of the evidence that Walker anticipates these claims.

Specifically concerning dependent claims 8 and 28, which recite that the "plasticized soft tissue graft is sterile" (Ex. 1002, 25:1–2, 26:23–24), Petitioner relies on Walker's sterilization of its grafts with EtO following plasticization with glycerol. *See* Pet. 29 (citing Ex. 1005, 4:29–32, 8:13–23, 9:8–15); Ex. 1034 ¶¶ 207, 231. We find a preponderance of the evidence supports this contention, regardless of the proper claim construction of the "cleaned" term in the independent claims. *See* Ex. 1005, 4:29–32, 8:16–23, 9:11–15.

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.[13] For reasons provided below, we do not reach this ground in this Decision. We begin with a brief summary of the law of obviousness, then we address Petitioner's contentions.

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. *See Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

"While the sequence of these questions might be reordered in any particular case," *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 407 (2007), the Federal Circuit has explained that an obviousness determination can be made only after consideration of all of the *Graham* factors. *Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342, 1360 (Fed. Cir. 2012).

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[13] We noted in the Institution Decision that there is some confusion in the Petition as to whether claims 3, 9, 11, 15, 29, and 31 are part of this ground. *See* Inst. Dec. 5 n.2, 21–22; Pet. 5, 38–42. Patent Owner agreed there is confusion, but nonetheless addressed these claims as part of this ground. *See* PO Resp. 29 n.7. We therefore continue to treat these claims as subject to this ground.

2. Claims 1–3, 5, 8, 10, 14–18, 20, 21, 24–28, 30, and 33–35

Petitioner provides arguments and evidence, including the testimony of Dr. McQuillan, in support of contending independent claims 1, 2, 3, 15, and 16 are unpatentable as having been obvious over Walker. Pet. 38–40 (citing Ex. 1034 ¶¶ 85–86, 88, 236–237); Pet. Reply 23–24 (citing Ex. 1034 ¶ 23; Ex. 1045 ¶¶ 21–24). Petitioner does not address the alleged obviousness of dependent claims 5, 8, 10, 14, 17, 18, 20, 21, 24–28, 30, and 33–35 separately from the independent claims. Pet. 38–42; Pet. Reply 23–25.

Having determined Petitioner has demonstrated by a preponderance of the evidence that claims 1–3, 5, 8, 10, 14–18, 20, 21, 24–28, 30, and 33–35 are anticipated by Walker, we need not reach the question of whether these same claims also would have been obvious based on Walker. *See Boston Scientific Scimed, Inc. v. Cook Group Inc.*, 809 Fed. Appx. 984, 990 (Fed. Cir. 2020) (rejecting argument that it is improper for the Board to decline to address a petitioner's alternative grounds with respect to claims it found unpatentable on other grounds, and determining that "the Board need not address issues that are not necessary to the resolution of the proceeding"); *see also Beloit Corp. v. Valmet Oy*, 742 F.2d 1421, 1423 (Fed. Cir. 1984) (explaining that an administrative agency "is at perfect liberty" to reach a decision based on a single dispositive issue because doing so "can not only save the parties, the [agency], and [the reviewing] court unnecessary cost and effort, it can greatly ease the burden on [the agency] faced with a . . . proceeding involving numerous complex issues and required by statute to reach its conclusion within rigid time limits.").

Thus, we do not reach Petitioner's contention that claims 1–3, 5, 8, 10, 14–18, 20, 21, 24–28, 30, and 33–35 are unpatentable as having been obvious over Walker.

3. Claim 7

Claim 7 recites: "The plasticized soft tissue graft of any one of claim 1, 2, or 3, wherein said cleaned soft tissue graft is selected from the group consisting of: dura, pericardium, fascia lata, tendons and ligaments." Ex. 1002, 24:64–67.

We find Petitioner has shown an ordinarily skilled artisan would have been motivated to apply Walker's teachings to these common, load-bearing types of soft tissue grafts. *See* Pet. 40–41 (citing Ex. 1034 ¶ 244); *see also* Ex. 2016 ¶ 32 (Dr. Kaplan explaining that load-bearing soft tissue structures include pericardium, fascia lata, dura mater, and various tendons and ligaments). As Petitioner points out, Walker teaches that bovine pericardium can be plasticized and sterilized using the same methods it teaches for bovine carotid and thoracic arteries, which are other types of load-bearing soft tissue. *See* Pet. 40–41; Ex. 1005, 9:19–20, 27:1–2.

Patent Owner does not present any argument against Petitioner's contentions that the additional limitation recited in dependent claim 7 would have been obvious to a person of ordinary skill in the art based on Walker. *See* PO Resp. 29–32. Patent Owner argues that objective indicia support nonobviousness, but Patent Owner's objective indicia evidence is not directed to the features recited in claim 7. *See id.* at 51–64. "For objective indicia of nonobviousness to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the claimed

invention." *Lectrosonics, Inc. v. Zaxcom, Inc.*, IPR2018-01129, Paper 33, 32 (PTAB Jan. 24, 2020) (precedential); *see also In re Affinity Labs of Tex., LLC*, 856 F.3d 883, 901 (Fed. Cir. 2017) ("Evidence of [objective indicia] is only relevant to the obviousness inquiry 'if there is a nexus between the claimed invention and the [objective indicia].'"). "[T]he patentee bears the burden of showing that a nexus exists.'" *Henny Penny Corp. v. Frymaster LLC*, 938 F.3d 1324, 1332 (Fed. Cir. 2019) (quoting *WMS Gaming, Inc. v. Int'l Game Tech.*, 184 F.3d 1339, 1359 (Fed. Cir. 1999)).

A presumption of nexus applies "when the patentee shows that the asserted objective evidence is tied to a specific product and that product embodies the claimed features, and is coextensive with them." *Lectrosonics*, Paper 33, 32 (quoting *Fox Factory, Inc. v. SRAM, LLC*, 944 F.3d 1366, 1373 (Fed. Cir. 2019)). Here, Patent Owner has not shown entitlement to a presumption of nexus for claim 7 because Patent Owner does not provide evidence that the commercial products underlying its objecting indicia arguments embody claim 7. *See* PO Resp. 63–64. Patent Owner cites Dr. Kaplan's testimony to support its argument regarding a presumption of nexus. *Id*. (citing Ex. 2016 ¶ 305). But Dr. Kaplan's claim chart for the '420 patent does not compare the commercial products to claim 7. *See* Ex. 2073 (charting claims 1–4, 6, 8–14, 16–18, 25, 28–32, and 34–36).

Absent a presumption of nexus, a "patent owner is still afforded an opportunity to prove nexus by showing that the evidence of secondary considerations is the direct result of the unique characteristics of the claimed invention." *Lectrosonics*, Paper 33, 33 (quoting *Fox Factory*, 944 F.3d at 1373–74). But here, Patent Owner does not tie its objective indicia evidence to the limitation recited in claim 7. The features Patent Owner

relies on to establish nexus are ready-to-use grafts that are stable for storage at room temperature. *See* PO Resp. 63–64; Tr. 76:1–12. Patent Owner does not tie those features to the limitations of claim 7. *See* Tr. 76:13–24; Ex. 2016 ¶¶ 306–309. Accordingly, we find Patent Owner has not established a nexus to support the nonobviousness of claim 7.

For the foregoing reasons, we determine Petitioner has demonstrated by a preponderance of the evidence that claim 7 would have been obvious based on Walker.

4. Claims 9, 11, 29, and 31

Claim 9 recites: "The plasticized soft tissue graft of any one of claim 1, 2, or 3, wherein said plasticized soft tissue graft does not require refrigeration or freezing." Ex. 1002, 25:3–5. Claim 29 depends from independent claim 16, to add the same limitation as claim 9. *Id.* at 26:25–26.

Claim 11 recites: "The plasticized soft tissue graft of any one of claim 1, 2, or 3, wherein said plasticized soft tissue graft is suitable for storage at room temperature." Ex. 1002, 25:8–10. Claim 31 depends from independent claim 16, to add the same limitation as claim 11. *Id.* at 26:29–30.

Petitioner provides arguments and evidence, including the testimony of Dr. McQuillan, in support of contending these four claims are unpatentable as having been obvious over Walker. Pet. 41; Ex. 1034 ¶¶ 238–243. Dr. McQuillan testifies in support that Walker "teaches" and "explicitly disclose[s]" its plasticized tissue is not required to be refrigerated or frozen, and can be stored at room temperature. Ex. 1034 ¶¶ 239–240. In

the alternative to such teaching or disclosure being found, Dr. McQuillan testifies an ordinarily skilled artisan would have understood Walker's plasticized tissue grafts were "dried" by the plasticization with glycerol, and dried grafts do not require refrigeration or freezing, and may be stored at room temperature. *Id.* ¶¶ 240–243. These opinions are stated without citation to evidence in the record. *Id.* ¶¶ 238–243.

Patent Owner asserts, and Dr. Kaplan testifies, that "Walker is silent on its storage requirements and thus nowhere teaches that its finished grafts do not require refrigeration or freezing for storage or that they may be stored at room temperature." PO Resp. 32; Ex. 2016 ¶ 204. And: "Without *some* teaching in Walker, a POSA [would] have no reason to assume specific storage conditions of Walker." PO Resp. 32; Ex. 2016 ¶ 204.

Petitioner replies that Patent Owner's position "turns scientific inquiry on its head," because "[r]efrigeration and freezing are special storage conditions." Pet. Reply 25. Petitioner concludes that "[i]f Walker's grafts required such special storage conditions, Walker would have expressly so stated." *Id.*

We agree with Patent Owner that Petitioner's arguments and evidence regarding these limitations are unpersuasive. Petitioner and Dr. McQuillan do not cite any express disclosure in Walker that its plasticized tissue does not require refrigeration or freezing, or that its plasticized tissue may be stored at room temperature. *See* Pet. 41; Ex. 1034 ¶¶238–239 ("Walker does not explicitly discuss whether the plasticized tissue product can be stored at room temperature or not."). Further, we do not follow Petitioner's inference that Walker's silence regarding storage conditions means that the grafts do not require refrigeration or freezing, and may be stored at room temperature.

That argument is undermined by the evidence that storage stability without refrigeration or freezing was noteworthy in this field, which suggests the contrary understanding of Walker's silence on storage conditions: if Walker's grafts were stable for storage without refrigeration or freezing, or at room temperature, Walker would have noted these advantageous features.

Most notable in this regard is Livesey, Petitioner's other primary reference, which touts that its "packaged dried tissue may be stored for extended time periods under ambient conditions," and "[t]ransportation may be accomplished via standard carriers and under standard conditions relative to normal temperature exposure and delivery times." Ex. 1004, 6:6–11. A graft that "can be easily stored and transported at ambient temperatures" is one of the "criteria" that Livesey states for its grafts. *Id.* at 4:43–46, 4:54–55. Petitioner's argument that it goes without saying that Walker's grafts are stable without special storage conditions is inconsistent with Livesey.

In addition, Patent Owner has presented evidence showing storage stability without refrigeration is a feature that manufacturers have highlighted in marketing their grafts. *See* PO Resp. 63–64; Ex. 2016 ¶¶ 310, 312; Ex. 2050, 1 (listing benefits of LifeCell's Strattice product, including that it "[o]ffers enhanced ease of use – Strattice™ Tissue Matrix requires no rehydration and can be stored at room temperature"); Ex. 2066, 4 (listing benefits of LifeCell's AlloDerm Ready to Use product, including "[n]o refrigeration required); Ex. 2080, 1 (advertising LifeNet's DermACELL product by stating that is "ready to use of the package and stored at room temperature, eliminating the need for refrigeration and rehydrating processes"); Ex. 2081, 1 (advertising LifeNet's OrACELL product by stating

that it "can be stored at room temperature"); Ex. 2084, 7 (noting a benefit of LifeNet's ArthroFlex product is that it is "stored at room temperature"). The significance of these features to the marketplace cuts against Petitioner's argument that Walker's silence on the issue of storage would have been understood to mean no refrigeration was needed, and Walker's tissue could be stored at room temperature.

We have considered Dr. McQuillan's testimony that skilled artisans would have understood in 1998 that soft tissue grafts preserved with glycerol do not require refrigeration, and could be stored at room temperature, but we note no underlying support is provided for that testimony. Ex. 1034 ¶¶ 238–243. We also do not find in that testimony any persuasive explanation of why an ordinarily skilled artisan would have had that understanding. We therefore give this testimony little weight. *See Am. Acad.*, 367 F.3d at 1368; *Skky*, 859 F.3d at 1022. The '420 patent places substantial emphasis on the benefit that its grafts do not require special storage conditions, calling out that feature in the first sentence of both the Abstract and the Field of the Invention. *See* Ex. 1002, Abstract, 1:12–17. Considering that emphasis, we also agree with Patent Owner that Petitioner's argument and Dr. McQuillan's testimony bear the imprint of improper hindsight. *See Otsuka Pharm. Co. v. Sandoz, Inc.*, 678 F.3d 1280, 1296 (Fed. Cir. 2012) ("The inventor's own path itself never leads to a conclusion of obviousness; that is hindsight.").

In short, Petitioner has not adequately shown that, absent any discussion of storage conditions in Walker, an ordinarily skilled artisan would have understood Walker to disclose that the grafts could be stored without refrigeration or freezing, or at room temperatures. Based on that

deficiency, we conclude Petitioner has not demonstrated by a preponderance of the evidence that claims 9, 11, 29, and 31 would have been obvious based on Walker.

5. Claim 13

Claim 13 recites: "The plasticized soft tissue graft of any one of claim 1, 2, or 3, wherein said plasticized soft tissue graft is essentially free from cellular elements." Ex. 1002, 25:15–17. As discussed above, we have determined Petitioner has not demonstrated by a preponderance of the evidence that Walker anticipates claim 13. *See supra* Section IV.C.5.

As to obviousness of claim 13 over Walker, the Petition does not directly address the subject matter of claim 13 separately from its parent claims 1, 2, and 3. Pet. 38–42. The Petition does, however, assert: "To the extent any limitation of [claims 1, 2, 3 and 13] is not explicitly disclosed in Walker, the subject matter as a whole of those claims would have been obvious." Pet. 38.

Patent Owner attacks this contention as an insufficient "vague and conclusory catch-all statement" that "is devoid of substance and reasoning." PO Resp. 31. Patent Owner urges us to reject Petitioner's reliance on this kind of statement of obviousness in the Petition, lest we encourage gamesmanship by petitioners in the future, by permitting the delay of substantive argument to a petitioner's reply brief rather than the petition, depriving a patent owner of the opportunity to respond effectively. *Id.* at 31–32.

In the Reply, Petitioner argues that if Walker does not "disclose a 'cleaned' graft [as recited in claims 1, 2, and 3] that is 'essentially free from

cellular elements' [as recited in claim 13]," then it would have been obvious "to clean the tissues of Walker to reduce the risk of adverse immunogenic responses after transplant." Pet. Reply 23–24 (citing Ex. 1034 ¶ 23; Ex. 1045 ¶¶ 21–24). We agree with Patent Owner's rebuttal that this obviousness position was not articulated in the Petition. *See* Sur-reply 18–19. The Petition argues Walker discloses a cleaned graft that is essentially free from cellular elements (Pet. 18–19, 22, 26, 28, 30), and does not contemplate that Walker might be deficient in these regards as part of the obviousness challenge (*id.* at 38–42).

The Petition's catch-all statement that obviousness applies to "any limitation" that is found not to be disclosed in Walker (*id.* at 38) is insufficient to meet the requirement that a petition must "identif[y] . . . with particularity . . . the grounds on which the challenge to each claim is based, and the evidence that supports the grounds." 35 U.S.C. § 312(a)(3); *Intelligent Bio-Systems, Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1369–70 (Fed. Cir. 2016) (affirming PTAB's refusal to consider obviousness theory presented for first time in a petitioner's reply brief). We therefore decline to consider whether it would have been obvious to modify Walker by cleaning its tissue to be essentially free from cellular elements. This theory of obviousness was improperly presented for the first time in Petitioner's Reply Brief.

6. Claim 22

Claim 22, in combination with its parent claims 16, 17, and 20, recites incubating a graft with a plasticizer composition including glycerol as a plasticizer, and isopropyl alcohol as a biocompatible solvent. Ex. 1002,

25:28–29 (claim 16), 25:37–40 (claim 17), 26:1–2 (claim 20), 26:8–9 (claim 22).

We find Petitioner has shown Walker teaches glycerol as a plasticizer and ethanol as a solvent. Pet. 41–42; Ex. 1005, 6:26–27, 9:20–23, 17:13–14. We further find Petitioner has shown that a skilled artisan would know ethanol is readily interchangeable with isopropyl alcohol, and isopropyl alcohol is less expensive such that an ordinarily skilled artisan would have been motivated to substitute isopropyl alcohol to decrease cost. Pet. 42; Ex. 1034 ¶¶ 136, 245.

Patent Owner does not present any argument against Petitioner's contention that the additional limitation recited in dependent claim 22 would have been obvious to a person of ordinary skill in the art based on Walker. *See* PO Resp. 29–32. Patent Owner argues objective indicia support nonobviousness, but Patent Owner's objective indicia evidence is not directed to the features recited in claim 22. *See id*. at 51–64. Patent Owner has not shown entitlement to a presumption of nexus for claim 22 because Patent Owner does not provide evidence that the commercial products underlying its objective indicia arguments embody claim 22. Patent Owner cites Dr. Kaplan's testimony to support its argument regarding a presumption of nexus, but Dr. Kaplan's claim chart for the '420 patent does not compare the commercial products to claim 22. *See* PO Resp. 63–64; Ex. 2016 ¶ 305; Ex. 2073 (charting claims 1–4, 6, 8–14, 16–18, 25, 28–32, and 34–36). Further, Patent Owner does not tie its objective indicia evidence to the limitation recited in claim 22, because the features Patent Owner relies on to establish nexus are ready-to-use grafts that are stable for storage at room temperature. *See* PO Resp. 63–64; Tr. 76:1–24; Ex. 2016

¶¶ 306–309. Accordingly, we find Patent Owner has not established a nexus to support the nonobviousness of claim 22.

For the foregoing reasons, we determine Petitioner has demonstrated by a preponderance of the evidence that claim 22 would have been obvious based on Walker.

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. We determine Petitioner has demonstrated, by a preponderance of the evidence, that each of these claims is anticipated by Livesey. 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 the freezing step (3), and minimize structural damage during the drying step (4). *Id.* at 3:35–38, 5:15–24, 11:9–24. Glyercol is disclosed as a suitable cryoprotectant. *Id.* at 3:35–38, 11:49–60.

In step (5), the biological tissue is stored for extended periods of time under ambient conditions. *Id.* at 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 arguments and evidence, including the testimony of Dr. McQuillan, in support of contending claim 1 is unpatentable as anticipated by Livesey. Pet. 42–49; Ex. 1034 ¶¶ 58–81, 246–251. Patent Owner provides arguments and evidence, including the testimony of Dr. Kaplan, in opposition. PO Resp. 4–9, 33–42; Ex. 2016 ¶¶ 85–87, 206–216.

a) Undisputed Limitations

The only disputed aspects of Petitioner's anticipation challenge to claim 1 based on Livesey are the "plasticized" limitation, and maintaining the native orientation of collagen fibers. "The Board is 'not required to address undisputed matters' or arguments about limitations with which it was never presented." *LG Elecs.*, 759 F. App'x at 925; *see also Papst*, 924 F.3d at 1250; *Bradium*, 923 F.3d at 1048. Nevertheless, to provide a

complete record, we briefly summarize our findings regarding the uncontested limitations.

The preamble recites "[a] plasticized soft tissue graft suitable for transplantation into a human." The "plasticized" term, which is also recited in the body of claim 1, is disputed and is separately discussed below. *See infra* § IV.E.2(b). Patent Owner presents no argument to show that the remaining aspects of the preamble are limiting, or (if limiting) are not disclosed by Livesey. *See* PO Resp. 14, 33–42. Petitioner's arguments account for the possibility that the preamble is limiting. *See* Pet. 42–43, 46. We are persuaded by Petitioner's argument that, to the extent the entire preamble is limiting, Livesey discloses a graft suitable for transplantation into a human. *See* Pet. 42–43, 46; Ex. 1034 ¶¶ 247–248. Livesey describes "a method for processing and preserving collagen-based biological tissues for transplantation" into a "host" without eliciting an immune response. Ex. 1004, 4:39–52; *see also id.* at 1:15–21 ("This invention relates to methods for procuring . . . tissues derived from humans and animals for transplantation into humans or other animals.").

Claim 1 further recites "a cleaned soft tissue graft having an internal matrix." We find Petitioner has shown Livesey's grafts are cleaned, and have an internal matrix. *See* Pet. 16–17, 43, 47; Ex. 1034 ¶¶ 61, 248. Livesey correspondingly describes "the tissue is . . . incubated in a processing solution to remove viable antigenic cells . . . from the structural matrix without damaging the basement membrane complex or the structural integrity of the collagen matrix," such that "the structural integrity of the matrix is maintained including collagen fibers and elastin." Ex. 1004, 5:1–14; *see also id.* at 23:62–67 (disclosing a specific decellularizing

solution used to clean human skin tissue). We credit Dr. McQuillan's unopposed testimony that an ordinarily skilled artisan would understand this disclosure to reflect cleaning of a graft having an internal matrix, under the claim construction we have adopted above. *See* Ex. 1034 ¶¶ 61, 248.

Next, claim 1 recites "one or more plasticizers contained in said internal matrix." We find Petitioner has shown the internal matrix of Livesey's tissue would contain the plasticizer glycerol in view of Livesey's disclosure of incubating tissue with a cryopreservation solution containing glycerol as a cryoprotectant, "until complete penetration of the components of the cryosolution is achieved." Ex. 1004, 11:49–51, 12:34–37, 14:47–50, 15:11–13; *see* Pet. 17, 44, 47–48; Ex. 1034 ¶¶ 28, 62–64, 249.

Finally, claim 1 recites "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." As construed above, this limitation requires that the native orientation of the collagen fibers is not altered by the plasticization process. *See supra* Section IV.B.3. We are persuaded by Petitioner's argument that Livesey's grafts comprise collagen fibers, which Patent Owner does not dispute. *See* Pet. 16, 49; Ex. 1034 ¶¶ 65, 250–251. For example, Livesey is entitled "Method for Processing and Preserving Collagen-Based Tissues for Transplantation." Ex. 1004, Title; *see also id.* at Abstract, 5:1–14, 25:12–17. To the extent Patent Owner disputes whether Livesey's cryopreservation process alters the native orientation of the collagen fibers, we consider Patent Owner's arguments below. *See infra* Section IV.E.2(b)(2).

b) "plasticized" and "the native orientation of the collagen fibers is maintained"

As discussed above in Section IV.B.1, the construction of the "plasticized" term in claim 1 we have adopted is that the graft is "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." Patent Owner's arguments address both (1) the replacement of waters of hydration in the matrix, and (2) the mechanical properties of the graft being similar to those of normal hydrated tissue. *See* PO Resp. 34. Claim 1 additionally recites that "the native orientation of the collagen fibers is maintained." Ex. 1002, 24:40–41. We discuss the plasticized requirements (1) and (2) separately, and we also address maintaining the native collagen fiber orientation in combination with the plasticized requirement (2).

(1) Whether Livesey Discloses that a Plasticizer Replaces Free and Loosely Bound Water in the Tissue Matrix

For the following reasons, we find Livesey discloses its cryoprotectants include plasticizers (such as glycerol) which replace free and loosely bound water in the tissue matrix of Livesey's grafts, as Petitioner contends.

Livesey describes incubating its grafts in a cryopreservation solution containing one or more cryoprotectants. Ex. 1004, 5:15–24, 11:49–51, 12:31–37; *see* Pet. 17, 44, 47–48. Many of Livesey's "cryoprotectants" are identified as "plasticizers" by the '420 patent. Ex. 1034 ¶¶ 62–64; *id.* ¶ 249

(testifying "Livesey's 'cryoprotectant' serves the same function as the 'plasticizer' in the 420 patent"); *see* Pet. 44, 47–48. These common substances include glycerol, sucrose[14], sorbitol, propylene glycol, proline, and combinations thereof. *Compare* Ex. 1004, 11:49–55, *with* Ex. 1002, 7:52–67. As described in Livesey, the incubation achieves "complete penetration" of the cryoprotectants within the graft tissue, such that the cryoprotectants "penetrate[] and exert[] colligative action within the cells." Ex. 1004, 12:34–37, 14:47–50, 15:11–17; *see* Pet. 17, 43, 44, 47–48.

Dr. McQuillan testifies that an ordinarily skilled artisan would understand the described penetration and colligative action of cryoprotectants "mean[s] that glycerol or other small cryoprotectants replace free or loosely bound water in the internal matrix and preserve the structural integrity of the tissue." Ex. 1034 ¶ 62; *see* Pet. 17. In support, Dr. McQuillan cites van Baare[15] as establishing that, as of the '420 patent's February 1998 priority date, "a person of ordinary skill would know that glycerol was a preferred preservative" in part because it "was ideal as a water replacement agent." Ex. 1034 ¶ 25 (citing Ex. 1031, S77–S80). Dr. McQuillan further testifies that the cryopreservation process of Livesey is "the same" as the plasticization process of the '420 patent, because both incubate a cleaned soft tissue graft in glycerol under conditions that obtain

[14] Curiously, Dr. McQuillan testifies that sucrose is *not* a "plasticizer as [he] understand[s] that term to be used in the ['420 patent]." Ex. 1045 ¶ 35; *see* Sur-reply 13. It is difficult to reconcile this testimony with the fact that the '420 patent identifies sucrose as a plasticizer. Ex. 1002, 7:56. Regardless, it remains true that many other identified substances are the same.

[15] Ex. 1031, J. van Baare et. al., *Virucidal effect of glycerol as used in donor skin preservation*, 20 Burns Suppl. 1, S77–S80 (1994).

complete penetration of the glycerol in the tissue matrix, and so will achieve the same results. Ex. 1034 ¶¶ 64, 249, 290; Pet. Reply 16–17 (citing Ex. 1004, 11:17–23, 11:49–51, 12:33–37).

Dr. Kaplan testifies that Livesey does not disclose replacing free or loosely bound waters of hydration with a cryoprotectant. Ex. 2016 ¶¶ 207–211; *see* PO Resp. 34–38; Sur-reply 14–16. According to Dr. Kaplan, Livesey instead discloses the cryoprotectant "simply reacts with the free water in the graft to keep the water from crystalizing during freezing," and "does nothing to" the loosely bound water. Ex. 2016 ¶ 207 (citing Ex. 1004, 11:32–35, 11:55–60); *see* PO Resp. 35. According to Dr. Kaplan, the penetration of Livesey's cryoprotectant into the tissue "thus *maintains* the water in the tissue in an amorphous state" (i.e., prevents the water from crystallizing into ice) during the subsequent freezing of the graft, so the cryoprotectant "does not *replace* the water in the matrix." Ex. 2016 ¶¶ 207–209 (citing Ex. 1004, 12:36–37, 15:15–18, 15:22–24, 17:15–19, 17:49–51); *see* PO Resp. 35–36. Based on this understanding of how Livesey's cryoprotectants function, Dr. Kaplan testifies "the fact that Livesey even uses a cryoprotectant proves that water remains in the graft." Ex. 2016 ¶ 208; *see* PO Resp. 35–36. Further according to Dr. Kaplan, the fact that Livesey *dries* its grafts *after* cryopreservation and freezing establishes that the cryopreservation does not plasticize the grafts, because otherwise the drying step would not be needed. Ex. 2016 ¶¶ 85–87, 139–143, 211; PO Resp. 33–34, 37–38.

Upon review of the foregoing, we note first that claim 1 does not specify a particular amount or percentage of free and loosely bound water in the tissue matrix that must be replaced by the plasticizer.

Dr. McQuillan and Dr. Kaplan agree that Livesey's cryoprotectant incubation achieves complete penetration of the cryoprotectants within the tissue, so the cryoprotectants exert colligative action within the cells. *See, e.g.*, Ex. 1004, 12:34–37, 14:47–50, 15:11–17; Ex. 1034 ¶ 62; Ex. 2016 ¶¶ 207–208. The witnesses disagree, however, as to whether such penetration and colligative action corresponds to the cryoprotectants replacing free and loosely bound in the tissue matrix. On that particular point, we find Dr. McQuillan's testimony to be more persuasive than Dr. Kaplan's testimony, because it is more consistent with Livesey's disclosure.

For example, Livesey discloses that "[t]he physicochemical effects of cryoprotectants" such as glycerol include "*dehydrative effects on cells by osmotic action*." Ex. 1004, 17:3–9 (emphasis added), 11:49–51. This is consistent with van Barre, which refers to "the dehydrating action of glycerol" and indicates "[g]lycerol will dehydrate the skin, *the extracted water being replaced by glycerol*, preserving the original structure" such that "[t]he remaining water is optimally distributed throughout the tissue." Ex. 1031, S77 (emphasis added); Ex. 1034 ¶ 25. Thus, Livesey and van Barre indicate at least a portion of the cryoprotectant that penetrates into the tissue matrix will dehydrate the tissue by replacing some, but perhaps not all, of the free and loosely bound water in the matrix.

This finding is not contradicted by the Livesey disclosures cited by Dr. Kaplan. These disclosures most pertinently reflect that "*[s]uitable cryoprotectants structure water molecules* such that the freezing point is reduced and/or the rate of cooling necessary to achieve the vitreous phase is reduced." Ex. 1004, 11:55–58 (emphasis added). Similarly: "*The action of*

glycerol and other small polar compounds has been interpreted as penetrating and exerting colligative action within the cells," such that "the colligative action of the penetrating compounds *maintains water in the liquid state* at temperatures below 0°C.," the freezing point of water. *Id.* at 15:11–22 (emphases added). These disclosures indicate at least a portion of the cryoprotectant that penetrates into the tissue matrix will maintain water in the liquid state during Livesey's freezing step following the cryopreservation step, to help prevent the formation of ice which can damage the tissue. *See id.* at 11:32–35, 15:20–30, 17:10–25, 17:47–53.

Reading Livesey as a whole, we find that the cryoprotectant dehydrates the tissue by replacing *some of* the free and loosely bound water in the matrix. At the same time, the cryoprotectant *also* preserves *other* water in the matrix in a liquid state during the freezing step. These actions combine to help protect the tissue from damage during the freezing step, by reducing and controlling ice crystal formation during the freezing step. The disclosed actions of the cryoprotectant (replacing some water in the matrix, and controlling ice formation by water that remains) are not mutually exclusive. Claim 1 does not require anything more, or different.

Our findings are not inconsistent with Livesey's additional disclosure of drying the graft after freezing the graft. *See, e.g.*, Ex. 1004, Abstract (stating Livesey's "method includes the steps of . . . treatment with a cryoprotectant solution followed by freezing, drying . . . "); Ex. 2016 ¶¶ 85–87, 139–142, 211 (discussing various disclosures of Livesey relating to the post-freeze drying step). Livesey's cryoprotectant preserves some (but not all) of the water in a liquid state during the freezing step, which may then be removed by Livesey's post-freeze drying step. Moreover, as

Petitioner points out, the '420 patent itself discloses processes that involve freeze-drying after plasticization, and claim 1 does not preclude freeze-drying after plasticization. *See* Ex. 1002, 10:24–46, 23:40–41, 24:26–27, 24:35–41; Pet. Reply 19–20; Dec. Inst. 25–26. Thus, we are not persuaded by Patent Owner's contention that the drying step of a free-drying process is necessarily inconsistent with plasticization of the graft before the freeze-drying.

Patent Owner finally contends Dr. McQuillan's testimony is deficient because he opines only that Livesey's cryoprotectant replaces "free *or* loosely bound water," not that the cryoprotectant would replace *both* kinds of water, as required by claim 1. PO Resp. 36–37 (citing Ex. 1034 ¶ 62). However, we agree with Petitioner's rebuttal that Dr. McQuillan's original declaration testimony, when read as a whole, properly addresses this claim requirement. *See* Pet. Reply 17; Ex. 1045 ¶ 37 n.5; Ex. 1034 ¶¶ 62, 377, 290.

Thus, we find Livesey discloses its cryoprotectants include plasticizers (such as glycerol) which replace free and loosely bound water in the tissue matrix of Livesey's grafts.

(2) Whether Livesey Discloses that Mechanical Properties, Including Material, Physical, and Use Properties, Are Similar to Normal Hydrated Tissue, and Whether Livesey Discloses that the Native Orientation of Collagen Fibers is Maintained

For the following reasons, we find Livesey discloses that the mechanical properties, including material, physical, and use properties, of its cryopreserved tissue grafts are similar to normal hydrated tissue, and that the

native orientation of the collagen fibers is not altered by cryopreservation, as Petitioner contends.

Livesey correspondingly describes that "analysis of the end product by light and electron microscopy has demonstrated it to be structurally intact with normal collagen banding and the presence of collagen bundles in the matrix of the dermis and with structural preservation of the lamina densa and anchoring fibrils of basement membrane complex." Ex. 1004, 25:12–17; *see* Pet. 17–18, 43, 44–45, 46, 49. Further, "degradation of the basement membrane complex is avoided and the structural integrity of the matrix is maintained including collagen fibers and elastin" by Livesey's pre-cryopreservation cleaning process. Ex. 1004, 5:1–14; *see* Pet. 43, 44–45, 46, 49. Thus, Livesey's method "attempts to cool and store biological samples without causing structural and functional damage." Ex. 1004, 14:59–63; Ex. 1034 ¶¶ 72, 79.

We credit Dr. McQuillan's testimony that an ordinarily skilled artisan would understand these disclosures to reflect that "the native orientation of the collagen fibers and the mechanical properties of the soft tissue are maintained." Ex. 1034 ¶ 65; *id.* ¶¶ 71–73, 78–81, 247, 250–251. For example, Dr. McQuillan states "anchoring fibrils are more difficult to preserve than collagen fibrils," so an ordinarily skilled artisan "would recognize that retaining these structural elements as described in Livesey is a sensitive surrogate for maintaining the overall structural integrity of the internal matrix," including the native orientation of collagen fibers. *Id.* ¶ 73. Further, "the functioning of [a] soft tissue graft is highly dependent on the structure of the soft tissue graft and, therefore, where the structure of a soft

tissue graft is maintained, the function would be maintained as well." *Id.* ¶ 81.

We have considered Patent Owner's counter-arguments, but we do not find them persuasive. *See* PO Resp. 34, 38–42; Ex. 2016 ¶¶ 212–216. First, Dr. Kaplan acknowledges Livesey's statement that the cryopreserved tissue is "structurally intact with normal collagen banding" (Ex. 1004, 25:12–17), but concludes this is not sufficient to satisfy claim 1. Ex. 2016 ¶ 213; PO Resp. 39. In support, Dr. Kaplan states: "Collagen banding is a pattern characteristic of *an assembled [individual] collagen fiber*," whereas claim 1 is directed to "the structure of a collection of several collagen fibers" which is what determines whether the tissue matrix structure and the resulting mechanical properties have been preserved. Ex. 2016 ¶¶ 147, 213 (citing Ex. 2018, 4); *id.* ¶¶ 34–36 (discussing structure of "collagen bundles" and "collagen fibers" in tissue matrix); PO Resp. 4–5, 39–40.

The foregoing testimony does not distinguish persuasively between the "normal collagen banding" seen in Livesey's cryopreserved tissue (Ex. 1004, 25:12–17) and maintaining the native orientation of collagen fibers as required by claim 1. Livesey focuses specifically on preserving the collagen structure in the tissue graft. *See, e.g.*, Ex. 1004, Abstract ("A method for processing and preserving an acellular collagen-based tissue matrix for transplantation is disclosed."), 1:15–30 (indicating the field of Livesey's invention is to preserve collagen-based tissues for transplantation, including "a selectively preserved extracellular protein matrix . . . made up of collagen and other proteins" to provide a structural template for population with new viable cells within the host), 14:36–63.

We find Dr. Kaplan's testimony attempting to differentiate between collagen banding or bundles on the one hand, and the orientation of collagen fibers on the other hand, to be confusing, undeveloped, and unsupported by citation to evidence. *See* Ex. 2016 ¶¶ 147, 213. Dr. Kaplan does cite Exhibit 2018, page 4, as part of his testimony, but he does not explain how Exhibit 2018 supports his testimony, and we are unable to draw the connection ourselves. *See id.* We further credit Dr. McQuillan's rebuttal testimony that "if the collagen is damaged such that it is no longer similar to normal hydrated tissue, the damage would be apparent in Livesey's light microscopy analysis," and "[i]f the orientation of collagen fibers is altered, this will be observed by changes in collagen bundles." Ex. 1045 ¶ 46; Pet. Reply 18.

Dr. Kaplan secondly takes issue with Dr. McQuillan's testimony that Livesey's "structural preservation of the . . . anchoring fibrils of basement membrane complex" (Ex. 1004, 25:12–17) is a sensitive surrogate for maintaining the native orientation of collagen fibers. Ex. 2016 ¶¶ 148, 214; PO Resp. 40–41. Dr. Kaplan states "the basement membrane complex is only a portion of the dermis layer of the skin," so "information regarding the basement membrane alone cannot inform a POSA about the state of the entire dermal matrix." Ex. 2016 ¶ 214 (citing Ex. 2041, 46, 47); PO Resp. 40–41.

We find Dr. McQuillan's testimony in this regard is somewhat overstated, in that he does not provide evidence that anchoring fibrils are more difficult to preserve than collagen fibrils. Ex. 1034 ¶ 73; Ex. 1045 ¶ 47; Pet Reply 18. Nonetheless, Livesey's disclosure that its cryopreservation process structurally preserves the lamina densa and

anchoring fibrils is consistent with, and does support if not as strongly as Dr. McQuillan indicates, our finding that Livesey's cryopreservation process also maintains the native orientation of collagen fibers in the tissue matrix.

Dr. Kaplan thirdly takes issue with Livesey's imaging methods, which he describes as "zoom[ing] in with an electron microscope [to] view[] a single point of the tissue," whereas the claimed invention requires "the internal matrix must remain unaltered across the entire tissue to maintain mechanical properties that are similar to normal hydrated tissue." Ex. 2016 ¶¶ 149, 215 (citing Ex. 2042, 477); *see* PO Resp. 41; Sur-reply 16–17. According to Dr. Kaplan, determining Livesey's cryopreserved tissue is "plasticized" as required by claim 1 requires more than viewing the tissue under a microscope, "such as through mechanical testing." Ex. 2016 ¶¶ 150, 215; *see* PO Resp. 41. Dr. Kaplan testifies that the stress testing of Livesey's Example 4 is the only such testing reported in Livesey, and this testing indicates the tissue's physical properties are "changed as a result of the freeze-drying and rehydration." Ex. 2016 ¶¶ 150, 216; Ex. 1004, 28:8–36, 28:52–53 (stating Livesey's cryopreserved, freeze-dried, and rehydrated grafts "w[ere] found to be able to withstand greater stress load than control samples"); *see* PO Resp. 41–42.

We find the foregoing testimony unpersuasive because it is inconsistent with Livesey's disclosure. Livesey concludes that microscopy "[a]nalysis . . . has demonstrated" the cryopreserved tissue to be structurally intact with normal collagen banding and other structural preservations. Ex. 1004, 25:12–17. We credit Dr. McQuillan's reply testimony that this disclosure reflects more than zooming in on a single point of the tissue matrix, as Dr. Kaplan would have it, and instead reflects "assessment across

multiple fields of tissue samples" in order to reach the disclosed conclusion. Ex. 1045 ¶ 48; Pet. Reply 18–19.

For all of the foregoing reasons, we find Livesey's cryopreservation process does not alter the native orientation of collagen fibers in the graft's tissue. Next, Dr. McQuillan and Dr. Kaplan agree that preserving the native orientation of collagen fibers is a crucial factor when ensuring that the mechanical properties of the graft, including material, physical, and use properties, are similar to normal hydrated tissue. Dr. McQuillan testifies that "the functioning of [a] soft tissue graft is highly dependent on the structure of the soft tissue graft and, therefore, where the structure of a soft tissue graft is maintained, the function would be maintained as well." Ex. 1034 ¶ 81. Dr. McQuillan further testifies Livesey's disclosure reflects that "the native orientation of the collagen fibers and the mechanical properties of the soft tissue are maintained." *Id.* ¶ 65; *id.* ¶¶ 71–73, 78–81, 247, 250–251. Dr. Kaplan similarly testifies that "[t]he structural hierarchy and the precise orientation and organization of the collagen chains is important in providing the properties of the tissue" such that an "intact, hierarchical structure defines the material, physical, and use features of that tissue." Ex. 2016 ¶¶ 35–36.

Livesey's disclosure is consistent with this testimony from the technical experts. Livesey discloses "incubat[ing]" soft tissue samples in glycerol, which is the same material disclosed by both Walker and the '420 patent as resulting in tissue plasticization when tissue is soaked in the composition. *See* Ex. 1004, 5:27–28, 11:17–18, 11:49–51, 12:31–33; Ex. 1002, 7:52–55. As discussed above with respect to Walker, it is unclear how or why subjecting the same materials (soft tissue) to the same

composition (glycerol) as part of the same process (incubation/soaking) would not result in the same product, i.e., a tissue graft with mechanical properties being similar to those of natural tissue. *See supra* Section IV.C.3(b); Ex. 1034 ¶ 64, 72, 79; Ex. 1045 ¶¶ 34–35, 37.

Patent Owner's rebuttal to the foregoing consideration directs us to Dr. Kaplan's testimony that Livesey provides stress test results of the tissue disclosed in Example 4, which reflect that the tissue's physical properties are "changed as a result of the freeze-drying and rehydration." Ex. 2016 ¶¶ 150, 216. In particular, Livesey indicates the cryopreserved, freeze-dried, and rehydrated grafts "w[ere] found to be able to withstand greater stress load than control samples." Ex. 1004, 28:8–36, 28:52–53. But, the issue here is whether Livesey's cryopreservation process — which Petitioner equates to the plasticization required by claim 1 — leads to the mechanical properties of the graft being similar to normal hydrated tissue. The testing of Example 4 instead evaluates samples that have been cryopreserved, *and additionally* freeze-dried and rehydrated. This testing therefore is not a fair analysis of whether Livesey's cryopreservation satisfies the plasticization requirements of claim 1.[16] Also, as Petitioner points out in reply, Livesey suggests that other Examples function in the same way as natural tissue, such as by supporting cell growth within the tissue graft. *See* Ex. 1004,

[16] The microscopy analysis that we cite above also was applied to cryopreserved, freeze-dried, and rehydrated grafts. *See* Ex. 1004, 24:6–29 (cryopreservation), 24:30–64 (freeze-drying), 25:4–11 (storage and rehydration), 25:12–17 (microscopy analysis of "the end product"). However, we rely on the microscopy analysis as support for finding that the native orientation of the collagen fibers is maintained, which holds true for each of the steps in the process if it holds true for the end product.

25:18–42 (Example 1), 26:51–54 (Example 2); Pet. Reply 17–18. Thus, Dr. Kaplan does not explain persuasively how or why Livesey's incubating of the same material within the same composition would not result in the same product, as in Walker and the '420 patent.

Patent Owner further attacks Petitioner's reliance on Livesey's Examples, on the basis that Dr. McQuillan admits the cryoprotectants used in the Examples are not plasticizers. *See* Sur-reply 13 (citing Ex. 1045 ¶ 35). Patent Owner, however, mischaracterizes Dr. McQuillan's testimony. Dr. McQuillan pertinently states only that: "Although not all of the cryoprotectants disclosed in Livesey are plasticizers as I understand that term to be used in the ['420 patent] (e.g., sucrose, dextran), glycerol certainly is." Ex. 1045 ¶ 35. Moreover, we disagree with Dr. McQuillan's testimony that sucrose is not a plasticizer, because the '420 patent expressly identifies sucrose as a plasticizer, along with propylene glycol. Ex. 1002, 7:52–56. The cryopreservation solutions used in each of Livesey's Examples all include sucrose, propylene glycol, or both. Ex. 1004, 24:7–18 (Example 1), 26:17–27 (Example 2), 27:28–34 (Example 3), 28:8–13 (Example 4), 29:40–47 (Example 5). Thus, we do not agree with Patent Owner's argument that Livesey's Examples are irrelevant here.

Finally, although not addressed by the parties in post-institution briefing, we note that during prosecution of the '420 patent, the applicant successfully argued claim 1 was different from Livesey. *See* Pet. 1–3, 7–9; Ex. 1034 ¶¶ 66–81. The Examiner rejected several claims as anticipated by or as obvious over Livesey. *See* Ex. 1024, 3–5. The applicant then argued Livesey failed to disclose or suggest maintaining the native orientation of collagen fibers. *See* Ex. 1025, 7–9. The applicant particularly argued

Livesey's disclosures indicating the tissue is "not damaged" were not sufficient to disclose the claimed invention, because "the orientation of collagen fibers may be altered without damaging the structural integrity of the collagen matrix" so the lack of damage "does not rule out the possibility of changes to collagen fiber orientation." *Id.* (citing Ex. 1004, 5:1–6, 7:36–51). The Examiner then allowed the claims "in light of the totality of Application's remarks." Ex. 1026, 2.

However, as discussed in detail above, Petitioner here relies on several other disclosures in Livesey, which are not addressed in the prosecution history record, and which specifically discuss preserving the native orientation of collagen fibers in the tissue matrix. Thus, the Examiner's reason for allowing the '420 patent over Livesey has little bearing on the merits of the issues presented in this proceeding.

For the foregoing reasons, we find Livesey discloses that the mechanical properties, including material, physical, and use properties, of its cryopreserved tissue grafts are similar to normal hydrated tissue, and that the native orientation of the collagen fibers is not altered by the cryopreservation.

c) Conclusion Regarding Claim 1

For the reasons discussed above, we determine Petitioner has demonstrated by a preponderance of the evidence that Livesey anticipates claim 1.

3. Claims 2 and 16

For its argument that Livesey teaches a graft impregnated with one or more plasticizers as recited in independent claims 2 and 16, Petitioner relies

on its arguments for claim 1 that Livesey discloses one or more plasticizers contained in the internal matrix. *See* Pet. 50 (claim 2), 55 (claim 16). Patent Owner argues Livesey's grafts "cannot be 'filled' by plasticizer as required by the definition of 'impregnating,'" because "Livesey does not disclose replacing the free or loosely bound waters of hydration . . . with a plasticizer," as discussed above. PO Resp. 38 (citing Ex. 2016 ¶ 217); *see also* Tr. 75:7–8 (Patent Owner's counsel stating: "I believe for the most part the parties simply relied on their arguments for [plasticized soft tissue graft] for whether impregnated/impregnating rises or falls."). For the reasons discussed above in Section IV.E.2(b), we are not persuaded by Patent Owner's argument, and we find Petitioner has shown Livesey describes a "plasticized" graft.

After considering the evidence and arguments of record, we find Petitioner has shown Livesey discloses each limitation in claims 2 and 16. *See* Pet. 50, 53–57. Apart from the "impregnated" limitation, Patent Owner does not present any argument for claims 2 and 16 separate from its arguments regarding claim 1, which we have already discussed above. We determine Petitioner has demonstrated by a preponderance of the evidence that Livesey anticipates claim 2 and 16.

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

Petitioner identifies disclosure in Livesey that discloses each limitation in claims 3, 6, 8, 9, 11–14, 17, 18, 24, 25, 28, 29, 31, 32, and 34–36. *See* Pet. 51–53, 57–59. Patent Owner does not present any argument for these claims other than what we have already considered with respect to claim 1. *See LG Elecs.,* 759 F. App'x at 925 ("The Board is 'not required to

address undisputed matters' or arguments about limitations with which it was never presented."); *Papst*, 924 F.3d at 1250; *Bradium*, 923 F.3d at 1048.

After considering the evidence and arguments of record, we determine Petitioner has demonstrated by a preponderance of the evidence that Livesey anticipates these claims. Specifically concerning dependent claim 14, which recites that the graft "has mechanical properties approximating mechanical properties of natural soft tissue" (Ex. 1002, 25:18–21), Petitioner relies on its arguments concerning a similar recitation in the claim construction of "plasticized," and considered above. *See* Pet. 53. Patent Owner, similarly, relies on its same arguments. *See* PO Resp. 38–42. Thus, for claim 14, we rely on the analysis provided above in connection with claim 1.

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.[17] Pet. 5, 59–61. Having determined Petitioner has demonstrated by a preponderance of the evidence that these claims are anticipated by Livesey, we need not reach the question of whether these same claims also would have been obvious based on Livesey. *See Boston Scientific*, 809 Fed. Appx. at 990; *Beloit*, 742 F.2d at 1423. Thus, we do not reach Petitioner's contention that these claims are unpatentable as having been obvious over Livesey.

[17] We noted in the Institution Decision that there is some confusion in the Petition as to whether claim 3 is part of this ground. *See* Inst. Dec. 5 n.4, 33; Pet. 5, 59–61. Patent Owner agreed there is confusion, but nonetheless addressed claim 3 as part of this ground. *See* PO Resp. 42 n.9. We therefore continue to treat claim 3 as subject to this ground.

G. Obviousness over Walker or Livesey, and Werner

Petitioner asserts claim 4 of the '420 patent is unpatentable under 35 U.S.C. § 103 as having been obvious over either Walker or Livesey, in view of Werner. Pet. 5, 61–63. We determine Petitioner has not demonstrated, by a preponderance of the evidence, that claim 4 would have been obvious under either theory. We first summarize the Werner disclosure, then we address Petitioner's and Patent Owner's contentions as to obviousness.

1. Werner Disclosure

Werner discloses methods of manufacturing "sclero protein transplants." Ex. 1006, 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[18] 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. Claim 4

Petitioner provides arguments and evidence, including the testimony of Dr. McQuillan, in support of contending claim 4 would have been obvious. Pet. 61–63; Ex. 1034 ¶¶ 291–297. Patent Owner provides arguments and evidence in opposition, including the technical testimony of Dr. Kaplan, and evidence of objective indicia of nonobviousness as

[18] As mentioned above, "glycerin" and "glycerol" refer to the same compound. *See* Ex. 1034 ¶ 37; Ex. 1002, 5:32 (referring to "glycerol (glycerin USP)").

explained by the testimony of Dr. Kaplan and Mr. Sharma. PO Resp. 43–64; Ex. 2016 ¶¶ 88, 225–238, 300–328.

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 argues Walker and Livesey each separately disclose the limitations of the claims from which claim 4 depends, and Petitioner relies on Werner to disclose the additional limitation recited in claim 4. *See* Pet. 61. In particular, Petitioner asserts Werner discloses that treating a tissue with glycerol increases biological stability, and that no rehydration of the resulting product is necessary before transplantation. *Id.* (citing Ex. 1006, Abstract, 2:37–41). Petitioner contends an ordinarily skilled artisan:

> would have recognized an advantage to be achieved by adapting Werner's teaching of the use of glycerol for use in the method of either Walker or Livesey; namely, that no rehydration of the tissue product is necessary before implantation and would have had a reasonable expectation of success in that adaptation.

Id. at 61–62 (citing Ex. 1034 ¶¶ 174–175, 292–293, 295–296); *see also* Pet. Reply 22–23 (citing Ex. 1045 ¶ 65).

a) Whether the Combination Teaches the Individual Limitations

We find Petitioner has shown Werner teaches a soft tissue graft suitable for transplantation without rehydration. *See* Pet. 61; Ex. 1006, 2:39–40. Indeed, Patent Owner does not dispute that point. As discussed above, we find Petitioner has shown Walker and Livesey both disclose, separately from each other, the limitations of the claims from which claim 4 depends. *See supra* § IV.C.3,4,7 & IV.E.2–4. Thus, Petitioner has shown

the proposed combination of Walker or Livesey, and Werner, teaches every individual limitation of claim 4.

b) Motivation to Combine and Reasonable Expectation of Success

We further find Petitioner has articulated a reason to combine that is rational, but only moderately persuasive. Petitioner's proposed combination is to follow the same process steps as described in Walker or Livesey, but to follow Werner's teaching to implant the graft into a patient without first rehydrating it. Pet. 61–62. Patent Owner argues, and Dr. Kaplan testifies, that it is unclear how Petitioner proposes to combine the references, *see* PO Resp. 44, 47–48; Ex. 2016 ¶¶ 227, 231, but we disagree with this criticism. In our view, the manner in which Petitioner proposes to combine the references is apparent from the Petition, has been consistent throughout this proceeding, and is how we summarized the proposed combination in our Institution Decision. *See* Pet. 61–62; Pet. Reply 22–23; Tr. 32:12–33:10; Inst. Dec. 34–35.

Petitioner contends an ordinarily skilled artisan would have been motivated to omit rehydration in Walker or Livesey in order "to simplify the processing of the soft tissue graft during implantation." Pet. 62 (citing Ex. 1034 ¶¶ 176–180, 292–293, 295–296); Pet. Reply 22–23. This argument is sensible in the abstract, but its persuasiveness depends on the extent to which an ordinarily skilled artisan would have expected success in omitting rehydration from Walker's or Livesey's process. And we find only moderately persuasive Petitioner's argument that an ordinarily skilled artisan would have had a reasonable expectation of success in making the proposed combination. *See* Pet. 62 (citing Ex. 1034 ¶¶ 176–180, 292–297).

Although Petitioner notes that Walker describes rehydration as optional, *see* Pet. Reply 22 (citing Ex. 1005, 5:14–15), Patent Owner points out that Walker's examples include rehydration and Walker explains the benefits rehydration provides. *See* PO Resp. 47; Ex. 1005, 5:25–27, 9:25–29, 18:7–15, 19:2–3, 19:27–28, 21:1–3, 26:26–29. In describing Example 5, Walker discloses "[t]he 50% glycerol samples with no humidification appeared dry and felt dry to the touch, though they were not rigid or too dehydrated. . . . Increasing periods of rehydration improved the appearance of 50–70% glycerol samples, they also felt softer and more natural." Ex. 1005, 26:19–29. Walker then explains "[p]ost sterili[z]ation humidification allows for a more fully hydrated end product." *Id.* at 27:4–5. In our view, although Walker states in its basic, high level description of the process that "humidifying the sterili[z]ing material" is "optional[]," *id.* at 5:14–15, Walker's disclosure as a whole casts some doubt on Petitioner's contention that an ordinarily skilled artisan reviewing Walker and Werner would have reasonably expected success in simply carrying out Walker's process but omitting rehydration, as Petitioner proposes.

Similarly, Petitioner's showing that an ordinarily skilled artisan would have had a reasonable expectation of success in combining Livesey and Werner in the proposed manner is, at best, only moderately persuasive. Petitioner relies on Dr. McQuillan's testimony, but neither Dr. McQuillan nor Petitioner explains *why* an ordinarily skilled artisan would have expected success in simply omitting rehydration from Livesey's process based on Werner's teaching. *See* Pet. 62; Ex. 1034 ¶¶ 183–184, 295–297. And Werner's criticism of the biological stability of products obtained through freeze-drying calls into question the extent to which an ordinarily skilled

artisan would have expected success in applying Werner's teachings to Livesey's processes, which include freeze-drying and then rehydrating. *See* PO Resp. 50–51 (citing Ex. 1006, 1:33–38); Ex. 1004, Abstract.

c) Objective Indicia of Nonobviousness

(1) Nexus

Turning to objective indicia of nonobviousness, we find Patent Owner has shown a nexus between the objective indicia of nonobviousness and claim 4. As noted above, a presumption of nexus applies "when the patentee shows that the asserted objective evidence is tied to a specific product and that product 'embodies the claimed features, and is coextensive with them.'" *Lectrosonics*, Paper 33, 32 (quoting *Fox Factory*, 944 F.3d at 1373). We find Patent Owner has established entitlement to this presumption of nexus based on its persuasive evidence that claim 4 is embodied by and coextensive with three of its products, DermACELL, ArthroFlex, and OrACELL, as well as three of LifeCell's products, Strattice, Conexa, and AlloDerm RTU. *See* PO Resp. 53–54. That evidence includes the testimony of Dr. Kaplan, which is supported by documentary product information and claim charts comparing the products to each limitation of claim 4, as well as the judgment from the LifeCell Litigation determining that the LifeCell products infringe claim 4 of the '200 patent. *See* Ex. 2016 ¶¶ 303–305 (testimony of Dr. Kaplan); Ex. 2076, 1–20, 28–29 (Dr. Kaplan's claim charts for LifeNet products); Ex. 2073, 1–5 (Dr. Kaplan's claim charts for LifeCell products, comparing claims 1–4 of '420 patent with infringed claims 1 and 4 of '200 patent); Ex. 1039, 1, 3–4 (jury verdict in LifeCell

Litigation); Ex. 2002, 4 (Federal Circuit's affirmance of judgment in LifeCell Litigation).

Aside from evidence supporting a presumption of nexus, Patent Owner also provides direct evidence of nexus. Patent Owner points out that product literature and marketing materials for the embodying products emphasize that the grafts are ready to use upon opening from the package without rehydration. *See* PO Resp. 63–64; Ex. 2016 ¶¶ 306–312; Ex. 2050, 1; Ex. 2051, 3; Ex. 2054, 2; Ex. 2072, 1; Ex. 2081, 1; Ex. 2084, 7. As Dr. Kaplan explains, a graft that is "'ready to use' means that it obviates the need for time-consuming preparation steps, such as thawing and re-hydrating, that used to be necessary to achieve the physical properties that are required for implantation." Ex. 2016 ¶ 307 (citing Ex. 2066). In this regard, we find compelling Patent Owner's point that "[t]he fact alone LifeCell named the plasticized version of AlloDerm RTM as AlloDerm 'Ready To Use' — as opposed to some other feature — firmly establishes the importance of the challenged claims' specific benefits." PO Resp. 64 (citing Ex. 2066, 1).

Petitioner does not provide any evidence or argument to challenge Patent Owner's showing that LifeNet's DermACELL, ArthroFlex, and OrACELL products, as well as LifeCell's Strattice, Conexa, and AlloDerm RTU products, all embody claim 4. *See* Pet. Reply 27–29, 31–34. Instead, Petitioner attacks the co-extensiveness of the secondary considerations evidence and the claim, arguing that another product not covered by the claim provides the features on which Patent Owner relies as objective indicia. *See* Pet. Reply 28, 31–32. In particular, Petitioner argues that its product, Fortiva, is storable at room temperature and ready to use out of the

package, but it is not encompassed by claim 4 because it has no plasticizer. *Id.* at 28 (citing Ex. 1054 ¶¶ 52–54, Ex. G at 2). The factual predicate for this argument has not been established; the question of whether Fortiva is encompassed by claim 4 is disputed and remains the subject of ongoing litigation in district court. *See* Sur-reply 23–24. And even assuming *arguendo* that Fortiva does not embody claim 4, it is unclear why a product launched some fifteen years after the date of the invention (*see* Pet. Reply 28 ("Fortiva was commercially launched in 2013")) that achieves the advantages of a claimed invention without embodying the claim undermines nexus for products that undisputedly did embody the claim in the years before launch of the later product. Petitioner does not explain why the ability to eventually create a non-infringing alternative cuts against the conclusion that previous products that used the patented technology were successful because of the merits of the invention.

Petitioner also counters Patent Owner's nexus argument on the ground that the merits of the claimed invention were in the prior art because Werner discloses that no rehydration is necessary. Pet. Reply 29 (citing Ex. 1034 ¶ 94; Ex. 1006, 2:37–40). But Petitioner does not contend that Werner discloses all the features of claim 4, including the limitations of the claims from which it depends. Nexus is not disproved simply because all of the features of claim 4 were individually known in various prior art references. *See Henny Penny Corp. v. Frymaster LLC*, 938 F.3d 1324, 1333 (Fed. Cir. 2019) ("It is true . . . that 'the identified objective indicia must be directed to what was not known in the prior art. But . . . 'what was not known in the prior art . . . may well be the novel combination or arrangement of known individual elements.'") (citation omitted).

Petitioner further argues that the success of LifeNet's and LifeCell's embodying products included other benefits and features beyond being ready to use without rehydration and storage stability at room temperature, so any commercial success of those products may have been due to the other features. Pet. Reply 33–34. But Petitioner does not offer any evidence to establish that factors other than the merits of the invention drove the success of the embodying products. *See id.*; *see also WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1329 (Fed. Cir. 2016) ("The presumption of nexus is rebuttable: a patent challenger may respond by presenting evidence that shows the proffered objective evidence was 'due to extraneous factors other than the patented invention.' . . . However, a patent challenger cannot successfully rebut the presumption with argument alone — it must present evidence.") (citations omitted). In addition, Patent Owner points out that "the displacement of AlloDerm RTM by AlloDerm RTU effectively neutralized all other factors . . . aside from the merits of the claimed invention because the two products are the same in all other respects." Sur-reply 26 (citing Ex. 1056, 126:5–21).

For the foregoing reasons, we find Patent Owner has shown a nexus between the objective indicia of nonobviousness and claim 4.

(2) Long-Felt Need

"Evidence of a long-felt but unresolved need can weigh in favor of the non-obviousness of an invention because it is reasonable to infer the need would not have persisted had the solution been obvious." *Apple Inc. v. Samsung Elecs. Co.*, 839 F.3d 1034, 1056 (Fed. Cir. 2016) (en banc).

Patent Owner argues that before the '420 patent, surgeons were dissatisfied with soft tissue graft offerings because they required lengthy preparation prior to use. PO Resp. 54–55. According to Patent Owner, industry participants like LifeCell recognized that a ready-to-use graft was needed to reduce preparation time and simplify inventory management. *Id.* at 55. Patent Owner contends that although LifeCell identified this unmet need by the early 2000's, it did not release its first plasticized soft tissue graft product until 2008. *Id.* at 55–56. Petitioner responds that Patent Owner's evidence of long-felt need post-dates the invention and is, therefore, irrelevant. Pet. Reply 29–30.

We agree with Petitioner that Patent Owner's evidence does not establish that the alleged need was long-felt and unmet in 1998, the claimed date of the invention. *See* Ex. 1002, Abstract, 1:5–11 (claiming the benefit of the filing date of an application filed June 30, 1998); *see also* Paper 62, 3 (Patent Owner referring to June 30, 1998 as "the critical date in this case"). The Federal Circuit has explained that "we look to the filing date of the challenged invention to assess the presence of a long-felt and unmet need." *Procter & Gamble Co. v. Teva Pharms. USA, Inc.*, 566 F.3d 989, 998 (Fed. Cir. 2009); *see also Perfect Web Techs., Inc. v. InfoUSA, Inc.*, 587 F.3d 1324, 1332 (Fed. Cir. 2009) ("Evidence that an invention satisfied a long-felt and unmet need that existed on the patent's filing date is a secondary consideration of nonobviousness."). Because Patent Owner's proffered objective indicia evidence is dated in the early 2000s and after, subsequent to the priority date in 1998, it cannot establish the existence of a *long felt* need as of the priority date.

Accordingly, we give no weight to Patent Owner's evidence of long-felt but unmet need.

(3) Failure of Others

"Evidence that others tried but failed to develop a claimed invention may carry significant weight in an obviousness inquiry." *In re Cyclobenzaprine Hydrocholride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1081 (Fed. Cir. 2012). "[A]lthough long-felt need is closely related to failure of others, these considerations are distinct and we treat each separately." *Millennium Pharms., Inc. v. Sandoz Inc.*, 862 F.3d 1356, 1369 n.5 (Fed. Cir. 2017).

Patent Owner argues "LifeCell repeatedly tried and failed over the course of a decade to develop a ready-to-use plasticized version of LifeCell's legacy freeze-dried AlloDerm RTM product." PO Resp. 57 (citing Ex. 2016 ¶¶ 318–319; Ex. 2049, 915:19–917:25). Patent Owner urges that "[t]hese repeated failures by LifeCell's highly trained, senior scientists over an extended period militate against the obviousness of the challenged claims." *Id.* (citing Ex. 2016 ¶ 320). Although Patent Owner's characterizations appear to somewhat overstate the evidence of LifeCell's efforts and failures, we nevertheless find Patent Owner's evidence of LifeCell's activities in attempting to develop a ready-to-use graft provides some evidence weighing toward nonobviousness.

Patent Owner's argument and Dr. Kaplan's testimony regarding failure of others is based on the testimony during the LifeCell Litigation of Dr. Nathaniel Bachrach, a LifeCell scientist. PO Resp. 57; Ex. 2016 ¶¶ 318–319. Dr. Bachrach testified that LifeCell attempted to create a

"glycerolized AlloDerm product" in the early 2000's. Ex. 2049, 915:19–917:23. LifeCell's initial approach was to remove as much water as possible in the tissue by replacing it with glycerol, but this low-water, high glycerol product "didn't make it" because "with all the glycerol in the product, it didn't have the handling attributes, and the time for preparation was just way too long." *Id.* at 917:2–17. LifeCell abandoned that approach in 2005 and later used a different approach for its Strattice, AlloDerm RTU, and Conexa products that involved "us[ing] components in a preservation solution to protect against the damages of water." *Id.* at 918:1–15.

We are persuaded by Patent Owner and Dr. Kaplan that LifeCell's initial failure to produce a suitable ready-to-use plasticized soft tissue graft to replace its existing, freeze-dried AlloDerm product tends to show the nonobviousness of a graft as recited in claim 4. We note that Patent Owner's evidence of failure of others is somewhat narrow in that it is limited to one entity and one failed approach, and that LifeCell did ultimately succeed in producing ready-to-use grafts having the desired characteristics. *Id.* at 918:1–15. However, LifeCell's position as an industry leader and the owner of the Livesey patent provides additional heft to Patent Owner's nonobviousness argument. *See* PO Resp. 57–58 (citing Ex. 2134, 1–3); *see also* Ex. 2125 ¶ 20 (Mr. Sharma testifying that "LifeCell has been the leading manufacturer of soft tissue graft products used in dental, chronic wound, and other soft tissue repair procedures since it launched AlloDerm® RTM in 1994").

Petitioner's arguments regarding failure of others are the same as its arguments regarding long-felt need: that the evidence is only relevant if it pre-dates the invention. *See* Pet. Reply 29–30. But the case law Petitioner

cites stands for the proposition that failure of others cannot be established where the evidence fails to indicate that others were aware of the problem solved by the patent, and does not support that evidence of failure of others must pre-date the invention. *See In re Gershon*, 372 F.2d 535, 538 (CCPA 1967). We are not aware of other authority limiting the scope of evidence of failure of others to the pre-invention time frame. Nor do we see any reason why failure of others *before* the invention would weigh toward nonobviousness, but failure of others *after* the invention would not. In general, scientific knowledge and technological skill advances over time, or at least does not diminish. As a logical matter, then, the failure of others after the time of invention would seem to support nonobviousness to at least the same degree as pre-invention failures of others.

For these reasons, we find Patent Owner's evidence of the failure of others provides some evidence weighing toward nonobviousness.

(4) Industry Adoption

Patent Owner argues freeze-dried grafts dominated the market until plasticized soft tissue grafts were introduced, at which point "competitors moved decisively in their direction." PO Resp. 58. Petitioner responds that "only widespread industry adoption is relevant," and Patent Owner's evidence is limited to LifeCell. Pet. Reply 30 (emphasis omitted).

Petitioner is correct in observing that Patent Owner's industry adoption evidence is focused on LifeCell and, in that respect, is somewhat narrower than a showing that the entire industry changed direction. Still, given the leading role of LifeCell and its soft tissue products in the market, Patent Owner's evidence supports its assertion that the dominant approach

for soft tissue grafts changed after the '420 patent to grafts that were ready-to-use without rehydration. That shift weighs in favor of nonobviousness.

Patent Owner presents unrebutted evidence that LifeCell has been a leading manufacturer of soft tissue graft products since 1994. Sur-reply 29; Ex. 2125 ¶¶ 20, 41. [redacted]. *See* PO Resp. 55 n.10, 59; Ex. 2125 ¶ 20; Ex. 2082, 2; Ex. 2089, 13; Ex. 2086, 18. When LifeCell introduced its ready-to-use Strattice product in 2008, it succeeded beyond internal expectations, accounting for 15% of LifeCell's revenue in the third quarter of 2008. PO Resp. 58–59; Ex. 2068, 5. [redacted] PO Resp. 59; Sur-reply 30; Ex. 2125 ¶ 32; Ex. 2053, 52.

In 2011, based on demand for ready-to-use products, LifeCell accelerated the schedule to release its ready-to-use AlloDerm RTU product. PO Resp. 59; Ex. 2125 ¶ 34; Ex. 2067, 11. [redacted]. PO Resp. 59–60; Ex. 2125 ¶¶ 36–37; Ex. 2065, 15. Mr. Sharma testifies, convincingly, that because AlloDerm RTU had the same features and performance characteristics as AlloDerm RTM, except being ready-to-use, AlloDerm RTU's cannibalization of AlloDerm RTM sales "provides direct economic evidence about the commercial importance of the [ready-to-use]

features made possible by" claim 4. Ex. 2125 ¶ 35. [redacted]. PO Resp. 59; Ex. 2125 ¶ 41. Against this backdrop, we find persuasive Patent Owner's argument that LifeCell's shift to ready-to-use grafts represents a change in the industry. Sur-reply 29–30.

We find Patent Owner's evidence demonstrates the market's preference for, and rapid adoption of, ready-to-use grafts weighs in favor of nonobviousness.

(5) Industry Praise

As instances of industry praise, Patent Owner cites a paper from a 2015 conference in Milan that preferred DermACELL to another product because of DermACELL's "convenience of storage at room temperature and ready to use without needing to be rehydrated or thawed." PO Resp. 60 (quoting Ex. 2131, 2). Patent Owner further cites a 2007 earnings call in which LifeCell reported positive feedback from surgeons who used Strattice. *Id.* at 60–61 (citing Ex. 2064, 3).

We accord little weight to this limited evidence of industry praise. Two instances of praise strikes us as far short of the recognition that one would expect to attend an innovation that significantly changed a segment of medical care, such as Patent Owner's industry adoption and commercial success evidence indicates. Further, a statement on an earnings call reporting positive feedback from unnamed sources provides little basis for evaluation and is promotional in nature — the opposite of the scenario when industry praise is usually deemed informative. *See Apple*, 839 F.3d at 1053 (observing that industry praise weighs against obviousness because

competitors "are not likely to praise an obvious advance over the known art"); *In re Cree*, 818 F.3d 694, 702 (Fed. Cir. 2016) ("While 'praise in the industry for a patented invention, and specifically praise from a competitor tends to "indicate that the invention was not obvious,"' self-serving statements from researchers about their own work do not have the same reliability.") (quoting *Power-One v. Artesyn Techs., Inc.*, 599 F.3d 1343, 1352 (Fed. Cir. 2010)).

Accordingly, we give Patent Owner's industry praise evidence little weight.

(6) Commercial Success

"Demonstrating that an invention has commercial value, that it is commercially successful, weighs in favor of . . . non-obviousness." *WBIP*, 829 F.3d at 1337. Commercial success is "usually shown by significant sales in a relevant market," coupled with a showing "that the successful product is the invention disclosed and claimed in the patent." *Ecolochem, Inc. v. Southern California Edison Co.*, 227 F.3d 1361, 1377 (Fed. Cir. 2000) (finding that patentee's evidence that its invention was practiced at 28 plants and generated $13 million in revenue constituted evidence of commercial success that shifted the burden to the patent challenger to prove that the commercial success was due to other factors extraneous to the patented invention).

Patent Owner presents unrebutted evidence that its products embodying claim 4 yielded [redacted] in revenues from their launch in 2010 through the third quarter of 2019. *See* PO Resp. 62; Ex. 2125 ¶ 26. The average annual growth rates of sales of Patent Owner's embodying

products between 2011 and 2018 was [redacted]. Ex. 2125 ¶ 27. Additionally, Patent Owner presents evidence — again unrebutted — that LifeCell's Strattice and AlloDerm RTU products produced [redacted] of revenue between 2008 and 2013, with an average annual growth rate of [redacted] during those years. PO Resp. 61; Ex. 2125 ¶¶ 29–30. While Patent Owner does not specify what market share these embodying products represent, Patent Owner does show that LifeCell's AlloDerm RTM product had over [redacted] before the embodying products were commercialized, and once the embodying products were introduced, AlloDerm RTU sales quickly displaced the sales of AlloDerm RTM. *See supra* § IV.G.2(c)(4).

Apart from its arguments concerning nexus, which we have discussed above, Petitioner's briefing does not specifically address Patent Owner's commercial success arguments. *See* Pet. Reply 27–34. At the hearing, Petitioner declined to concede that the embodying products have been commercially successful, *see* Tr. 34:7–19, but the evidence and arguments in the record provide no basis to conclude otherwise.

We find Patent Owner's commercial success evidence weighs in favor of nonobviousness.

d) Conclusion Regarding Claim 4

Although Petitioner has shown that the individual limitations of claim 4 (including the limitations in the claims from which it depends) are disclosed by the combination of either Walker or Livesey with Werner, Petitioner's arguments and evidence regarding motivation to combine and reasonable expectation of success are only moderately persuasive. Patent Owner's objective indicia, particularly industry adoption and commercial

success, provide strong evidence of nonobviousness. When considering all of the evidence of obviousness and nonobviousness together (*see Cyclobenzaprine*, 676 F.3d at 1079), we conclude Petitioner has not shown by a preponderance of the evidence that the subject matter of claim 4 would have been obvious over the prior art.

V. SUMMARY OF CONCLUSIONS[19]

In summary, we determine a preponderance of the evidence establishes claims 1–3, 5–18, 20–22, and 24–36, but not claim 4, of the '420 patent are unpatentable, as shown in the following table:

Claims	35 U.S.C. §	Reference(s)	Claims Shown Unpatentable	Claims Not Shown Unpatentable
1–3, 5, 8, 10, 13–18, 20, 21, 24–28, 30, 33–35	102(b)	Walker	1–3, 5, 8, 10, 14–18, 20, 21, 24–28, 30, 33–35	13

[19] Should Patent Owner wish to pursue amendment of the challenged claims in a reissue or reexamination proceeding subsequent to the issuance of this decision, we draw Patent Owner's attention to the April 2019 *Notice Regarding Options for Amendments by Patent Owner Through Reissue or Reexamination During a Pending AIA Trial Proceeding*. *See* 84 Fed. Reg. 16,654 (Apr. 22, 2019). If Patent Owner chooses to file a reissue application or a request for reexamination of the challenged patent, we remind Patent Owner of its continuing obligation to notify the Board of any such related matters in updated mandatory notices. *See* 37 C.F.R. § 42.8(a)(3), (b)(2).

Claims	35 U.S.C. §	Reference(s)	Claims Shown Unpatentable	Claims Not Shown Unpatentable
1–3, 5, 7–11, 13–18, 20–22, 24–31, 33–35	103(a)	Walker[20]	7, 22	9, 11, 29, 31
1–3, 6, 8, 9, 11–14, 16–18, 24, 25, 28, 29, 31, 32, 34–36	102(b)	Livesey	1–3, 6, 8, 9, 11–14, 16–18, 24, 25, 28, 29, 31, 32, 34–36	
1–3, 6, 8, 9, 11–14, 16–18, 24, 25, 28, 29, 31, 32, 34–36	103(a)	Livesey[21]		
4	103(a)	Walker or Livesey, and Werner		4
Overall Outcome			1–3, 5–18, 20–22, 24–36	4

VI. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that claims 1–3, 5–18, 20–22, and 24–36 of the '420 patent have been proven by a preponderance of the evidence to be unpatentable;

[20] As explained above in Section IV.D.2,5, we do not reach this ground as to claims 1–3, 5, 8, 10, 13–18, 20, 21, 24–28, 30, and 33–35.

[21] As explained above in Section IV.F, we do not reach this ground as to any claim.

FURTHER ORDERED that claim 4 of the ’420 patent has not been proven by a preponderance of the evidence to be unpatentable;

FURTHER ORDERED that Petitioner’s Motion to Exclude is denied;

FURTHER ORDERED that Patent Owner’s Motion to Exclude is dismissed as moot;

FURTHER ORDERED that, no later than ten days after the issuance of this Decision, the parties may file a joint motion to seal, explaining why this Decision should remain under seal, and including a redacted version of this Decision that can be made publicly available;

FURTHER ORDERED that this Decision shall remain under seal until any joint motion to seal this Decision is resolved;

FURTHER ORDERED that this Decision shall be made public if, after the expiration of the time for the parties to file a joint motion to seal, no such motion has been filed; and

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

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