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"), Integra LifeSciences Sales LLC ("Integra Sales"), Confluent Surgical, Inc. ("Confluent") and Incept LLC ("Incept," and collectively with Integra, Integra Sales and Confluent, "Plaintiffs") against Defendant HyperBranch Medical Technology, Inc. ("Defendant" or "HyperBranch"), Plaintiffs allege infringement of United States Patent Nos. 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").[1] Presently before the Court is HyperBranch's motion for summary judgment of non-infringement of claims 1, 6, 12 and 17 of the '5705 patent (the "Motion"). (D.I. 393)[2] The Court recommends that

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[1] Plaintiffs originally also alleged infringement of United States Patent No. 6,566,406, but Plaintiffs do not appear to currently be asserting any claims from that patent. (*See, e.g.*, D.I. 402 at ix)

[2] The Court notes that the Motion is included in HyperBranch's "Motion for Summary Judgment of Non-Infringement and Invalidity of the Patents-in-Suit," in which it, *inter alia*, moves for summary judgment with respect to other issues in addition to this infringement issue. (D.I. 393, 402) This Report and Recommendation solely addresses HyperBranch's

HyperBranch's Motion be GRANTED.

I. BACKGROUND

A. The Parties

Integra is involved in the design, development and manufacturing of medical devices for orthopedics, tissue technologies and speciality surgical solutions, with an emphasis on products that help heal and/or regenerate tissue. (D.I. 1 at ¶ 7) Integra Sales sells and distributes Integra's medical technology products, including Integra's dural sealant products. (*Id.* at ¶¶ 8, 25) Integra and Integra Sales are affiliates of Confluent, which is a medical device company that has developed in-situ polymerized biomaterials with applications as synthetic sealants and hemostats in minimally invasive surgery, adhesion prevention and interventional procedures. (*Id.* at ¶¶ 5, 9) Incept is a medical technology company that promotes and advances technological innovation and entrepreneurship. (*Id.* at ¶ 10) The asserted patents "relate to Integra's and Integra Sales' dural sealant products and technology, particularly those used by neurosurgeons and orthopedic spine surgeons." (*Id.* at ¶ 25) Integra, Integra Sales and Confluent are the exclusive licensees of the asserted patents, and Incept owns them by assignment. (*Id.* at ¶¶ 11-16; D.I. 35, ex. 1 at ¶ 5)

Defendant HyperBranch is a medical device company that is involved in the business of designing, developing, manufacturing and selling surgical sealants. (D.I. 1 at ¶ 19; D.I. 25 at ¶ 2; D.I. 37 at ¶ 19) In this action, Plaintiffs allege that HyperBranch directly and indirectly infringes the asserted patents by, *inter alia*, the manufacture, use, sale, and offers to sell of HyperBranch's Adherus Dural Sealant, Adherus Spinal Sealant, Adherus AutoSpray Dural Sealant, and Adherus

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arguments relating to infringement of the "the biodegradable groups of the hydrogel consist of the esters" limitation of claims 1, 6, 12 and 17 of the '5705 patent.

AutoSpray Extended Tip (ET) Dural Sealant (the "Accused Products"). (D.I. 1 at ¶¶ 28, 35, 42, 49, 56; D.I. 402 at vii-viii)

B. The '5705 Patent

The '5705 patent, entitled "Biocompatible Polymers and Hydrogels and Methods of Use" was issued on September 17, 2013, with the application having been filed on November 16, 2007. (D.I. 246, ex. F)[3] The patent contains 18 claims directed to methods of making a biocompatible degradable hydrogel. ('5705 patent, cols. 30:34-32:19) Plaintiffs assert claims 1, 6, 12 and 17 of the '5705 patent. (*See* D.I. 402 at ix)

Claim 1 of the '5705 patent, the only independent claim, is representative, and it recites:

> **1.** A method of making a biocompatible degradable hydrogel to treat a medical condition of a patient comprising:
> identifying a medical condition for treatment by use of a hydrogel formed in situ in a patient and fully degradable in a patient in less than about 180 days; and
> mixing a first precursor with a second precursor in situ in the patient to form the hydro gel for treatment of the medical condition,
> with the first biocompatible synthetic hydrophilic polymer precursor having a water solubility of at least 1 gram per 100 milliliters and comprising at least two electrophilic functional groups; and the second biocompatible synthetic hydrophilic polymer precursor comprising at least two nucleophilic amine functional groups; and wherein
> (i) the first precursor is selected to have only one or two chemically hydrolytically degradable ester bonds per every electrophilic functional group on the first precursor; and
> (ii) the second precursor comprises at least three nucleophilic functional groups;
> wherein *the biodegradable groups of the hydrogel consist of the esters* and the hydrogel as placed in situ in the patient is essentially

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[3] The asserted patents appear on the docket in this action more than once, including as exhibits to the Joint Claim Construction Chart. (D.I. 246, exs. A-F) Citations to the patents will simply be to the '406 patent, the '034 patent, the '566 patent, the '418 patent, the '3705 patent and the '5705 patent.

> fully degradable in a patient in less than about 180 days, and wherein mixing the first and the second synthetic hydrophilic polymer precursors forms crosslinking covalent bonds that are reaction products of the electrophilic and the nucleophilic groups, wherein essentially every ester bond in the hydrogel is separated from other ester bonds in the hydrogel by at least three covalent bonds when the hydrogel is formed.

('5705 patent, col. 30:34-65 (emphasis added))

C. Procedural History

Plaintiffs filed the instant case on September 15, 2015. (D.I. 1) On September 25, 2015, Chief Judge Leonard P. Stark referred this case to the Court to hear and resolve all pretrial matters, up to and including the resolution of case-dispositive motions. (D.I. 15)

Briefing on the instant Motion was completed on December 21, 2017, (D.I. 463), and the Court heard oral argument on the Motion (and various other summary judgment and *Daubert* motions filed in the case) on January 5, 2018, (D.I. 482 (hereinafter, "Tr.")). A 7-day trial is set to begin on April 16, 2018. (D.I. 173)

II. STANDARD OF REVIEW

A. Summary Judgment

A grant of summary judgment is appropriate where "the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). The moving party bears the burden of demonstrating the absence of a genuine issue of material fact. *See Matsushita Elec. Indus. Co., Ltd. v. Zenith Radio Corp.*, 475 U.S. 574, 585-86 n.10 (1986). If the moving party meets this burden, the nonmovant must then "come forward with specific facts showing that there is a *genuine issue for trial*." *Id.* at 587 (emphasis in original) (internal quotation marks and citation omitted). If the nonmoving party

fails to make a sufficient showing on an essential element of its case with respect to which it has the burden of proof, the moving party is entitled to judgment as a matter of law. *Celotex Corp. v. Catrett*, 477 U.S. 317, 322-23 (1986). During this process, the Court will "draw all reasonable inferences in favor of the nonmoving party, and it may not make credibility determinations or weigh the evidence." *Reeves v. Sanderson Plumbing Prods., Inc.*, 530 U.S. 133, 150 (2000).

However, in order to defeat a motion for summary judgment, the nonmoving party must "do more than simply show that there is some metaphysical doubt as to the material facts." *Matsushita*, 475 U.S. at 586-87; *see also Podobnik v. U.S. Postal Serv.*, 409 F.3d 584, 594 (3d Cir. 2005) (party opposing summary judgment "must present more than just bare assertions, conclusory allegations or suspicions to show the existence of a genuine issue") (internal quotation marks and citation omitted). The "mere existence of *some* alleged factual dispute between the parties will not defeat an otherwise properly supported motion for summary judgment; the requirement is that there be no *genuine* issue of *material* fact." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 247-48 (1986) (emphasis in original). Facts that could alter the outcome are "material," and a factual dispute is genuine only where "the evidence is such that a reasonable jury could return a verdict for the nonmoving party." *Id.* at 248. "If the evidence is merely colorable . . . or is not significantly probative . . . summary judgment may be granted." *Id.* at 249-50 (internal citations omitted). A party asserting that a fact cannot be—or, alternatively, is—genuinely disputed must support the assertion either by citing to "particular parts of materials in the record, including depositions, documents, electronically stored information, affidavits or declarations, stipulations (including those made for purposes of the motion only), admissions, interrogatory answers, or other materials"; or by "showing that the

materials cited do not establish the absence or presence of a genuine dispute, or that an adverse party cannot produce admissible evidence to support the fact." Fed. R. Civ. P. 56(c)(1)(A) & (B).

B. Infringement

The patent infringement analysis consists of two steps. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995). First, the court must determine the meaning and scope of the patent claims asserted to be infringed. *Id.* Claim construction is generally a question of law, although subsidiary fact finding is sometimes necessary. *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 837-38 (2015). Second, the trier of fact must compare the properly construed claims to the allegedly infringing device. *Markman*, 52 F.3d at 976. This second step is a question of fact. *ActiveVideo Networks, Inc. v. Verizon Commc'ns, Inc.*, 694 F.3d 1312, 1319 (Fed. Cir. 2012).

"Literal infringement of a claim exists when every limitation recited in the claim is found in the accused device." *Kahn v. Gen. Motors Corp.*, 135 F.3d 1472, 1477 (Fed. Cir. 1998). If any claim limitation is absent from the accused product, there is no literal infringement as a matter of law. *Amgen Inc. v. F. Hoffman-La Roche Ltd*, 580 F.3d 1340, 1374 (Fed. Cir. 2009). A product that does not literally infringe a patent claim may still infringe under the doctrine of equivalents if the differences between the claimed invention and the accused product are insubstantial. *See Warner-Jenkinson Co., Inc. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 24, 40 (1997); *Virnetx, Inc. v. Cisco Sys., Inc.*, 767 F.3d 1308, 1322 (Fed. Cir. 2014).

The patent owner has the burden of proving infringement, and must do so by a preponderance of the evidence. *SmithKline Diagnostics, Inc. v. Helena Labs. Corp.*, 859 F.2d

878, 889 (Fed. Cir. 1988). When an accused infringer moves for summary judgment of non-infringement, such relief is only appropriate if, viewing the facts in the light most favorable to the patentee, no reasonable jury could find that every limitation recited in the properly construed claim is found in the accused device, either literally or under the doctrine of equivalents. *See Chimie v. PPG Indus., Inc.*, 402 F.3d 1371, 1376 (Fed. Cir. 2005); *see also Bell Atl. Network Servs., Inc. v. Covad Commc'ns Grp., Inc.*, 262 F.3d 1258, 1267 (Fed. Cir. 2001) ("[S]ummary judgment is proper only if no reasonable jury could return a verdict for the nonmoving party.") (internal quotation marks and citation omitted).

III. DISCUSSION

The asserted claims of the '5705 patent, which recite methods of making a biocompatible degradable hydrogel formed "in situ in a patient" to treat a medical condition, require that "the biodegradable groups of the hydrogel consist of the esters" (the "esters limitation"). HyperBranch argues that its Accused Products do not infringe the asserted claims of the '5705 patent, either literally or under the doctrine of equivalents, because the Accused Products form hydrogels that have biodegradable amide linkages, and they therefore do not read on the esters limitation. (D.I. 402 at 2)[4]

The Court will first provide background information regarding claim construction of the

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[4] In its Motion, HyperBranch also argues that the Accused Products do not infringe the asserted claims of the '5705 patent because they do not read on a second limitation: "mixing a first precursor with a second precursor in situ in the patient to form the hydro gel" (the "mixing limitation"). (D.I. 402 at 2-3) Because the parties' arguments with respect to that limitation appear to have some overlap with the parties' arguments relating to Plaintiffs' Motion for Summary Judgment of infringement of claim 10 of the '034 patent, (*see, e.g.* Tr. at 118), the Court will address the infringement arguments relating to the mixing limitation of the '5705 patent in a forthcoming Report and Recommendation that also addresses claim 10 of the '034 patent.

esters limitation. Then, the Court will assess the parties' arguments with respect to infringement.

A. Claim Construction of the Esters Limitation

During the claim construction process, Plaintiffs proposed that the esters limitation be construed to mean "the esters are the only biodegradable group responsible for degradation in a patient in less than about 180 days[.]" (*See* D.I. 316 at 8 (internal quotation marks omitted)) To that end, Plaintiffs contended that the claims of the '5705 patent did not "'exclude the presence of other biodegradable groups, but at physiological conditions in vivo, the claim requires that the biodegradable groups responsible for degradation in less than about [180] days only be ester groups.'" (*See* D.I. 230 at 11-12 (quoting D.I. 233, ex. 13 at ¶ 167)) Meanwhile, HyperBranch asserted that the term be construed to mean "the hydrogel does not contain any biodegradable linkages other than ester linkages[.]" (D.I. 316 at 8 (internal quotation marks omitted)) The Court framed the parties' dispute as follows:

> The crux of the dispute with respect to this term is whether its effect is that (1) the claimed hydrogel must not contain any biodegradable linkages other than ester linkages (as Defendant argues), or (2) whether the hydrogel can include other biodegradable linkages, but that those linkages that are biodegradable linkages under the conditions specified in the claims (i.e., in a patient in less than about 180 (or 90) days) must be ester groups (as Plaintiffs contend).

(*Id.* at 9) In view of the intrinsic record, the Court recommended that HyperBranch's construction be adopted for the term. (*Id.* at 9-16)

Plaintiffs objected to the Court's recommended construction, arguing that:

> When considered in context of the claim language as a whole, the term "biodegradable groups consist of the esters" means that the claimed hydrogel may include other non-ester groups, *which may be considered "biodegradable" to some extent under certain*

> *conditions*, but the "biodegradable" groups that cause degradation in a patient within 180 days must be the ester groups. The claim rightly excludes "biodegradable" groups other than esters that cause degradation in a patient within 180 days. But, [the Court's] construction wrongly excludes *any non-ester group that may be "biodegradable" to even a small or insignificant extent under certain conditions and over a very long period of time beyond 180 days*, and that does not usefully contribute to degradation of the hydrogel within 180 days. . . . Any non-ester groups *that may be "biodegradable" under certain conditions* but that have no effect on degradation of the hydrogel in the body within 180 days, should not be excluded from within the scope of the claim.

(D.I. 325 at 1 (emphasis added, certain emphasis omitted)) Chief Judge Stark overruled Plaintiffs' objection, finding that the import of the claim language and the prosecution history is that the claim term "limits the biodegradable groups of the claimed hydrogel to ester groups only." (D.I. 379 at 9) Chief Judge Stark thus adopted the Court's recommendation, and construed the term "the biodegradable groups of the hydrogel consist of the esters" to mean "the hydrogel does not contain any biodegradable linkages other than ester linkages." (*Id.* at 8-10)

B. Literal Infringement

Before delving into the parties' specific arguments and evidence, the Court pauses to consider how, in light of the claim and the claim construction of the esters limitation, a hydrogel would generally avoid infringement of the asserted claims of the '5705 patent. It is undisputed that, in the context of the asserted claims, "biodegradable" means groups or linkages that are "susceptible to biodegradation" or "able to be degraded." (D.I. 402 at 15 n.6; D.I. 443 at 7-8; Tr. at 94) And as Plaintiffs point out, in determining whether a particular linkage is "biodegradable," the context of the claim must be considered. (D.I. 443 at 6) The claimed hydrogel, after all, is formed "in situ in a patient" and is used to treat a medical condition. ('5705

patent, col. 30:35-41) Thus, if an accused hydrogel includes a linkage other than an ester linkage that is able to be degraded in the human body, that would put it outside of the scope of the asserted claims.

HyperBranch's Accused Products are used to coat a dural incision in a patient. (Plaintiffs' Opposition to Defendant's Motion for Summary Judgment of Non-infringement of the '3705 Patent and '5705 Patent Slide Presentation, Slide 5; D.I. 443 at 5; D.I. 429, ex. 90 at ¶ 274) And there is no dispute that the Accused Products contain amide (i.e., non-ester) linkages. (*See, e.g.*, D.I. 403, ex. A at ¶ 213; D.I. 456, ex. 5 at ¶ 32) The key issue here is whether the amide linkages found in the Accused Products are able to be degraded when used in situ in a patient to treat a medical condition. In view of the Court's claim construction described above, however, such linkages need *not* cause degradation of the hydrogel within 180 days (or 90 days pursuant to claim 17)—they just need to be able to be degraded "'to even a small or insignificant extent . . . [and even] over a very long period of time beyond 180 days[.]'" (*See* D.I. 379 at 8-9 (internal citation omitted))

With all this in mind, the Court now turns to the parties' arguments and evidence on the disputed issue. As noted above, HyperBranch argues that the amide linkages in its Accused Products are biodegradable, and that their presence thus removes the Accused Products from the scope of the asserted claims of the '5705 patent. (D.I. 402 at 10-12; D.I. 463 at 3) For the reasons discussed below, the Court agrees with HyperBranch that: (1) there is no genuine dispute of fact that the amide linkages in the Accused Products are biodegradable; and (2) the Accused Products thus do not read on the asserted claims of the '5705 patent because they do not read on the esters limitation.

The Court starts by noting that the record is robust with several categories of evidence indicating that, at least as a general matter, amide linkages can be and are biodegradable (including when they are used on a patient).

First, HyperBranch points to the text of the asserted patents to make this showing. (D.I. 402 at 11-12; D.I. 463 at 3) The specifications of some of the asserted patents (other than the '5705 patent) specifically identify amide linkages as biodegradable linkages in the context of biocompatible hydrogels used for medical applications on a patient. The '034 patent, '566 patent, and '418 patent specifications, after explaining that "[a]n embodiment of the invention is a hydrogel for use on a patient's tissue[,]" note that "[t]he polymers preferably also have *a hydrolytically biodegradable portion or linkage, for example* an ester, carbonate or *an amide linkage*." ('034 patent, col. 6:22-23, 44-47; '566 patent, col. 6:22-23, 44-47; '418 patent, col. 6:20-21, 42-44 (emphasis added)) In discussing the "[p]reparation of [b]iocompatible [p]olymers," the '3705 patent explains that "[t]he polymers may also have *a hydrolytically biodegradable portion or linkage*, for example an ester, carbonate, or *an amide linkage*." ('3705 patent, cols. 21:47, 23:38-40 (emphasis added)) In view of this intrinsic record, the District Court's claim construction order noted that "amide linkages are considered biodegradable in the context of the asserted patents[.]" (D.I. 379 at 9 n.8)[5]

Second, the prosecution history of the '034 patent provides further evidence that amide linkages in hydrogels used on patients are biodegradable. (*See* D.I. 402 at 11 n.3; D.I. 463 at 3;

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[5] These patents come from the same patent family and are related. The '5705 patent and the '3705 patent are both continuations-in-part of the '406 patent, and the '034 patent, '418 patent, and '566 patent are all continuations of the '406 patent. (*See, e.g.*, D.I. 379 at 11; Plaintiffs' Claim Construction Presentation, Slide 2)

Tr. at 87-88) During prosecution of that patent—entitled "Biocompatible Crosslinked Polymers"—the patentees actually sought claims reciting a "biodegradable hydrogel . . . wherein the crosslinked hydrophilic polymers comprise polyethylene glycol and a *hydrolytically biodegradable portion chosen from the group consisting* of an ester, *amide*, or carbonate *linkage*[.]" (D.I. 412, ex. 129 at HBMT0405966-67 (emphasis added); *see also* D.I. 410, ex. 123 at 68-69)

Third, HyperBranch points to the initial report of Plaintiffs' expert Dr. Jimmy Mays, which was prepared during the preliminary injunction stage of this proceeding. (D.I. 402 at 11; D.I. 463 at 7) There, Dr. Mays acknowledged that the intrinsic record of the asserted patents taught that amide linkages are biodegradable in the context of the patents. With respect to the '3705 patent, Dr. Mays explained that:

> [T]he '3705 patent teaches that "[t]he polymers may also have a hydrolytically biodegradable portion or linkage for example an ester, carbonate, or an amide linkage." See col. 23, lines 38-40. The '3705 patent therefore teaches that amide linkages, such as those created by reacting the preferred NHS ester of a first precursor with a primary amine of a second precursor is a hydrolytically biodegradable linkage.

(D.I. 10, ex. 13 at ¶ 454) HyperBranch asserts that "[t]his is the exact way the amide linkages are created in the hydrogels of the Accused Products." (D.I. 402 at 11 (citing D.I. 403, ex. A at ¶ 218 (HyperBranch's expert Dr. Anthony Lowman opining that the hydrogels made by the Accused Products have these exact amide bonds, formed by the reaction of an NHS ester and a primary amine)); *see also* Tr. at 76-77) And Plaintiffs' expert Dr. Mark Distefano appears to confirm that this is so. (D.I. 456, ex. 5 at ¶ 32 (explaining his understanding that the nature of the synthetic amide linkages in the Accused Products are "formed from the electrophilic NHS groups and the

nucleophilic amine groups of the reactive precursor compounds"))

Fourth, HyperBranch cites to many references that are called out in the patents-in-suit or that are otherwise in the field, all of which identify amide bonds as hydrolytically biodegradable linkages. (D.I. 402 at 12; D.I. 463 at 4 n.1; D.I. 403, ex. A at ¶¶ 223-38) For instance, a textbook known as *Contemporary Polymer Chemistry* by Allcock and Lampe teaches that "[t]he amide linkage is moderately sensitive to hydrolysis, but the behavior of a synthetic polymer under hydrolytic conditions will depend more on materials and surface effects than on the chemistry of the linkage itself." (D.I. 403, ex. A at ¶ 259) There are also several patents cited on the face of the '5705 patent that identify amide linkages as biodegradable, (*see id.* at ¶¶ 224-26), as listed below:

(1) United States Patent No. 5,514,380, issued to Song and entitled "Biodegradable Hydrogel Copolymer as Drug Delivery Matrix" describes a claimed hydrogel structure that is "easily degraded and excreted in human body by the hydrolysis of intramolecular ester and amide bonds" and it further references "a biodegradable chemical linkage, such as an amide linkage, ester linkage, and/or carbonate linkage[.]" (D.I. 409, ex. 108, at Abstract & cols. 1:9-12, 3:15-16)

(2) United States Patent No. 6,162,241, issued to Coury and entitled "Hemostatic Tissue Sealants" recites that "[b]iodegradable regions can be constructed from polymers or monomers using linkages susceptible to biodegradation, such as ester, amide, peptide, carbonate, urea, anhydride, orthoester, phosphazine and phosphoester bonds. . . . initial polymer molecular weight and structure will influence the degradation rate." (D.I. 413, ex. 133, col. 5:18-28)

(3) United States Patent No. 6,458,889, issued to Trollsas and entitled "Compositions and Systems for Forming Crosslinked Biomaterials and Associated Methods of Preparation and Use" teaches that "[e]xamples of linking

groups that provide hydrolyzable sites, include . . . amide linkages[.]" (*Id.*, ex. 134, col. 15:47-60)

There are several other patents and references in the field that teach that amide linkages are biodegradable linkages. (D.I. 403, ex. A at ¶¶ 227-37) To summarize just a few of them:

(1) United States Patent No. 7,347,850, issued to Sawhney (who is also a named inventor on the '5705 patent), is entitled "Adhesion Barriers Applicable by Minimally Invasive Surgery and Methods of Use Thereof," and recites that "[t]he polymers preferably also have a hydrolytically biodegradable portion or linkage, for example an ester, carbonate or an amide linkage[.]" (D.I. 413, ex. 135, col. 8:23-25)

(2) United States Patent No. 7,919,112 issued to Pathak (who is also a named inventor on the '5705 patent), is entitled "Implantable Tissue Compositions and Method," and explains that "[i]llustrative chemically hydrolyzable biodegradable linkages are ester or amide bonds that undergo cleavage under physiological conditions such as, by way of example, and not limitation, found in human body (pH 7.2)." (*Id.*, ex. 136, col. 37:11-14)

(3) United States Patent No. 6,652,886, issued to Ahn and entitled "Biodegradable Cationic Copolymers of Poly(alkylenimine) and Poly(ethylene glycol) for the Delivery of Bioactive Agents" recites "a biodegradable linkage which can be an ester, amide or urethane, depending on the required degradation rate." (D.I. 414, ex. 141, col. 3:64-66)

(4) Lakshmi S. Nair & Cato T. Laurencin, "Biodegradable Polymers as Biomaterials," *Progress in Polymer Sci.*, 32:762-98 (2007), explains, in a section entitled "Hydrolytically degradable polymers as biomaterials[,]" that "[h]ydrolytically degradable polymers are polymers that have hydrolytically labile chemical bonds in their back bone. The functional groups susceptible to hydrolysis include esters, orthoesters, anyhdrides, carbonates, amides, urethanes, ureas, etc." (*Id.*, ex. 144 at 765)

In addition to the above-referenced evidence indicating that, as a general matter, amide linkages are understood to be biodegradable, HyperBranch has identified other evidence relating more directly to the Accused Products that shows that the amide linkages therein are indeed biodegradable.

For example, HyperBranch points to the testimony of Plaintiffs' expert Dr. Distefano. (D.I. 402 at 14; D.I. 463 at 5; Tr. at 86, 100-03) During his deposition, Dr. Distefano acknowledged that one could calculate the fraction of bonds that would be expected to break by hydrolysis using the half life for those bonds. (D.I. 418, ex. 172 at 190-92) Dr. Distefano further agreed that seven years is a reasonable number for the half life of the amide bonds in the Accused Products, and that one could use this half life to do a "straightforward calculation" to determine the fraction of amide bonds that would be expected to degrade in 180 days. (*Id.* at 195-96) And Dr. Distefano agreed that, after performing this calculation, approximately 5% of the amide linkages in the hydrogels of the Accused Products would be broken by reaction of water within 180 days. (*Id.* at 196-200; *see also id.* at 143 ("I would say that in 180 days you will only have a few percent of the amide bonds cleaved, and that would not be sufficient to alter the properties of the material"))

Additionally, HyperBranch offers Dr. Lowman's opinion that the Accused Products contain biodegradable amide linkages. (D.I. 402 at 11-12; D.I. 403, ex. A at ¶ 213) This conclusion rests on the intrinsic record of the patents, the prosecution history of the '034 patent, and the many pieces of art cited in the patents-in-suit and otherwise in the field that identify amide bonds as biodegradable. (D.I. 403, ex. A at ¶ 240)

For their part, Plaintiffs assert that the Accused Products infringe the esters imitation

because "the amide linkage in the accused hydrogels *is not hydrolytically biodegradable within the meaning of the claim (i.e., it does not cause degradation of the hydrogel within less than 180 days or less than 90 days) when the accused hydrogels are placed on the dura mater of a patient.*". (D.I. 429, ex. 76 at ¶ 198 (emphasis added); *see also* D.I. 443 at 6 ("The amide linkages simply do not biodegrade within 180 days or 90 days when Adherus hydrogel is used to coat a patient's dural incision. This fact alone prevents summary judgment of noninfringement.")) Dr. Mays explains that the Accused Products degrade because they include ester linkages, which "hydrolyze and break so quickly to degrade the hydrogel that the amide linkages provide no useful biodegradation effect, if any biodegradation effect at all" in the context of the claims—(i.e., within less than 180 days or less than 90 days). (D.I. 429, ex. 76 at ¶ 184; *see also id.* at ¶ 187)

Plaintiffs' contrary position really relies on the opinions of their experts, Dr. Mays and Dr. Distefano. But it is clear that they approached the infringement question by assessing whether the amide linkages in the Accused Products were responsible for degradation of the hydrogel in a patient in less than 180/90 days. For example, elsewhere in his report Dr. Mays reiterates his infringement opinion:

> For the amide linkages in the hydrogel to be "biodegradable" within the context of the claims, the amide linkages need to break under physiological conditions *and cause degradation of the hydrogel in less than about 180 days or less than about 90 days*, as the hydrogel is formed in situ in a patient as required by the claims. *If the amide is stable* under such conditions at the point where the hydrogel is essentially fully degraded in the patient in less than about 180 days, or less than about 90 days due to ester linkages *i.e., the amide linkages do not break to cause the claimed degradation*, then the amide linkage is not biodegradable within the context of the claim.

(*Id.* at ¶ 173 (emphasis added); *see also id.* at ¶ 182 ("I understand 'stable' to mean that the amide linkages do not biodegrade *relative to the ester linkages* in the accused HyperBranch hydrogels") (emphasis added); *id.* at ¶ 183 ("[i]f a linkage does not *contribute to degradation of the hydrogel within less than 180 days or less than 90 days*, the linkage is stable") (emphasis added)) This position is further repeated throughout Dr. Mays' report. (*See also, e.g.*, *id.* at ¶ 169 (Dr. Mays asserting that "any amide linkages present in the accused HyperBranch products *must biodegrade within the meaning of the claim to avoid infringement, i.e., the amide linkages being broken result in essentially full degradation of the hydrogel in a patient in less than about 180 days (claim 1) or less than 90 days* (claim 17)") (emphasis added); *id.* at ¶ 171 ("Since the hydrogels are biodegradable, the biodegradable groups are responsible for no more than a small amount of the hydrogel remaining in less than about 180 days or in less than about 90 days. This is how the claim defines the biodegradable groups."); *id.* at ¶ 172 ("If amide linkages do not cause a hydrogel to degrade such that no more than a small amount of the hydrogel remains in less than about 180 days or less than about 90 days at an aqueous physiological pH of 7.4, then the amide linkages are not biodegradable linkages"))

Dr. Distefano's interpretation of a hydrogel with non-ester linkages that reads on the asserted claims is consistent with that of Dr. Mays. For instance, Dr. Distefano explains that "[t]he synthetic amide groups [of the Accused Products] *do not contribute to biodegradation of the claimed hydrogel within 180 days* within a patient under physiological conditions." (D.I. 456, ex. 5 at ¶ 32 (emphasis added)) Similarly, he later opines that "[b]ecause amide linkages are inherently stable under physiological conditions, *they are not going to biodegrade in situ in less*

than 180 days so as to contribute to biodegradation of the synthetic hydrogel, which is what claim 1 requires." (*Id.* at ¶ 33 (emphasis added); *see also, e.g.*, D.I. 418, ex. 172 at 140 (Dr. Distefano testifying that, in determining whether or not the amide linkages in the Accused Products are a biodegradable group under the Court's construction, "time was a factor because the [amide] linkage would have to be cleaved in 180 days. So if it was ten years, that could be a different situation.")) Dr. Distefano based his understanding of whether the amide linkage would be biodegradable "based on the . . . rates of bond cleavage of esters versus amides in this case." (D.I. 418, ex. 172 at 143)

However, Plaintiffs' position is inconsistent with the Court's claim construction, and it is therefore fatally flawed. (*See* D.I. 402 at 12-13; D.I. 463 at 3 & 5 n.3; Tr. at 82, 89) As described above, the Court rejected Plaintiffs' proposal that the term "the biodegradable groups of the hydrogel consist of the esters" be construed as "the esters are the only biodegradable group responsible for degradation in a patient in less than about 180 days[.]" Instead, the esters limitation places a hydrogel outside of the scope of the claims when it includes biodegradable groups other than ester linkages that are able to be degraded when used in a patient *at all*—i.e., to even a small or insignificant extent or if the degradation would take place beyond 180 days. (*See* D.I. 379 at 8-10) Thus, Plaintiffs' experts are, in essence, construing the term in a manner that the Court has already rejected during the *Markman* process.[6]

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[6] Dr. Mays' erroneous interpretation of the claim construction is further highlighted by his testimony that a hydrogel with ester linkages and anhydride linkages would not automatically fall outside of the scope of the asserted claims. (D.I. 402 at 13-14; Tr. at 89-91) As the Court explained in its Report and Recommendation regarding claim construction, during prosecution of the '5705 patent application, the applicants explained that claim 1 was amended to clarify that "'the biodegradable groups are the isolated esters[]'" and that adding a "'polyanhydride places the precursor outside of the claims.'" (D.I. 316 at 13 (internal citation

Plaintiffs' flawed view of the meaning of "the biodegradable groups consists of the esters" infects their assessment of the evidence. For example, Plaintiffs point to HyperBranch's own internal documents in support of their argument that the Accused Products infringe because the amide linkages therein do not biodegrade within 180 days or 90 days. One such document describes the degradative profile of HyperBranch's NuSeal 100 hydrogel, (D.I. 429, ex. 76 at ¶ 165), which includes the same precursors and reaction chemistry as the Accused Products, (*id.* at ¶ 163). HyperBranch reported that:

> [I]f completely hydrolyzed, the ultimate shift for free PEG in the forced degradation study strongly suggests that the PEI remains in the form of a sebacate derivative. This is also supported theoretically by the strength and stability of the amide bond between the PEI and the sebacate previously bound to PEG by ester linkage.

(*Id.* at ¶ 165) Dr. Mays opines that this study "confirms that degradation occurs by ester hydrolysis and that there is no amide linkage hydrolysis. . . . [i]f there was amide linkage hydrolysis, then HyperBranch would have found free PEI during the degradation study, which it did not." (*Id.* at ¶ 166) While this document could be used to show that the biodegradable groups that are responsible for degradation in a patient in less than about 180 days are the ester

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omitted) (emphasis omitted)) These statements came in the course of distinguishing the claims over a prior art reference ("Rhee '500") which taught the artisan to add certain biodegradable materials that included poly(anhydride) but not ester groups. (*Id.*) As the Court noted, the applicants there "explained how adding a degradable material to the precursor that was *not* an ester (i.e., a polyanhydride) would remove it from the scope of the claimed invention." (*Id.* at 14) Yet Dr. Mays testified that to assess infringement of such a hydrogel, one would have to "look at the relative rates of degradation of those two groups under the conditions that you're putting the material in"—if the anhydride groups did not "contribute significantly" to the degradation, then Dr. Mays "believe[d]" such a hydrogel would still fall within the scope of the claim. (D.I. 418, ex. 171 at 139-40) Dr. Mays' testimony on this point thus underscores his continued application of Plaintiffs' rejected claim construction in the infringement analysis.

groups (and that the amide linkages are relatively "stable" in this timeframe), (*see, e.g.*, D.I. 443 at 6), it does not speak to whether the amide linkages are biodegradable *at all*—and that is the pertinent inquiry here.

Plaintiffs also cite in support to HyperBranch's statements to the United States Patent and Trademark Office in prosecuting U.S. Patent Application 11/653,433, which relates to the Accused Products. (D.I. 443 at 9) In a December 21, 2011 Amendment and Response in which HyperBranch argued that certain claims were not obvious over another patent, HyperBranch explained:

> **Second, and more importantly in terms of suitability for use in the claimed methods, the PEG core in Formula 5 of Rhee is -NH-PEG-NH-, so the linkers are attached to the PEG core via *amide linkages.*** In contrast, the structure cited by the Examiner implies a PEG core represented by -O-PEG-O-, so that the linkers would be attached to the PEG core via *ester* linkages. ***Critically, ester linkages are degraded significantly more rapidly in the physiologic milieu than amide linkages.*** Consequently, the crosslinker actually disclosed by Rhee (i.e., Formula 5) ***would degrade too slowly to be efficacious in the claimed methods due to the intrinsic stability of amide linkages at physiological pH.*** *This distinction is critical* because one of ordinary skill in the art would not have had a reasonable expectation of success in developing the claimed methods by utilizing a crosslinker with amide linkages between the PEG core and the diacid linkers due to ***the robustness of the amide linkages at physiological pH.***

(*See* D.I. 429, ex. 76 at ¶ 183 (emphasis added by Dr. Mays)) What is critical in the Court's view is that this document does *not* say that the amide linkages simply will not biodegrade in situ—rather, it says that they will degrade *more slowly* than the ester linkages. (*See* D.I. 403, ex. A at ¶ 248) And as HyperBranch accurately notes, "there is no [] significance or relative rate cutoff for a biodegradable linkage to remove a hydrogel from the scope of the claims under the Court's construction." (D.I. 402 at 15 (emphasis omitted); *see also id.* at 14; D.I. 463 at 6; Tr. at

102)

Additionally, Plaintiffs assert that Dr. Mays' degradation experiments performed on the Accused Products also contribute to generating a genuine dispute of material fact here. (D.I. 443 at 9-10) Dr. Mays performed an experiment where he prepared hydrogels representative of the Accused Products except with the ester linkages removed, and he reported that "no noticeable degradation" occurred in the test hydrogels upon visual inspection after 53 days. (D.I. 456, ex. 6 at ¶¶ 4-6) Dr. Mays opines that the results of this testing "demonstrate that amide linkages in the accused Adherus hydrogels do not degrade under physiological conditions *within 90 days or within 180 days*[.]" (*Id.* at ¶ 1 (emphasis added)) When viewed in light of the Court's claim construction, however, Dr. Mays' testing does not create a dispute of fact, because the absence of visible degradation in 53 days does not speak to whether the amide linkages are biodegradable *at all* when used in a patient.[7]

If there was some credible evidence in the record that amide linkages simply would never biodegrade at all in a patient, then there would be at least a genuine dispute of material fact here about whether the Accused Products satisfied the esters limitation. But there is not. The evidence that Plaintiffs point to is all geared to showing that the amide linkages in the hydrogels of the Accused Products *are not responsible for the degradation of the hydrogel in 180 or 90 days*, and Plaintiffs' experts did *not* opine that the amide linkages would *never* degrade. (*See, e.g.*, D.I. 429, ex. 76 at ¶ 195 (Dr. Mays opining that "the rate of hydrolysis of the ester linkages

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[7] Furthermore, the record indicates that visual inspection is not sufficient to indicate whether there is any degradation. (*See, e.g.*, D.I. 418, ex. 172 at 161-62 (Dr. Distefano testifying that you could use a "spectroscopic technique" to assess whether particular bonds have cleaved); D.I. 429, ex. 39 at 255-57 (Dr. Lowman explaining that hydrogel samples in a photograph could be undergoing degradation regardless of visual appearance))

in the accused HyperBranch hydrogels, i.e. on the order of 45 days, even if 90 days or 180 days, is so quick compared to the 350 year half-life for hydrolysis of a single amide linkage that the accused [] products are long degraded before even a single amide linkage is broken due to hydrolysis")) Indeed, both Dr. Distefano and Dr. Mays acknowledged that *even within 90 or 180 days*, some small amount of the amide linkages *would* degrade. (D.I. 418, ex. 172 at 143, 196-200 (Dr. Distefano testifying that a few percent of the amide linkages would cleave within 180 days); *id.*, ex. 171 at 143-44 (Dr. Mays acknowledging that a "[n]egligible" amount of amide bonds would biodegrade in 90 days "compared to any degradation that's taking place with the ester groups"))

In view of all of the evidence discussed above, then, the Court agrees with HyperBranch that no reasonable jury could find that the Accused Products satisfy the claim limitation "the biodegradable groups of the hydrogel consist of the esters" in the asserted claims of the '5705 patent. Plaintiffs' experts' opinions to the contrary, which were based on an erroneous understanding of the Court's claim construction, cannot persuade the Court otherwise. *See Cordis Corp. v. Boston Sci. Corp.*, 658 F.3d 1347, 1357-58 (Fed. Cir. 2011) (concluding that expert testimony regarding infringement must be disregarded where it was "based on an incorrect understanding of the claim construction"); *Quest Licensing Corp. v. Bloomberg L.P.*, C.A.No. 14-cv-561(GMS), 2017 WL 239345, at *3 (D. Del. Jan. 19, 2017) (finding that there was not a difference in expert opinion that should preclude summary judgment of noninfringement where the plaintiff's expert "failed to apply the court's claim construction"); *see also Luminara Worldwide, LLC v. Liown Elecs. Co.. Ltd.*, Case No. 14-cv-03103 (SRN/FLN), 2017 WL 1555881, at *6 (D. Minn. Mar. 29, 2017) ("Expert testimony based on erroneous constructions is

insufficient—as a matter of law—to create a triable issue of fact.") (citing cases).[8] Accordingly, the Court recommends that summary judgment of non-infringement be granted for the Accused Products as to literal infringement of the asserted claims of the '5705 patent.[9]

C. Doctrine of Equivalents

HyperBranch additionally seeks summary judgment that Plaintiffs are precluded from relying on the doctrine of equivalents to establish infringement of the asserted claims of the '5705 patent, asserting that the esters limitation "was a narrowing amendment added to the claims during prosecution to overcome the prior art." (D.I. 402 at 17; *see also* D.I. 463 at 7) The United States Court of Appeals for the Federal Circuit has explained that "[p]rosecution history estoppel applies as part of an infringement analysis to prevent a patentee from using the doctrine of equivalents to recapture subject matter surrendered from the literal scope of a claim during prosecution." *Trading Techs. Int'l, Inc. v. Open E Cry, LLC*, 728 F.3d 1309, 1322 (Fed. Cir. 2013). "Estoppel arises when an amendment is made to secure the patent, and the amendment narrows the patent's scope." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 736 (2002); *see also Honeywell Int'l Inc. v. Hamilton Sundstrand Corp.*, 370 F.3d 1131, 1139 (Fed. Cir. 2004) (prosecution history estoppel "bar[s] the patentee from asserting

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[8] Dr. Mays' experimental testing described above is the subject of HyperBranch's Motion to Strike Plaintiffs' Untimely Production of New Test Results and New Evidence Regarding the Degradation of Amide Linkages. (D.I. 424) In light of the Court's recommendation, however, the Court hereby DENIES AS MOOT the Motion to Strike.

[9] In light of the Court's recommendation in this regard, it further recommends that HyperBranch's Motion for Summary Judgment of Invalidity of the '5705 patent be DENIED AS MOOT, as HyperBranch's invalidity arguments were applicable only "[u]nder Plaintiffs' interpretation of the [esters limitation]." (*See* D.I. 402 at 3; *see also id.* at 20, 25) As the Court has explained, it does not agree with Plaintiffs' interpretation, as it is in conflict with the Court's claim construction.

equivalents if the scope of the claims has been narrowed by amendment during prosecution").

When presented with a narrowing amendment that was made for reasons related to patentability, the Court must "presum[e] that prosecution history estoppel applies." *EMD Millipore Corp. v. AllPure Techs., Inc.*, 768 F.3d 1196, 1204 (Fed. Cir. 2014). The patentee may rebut the presumption by establishing one of three exceptions to estoppel: "the equivalent [was] unforeseeable at the time of the application; the rationale underlying the amendment [bore] no more than a tangential relation to the equivalent in question; or there [was] some other reason suggesting that the patentee could not reasonably be expected to have described the [equivalent]." *Festo*, 535 U.S. at 740-41. Whether prosecution history estoppel applies, and therefore whether a patentee may assert the doctrine of equivalents for a particular claim limitation, is a question of law. *Spectrum Pharms., Inc. v. Sandoz Inc.*, 802 F.3d 1326, 1337 (Fed. Cir. 2015); *Intellectual Ventures I LLC v. T-Mobile USA, Inc.*, C.A. No. 13-1632-LPS, 2017 WL 3723934, at *5 (D. Del. Aug. 29, 2017).

In connection with the claim construction process, the Court examined the relevant prosecution history of the '5705 patent in detail; in doing so, it found that the applicants narrowed the claims to exclude biodegradable linkages other than ester linkages. (D.I. 316 at 11-15; D.I. 379 at 9-10) Thus, the presumption of prosecution history estoppel applies, and would prevent operation of the doctrine of equivalents to extend the coverage of the asserted claims to include other biodegradable linkages, such as amide linkages. *See, e.g.*, *Trading Techs. Int'l, Inc.*, 728 F.3d at 1322 ("[A] single action during prosecution can engender both a prosecution disclaimer and prosecution history estoppel."); *Elkay Mfg. Co. v. Ebco Mfg. Co.*, 192 F.3d 973, 978-79, 981 (Fed. Cir. 1999) (finding that the "prosecution history of the patents shows that Elkay gave up a

construction of the feed tube/probe limitation that could include an apparatus with separate flow paths for liquid and air" in construing claims, and that prosecution history estoppel applied to prevent operation of the doctrine of equivalents "to extend the coverage of those claims to include a separate feed tube or flow path for liquid and air").

Plaintiffs argue that they have overcome any presumption of estoppel because there are factual questions as to whether the inclusion of an amide linkage was unforeseeable at the time of the applicants' amendment. They assert that "an amide linkage was not foreseeable because the degradation rate of esters linkages and amide linkages were so significantly different that when comparing the two[,] those of ordinary skill in the art (and even HyperBranch themselves) considered the amide linkages 'stable' as opposed to biodegradable at the time of the amendment." (D.I. 443 at 12-13)

The Federal Circuit has explained that "[a]n equivalent is foreseeable if one skilled in the art would have known that the alternative existed in the field of art as defined by the original claim scope, even if the suitability of the alternative for the particular purposes defined by the amended claim scope were unknown." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 493 F.3d 1368, 1382 (Fed. Cir. 2007). If the alleged equivalent were known in the prior art in the field of the invention, it "certainly should have been foreseeable at the time of the amendment." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 344 F.3d 1359, 1369 (Fed. Cir. 2003).

Here, the Court easily finds that "at the time of the amendment one skilled in the art could . . . reasonably [have been] expected to have drafted a claim that would have literally encompassed the alleged equivalent." *Festo*, 535 U.S. at 741. As described above, (*see supra* at

11), at the time of the amendment—submitted on May 1, 2012, (D.I. 232, ex. 6 at HBMT0409334-35)—the specifications of some of the other asserted, related patents specifically identified amide linkages as biodegradable linkages in the context of biocompatible hydrogels used for medical applications on a patient. Moreover, as also discussed above, (*see supra* at 12), in 2001, the applicants actually sought claims reciting a "biodegradable hydrogel . . . wherein the crosslinked hydrophilic polymers comprise polyethylene glycol and a *hydrolytically biodegradable portion chosen from the group consisting* of an ester, *amide*, or carbonate *linkage*[.]" (D.I. 412, ex. 129 at HBMT0405894-96, 966-67 (emphasis added)) Finally, the art described amide linkages as biodegradable linkages. (*See supra* at 13-15)

For these reasons, the Court finds that there can be no genuine fact dispute that the alleged equivalent (biodegradable groups consisting of ester linkages and amide linkages) would have been foreseeable to a person of ordinary skill in the art at the time of the amendment. And thus, the Court recommends that summary judgement of non-infringement be granted as to Plaintiffs' doctrine of equivalents argument.

IV. CONCLUSION

For the reasons set forth above, the Court recommends that HyperBranch's motion for summary judgment of non-infringement of the esters limitation of claims 1, 6, 12 and 17 of the '5705 patent be GRANTED.

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 by no later than **March 2, 2018**; responses are due by no later than **March 12, 2018**. 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 Sincavage v. Barnhart*, 171 F. App'x 924, 925 n.1 (3d Cir. 2006); *Henderson v. Carlson*, 812 F.2d 874, 878-79 (3d Cir. 1987).

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.

Because this Report and Recommendation may contain confidential information, it has been released under seal, pending review by the parties to allow them to submit a single, jointly proposed, redacted version (if necessary) of the Report and Recommendation. Any such redacted version shall be submitted no later than **February 23, 2018** for review by the Court, along with a clear, factually detailed explanation as to why disclosure of any proposed redacted material would "work a clearly defined and serious injury to the party seeking closure." *Pansy v. Borough of Stroudsburg*, 23 F.3d 772, 786 (3d Cir. 1994) (internal quotation marks and citation omitted). The Court will subsequently issue a publicly-available version of its Report and Recommendation.

Dated: February 20, 2018

Christopher J. Burke
UNITED STATES MAGISTRATE JUDGE