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Paper 14
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

HYPERBRANCH MEDICAL TECHNOLOGY, INC.,
Petitioner,

v.

INCEPT LLC,
Patent Owner.

Case IPR2016-01836
Patent 7,009,034 B2

Before LORA M. GREEN, BRIAN P. MURPHY, and KRISTI L. R. SAWERT, *Administrative Patent Judges.*

SAWERT, *Administrative Patent Judge.*

DECISION
Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

HyperBranch Medical Technology, Inc. ("Petitioner") filed a corrected Petition for an *inter partes* review of claims 1–12 of U.S. Patent No. 7,009,034 B2 ("the '034 patent," Ex. 1001). Paper 4 ("Pet."). Incept LLC ("Patent Owner") timely filed a Preliminary Response. Paper 13 ("Prelim. Resp.").

Institution of an *inter partes* review is authorized by statute when "the information presented in the petition . . . and any response . . . shows that 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); *see also* 37 C.F.R. §§ 42.4, 42.108.

For the reasons provided below, we determine that Petitioner has satisfied the threshold requirement set forth in 35 U.S.C. § 314(a) as to claims 1–6 and 8–12 of the '034 patent, and we institute an *inter partes* review of those claims. As to claim 7, we exercise our discretion to not institute *inter partes* review of this claim.

A. Related Proceedings

The parties identify the following district court action as a related matter under 37 C.F.R. § 42.8(b)(2): *Integra LifeSciences Corp. v. HyperBranch Med. Tech., Inc.*, C.A. No. 15-819-LPS-CJB (D. Del.). Pet. 6; Paper 6, 2.

B. The ’034 Patent

The ’034 patent discloses and claims biocompatible crosslinked polymers that “are formed from water soluble precursors having electrophilic and nucleophilic functional groups capable of reacting and crosslinking in situ.” Ex. 1001 (Abstract). Biocompatible crosslinked polymers, and especially hydrogels, were known in the art as useful for the prevention and treatment of surgical adhesions (i.e., the adhesion of tissues exposed during surgery to one another), tissue augmentation, medical device coating, surgical sealing, and drug delivery. *Id.* (col. 1, ll. 30–60). The ’034 patent explains, however, that these prior-art hydrogels “are essentially colorless” and, therefore, “difficult to visualize, especially in the typically wet and moist surgical environment” and under “laparoscopic conditions.” *Id.* (col. 2, ll. 4–14). The inventors of the ’034 patent “realized that the use of color in biocompatible crosslinked polymers and precursors greatly improves their performance in a surgical environment.” *Id.* (col. 2, ll. 18–22). Thus, the hydrogel may contain a “visualization agent” that “reflects or emits light at a wavelength detectable to a human eye.” *Id.* (col. 2, ll. 30–32); *see also id.* (col. 10, ll. 47–50) (“Where convenient, the biocompatible crosslinked polymer or precursor solutions (or both) may contain visualization agents to improve their visibility during surgical procedures.”).

The visualization agent, the ’034 patent explains, allows a user to determine the thickness of the hydrogel as it is being applied. *Id.* (col. 5, ll. 9–10). Specifically, the visualization agent “lets a user applying the hydrogel observe the hydrogel and estimate its thickness and apply the hydrogel until it reaches a predetermined thickness.” *Id.* (col. 2, ll. 32–35);

see also id. (col. 2, ll. 63–66) ("A preferred method of use is to form a hydrogel on the tissue until the color and/or color intensity of the hydrogel indicates that a pre-determined thickness of hydrogel has been deposited on the tissue."). The visualization agent "makes the hydrogel change in its appearance until the user determines [its] thickness." *Id.* (col. 5, ll. 50–51). "For example," the '034 patent explains, "a blue dye in the hydrogel makes the hydrogel increasingly opaque as the thickness of the hydrogel increases." *Id.* (col. 5, ll. 53–55). The '034 patent further explains that the hydrogel's thickness may affect surgical outcomes: a hydrogel that is "too thick" will interfere with, for example, the closure of a wound or tissue movement, whereas "[a] hydrogel that is too thin will not serve its purpose, e.g., providing a barrier that prevents surgical adhesions or provides a strong seal against fluid leakage." *Id.* (col. 5, ll. 2–9).

The '034 patent teaches that the visualization agents "may be selected from among any of the various non-toxic colored substances suitable for use in medical implantable medical devices," *id.* (col. 10, ll. 53–55), and lists the preferred visualization agents as "FD&C Blue #1, #2, #3, D&C Green #6, and methylene blue," *id.* (col. 2, ll. 46–47). The '034 patent also states that the visualization agent may be a fluorescent molecule. *Id.* (col. 2, ll. 47–48; col. 7, ll. 2–3).

The visualization agent "provides a color that is visible to the human eye, e.g., a color that is detected visually by the user or detected by a video camera and relayed to a video screen observed by the user." *Id.* (col. 5, ll. 10–14). The '034 patent teaches that visually-observable visualization agents, i.e., those agents having a color detectable to a human eye, are

preferred. *Id.* (col. 11, l. 11); *see also id.* (col. 7, ll. 56–57) ("A visually observable visualization agent is an agent that has a color detectable by a human eye."). But visualization agents not normally visible to the human eye may also be used, so long as those agents are "detectable at a different wavelength, e.g., the infra red or ultraviolet, when used in combination with a suitable imaging device, e.g., a video-camera." *Id.* (col. 7, ll. 60–65).

Finally, the '034 patent teaches that "[c]onventional polymeric hydrogels" "have sometimes been mixed with image contrast agents to increase their visibility for medical imaging devices such as X-ray or magnetic resonance imaging (MRI) machines." *Id.* (col. 5, ll. 15–22). But, "[a] characteristic of providing imaging to an X-ray or MRI machine is not a characteristic sufficient to establish function as a visually observable visualization agent." *Id.* (col. 7, ll. 58–60).

C. Challenged Claims

Petitioner challenges claims 1–12 of the '034 patent. Claim 1 is the only independent claim and is illustrative:

> 1. A method of preparing a composition suitable to coat a tissue of a patient, the method comprising:
>
> mixing reactive precursor species comprising nucleophilic functional groups, reactive precursor species comprising electrophilic functional groups, and a *visualization agent* such that the nucleophilic functional groups and electrophilic functional groups crosslink after contact with the tissue to form a hydrogel having an interior and an exterior, with the exterior having at least one substrate coating surface and *the visualization agent being at least partially disposed within the interior and reflecting or emitting light at a wavelength detectable to a human eye*

> *to thereby provide a means for visualization of the coating by a human eye*.

Ex. 1001 (col. 39, l. 56–col. 40, l. 2) (emphases added).

D. The Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–12 of the '034 patent on the following grounds:

Ground	Claims	Basis
I	1–5, 7–12	Anticipation under 35 U.S.C. § 102(b) by Rhee '500[1]
II	1–6, 8–12	Obviousness under 35 U.S.C. § 103 over Rhee '500 in view of Bass[2]
III	1–6, 8–12	Obviousness under 35 U.S.C. § 103 over Rhee '500 in view of Tse[3]
IV	1–5, 7–12	Anticipation under 35 U.S.C. § 102(b) by Rhee '587[4]
V	1–6, 8–12	Obviousness under 35 U.S.C. § 103 over Rhee '587 in view of Bass
VI	1–6, 8–12	Obviousness under 35 U.S.C. § 103 over Rhee '587 in view of Tse

Pet. 8–9. Petitioner also relies on the Declaration of Anthony M. Lowman, Ph.D. *See* Pet. 8 (citing Ex. 1003).

[1] Woonza M. Rhee, et al., U.S. Patent 5,874,500 (filed Dec. 18, 1996) (issued Feb. 23, 1999) ("Rhee '500"). Ex. 1004.

[2] Lawrence S. Bass, et al., U.S. Patent 5,292,362 (filed Jul. 9, 1991) (issued Mar. 8, 1994) ("Bass"). Ex. 1006.

[3] David S. Tse, et al., *Cyanoacrylate Adhesive Used to Stop CSF Leaks During Orbital Surgery*, ARCH OPHTHALMOL, 102:1337–39 (Sept. 1984) ("Tse"). Ex. 1007.

[4] Woonza M. Rhee, et al., U.S. Patent 5,614,587 (filed Jun. 7, 1995) (issued Mar. 25, 1997) ("Rhee '587"). Ex. 1005.

II. ANALYSIS

A. Claim Construction

In an *inter partes* review, claim terms in an unexpired patent are interpreted according to their broadest reasonable construction in light of the specification of the patent in which they appear. *See* 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2144–46 (2016) (upholding the use of the broadest reasonable interpretation standard).

Under that standard, we presume that a claim term carries its "ordinary and customary meaning," which "is the meaning that the term would have to a person of ordinary skill in the art in question" at the time of the invention. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007); *see also Trivascular, Inc. v. Samuels*, 812 F.3d 1056, 1062 (Fed. Cir. 2016) ("Under a broadest reasonable interpretation, words of the claim must be given their plain meaning, unless such meaning is inconsistent with the specification and prosecution history."). Any special definition for a claim term must be set forth in the specification with reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

Petitioner proposes interpretations of certain claim terms. Pet. 18–22. Patent Owner states that the interpretations "of th[ose] specified claim terms do not matter except to the extent that Petitioner's proposed broadest reasonable construction of 'visualization agent' is inconsistent with what a POSA would understand" based on the specification of the '034 patent. Prelim. Resp. 12. Patent Owner, however, does not propose an explicit construction for the claim term "visualization agent." *Id.*

For purposes of this decision, in order to determine whether to institute an *inter partes* review, we need not explicitly interpret every claim term for which Petitioner propose a construction. *See* 35 U.S.C. § 314(a); *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) ("[O]nly those terms need be construed that are in controversy, and only to the extent necessary to resolve the controversy."). We find that, to resolve whether Petitioner has demonstrated a reasonable likelihood of prevailing, we need only address Petitioner's proposed construction of "visualization agent."

Petitioner contends that the broadest reasonable interpretation of that term is "a substance or material that imparts a visibly discernable color or obscures the optical clarity of the hydrogel." Pet. 18–19. In support of the "imparts a visibly discernable color" portion of its definition, Petitioner cites to statements in the written description of the '034 patent that a "visualization agent" "reflects or emits light at a wavelength detectable to a human eye." *Id.* at 19 (citing Ex. 1001, col. 2, ll. 31–32, 62–63; col. 3, ll. 10–11). And as to "or obscures the optical clarity of the hydrogel," Petitioner asserts that any substance or material that emits or reflects light, such as a particle entrapped within the hydrogel, may serve as a visualization agent. *Id.* at 19–20 (citing Ex. 1001, col. 34, ll. 28–32). Put differently, because the visualization agent "need only be able to obscure the user's ability to view the underlying tissue," Petitioner asserts, a visualization agent must include "materials that impart *any* visually observable opacity to the hydrogel." *Id.* at 20 (citing Ex. 1001, col. 7, ll. 32–33).

Claim 1 expressly provides that the visualization agent "reflect[s] or emit[s] light at a wavelength detectable to a human eye to thereby provide a means for visualization of the coating by a human eye." Ex 1001 (col. 39, l. 65–col. 40, l. 2). Thus, by its plain terms, the "visualization agent" is an agent that reflects or emits light at a wavelength detectable to a human eye so that a human eye may visualize the hydrogel coating. *See, e.g.*, *Veritas Techs. LLC v. Veeam Software Corp.*, 835 F.3d 1406, 1411 (Fed. Cir. 2016) (claim construction begins with the plain language of the claims). The written description supports this plain reading of the claim: the "visualization agent" is consistently and repeatedly described as an agent that "reflects or emits light at a wavelength detectable to a human eye." Ex. 1001 (col. 2, ll. 30–32, ll. 61–63; col. 3, ll. 9–11; col. 6, ll. 26–28). Moreover, the written description discloses several examples of colors that reflect or emit light at a wavelength detectable to a human eye. *See, e.g.*, *id.* (col. 2, ll. 46–47 (listing "FD&C Blue #1, #2, #3, D&C Green #6, and methylene blue" as preferred visualization agents)).

Given this interpretation, for purposes of this Decision, we determine that a "visualization agent" encompasses an agent with a visually discernable color—the first portion of Petitioner's proposed interpretation. Pet. 18–19. But, at this stage of the proceeding, we are not persuaded that the broadest reasonable interpretation of "visualization agent" includes *any* substance or material that merely "obscures the optical clarity of the hydrogel"—the remaining portion of Petitioner's proposed interpretation. *Id.* at 19; *see also id.* at 20 (stating that the broadest reasonable interpretation must include "materials that impart *any* visually observable opacity to the

hydrogel"). Specifically, the written description does not appear to support Petitioner's assertion that the visualization agent "need only be able to obscure the user's ability to view the underlying tissue." *Id.* at 20 (citing Ex. 1001, col. 7, ll. 32–33).

We note that the written description only uses variations of the term "obscure" twice: both instances in conjunction with an explanation of how a user may utilize the visualization agent to determine the thickness of the hydrogel as it is being applied. Ex. 1001 (col. 7, ll. 34–45). Specifically, the written description describes two "thickness evaluation approaches." *Id.* (col. 7, ll. 38–39). In the first approach, the user applies the hydrogel until the underlying tissue is no longer visible. *Id.* (col. 7, ll. 28–32). And in the second approach, the user applies the hydrogel "until the underlying tissue is *obscured*." *Id.* (col. 7, ll. 32–33 (emphasis added)).

Neither approach involves the use of a hydrogel that lacks color as the visualization agent, as Petitioner appears to imply. *See* Pet. 20 (stating that the '034 patent only teaches color as a preferable visualization agent). Put differently, both "thickness evaluation approaches" result from "form[ing] a hydrogel on the tissue until the *color* of the hydrogel indicates that a predetermined thickness of hydrogel has been deposited on the tissue." Ex. 1001 (col. 7, ll. 17–19 (emphasis added)). And the color, in turn, results from an "appropriately selected concentration of visualization agent." *Id.* (col. 7, ll. 34–36). If a user selects a concentration of visualization agent "that is too low," then the resulting hydrogel will be "too thick," and if the concentration "is too high," then the resulting hydrogel will be "too thin." *Id.* (col. 7, ll. 39–41). Thus, we find nothing in this section of the written

description that would support an interpretation of "visualization agent" that merely obscures the optical clarity of the hydrogel.

B. Anticipation by Rhee '500 (Ground I) and Rhee '587 (Ground IV)

Patent Owner argues that we should invoke our discretion under 35 U.S.C. § 325(d) and deny the anticipation challenges over Rhee '500 and Rhee '587. Prelim. Resp. 13–15. We agree.

As an initial matter, institution of an *inter partes* review is discretionary. *See* 35 U.S.C. § 314(a) (authorizing institution of an *inter partes* review under particular circumstances, but not requiring institution under any circumstances); 37 C.F.R. § 42.108(a) ("the Board *may* authorize the review to proceed" (emphasis added)); *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1367 (Fed. Cir. 2016) (explaining that under § 314(a), "the PTO is permitted, but never compelled, to institute an [*inter partes* review] proceeding"). Even so, we have express discretion under § 325(d) to reject a petition when the same or substantially the same prior art or arguments were presented previously in another proceeding before the Office.

Specifically, "[i]n determining whether to institute or order a proceeding under this chapter, chapter 30, or chapter 31, the Director may take into account whether, and reject the petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office." 35 U.S.C. § 325(d). Although a petitioner may have sound reasons for raising art or arguments similar to those previously considered by the Office, the Board weighs petitioners' desires to be heard against the interests of patent owners, who seek to avoid harassment. *See* H.R. Rep. No. 112-98, pt.1, at 48 (2011) (AIA proceedings "are not to be

used as tools for harassment or a means to prevent market entry through repeated litigation and administrative attacks on the validity of a patent. Doing so would frustrate the purpose of the section as providing quick and cost effective alternatives to litigation.").

Patent Owner states that Rhee '500 was explicitly considered by the Office during examination of the '034 patent. Prelim. Resp. 13–15. Patent Owner explains that the Examiner relied on Rhee '500 for the same purpose that Petitioner relies on Rhee '500 here: to teach the claimed "visualization agent." *Id.* at 13. Patent Owner further explains that it "successfully overcame" a rejection based on Rhee '500 by arguing that the "imaging agents" utilized in Rhee '500 (i.e., iodine, barium sulfate, and fluorine) aided visualization via X-ray or ^{19}F-MRI, and that those imaging agents therefore require procedures and machines that do not involve detection of the imaging agent by the human eye. *Id.* at 14–15 (citing Ex. 2001, 21–22). Petitioner, in contrast, states that the Examiner did not rely on Rhee '500 to teach a visualization agent. Pet.14–16; *see also* Pet. 30 n.4. Instead, Petitioner explains, "Rhee '500 was cited for the use of the chemistry claimed." *Id.* at 15 (citing Ex. 1002, 170–182).

We are persuaded by Patent Owner's evidence and argument. Rhee '500 was expressly considered by the Examiner during prosecution of the application leading to the '034 patent, and expressly relied upon as a reference teaching the claimed "visualization agent." For example, the Examiner described Rhee '500 in the first Office Action as disclosing "crosslinked polymer compositions [that] may contain various imaging agents such as iodine or barium sulfate, or fluorine, in order to aid

visualization of the composition." Ex. 1002, 175. "Thus," the Examiner continued, Rhee '500 "suggest[s] the use of various *visualization agents* including fluorine to improve visibility and performance in a surgical environment." *Id.* (emphasis added). For this reason, Petitioner's assertion that the Examiner did not rely on Rhee '500 to teach a visualization agent, Pet. 15, 30 n.4, is not well taken.

We recognize that Petitioner relies on Rhee '500 to teach two types of alleged visualization agents: barium sulfate and fibrillar collagen. Pet. 31–33. And although barium sulfate was expressly considered as a type "visualization agent" during prosecution, fibrillar collagen was not. Nevertheless, § 325(d) gives us discretion to reject grounds based on previous presentation of "the same or substantially the same prior art *or* arguments." 35 U.S.C. § 325(d) (emphasis added). We find that the Examiner thoroughly considered the written description of Rhee '500 during prosecution, as well as the issue of whether Rhee '500 teaches a visualization agent. *See, e.g.*, Ex. 1002, 126–38. And, given the Examiner's thorough discussion of Rhee '500, we infer that the Examiner simply did not consider fibrillar collagen as satisfying the "visualization agent" claim limitation. Such an inference is consistent the broadest reasonable interpretation of "visualization agent," as explained above.

Finally, we find that Rhee '587 constitutes "substantially the same prior art" as Rhee '500 so as to satisfy § 325(d). In this regard, Petitioner relies on the same disclosure in both Rhee '500 and Rhee '587 to teach the "visualization agent" limitation of the challenged claims. *Compare* Pet. 23–24 (asserting that Rhee '500 teaches the use of opaque fibrillar collagen if

optical clarity is not a requirement and "therefore discloses that its compositions may include a visualization agent"), *with* Pet. 25 (asserting that Rhee '587 teaches that opaque fibrillar collagen may be used "if optical clarity is not a requirement" and "therefore discloses that its compositions may include a visualization agent").

For these reasons, we exercise our discretion under 35 U.S.C. § 325(d) to decline to institute an *inter partes* review based on anticipation by Rhee '500 (Ground I) and by Rhee '587 (Ground IV).

C. Asserted Obviousness over Rhee '500 in view of Bass (Ground II) or Rhee '587 in view of Bass (Ground V)

Petitioner contends that claims 1–6 and 8–12 are unpatentable as obvious over Rhee '500 in view of Bass (Ground II), and Rhee '587 in view of Bass (Ground V). Pet. 8. Relying on the Declaration of Dr. Lowman, Ex. 1003, Petitioner explains how the references teach or suggest the claim limitations and provides reasoning for combining the references. *See* Pet. 39–45 (Ground II), 54–56 (Ground V).

1. Overview of Rhee '500

Rhee '500 discloses crosslinked polymer compositions that comprise "a first synthetic polymer containing multiple nucleophilic groups" and "a second synthetic polymer containing multiple electrophilic groups." Ex. 1004 (Abstract). The first synthetic polymer and the second synthetic polymer "covalently bond[] to one another to form a three dimensional matrix." *Id.* (col. 2, ll. 27–32). Rhee '500 teaches that the crosslinked polymer compositions may be used as, for example, "bioadhesives, for tissue augmentation, in the prevention of surgical adhesions." *Id.* (col. 1, ll. 17–19). Specifically, the crosslinked polymer compositions may be used to

"coat tissues in order to prevent the formation of adhesions following surgery or injury to internal tissues or organs." *Id.* (col. 19, ll. 6–9).

Rhee '500 teaches that the crosslinked polymer composition is made by mixing the first synthetic polymer with the second synthetic polymer. *Id.* (col. 3, ll. 9–19). The resulting "reaction mixture" may then be "applied to tissue comprising, surrounding, or adjacent to a surgical site." *Id.* Rhee '500 teaches to apply the resulting mixture "before substantial crosslinking has occurred between" the nucleophilic groups of the first synthetic polymer and the electrophilic groups of the second synthetic polymer. *Id.* "[T]he reaction mixture is allowed to continue crosslinking in situ until equilibrium crosslinking has been achieved." *Id.*

Rhee '500 teaches that the time required for crosslinking varies, depending on "the types and molecular weights of the two synthetic polymers and, most particularly, the concentrations of the two synthetic polymers." *Id.* (col. 17, ll. 33–38). In particular, Rhee '500 discloses crosslinking times from 5.0 seconds to more than 90 minutes. *Id.* (col. 24, ll. 8–24) (Table 6).

Rhee '500 teaches that the preferred synthetic polymers are hydrophilic in nature, such as various polyethylene glycols. *Id.* (col. 7, ll. 52–55). And Rhee '500 discloses several examples of crosslinked polymer compositions comprising hydrophilic polymers, *see id.* (col. 4, ll. 17–18) (Figs. 4–13), including crosslinked polymer compositions containing linkages "subject to hydrolysis under physiological conditions," *id.* (col. 8, ll. 8–12).

Finally, Rhee ’500 teaches that the crosslinked polymer composition may also comprise “[n]aturally occurring proteins,” such as collagen, albumin, fibrin, and fibrinogen. *Id.* (col. 11, ll. 3–12; col. 13, ll. 30–33). These proteins may react with the functional groups of the synthetic polymers, such that “their presence during mixing and/or crosslinking of the first and second synthetic polymer will result in formation of a crosslinked synthetic polymer-naturally occurring polymer matrix.” *Id.* Rhee ’500 further teaches the incorporation of biologically active agents into the crosslinked synthetic polymer compositions “for localized delivery” of the agents. *Id.* (col. 14, ll. 60–65; col. 15, ll. 38–43).

2. Overview of Rhee ’587

Rhee ’587 also discloses crosslinked polymer compositions, but limited to those comprising collagen crosslinked with a multifunctionally activated synthetic hydrophilic polymer. Ex. 1005 (col. 4, ll. 51–54). Rhee ’587 defines “multifunctionally activated” polymers as “synthetic hydrophilic polymers which have, or have been chemically modified to have, two or more functional groups located at various sites along the polymer chain and are capable of reacting with primary amino groups on collagen molecules.” *Id.* (col. 8, ll. 16–22). Rhee ’587 teaches that the compositions are “useful as biological or surgical adhesives” “to effect adhesion between a first surface and a second surface, wherein at least one of the first and second surfaces is preferably a native tissue surface.” *Id.* (col. 1, ll. 20–27).

In one example, Rhee ’587 prepares a bioadhesive composition by mixing methylated collagen with “difunctionally activated” SG-PEG

(succinimidyl glutarate-polyethylene glycol). *Id.* (col. 8, ll. 50–67). Rhee '587 explains that the difunctionally activated SG-PEG was obtained by chemically modifying the PEG molecule to provide functional groups along its length capable of "covalent binding" with collagen reactive groups. *Id.* Rhee '587 applied the mixture "onto a bloody wound site on the liver of a previously sacrificed rabbit and allowed to gel for 1 minute." *Id.* (col. 19, ll. 11–23). Rhee '587 states that the methylated collagen—SG-PEG gel "adhered very well to the liver, [but] not as well to the skin." *Id.* (col. 19, ll. 22–23),

Finally, Rhee '587 teaches that the collagen-based bioadhesive compositions may also comprise biologically active agents "in order to facilitate adhesion of tissues or healing of adhered tissues." *Id.* (col. 7, ll. 12–15).

3. Overview of Bass

Bass discloses a composition "adapted to bond separated tissues together or to coat tissues or prosthetic materials." Ex. 1006 (col. 1, ll. 9–11). The composition comprises, as a first component, naturally occurring peptides and/or synthetic peptides, which function to provide tensile strength. *Id.* (col. 4, ll. 29–34, 53–56). The composition further comprises, as a second component, a compound "adapted to support the first component producing an improved degree of inter-relationship among the molecules of the first component." *Id.* (col. 4, ll. 34–38). These include "natural or synthetic proteoglycans, glycoproteins, saccharides, polyalcohols, protein gels, gelatins, . . . and mixtures thereof." *Id.* (col. 5, ll. 12–14).

Bass teaches that "[t]he composition of the present invention may also include indogenous [sic] or exogenous chromophores to facilitate visualization of the material during placement into warm blooded animals." *Id.* (col. 11, ll. 18–21) (emphasis added). In particular, Bass explains, the "[u]se of a chromophore will allow material which becomes displaced from the desired application site to be easily visualized, and subsequently removed using a cellulose sponge, gauze pad, or other absorbing material." *Id.* (col. 11, ll. 21–25). Bass also teaches that exogenous chromophores may be used "for aid in the placement of biological glues." *Id.* (col. 11, ll. 29–34).

Examples of chromophores include "fluorescein isothiocyanate, indocyanine green, silver compounds such as silver nitrate, rose bengal, nile blue and Evans Blue, Q-Switch™, a dye made by Kodak, Inc., Sudan III, Sudan Black B and India Ink." *Id.* (col. 11, ll. 35–40). Bass also claims "methylene blue" as a preferred chromophore. *Id.* (col. 20, ll. 1–3) (claim 31).

4. Analysis

Petitioner generally contends that Rhee '500 and Rhee '587 teach biocompatible crosslinked polymers formed by a chemical reaction between electrophilic and nucleophilic reaction groups for use in medical applications such as tissue coating, and that Bass teaches the use of dyes to allow visualization of polymeric compositions used to bond or coat tissues. *See generally* Pet. 1–5. Petitioner contends that it would have been obvious to a skilled artisan "who wanted to visualize the hydrogels" of Rhee to "take advantage of the general knowledge in the art that dyes and other colorants

can be mixed with the hydrogel precursors." *Id.* at 41. In particular, Petitioner asserts that an ordinarily skilled artisan would look to the "visualization teachings" of Bass, which also discloses bonding or coating tissues. *Id.*; *see also id.* at 55–56.

Having reviewed the record, we determine that Petitioner has shown sufficiently for the purpose of institution that the combination of either Rhee reference with Bass discloses each and every limitation of illustrative claim 1. *See id.* at 34–35 (Ground II), 50–51 (Ground V). As to the preamble (i.e., "[a] method of preparing a composition suitable to coat a tissue of a patient"), Petitioner reasonably points to passages in the Rhee references teaching crosslinked polymer compositions used to coat tissues in a surgical patient. *Id.* at 34 (citing Ex. 1004, col. 19, ll. 6-10); *id.* at 50 (citing Ex. 1005, col. 1, ll. 20–27). Petitioner also reasonably points to passages in the Rhee references as teaching the reactive precursor species recited in claim 1 (i.e., the reactive precursor species comprising nucleophilic functional groups and the reactive precursor species comprising electrophilic functional groups). Specifically, Petitioner points out that Rhee '500 explicitly teaches mixing "a first synthetic polymer containing two or more nucleophilic groups" with "a second synthetic polymer containing two or more electrophilic groups." *Id.* at 34 (citing Ex. 1004, col. 3, ll. 9–19). Petitioner also reasonably contends that, in Rhee '587, methylated collagen is the reactive precursor species comprising nucleophilic functional groups, and that, for example, SG-PEG is the second synthetic polymer containing two or more electrophilic groups. *Id.* at 50 (citing Ex. 1005, col. 19, ll. 12–19); *see also* Ex. 1003 ¶ 104 (explaining that "methylated collagen" is a

"reactive precursor species comprising nucleophilic functional groups" and that "SG-PEG" is a "reactive precursor species comprising electrophilic functional groups"). And Petitioner reasonably contends that these reactive precursor species crosslink in situ to form a hydrogel on the tissue. Pet. 35 (citing Ex. 1004, col. 3, ll. 9–19); *id.* at 50–51 (citing Ex. 1005, col. 19, ll. 12–23); Ex. 1003 ¶ 106. Finally, as to the "visualization agent" limitation of illustrative claim 1, Petitioner relies on Bass. Specifically, Petitioner reasonably contends that Bass teaches a visualization agent in the form of an "[e]ndogenous or exogenous chromophore[]" that is used to "facilitate visualization of the material during placement into warm blooded animals." Pet. 43 (citing Ex. 1006, col. 11, ll. 18–21).

We note that, on the present record, Patent Owner does not dispute Petitioner's position that the combinations of Rhee '500 and Bass and of Rhee '587 and Bass teach every limitation of claim 1. Instead, Patent Owner argues in its Preliminary Response that an ordinarily skilled artisan would not have combined Bass with either Rhee reference, and that an ordinarily skilled artisan would not have had a reasonable expectation of success. Prelim. Resp. 28–37. Having reviewed the present record, we are persuaded that Petitioner has articulated sufficient reasoning with rational underpinning for combining the teachings of Rhee '500 and Bass, and the teachings of Rhee '587 and Bass, to meet the "reasonable likelihood" standard for instituting trial.

Specifically, Petitioner points out that Bass expressly uses chromophores "to facilitate visualization of the [bioadhesive] material during placement into warm blooded animals." Pet. 5 (citing Ex. 1006,

col. 11, ll. 18–21). We also note that Bass teaches that exogenous chromophores may be used "for aid in the placement of biological glues." Ex. 1006 (col. 11, ll. 29–34). An ordinarily skilled artisan, therefore, wanting to visualize the hydrogels of either Rhee reference during use, would reasonably look to Bass for its teaching of chromophores as visualization agents for medical applications. Indeed, Bass specifically claims methylene blue as a specific chromophore that "allow[s] visualization of the composition." *Id.* (col. 19, l. 66–col. 20, l. 3).

Although we acknowledge that Bass is directed to bioadhesive compositions rather than aqueously degradable hydrogels, *see* Prelim. Resp. 32–33, we are not persuaded on this record that an ordinarily skilled artisan would not look to Bass for that reason. We are instead persuaded by Petitioner's explanation that visualization agents have been used in polymeric materials for medical applications for many years, and that an ordinarily skilled artisan seeking to visualize the newer-generation hydrogels would reasonably look to the visualization agents previously employed in other biocompatible polymers used to coat tissues during surgical operations. Pet. 10–12 (citing Ex. 1003 ¶¶ 33–38; Ex. 1007, 7; Ex. 1009, 1; Ex. 1010; Ex. 1011, 2; Ex. 1012, col. 3, ll. 41–43, col. 8, ll. 56–58; Ex. 1018, 1154).

Finally, we acknowledge Patent Owner's argument that a skilled artisan would not have reasonably expected success in adding a visualization agent to the electrophilic/nucleophilic reaction chemistry disclosed in the Rhee references. Prelim. Resp. 33–36. And we note that Petitioner's reasonable-expectation-of-success argument relies on the testimony of Dr.

Lowman. *See e.g.*, Ex. 1003 ¶¶ 89–90 (testimony of Dr. Lowman that "given the disclosures in Bass (and the general knowledge of color additives in polymers), a POSA would have every reason to expect success in combining the hydrogels of Rhee '500 with the visualization agents of Bass to produce colored hydrogels"). Based on the present record and information before us, we are persuaded to institute a trial. The parties are cautioned that the Board gives little or no weight to attorney arguments and/or testimony unsupported by record evidence. *See* 37 C.F.R. § 42.65(a) (opinion testimony that does not disclose underlying facts "is entitled to little or no weight").

For the reasons explained above, we determine that the information presented establishes a reasonable likelihood that Petitioner would prevail in showing that independent claim 1 is unpatentable under 35 U.S.C. § 103(a) as obvious over the combination of Rhee '500 and Bass (Ground II), as well as the combination of Rhee '587 and Bass (Ground IV). We note that Patent Owner does not raise any additional arguments specific to the dependent claims 2–6 and 8–12. *See generally* Prelim. Resp. 28–37. We have reviewed the information presented in the Petition and supporting evidence with respect to the challenged dependent claims and determine that the information presented establishes a reasonable likelihood that Petitioner also would prevail in showing that those claims are unpatentable under 35 U.S.C. § 103(a) on the same grounds.

D. Obviousness over Rhee '500 in view of Tse (Ground III) or Rhee '587 in view of Tse (Ground VI)

Petitioner contends that claims 1–6 and 8–12 are unpatentable as obvious over Rhee '500 in view of Tse (Ground III), and Rhee '587 in view

of Tse (Ground VI). Pet. 8. Relying on the Declaration of Dr. Lowman, Ex. 1003, Petitioner explains how the references teach or suggest the claim limitations and provides reasoning for combining the references. *See* Pet. 45–48 (Ground III), 57–59 (Ground VI).

1. Overview of Tse

Tse teaches the use of cyanoacrylate adhesive to stop leakage of CSF (cerebrospinal fluid) during orbital surgery. Ex. 1007, 7. Specifically, Tse reports that topical application of butyl-2-cyanoacrylate (Histoacryl Blue) immediately stopped CSF leakages during surgery. *Id.* Tse explains that the tissue adhesive is "applied as a thin film over the prepared" tissue site to form an "adhesive plaque." *Id.* Tse further teaches that the tissue adhesive contains a "color additive" "which facilitates visualization and assessment of plaque thickness." *Id.*

2. Analysis

We find that Petitioner reasonably contends that Tse teaches a visualization agent in the form of "color additive which 'facilitates visualization and assessment of . . . thickness' of the applied adhesive." Pet. 46 (quoting Ex. 1007, 7). And, as explained above, we find that Petitioner reasonably contends that Rhee '500 and Rhee '587 teach the remaining limitations of illustrative claim 1. *Supra* at § II.C.4. Thus, we determine that Petitioner has shown sufficiently for the purpose of institution that the combination of either Rhee reference with Tse discloses each and every limitation of illustrative claim 1. *See* Pet. 45–48 (Ground III), 57–59 (Ground VI).

Petitioner contends that it would have been obvious to a skilled artisan "who wanted to visualize the hydrogels" of Rhee to "take advantage of the general knowledge in the art that dyes and other colorants can be mixed with the hydrogel precursors." Pet. 47. In particular, Petitioner asserts that an ordinarily skilled artisan would look to the "visualization teachings" of Tse, which also "concerns coating the tissue of a patient with an adherent material." *Id.*; *see also id.* at 58–59. We find that Petitioner also has articulated sufficient reasoning with rational underpinning for combining the teachings of Rhee '500 and Tse, and the teachings of Rhee '587 and Tse, to meet the "reasonable likelihood" standard for instituting trial.

Patent Owner does not dispute that the combination of either Rhee reference with Tse teaches each and every limitation of illustrative claim 1. Instead, Patent Owner again argues that an ordinarily skilled artisan would not have combined Tse with the Rhee references and would not have had a reasonable expectation of success. Prelim. Resp. 28–32. Patent Owner points out that Tse is directed to butyl-2-cyanoacrylate (Histoacryl Blue)—a type of "super glue"—and asserts that butyl-2-cyanoacrylate is "entirely different from [the] nucleophilic-electrophilic chemistry" described in the Rhee references. *Id.* at 29–30.

Even so, we find on this record that Petitioner reasonably relies on Tse for its teaching of a blue dye that serves as a visualization agent during surgery. Specifically, the blue dye "facilitates visualization and assessment of . . . thickness" of the applied glue. Pet. 27 (quoting Ex. 1007, 7). Moreover, we are not persuaded on this record that an ordinarily skilled artisan would disqualify the teachings of Tse merely because Tse teaches a

different type of biocompatible polymer. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2007) ("[I]f a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill."). As noted above, we are instead persuaded by Petitioner's explanation that visualization agents have been used in polymeric materials for medical applications for many years, and that an ordinarily skilled artisan seeking to visualize the newer-generation hydrogels would reasonably look to the visualization agents previously employed in other biocompatible polymers used to coat tissues during surgical operations. Pet. 10–12 (citing Ex. 1003 ¶¶ 33–38; Ex. 1007, 7; Ex. 1009, 1; Ex. 1010; Ex. 1011, 2; Ex. 1012, col. 3, ll. 41–43, col. 8, ll. 56–58; Ex. 1018, 1154).

Patent Owner also argues that, following the publication of Tse, "the art taught away from the use of cyanoacrylates for applications involving contact with tissue because of toxicity and other negative factors associated with cyanoacrylates in the body." Prelim. Resp. 31. Nevertheless, it appears to us on this record that, even if the ordinarily skilled artisan would have avoided the use of the tissue adhesive Histoacryl (i.e., the cyanoacrylate without blue dye), the ordinarily skilled artisan would still have had a reason to utilize the blue dye, such as that added to Histoacryl Blue, "to make it easier to see the adhesive being applied." Pet. 3 (citing Ex. 1010); *see also* Ex. 1011, 2 (Col. 1) (stating that "Histoacryl Blue . . . is colored to increase its visibility in surgical use."); Ex. 1003 ¶ 97 (testimony of Dr. Lowman that "Histoacryl® Blue . . . was known to differ from the clear Histoacryl® only

by the addition of a blue dye"). Indeed, as Tse explains, the "color additive in the tissue adhesive . . . facilitates visualization" during application of the adhesive. Ex. 1007, 7.

For these reasons, we determine that the information presented establishes a reasonable likelihood that Petitioner would prevail in showing that independent claim 1 is unpatentable under 35 U.S.C. § 103(a) as obvious over Rhee '500 and Tse (Ground III) and Rhee '587 and Tse (Ground VI). Again, Patent Owner does not raise any additional arguments specific to the dependent claims 2–6 and 8–12. *See generally* Prelim. Resp. 28–37. We have reviewed the information presented in the Petition and supporting evidence with respect to the challenged dependent claims and determine that the information presented establishes a reasonable likelihood that Petitioner would also prevail in showing that those claims are unpatentable under 35 U.S.C. § 103(a) on the same grounds.

III. CONCLUSION

For the foregoing reasons, we are persuaded that the Petition establishes a reasonable likelihood that Petitioner would prevail in showing that claims 1–6 and 8–12 of the '034 patent are unpatentable under 35 U.S.C. § 103(a).

Our determinations at this stage of the proceeding are based on the evidentiary record currently before us. This decision to institute trial is not a final decision as to patentability of any claim for which *inter partes* review has been instituted. Our final decision will be based on the full record developed during trial.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that pursuant to 35 U.S.C. § 314(a), an *inter partes* review is hereby instituted on the following grounds:

Claims 1–6 and 8–12 as unpatentable under 35 U.S.C. § 103 for obviousness over Rhee ’500 in view of Bass (Ground II);

Claims 1–6 and 8–12 as unpatentable under 35 U.S.C. § 103 for obviousness over Rhee ’500 in view of Tse (Ground III);

Claims 1–6 and 8–12 as unpatentable under 35 U.S.C. § 103 for obviousness over Rhee ’587 in view of Bass (Ground V); and

Claims 1–6 and 8–12 as unpatentable under 35 U.S.C. § 103 for obviousness over Rhee ’587 in view of Tse (Ground VI).

FURTHER ORDERED that no other proposed grounds of unpatentability are authorized; 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 a trial commencing on the entry date of this Decision.

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