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Paper 75
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.

IPR2019-00571
Patent 6,569,200 B2

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

GOODSON, *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

A. Background and Summary

Petitioner RTI Surgical, Inc., filed a Petition (Paper 2, "Pet.") requesting *inter partes* review of claims 1–10, 12, 13, and 15 of U.S. Patent

No. 6,569,200 B2 (Ex. 1001, "the '200 patent"). Patent Owner LifeNet Health filed a Preliminary Response. Paper 9. The record of the preliminary proceeding also included a Reply from Petitioner and a Sur-Reply from Patent Owner. *See* Papers 16, 19. We instituted an *inter partes* review on all claims and all grounds asserted in the Petition. *See* Paper 20 ("Dec. on Inst.").

After institution of trial, Patent Owner filed a Patent Owner Response. Paper 34 ("PO Resp.").[1] Petitioner filed a Reply. Paper 43 ("Pet. Reply"). Patent Owner filed a Sur-Reply. Paper 55 ("Sur-Reply").[2] We held a hearing on May 11, 2020, a transcript of which is included in the record. *See* Paper 74 ("Tr.").

The parties have also filed motions to exclude, which we address below in Section II. For the reasons discussed therein, we deny Petitioner's motion to exclude and dismiss as moot Patent Owner's motion to exclude.

We have authority under 35 U.S.C. § 6. 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 Final Written Decision is issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73.

For the reasons discussed below, we determine that Petitioner has shown by a preponderance of the evidence that claims 1–3, 5–10, 12, 13, and

[1] A public, redacted version of the Patent Owner Response was filed as Paper 32.
[2] A public, redacted version of the Sur-Reply was filed as Paper 56.

15 of the ’200 patent are unpatentable, but Petitioner has not shown by a preponderance of the evidence that claim 4 is unpatentable.

B. Real Parties in Interest

The parties list only themselves as real parties in interest. *See* Pet. 3; Paper 4, 2.

C. Related Matters

Patent Owner asserted the ’200 patent against Petitioner in *LifeNet Health v. RTI Surgical, Inc.*, No. 3:18-cv-817 (M.D. Fla.), filed June 25, 2018. *See* Pet. 3. That case was transferred to another judicial district and is now captioned as *LifeNet Health v. RTI Surgical, Inc.*, No. 1:18-cv-00146-MW-GRJ (N.D. Fla.). *See* Paper 4, 1.

Previously, the ’200 patent was asserted in *LifeNet Health v. LifeCell Corp.*, No. 2:13-cv-486 (E.D. Va.) (“LifeCell Litigation”). In that case, after a two-week trial, a jury found that the accused products infringed the ’200 patent and that the defendant failed to establish the invalidity of the asserted claims, and awarded approximately $35 million in damages. The district court denied the defendant’s post-trial motions, and the Federal Circuit affirmed. *See LifeNet Health v. LifeCell Corp.*, 837 F.3d 1316, 1321 (Fed. Cir. 2016) (Ex. 2002, 6). 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 this Petition were not considered during the trial or appeal of the LifeCell Litigation. *See* Dec. on Inst. 8–10.

Patent Owner also lists two Board proceedings as related: Case IPR2019-00572, which challenges U.S. Patent No. 9,579,420 B2 (Ex. 1002, “the ’420 patent”), and Case IPR2019-00573, which challenges U.S. Patent No. 9,585,986 B2 (Ex. 1003, “the ’986 patent”). *See* Paper 4, 1.

D. The '200 Patent

The '200 patent relates to plasticized tissue grafts. *E.g.*, Ex. 1001, code (54). The '200 patent discloses that "[s]oft tissue products are typically provided as fresh-frozen or freeze-dried," but that "freeze-drying causes grafts to be brittle and typically causes shrinkage where the shrinkage is often not uniform, thereby causing graft failure." *Id.* at 3:38–39, 3:49–52. The patent further discloses that "solvent preservation . . . can cause irreversible denaturation of proteins, and solubilization of solvent soluble components, including for example, lipids." *Id.* at 3:52–55. According to the '200 patent, typical methods of preparing tissue grafts necessitate a rehydration step for implantation. *Id.* at 3:55–58.

The '200 patent discloses the use of a plasticizer, such as glycerol, in the preparation of tissue grafts. *See id.* at code (57), 5:21–27. The plasticizer "replaces water in the molecular structure of the bone or soft tissue matrix." *Id.* at code (57). The patent purports to solve problems in the prior art "by providing a plasticized dehydrated bone and/or soft tissue product that exhibits materials properties that approximate those properties present in normal hydrated tissue, is not brittle and does not necessitate rehydration prior to implantation." *Id.* at 5:36–40. Consequently, "the dehydrated bone or soft tissue plasticized product can be placed directly into an implant site without significant preparation in the operating room." *Id.* at code (57).

E. Illustrative Claim

Petitioner challenges claims 1–10, 12, 13, and 15. Of these, claims 1–3, 7, and 15 are independent claims. Claim 1, reproduced below, is illustrative of the challenged claims:

1. A plasticized soft tissue graft suitable for transplantation into a human, comprising:

   a cleaned soft tissue graft having an internal matrix; and

   one or more plasticizers contained in said internal matrix;

   said one or more plasticizers are not removed from said internal matrix of said plasticized soft tissue graft prior to transplantation into a human.

Ex. 1001, 24:10–16.

F. Prior Art References and Testimonial Evidence

Petitioner relies on three references for its challenges:

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

The parties have also 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[3]	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).

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

Witness	Role	Exhibits
David L. Kaplan, Ph.D.	Patent Owner's technical expert[4]	Ex. 1018 (declaration of June 24, 2014); Ex. 2016 (declaration of Nov. 11, 2019);[5] Ex. 1057 (declaration of Dec. 4, 2019); Ex. 1046 (transcript of deposition of Jan. 10, 2020).
Arun Sharma	Patent Owner's commercial success expert[6]	Ex. 2125 (declaration of Nov. 12, 2019);[7] Ex. 1044 (declaration of Dec. 6, 2019); Ex. 1056 (transcript of deposition of Jan. 24, 2020).

G. Prior Art and Asserted Grounds

Petitioner asserts that claims 1–10, 12, 13, and 15 would have been unpatentable on the following grounds:

Claim(s) Challenged	35 U.S.C. §[8]	Reference(s)/Basis
1–3, 5, 7–10, 12, 15	102(b)	Walker
1–3, 5–10, 12, 13, 15	103(a)	Walker
1–3, 7, 8, 10, 15	102(b)	Livesey

[4] *See* Ex. 2016 ¶ 1 ("I have been retained as an expert witness on behalf of Patent Owner . . . ."); *id.* ¶ 11 ("Based on 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 processing and use of bone and soft-tissue for transplantation into humans.").

[5] A redacted public version of this declaration is at Exhibit 2136.

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

[7] A redacted public version of this declaration is at Exhibit 2137.

[8] 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 '200 patent issued from an application filed before March 16, 2013, we apply the pre-AIA versions of the statutory bases for unpatentability.

Claim(s) Challenged	35 U.S.C. §[8]	Reference(s)/Basis
1–3, 7, 8, 10, 15	103(a)	Livesey
4	103(a)	Walker or Livesey in view of Werner

See Pet. 5.

II. 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 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 level 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 that 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.").[9] 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.

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.

III. LEVEL OF ORDINARY SKILL IN THE ART

In our Decision on Institution, based on the parties' proposals and the record at that stage, we found that the following background and experience reflected the level of ordinary skill in the art:

> (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

[9] One panel determined that 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.

> 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.

Dec. on Inst. 11. The parties do not address the level of ordinary skill in the art in the post-institution briefing, and the full trial record does not alter our preliminary determination of the level of ordinary skill in the art. Thus, we maintain our finding quoted above regarding the level of ordinary skill in the art.

IV. CLAIM CONSTRUCTION

"In an *inter partes* review proceeding, a claim of a patent . . . shall be construed using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. 282(b)." 37 C.F.R. § 42.100(b) (2019).[10] That standard "includ[es] construing the claim in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent." *Id.*; *see also Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (en banc).

We discuss three terms below, which are the only terms that require express construction. *See Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) (claim terms need only be construed "to the extent necessary to resolve the controversy"); *see also Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (applying *Vivid Techs.* in the context of an *inter partes* review).

[10] The Petition in this case was filed January 29, 2019. *See* Paper 3, 1. Moreover, the *Phillips* standard applies in this proceeding for the additional reason that the '200 patent is expired. *See* Prelim. Resp. 12 n.4.

A. "plasticized"

Each of the independent claims in the '200 patent includes the phrase "plasticized soft tissue graft," both in the preamble and in the bodies of the claims. In the LifeCell Litigation, the district court construed a "plasticized" graft 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.

Ex. 1019, 7–8. The Federal Circuit did not disturb that construction on appeal. Ex. 2002, 10–11.

For purposes of our Decision on Institution, we adopted this same construction, noting that the construction was agreed-upon by the parties and was supported by the Specification of the '200 patent. Dec. on Inst. 12 (citing Pet. 16–17; Prelim. Resp. 15; Ex. 1001, 7:24–28, 8:3–12, 9:14–18). Following institution, Patent Owner continues to advocate for this construction. *See* PO Resp. 13 (stating that "[t]he Board correctly adopted the parties' proposed construction" of this term in the Decision on Institution). Petitioner's post-institution briefing presents no claim construction argument on this term, or any other modification of its initial position that this construction should govern. *See* Pet. 16–17; *see also* Pet. Reply 2–5 (presenting claim construction arguments on other terms but not "plasticized").

Thus, we adopt the parties' agreed construction of this term, as set forth above.

B. "impregnated"

Claim 7 recites "impregnating a cleaned, soft tissue graft with one or more plasticizers." The '200 patent defines "impregnating" to mean "any processing conditions which result in filling the matrix of a bone graft with a plasticizer composition." Ex. 1001, 6:55–58. Patent's Owner's proposed construction of "impregnated" is "filled," which is the construction the district court adopted in the LifeCell Litigation. *See* PO Resp. 18; Ex. 1019, 11. Petitioner's only claim construction argument regarding this term is that it does not require completely filling, but Patent Owner subsequently confirmed its agreement that impregnating does not require completely filling. *See* Pet. Reply 4–5; Sur-Reply 4. Based on the express definition in the patent and the parties' apparent agreement, we construe "impregnated" to mean "filled."

C. "cleaned"

1. Background

Each of the independent claims in the '200 patent recites that the soft tissue graft is "cleaned." Like the two terms discussed above, "cleaned" was also 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. 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 that the 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.

At the institution stage in this proceeding, the parties disputed whether the proper construction of "cleaned" encompasses partial removal of cellular elements and small molecular weight solutes. *See* Dec. on Inst. 13 (citing Pet. 16; Prelim. Resp. 14). Based on the preliminary record at that stage, we agreed with Petitioner that "'cleaned' . . . encompasses soft tissue grafts in which some, but not necessarily all, cellular elements and small molecular weight solutes have been removed." *Id.* at 14. In reaching that preliminary determination, we noted that the "the '200 patent discloses that tissue that has been 'cleaned' can still be 'further cleaned,' suggesting that 'cleaned' tissue retains at least some elements that can be 'further cleaned' if desired." *Id.* at 13–14 (citing Ex. 1001, 9:57–65).

2. Summary of the Parties' Contentions During Trial

Following institution, Patent Owner agreed that "'cleaned' does not require all of the cellular elements and small molecular weight solutes to have been removed, but with a caveat." PO Resp. 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 ¶ 62). Patent Owner asserts that "[t]he processes to create a 'cleaned' graft in the '200 patent are conventional, known in the art, and described in several cited patents and applications." *Id.* at 16 (citing Ex. 2016 ¶¶ 64–70; Ex. 1001, 6:31–34, 9:21–37, 10:7–8, 11:1–15). 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. 1001, 9:57–65, 10:52–55; Ex. 1045 ¶¶ 21, 26). Petitioner further argues that Patent Owner's construction conflates cleaning, which is intended to reduce the likelihood of rejection by the patient, with sterilization, which prevents disease transmission. *Id.* at 3–4 (citing Ex. 1045 ¶¶ 27, 62). And Petitioner argues that Patent Owner's construction conflicts with the construction adopted by the district court in the LifeCell Litigation. *Id.* at 4. Petitioner's proposed construction is the one adopted in the LifeCell Litigation. 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 '200 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. 1001, 9:21–37, 10:30–39; Ex. 2044, 3:21–37).

3. 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 '200 patent's independent claims themselves, which simply recite that the soft tissue graft is "cleaned," is broad and generic. In assessing that 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.'"); *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 the related '420 patent, the independent claims include the same broad "cleaned" term and dependent claim 13 adds the limitation that "said plasticized soft tissue graft is essentially free from cellular elements." Ex. 1002, 25:15–17. 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 those claims in related patents 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 '200 patent, the patentee chose the broad term "cleaned."

The genericness of the term "cleaned," in comparison to the specificity of the language used in 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 '200 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 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. 1001, 6:31–34; *see also id.* at 9:21–23 ("Bone processing and cleaning procedures suitable for use with the present invention include known processes. . . ."). Likewise, the patent explains that "[b]one and soft tissue grafts can be cleaned and processed using conventional methods." *Id.* at 10:7–8; *see also id.* at 11:2–4 ("For example, tissue can be processed and cleaned according to any method including known methods . . . ."). In the 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 22:45–47, 23:29–31. Thus, we agree with Patent Owner's frank acknowledgement that the cleaning methods described in the '200 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 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 '200 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 that 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 that 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. 1001, 11:5–8. However, that description does not purport to define "cleaned" but simply describes one "example." *Id.* at 11:2. 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. 15.

We have also considered the extrinsic evidence that 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.

V. ANTICIPATION BASED ON WALKER

A. Legal Standards

"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.").

B. Summary of Walker

Walker discloses "[a] method of sterili[z]ing material . . . for implantation into a human or animal body" in which the material is treated with "a substance . . . selected so as to maintain certain physical

characteristics of the material such as flexibility and/or structure of cells or extra cellular material." Ex. 1005, 1 at code (57).[11] "Suitable substances include . . . glycerol." *Id.* Walker teaches that its method "can be used on gra[ft]s for implantation or on biological material such as vascular tissue etc. and has the advantage that the substance does not react with water and so the material can be treated in solution without drying out or becoming brittle." *Id.* Walker's method includes storing the material in an ethanol solution, treating with glycerol, and treating with ethylene oxide to sterilize. *See id.* at 4:2–3, 5:17–20. Walker discloses that the "pre-sterili[z]ing treatment," which may include treatment with glycerol, "enables the material substantially to retain certain physical characteristics, such as flexibility, and can suitably replace at least some of the water contained in the material." *Id.* at 6:20–24.

C. Claim 1

1. 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)).[12]

[11] In our pin cites to Walker, page numbers refer to the stamp added by Petitioner to the lower right corner of each page of Walker.

[12] *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).

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* § V.C.2. 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. 25–26; 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. 25–26; Ex. 1034 ¶ 97. Walker describes "a method of sterilizing material for implantation into a human or animal body." Ex. 1005, 4:14–16; *see also id.* at 1 (code (57)); *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* § V.C.3. As to a soft tissue graft having an internal matrix, we find that Petitioner has shown that Walker teaches those features. *See* Pet. 26–27; Ex. 1034 ¶¶ 98–99. 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 that Petitioner has shown that 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. 26–27, 29; Ex. 1005, 4:33, 5:23–24, 7:11–14, 21:9–12; Ex. 1034 ¶ 99.

Finally, claim 1 recites "said one or more plasticizers are not removed from said internal matrix of said plasticized soft tissue graft prior to transplantation into a human." We are persuaded by Petitioner's argument that glycerol is incorporated into the internal matrix of Walker's tissue, and that the glycerol would not be removed with the brief washing that Walker teaches to carry out. *See* Pet. 27, 30; Ex. 1005, 4:29–31; Ex. 1034 ¶ 100.

2. "plasticized"

As discussed in Section IV.A., 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 that Petitioner has shown that 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. 25–26, 28; Pet. Reply 6–12. Walker's process is carried out on "material . . . for implantation into a human or animal body" such as vascular tissue. Ex. 1005, 1 at code (57),

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. *Id.* at 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. Suitable 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[13] sterilization." *Id.* at 7:4–5. In that example, tissue samples are incubated in glycerol "for around 16 hours or more." *Id.* at 7:7–13. 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 that 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

[13] EtO refers to ethylene oxide. *See* Ex. 1005, 4:3.

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.[14] PO Resp. 18–28; *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 that 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, 1 at code (57). 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.

[14] Patent Owner provides a detailed background discussion concerning waters of hydration in tissue. *See* PO Resp. 4–8; Ex. 2016 ¶¶ 34–42. However, Patent Owner does not apply this background discussion to Walker as a basis for distinguishing Walker from claim 1 of the '200 patent, apart from an argument concerning crosslinking which we address below. *See* PO Resp. 4–8, 18–28.

In addition, Walker discloses the results of testing conducted to compare a treated graft to natural tissue. Ex. 1005, 9–15. Specifically, bovine artery samples were plasticized in 50% glycerol and 50% ethanol, 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." Ex. 1034 ¶ 86; *see also* Pet. 21 ("Like the plasticization method disclosed in the 200 patent, Walker discloses the incorporation of glycerol . . . into the internal matrix of the material."); Pet. Reply 8 (arguing that "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 '200 patent similarly describes plasticizing by soaking the graft in a solution of glycerol and alcohol.

Specifically, the '200 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. 1001, 8:31–45, 9:4–8. In the section titled "Plasticization," the '200 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. Suitable solvents include for example, 70% isopropyl alcohol." *Id.* at 10:6, 10:34–40. "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 10:48–52.

The two examples in the '200 patent relating to processing of soft tissue grafts (as opposed to bone grafts, which are the subject of Examples 1–8, *see id.* at 12:40–22:31) also describe soaking the graft in a solution of glycerin and alcohol. *See id.* at 22:55–23:5, 23:40–58. In Example 9, describing processing of fascia lata, the '200 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 22:55–58. The graft is "then placed into the basin containing the antibiotic solution in 30% glycerin USP for at least 15 minutes." *Id.* at 22:61–63.

Example 10 describes plasticizing a pericardium sample using a very similar process. *Id.* at 23:40–58.

We asked Patent Owner at the hearing what steps the '200 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 '200 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 '200 patent have been apparent since institution, and Patent Owner has not persuasively identified any material differences. *See* Dec. on Inst. 18–20. The similarity of Walker's plasticization process to that of the '200 patent further supports that Walker's treated graft would have mechanical properties similar to natural tissue, just as in the '200 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 5–9. Patent Owner argues that 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 (citing Ex. 2016 ¶¶ 93–96). 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 (citing Ex. 2016 ¶ 94). Cross-linking also makes the tissue

stiffer and more durable than normal hydrated tissue. *Id.* at 20–21 (citing Ex. 2016 ¶¶ 95–96).

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 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 sterilization 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 that 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 photo oxidation) 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 (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 11; 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* § IX.B.

Patent Owner further argues that 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. 21–22 (citing Ex. 2016 ¶ 100). 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 that Walker does not disclose that the material, physical, and use properties of the treated tissue are similar to normal hydrated tissue. PO Resp. 23; Sur-Reply 7. 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 24 (citing Ex. 2016 ¶¶ 106–108). Patent Owner also argues that "the variance in [Walker's] data

is too great to draw any statistically significant conclusion from it." *Id.* at 25 (citing Ex. 2016 ¶¶ 103–108); Sur-Reply 9.

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, 1 at code (57), 4:23–27, 6:6–8, 6:20–24, 21:9–12.

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

3. "cleaned"

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

We find that Petitioner has shown that Walker discloses cleaning under that construction. *See* Pet. 26, 29; Pet. Reply 12–13. Petitioner contends that Walker discloses cleaning because it describes storing the graft in ethanol before the glycerol treatment. *See* Pet. 26; Pet. Reply 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. 25–27; Sur-Reply 10–12. Patent Owner argues that Walker traps cellular elements and small molecular weight solutes rather than removing them because that is what cross-linking does. PO Resp. 25–26 (citing Ex. 2016 ¶ 110). 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 that 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 ¶ 111). This argument is based on Patent Owner's proposed construction of "cleaned," which we have not adopted for the reasons explained in Section IV.C.

Patent Owner also argues that Petitioner's understanding of Walker "sets up a paradox that relates to three requirements of the challenged claims." PO Resp. 27. 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, 1 at code (57), 4:14–16, 6:33–36, 33:3–4.

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

4. Conclusion

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

D. Claim 2

Independent claim 2 recites many of the same limitations as claim 1, except that claim 2 recites that the cleaned soft tissue is "impregnated" with one or more plasticizers. Ex. 1001, 24:20. As discussed in Section IV.B, we construe "impregnated" to mean "filled," and the parties agree that the term does not require completely filling.

For its argument that Walker teaches a graft impregnated with one or more plasticizers, Petitioner refers back to its arguments for claim 1 that Walker discloses one or more plasticizers contained in the internal matrix. *See* Pet. 29, 31. 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. 28 (citing Ex. 2016 ¶¶ 115–120); *see also* Sur-Reply 12 ("The tissue of Walker cannot be impregnated because 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 in Section V.C.2, we are not persuaded by Patent Owner's arguments regarding cross-linking and we find that Petitioner has shown that Walker describes a "plasticized" graft.

After considering the evidence and arguments of record, we find that Petitioner has shown that Walker discloses each limitation in claim 2. *See* Pet. 30–31. Apart from the "impregnated" limitation, Patent Owner does not present any argument for claim 2 separate from its arguments regarding claim 1, which we have already discussed above. We determine that Petitioner has demonstrated by a preponderance of the evidence that Walker anticipates claim 2.

E. Claims 3, 5, 7–10, 12, 15

Petitioner identifies disclosure in Walker that discloses each limitation in claims 3, 5, 7–10, 12, and 15. *See* Pet. 31–39. 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 that Petitioner has demonstrated by a preponderance of the evidence that Walker anticipates claims 3, 5, 7–10, 12, and 15.

VI. OBVIOUSNESS BASED ON WALKER

A. Legal Standards

In *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966), the Supreme Court set out a framework for assessing obviousness under § 103 that requires consideration of four factors: (1) the "level of ordinary skill in the pertinent art," (2) the "scope and content of the prior art," (3) the "differences between the prior art and the claims at issue," and (4) "secondary considerations" of nonobviousness such as "commercial success, long-felt but unsolved needs, failure of others, etc." *Id.* at 17–18. "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).

B. Claims 1–3, 5, 7–10, 12, and 15

Petitioner argues that claims 1–3, 5, 7–10, 12, and 15 would have been obvious to an ordinarily skilled artisan in view of Walker "[t]o the extent any limitation of those claims is not explicitly disclosed in Walker." Pet. 39. The only limitation in these claims that the Petition specifically addresses is that "the plasticizers are not removed from the internal matrix." *See id.* at 39–41. Petitioner argues that "if it is determined that Walker does not explicitly disclose" this limitation, an ordinarily skilled artisan would

have known that it was advantageous not to remove the plasticizer from the internal matrix because incorporating the plasticizer into the matrix would have benefits, whereas removing it would be difficult and would leave the tissue vulnerable to degradation. *Id.* at 40–41 (citing Ex. 1034 ¶¶ 129–134). As we noted above, Patent Owner does not challenge Petitioner's assertion that Walker discloses the limitation in question, and we find that Walker discloses it. *See supra* § V.C.1. Thus, the contingency for which Petitioner offered this ground has not occurred.

Because Petitioner's predicate for offering this back-up obviousness ground is not met, we do not reach this ground. Having determined that Petitioner has demonstrated by a preponderance of the evidence that 1–3, 5, 7–10, 12, and 15 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.*, __ Fed. Appx. __, 2020 WL 2071962, at *4 (Fed. Cir. Apr. 30, 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.").

C. Claims 6 and 13

Claim 6 depends from any one of claims 1, 2, or 3 and adds that the "soft tissue graft is selected from the group consisting of: dura, pericardium, fascia lata, tendons and ligaments." Ex. 1001, 24:35–38. We find that Petitioner has shown that 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. 41–42 (citing Ex. 1034 ¶ 135); *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. 32, 42; Ex. 1005, 9:19–20, 27:1–2.

Claim 13 depends from claim 12 and adds that the "plasticer [sic] is glycerol and said alcohol is isopropyl alcohol." Ex. 1001, 24:63–64. We find that Petitioner has shown that Walker teaches glycerol as a plasticizer and ethanol as a solvent. Pet. 42; Ex. 1005, 6:26–27, 9:20–23, 17:13–14. We further find that Petitioner has shown that a skilled artisan would know that ethanol is readily interchangeable with isopropyl alcohol, and that isopropyl alcohol is less expensive such that an ordinarily skilled artisan would have been motivated to substitute isopropyl alcohol to decrease cost. Pet. 42–43; Ex. 1034 ¶ 136.

Patent Owner does not present any argument against Petitioner's contentions that the additional limitations recited in dependent claims 6 and 13 would have been obvious to a person of ordinary skill in the art based on Walker. *See* PO Resp. 18–30. Patent Owner argues that objective indicia support nonobviousness, but Patent Owner's objective indicia evidence is

not directed to the features recited in claims 6 and 13. *See id.* at 50–63. "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 6 or 13 because it does not provide evidence that the commercial products underlying its objective indicia arguments embody claims 6 and 13. *See* PO Resp. 61–62 (arguing that "[t]he Board should presume that that nexus requirement has been met . . . because these products embody *certain* challenged claims . . . .") (emphasis added). Patent Owner cites Dr. Kaplan's testimony to support its argument regarding a presumption of nexus. *Id.* at 62 (citing Ex. 2016 ¶ 305). But Dr. Kaplan's claim chart for the '200 patent does not compare the commercial products to either claim 6 or 13. *See* Ex. 2075 (charting claims 1–4, 7, 8, and 10).

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 limitations recited in claim 6 or 13. The features Patent Owner relies on to establish nexus are grafts that are ready-to-use and stable for storage at room temperature. *See* PO Resp. 62–63; Tr. 76:1–12. Patent Owner does not tie those features to the limitations of either claim 6 or 13. *See* Tr. 76:13–24; Ex. 2016 ¶¶ 306–309. Accordingly, we find that Patent Owner has not established a nexus to support the nonobviousness of claims 6 and 13.

For the foregoing reasons, we determine that Petitioner has demonstrated by a preponderance of the evidence that claims 6 and 13 would have been obvious based on Walker.

VII. CHALLENGES BASED ON LIVESEY

A. Summary of Livesey

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.

B. Discussion

Petitioner contends that Livesey anticipates claims 1–3, 7, 8, 10, and 15. Pet. 43–59. As a backup, "[t]o the extent any limitation of those claims is not explicitly disclosed in Livesey," Petitioner argues that the claims would have been obvious based on Livesey. *Id.* at 59–61. We have found each of the claims challenged in these grounds to be anticipated by Walker. *See supra* § V.C–E. Therefore, we need not determine whether the same claims are additionally anticipated by or obvious over Livesey. *See Boston Scientific*, 2020 WL 2071962, at *4 (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"); *Beloit*, 742 F.2d at 1423 (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.").

VIII. OBVIOUSNESS OVER WALKER OR LIVESEY IN VIEW OF WERNER

A. Summary of Werner

Werner discloses methods of manufacturing "sclero protein transplants." Ex. 1006 at [57] (abstract). In particular, Werner discloses a method in which tissue such as "raw dura matter from humans" is treated with H_2O_2, degreased, rinsed, treated with a glycerin[15] 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.

B. Analysis

In this ground, Petitioner challenges claim 4, which depends from "any one of claim 1, 2, or 3," and further recites that "said soft tissue graft is suitable for direct transplant into a human without rehydration." Ex. 1001, 24:29–31.

Petitioner argues that 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. 62. In particular, Petitioner asserts that Werner discloses treating a tissue

[15] As mentioned above, "glycerin" and "glycerol" refer to the same compound. *See* Ex. 1034 ¶ 37; Ex. 1001, 5:25 (referring to "glycerol (glycerin USP)").

with glycerol increases biological stability, and that no rehydration of the resulting product is necessary before transplantation. *Id.* (citing Ex. 1006, at code (57), 2:37–41). Petitioner contends that 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. (citing Ex. 1034 ¶¶ 173–175); *see also* Pet. Reply 22–23 (citing Ex. 1045 ¶ 65).

1. Whether the Combination Teaches the Individual Limitations

We find that Petitioner has shown that Werner teaches a soft tissue graft suitable for transplantation without rehydration. *See* Pet. 62; Ex. 1006, 2:39–40. Indeed, Patent Owner does not dispute that point. As discussed above, we find that Petitioner has shown that Walker discloses the limitations of the claims from which claim 4 depends. *See supra* § V.C–E. Thus, Petitioner has shown that the proposed combination of Walker and Werner teaches every individual limitation of claim 4. We need not decide whether the combination of Livesey and Werner also teaches every limitation of claim 4 because even if it did, the factors discussed below would outweigh such evidence of obviousness.

2. Motivation to Combine and Reasonable Expectation of Success

We further find that 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 without first rehydrating it. Pet. 63. Patent Owner argues, and Dr. Kaplan testifies, that it is unclear how Petitioner proposes the combine the references, *see* PO Resp.

46; Ex. 2016 ¶¶ 170, 178, 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 Decision on Institution. *See* Pet. 63; Pet. Reply 22–23; Tr. 32:12–33:10; Dec. on Inst. 25–26.

Petitioner contends that an ordinarily skilled artisan would have been motivated to omit rehydration in order "to simplify the processing of the soft tissue graft during implantation." Pet. 62 (citing Ex. 1034 ¶ 177); Pet. Reply 22. 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. 63 (citing Ex. 1034 ¶¶ 178, 183).

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. 46; 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 that "[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 that "[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. 63; Ex. 1034 ¶¶ 183–184. 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. 48 (citing Ex. 1006, 1:33–38); Ex. 1004, 1 code [57].

3. Objective Indicia of Nonobviousness

a) Nexus

Turning to objective indicia of nonobviousness, we find that 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 that 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. 51–53. 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. *See* Ex. 2016 ¶¶ 303–305 (testimony of Dr. Kaplan); Ex. 2075, 1–21, 30–31 (Dr. Kaplan's claim charts); 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. 62–63; 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 that 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. 63 (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 26–28, 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 27, 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 27 (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 27 ("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 28 (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 32–33. 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 that Patent Owner has shown a nexus between the objective indicia of nonobviousness and claim 4.

b) 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 '200 patent, surgeons were dissatisfied with soft tissue graft offerings because they required lengthy preparation prior to use. PO Resp. 53–54. 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 54–55. 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. Petitioner responds that Patent Owner's evidence of long-felt need post-dates the invention and is, therefore, irrelevant. Pet. Reply 28–29.

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. 1001, at code (62), 1:4–5 (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 Pharmaceuticals 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 claimed priority date in 1998, it cannot establish the existence of a *long felt* need as of the claimed priority date.

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

c) 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 that "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. 56 (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 that 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. 56; 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. 56–57 (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 28–29. 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 that Patent Owner's evidence of the failure of others provides some evidence weighing toward nonobviousness.

d) Industry Adoption

Patent Owner argues that freeze-dried grafts dominated the market until plasticized soft tissue grafts were introduced, at which point "competitors moved decisively in their direction." PO Resp. 57. Petitioner responds that "only widespread industry adoption is relevant," and Patent Owner's evidence is limited to LifeCell. Pet. Reply 29 (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 '200 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. 54 n.8, 57; 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. 57; Ex. 2068, 5. [redacted] PO Resp. 58; 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. 57; Ex. 2125 ¶ 34; Ex. 2067, 11. [redacted] PO Resp. 58; 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. 58; 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.

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

e) 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. 59 (quoting Ex. 2131, 2). Patent Owner further cites a 2007 earnings call in which LifeCell reported positive feedback from surgeons who used Strattice. *Id.* (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.

f) Commercial Success

"Demonstrating that an invention has commercial value, that it is commercially successful, weighs in favor of . . . non-obviousness." *WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1337 (Fed. Cir. 2016). 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. 60; Ex. 2125 ¶ 26. The average annual growth rates of sales of Patent Owner's embodying products between 2011 and 2018 [redacted] Ex. 2125 ¶ 27. Additionally, Patent Owner presents evidence—again unrebutted—that LifeCell's Strattice and AlloDerm RTU products produced [redacted] revenue between 2008 and 2013, with an average annual growth rate of [redacted] during those years. PO Resp. 60; 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* § VIII.B.3.d.

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 26–34. 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 that Patent Owner's commercial success evidence weighs in favor of nonobviousness.

4. 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 at least the proposed combination of Walker and 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 1063, 1079 (Fed. Cir. 2012)), we conclude that 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.

IX. CONCLUSION

The outcome for the challenged claims in this proceeding is set forth below.[16] In summary:

Claims	35 U.S.C. §	Reference(s)/Basis	Claims Shown Unpatentable	Claims Not Shown Unpatentable
1–3, 5, 7–10, 12, 15	102(b)	Walker	1–3, 5, 7–10, 12, 15	
1–3, 5–10, 12, 13, 15	103(a)	Walker[17]	6, 13	
1–3, 7, 8, 10, 15	102(b)	Livesey[18]		
1–3, 7, 8, 10, 15	103(a)	Livesey[19]		
4	103(a)	Walker or Livesey in view of Werner		4
Overall Outcome			1–3, 5–10, 12, 13, 15	4

[16] 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).

[17] As explained above in Section VI.B, we do not reach this ground as to claims 1–3, 5, 7–10, 12, and 15.

[18] As explained above in Section VII.B, we do not reach this ground as to any claim.

[19] As explained above in Section VII.B, we do not reach this ground as to any claim.

X. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that claims 1–3, 5–10, 12, 13, and 15 have been proven by a preponderance of the evidence to be unpatentable;

FURTHER ORDERED that claim 4 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 the present decision should remain under seal, and including a redacted version of this decision that can be made publicly available;

FURTHER ORDERED that the present decision shall remain under seal until any joint motion to seal the present decision is resolved;

FURTHER ORDERED that the present 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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