UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MEDTRONIC, INC., and TYRX, INC.
Petitioner,

v.

BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM and TISSUEGEN, INC.
Patent Owner.

Case: IPR2019-00038
U.S. Patent No. 7,033,603

PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 7,033,603

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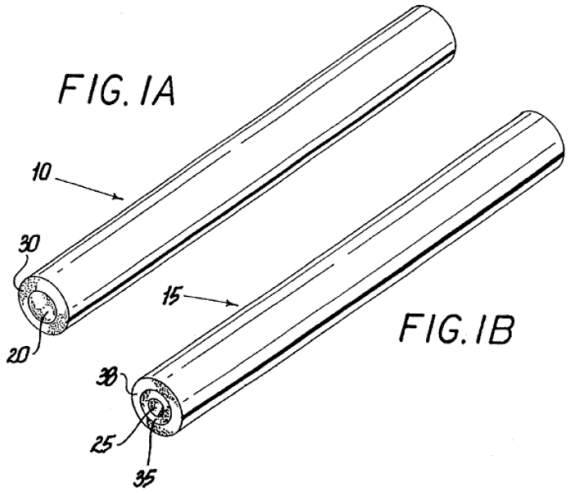
Medtronic, Inc., and Tyrx, Inc. (collectively, "Petitioner") petition for *Inter Partes* Review under 35 U.S.C. §§ 311–319 and 37 C.F.R., Part 42 of claims 1, 2, 4–6, 11–13, 15–19, 21, 22, 24–26, and 31–33 of U.S. Patent No. 7,033,603 (the "'603 patent"). As shown herein, Petitioner is reasonably likely to prove these challenged claims unpatentable. Accordingly, Petitioner requests that the Board institute trial and cancel all challenged claims.

I. INTRODUCTION

The '603 patent claims simple drug-delivery fibers with two components, where one of the components is a biodegradable polymer and another component is a gel or hydrogel. Drug-delivery fibers, including those using biodegradable polymers, gels, and hydrogels, were well known before the claimed effective filing date of the '603 patent. *Infra* § V. For example, U.S. Patent No. 5,578,046 to Liu *et al*. ("Liu") (Ex. 1005) discloses multi-component fibers which include different layers that each may be comprised of polymers, gels, and/or hydrogels:



Liu explains that its fibers can incorporate various drugs, which will be delivered into the body as the device biodegrades. As shown in detail herein, the challenged claims of the '603 patent are directed only to what was old and obvious.

Petitioners therefore respectfully request the Board institute an *inter partes* review and ultimately cancel claims 1, 2, 4–6, 11–13, 15–19, 21, 22, 24–26, and 31–33 of the '603 patent as unpatentable.

II. MANDATORY NOTICES – 37 C.F.R. § 42.8

A. Real Party-In-Interest Under 37 C.F.R. § 42.8(b)(1)

Medtronic, Inc., and Tyrx, Inc. are the real-parties-in-interest for the purposes of this proceeding.

B. Related Matters Under 37 C.F.R. § 42.8(b)(2)

Patent Owner is asserting the '603 patent in the following currently pending cases:

- *Board of Regents, the University of Texas Sys. et al. v. Ethicon, Inc. et al.*, No. 1:17-cv-01084 (W.D. Tex.);
- *Board of Regents, the University of Texas Sys. et al. v. Boston Scientific Corp.*, No. 1:18-cv-00392 (D. Del.); and
- *Board of Regents v. Boston Scientific Corp.*, No. 18-1700 (Fed. Cir.)

Patent Owner also previously asserted the '603 patent against Petitioner in *Board of Regents, the University of Texas System et al. v. Medtronic, Inc. et al.*, No. 1:17-cv-

00942 (W.D. Tex.). The complaint in that action was served on October 11, 2017 (Ex. 1041; Ex. 1042) and the suit was dismissed without prejudice on July 19, 2018.

The '603 patent is related to U.S. Patent No. 6,596,296, which is also asserted in each of the above-referenced cases. Petitioner will file a Petition for *Inter Partes* Review regarding the '296 patent concurrently with this Petition. *See* IPR2019-00037.

C. Lead and Back-Up Counsel Under 37 C.F.R. § 42.8(b)(3)

Lead Counsel: Andrew R. Sommer (Reg. #53,932). **Backup Counsel:** Nimalka R. Wickramasekera, Shilpa A. Coorg, Katherine Hundt, Matthew R. McCullough (*pro hac vice* to be filed).

D. Service Information Under 37 C.F.R. § 42.8(b)(4)

Petitioners consent to service by email on the following email addresses: Medtronic-TissueGen-IPRs@winston.com.

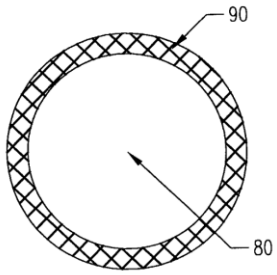
III. PETITIONER HAS STANDING TO BRING THIS PROCEEDING

Petitioner certifies (1) the '603 patent is available for IPR, (2) none of the parties constituting Petitioner are the Patent Owner, and (3) it is not barred or estopped from requesting this IPR. The '603 patent was first asserted in a complaint served on Medtronic, Inc. and Tyrx, Inc. on October 11, 2017. Ex. 1041; Ex. 1042.

IV. THE '603 PATENT

The '603 patent relates to "gel or hydrogel loaded biodegradable fiber[s]." Ex. 1001, Abstract. The fibers have at least two components, as depicted in Figure

3B, for example, which is described as a "bicomponent fiber with a polymer bore (80) surrounded by a gel or hydrogel wall (90)":

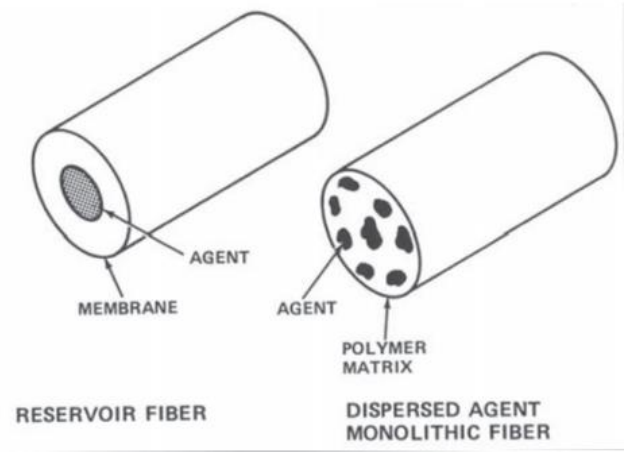


Id., Fig. 3, 4:4–5. The '603 patent describes that its fibers may incorporate various types of known drugs, such as antibiotics or growth factors. *Id.*, 7:57–8:57. The patent admits that gels and hydrogels were known and could be prepared "by a variety of methods well known to those of ordinary skill in the art." *Id.*, 9:9–32; *see also id.*, 25:10–11.

V. PRIOR ART FIBERS FOR DRUG DELIVERY USING GELS AND HYDROGELS WERE WELL KNOWN

Uses of polymeric devices for controlled drug delivery are described as early as 1963. Ex. 1002, ¶ 26 (citing Ex. 1023 at 1135–49). Real-world devices became known by the 1970s, with disclosures relating to polymer-coated pharmaceutical compositions for the controlled release of drugs over a predetermined time period. *See, e.g.*, Ex. 1024, 9–15; Ex. 1002, ¶ 26. By the mid-1970s, fibers formed of polymers—including biodegradable polymers—for the purpose of providing the controlled delivery of drugs were disclosed in the art. Ex. 1002, ¶ 31. For example, U.S. Patent No. 3,991,766 (1976) describes the formation of implantable controlled-

release biodegradable polymer fibers or sutures. Ex. 1033. The technology continued advancing in the 1980s. For example, Dunn discloses polymer fibers incorporating a drug within the lumen of the fiber and fibers with a drug dispersed throughout the polymer matrix:



Ex. 1035, 128. Dunn teaches such fibers can be manufactured through "wet-, dry-, and melt-spinning processes." *Id*. at 127–129.

By at least 1990, the advantages of using polymeric fibers for controlled drug release were well known. Ex. 1002, ¶ 33. "Major advantages of drug-loaded fibers include ease of fabrication, high surface area for drug release, wide range of physical structures possible, and localized delivery of the bioactive agent to the target." Ex. 1028, 12.

It was also well known that gels and hydrogels could be used in controlled drug delivery devices. For example, dating back to at least 1976, it was known that hydrogel polymers could be made into fibers for medical uses. Ex. 1002, ¶ 36. By

the 1990s, it was well known that a variety of hydrogels, including those derived from dextran, alginate, and gelatin, could be used to create drug delivery devices.

Thus, by August 1999, the claimed effective filing date of the '603 patent, the use of polymeric fibers, including those with gels and hydrogels, for controlled drug release had long been known in the art.

VI. IDENTIFICATION OF THE CHALLENGES

Claims 1, 2, 4–6, 11–13, 15–19, 21, 22, 24–26, and 31–33 should be canceled in view of the following prior art: U.S. Patent No. 5,578,046 to Liu *et al*. ("Liu") (Ex. 1005), U.S. Patent No. 5,186,936 to Groves ("Groves") (Ex. 1006), U.S. Patent No. 5,538,735 to Ahn ("Ahn") (Ex. 1007), and U.S. Patent No. 5,364,627 to Song ("Song") (Ex. 1008). All of these references are prior art under pre-AIA § 102. None of these references were considered by the Patent Office during prosecution.

Petitioner presents the following grounds for trial:

- **Ground 1:** Claims 1, 4, 5, 12, 21, 24, 25, and 32 are anticipated under 35 U.S.C. § 102(a), (b), and (e) by Liu;
- **Ground 2:** Claims 2, 6, 11, 13, 22, 26, 31, and 33 are anticipated under 35 U.S.C. § 102(a), (b), and (e), or in the alternative, rendered obvious under 35 U.S.C. § 103(a) by Liu;
- **Ground 3:** Claims 1, 2, 6, 11–13, 21, 22, 26, and 31–33 are anticipated under 35 U.S.C. § 102(a), (b), and (e) by Groves;

- **Ground 4:** Claims 15 and 18 are anticipated under 35 U.S.C. § 102(a), (b), and (e) by Ahn;
- **Ground 5:** Claims 16 and 17 are rendered obvious under 35 U.S.C. § 103(a) by Ahn in view of Liu;
- **Ground 6:** Claim 19 is anticipated under 35 U.S.C. § 102(a), (b), and (e) by Song.

VII. PROSECUTION HISTORY OF THE '603 PATENT

During prosecution, the challenged claims were allowed without any substantive rejection or discussion, other than a double-patenting rejection, which applicant overcame by filing a terminal disclaimer. Ex. 1004, 49, 47, 43.

VIII. CLAIM CONSTRUCTION UNDER 37 C.F.R. §§ 42.100(b), 42.104(b)(3)

Pursuant to 37 C.F.R. § 41.100(b), a claim of an unexpired patent is given its broadest reasonable interpretation in light of the specification. *See Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131 (2016); 37 C.F.R. § 42.100(b). For purposes of this proceeding, Petitioner submits that the following phrases should be construed: "***gel***" and "***hydrogel***" (claims 1, 19, 21) and "***said fiber comprises an emulsion consisting essentially of a gel or hydrogel***" (claim 19).

A. "gel" and "hydrogel" (Claims 1, 19, 21)

Each of claims 1, 19, and 21 recite the terms "gel" or "hydrogel." The '603 patent defines the terms "gel" and "hydrogel" to encompass both formed gels and

precursors (materials which can make gels/hydrogels):

> The terms "gel" or "hydrogel" as used herein is [sic] intended to include the formed gel or hydrogel as well as the appropriate precursor molecules involved in the formation of gels and hydrogels.

Ex. 1001, 9:33–55. Since the applicant defined the term, this definition controls. *See Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1380 (Fed. Cir. 2009) ("When a patentee explicitly defines a claim term in the patent specification, the patentee's definition controls."). Additionally, the independent claims must encompass the dependent claims, which also show that the phrase "gel or hydrogel" include precursors thereof. *See* Ex. 1001, cl. 12 ("wherein said gel or hydrogel is a precursor gel or precursor hydrogel"); *cf. Free Motion Fitness, Inc. v. Cybex Int'l, Inc.*, 423 F.3d 1343, 1351 (Fed. Cir. 2005) ("[D]ependent claims limiting the claim to a single cable confirm that the independent claims may encompass more than one cable."). Thus, the broadest reasonable interpretation of "gel" and "hydrogel" is that it includes both formed gels or hydrogels and gel or hydrogel precursors.

B. "said fiber comprises an emulsion consisting essentially of a gel or hydrogel" (Claim 19)

Claim 19 recites "said fiber comprises an emulsion consisting essentially of a gel or hydrogel." For purposes of this proceeding, based on the intrinsic evidence, the proper construction of this phrase is "said fiber comprises a dispersed component

consisting essentially of a gel or hydrogel (including precursors)."[1]

The intrinsic evidence demonstrates that the patentee described a gel or hydrogel dispersed within a fiber as a "fiber compris[ing] an emulsion" as recited by claim 19. The ordinary meaning of the term "emulsion" is one liquid dispersed in another liquid (*i.e.*, the liquids are immiscible and do not mix, such as an oil-in-water emulsion) (*see* Ex. 1002, ¶ 59 (quoting Ex. 1040)), but the specification does not use the term in that manner. Instead, the specification uses the term "emulsion" to refer to one component (*e.g.*, gel or hydrogel) dispersed in a fiber. Specifically, although the '603 patent refers to ordinary emulsions during the manufacturing process, its sole description of emulsions in formed fibers pertains to Figures 1B–1D, 2B–2D, 3C–3D, 4A–4D, 5A–5D, 6A–6D, and 11. Ex. 1001, 3:44–5:2.[2] For example, Figure 3D is described as a "bicomponent fiber with a polymer bore (80) ***comprising a gel***

[1] Petitioner has not performed an analysis under *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (*en banc*) in this Petition and has only provided the broadest reasonable interpretation of the claim language.

[2] The only other references to a fiber comprising an "emulsion" in the specification are two instances where the specification quotes the claim language, "said fiber comprises an emulsion consisting essentially of a gel or hydrogel" without further elaboration. Ex. 1001, 3:18–22, 5:17–21; *compare id.*, cl. 19.

or hydrogel emulsion (40) that is surrounded by a gel or hydrogel wall (90)":

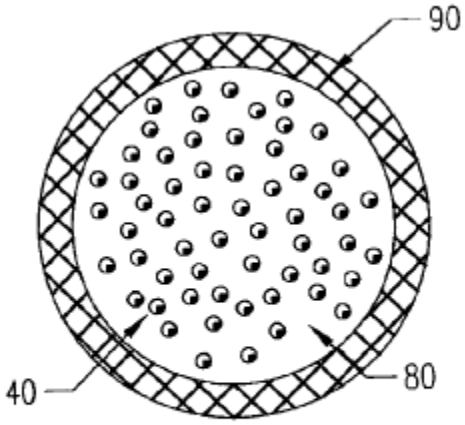


FIG. 3D

Id., 4:9–11. The description of the other figures is similar. In each of these figures, the patent identifies an "emulsion" as a component dispersed within the fiber. Ex. 1001, 3:44–5:2. The dispersed component may be water, gel, or hydrogel, depending on the figure. *Id.*

The additional claim language "consisting essentially of" means "the invention necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention." *PPG Indus. v. Guardian Indus. Corp.*, 156 F.3d 1351, 1354 (Fed. Cir. 1998). And, as discussed above, the '603 patent expressly defines gels and hydrogels to include gel and hydrogel precursors, respectively. *Supra* § VIII.A. Thus, the broadest reasonable interpretation of "fiber comprises an emulsion consisting essentially of a gel or hydrogel" encompasses fibers with dispersed gels

or hydrogels (including precursors). Ex. 1002, ¶¶ 57–66.

Petitioner's proposed construction is consistent with Patent Owner's position in pending litigation. There, Patent Owner proposed to construe the phrase "an emulsion consisting essentially of a gel or hydrogel" as "an emulsion consisting essentially of a dispersed gel or hydrogel phase." Ex. 1036 at 17. That construction requires a gel or hydrogel "dispersed" within the fiber. To support its construction, Patent Owner's expert contended that claim 19 of the '603 patent requires "a dispersed gel or hydrogel phase." Ex. 1009, ¶ 47. Patent Owner's expert also noted the same descriptions of Figures 1B–1D, 2B–2D, 3C–3D, 4A–4D, 5A–5D, and 6A–6D discussed above as supporting this construction. *Id.*, ¶ 50.

Therefore, the Board should construe the term "said fiber comprises an emulsion consisting essentially of a gel or hydrogel" of claim 19 to have a broadest reasonable interpretation of "said fiber comprises a dispersed component consisting essentially of a gel or hydrogel (including precursors)."

IX. DETAILED EXPLANATION UNDER 37 C.F.R. § 42.104(b)

A. The Grounds for Trial Are Based on Prior Art Patents Not Considered by the Patent Office

The '603 patent claims priority to U.S. Provisional Patent Application No. 60/147,827, filed August 6, 1999. For purposes of this IPR, the Board need not evaluate whether the '603 patent is entitled to claim priority to that date, as all of Petitioner's prior art qualifies as prior art even under this earliest possible effective

filing date. None of Petitioner's art was considered by the Patent Office during prosecution of the '603 patent. *Compare* Ex. 1001, cover & page 2 (listing prior art considered) *with* § VI, *supra* (identifying different prior art).

1. *Liu is a Prior Art Patent*

Liu qualifies as prior art under 35 U.S.C. § 102(a), (b), and (e) because it issued as a U.S. patent on November 26, 1996, more than one year before the claimed effective filing date of the '603 patent. Ex. 1005, cover.

2. *Groves is a Prior Art Patent*

Groves qualifies as prior art under 35 U.S.C. § 102(a), (b), and (e) because it issued as a U.S. patent on February 16, 1993, more than one year before the claimed effective filing date of the '603 patent. Ex. 1006, cover.

3. *Ahn is a Prior Art Patent*

Ahn qualifies as prior art under 35 U.S.C. § 102(a), (b), and (e) because it issued as a U.S. patent on July 23, 1996, more than one year before the claimed effective filing date of the '603 patent. Ex. 1007, cover.

4. *Song is a Prior Art Patent*

Song qualifies as prior art under 35 U.S.C. § 102(a), (b), and (e) because it issued as a U.S. patent on November 15, 1994, more than one year before the claimed effective filing date of the '603 patent. Ex. 1008, cover.

B. Level of Ordinary Skill in the Art

By the claimed effective filing date of the '603 patent, a person of ordinary

skill in the art ("POSA") would have a master's or doctorate degree in one or more of the following: basic chemistry, polymer and materials science, pharmaceutics, and biomedical engineering; or would have a bachelor's degree and at least five years' experience in research and development in one or more of the following: basic chemistry, polymer and materials science, pharmaceutics, and biomedical engineering. Ex. 1002, ¶ 13.

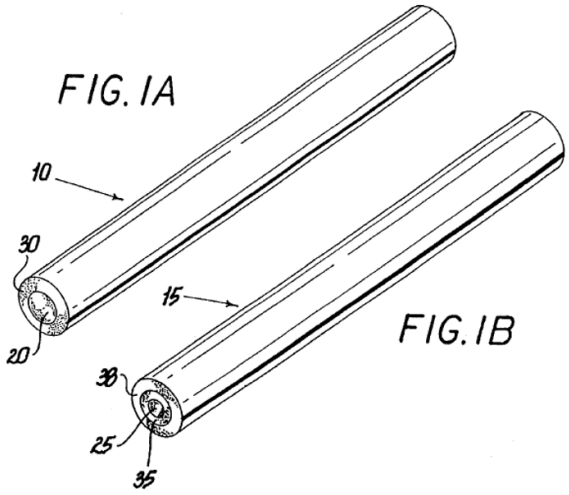
In a pending litigation, Patent Owner's expert has proposed a level of skill that is similar (Ex. 1009, ¶ 11), and the prior art described below would also invalidate under this proposed level of skill. Ex. 1002, ¶ 17.

C. Ground 1: Claims 1, 4, 5, 12, 21, 24, 25, and 32 are Anticipated by Liu

Petitioner requests cancellation of claims 1, 4, 5, 12, 21, 24, 25, and 32 because they are anticipated by Liu.

1. *Overview of Liu*

Liu describes "composite materials having a core portion formed from a first bioabsorbable material and at least one shell portion of a second bioabsorbable material joined to the core portion." Ex. 1005, Abstract. These composite materials can be formed into fibers as shown in Figures 1A and 1B:



Liu further explains that the fibers can be used in different types of implants including "sutures, soft tissue patches, surgical mesh, wound dressings, surgical felts, vascular grafts, nerve repair devices, artificial skin and sternum tape." *Id.*, 4:63–67. Liu teaches that the bioabsorbable materials be "coat[ed] or impregnate[ed] . . . with one or more . . . surgically useful substances" such as "broad spectrum antibiotics" or "human growth factors" for "wound repair and/or tissue growth." *Id.*, 6:66–7:50.

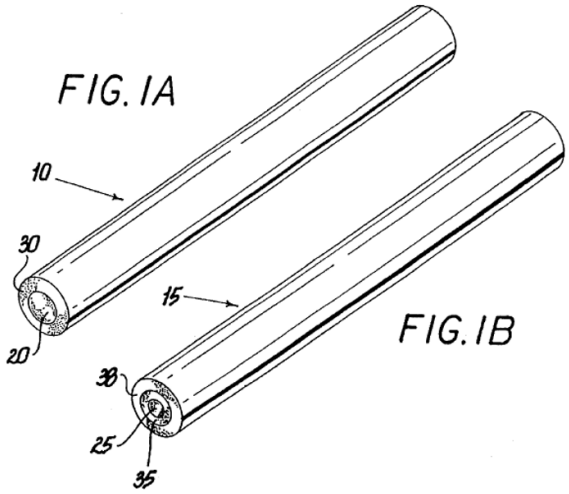
Liu teaches that the core and shell materials can be made of numerous different bioabsorbable materials, including "absorbable polymers made from glycolide, glycolic acid, lactide, lactic acid, caprolactone . . . and/or copolymers" as well as other materials with different "strength and bioabsorption characteristics," such as "collagen, chitin, chitin derivatives (e.g., chitosan), amino acid polymers (e.g., gelatin), and polysaccharides (e.g., dextran)." *Id.*, 3:32–37, 4:40–49. These are some of the same polymers and gel/hydrogel materials described in the '603

patent. Ex. 1001, 15:56–61 (referencing "poly(L-lactic acid), poly(DL-lactic acid), polycaprolactone, poly(glycolic acid)" and "co-polymers"), 17:36–67 (referencing "chitin," "collagen (and gelatin)," "chitosan," and "dextran" as "materials which can form hydrogels").

2. *Claim 1*

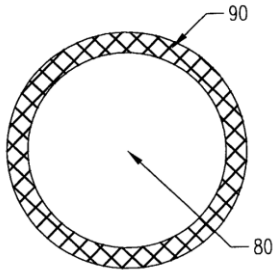
a. <u>"A drug delivery composition comprising at least one fiber having a bore and a wall"</u>

Liu discloses a drug delivery composition that includes "at least one fiber having a bore and a wall." Ex. 1002, ¶¶ 111–13. Liu describes "composite materials having a core portion formed from a first bioabsorbable material and at least one shell portion of a second bioabsorbable material joined to the core portion" that may be formed into a fiber as depicted in Figures 1A and 1B:



Ex. 1005, Abstract & Figs. 1A–1B. The "core" of Liu's fiber (*e.g.*, item 20 in Fig. 1A) is the bore and the "shell portion" (*e.g.*, item 30 in Fig. 1A) is the wall, as recited

in the claim. Ex. 1002, ¶ 112. Indeed, this figure is similar to the structure described in the '603 patent, for example, Figure 3B which is described as a "bicomponent fiber with a polymer bore (80) surrounded by a gel or hydrogel wall (90)":

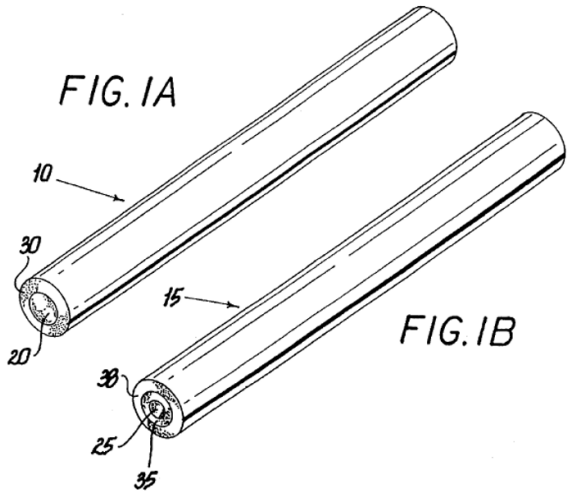


Ex. 1001, Fig. 3, 4:4–5.

Liu explains that its fibers can be used in different types of implants, including drug delivery devices, such as "sutures, soft tissue patches, surgical mesh, wound dressings, surgical felts, vascular grafts, nerve repair devices, artificial skin and sternum tape." Ex. 1005, 4:63–67. Liu teaches that the bioabsorbable materials be "coat[ed] or impregnate[ed] . . . with one or more . . . surgically useful substances" such as "broad spectrum antibiotics" or "human growth factors" for "wound repair and/or tissue growth." *Id.*, 6:66–7:50. Liu teaches that this allows the device to "aid in combating clinical and sub-clinical infections in a surgical or trauma wound side." *Id.*, 7:6–11. These substances are the same types disclosed in the '603 patent. *See* Ex. 1001, 7:57–8:57 (noting both "antibiotic[s]" and various "growth factor[s]").

b. <u>"wherein said fiber comprises a first component and a second component, and"</u>

Liu discloses a fiber that comprises a first and second component. Ex. 1002, ¶¶ 114–15. As noted above, Liu's fiber has a "core" formed from a "first bioabsorbable material" and a "shell" formed from "a second bioabsorbable material" that may be formed into a fiber as depicted in Figures 1A and 1B:



Ex. 1005, Abstract & Figs. 1A–1B. The "core" and "shell" in Liu's fibers are two components, which Liu teaches are made of different materials that have different rates of bioabsorption. Ex. 1005, 4:40–46 ("those of skill may select any two bioabsorbable materials having different rates of bioabsorption"); Ex. 1002, ¶ 115.

c. <u>"wherein said first component is a biodegradable polymer and"</u>

Liu discloses that the first component is a biodegradable polymer. Ex. 1002, ¶ 116. Liu teaches that its fiber is comprised of "any two bioabsorbable materials having different rates of bioabsorption." Ex. 1005, 4:39–49. Liu teaches that one

of the materials may be "absorbable polymers made from glycolide, glycolic acid, lactide, lactic acid, caprolactone," including "[c]opolymers" and "blends." Ex. 1005, 3:22–41 (describing use of such materials in either the core or shell of the fiber). Liu's "absorbable" polymers are biodegradable polymers; indeed, they are some of the very same polymers mentioned in the '603 patent. Ex. 1002, ¶ 116 (citing Ex. 1001, 15:56–16:29 (identifying "single polymer, co-polymer or a blend of polymers of poly(L-lactic acid), poly(DL-lactic acid), polycaprolactone, poly(glycolic acid)").

d. "said second component is selected from the group consisting of a gel and a hydrogel."

Liu discloses that the second component is a gel or hydrogel. Ex. 1002, ¶¶ 117–19. Liu explains that gel and hydrogel materials may be used for either the core or shell portion of Liu's fiber:

> Although the above descriptions of preferred embodiments focus on bioabsorbable polymers, it is understood that ***those of skill may select any two bioabsorbable materials having different rates of bioabsorption*** to construct a bioabsorbable composite having the desired strength and bioabsorption characteristics needed for a particular medical or surgical application. ***Such bioabsorbable materials include***, but are not limited to, ***collagen***, ***chitin***, chitin derivatives (e.g.,

chitosan), amino acid polymers (e.g., ***gelatin***), and polysaccharides (e.g., ***dextran***).

Ex. 1005, 4:39–49 (emphasis added). The '603 patent admits that "chitin" is a "gel material[]" and that "collagen," "chitin," "chitosan," "gelatin," and "dextran" are "materials which can form hydrogels." Ex. 1001, 17:28–67. This is consistent with the understanding of a person of ordinary skill in the art. *See* Ex. 1002, ¶ 118. Therefore, Liu discloses both gels and hydrogels for use in one or more components of the fiber as encompassed by the claims of the '603 patent. Ex. 1002, ¶ 119; *supra* § VIII.A.

3. *Claim 4*

a. "The composition of claim 1 further comprising at least one additional fiber,"

Liu discloses the composition of claim 1. *Supra* § IX.C.2. Liu discloses claim 4 in two separate ways. Ex. 1002, ¶¶ 121–23.

First, Liu discloses a filament with two or more shells surrounding the core, as shown in Figure 1B:

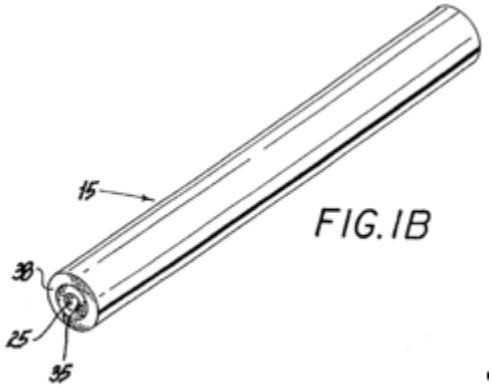
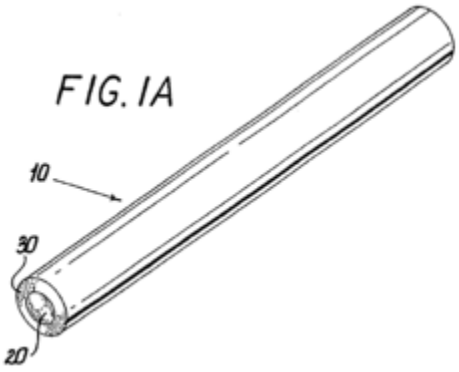


FIG. 1B

As discussed above with respect to claim 1, Liu's inner core (25) and the shell (35) surrounding it satisfy the limitations of claim 1. *Supra* § IX.C.2. In the embodiment of Fig. 1B, there is an additional shell (38) which surrounds the inner shell (35), thus satisfying the requirement that there be at least one additional fiber. Ex. 1002, ¶ 122.

Liu also discloses this claim limitation in a second way. Liu explains that there are drug delivery devices which can be fabricated using multiples of Liu's filaments woven or joined together, where each of the filaments would have a core (20) and shell (30) as depicted in Figure 1A:

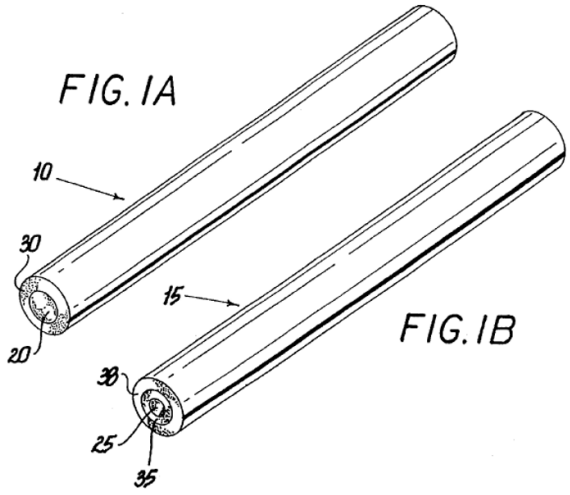


For example, Liu teaches that multiple filaments can be combined into "multifilament sutures" (Ex. 1005, 6:48–58) or used to form "biocompatible implants such as . . . surgical mesh" (*id.*, 4:53–67). A person of ordinary skill would understand that these structures involve the use of multiple of Liu's filaments (each of which has a core and at least one shell, as in Figure A). Ex. 1002, ¶ 123. For example, a multifilament suture would require multiple fibers braided together and a surgical mesh would require multiple fibers woven in a mesh pattern. *Id*. Thus,

Liu discloses the limitation of an additional fiber when an additional filament is used to create a device such as a multifilament suture or surgical mesh.

b. "wherein said additional fiber circumscribes an adjacent inner fiber."

As discussed above, Liu discloses an additional fiber in at least two different ways: either as an additional shell (38) surrounding the inner shell, as in Figure 1B, or as a device formed of multiple filaments, each of which has a core and shell, as shown in Figure 1A:



See also Ex. 1005 at 2:26–44 (describing coatings in Figs. 1A–1B). Liu explains that "[i]n particularly useful embodiments, the core portion and shell portion are substantially co-extensive," and specifically contrasts this with composites where "the shell portion only partially covers the core portion." Ex. 1005, 3:15–19. Thus, in both embodiments, the outermost shell completely surrounds (or circumscribes)

the interior (either just an inner core in Fig. 1A, or an inner core and inner shell in Fig. 1B). Ex. 1002, ¶¶ 124–27.[3]

Liu also discloses a die for extruding a filament according to Figure 1A, such that the core is extruded through exit 72 and the surrounding shell is extruded through exit 82:

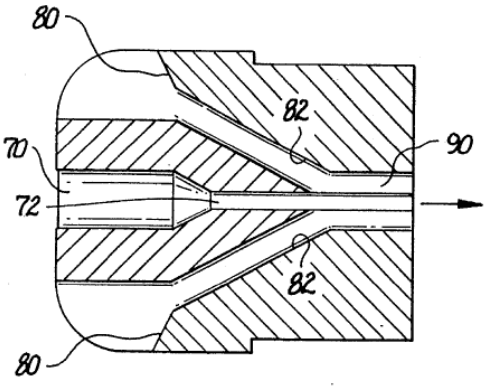


FIG. 3

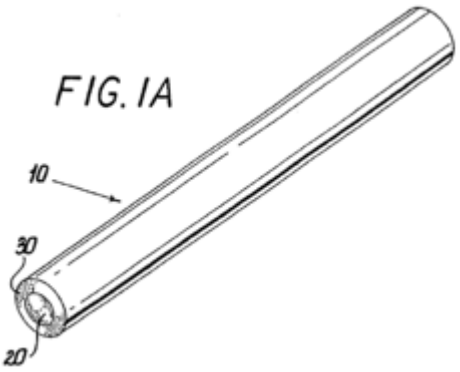


FIG. 1A

Ex. 1005, 5:12–22. Liu explains that these "***concentric*** polymer melts are joined at die exit 90" forming the filament depicted in Figure 1A. *Id.* The fact that these exits are "concentric" as depicted in Figure 3 further confirms that the outermost shell

[3] According to the '603 patent, "[i]n certain embodiments of the invention, a layer of a fiber circumscribes a layer of an adjacent inner fiber. The inner fiber is approximately centered within the outer fiber." *See, e.g.*, Ex. 1001, 6:15–16. This is the only use of the word "circumscribes" in the specification.

completely surrounds (or circumscribes) the interior of the filament. Ex. 1002, ¶¶ 125–26.

4. *Claim 5: "The composition of claim 4 wherein said adjacent inner fiber is approximately centered within the outer fiber."*

Liu discloses the composition of claim 4 in two separate ways: a second shell surrounding an inner shell and core (as in Fig. 1B) or as multiple filaments each of which has a shell and core (as in Fig. 1A). *Supra* § IX.C.3. As discussed above, in each of those embodiments, Liu depicts that a shell is extruded along with the core from a die with "concentric" exits, as in Figure 3, to create a fiber as in Figure 1A:

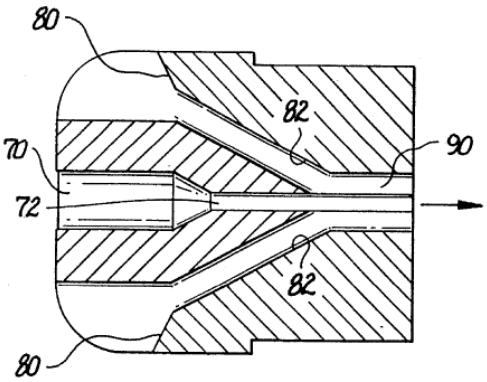


FIG. 3

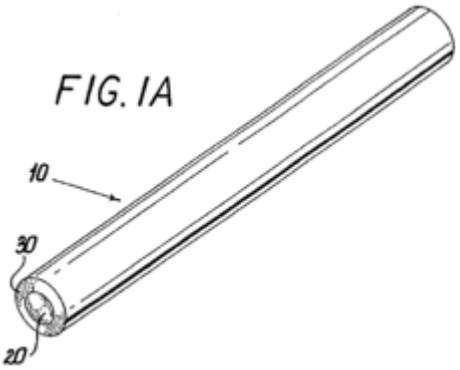


FIG. 1A

Ex. 1005, 5:12–22. Liu expressly states that these exits are "concentric," confirming that the interior is center within the outermost shell. *Id.*; Ex. 1002, ¶¶ 128–31.

5. *Claim 12: "The composition of claim 1, wherein said gel or hydrogel is a precursor gel or precursor hydrogel."*

Liu discloses the composition of claim 1. *Supra* § IX.C.2. Liu discloses that the second component may be "collagen," "chitin," "chitosan," "gelatin," or "dextran." Ex. 1005, 4:39–49. The '603 patent admits that these are gel/hydrogel precursors by admitting that "collagen," "chitin," "chitosan," "gelatin," and "dextran" are "materials which can form hydrogels." Ex. 1001, 17:28–67; Ex. 1002, Ex. ¶¶ 132–33.

6. *Claim 21*

a. "A scaffold composition comprising one or more fibers,"

Liu discloses one or more fibers for the reasons explained above with respect to substantially similar limitation 1[a]. *Supra* § IX.C.2.a. Liu additionally discloses a "scaffold composition" made up of these fibers. Ex. 1002, ¶ 135. For example, Liu teaches that multiple filaments (*i.e.*, multiple fibers) can be combined into various medical devices such as "multifilament sutures" or be "woven" together. Ex. 1005, 6:48–58. Liu also explains that its fibers may be used to form "biocompatible implants such as . . . ***surgical mesh***." *Id.*, 4:53–67 (emphasis added). The '603 patent admits that "woven" fibers and a "non-woven mesh" are examples of scaffolds. Ex. 1001, 6:41–45. Additionally, the parent of the '603 patent, U.S. Patent No. 6,596,296, identifies a mesh as an example of a "complex three-dimensional woven scaffolding with patterning":

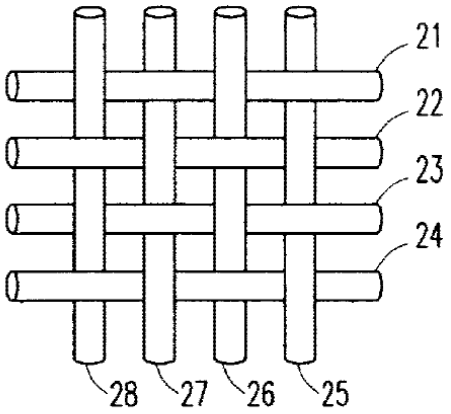


FIG. 1

Ex. 1043, 6:63–67.

b. "wherein said fibers comprise a first component and a second component and"

Liu discloses a fiber comprised of a first and second component for the reasons explained above with respect to substantially similar limitation 1[b]. *Supra* § IX.C.2.b; Ex. 1002, ¶ 136.

c. "wherein said first component is a biodegradable polymer and"

Liu discloses the first component is a biodegradable polymer for the reasons explained above with respect to substantially similar limitation 1[c]. *Supra* § IX.C.2.c; Ex. 1002, ¶ 137.

d. "said second component is selected from the group consisting of a gel and a hydrogel."

Liu discloses the second component is gel or hydrogel for the reasons explained above with respect to substantially similar limitation 1[d]. *Supra* § IX.C.2.d; Ex. 1002, ¶ 138-39.

7. *Claim 24*

a. "The composition of claim 21 further comprising at least one additional fiber,"

Liu discloses the composition of claim 21. *Supra* § IX.C.6. Liu also discloses at least one additional fiber for the reasons explained above with respect to substantially similar limitation 4[a]. *Supra* § IX.C.3.a; Ex. 1002, ¶ 141.

b. "wherein said additional fiber circumscribes an adjacent inner fiber."

Liu discloses that the additional fiber circumscribes an adjacent inner fiber for the reasons explained above with respect to substantially similar limitation 4[b]. *Supra* § IX.C.3.b; Ex. 1002, ¶¶ 142–43.

8. *Claim 25: "The composition of claim 24 wherein said adjacent inner fiber is approximately centered within the outer fiber."*

Liu discloses the composition of claim 24. *Supra* § IX.C.7. Liu also discloses that the adjacent inner fiber is approximately centered within the outer fiber for the reasons explained above with respect to substantially similar claim 5. *Supra* § IX.C.4; Ex. 1002, ¶¶ 144–45.

9. *Claim 32: "The composition of claim 21, wherein said gel or hydrogel is a precursor gel or precursor hydrogel."*

Liu discloses the composition of claim 21. *Supra* § IX.C.6. Liu also discloses that the gel or hydrogel is a precursor gel or precursor hydrogel for the reasons explained above with respect to substantially similar claim 12. *Supra* § IX.C.5; Ex. 1002, ¶ 146.

D. Ground 2: Claims 2, 6, 11, 13, 22, 26, 31, and 33 are Anticipated, or in the Alternative, Rendered Obvious by Liu

Petitioner requests cancellation of claims 2, 6, 11, 13, 22, 26, 31, and 33 because they are anticipated, or in the alternative, rendered obvious by Liu.

1. *Claim 2*

a. "The composition of claim 1 wherein said first component is present in the fiber bore and"

Liu discloses the composition of claim 1. *Supra* § IX.C.2. Liu further describes that the core of the fiber (the bore) is made of a biodegradable polymer (the first component):

> ***Bioabsorbable materials*** used to form the core portions of these composites ***include***, but are not limited to ***absorbable polymers made from glycolide, glycolic acid, lactide, lactic acid, caprolactone***, dioxanone, trimethylene carbonate and dimethyl trimethylene carbonate. ***Copolymers*** (block or random) and mixtures ***and blends*** of such polymers or copolymers are also useful.

Ex. 1005, 3:22–29 (emphasis added); Ex. 1002, ¶ 151. As noted above, Liu's "bioabsorbable" polymers are biodegradable polymers and some of the same polymers mentioned in the '603 patent. *Supra* § IX.C.2.c; *see also* Ex. 1002, ¶ 116.

b. "said second component is present in the fiber wall."

Liu describes that the shell of the fiber (the wall) is made of a gel or hydrogel (the second component). Ex. 1002, ¶¶ 152–55. Liu teaches that gel and hydrogel materials may be used for either the core or shell portion of Liu's fiber:

> Although the above descriptions of preferred embodiments focus on bioabsorbable polymers, it is understood that ***those of skill may select any two bioabsorbable materials having different rates of bioabsorption*** to construct a bioabsorbable composite having the desired strength and bioabsorption characteristics needed for a particular medical or surgical application. ***Such bioabsorbable materials include***, but are not limited to, ***collagen***, ***chitin***, chitin derivatives (e.g., ***chitosan***), amino acid polymers (e.g., ***gelatin***), and polysaccharides (e.g., ***dextran***).

Ex. 1005, 4:39–49 (emphasis added). As noted above, a person of ordinary skill would have understood, and the '603 patent admits, that "collagen," "chitin," "chitosan," "gelatin," and "dextran" are gels and/or hydrogels (including precursors). *Supra* § IX.C.2.d.

To the extent that Patent Owner argues that Liu does not anticipate claim 2 because it does not disclose a specific example fiber with a gel or hydrogel (or precursor) used as a wall, that argument is unavailing. Liu expressly teaches using "any two bioabsorbable materials having different rates of bioabsorption" for the core and shell. Ex. 1005, 4:39–49. One of ordinary skill would have been motivated to use these gel/hydrogel precursors based on Liu's express suggestion. Ex. 1002, ¶ 153. Additionally, Liu's disclosure would cause one of ordinary skill in the art to create a fiber using a gel/hydrogel in the wall. Specifically, Liu teaches that embodiments with a "higher rate of bioabsorption for the shell may, in some applications, serve to enhance tissue ingrowth and subsequent healing and wound closures." Ex. 1005, 4:12–15. Liu further teaches that "it is known that amorphous polymers have higher rates of hydrolysis than crystalline versions of the same polymer." *Id.*, 4:29–34, *see also id.*, 3:43–59 (correlating higher rate of bioabsorption to higher rate of hydrolysis for the materials disclosed in Liu). Thus, one of ordinary skill would have been motivated to consider using an amorphous polymer (*e.g.*, as mentioned above, "***collagen***, ***chitin***, chitin derivatives (e.g., ***chitosan***), amino acid polymers (e.g., ***gelatin***), and polysaccharides (e.g., ***dextran***)") as the shell of Liu's fiber. Ex. 1002, ¶ 154. Thus, Liu at least renders this claim obvious based on the explicit suggestions within Liu to consider gel/hydrogel materials and to consider "amorphous" polymers for use in the shell.

2. *Claim 6: "The composition of claim 1, wherein a therapeutic agent is loaded into the gel or hydrogel."*

Liu discloses the composition of claim 1. *Supra* § IX.C.2. Liu further discloses a therapeutic agent loaded into the gel or hydrogel. Ex. 1002, ¶¶ 156–59. Liu teaches that the bioabsorbable materials of its fibers be "coat[ed] or impregnate[ed] . . . with one or more . . . surgically useful substances" such as "broad spectrum antibiotics" or "human growth factors" for "wound repair and/or tissue growth." *Id.*, 6:66–7:50. Liu explains that this allows the device to "aid in combating clinical and sub-clinical infections in a surgical or trauma wound site." *Id.*, 7:6–11. These substances are the same types disclosed in the '603 patent. *See* Ex. 1001, 7:57–8:57 (noting both "antibiotic[s]" and various "growth factor[s]").

To the extent Patent Owner argues that Liu does not anticipate a drug being loaded into a gel or hydrogel, Liu would have rendered this limitation obvious. Liu teaches that the use of such therapeutic agents is particularly useful where the shell has a higher rate of bioabsorption:

> ***When incorporating wound healing substances*** such as those discussed above, ***it may be advantageous to use*** composite materials having ***at least one shell layer*** are ***formed from a bioabsorbable material having a relatively high rate of bioabsorption***. By incorporating wound healing substances in a high rate bioabsorption layer, ***the substance will be more quickly absorbed while the remaining composite material will still retain sufficiently***

good mechanical properties to perform its medicaid or surgical function.

Ex. 1005, 7:42–50 (emphasis added). As described above, one of ordinary skill would be motivated to use an amorphous gel/hydrogel for the shell because, *e.g.*, it has a higher rate of bioabsorption and therefore may "serve to enhance tissue ingrowth and subsequent healing and wound closures." *Id.*, 4:12–15; *supra* § IX.D.1. Based on these teachings, one of ordinary skill would be motivated to incorporate a drug into the amorphous gel layer of Liu's fiber so that it would "be more quickly absorbed" and therefore provide quicker healing to a patient. Ex. 1002, ¶ 157. Thus, Liu renders obvious that a therapeutic agent would be loaded into its gel/hydrogel layer.

3. *Claim 11: "The composition of claim 6, wherein the therapeutic agent is selected from the group consisting of . . . antibiotics, . . . [and] growth factors . . ."*

Liu anticipates, or in the alternative, renders obvious the composition of claim 6. *Supra* § IX.D.2. Liu further discloses that the therapeutic agent may be "broad spectrum antibiotics" or "human growth factors." *Id.*, 6:66–7:50; Ex. 1002, ¶ 160–62.

4. *Claim 13: "The composition of claim 1, wherein said biodegradable polymer fiber comprises a hydrophobic drug."*

Liu discloses the composition of claim 1. *Supra* § IX.C.2. Liu discloses that the bioabsorbable polymer (the first component of claim 1) comprises a hydrophobic

drug. Ex. 1002, ¶¶ 163–66. Liu discloses that the bioabsorbable materials in its fiber may be "impregnate[ed] . . . with one or more . . . surgically useful substances" such as "broad spectrum antibiotics," including "erythromycin." Ex. 1005, 6:66–7:50. Erythromycin is a known hydrophobic drug. Ex. 1002, ¶ 163 (citing Ex. 1037 and Ex. 1038, which discuss "erythromycin" as a "hydrophobic antibiotic"). Thus, Liu discloses the use of hydrophobic drugs.

To the extent Patent Owner argues that Liu fails to anticipate the use of a hydrophobic drug, using such a drug would have been obvious to one of ordinary skill. One of ordinary skill would have understood that choosing a hydrophobic or hydrophilic drug was a simple choice that would affect the release profile for the drug and the bioabsorption profile of the device. Ex. 1002, ¶ 164. Liu acknowledges the importance of controlling the rate of bioabsorption of its fibers. Ex. 1005, 4:39–46 ("***those of skill may select any two bioabsorbable materials having different rates of bioabsorption to construct*** a bioabsorbable composite having ***the desired*** strength and ***bioabsorption characteristics***" (emphasis added)). A hydrophilic drug would absorb water from the body into the polymer, accelerating the degradation of the polymer and the release of the drug into the body. Ex. 1002, ¶ 165. A hydrophobic drug would not absorb water, and therefore the polymer would degrade more slowly and the drug would be released more slowly. *Id.* Thus, to achieve a more gradual drug release, which would be desirable for longer term implants (such

as the surgical mesh, vascular grafts, and nerve repair devices mentioned in Liu, Ex. 1007, 4:60–67), one of ordinary skill would have found it obvious to choose a hydrophobic drug. Ex. 1002, ¶ 165.

5. *Claim 22*

a. "The composition of claim 21 wherein said first component is present in the fiber bore and"

Liu discloses the composition of claim 21. *Supra* § IX.C.6. Liu also discloses that the fiber has a bore (*supra* § IX.C.2.a) and that the first component is present in the bore, for the reasons explained above with respect to substantially similar limitation 2[a]. *Supra* § IX.D.1.a; Ex. 1002, ¶ 167.

b. "said second component is present in the fiber wall."

Liu discloses, or alternatively renders obvious, that the fiber has a wall (*supra* § IX.C.2.a) and that the second component is present in the wall, for the reasons explained above with respect to substantially similar limitation 2[b]. *Supra* § IX.D.1.b; Ex. 1002, ¶¶ 169–70.

6. *Claim 26: "The composition of claim 21, wherein therapeutic agent is loaded into the gel or hydrogel."*

Liu discloses the composition of claim 21. *Supra* § IX.C.6. Additionally, Liu anticipates, or alternatively renders obvious, that a therapeutic agent is loaded into the gel or hydrogel, for the reasons explained above with respect to substantially similar claim 6. *Supra* § IX.D.2; Ex. 1002, ¶¶ 171–72.

7. *Claim 31: "The composition of claim 26, wherein the therapeutic agent is selected from the group consisting of . . . antibiotics, . . . [and] growth factors"*

Liu discloses the composition of claim 26. *Supra* § IX.D.6. Liu anticipates, or alternatively renders obvious, that the therapeutic agent is an antibiotic or growth factor, for the reasons explained above with respect to substantially similar claim 11. *Supra* § IX.D.3; Ex. 1002, ¶¶ 173–74.

8. *Claim 33: "The composition of claim 21, wherein said biodegradable polymer fiber comprises a hydrophobic drug."*

Liu discloses the composition of claim 21. *Supra* § IX.C.6. Additionally, Liu anticipates, or alternatively renders obvious, that the bioabsorbable polymer (the first component of claim 21) comprises a hydrophobic drug, for the reasons explained above with respect to substantially similar claim 13. *Supra* § IX.D.4; Ex. 1002, ¶ 175.

E. Ground 3: Claims 1, 2, 6, 11–13, 21, 22, 26, and 31–33 are Anticipated by Groves

Petitioner requests cancellation of claims 1, 2, 6, 11–13, 21, 22, 26, and 31–33 because they are anticipated by Groves.

1. *Overview of Groves*

Groves describes a "packing material for the treatment of infections, particularly of the teeth and gums." Ex. 1006, Abstract. Groves explains that this material is made of a "biocompatible, polymeric carrier" with an antibiotic "dispersed therein." *Id.* The material is preferably a fiber, and may have an "inner

core" and an "outer coating." *Id.*, 3:53–4:4. The patent identifies different biocompatible polymers for use in the fiber, including "calcium or magnesium alginate . . . or other hydrogels such as pectin, chitosan, or chitin." *Id.*, 3:5–9.

2. *Claim 1*

a. "A drug delivery composition comprising at least one fiber having a bore and a wall"

Groves discloses a drug delivery composition that includes "at least one fiber having a bore and a wall." Ex. 1002, ¶ 180. Groves describes a "packing material for the treatment of infections" which includes a "biocompatible, polymeric carrier" with an antibiotic "dispersed therein." Ex. 1006, Abstract. Groves teaches that it is "desirable to provide a controlled release vehicle for antibiotics in a packing." *Id.*, 1:30–51. Groves explains that its polymer "may be of any desired shape, preferably being of string or fibrous form" and may have an "inner core" and an "outer coating." *Id.*, 3:54–4:4. The core of Groves' fiber is the bore and the outer coating is the wall, as recited in the claim.

b. "wherein said fiber comprises a first component and a second component, and"

Groves discloses that the fiber comprises a first and second component. Ex. 1002, ¶ 181–82. Groves teaches that the fiber's inner core and outer coating are made of two different components. For example, Groves discloses that the "inner core may comprise an alginate salt such as calcium or magnesium alginate, while the outer coating comprises a material such as pectin, chitosan, or chitin." Ex. 1006,

4:9–12. As another example, Groves discloses that the inner core may contain "as a polymeric carrier a hydrogel which defines ionic polymer units of one charge" and the outer coating may contain "a hydrogel which defines ionic polymer units of the opposite charge to that of the hydrogel of the inner core." *Id.*, 3:53–4:4.

c. "wherein said first component is a biodegradable polymer and"

Groves discloses that the first component is a biodegradable polymer. Ex. 1002, ¶ 183. For example, Groves discloses that the "biocompatible polymers used herein may be any of a wide variety" including "calcium or magnesium alginate" or "other hydrogels such as pectin, chitosan, or chitin." Ex. 1006, 3:5–9. The '603 patent admits that "alginates," "pectin," "chitosan," and "chitin" are polymers. Ex. 1001, 17:36–67 (identifying these substances as examples of "[s]uitable polysaccharides and polymers"); *see also id.*, 16:1–29 (identifying "chitin" as a "biodegradable polymer[]"). Additionally, a person of ordinary skill would have known that calcium and magnesium alginate, pectin, and chitosan are known biodegradable polymers. Ex. 1002, ¶ 183.

d. "said second component is selected from the group consisting of a gel and a hydrogel."

Groves discloses that the second component is a gel or hydrogel. Ex. 1002, ¶¶ 184–85. For example, Groves discloses that the "biocompatible polymers used herein may be any of a wide variety" including "calcium or magnesium alginate" or

"other hydrogels such as pectin, chitosan, or chitin." Ex. 1006, 3:5–9. The '603 patent admits that "chitin" is a "gel material[]" and that "alginates," "chitin," "chitosan," and "pectin" are "materials which can form hydrogels" and are therefore hydrogel precursors. Ex. 1001, 17:28–67; Ex. 1002, ¶ 184. Thus, Groves discloses that its shell can be made of hydrogels and/or materials which can form gels/hydrogels (*i.e.*, precursors), thus falling within the scope of claim 1. Ex. 1002, ¶¶ 184–85; *supra* § VIII.A (construction of "gel" and "hydrogel" to include precursors to gels and hydrogels based on definition in '603 patent specification).

3. *Claim 2*

a. <u>"The composition of claim 1 wherein said first component is present in the fiber bore and"</u>

Groves discloses the composition of claim 1. *Supra* § IX.E.2. Groves further describes that the inner core is made of a biodegradable polymer (the first component):

> For example, ***the inner core may comprise an alginate salt such as calcium or magnesium alginate***, while the outer coating comprises a material such as pectin, chitosan, or chitin.

Ex. 1006, 4:9–12 (emphasis added); Ex. 1002, ¶ 187. As noted above, alginates are example polymers discussed in the '603 patent. *Supra* § IX.E.2.c.

b. "said second component is present in the fiber wall."

Groves describes that the outer coating of the fiber (the wall) is made of a gel or hydrogel (the second component):

> For example, the inner core may comprise an alginate salt such as calcium or magnesium alginate, while ***the outer coating comprises a material such as pectin, chitosan, or chitin***.

Ex. 1006, 4:9–12 (emphasis added); Ex. 1002, ¶ 188. As noted above, pectin, chitosan, and chitin are each examples of gels or hydrogels discussed in the '603 patent. *Supra* § IX.E.2.d.

4. *Claim 6: "The composition of claim 1, wherein a therapeutic agent is loaded into the gel or hydrogel."*

Groves discloses the composition of claim 1. *Supra* § IX.E.2. Groves further discloses a therapeutic agent loaded into the gel or hydrogel. Ex. 1002, ¶¶ 190–91. The inner core of Groves' fiber may contain "as a polymeric carrier a hydrogel" which includes an "antibiotic ester . . . substantially carried in the inner core." Ex. 1006, 3:53–4:4. As discussed above, "calcium or magnesium alginate" is disclosed as an exemplary "inner core" in Groves (*id.*, 4:9–12) and is also admitted as a material which may form a hydrogel in the '603 patent (Ex. 1001, 17:28–67). Thus,

Groves discloses a therapeutic agent loaded into an inner core which is a gel or hydrogel.[4]

5. *Claim 11: "The composition of claim 6, wherein the therapeutic agent is selected from the group consisting of . . . antibiotics . . ."*

Groves discloses the composition of claim 6. *Supra* § IX.E.4. Groves further discloses that the therapeutic agent may be an "antibiotic ester" which refers to "any conventional, medically available antibiotic which has at least one hydroxyl or carboxylic acid group." Ex. 1006, 2:6–13. Groves further identifies "metronidazole" as a "preferred antibiotic for use in this invention." *Id.*, 2:51–56; Ex. 1002, ¶¶ 192–94.

[4] As discussed above, Groves teaches several materials (alginates, chitin, chitosan, and pectin) which are both biodegradable polymers, as admitted by the '603 patent (*supra* § IX.E.2.c), and capable of forming hydrogels, as admitted by the '603 patent (*supra* § IX.E.2.cIX.E.2.d). Thus, Groves discloses an embodiment using biodegradable polymer hydrogels in both the inner core and wall component, and thereby anticipates both claim 2 (which requires the gel/hydrogel be the wall component) and claim 6 (which does not require the gel/hydrogel be the wall component, and under which Petitioner contends that the gel/hydrogel loaded with a therapeutic agent is the inner core). Ex. 1002, ¶ 189, n.9.

6. *Claim 12: "The composition of claim 1, wherein said gel or hydrogel is a precursor gel or precursor hydrogel."*

Groves discloses the composition of claim 1. *Supra* § IX.E.2. Groves discloses that the second component may be "calcium or magnesium alginate" or "other hydrogels such as pectin, chitosan, or chitin." Ex. 1006, 3:5–9. The '603 patent admits that "chitin" is a "gel material[]" and that "alginates," "chitin," "chitosan," and "pectin" are "materials which can form hydrogels." Ex. 1001, 17:28–67. Thus, Groves discloses that its shell can be made of materials which can form gels/hydrogels (precursors). Ex. 1002, ¶¶ 195–96.

7. *Claim 13: "The composition of claim 1, wherein said biodegradable polymer fiber comprises a hydrophobic drug."*

Groves discloses the composition of claim 1. *Supra* § IX.E.2IX.C.2. Groves further discloses that the bioabsorbable polymer (the first component of claim 1) comprises a hydrophobic drug. Ex. 1002, ¶¶ 197–99. Groves discloses an "antibiotic ester . . . substantially carried in the inner core." Ex. 1006, 3:53–4:4. As discussed above, "calcium or magnesium alginate" is disclosed as an exemplary "inner core" in Groves (*id.*, 4:9–12) and is also is a polymer as admitted in the '603 patent (Ex. 1001, 17:28–67). Groves provides a specific example of metronidazole palmitate, which is a known hydrophobic drug. Ex. 1002, ¶ 198. Groves also confirms that metronidazole is hydrophobic by describing that it forms a "suspension" when mixed in solution. Ex. 1006, 5:1–20. These passages confirm

that the metronidazole does not dissolve in water, showing that it is hydrophobic. Ex. 1002, ¶ 198.

8. *Claim 21*

a. "A scaffold composition comprising one or more fibers,"

Groves discloses one or more fibers, for the reasons explained above with respect to substantially similar limitation 1[a]. *Supra* § IX.E.2.a. Groves additionally discloses a "scaffold composition" made up of one or more fibers. Ex. 1002, ¶¶ 201–03. Groves is directed at a "packing material" for the treatment of infections. Ex. 1006, Abstract. Groves teaches that this material is comprised of fibers and "may be packed into a periodontal pocket formed in the gum tissue against the root of the tooth." *Id.*, 1:8–11. Groves further explains that in the packing, "the hydrated strings or fibers release free metronidazole." *Id.*, 5:34–42. Groves therefore confirms that multiple strings are used in the "packing material" and that these are arranged in a three-dimensional structure to be placed in a pocket in the gum tissue, for example. Ex. 1002, ¶ 202. This is consistent with the discussion of "scaffolds" in the '603 patent, which covers various arrangements, including "random arrays" of multiple fibers. Ex. 1001, 6:41–45. Additionally, the parent of the '603 patent, U.S. Patent No. 6,596,296, identifies an unordered arrangement of multiple fibers as an example of a "three-dimensional non-woven scaffolding without patterning":

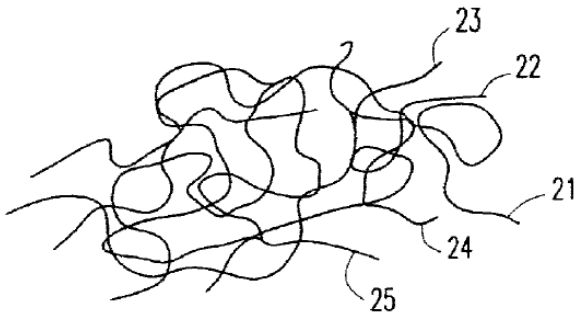


FIG. 2

Ex. 1043, 7:1–7. Thus, Groves discloses a scaffold. Ex. 1002, ¶ 203.

b. "wherein said fibers comprise a first component and a second component and"

Groves discloses a fiber comprised of a first and second component for the reasons explained above with respect to substantially similar limitation 1[b]. *Supra* § IX.E.2.b; Ex. 1002, ¶ 204.

c. "wherein said first component is a biodegradable polymer and"

Groves discloses the first component is a biodegradable polymer for the reasons explained above with respect to substantially similar limitation 1[c]. *Supra* § IX.E.2.c; Ex. 1002, ¶ 205.

d. "said second component is selected from the group consisting of a gel and a hydrogel."

Groves discloses the second component is gel or hydrogel for the reasons explained above with respect to substantially similar limitation 1[d]. *Supra* § IX.E.2.d; Ex. 1002, ¶¶ 206–07.

9. *Claim 22*

a. "The composition of claim 21 wherein said first component is present in the fiber bore and"

Groves discloses the composition of claim 21. *Supra* § IX.E.8. Groves also discloses the fiber has a bore (*supra* § IX.E.2.a) and that the first component is present in the bore for the reasons explained above with respect to substantially similar limitation 2[a]. *Supra* § IX.E.3.a; Ex. 1002, ¶ 209.

b. "said second component is present in the fiber wall."

Groves discloses the fiber has a wall (*supra* § IX.E.2.a) and that the second component is present in the wall for the reasons explained above with respect to substantially similar limitation 2[b]. *Supra* § IX.E.3.b; Ex. 1002, ¶¶ 210–11.

10. *Claim 26: "The composition of claim 21, wherein therapeutic agent is loaded into the gel or hydrogel."*

Groves discloses the composition of claim 21. *Supra* § IX.E.8. Groves also discloses that a therapeutic agent is loaded into the gel or hydrogel for the reasons explained above with respect to substantially similar claim 6. *Supra* § IX.E.4;Ex. 1002, ¶ 212.

11. *Claim 31: "The composition of claim 26, wherein the therapeutic agent is selected from the group consisting of . . . antibiotics"*

Groves discloses the composition of claim 26. *Supra* § IX.D.6. Groves also discloses that the therapeutic agent is an antibiotic for the reasons explained above with respect to substantially similar claim 11. *Supra* § IX.E.5; Ex. 1002, ¶¶ 213–14.

12. *Claim 32: "The composition of claim 21, wherein said gel or hydrogel is a precursor gel or precursor hydrogel."*

Groves discloses the composition of claim 21. *Supra* § IX.E.8. Groves also discloses that the gel or hydrogel is a precursor gel or precursor hydrogel for the reasons explained above with respect to substantially similar claim 12. *Supra* § IX.E.6; Ex. 1002, ¶ 215.

13. *Claim 33: "The composition of claim 21, wherein said biodegradable polymer fiber comprises a hydrophobic drug."*

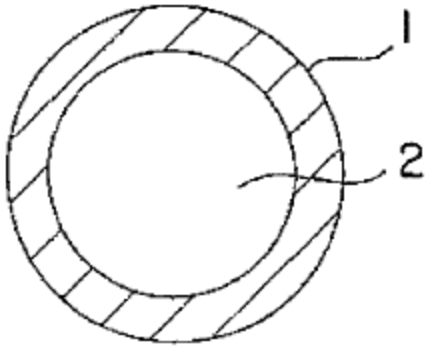
Groves discloses the composition of claim 21. *Supra* § IX.E.8. Groves also discloses that the bioabsorbable polymer (the first component of claim 21) comprises a hydrophobic drug for the reasons explained above with respect to substantially similar claim 13. *Supra* § IX.E.7; Ex. 1002, ¶ 216.

F. Ground 4: Claims 15 and 18 are Anticipated by Ahn

Petitioner requests cancellation of claims 15 and 18 because they are anticipated by Ahn.

1. *Overview of Ahn*

Ahn describes a "timed release drug delivery system using hollow fibers." Ex. 1007, Abstract. An exemplary hollow fiber is depicted in Figure 1:



Ahn's hollow fibers are filled with drugs including "[b]asically any liquid or dissolved drug or chemical," such as "antibiotics" and "anticoagulants." *Id.*, 3:39–46. To fill the fiber, fibers are submerged in a liquid solution, a partial vacuum is created to withdraw the air from the hollow portion of the fibers, then normal pressure is returned, and "[l]iquid 11 [is] drawn into the fiber filling the entire hollow" as depicted in Figure 6:

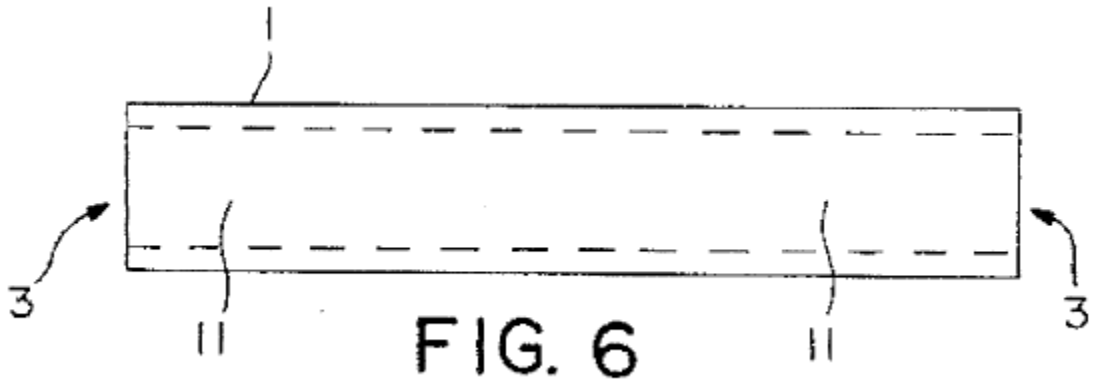


FIG. 6

Id., 2:40–58.

2. *Claim 15*

a. "A drug delivery composition comprising a fiber,"

Ahn discloses a drug delivery composition that is a fiber:

> The field of this invention is ***drug delivery systems***. More specifically the field of this invention is fabrics or ***fibers that contain drugs*** or other chemicals for various purposes, ***and which deliver these substances*** outside the fabric or fiber at a later time for various purposes. Furthermore ***the invention includes a method for filling such chemicals into such fibers*** or fabrics.

Ex. 1007, 1:6–12 (emphasis added); Ex. 1002, ¶ 221. Ahn explains that a hollow fiber can be filled with "[b]asically any liquid or dissolved drug or chemical," such as "antibiotics" and "anticoagulants." Ex. 1007, 3:39–46.

b. "wherein said fiber comprises a first component and a second component, and"

Ahn's discloses that the fiber has a first and second component. The fiber is originally a hollow fiber made up of "fiber material 1" which is then filled with a "[l]iquid 11." Ex. 1007, 2:21–58. Thus, Ahn discloses a first component (fiber material) and a second component (the liquid filling). Ex. 1002, ¶ 222.

c. "wherein said first component is a biodegradable polymer"

Ahn discloses that the first component is a biodegradable polymer. Ex. 1002, ¶ 223. Ahn identifies numerous materials which can be used to make the fibers, including "cellulose" and "polypeptide." Ex. 1007, 4:66–5:3. The '603 patent admits that cellulose and polypeptides are known biodegradable polymers. Ex. 1001, 16:1–29.

d. "said second component is water, and"

Ahn discloses wherein the second component is water. Ex. 1002, ¶ 224. Ahn explains that drugs are incorporated into the fibers in liquid form, and may be "dissolved in water." Ex. 1007, 4:21–25.[5] Ahn also notes that the types of drugs which can be incorporated include "hydrophilic (aqueous based)" drugs, *i.e.*, drugs dissolved in a solution with water. *Id.*, 5:7–10; Ex. 1002, ¶ 224. Ahn further explains that the final fiber may release the drug within via "liquid flow" or "liquid leakage," confirming that the final fiber has a liquid (such as water) in it. Ex. 1007, 5:11–22. Ex. 1002, ¶ 224.

e. "further wherein said water is present as an inner core."

Ahn discloses that the water is present as an inner core. Ex. 1002, ¶ 225–26. Ahn's fiber is a hollow fiber where the drug (which may be dissolved in water) is filled in the center of the fiber by submerging the fiber in liquid and using a vacuum to fill the fiber. Ex. 1007, 2:40–58. For example, Figure 1 depicts hollow region 2

[5] It is immaterial to the claims that the drug is additionally present. The claims recite the open-ended phrase "said fiber ***comprises*** a first component and a second component" confirming that the presence of additional components (e.g., drugs dissolved in the water) is permitted.

which will be filled with the water-drug solution and Figure 6 shows how the liquid 11 has filled throughout the center of the fiber:

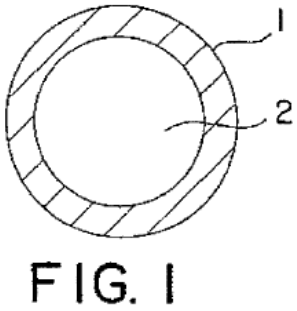


FIG. 1

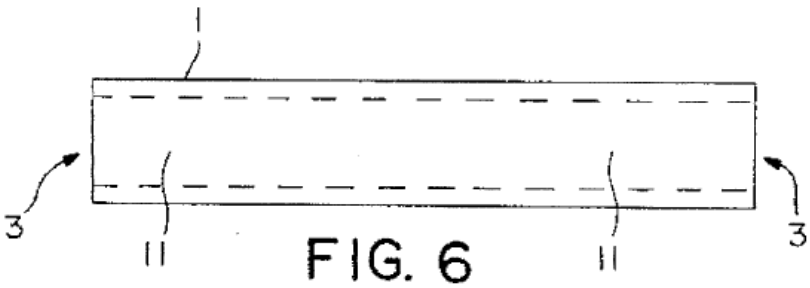


FIG. 6

Thus, Ahn discloses that the water is present as an inner core of the fiber. Ex. 1002, ¶¶ 225–26.

3. *Claim 18: "The composition of claim 15, wherein said biodegradable polymer fiber comprises a hydrophobic drug."*

Ahn discloses the composition of claim 15. *Supra* § IX.F.2. Ahn further discloses that the fiber comprises a hydrophobic drug. Ahn teaches that its fibers are "treated with antibiotics to prevent infection and to encourage healing." Ex. 1007, 3:61–64. Ahn expressly discloses that the drugs used may be "hydrophobic (oil or lipid based)." *Id.*, 5:7–10; Ex. 1002, ¶¶ 227–28.

G. Ground 5: Claims 16 and 17 are Rendered Obvious by Ahn in View of Liu

Petitioner requests cancellation of claims 16 and 17 because they are rendered obvious by Ahn in view of Liu.

1. *Motivation to Combine Ahn and Liu*

Both Ahn and Liu disclose drug-releasing fibers. Both Ahn and Liu disclose that their fibers can be woven with other fibers to form various medical devices. For example, Ahn teaches that its fibers can be "[k]nitted or woven" to make "vascular grafts, other prosthetic grafts, [or] sutures." Ex. 1007, 5:36–39. Liu similarly discloses that its fibers may be combined to make "multifilament sutures" or "woven to form . . . vascular grafts, [or] muscle grafts." Ex. 1005, 6:48–58. Ahn and Liu are thus directed at similar fibers for use in forming medical devices.

Ahn and Liu are also similar because they both highlight the importance of considering the release rate of a drug from the fiber. For example, Ahn emphasizes the importance of controlling the drug's release rate from the fiber. Ex. 1007, Abstract ("The present invention further includes . . . a method . . . to obtain a certain rate of drug release."). Ahn explains that the rate of release can be controlled in several ways, including by adjusting the length of fiber, cross-sectional area, fiber size, or concentration. *Id.*, 2:59–3:15.

Liu likewise teaches the importance of considering a drug's release rate. Liu teaches one of skill to select different bioabsorbable materials "having different rates of bioabsorption ***to construct a bioabsorbable composite having the desired*** strength and ***bioabsorption characteristics*** needed for a particular medical or surgical application." Ex. 1005, 4:39–46. Liu also explains that the bioabsorption

rate affects how quickly the drug will be absorbed by the body. *Id.*, 7:46–50 ("By incorporating wound healing substances in a high rate bioabsorption layer, the substance will be more quickly absorbed . . . .").

Ahn further teaches that its filled fibers "may be mixed and used with a variety of other fibers that are untreated or treated to form composite materials for uses incorporating delivery of the drugs or other carried agents." Ex. 1007, 4:53–58. Thus, Ahn suggests combining its fibers with other "treated" (*i.e.*, drug-loaded fibers) for incorporating into drug delivery devices, such as a graft or suture. Ex. 1002, ¶ 233.

Based on Ahn and Liu's similar drug-delivery fibers and their common teachings about the importance of considering the release rate of the drug, and further based on Ahn's express suggestion to mix its fibers with other treated fibers to form composite materials, one of ordinary skill in the art would have been motivated to consider combining Ahn's fibers with Liu's fibers in a medical device (e.g., weaving them together into a suture or graft as suggested by both Ahn and Liu). Ex. 1002, ¶¶ 229–34. This would have allowed one of ordinary skill to more precisely control the drug release rate and achieve different release rate profiles than if the device were comprised solely of Ahn's fibers or solely of Liu's fibers. *Id.* Such a combination would have been obvious to one of ordinary skill given the

similarities in Ahn's and Liu's fibers and the similar types of medical devices (*e.g.*, sutures or grafts) that can be made from such fibers.

2. *Claim 16*

a. "The composition of claim 15 Anther [sic][6] comprising at least one additional fiber,"

Ahn discloses the composition of claim 15. *Supra* § IX.F.2. As discussed above, one of ordinary skill would have been motivated to combine Ahn's and Liu's fibers into a drug delivery device (*e.g.*, a suture or a graft). Thus, Liu's fiber, in this combined drug delivery device, would disclose at least one additional fiber. Ex. 1002, ¶ 236.

b. "wherein said additional fiber circumscribes an adjacent inner fiber."

Liu's fiber (*i.e.*, the additional fiber that a person of ordinary skill would be motivated to add to Ahn's fiber to create a drug delivery device) discloses this limitation for the reasons explained above with respect to similar limitations in claim 4. *Supra* § IX.C.3; Ex. 1002, ¶ 237. As explained above, Liu discloses that its fiber has one or more outer shells, where the outer shell circumscribes an adjacent inner fiber. *Id.*

[6] This appears to be a typo in the printing of the patent. The claim as presented in the file history consistently read "further" rather than "Anther."

3. *Claim 17: "The composition of claim 16 wherein said adjacent inner fiber is approximately centered within the outer fiber."*

The combination of Ahn and Liu discloses the composition of claim 16. *Supra* § IX.G.2. Liu's fiber (*i.e.*, the additional fiber that a person of ordinary skill would be motivated to add to Ahn's fiber to create a drug delivery device) discloses this limitation for the reasons explained above with respect to similar limitations in claim 5. *Supra* § IX.C.4; Ex. 1002, ¶ 238. As explained above, Liu discloses that the inner fiber is centered within the outer fiber, for example, when it is made by a die that extrudes "concentric" fibers. *Id.*

H. Ground 6: Claim 19 is Anticipated by Song

Petitioner requests cancellation of claim 19 because it is anticipated by Song.

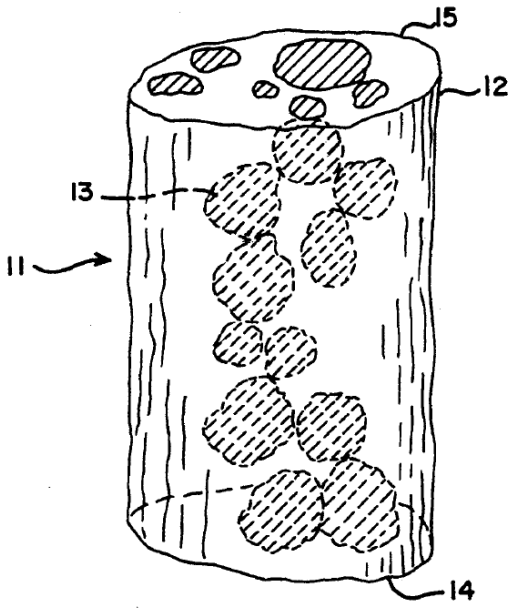
1. *Overview of Song*

Song discloses a biodegradable polymer fiber that contains an active agent (*e.g.*, drug) dispersed throughout a wall material (*e.g.*, polymer) such that the active agent is gradually released from the fiber:

> A delivery system and a process for making the system is provided for the gradual release of an active agent. The system comprises an active agent and a wall material. The delivery system is formed by melt spinning a mixture of particles of active agent and wall material into a fiber. . . . The particles of active agent are dispersed throughout the wall material such that the particles of active agent are

gradually released from the fiber when the fiber is contacted with a solvent specific to the active agent.

Ex. 1008 at Abstract. Figure 1 of Song illustrates a gradual release fiber with an active agent dispersed in physically distinct pockets (marked 13, diagonally shaded) throughout the fiber:



Id. at Fig. 1. Song explains that the drug may be "adsorbed or absorbed into or onto a supporting matrix, *i.e.*, silica." *Id.*, 4:32–40.

2. *Claim 19*

a. "A drug delivery composition comprising a fiber"

Song discloses the claimed composition that includes a fiber. Ex. 1002, ¶ 243. Song teaches a "delivery system" that can gradually release "an active agent." Ex. 1008, Abst. "The delivery system is formed by melt spinning a mixture of particles of active agent and wall material into a fiber." *Id.*; *see also id.*, 1:52–60. "[P]articles

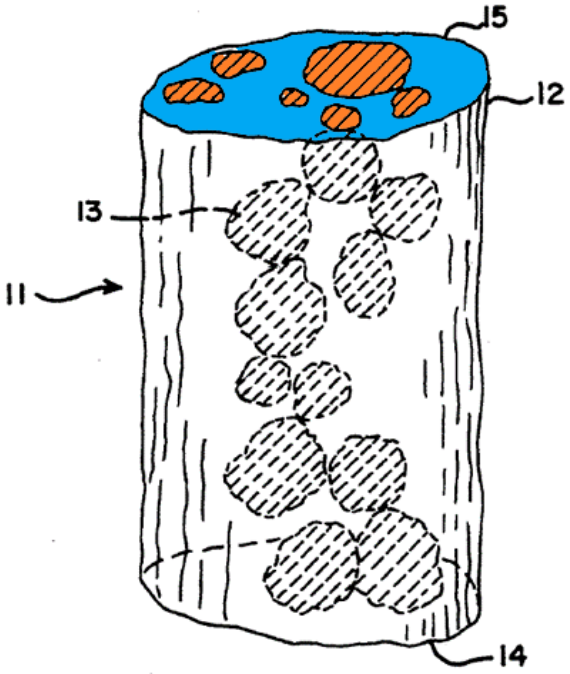
of active agent are dispersed throughout the wall material such that the particles of active agent are gradually released from the fiber . . . ." *Id.*, Abst.; *see also id.*, 1:61–65, 2:38–40. Song's active agent may include "drugs" including "anti-hypertensive drugs" and "anti-arrhythmics," (Ex. 1008, 4:40–66), which are the same type of therapeutic agents disclosed in the '603 patent. *See* Ex. 1001, 8:2–9 (disclosing "therapeutic agents" including drugs for "blood pressure" and "anti-arrhythmia" drugs).

b. <u>"wherein said fiber comprises an emulsion consisting essentially of a gel or hydrogel."</u>

Song discloses wherein the fiber comprises an emulsion consisting essentially of a gel or hydrogel because Song discloses a fiber that has a dispersed component that is a hydrogel precursor, satisfying Petitioner's proposed construction of "said fiber comprises a dispersed component consisting essentially of a gel or hydrogel (including precursors)." *Supra* § VIII.B; Ex. 1002, ¶¶ 244–50.

Song discloses that the active agent dispersed throughout its fiber may include "liquids adsorbed or absorbed into or onto a supporting matrix" *i.e.*, "silica." Ex. 1008, 4:32–38. The liquids adsorbed or absorbed into the silica include "drugs." *Id.*; *see also id.*, 4:57–66 (listing numerous exemplary pharmaceuticals which may be incorporated into Song's fiber). Silica is a well-known hydrogel precursor in common use (*e.g.*, the silica gel packets used in packing to keep objects dry) which gels in the presence of water. Ex. 1002, ¶ 245. As discussed above, Song discloses

that its active agent (*i.e.*, the drug adsorbed into silica) is "dispersed throughout the wall material such that the particles of active agent are gradually released from the fiber." Ex. 1008, 1:52–65. This is clearly depicted in Song's Figure 1, where the active agent (highlighted in orange) is dispersed throughout the fiber (made of a polymer, highlighted in blue):



Song also explains that the wall material and dispersed active agent "must be immiscible with each other." Ex. 1008, 5:5–9. This confirms that the active agent will not dissolve into the polymer and form a single component, but will remain a dispersed component in the fiber. Thus Song discloses that its active agent, which may be a drug adsorbed or absorbed into the hydrogel precursor silica, is dispersed throughout the fiber. Ex. 1002, ¶ 247. This satisfies Petitioner's proposed

construction of "said fiber comprises a dispersed component consisting essentially of a gel or hydrogel (including precursors)."

The fact that Song's dispersed component includes a drug adsorbed onto silica does not alter this conclusion. The phrase "consisting essentially of . . . is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention." *PPG Indus.*, 156 F.3d at 1354. The basic property of the '603 patent's alleged invention is drug delivery, as is shown by the patent's title, "Drug Releasing Biodegradable Fiber For Delivery of Therapeutics." Ex. 1001, cover. The '603 patent also specifically confirms that the embodiments with dispersed gel or hydrogel may also contain a therapeutic agent in the gel or hydrogel, teaching that the fibers "may also contain therapeutic agents in a dispersed aqueous, gel or hydrogel phase." Ex. 1001, 32:45–49; *see also id.*, 32:50-54 (describing manufacturing process, where "an aqueous solution or a gel or a hydrogel (including precursors) containing both the biomolecule(s) of interest and a surfactant" is used to create dispersed gel or hydrogel inside a fiber). Thus, Song's dispersed phase (of a drug adsorbed or absorbed into silica) consists essentially of a hydrogel precursor, and Song therefore satisfies Petitioner's proposed construction.

X. PAYMENT OF FEES – 37 C.F.R. § 42.103

The required fee is being paid through PTABE2E.

XI. CONCLUSION

For the foregoing reasons, Petitioner requests that the Board institute *inter partes* review of claims 1, 2, 4–6, 11–13, 15–19, 21, 22, 24–26, and 31–33 of the ’603 patent and cancel those claims as unpatentable.

Dated: October 9, 2018

Respectfully submitted,

/Andrew R. Sommer/

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CERTIFICATE OF COMPLIANCE

This petition complies with the word count limits set forth in 37 C.F.R. § 42.24(a)(i), effective May 2, 2016, because this Petition contains 11,107 words, excluding the parts of the petition exempted by 37 C.F.R. § 42.24(a), as corrected in *Amendments to the Rules of Practice for Trials Before the Patent Trial and Appeal Board*, 81 Fed. Reg. 24,702 (Apr. 27, 2016) and determined using the word count provided by Microsoft Word, which was used to prepare this Petition.

Dated: October 9, 2018

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CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. §§ 42.6(e) and 42.105(a), this is to certify that on October 9, 2018, I caused to be served a true and correct copy of the foregoing PETITION FOR *INTER PARTES* REVIEW and Exhibits 1001–1043 by EXPRESS MAIL on Patent Owner the correspondence address of record for U.S. Patent No. 7,033,603, as follows:

Correspondence Address	WINSTEAD PC P.O. Box 131851 Dallas, TX 75313-1851
Litigation Counsel:	Michael W. Shore SHORE CHAN DEPUMPO LLP 901 Main Street, Suite 3300 Dallas, TX 75202

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