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Paper No. 8
Date: April 17, 2020

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PALETTE LIFE SCIENCES, INC.,
Petitioner,

v.

INCEPT LLC.,
Patent Owner.

IPR2020-00004
Patent US 7,744,913 B2

Before ERICA A. FRANKLIN, ULRIKE W. JENKS, and TINA E. HULSE, *Administrative Patent Judges.*

HULSE, *Administrative Patent Judge*.

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

I. INTRODUCTION

Palette Life Sciences, Inc. ("Petitioner") filed a Petition requesting an *inter partes* review of claims 1–25 of U.S. Patent No. 7,744,913 B2 (Ex. 1001, "the '913 patent"). Paper 2 ("Petition" or "Pet."). Incept LLC ("Patent Owner") filed a Preliminary Response to the Petition. Paper 7 ("Prelim. Resp.").

We have authority under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted "unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a). Upon considering the argument and evidence presented in the Petition and Preliminary Response, we determine that Petitioner has established a reasonable likelihood that it would prevail in showing the unpatentability of at least one claim challenged in the Petition. Accordingly, we institute an *inter partes* review of claims 1–25 of the '913 patent.

A. Real Parties-in-Interest

Petitioner identifies Palette Life Sciences, Inc. and Pharmanest AB as real parties-in-interest. Pet. 1. Petitioner also identifies Galderma S.A., Galderma Laboratories, Inc., Galderma Laboratories LP, Galderma Research & Development SNC, Nestlé Skin Health, Inc., Nestlé Skin Health S.A., Nestlé S.A., EQT Partners AB, Public Sector Pension Investment Board (PSP Investments), Luxinva, and Abu Dhabi Investment Authority as possible real parties-in-interest. *Id.*

Patent Owner identifies Incept LLC and Boston Scientific Corporation as real parties-in-interest. Paper 5, 1.

B. Related Proceedings

Petitioner has filed a second petition for *inter partes* review of the '913 patent as IPR2020-00005 ("the -005 Petition"). Pet. 2. Petitioner also filed petitions for *inter partes* review of related U.S. Patent No. 8,257,723 B2 in IPR2020-00002 and IPR2020-00003. Pet. 2.

Patent Owner states that it "is not presently aware of any proceedings other than those cited in the Petition." Paper 5, 1.

C. The '913 Patent

The '913 patent relates to a method of placing a degradable filler between the radiation target tissue (e.g., prostate) and other tissues (e.g., rectum) to increase the distance between the two tissues, so that the other tissues receive less radiation than the target tissue. *Id.* at 2:28–31. The degradable filler is installed once before radiation treatment and does not require subsequent manipulation, repositioning, or removal. *Id.* at 2:31–35.

The '913 patent describes a filler as "a substance that occupies a volume after its introduction into a body." *Id.* at 4:34–35. Filler materials include alginate, collagen, gelatin, fibrin, fibrinogen, albumin, polyethylene glycol, thixotropic polymers, and thermoreversible polymers. *Id.* at 4:37–46. Biocompatible materials are preferred, especially collagen or hyaluronic acid. *Id.* at 5:3–4. Biodegradation is measured by palpitation or other methods to detect the change in volume of the filler after its introduction into a patient. *Id.* at 4:66–5:3. Biodegradation may occur over the course of weeks or months after introduction depending on the requirements for administering radiation therapy. *Id.* at 5:4–16.

The filler maybe injected through a needle into the patient's body. *Id.* at 10:51–53. After introduction into the body, the filler may increase in volume and form a gel *in situ* through a variety of processes, depending on

the material. *See id.* at 5:30–56, 7:42–53. A filler solution may have low viscosity when stored and higher viscosity after *in situ* self-assembly in the patient. *Id.* at 5:48–50.

The '913 patent also describes a study that shows a method of injecting collagen into Denonvillier's space, i.e., the region located between the rectum and the prostate, to displace the rectum away from the prostate during radiation therapy. *Id.* at 3:15–26. The combination of body temperature and pH causes the collagen fibrils to cooperate to form a fibrin gel. *Id.* at 5:43–48. "The collagen degraded in less than about sixty days and required no procedures after its initial introduction into the patients." *Id.* at 3:20–22. Patients receiving the collagen injections "appeared to have minimal rectal side effects associated from their radiotherapy." *Id.* at 3:30–32.

D. Illustrative Claims

Petitioner challenges claims 1–25 of the '913 patent, of which claims 1 and 17 are independent. Claims 1 and 17 are illustrative and are reproduced below.

> 1. A method of delivering a therapeutic dose of radiation to a patient comprising introducing a biocompatible, biodegradable filler device between a first tissue location and a second tissue location to increase a distance between the first tissue location and the second tissue location, and treating the second tissue location with the therapeutic dose of radiation so that the presence of the filler device causes the first tissue location to receive less of the dose of radioactivity compared to the amount of the dose of radioactivity the first tissue location would receive in the absence of the filler device, wherein the filler device [that] is introduced an injectable material and is a gel in the patient that is removed by biodegradation of the filler device in the patient wherein the first tissue location is associated

> with the rectum and the second tissue location is associated with the prostate gland.

Ex. 1001, 16:43–57.

> 17. A method of delivery a therapeutic dose of radiation to a patient comprising: (i) injecting anesthesia and (ii) injecting saline to expand the space between the first and second tissue location, wherein the first tissue location is associated with the rectum and the second tissue location is associated with the prostate gland and introducing a biocompatible, biodegradable filler device between the first tissue location and the second tissue location to increase a distance between the first tissue location and the second tissue location, said biocompatible, biodegradable filler being collagen and introducing collagen into Deno[n]villier's space and treating the second tissue location with a therapeutic dose of radiation, said therapeutic dose of radiation being 70 to 100 Gy, so that the presence of the filler device causes the first tissue location to receive less than 50% of the dose of radioactivity compared to the amount of the dose of radioactivity the first tissue location would have received in the absence of the filler device, wherein the filler device is removed by biodegradation of the filler device in the patient.

Id. at 17:31–18:15.

E. The Asserted Grounds of Unpatentability

Petitioner asserts that claims 1–25 would have been unpatentable on the following grounds.

Claim(s) Challenged	35 U.S.C. §	References
1–18, 20–24	103	Wallace,[1] Ein-Gal[2]
19, 25	103	Wallace, Ein-Gal, Griffith-Cima[3]

[1] Wallace et al., US 6,624,245 B2, issued Sep. 23, 2003 ("Wallace," Ex. 1010).
[2] Moshe Ein-Gal, US 6,210,314 B1, issued Apr. 3, 2001 ("Ein-Gal," Ex. 1049).
[3] Griffith-Cima et al., PCT Publication No. WO 94/25080 ("Griffith-Cima," Ex. 1011).

Claim(s) Challenged	35 U.S.C. §	References
1–24	103	Ball,[4] Carroll[5]
25	103	Ball, Carroll, Ein-Gal, Griffith-Cima

Petitioner also relies on the Declaration of Adam Dicker, M.D., Ph.D. Ex. 1003.

II. ANALYSIS

A. Person of Ordinary Skill in the Art

Petitioner asserts that a person of ordinary skill in the art at the time of the invention would include someone having a medical degree with experience in radiation oncology, including knowledge of the side effects of radiation treatment. Pet. 11–12 (citing Ex. 1003 ¶¶ 30–31). Petitioner also asserts that a person of ordinary skill in the art at the time of the invention would have experience in performing radiation treatments and shielding normal tissue or organs from radiation. *Id.* at 12. Dr. Dicker explains that such experience "may come from the POSA's own experience, or may come through research or work collaborations with other individual(s) with experience in the medical or biotechnology industry, *e.g.*, as members of a research team or group." Ex. 1003 ¶ 29.

Patent Owner contests Petitioner's definition of the person of ordinary skill. Prelim. Resp. 1. Patent Owner argues that a physician would not have the necessary experience in polymer science to design or select the claimed "biocompatible, biodegradable filler device." *Id.* at 1–3. Patent Owner

[4] Ball, A. B. S. et al., *Silicone Implant to Prevent Visceral Damage During Adjuvant Radiotherapy for Retroperitoneal Sarcoma*, 63 BRITISH J. RADIOLOGY 346–48 (1990) ("Ball," Ex. 1012).
[5] Carroll, US 6,375,634 B1, issued Apr. 23, 2002 ("Carroll," Ex. 1013).

does not, however, propose its own definition of the level of ordinary skill in the art in the Preliminary Response. *See generally* Prelim. Resp.

At this stage of the proceeding, we adopt Petitioner's definition, with the clarification that the experience of the hypothetical person of ordinary skill in the art includes an understanding of polymer science via their own research or collaborative work with a research team or group in the medical or biotechnology industry. *See* Ex. 1003 ¶ 29. That definition is consistent with the level of skill in the art at the time of the invention as reflected by the prior art. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that specific findings regarding ordinary skill level are not required "where the prior art itself reflects an appropriate level and a need for testimony is not shown" (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp*., 755 F.2d 158, 163 (Fed. Cir. 1985))).

If either party disagrees with our finding of the level of ordinary skill, they are encouraged to develop the argument further at trial.

B. Claim Construction

Where, as here, a Petition is filed on or after November 13, 2018, the Board applies 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. § 100(b) (2019); *see* Changes to the Claim Construction Standard for Interpreting Claims in Trial Proceedings Before the Patent Trial and Appeal Board, 83 Fed. Reg. 51,340 (Oct. 11, 2018).

Under that standard, claim terms "are generally given their ordinary and customary meaning" as understood by a person of ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc). "In determining the meaning of the disputed claim limitation, we look principally to the intrinsic evidence of

record, examining the claim language itself, the written description, and the prosecution history, if in evidence." *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 469 F.3d 1005, 1014 (Fed. Cir. 2006) (citing *Phillips*, 415 F.3d at 1312–17). Extrinsic evidence is "less significant than the intrinsic record in determining 'the legally operative meaning of claim language.'" *Phillips*, 415 F.3d at 1317.

Petitioner offers proposed claim constructions for the terms "filler device"/"filler" and "consists essentially of collagen." Pet. 13–15. Patent Owner does not propose any constructions of its own for any claim terms. *See generally* Prelim. Resp. We address the term "consists essentially of collagen" below.[6]

1. "Consists essentially of collagen"

Claim 8 recites that the "filler consists essentially of collagen." Ex. 1001, 17:7–8. Petitioner asserts that the transition phrase "consists essentially of" "limits the scope of a claim to the specified ingredients and those that do not *materially affect the basic* and *novel* characteristic(s) of a composition." Pet. 14–15 (citing *In re Herz*, 537 F.2d 549, 551–52 (CCPA 1976)). Petitioner therefore argues that claim 8 "allows components other than collagen to be present so long as they do not prevent collagen from being used as a biocompatible, bioabsorbable filler." *Id.* at 14–15.

On this record, we agree with Petitioner's construction as consistent with the Specification and case law. We also note that the term "collagen" is

[6] Construing "filler device" and "filler" is not necessary for purposes of this Decision, as the issue of whether the term includes a "balloon that is itself not an injectable, gel material, but is instead filled with an 'injectable material' that 'is a gel in the patient'" (Pet. 14) is not at issue in this proceeding.

used broadly by the Specification, encompassing more than just naturally occurring collagen. According to the Specification, "collagen" may be "natural or synthetic," "human origin or non-human origin," and "material intelligently designed to mimic collagen or some of the structural or functional features of collagen." Ex. 1001, 7:65–8:10.

2. Remaining Claim Terms

At this stage of the proceeding, we determine that it is unnecessary to expressly construe any other claim terms for purposes of rendering this Decision. *See Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011) ("[C]laim terms need only be construed 'to the extent necessary to resolve the controversy.'" (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc*., 200 F.3d 795, 803 (Fed. Cir. 1999))).

C. Obviousness over Wallace and Ein-Gal

Petitioner asserts that claims 1–18 and 20–24 are unpatentable as obvious over Wallace and Ein-Gal. Pet. 26–44. Patent Owner opposes Petitioner's assertion. Prelim. Resp. 4–25.

1. Wallace (Ex. 1010)

Wallace relates to a method of forming a biocompatible gel at a selected site within a patient's body. Ex. 1010, Abstract. In particular, Wallace relates to a "composition prepared by admixture of individually reactive polymer components, wherein the admixture initiates rapid crosslinking and gel formation." *Id.* at 1:16–19. The gel may be formed from an injectable reaction mixture, injected at a specific site within a patient's body, that crosslinks at the site of the injection. *Id.* at 10:8–12. Wallace states that the gel can "be used as a large space-filling device for organ displacement in a body cavity during surgical or radiation procedures,

for example, to protect the intestines during a planned course of radiation to the pelvis." *Id.* at 33:64–67.

Wallace explains that the gel may be formed from a polymer including biodegradable segments or blocks that are hydrolyzed in the presence of water or enzymatically cleaved *in situ*. *Id.* at 19:3–19. Preferred naturally occurring hydrophilic polymers include collagen, albumin, fibrin, fibrinogen, carboxylated polysaccharides, and aminated polysaccharides, such as hyaluronic acid. *Id.* at 19:59–65, 20:1–3. The gels may include tensile strength enhancers, such as polyglycolide and polylactide fibers. *Id.* at 24:21–23.

2. Ein-Gal (Ex. 1049)

Ein-Gal relates to a method of treating prostate cancer using radiation therapy. Ex. 1049, 1:4–6. Ein-Gal teaches injecting water in the area of Denonvillier's fascia to reflect the rectal wall away from the prostate and thus "reduce the adverse effects of radiation on healthy tissue, e.g., the rectal wall." *Id.* at 1:31–36; *see also id.* at 3:51–56.

3. Analysis

A patent claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the claimed subject matter and the prior art are such that the subject matter, as a whole, would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations, including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of skill in the art; and (4) objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

"[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 550 U.S. at 418. "[I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *Id.* Moreover, a person of ordinary skill in the art must have had a reasonable expectation of success of doing so. *PAR Pharm., Inc. v. TWi Pharms., Inc.*, 773 F.3d 1186, 1193 (Fed. Cir. 2014).

Regarding claim 1, Petitioner provides a detailed analysis of each claim limitation as taught or suggested by Wallace and Ein-Gal. *Id.* at 27–33. Petitioner asserts that Wallace teaches or suggests each and every limitation of the claim, except for displacing the rectum relative to the prostate gland. Pet. 26–27. Petitioner asserts that Ein-Gal teaches introducing an injectable material to displace the rectum relative to the prostate gland during radiation therapy. *Id.* at 27.

For example, Petitioner asserts Wallace teaches introducing a biocompatible and biodegradable gel as a space-filling device to displace tissues relative to one another during radiation therapy. *Id.* at 28–30 (citing, e.g., Ex. 1010, Abstract, 1:14–15, 3:43–49, 19:3–9, 19:9–19, 28:7–19, 33:64–67; Ex. 1003 ¶¶ 143–145). Moreover, Petitioner asserts that Wallace teaches introducing an injectable material that forms a gel in the patient. *Id.* at 32 (citing Ex. 1010, 1:39–45, 2:5–9, 10:9–12; Ex. 1003 ¶ 148). Petitioner further asserts that Wallace teaches polymers that include linking groups to promote hydrolysis or provide a site for enzymatic degradation. *Id.* at 32–33 (citing Ex. 1010, 16:44–47; Ex. 1003 ¶¶ 143–144). In view of those teachings, Petitioner asserts that Wallace teaches a biodegradable filler

removable by biodegradation. *Id.* (citing Ex. 19:3–19; Ex. 1003 ¶¶ 148–149).

To the extent Wallace does not explicitly teach a biocompatible and biodegradable gel, Petitioner asserts the use of such a gel would have been obvious. Specifically, Petitioner argues that a person of ordinary skill in the art would have been aware that biocompatible filler devices were commonly used to displace organs during radiation therapy. *Id.* at 29 (citing Ex. 1003 ¶¶ 133–138). Petitioner also argues that a person of ordinary skill would have understood that non-biodegradable fillers "would need to be removed from the patient subsequent to therapy so that the displaced organ could return to its original position." *Id.* (citing Ex. 1003 ¶ 137). In the alternative, Petitioner argues that a person of ordinary skill in the art would have known that a biodegradable filler could be left in the patient's body to be absorbed over time, and obviate the need for surgical removal. *Id.* at 29–30 (citing Ex. 1003 ¶ 137, 143–152).

Petitioner asserts that a person of ordinary skill in the art at the time would have had a reasonable expectation of success injecting Wallace's biocompatible, biodegradable material to displace the rectum relative to the prostate during radiation therapy as taught by Ein-Gal. *Id.* at 33–34. Petitioner asserts that "[b]oth Wallace and Ein-Gal recognize and appreciate the benefit of displacing tissue away from a site intended to be irradiated, as doing so would protect the tissue from the harmful effects of radiation." *Id.* at 34 (citing Ex. 1010, 33:64–67; Ex. 1049, 1:31–36; Ex. 1003 ¶ 151). Petitioner also asserts that Wallace teaches a person of ordinary skill would have "easily determine[d] the appropriate administration protocol to use with any particular composition having a known gel strength and gelation time." *Id.* at 34–35 (citing Ex. 1010, 28:39–41; Ex. 1003 ¶ 151).

Patent Owner opposes Petitioner's arguments, arguing Petitioner's analysis is flawed and its declarant, Dr. Dicker, offers conclusory opinions. Prelim. Resp. 4–23. For example, Patent Owner argues that Petitioner's person of ordinary skill in the art lacks the knowledge of polymer science needed to pick and choose among the many options disclosed by Wallace. *See id.* at 4–6. Regarding the "biodegradable" limitation, Patent Owner argues Wallace does not describe compositions that are biodegradable or removed by biodegradation, nor would Petitioner's person of ordinary skill in the art have reasonably expected to have been able to prepare polymers that are removed by biodegradation while also simultaneously possessing all of the other claimed features. *Id.* at 9–18. Regarding the "space-filling device" limitation, Patent Owner argues that Wallace does not specifically teach the space-filling device is a composition that is "removed by biodegradation." *Id.* at 19–20. Patent Owner further argues Petitioner cites no evidence to support its rationale that the device should be biodegradable so the displaced organ could return to its original position. *Id.* at 21–22.

We have considered each of Patent Owner's arguments, but do not find them sufficient at this stage of the proceeding to deny the Petition. As explained above, on this record, we find Petitioner's arguments and evidence sufficient to show that each limitation of claim 1 is taught or suggested by the combination of Wallace and Ein-Gal and that a person of ordinary skill in the art would have had a reason to use Wallace's biocompatible, biodegradable polymer gel instead of Ein-Gal's water to treat the prostate gland and avoid radiation damage to the rectum with a reasonable expectation of success to eliminate the need to remove the filler surgically. Ex. 1003 ¶¶ 132–152.

To the extent Patent Owner questions the credibility of Dr. Dicker's testimony for lack of expertise in polymer chemistry, we find his testimony to be sufficiently supported at this stage of the proceeding. For example, Dr. Dicker explains that Wallace teaches "introducing a biocompatible, biodegradable gel within a patient's body for the specific purpose of filling a space between a first tissue location and a second tissue location (*i.e.*, increasing the distance between a first tissue location and a second tissue location)." Ex. 1003 ¶¶ 143–144 (citing Ex. 1010, Abstract, 7:25–29, 32:45–49, 16:44–47, 19:3–19, 33:64–67). Dr. Dicker also notes that Wallace states that a person of ordinary skill in the art would have "easily determine[d] the appropriate administration protocol to use with any particular composition having a known gel strength and gelation time." *Id.* ¶ 151 (quoting Ex. 1010, 28:39–41). As explained above, on this record, we consider the level of ordinary skill in the art to include experience with polymer science via their own research or collaborative work with a research team in the medical or biotechnology industry. To the extent Patent Owner questions Dr. Dicker's expertise during trial, we will consider his experience (particularly relative to Patent Owner's expert) when weighing each experts' testimony.

As for Patent Owner's remaining arguments, we find them to be largely technical arguments that can be further developed at trial with the benefit of expert testimony from both sides. For example, Patent Owner questions whether Wallace teaches biodegradable compositions that are "removed by biodegradation."[7] Prelim. Resp. 9–14. Dr. Dicker opines that

[7] Patent Owner appears to construe "removed by biodegradation" to require that the filler device biodegrade completely such that nothing remains. We do not discern anything in the '913 patent specification that appears to

it does based on Wallace's teaching of biodegradable segments and blocks. Ex. 1003 ¶ 149 (citing Ex. 1010, 19:3–9). On this record, we find Dr. Dicker's unrebutted testimony sufficient, particularly given Wallace's teaching that biodegradable segments may be "distributed throughout the polymer's molecular structure" and "may be composed of small molecular segments." Ex. 1010, 19:3–10. At trial, Patent Owner may cross-examine Dr. Dicker and submit evidence of its own to support its position that Wallace does not teach fillers that are "removed by biodegradation."

Patent Owner also asserts that Dr. Dicker cites no evidence that the device needs to be removed after therapy and simply assumes that removal is required. Prelim. Resp. 21. We disagree as Dr. Dicker explains, for example, that in 2002, an ordinary artisan "recognized the shortcomings of surgically implanted physical shields or barriers to reduce exposure of harmful radiation on surrounding normal tissue, and suggested mitigating the risk by using 'a prosthesis made entirely from absorbable material.'" Ex. 1003 ¶ 125 (citing Ex. 1012, 348); *see also id.* ¶¶ 97–100. We find that testimony to be sufficient at this stage of the proceeding.

Accordingly, having considered the arguments and evidence presented by the parties, we find Petitioner has shown a reasonable likelihood of prevailing on its assertion that claim 1 of the '913 patent is unpatentable as obvious over Wallace and Ein-Gal.

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require 100% biodegradation of the filler to be considered "removed." For example, the Specification states "[b]iodegradation may be measured by palpitation or other observations to detect the change in volume of a filler after its introduction into a patient." Ex. 1001, 5:1–3. We invite the parties to brief the construction of "removed by biodegradation" and address what constitutes sufficient biodegradation to constitute "remov[al]" of the filler device.

4. Analysis of Claim 17

Regarding claim 17, we have considered the arguments and evidence presented by Petitioner and find Petitioner has shown sufficiently that each limitation of claim 17 is taught by the combination of Wallace and Ein-Gal. Pet. 35–39 (citing Ex. 1010, 3:50–55, 9:1–19, 19:59–60, 20:2–21:35; Ex. 1049, 1:31–36; Ex. 1003 ¶¶ 155–160). We also find Petitioner has shown sufficiently that a person of ordinary skill in the art would have had a reason to combine Wallace and Ein-Gal with a reasonable expectation of success for the same reasons discussed above with respect to claim 1.

In response, Patent Owner argues that Wallace does not teach the "filler being collagen," because Wallace teaches a chemically modified form of collagen that includes reactive groups and optional linkers. Prelim. Resp. 8–9. Patent Owner also argues that "Petitioner relies on unsupported expert testimony to gap-fill the prior art with respect to the specific therapeutic radiation dose applied to the second tissue location, and the specific reduction in dose to the first tissue location." Prelim. Resp. at 23–24. Patent Owner also argues that Petitioner offers no evidence for why a person of ordinary skill in the art would have selected a radiation dose in the range of 70 to 100 Gy. *Id.* at 24. Patent Owner argues further that Dr. Dicker "offers no evidence or explanation for his conclusion that the [person of ordinary skill in the art] would have been able to decrease the radiation dose to the surrounding tissue by the specific amount of '50% or less than the dose of radiation received by the target tissue.'" *Id.* at 25–26 (citing Ex. 1003 ¶ 60).

At this stage of the proceeding, we find Dr. Dicker's testimony to be sufficient. We agree with Patent Owner that Wallace teaches chemically modifying collagen. But on this record, we find the '913 patent specification defines "collagen" broadly, as explained above, such that the

term includes "materials intelligently designed to mimic collagen or some of the structural or functional features of collagen." *See* Ex. 1001, 7:65–8:10. Moreover, we find Dr. Dicker is entitled to rely on the '913 patent's statement regarding the state of the art that "[t]he traditional radiation dose delivered to the prostate ranges from 70-76 Gy. However, modern technology using 3-D conformal radiation or Intensity Modulated Radiotherapy (IMRT) has allowed dose escalation upwards to 100 Gy." Ex. 1003 ¶ 41 (quoting Ex. 1001, 14:6–15) (emphasis omitted). The '913 patent does not cite those dose ranges as knowledge that was unique to the patentee, as Patent Owner suggests. *See* Prelim. Resp. 25 (arguing "what the '913 patent's inventor recognized as a suitable dose for the claimed method is irrelevant to the obviousness inquiry"). Rather, the '913 patent refers to the 70–76 Gy radiation dose as "traditional" and the dose of up to 100 Gy as a known dose that is possible due to modern technology. *See* Ex. 1001, 14:6–15.

On this record, we also find sufficiently supported Dr. Dicker's explanation that a person of ordinary skill in the art in 2002 was "well aware that radiation energy diminishes rapidly from the source or origin of the ionizing radiation during radiation treatment." Ex. 1003 ¶ 81 (citing Ex. 1050, 185, 186). Dr. Dicker then explains an ordinary artisan "will routinely calculate as part of the clinical treatment the expected radiation dose to normal tissue, taking into account and weighing whether the therapy will cause more harm than good." *Id.* ¶ 83 (citing 1044, 103).

Accordingly, having considered the arguments and evidence presented by the parties, we find Petitioner has shown a reasonable likelihood of prevailing on its assertion that independent claim 17 of the '913 patent is unpatentable as obvious over Wallace and Ein-Gal.

5. Analysis of Dependent Claims

Petitioner asserts that dependent claims 2–16, 18, and 20–24, which depend from claim 1, are unpatentable as obvious over Wallace and Ein-Gal. Pet. 39–44. Regarding dependent claims 3, 7–10, 15, 18, and 20–24, Patent Owner asserts that Petitioner's person of ordinary skill in the art would have lacked sufficient knowledge of polymer science to reach the claimed composition and that Wallace does not teach the specific materials recited. Prelim. Resp. 7–9. Specifically, Patent Owner argues that Wallace teaches chemically modifying the component core, which results in a different compound. *Id.*

Having considered the arguments and evidence presented by the parties, we find Petitioner has shown sufficiently that the combination of Wallace and Ein-Gal teaches each limitation of dependent claims 2–16, 18, and 20–24. *See* Pet. 39–44 (citing Ex. 1003 ¶¶ 162–176). We also find there was a reason to combine Wallace and Ein-Gal with a reasonable expectation of success for the same reasons stated above with respect to claim 1. For the same reasons stated above, we are not persuaded at this stage of the proceeding that Petitioner's person of ordinary skill in the art would have lacked sufficient knowledge to reach the claimed composition. Moreover, on this record, we find the specific materials recited in the claims should be construed to include derivatives of the materials, as set forth in the '913 patent specification, which, for example, refers to "alginate" to include both naturally occurring alginate and modified derivatives. *See, e.g.*, Ex. 1001, 8:21–48 (describing "[n]aturally occurring alginate" and "modified alginate" derivatives).

Accordingly, we find Petitioner has shown a reasonable likelihood of prevailing on its assertion that claims 2–16, 18, and 20–24 are unpatentable as obvious over Wallace and Ein-Gal.

D. Obviousness over Wallace, Ein-Gal, and Griffith-Cima

Petitioner asserts that claims 19 and 25 are unpatentable as obvious over Wallace, Ein-Gal, and Griffith-Cima. Pet. 44–45. Patent Owner opposes Petitioner's assertion. Prelim. Resp. 26–29.

We incorporate here our discussion of Wallace and Ein-Gal above.

1. Griffith-Cima (Ex. 1011)

Griffith-Cima relates to slowly polymerizing, biocompatible, biodegradable hydrogels that promote engraftment and provide three dimensional templates for new cell growth. Ex. 1011, 9:32–37. Griffith-Cima teaches a method of suspending cells in a hydrogel solution and injecting the solution directly into a site in a patient, where the hydrogel hardens into a matrix with cells dispersed in it. *Id.* at 10:3–7. Ultimately, the hydrogel degrades, leaving only the resulting tissue. *Id.* at 12–13. Griffith-Cima teaches that hydrogel materials include polysaccharides such as alginate. *Id.* at 15:27–34.

2. Analysis

Claims 19 and 25 depend from claim 1 and further recite that the filler includes alginate and a thermoreversible polymer, respectively. Ex. 1001, 18:19–20, 31–32. Regarding claim 19, Petitioner asserts that Wallace discloses that the compositions may include a carboxylated polysaccharide and that an ordinary artisan would have understood alginate to be a carboxylated polysaccharide that was known to form a hydrogel in situ, as taught by Griffith-Cima. Pet. 44 (citing Ex. 1010, 19:59–67; Ex. 1003 ¶¶ 177–178). Moreover, Petitioner asserts that "Applicant cited to Griffith-

Cima to overcome an enablement rejection as evidence that alginate was known to form a hydrogel prior to the time of invention," during prosecution of the '913 patent. *Id.* at 44–45 (citing Ex. 1005, 199, 254).

Regarding claim 25, Petitioner asserts that Wallace teaches that the gel compositions may include synthetic hydrophilic polymers, including poly(ethylene oxide)-poly(propylene oxide) copolymers and block polymers. Pet. 45 (citing Ex. 1010, 8:26–30; Ex. 1003 ¶ 179). Petitioner notes that during prosecution, Applicant cited Pluronics as an example of a block copolymer based on ethylene oxide and propylene oxide that is a well-known thermoreversible polymer that can form a gel. *Id.* (citing Ex. 1005, 256, 273). Petitioner asserts that Griffith-Cima teaches the use of Pluronics to form a biocompatible hydrogel that may be crosslinked by temperature. *Id.* (citing Ex. 1011, 15:20–34). Thus, Petitioner asserts that a person of ordinary skill in the art would have found the use of thermoreversible polymers in the gel compositions to be well known, well understood, and predictable. *Id.* (citing Ex. 1003 ¶¶181–182).

In response, Patent Owner argues that Petitioner fails to explain how its person of ordinary skill in the art would have been able to reach the claimed subject matter (*see* Prelim. Resp. 6–7) or why a person of ordinary skill in the art would have selected a filler comprising alginate or a thermoreversible polymer such as Pluronics (*id.* at 26–29).

For the same reasons stated above, we find Petitioner's arguments and evidence with respect to the knowledge of the person of ordinary skill the art to be sufficient at this stage of the proceeding. We also find Dr. Dicker's testimony that a person of ordinary skill in the art would have found it obvious to use alginate and Pluronics based on Wallace's general teaching and Griffith-Cima's specific use of those gel compositions sufficient on this

record, with the understanding that the record will be developed further at trial.

Accordingly, having considered the arguments and evidence presented by the parties, we find Petitioner has shown a reasonable likelihood that it would prevail on its assertion that claims 19 and 25 are unpatentable as obvious over Wallace, Ein-Gal, and Griffith-Cima.

E. Obviousness over Ball, Carroll, Ein-Gal, and Griffith-Cima

Petitioner asserts that claims 1–24 are unpatentable as obvious over Ball, Carroll, and Ein-Gal. Pet. 45–62. Petitioner also asserts that dependent claim 25 is unpatentable as obvious over Ball, Carroll, Ein-Gal, and Griffith-Cima. *Id.* at 62–63. Patent Owner opposes Petitioner's assertions. Prelim. Resp. 29–36.

We incorporate here our findings above regarding the disclosures of Ein-Gal and Griffith-Cima.

1. Ball (Ex. 1012)

Ball relates to the use of a silicone implant to prevent visceral damage during adjuvant radiation therapy for cancerous tissue. Ex. 1012, 346. Ball states that "[b]y securing a silicone gel-filled implant . . . in the tumour bed after excision of the tumour, adjacent viscera are displaced from the site of maximum irradiation and may thereby be protected." *Id.* Ball teaches surgically removing the implant after radiation therapy. *Id.* However, Ball reports side effects potentially caused by the silicone implant, including infection and bowel perforation. *Id.* at 348. Because removing the implant at an earlier stage would inflict further surgery on the patient, Ball proposes using an expandable prosthesis that could be withdrawn during the initial treatment, "or a prosthesis made entirely from absorbable material." *Id.*

2. Carroll (Ex. 1013)

Carroll relates to a method of encapsulating a tissue and treating the tissue with radiation therapy. Ex. 1013, Abstract. Carroll explains that "collateral damage to normal tissues adjacent to cancerous tumors [] limits the effectiveness of radiation therapy." *Id.* at 2:38–39. Carroll states that improved radiation therapy can be conducted with encapsulation. *Id.* at 3:3–7.

Carroll describes the encapsulating material as physiologically compatible, biodegradable, and resorbable. *Id.* at 10:23–25, 15:1–4, 23:32. The material may be injected and *in situ* crosslinked in the patient. *Id.* at 4:14–21. Carroll describes encapsulating materials as including hydrogel-forming materials, such as hyaluronic acid, and synthetic or naturally occurring resorbable materials, such as collagen, polyethylene glycol polymers, alginate, and polymers of polyglycolic and polylactic acids. *Id.* at 7:62–8:59.

3. Analysis

Petitioner asserts that Ball describes a method of radiation therapy including the step of introducing a biocompatible implant between normal tissue and cancerous tissue to increase distance between tissues and reduce the amount of radiation to the normal tissue. Pet. 46–48 (citing Ex. 1012, 346; Ex. 1003 ¶¶ 229–231, 235). Petitioner asserts Ball teaches the implant must be surgically removed after treatment, and recognizes the advantage of a biodegradable implant that would not require surgical removal. *Id.* at 46–47 (citing Ex. 1012, 348; Ex. 1003 ¶¶ 230–231). Petitioner asserts that Carroll describes biocompatible, biodegradable hydrogels used to encapsulate malignant tumors treated with radiation therapy. *Id.* at 47 (citing Ex. 1013, 1:18–20, 1:62–65; 3:66–4:17, 6:26–28, 17:32–35,

23:25–32; Ex. 1003 ¶ 232). Petitioner asserts Carroll's hydrogel is introduced as an injectable material and forms an elastic solid or semi-solid in the patient's body. *Id.* at 49 (citing Ex. 1013, 3:66–4:17, 7:54–57, 9:28–42; Ex. 1003 ¶¶ 237–238). Petitioner asserts that Ein-Gal describes introducing an injectable material to displace the rectum away from the prostate gland during radiation therapy. *Id.* at 49–50 (Ex. 1049, 1:31–36; Ex. 1003 ¶ 239).

Petitioner asserts that Ball describes the need for absorbable implants to be used in radiation therapy. *Id.* at 52 (Ex. 1012, 348; Ex. 1003 ¶ 231). Petitioner asserts that the person of ordinary skill in the art would have had a reason to use Carroll's biodegradable material to displace healthy tissue during radiation therapy, as taught by Ball and Ein-Gal, to eliminate the need for further surgery to remove the implant device. *Id.* at 52–53 (citing Ex. 1003 ¶ 234). Petitioner asserts that the person of ordinary skill in the art would have had a reasonable expectation of success in combining the references because Carroll teaches biodegradable hydrogels for filling a desired space within the patient's body for protecting healthy tissue and Ball suggests using biodegradable spacers. *Id.* at 53 (citing Ex. 1003 ¶ 241).

Patent Owner opposes Petitioner's arguments, arguing Petitioner's analysis is vague and fails to provide a rationale to combine the references. Prelim. Resp. 29–30. For example, Patent Owner argues Petitioner does not explain how Ball would have been modified by a person of ordinary skill in the art in view of Carroll or Ein-Gal. *Id.* at 30. Patent Owner argues Petitioner has failed to explain its challenge with particularity in this regard. *Id.* at 30–31. Additionally, Patent Owner argues that "Petitioner does not explain how any material from Carroll could replace a part of Ball's implant while allowing the implant to maintain its structure as a gel-filled prosthesis

and be securable in a tumor bed." *Id.* at 31–32. More specifically, Patent Owner argues that replacing Ball's silicone implant with Carroll's hydrogel would render Ball's implant unsuitable for its intended purpose of being fastened in place. *Id.* at 32.

Having considered the arguments and evidence, we agree with Patent Owner that Petitioner has not explained sufficiently how a person of ordinary skill in the art would have combined Ball, Carroll, and Ein-Gal to reach the claimed invention of claims 1–24 and Ball, Carroll, Ein-Gal, and Griffith-Cima to reach claim 25.

Specifically, it is unclear how Petitioner combines the implant device of Ball with the encapsulating hydrogel of Carroll. Petitioner asserts Ball recognizes the advantages of using "a prosthesis made entirely from absorbable material" to eliminate the need for surgical removal. Pet. 52 (citing Ex. 1012, 348; Ex. 1003 ¶ 231). And Petitioner asserts that a person of ordinary skill in the art would have considered it obvious to inject a biocompatible, biodegradable hydrogel composition like Carroll to displace a tissue location to protect an organ from radiation's harmful effects, as taught by Ball and Ein-Gal. *Id.* at 50 (citing Ex. 1003 ¶¶ 229–241).

It is unclear from the Petition, however, whether Petitioner argues a person of ordinary skill in the art would have filled the Ball implant with the hydrogel of Carroll, or if Petitioner argues that it would have been obvious to replace the Ball implant altogether with the encapsulating hydrogel of Carroll. According to Petitioner's Explanation of Multiple Petitions, the approach of the instant Petition "is the use of an injection of a gel filler to displace an organ from a tissue that is the target of radiation, without using a biodegradable envelope for the gel filler." Paper 3, 3. This approach is not

clear from the argument set forth in the Petition and should not be considered on the merits because it presents a new argument.

But even if we do consider Petitioner's explanation and assume Petitioner argues the latter, it is unclear why or how a person of ordinary skill in the art would have combined the encapsulating hydrogel of Carroll with Ein-Gal. According to Petitioner, Carroll teaches placing a biocompatible, biodegradable hydrogel "between a tumor's site and surrounding healthy tissue to act as a barrier that protects the healthy tissue during a course of treatment." Pet. 51 (citing Ex. 1013, 10:46–52). We find this to be an oversimplification of Carroll. Carroll teaches "methods in which a channel is provided around a tissue of the organism, and an encapsulating composition is infused into the channel to encapsulate the tissue in a capsule." Ex. 1013, Abstract. Petitioner fails to explain sufficiently how a person of ordinary skill in the art reading Carroll's encapsulation method would have combined Carroll's teaching with that of Ball and Ein-Gal to reach the claimed invention.

Put simply, Petitioner's argument lacks clarity and we are not inclined to decipher Petitioner's argument for ourselves. We, therefore, find Petitioner has not established a reasonable likelihood of succeeding on its assertion that claims 1–24 are unpatentable over Ball, Carroll, and Ein-Gal or claim 25 is unpatentable over Ball, Carroll, Ein-Gal, and Griffith-Cima.

III. CONCLUSION

For the foregoing reasons, we conclude that Petitioner has established a reasonable likelihood of prevailing on its assertion that at least one claim of the '913 patent is unpatentable. In *SAS Institute Inc. v. Iancu*, the Supreme Court held that the Board's final written decision in an instituted *inter partes* review must address every claim challenged by a petitioner.

138 S. Ct. 1348, 1354 (2018). In light of *SAS*, the "the Board will either (1) institute as to all claims challenged in the petition and on all grounds in the petition, or (2) institute on no claims and deny institution." Patent Trial and Appeal Board Consolidated Trial Practice Guide 64 (Nov. 2019), *available at* https://www.uspto.gov/sites/default/files/documents/tpgnov.pdf. We, accordingly, institute an *inter partes* review of all of the challenged claims on all asserted grounds.

Our determination in this Decision is not a final determination on either the patentability of any challenged claims or the construction of any claim term and, thus, leaves undecided any remaining fact issues necessary to determine whether sufficient evidence supports Petitioner's contentions by a preponderance of the evidence in the final written decision. *See Trivascular, Inc. v. Samuels*, 812 F.3d 1056, 1068 (Fed. Cir. 2016) (noting that "there is a significant difference between a petitioner's burden to establish a 'reasonable likelihood of success' at institution, and actually proving invalidity by a preponderance of the evidence at trial") (quoting 35 U.S.C. § 314(a) and comparing *id.* § 316(e)).

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that pursuant to 35 U.S.C. § 314(a), an *inter partes* review of claims 1–25 of the '913 patent is instituted, commencing on the entry date of this decision; and

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of review.

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