IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

INTEGRA LIFESCIENCES CORP., INTEGRA LIFESCIENCES SALES LLC, CONFLUENT SURGICAL, INC., and INCEPT LLC,	)	
Plaintiffs,	)	
v.	)	Civil Action No. 15-819-LPS-CJB
HYPERBRANCH MEDICAL TECHNOLOGY, INC.,	)	
Defendant.	)	

REPORT AND RECOMMENDATION

In this action filed by Plaintiffs Integra LifeSciences Corp., Integra LifeSciences Sales LLC, Confluent Surgical, Inc. and Incept LLC (collectively, "Plaintiffs") against Defendant HyperBranch Medical Technology, Inc. ("Defendant" or "HyperBranch"), Plaintiffs allege infringement of United States Patent Nos. 6,566,406 (the "'406 patent"), 7,009,034 (the "'034 patent"), 7,332,566 (the "'566 patent"), 7,592,418 (the "'418 patent"), 8,003,705 (the "'3705 patent") and 8,535,705 (the "'5705 patent") (collectively, the "patents-in-suit" or "asserted patents"). Presently before the Court is the matter of claim construction. The Court recommends that the District Court adopt the constructions set forth below for the four terms discussed in this Report and Recommendation.[1]

I. BACKGROUND

[1] The parties submitted 18 terms or sets of terms for claim construction. (D.I. 248 at 2) The parties grouped the 18 terms/term sets into seven groups for purposes of the *Markman* hearing. (*Id.* at 1-2) This Report and Recommendation addresses the final three groups (i.e., Groups E, F and G). On July 27, 2017, August 4, 2017, and August 18, 2017, the Court issued Reports and Recommendations regarding claim construction for the first four groups of terms (which included 14 terms/term sets). (D.I. 307, 310, 316, 317)

The Court incorporates by reference herein the factual and procedural background about this case and the patents-in-suit that was set out in the Court's July 27, 2017 Report and Recommendation regarding claim construction. (D.I. 307 at 2-5)

II. STANDARD OF REVIEW

The Court also incorporates by reference herein the discussion of general principles of claim construction, as well as the legal standard relating to the definiteness requirement, which were also set out in its July 27, 2017 Report and Recommendation. (*Id.* at 5-7, 30-32)

III. DISCUSSION

The Court takes up the four disputed terms in the order in which the parties addressed them at the *Markman* hearing.

A. "the first biocompatible precursor, the second biocompatible precursor, and the third biocompatible precursor are reactable with each other to form a crosslinked hydrogel" / "the first biocompatible precursor, the second biocompatible precursor, and the third biocompatible precursor are reactable with each other"[2]

The term that is ultimately at issue here is "the first biocompatible precursor, the second biocompatible precursor, and the third biocompatible precursor are reactable with each other to form a crosslinked hydrogel[,]" which is found in certain claims of the '3705 patent, including

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[2] These were presented to the Court as two terms, with the parties disputing whether the language "to form a crosslinked hydrogel" should be included in the term to be construed. (*See, e.g.*, D.I. 230 at 8; D.I. 231 at 27 n.8) Plaintiffs sought the construction of the term including this additional language "to ensure that the entire context of the claim could be taken into account." (D.I. 230 at 8) During the *Markman* hearing, however, Defendant acknowledged that it was "fine with including the 'to form a [crosslinked] hydrogel'" language in the term to be construed. (Tr. at 179) Therefore, the Court will include that language in the term to be construed here, and will thus provide a construction for "the first biocompatible precursor, the second biocompatible precursor, and the third biocompatible precursor are reactable with each other to form a crosslinked hydrogel."

claim 4. Plaintiffs propose that the term be construed to mean "the electrophilic functional groups of the first biocompatible precursor are reactable with the primary amine functional groups of the second and third biocompatible precursors to form a crosslinked hydrogel[,]" while Defendant proposes that the term be construed to mean "the first biocompatible precursor, the second biocompatible precursor, and the third biocompatible precursor each react with the other two [to form a crosslinked hydrogel.]" (D.I. 230 at 8-9 (internal quotation marks omitted); D.I. 231 at 27) Claim 4 of the '3705 patent is set out below:

> **4.** A kit comprising:
> a first biocompatible precursor having at least two electrophilic functional groups, and a second biocompatible precursor comprising at least two primary amine functional groups, a third biocompatible precursor comprising at least two primary amine functional groups and, an applicator;
> wherein *the first biocompatible precursor, the second biocompatible precursor, and the third biocompatible precursor are reactable with each other to form a crosslinked hydrogel*, are resistant to enzymatic degradation, and at least one of the first, second, or third biocompatible precursors comprises at least one isolated hydrolytically degradable ester group;
> wherein the applicator is configured to mix at least the first precursor, the second precursor, and the third precursor to form a crosslinked hydrogel in situ comprising covalent bonds formed by reaction of the functional groups of the precursors and further comprising the at least one isolated hydrolytically degradable ester group;
> wherein the hydrogel comprises a sufficient number of the at least one isolated hydrolytically degradable ester groups in the crosslinked hydrogel so that the crosslinked hydrogel is degradable in less than about 180 days, is resistant to enzymatic degradation, and is degradable by hydrolysis of the at least one isolated hydrolytically degradable ester group; and
> wherein the kit further comprises instructions that comprise directions for making a hydrogel that is degradable in an amount of time, with the amount of time being less than about 180 days.

('3705 patent, cols. 42:41-43:4 (emphasis added))

From this representative claim, we know, then, that the claims at issue require three precursors—a first precursor, a second precursor, and a third precursor. (*See* D.I. 241 at 19) Further, the claims require that the first precursor has electrophilic functional groups, and the second and third precursors each have primary amine functional groups. (*Id.*) The crux of the dispute here is whether the construction for this term must require the *second* and *third* biocompatible precursors *to react with each other* to form a crosslinked hydrogel, as Defendant contends, or whether it instead requires the first biocompatible precursor to react with the second and third precursors to form a crosslinked hydrogel, as Plaintiffs propose. (*See* D.I. 230 at 9; D.I. 231 at 27-28) Plaintiffs' proposal would not require the second and third precursors to react with each other.

The person of ordinary skill in the art ("POSITA") would consider the claims as a whole, Plaintiffs assert, and would know how to form a crosslinked hydrogel. (D.I. 230 at 9) Plaintiffs' expert, Dr. Jimmy Mays, then explained that in conjunction with this knowledge, the POSITA would additionally know that: "(1) electrophilic groups cannot react with other electrophilic groups; and (2) that primary amine groups cannot react with other primary amine groups." (D.I. 242, ex. 14 at ¶ 22; *see also* Tr. at 177) Thus, according to Plaintiffs, the POSITA would understand the claims at issue to teach that the first precursor (with electrophilic functional groups) reacts with the second and third precursors (both with primary amine functional groups) in order to form a crosslinked hydrogel. (D.I. 230 at 9 (citing D.I. 122, ex. 6 at ¶¶ 148-49); *see also* D.I. 242, ex. 14 at ¶ 21) With respect to the second and third precursors, Plaintiffs argue that the POSITA would know that the claims do not specifically identify any functional groups of the second and third precursors that would react with each other, and that those two precursors

thus "do not react together [to form a crosslinked hydrogel][.]" (D.I. 230 at 9) Plaintiffs argue that this interpretation is in line with the patent's teaching that the claimed crosslinked hydrogels of the invention "are made by reacting electrophilic functional groups with primary amine functional groups[,]" (*id.*), and in support, they cite to the following portion of the specification:

> Some embodiments are methods for making a readily degradable hydrogel by providing at least a first biocompatible precursor having at least two electrophilic functional groups, providing at least a second biocompatible precursor comprising at least two primary amine functional groups; optionally providing at least a third biocompatible precursor comprising at least two primary amine functional groups; wherein the first precursor, the second precursor, and the third precursor are reactable with each other to form a crosslinked hydrogel, are resistant to enzymatic degradation, and at least one of the first, second, or third precursors includes at least one isolated hydrolytically degradable ester group. And mixing at least the first precursor, the second precursor, and optionally the third precursor to form a crosslinked hydrogel in situ including covalent bonds *formed by reaction of the functional groups of the precursors* and further including the at least one isolated hydrolytically degradable ester group[.]

('3705 patent, cols. 1:58-2:7 (emphasis added))[3]

For its part, Defendant argues that Plaintiffs' proposal improperly reads out the requirement in the claims that the first precursor, the second precursor, and the third precursor "are reactable *with each other*." (D.I. 231 at 28; D.I. 243 at 18-19) Defendant points out that the plain meaning of "'each'" is "'every one of two or more considered separately'" and that "'each other'" means "'each one the other.'" (*See* D.I. 231 at 27 (citing D.I. 232, ex. 8 at 4)) The plain language of the claims, Defendant asserts, thus requires that "each of the three precursors considered separately must be able to react with each of the other two precursors." (*Id.* at 27-28)

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[3] The language in this portion of the specification largely mirrors that found in claim 4 itself.

Defendant does not dispute that primary amine functional groups are not reactable with each other to form a crosslinked hydrogel (and that, as a result, a second and third precursor that each contained only "at least two primary amine functional groups" could not react with each other to form a hydrogel). But Defendant argues that its proposed construction is nevertheless sensible, and points to the "comprising" language found in the claim term at issue. "Comprising," notes Defendant, is a term that means that the claim does not exclude additional unrecited elements; it equates to "'including at least.'" (D.I. 243 at 19 (citing *Mars, Inc. v. H.J. Heinz Co.*, 377 F.3d 1369, 1375-76 (Fed. Cir. 2004)). Therefore, Defendant argues, since the claims at issue recite second and third precursors each "*comprising* at least two primary amine functional groups[,]" this means that "the second and third biocompatible precursors could have other functional groups besides amines, which are indeed reactable with each other as the claim requires." (*Id.*; *see also* Tr. at 179 (Defendant's counsel asserting that "it's possible for the second and third precursors to have both electrophilic and nucleophilic with some projected groups in there as well and that they would be able to react with one another"))

The Court agrees with Defendant that, at least at first blush, the plain language of the claims seems to require that each of the first, second and third precursors must each react with every other precursor in order to form a crosslinked hydrogel. But with no dispute that two precursors having primary amine functional groups *are not capable of* reacting with each other to form a hydrogel, the Court is ultimately persuaded that Plaintiffs' proposal should be adopted.

After all, the specific result called for by the claims is that a "crosslinked hydrogel" is to be formed. The Court does not believe that Defendant's "comprising" argument is the answer here, as it relies on unclaimed, unrecited, unidentified functional groups to be present in order to

help achieve the very result that is expressly called for by the claims. The United States Court of Appeals for the Federal Circuit has explained that the term "comprising" has consistently been interpreted to mean "that the listed elements . . . *are essential* but other elements may be added." *Lochner Techs., LLC v. Vizio, Inc.*, 567 F. App'x 931, 939 (Fed. Cir. 2014) (emphasis added) (internal quotation marks and citations omitted). In other words, in order to read on the claims, *every limitation* must be present in the accused kit, and the import of the "comprising" language is simply that a kit that includes additional elements not claimed may still infringe. (*See* Tr. at 178 (Plaintiffs' counsel explaining that "comprising" means that "there may be [another] group in there, but that's not what you use to form a crosslinked hydrogel")) And here, it does not make sense that (assuming Defendant's construction was correct) the patentees would have drafted a method claim wherein—if the precursors contained nothing more than what was absolutely required by the claim language—(1) the process of generating a crosslinked hydrogel would require the second and third precursors to react with each other, but (2) their functional groups *cannot* react with each other. Accordingly, the Court is persuaded that the POSITA reviewing the claim and the specific groups recited therein will know that "to form crosslinked hydrogels, you're reacting the electrophilic functional groups in the first precursor with the primary amine functional groups of the second and third, and that's how you form a crosslinked hydrogel." (*Id.* at 177-78)

For these reasons, the Court recommends that the term "the first biocompatible precursor, the second biocompatible precursor, and the third biocompatible precursor are reactable with each other to form a crosslinked hydrogel" be construed to mean "the electrophilic functional groups of the first biocompatible precursor are reactable with the primary amine functional

groups of the second and third biocompatible precursors to form a crosslinked hydrogel."

B. "free of amino acid sequences of more than about four residues in number"

Plaintiffs propose that the term "free of amino acid sequences of more than about four residues in number" be construed to mean "[n]ot having a sequence of amino acids of more than about 4 amino acids[,]" while Defendant contends that the term is indefinite. (D.I. 230 at 17) The term appears in certain claims of the '566 patent and the '418 patent directed to a hydrogel that is "free of amino acid sequences of more than about four residues in number." ('566 patent, cols. 39:36-38, 40:25-27, 41:10-12; '418 patent, col. 39:34-36) It is undisputed that in this context, the reference to "residues" is "another name for amino acids that have lost a water molecule due to being bonded to another amino acid to form a sequence of amino acids." (D.I. 230 at 17; D.I. 243 at 19 n.2)

The core of Defendant's indefiniteness argument relates to the word "about" found in this claim term. Defendant's expert, Dr. Anthony Lowman, explains that an amino acid sequence is made up of a string of *discrete* amino acid residues. (D.I. 232 at ¶ 154) Accordingly, the number of amino acid residues present in a sequence would only be described as an integar value, and cannot and would not be described by a fractional number (such as, for example, 3 ¾, 3.99, 4.01 or 4 ¼ amino acid residues). (*Id.*) For this reason, Defendant contends, the term "about" renders the claims indefinite—"saying 'about four residues' has no precise meaning in the art because it could mean three, four, five, and/or six residues." (*Id.*; *see also* D.I. 231 at 29 (explaining that the POSITA "would not know how many amino acid residues would be required in order to escape the claim. It is five? Is it six? Is it something more?"); D.I. 243 at 19) While acknowledging that courts have found terms including the word "about" definite in situations

where the word is used to account for inherent measurement imprecision, (D.I. 231 at 29 (citing *GlaxoSmithKline Intellectual Prop. Mgmt. Ltd. v. Sandoz, Inc.*, C.A. No. 11-1284-RGA, 2013 WL 1163759, at *2-4 (D. Del. Mar. 20, 2013)); D.I. 243 at 19-20), Defendant asserts that there is no such imprecision at play here, where the number of residues are discrete, complete units, (D.I. 243 at 19-20). Defendant further argues that the intrinsic record sheds no light on the number of amino acid residues that may be added to a sequence with four residues and still be in the scope of the "about four residues in number" claim language. (D.I. 231 at 29)

Plaintiffs' briefing, unfortunately, did not provide much help with the dispute. Their opening brief does not even address the issue, and instead is solely focused on arguing an undisputed point: that the inclusion of the term "residues" in the claim does not render it indefinite. (D.I. 230 at 17; *see also* D.I. 243 at 19 n.2 (Defendant responding that its "dispute is not with the meaning of 'residues[]'")) In their answering brief, Plaintiffs first retorted that Defendant's argument relating to "about" "disregards the overwhelming number of cases that have found the term 'about' definite[.]" (D.I. 241 at 8 (citing cases)) As for the facts of this case, Plaintiffs then asserted that:

> Here the '566 prosecution history and specification makes clear that "free of amino acid sequences of more than about four residues . . ." is important for a hydrogel with an acceptable gel time in a patient. *See* D.I. 233, Ex. 11, p. 16-17 (citing Example 15, which references Fig. 12 and Fig. 11, as support for this limitation). Fig. 12 discloses gel times for di-lysine, tri-lysine and tetra-lysine, which have 2, 3, and 4 residues respectively. *See* ['566 patent, col.] 34:50-67, Fig. 11, 12.

(*Id.* at 8-9)

With regard to the "prosecution history" referenced in those two sentences, there the

patentees added claims containing the claim term at issue, (*see* D.I. 233, ex. 11 at 12, 15), and they cited to "Figure 11, Example 15" in support of these new claims, (*id.* at 17). Example 15, in turn, is directed to measuring the change in gel time as a function of ester solution age. ('566 patent, col. 34:51-67) Example 15 also references Figure 12, which "shows the variation in gelation time with the solution age of the electrophilic functional polymer." (*Id.*, col. 4:47-48; *see also* FIG. 12) And as for the reference to Figure 11, it "shows the variation in gelation time with the number of amino groups for the reaction of 4 arm 10 kDa succinimidyl glutarate PEG ('SG-PEG') with di-, tri- or tetra-lysine." (*Id.*, col. 4:43-46; *see also* FIG. 11)

The Court cannot see how any of this information elucidates the meaning of "about." Plaintiffs' briefing does not directly explain the connection between "about" and these particular references. (*See* D.I. 241 at 8-9) Nor did Plaintiffs cite to any expert testimony confirming that the POSITA would glean the meaning of "about" from these references. (*Id.*)[4]

Thus, Plaintiffs' explanation in their answering brief really did not advance the ball. In that explanation (set out above), Plaintiffs did note that the polymers represented in Figure 12 have 2, 3, and 4 residues respectively (i.e., that each has no more than 4 residues). (*Id.* at 9) But the claim term does not recite a hydrogel that is free of amino acid sequences of more than four residues in number—it recites one free of more than *about* four residues in number. After

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[4] Plaintiffs did submit a Rebuttal Declaration of their expert, Dr. Mays, "in response to [] HyperBranch's [o]pening [c]laim [c]onstruction [b]rief[,]" (D.I. 242, ex. 14 at ¶ 2), and Plaintiffs cited to that declaration in their answering brief in support of their assertion that the meaning of this claim term is straightforward, (D.I. 241 at 8 (citing D.I. 242, ex. 14 at ¶ 56)). Tellingly, however, while HyperBranch's opening brief with respect to this term focused on why the word "about" renders the term indefinite, Dr. Mays' "response" for this term does not address the "about" issue at all. Instead, Dr. Mays simply reiterates that the undisputed definition of "residues" renders this term understandable to the POSITA. (D.I. 242, ex. 14 at ¶ 56)

reading the entirety of Plaintiffs' briefing, the question still remained unanswered: What does the word "about" allow for and why is the word present in the claims?

When pressed about the issue during the *Markman* hearing, Plaintiffs directly asserted, for the first time, that "about four" in this context means "four[,]" since "you can see [in looking at Figure 12 that] right where you hit four that's where the gel times skyrocket up." (Tr. at 181-82) In other words, Plaintiffs were now claiming that the term "free of amino acid sequences of more than about four residues in number" means that there are "no more than four" residues—"[i]t could not be five or six[.]" (*Id.* at 182)

In one of their *Markman* hearing slides, Plaintiffs also cited to the Federal Circuit's holding in *Cohesive Tech., Inc. v. Waters Corp.*, 543 F.3d 1351, 1368 (Fed. Cir. 2008). Plaintiffs were citing to that case for the proposition that "[t]he use of the word 'about' avoids a strict numerical boundary to the specified parameter. Its range must be interpreted in its technological and stylistic context." (Plaintiffs' Claim Construction Presentation, Slide 72 (certain internal quotation marks omitted)) And then Plaintiffs asserted in the slide that the '566 patent and specification "make clear what the technological and stylistic context 'about' is used in[.]" (*Id.*) But by way of further explanation as to what that "context" is, Plaintiffs simply pasted the chart of Figure 12 onto the slide, and went on to state that it depicts the "[e]xemplary effect of number of specific amino acid sequences (2, 3, or 4) on gel times for forming specific exemplary hydrogels (*See* description of Example 15)." (*Id.*)

These arguments at the *Markman* hearing (unsupported by any citation to expert testimony) also did not clear up the uncertainty relating to the use of "about" in the claims. For one thing, as Defendant retorted, Plaintiffs' position that "about four" means "four" reads the

term "about" right out of the claims. (Tr. at 184) In similar situations, courts have rejected constructions that would render terms of degree such as "about" meaningless. *See, e.g.*, *Messer v. Ho Sports Co.*, No. CV 06-826-PK, 2007 WL 2011210, at *10 (D. Or. July 9, 2007) (rejecting the parties' proposal to construe "'approximately one fourth to one fifth'" to mean "'no less than one fifth and no greater than one fourth'" as that proposal "ignore[s] the presence of the word 'approximately', which the parties would treat as meaningless (or as having the same meaning as 'precisely'")); *Crown Packaging Tech., Inc. v. Rexam Beverage Can Co.*, 486 F. Supp. 2d 366, 381-82 (D. Del. 2007) (rejecting the defendant's proposal to construe "between about 20° and about 60°" to mean "'[b]etween 20° and 60°'" as that proposal "elides the word 'about' from the claim language"); *Novartis Pharms. Corp. v. Apotex Corp.*, No. 02Civ.8917(KMW)(HBP), 2006 WL 626058, at *9 (S.D.N.Y. Mar. 13, 2006) (rejecting defendant's proposal to construe "about" to mean "'limited to the precise lower and upper limits of the recited range'" as such a construction "would render the term 'about' meaningless"); *cf. Merck & Co., Inc. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1369-70 (Fed. Cir. 2005) (reversing the district court's construction of "about" to mean "exactly" where the intrinsic evidence did not "redefine 'about' to mean 'exactly' in clear enough terms to justify such a counterintuitive definition of 'about'").

Moreover, Plaintiffs' suggestion in its slide to the effect that Figure 12 somehow sheds light on the issue—in that the figure purportedly depicts the "[e]xemplary effect of number of specific amino acid sequences (2, 3, or 4) on gel times for forming specific exemplary hydrogels"—was also unhelpful. That figure does little to explain why the term "about" was included in these *claims*, which (if the presence of "about" were not considered) would otherwise *already* recite a hydrogel with amino acid sequences of no more than four residues.

In sum, the intrinsic record does not support an interpretation of the claim term that would read the word "about" entirely out of the claims. And the entire record, including Dr. Lowman's declaration, strongly indicates that a POSITA would be in the dark as to what "about" *is* intended to mean in the context of these claims.[5] For these reasons, the Court agrees with Defendant that there is clear and convincing evidence that the scope of the claims are not discernable, and that the term "free of amino acid sequences of more than about four residues in number" is indefinite in the context of these claims.

C. "unbleached"

Plaintiffs propose that the term "unbleached" be construed to mean "[n]ot altered by light to effectively become clear[,]" while Defendant proposes that the term be construed to mean "[h]as not been bleached to remove its color[.]" (D.I. 230 at 26) The term is found in claim 12 of the '566 patent, which is set out below:

> **12.** A method of preparing a composition suitable to coat a tissue substrate of a patient, the method comprising:
> mixing reactive precursor species comprising nucleophilic functional groups, reactive precursor species comprising electrophilic functional groups, and at least about 0.1 mg/ml of an

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[5] This is an instance where, in the Court's view, it is appropriate to resolve the definiteness dispute at the claim construction stage. The issue here ("What does 'about' mean?") was and is a discrete one. It is also an issue that (as the case law cited above demonstrates) is not unfamiliar in patent law. And this is a situation where, despite having multiple opportunities to bring further clarity to the record, Plaintiffs did not do so during the briefing process, nor during the *Markman* hearing. In contrast, Defendant set out its position clearly, and supported it with expert testimony. Ultimately, it is fair and appropriate to resolve this legal question at this stage. *See, e.g.*, *Integra Lifesciences Corp. v. HyperBranch Med. Tech., Inc.*, Civil Action No. 15-819-LPS-CJB, 2017 WL 3331739, at *1 n.2 (D. Del. Aug. 4, 2017) (concluding that the issue of whether a claim term was indefinite was "ripe" for consideration where Plaintiffs did not specifically identify how additional time would better advance the record, the parties' experts had the opportunity to address the issue, and the parties had a "full, fair opportunity" to litigate the issue) (internal quotation marks and citation omitted).

> *unbleached* visualization agent such that the nucleophilic functional groups react with the electrophilic functional groups to form covalent bonds and crosslink the reactive precursor species after the mixing to form a covalently crosslinked biodegradable hydrogel contacting the tissue substrate and having an interior and an exterior, with the exterior having at least one tissue substrate coating surface and the visualization agent being at least partially disposed within the interior,
> wherein the hydrogel comprises chemical groups that are prone to aqueous hydrolysis and is thereby degradable in vitro by exposure to aqueous solution, and
> wherein the visualization agent has a predetermined concentration that indicates a predetermined thickness of the hydrogel as deposited on substrate.

('566 patent, cols. 39:50-40:3 (emphasis added)) The crux of the dispute between the parties with respect to the term "unbleached" is whether it means that the visualization agent has not been altered by light to become *clear* (with clarity not being strictly equated with the absence of color), as Plaintiffs contend, or whether it means that the visualization agent has not been bleached to remove its *color*, as Defendant argues. (*See* D.I. 241 at 20; D.I. 243 at 20; Plaintiffs' Claim Construction Presentation, Slide 74)[6] The Court finds that the intrinsic evidence best aligns with Defendant's proposal.

In support of their proposed construction, Plaintiffs point to the prosecution history of the '566 patent. (D.I. 230 at 26) Plaintiffs explain that the claim limitation reciting an "unbleached visualization agent" was added to overcome a rejection based on United States Patent No. 5,410,016 ("Hubbell et al."), and that in the amendment, the patentees explained the following:

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[6] Plaintiffs assert that Defendant's proposed construction should be rejected as it does not address any fundamental dispute between the parties regarding the scope of the claim. (D.I. 230 at 27; D.I. 241 at 20) The Court does not understand how this is so, as the parties' competing proposals do, in fact, underscore the dispute between them: is an unbleached visualization agent one that has not had its color removed, or one that has not effectively become clear?

> A copy of an affidavit previously submitted in the parent case U.S. Ser. No. 10/010,075, now U.S. Pat. No. 7,009,034 (Affidavit) is hereby submitted under 37 C.F.R. § 1.132. The **Affidavit is a declaration of Amarpreet Sawhney, [] who is an inventor on the Application and also an inventor on the Hubbell et al. reference.**
>
> As explained in the Affidavit, **Hubbell et al., in general, uses dyes (such as Eosin Y or Methylene Blue) as part of a photoinitiation process that requires exposure to light wavelengths that bleach the dyes. When bleached, they no longer serve the function of visualization agents.** This testimony is corroborated by Gruber et al. (attached) and the FDA FOCAL SEAL approval materials (attached) **that describe how the dyes change from colored to clear during use**.
>
> **A dye that has been bleached as in the Hubbell et al. process yields a product that is not a visualization agent because it has effectively lost its coloration. Indeed, the term "unbleached" is, strictly speaking, superfluous since a bleached dye can not be a visualization agent and a visualization agent is unbleached. Even if some concentration of unbleached dye were to remain after the bleaching process, the concentration of unbleached dye would not be the concentration of visualization agent that is claimed. A bleached dye is not the claimed visualization agent**. Accordingly, withdrawal of this rejection is requested.

(D.I. 233, ex. 11 at 18 (*cited in* D.I. 230 at 26-27) (with the emphasis above matching that used in Plaintiffs' citation))

In the Court's view, this passage actually supports Defendant's proposal. The patentees were there attaching documentation that describes how the substances undergoing the bleaching process "change from colored to clear"—i.e., these dyes have had their color removed. In other words, it is evident from this passage that when the patentees referred to "clear" here, they meant "colorless." This is reiterated when the patentees explain that a dye that has been bleached as in Hubbell et al. is not a visualization agent "because it has effectively lost its coloration"—i.e., it

has had its color removed.

Other portions of the prosecution history of the '566 patent (and related patents) underscore that a visualization agent that has been "bleached" is one that has had its color removed. (*See* Tr. at 184-85 (Defendant's counsel asserting that "[t]here are numerous statements in [the intrinsic evidence] . . . about bleached, removing color or visualization agent[s] losing their color and, therefore, not a visualization agent")) At least three pieces of such evidence further bolster Defendant's case.

The first relates to the Examiner's further rejection of the claim that ultimately issued as claim 12 of the '566 patent, on the ground that the claim was unpatentable over Hubbell et al. combined with other prior art references. (D.I. 232, ex. 3 at HBMT0407020) In responding to this rejection, and in explaining why there would be no reasonable expectation of success in combining the references to arrive at the patented invention, the patentees explained that "a dye that participates in the photo-reaction process [as in Hubbell et al.] *could be bleached and thereby made colorless* . . . and not be useful for establishing the claimed predetermined thicknesses [] or claimed visually observable changes[.]" (*Id.* at HBMT0407058 (emphasis added))

Second, the patentees drew this same connection between the bleaching process and removing color from a substance during prosecution of the '034 patent. That patent's claims recite a "visualization agent," and in overcoming a rejection based on Hubbell et al., the patentees submitted the above-referenced affidavit of Dr. Sawhney, and explained that:

> Dr. Sawhney, in the Affidavit, states that a [POSITA] would understand that the dyes used as photoinitiators in the photoinitiation process of the Hubbell et al. *would be bleached*

> during that process . . . . The PMA is provided as further support. The PMA states that the FOCAL [] SEAL, which is covered by [Hubbell et al.], *has a pink color before photoinitiation and is colorless after photoinitiation.* The pink color is contributed by the dye EOSIN Y, which is a photoinitiator that is consumed by the photopolymerization process.

(*Id.*, ex. 2 at HBMT0406639-40 (emphasis added)) In the referenced Affidavit, Dr. Sawhney explains that FOCAL SEAL uses a dye that imparts a red or pinkish color, and this dye "becomes bleached during the photopolymerization process to produce a clear hydrogel"—i.e., a hydrogel that has had the red/pinkish *color* removed. (D.I. 247, ex. J at HBMT0406962)

Third, the Court notes that when the applicants added the "unbleached" limitation to the '566 patent, they explained that "[c]laim 1 was amended to recite at least about 0.1 mg/ml of an unbleached visualization agent as supported at, e.g., page 13 lines 11-15, with the agent being unbleached because it is in the final hydrogel composition and serve[s] the function of being visualization agent which must be visible, i.e., unbleached." (D.I. 232, ex. 3 at HBMT0406948) The above-referenced portion of the specification ("page 13[,] lines 11-15"), in turn, explains that preferred biocompatible visualization agents consisting of blue dyes are preferably present in the final precursor at a concentration of more than 0.05 mg/ml, and more preferably in a concentration range of 0.1 to 4.0 mg/ml, although greater concentrations may potentially be used, up to the limit of solubility of the visualization agent. (*Id.* at HBMT0406788) It goes on to say that such "concentration ranges were found to give a color to the hydrogel that was desirable without interfering with crosslinking times[.]" (*Id.*) This "support[]" for the unbleached limitation is all about a colored (i.e., unbleached) visualization agent—that is, a visualization agent that "has not been bleached to remove its color."

For these reasons, the Court recommends that "unbleached" should be construed to mean "has not been bleached to remove its color."

IV. CONCLUSION

For the foregoing reasons, the Court recommends that the District Court adopt the following constructions:

1. "the first biocompatible precursor, the second biocompatible precursor, and the third biocompatible precursor are reactable with each other to form a crosslinked hydrogel" should be construed to mean "the electrophilic functional groups of the first biocompatible precursor are reactable with the primary amine functional groups of the second and third biocompatible precursors to form a crosslinked hydrogel"

2. "free of amino acid sequences of more than about four residues in number" is indefinite

3. "unbleached" should be construed to mean "has not been bleached to remove its color"

This Report and Recommendation is filed pursuant to 28 U.S.C. § 636(b)(1)(B), Fed. R. Civ. P. 72(b)(1), and D. Del. LR 72.1. The parties may serve and file specific written objections within fourteen (14) days after being served with a copy of this Report and Recommendation. Fed. R. Civ. P. 72(b)(2). The failure of a party to object to legal conclusions may result in the loss of the right to de novo review in the district court. *See Henderson v. Carlson*, 812 F.2d 874, 878–79 (3d Cir. 1987); *Sincavage v. Barnhart*, 171 F. App'x 924, 925 n.1 (3d Cir. 2006).

The parties are directed to the Court's Standing Order for Objections Filed Under Fed. R. Civ. P. 72, dated October 9, 2013, a copy of which is available on the District Court's website,

located at http://www.ded.uscourts.gov.

Dated: August 30, 2017

Christopher J. Burke
UNITED STATES MAGISTRATE JUDGE