UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ETHICON, INC.,

Petitioner,

v.

BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM,

Patent Owner.

Patent No. 6,596,296
Issued: July 22, 2003
Filed: August 4, 2000

Inter Partes Review No. IPR2019-00406

PETITION FOR *INTER PARTES* REVIEW

Mail Stop PATENT BOARD
Patent Trial and Appeal Board
US Patent and Trademark Office
PO Box 1450
Alexandria, Virginia 22313-1450
Submitted Electronically via the PTAB E2E System

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Ethicon, Inc. ("Ethicon" or "Petitioner") respectfully requests *inter partes* review ("IPR") under 35 U.S.C. §§ 311-319 and 37 C.F.R., Part 42 of claims 1, 4, 11, 16-17, 20, and 26 ("the challenged claims") of U.S. Patent No. 6,596,296 ("the '296 patent," Ex. 1001) issued July 22, 2003. As demonstrated herein, there is a reasonable likelihood that Petitioner will prevail in establishing that at least one challenged claim is unpatentable.

I. INTRODUCTION

The '296 patent discloses and claims the basic, art-known combination of a biodegradable polymer and a drug in a fiber. Ex. 1001 at, *e.g.*, 2:44-45, 4:58-60, 27:54-58 (claim 1). Such compositions were known and used long before the alleged August 6, 1999 priority date of the '296 patent. The U.S. Patent and Trademark Office ("PTO") therefore repeatedly rejected Patent Owner's claims to biodegradable polymer fibers containing drugs. Patent Owner only obtained the challenged claims by adding limitations requiring that the polymer and drug form separate "phases" in the fiber that are "immiscible" with each other. But there is nothing novel about a drug region that is immiscible with the polymer portion of the fiber. The challenged claims are unpatentable and should not have issued. This Petition is based on references not considered by the PTO during prosecution of the '296 patent that are prior art under 35 U.S.C. § 102(b) and anticipate or render obvious each of the challenged claims.

Patent Owner has asserted the '296 patent against Ethicon and other defendants in U.S. district court. No discovery has been taken and no trial date has been set in the district court case. For the reasons discussed below, the Board should institute IPR.

II. MANDATORY NOTICES (37 CFR § 42.8)

A. Real Party-In-Interest

Petitioner Ethicon, Inc. as well as Ethicon US, LLC, Ethicon Endo-Surgery, Inc., Ethicon LLC, Ethicon Holding S.A.R.L., Ethicon PR Holdings Unlimited Company, Janssen Pharmaceutical, JNJ Irish Investments ULC, JNJ International Investment LLC, OMJ Pharmaceuticals, Inc., Medical Device Business Services, Inc., Synthes, Inc., DePuy Synthes, Inc., Johnson & Johnson International and Johnson & Johnson are real parties-in-interest. No other party is a real party-in-interest or a privy of Ethicon, Inc. for this Petition.

B. Related Matters

In *Board of Regents, The University of Texas System et al. v. Ethicon, Inc. et al.*, No. 1:17-cv-01084 (W.D. Tex.) (the "District Court Action"), Patent Owner and its licensee, TissueGen, Inc. accuse Ethicon's antibacterial sutures of infringing the '296 patent and U.S. Patent No. 7,033,603 ("the '603 patent," Ex. 1012), which is a continuation-in-part of the '296 patent. The '603 patent is the subject of a separate IPR petition that Ethicon is filing concurrently with this Petition. *See*

IPR2019-00407. Ethicon, Inc. and Ethicon US, LLC were served with the complaint in the District Court Action on December 11, 2017. Ex. 1015; Ex. 1016. The court in the District Court Action has stayed all proceedings other than claim construction. *See* Ex. 1017 (setting initial schedule limited to claim construction). Thus, no fact or expert discovery has occurred and no trial date has been set in the District Court Action. *See id.*

On December 3, 2018, the court entered its claim construction decision in the District Court Action. *See* Ex. 1018. In the same order, the court set a scheduling conference for February 15, 2019, based on which the court will render a scheduling order for the remainder of the case. *Id.* at 18. Thus, no discovery of any kind will be exchanged in the District Court Action until mid-February 2019 at the earliest. *See id.*

Patent Owner has also brought other suits against other defendants alleging infringement of the '296 and '603 patents. In *Board of Regents, The University of Texas System et al. v. Boston Scientific Corp.*, No. 1:18-cv-00392-MN (D. Del.), Patent Owner alleges that Boston Scientific Corp.'s drug-eluting stents infringe the '296 and '603 patents. That action is stayed pending interlocutory appeal of an order transferring the case to the District of Delaware from the Western District of Texas. *See* No. 18-1700 (Fed. Cir.).

In *Board of Regents, The University of Texas System et al. v. Medtronic, Inc. et al.*, No. 1:17-cv-00942 (W.D. Tex.), Patent Owner alleged that antibacterial pacemaker envelopes sold by Medtronic Inc. and TYRX, Inc. (together, "Medtronic") infringe the '296 and '603 patents. That case was dismissed without prejudice on July 19, 2018.

On October 9, 2018, Medtronic filed IPR petitions regarding the '296 and '603 patents, assigned No. IPR2019-00037 and No. IPR2019-00038, respectively. Medtronic challenges claims 1, 4, 11, 16, 20 and 26, which are also challenged in this Petition, as well as claims 2-3, 5-7, 10, 21-23, 25 and 31-32, which are not. Further, Ethicon challenges claim 17, which is not addressed in Medtronic's petition. *Compare* IPR2019-00037, Paper 2 (Petition) at 7, *with* § V, *infra*. Further, with the exception of U.S. Patent No. 5,364,627 to Song ("Song," Ex. 1005), Medtronic and Ethicon rely on different art in the respective petitions. At this time, Patent Owner has not submitted preliminary responses to Medtronic's petitions and the Board has not issued a decision on institution of either petition.

Petitioner is not aware of any other pending administrative matter or litigation that would affect, or be affected by, a decision in this proceeding.

C. Lead and Back-up Counsel and Service Information

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Petitioner consents to electronic service by email at UTexasIPRs@pbwt.com.

III. PAYMENT OF FEES

The Director is authorized to charge the fee specified by 37 CFR § 42.15(a), and any other required fees, to Deposit Account No. 50-6642.

IV. GROUNDS FOR STANDING

Petitioner certifies that the '296 patent is available for IPR and that Petitioner is not barred or estopped from requesting IPR of the '296 patent. This Petition is being filed less than one year after the date on which Petitioner was served with a complaint alleging infringement of the '296 patent. The challenged claims have not been the subject of any prior petitions by Petitioner, nor by any real party-in-interest or privies of Petitioner.

V. THE CHALLENGED CLAIMS

Petitioner challenges claims 1, 4, 11, 16-17, 20, and 26 of the '296 patent as unpatentable over the prior art under 35 U.S.C. §§ 102 and 103.

Claim 1 of the '296 patent recites:

> A composition comprising at least one biodegradable polymer fiber wherein said fiber is composed of a first phase and a second phase, the first and second phases being immiscible, and wherein the second phase comprises one or more therapeutic agents.

Ex. 1001 at 27:54-58. In brief, the claim requires: (i) a biodegradable polymer fiber, (ii) composed of two immiscible phases, (iii) wherein the second phase contains one or more therapeutic agents.

Claims 4, 11, 16, 20, and 26 all depend directly from claim 1. Claim 17 depends from claim 16.

Claim 4 recites "[t]he composition of claim 1, wherein said fiber is woven, braided or knitted in an assembly with other fibers, and at least one fiber in the assembly comprises one or more therapeutic agents."

Claim 11 requires that the "one or more therapeutic agents" contained in the second phase of the fiber be "selected from [a] group" that includes a broad range of known therapeutic agents.

Claim 16 requires the "biodegradable polymer" of the fiber be "a single polymer, a co-polymer, or a mixture of polymers selected from [a] group" consisting of various art-known biodegradable polymers, including "aliphatic polyesters" and "poly(ortho ester)," among others.

Claim 17 depends from claim 16 and requires that "said aliphatic polyesters are selected from [a] group" consisting of various art-known aliphatic polyesters such as "poly (glycolic acid)," "poly(lactic acid)" and "copolymers, blends and mixtures thereof."

Claim 20 depends from claim 1 and requires the fiber to comprise "a plurality of polymer layers, wherein an outer layer circumscribes an adjacent inner layer."

Claim 26 depends from claim 1 and requires that "said one or more therapeutic agents are released at varying rates over time from said fiber."

The challenged claims have been asserted against Ethicon in the District Court Action. No other claims are asserted in that action.

VI. IDENTIFICATION OF GROUNDS AND PRECISE RELIEF REQUESTED

Petitioner requests that claims 1, 4, 11, 16-17, 20, and 26 of the '296 patent be cancelled as unpatentable because they are anticipated under 35 U.S.C. § 102 and/or obvious under 35 U.S.C. § 103 in view of the following prior art: U.S. Patent No. 5,364,627 to Song (previously defined as "Song," Ex. 1005); U.S. Patent No. 4,093,709 to Choi ("Choi," Ex. 1007); U.S. Patent No. 4,351,337 to Sidman

("Sidman," Ex. 1006); Fred W. Billmeyer, Jr., *Chapter 18: Fiber Technology, in* TEXTBOOK OF POLYMER SCIENCE 513-532 (2d ed. 1971) ("Billmeyer," Ex. 1008), European Patent App. Pub. No. 0253554 to Curatolo ("Curatolo," Ex. 1009). These references are prior art under pre-AIA § 102(b) and were not considered by the PTO during prosecution.

Petitioner presents the following grounds for trial:

Ground 1: Claims 1, 11, 16-17, and 26 are anticipated under 35 U.S.C. § 102 or, at a minimum, rendered obvious under 35 U.SC. § 103 by Song in view of the knowledge of a person having ordinary skill in the art ("POSA");

Ground 2: Claims 4 and 20 are obvious under 35 U.S.C. § 103 over Song combined with the knowledge of a POSA;

Ground 3: Claim 4 is obvious under 35 U.S.C. § 103 over Song in view of Billmeyer or Curatolo;

Ground 4: Claim 20 is obvious under 35 U.S.C. § 103 over Song in view of Sidman;

Ground 5: Claims 1, 4, 11, 16-17, 20, and 26 are anticipated under 35 U.S.C. § 102 or, at a minimum, rendered obvious under 35 U.S.C. § 103 by Choi in view of the knowledge of a POSA.

VII. LEGAL STANDARDS

A. Anticipation (35 U.S.C. § 102)

"A patent is invalid for anticipation under 35 U.S.C. § 102 if a single prior art reference discloses all limitations of the claimed invention." *CRFD Research, Inc. v. Matal*, 876 F.3d 1330, 1338 (Fed. Cir. 2017) (citation omitted) (affirming the Board's finding of anticipation). In an anticipation analysis, "extrinsic evidence may be considered when it is used to explain, but not expand, the meaning of a reference." *In re Baxter Travenol Labs*, 952 F.2d 388, 390 (Fed. Cir. 1991); *see also* MPEP § 2131.01.II (Ninth Edition, Rev. 08.2017, last revised January 2018).

B. Obviousness (35 U.S.C. § 103)

"Obviousness is a question of law with underlying factual determinations, including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of skill in the art; and (4) objective evidence of nonobviousness." *IXI IP, LLC v. Samsung Elecs. Co.*, 903 F.3d 1257, 1262 (Fed. Cir. 2018) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966)) (affirming the Board's finding of obviousness). The obviousness inquiry includes considering "whether a person of ordinary skill in the art would have been motivated to combine the prior art to achieve the claimed invention and whether there would have been a reasonable expectation of success in doing so." *Dystar Textilfarben GmbH v. C.H. Patrick Co.*, 464 F.3d 1356, 1360 (Fed. Cir. 2006).

C. Claim Construction

In an *inter partes* review filed on or after November 13, 2018, claim terms are interpreted using the same standard that is used in a civil action in federal district court: "construing the claim in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent." 37 C.F.R. § 42.100(b). Further, "[a]ny prior claim construction determination concerning a term of the claim in a civil action … that is timely made of record in the inter partes review proceeding will be considered." *Id.*

VIII. THE '296 PATENT

A. The State of the Art and the '296 Patent

The '296 patent is entitled "Drug Releasing Biodegradable Fiber Implant." The patent is directed to "tissue engineering compositions and methods wherein three-dimensional matrices for growing cells are prepared for in vitro and in vivo use." Ex. 1001 at 2:41-43. The "matrices" described in the '296 patent (also referred to as "scaffolds" or "fiber scaffolds") are made of "biodegradable polymer fibers capable of the controlled delivery of therapeutic agents." *Id.* at 2:44-52. The '296 patent thus describes "a drug-delivery fiber composition comprising a biodegradable polymer fiber containing one or more therapeutic agents." *Id.* at 4:58-60.

Artisans had been making drug-releasing biodegradable polymer fibers long before August 6, 1999, the claimed priority date of the '296 patent. Ex. 1002 ¶¶

28-29. As explained in the 1990 book, BIODEGRADABLE POLYMERS AS DRUG DELIVERY SYSTEMS, "[f]or more than two decades, the delivery of bioactive agents from polymeric materials has attracted the considerable attention of investigators throughout the scientific community." Ex. 1019 (Lewis 1990) at 1.

Further, "[t]he advantages of biodegradable polymers ha[d] been described," and "the trend in drug delivery technology [was] toward biodegradable polymer excipients." Ex. 1019 (Lewis 1990) at 1; Ex. 1002 ¶ 28. Indeed, "[t]he biodegradable polyesters ha[d] attracted attention in a variety of biomaterial applications" in which "research teams were seeking delivery systems for such agents as narcotic antagonists, contraceptive hormones, and other conventional drug compounds." Ex. 1019 (Lewis 1990) at 2. "Controlled release fiber systems based on aliphatic polyesters" (a widely used class of biodegradable polymers "preferred" in the '296 patent (Ex. 1001 at 9:65-10:38)), had been investigated and put into practice. *Id.* at 11 (citing work published in 1981-1987); Ex. 1002 ¶ 29.

The '296 patent adds nothing new. It discusses making drug-delivery fibers out of the same widely used biodegradable polymers catalogued in the literature. Ex. 1001 at 10:13-38; *see also id.* at 4:52-57; Ex, 1002 ¶¶ 30-31. The patent contains a general list of art-known polymers, borrowing from a 1997 book chapter by Wai Hung Wong and David Mooney. *Id.* at 10:13-38 (adapting Table 1 from Wong and Mooney 1997); Ex. 1021 (Wong and Mooney 1997) at 55-56. The

"[p]referred polymers for use" in the '296 patent include single polymers and copolymers of polyglycolic acid (PGA) and polylactic acid (PLA). *Id.* at 9:65-10:2. These polymers had "received considerable attention since about 1973 as excipients for drug delivery," and by 1990, were "[t]he most widely investigated and advanced polymers in regard to available toxicological and clinical data." Ex. 1019 (Lewis 1990) at 2; *see also* Ex. 1021 (Wong and Mooney 1997) at 53-54 (describing PGA and PLA as "extensively utilized in … biomedical applications such as drug delivery"); Ex. 1002 ¶ 31.

With regard to the therapeutic agents to incorporate into its fibers, the '296 patent contains a general, column-long list of known therapeutic agents and drugs. *Id.* at 3:66-4:51. In fact, the patent "contemplates the use of any drug" in its fibers (Ex. 1001 at 4:32-34), and "incorporate[s] by reference" the U.S. Pharmacopeia. *Id.* at 4:32-51. The '296 patent thus describes the well-known combination of a biodegradable polymer and a drug in a fiber, choosing the most widely known biodegradable polymers and combining them with any drug. Further, the patent's examples of potential uses for its fibers are entirely prophetic, with no evidence that the fibers had been used in any of the ways hypothesized by the inventors. *See id.* at 22:17-25:12 (Examples 6-14). The patent provides no testing or data concerning drug release from its fibers. *See generally* Ex. 1001; Ex. 1002 ¶ 32.

The patent also generally states that its polymer fibers "may be woven, non-woven, braided, knitted, or a combination of two or more such preparations," (*id.* at 3:34-42), or "may comprise a plurality of co-axial biodegradable polymer layers." *Id.* at 3:48-49. The patent provides no special teachings of these art-known fiber formats. The inventors note that "braiding may, for example, provide superior strength" (*id.* at 3:41-42), and acknowledge that multilayered fibers were "well known to those familiar in the art." *Id.* at 20:33-36. The patent's examples of woven, braided or knitted structures or multilayered fibers are all present-tense prophetic discussions. *Id.* at 20:7-36, 22:39-51, 23:7-29, 24:9-30 (Examples 3, 7, 9 and 12).

As demonstrated below, the challenged claims of the '296 patent are unpatentable as anticipated and obvious over the prior art. *See* § X, *infra*.

B. Prosecution History of the '296 Patent

The application that issued as the '296 patent was filed on Aug. 4, 2000 as U.S. Application No. 09/632,457 ("the '457 application"). Claim 1, as originally proposed, recited compositions "comprising biodegradable polymer fibers, said fibers containing one or more therapeutic agent [sic] that are released over time." Ex. 1004 at 47. In response to a restriction requirement, Patent Owner cancelled all pending claims and replaced them with claims that again recited "biodegradable

polymer fibers" that "contain one or more therapeutic agents." *Id.* at 105 (new claims 199 and 202).

In an Office Action dated June 12, 2002, the Examiner rejected the proposed claims as "clearly anticipated by Martin et al. (WO'190)." *Id.* at 129; *see also* WO 98/20190 ("Martin," Ex. 1013). Martin discloses biodegradable polymer fibers that contain a "pharmaceutically active agent." Ex. 1013 at, *e.g.*, 1:3-8, 2:15-22, 5:20-23, 9:15-24, 14:27-33. It includes a list of art-known biodegradable polymers that largely overlaps with the list in the '296 patent (*id.* at 11:20-12:20), and describes "useful agents" that can be incorporated into the biodegradable polymer fibers. *Id.* at 15:17-16:10.

In response to the rejection over Martin, on September 13, 2002, Patent Owner amended the claims to recite compositions of biodegradable polymer fibers that "comprise an emulsion containing one or more therapeutic agents within the aqueous phase of said emulsion." Ex. 1004 at 132-133, 138. Patent Owner argued: "Although Martin teaches that a scaffold comprising fibers may comprise therapeutic agents, there is no mention in Martin of the manner in which the therapeutic agents are introduced into the fibers. Martin does not teach the presence of therapeutic agents in an emulsion wherein the therapeutic agents are present in the aqueous phase of the emulsion." *Id.* at 136.

The Examiner disagreed, and maintained the rejection over Martin in an October 4, 2002 final rejection on the basis that "applicant has claimed a composition, not a method of making said composition." *Id.* at 147. Thus, the Examiner explained, "[t]here is no requirement that the reference teach how the therapeutics are incorporated into the claimed fibers." *Id.* "[T]he only requirement of the Martin reference was that it disclose the limitations of the instantly claimed fibers. This requirement is clearly fulfilled." *Id.*

The Examiner further explained that "while [Patent Owner] has amended the claims to read on fibers containing an emulsion, there is no support in the original specification for a final product containing said formulation." *Id.* The Examiner stated: "It is clear from … the disclosure that the resultant fiber no longer contains any fluid, let alone an emulsion. [Patent Owner's] argument[s] concerning the emulsion content of the fiber claimed are therefore erroneous." *Id.* at 147-48.

In a renewed attempt to overcome Martin, on January 8, 2003, Patent Owner cancelled all pending claims and proposed the claims that ultimately issued. Ex. 1004 at 153-162. New claim 248 (issued as claim 1) recited "[a] composition comprising at least one biodegradable polymer fiber wherein said fiber is composed of a first phase and a second phase, the first and second phases being immiscible, and wherein the second phase comprises one or more therapeutic agents." *Id.* at 153, 160. Patent Owner argued that Martin "does not anticipate the amended

claims," "[b]ecause [it] does not teach a composition where the fibers comprise a first phase (*i.e.*, the polymer that makes up the fiber) and a second (inner) phase, wherein the second phase comprises one or more therapeutic agents." *Id.* at 158.

The Examiner allowed the amended claims. *Id.* at 170. The PTO did not consider the prior art references discussed in this Petition during prosecution. Patent Owner did not submit any of these references, and the PTO did not identify these references in its review of the prior art.

After 18 years of prosecution, no claims have issued from the European counterpart application to the '296 patent. *See generally* Ex. 1014.

C. Claim Construction

As noted above, claim 1 of the '296 patent recites: "a composition comprising at least one biodegradable polymer fiber wherein said fiber is composed of a **first phase** and a **second phase**, the **first and second phases being immiscible**, and wherein the **second phase** comprises one or more therapeutic agents. Ex. 1001 at 27:54-58 (terms for construction emphasized). In order to understand the scope of claim 1 and its dependent claims, it is necessary to construe the terms "first phase," "second phase," and "immiscible." The dependent claims do not introduce additional claim construction issues.

In the District Court Action, the court construed the relevant terms as follows:

- "**first phase**": "the polymer portion of the fiber"

- "**second phase**": "the discrete drug-containing regions dispersed throughout the fiber"
- "**immiscible**": "incapable of dissolving into one another"

Ex. 1018 at 8-14.

For purposes of this proceeding, Petitioner adopts the district court's constructions. *See* 37 C.F.R. § 42.100(b). As described below, each of the challenged claims is unpatentable over the prior art under these constructions.

1. "First Phase" and "Second Phase"

"First phase" should be construed to mean "**the polymer portion of the fiber**." This construction was adopted in the District Court Action. Ex. 1018 at 8-9. It is consistent with the prosecution history, where Patent Owner described the "first phase" as "the polymer that makes up the fiber." Ex. 1004 at 157; *id.* at 158 (same). As the court noted, "the parties agree that 'first phase' refers to the polymer portion of the fiber." Ex. 1018 at 9.

"Second phase" should be construed to mean "**the discrete drug-containing regions dispersed throughout the fiber**," as in the District Court Action. Ex. 1018 at 9-10. This construction is consistent with the specification and the prosecution history. *See* Ex. 1018 at 10. As the district court observed, Patent Owner distinguished the '296 patent from the prior art that was before the Patent Office

during prosecution "on the basis of the therapeutic agents being 'within an immiscible discontinuous phase or internal porous structure of the fiber.'" *Id*.

2. "Immiscible"

"Immiscible" should be construed to mean "**incapable of dissolving into one another**." This construction was adopted in the District Court Action, and is consistent with the intrinsic record and the term's ordinary meaning. Ex. 1018 at 11-14; Ex. 1002 ¶¶ 56-60.

The '296 patent does not use the term "immiscible" other than in claim 1. *See generally* Ex. 1001; Ex. 1018 at 12. The original claims, however (which were later cancelled), included claims to methods of making fibers with a solvent that is "*substantially* immiscible" with water and "*highly* miscible" with another solvent. Ex. 1004 at 58 (claim 103) (italics added). Similarly, the specification refers to a solvent having "*low* miscibility with water." Ex. 1001 at 17:48-50 (emphasis added); Ex. 1018 at 13. As the district court observed, however, "Claim 1 simply does not use the phrase 'low miscibility.'" Ex. 1018 at 13. By contrast, to gain allowance of claim 1 after repeated rejections, Patent Owner used the absolute term, "immiscible." *See* § VIII.B., *supra*. Thus, the claim language chosen by Patent Owner to overcome the prior art reflects that "immiscible" in the claims of the '296 patent means "incapable of dissolving into one another." Ex. 1002 ¶¶ 57-58.

Further, as the district court concluded, "the extrinsic evidence [] weighs heavily in favor of 'immiscible' meaning incapable of dissolving." *Id.* at 13 (citing MCGRAW-HILL DICTIONARY OF CHEMICAL TERMS 216 (1984) ("Pertaining to liquids that will not mix with each other")). Other technical and standard dictionaries also support the district court's construction. *See* Ex. 1025 (Academic Press) at 1086 ("not miscible; describing two liquids that do not mix, such as oil and water."); Ex. 1022 (American Heritage) at 643 ("Incapable of mixing or blending"); Ex. 1023 (Webster's II) at 553 ("Incapable of blending or mixing"); Ex. 1024 (Random House) at 957 ("not miscible; incapable of being mixed").

While the dictionaries use the word "mix," the parties and district court agreed that the term "immiscible," as used in the '296 patent, refers to the inability of the two phases to "dissolve" in one another. Ex. 1018 at 12 *id.* at 12 n.4. Accordingly, "immiscible" should be construed to mean "incapable of dissolving into one another," as the district court concluded. Ex. 1002 ¶ 60; Ex. 1018 at 11-14.

In the District Court Action, Patent Owner proposed construing "immiscible" to mean either "not miscible" or "incapable of mutual solution at the proportions used." Ex. 1018 at 11. Both of these proposed constructions are incorrect and should be rejected. "Not miscible" fails to provide any meaningful construction. Ex. 1002 ¶ 61. It was thus properly rejected by the district court. Ex. 1018 at 11.

The district court also correctly rejected Patent Owner's proposed construction of "immiscible" as "incapable of mutual solution at the proportions used," based on the intrinsic record. *Id.* at 12. As the court observed, "[d]ependent claims 6-9, 24, and 32 describe a variation of the fiber of Claim 1 in which the concentration of therapeutic agents varies along the length of the fiber." *Id.* (citing Ex. 1001 ('296 patent) at 19:40-55, 28:4-18, 29:6-8, 30:13-16, Figure 6). "Although the ratio of therapeutic agent to polymer varies in such a fiber, the first and second phases must still be 'immiscible,' suggesting that **immiscibility does not depend on the proportions used**." *Id.* (emphasis added).

IX. PERSON OF ORDINARY SKILL IN THE ART

For purposes of the '296 patent, a POSA would have had a Ph.D. in chemistry, chemical engineering, materials science, or a related field and several years of experience working in the fields of the patent, drug delivery and tissue engineering. *See* Ex. 1002 ¶¶ 22-23.

X. THERE IS A REASONABLE LIKELIHOOD THAT AT LEAST ONE CLAIM OF THE '296 PATENT IS UNPATENTABLE

A. Ground 1: Claims 1, 11, 16-17, and 26 Are Anticipated or Obvious Over Song

1. Song is Prior Art Not Considered by the Patent Office

Song issued on November 15, 1994, more than four years before the earliest claimed effective filing date of the '296 patent. Ex. 1005, Cover. Song is therefore

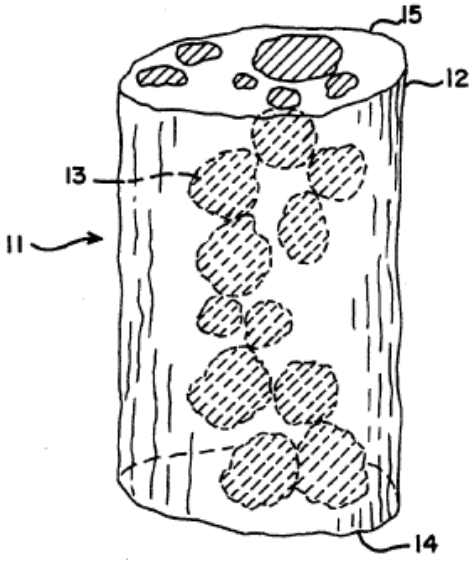
prior art under 35 U.S.C. § 102(b). Song was not provided to or considered by the PTO during prosecution of the '296 patent. Patent Owner did not cite Song to the Patent Office and the Patent Office did not identify Song.

2. Overview of Song

Song describes a "delivery system … for the gradual release of an active agent." Ex. 1005, Abstract; *see also id.* at 1:51-65. The delivery system is a "fiber" made of "an active agent and a wall material," in which "particles of active agent are dispersed throughout the wall material." *Id.*, Abstract; *see also id.* at 1:51-65. Song is "particularly directed to delivery systems" in which the wall material is made of "biodegradable polymers." *Id.* at 1:12-15.

The "active agent" in the fibers of Song can be any substance, including "drugs" such as "anti-inflammatory substance" or "anti-coagulants," among others. *Id.* at 4:32-66. The "active agent is dispersed throughout the support matrix," and may form a "contiguous phase," although the active agent phase "does not necessarily have to be in a contiguous phase." *Id.* at 2:38-42.

The biodegradable polymer "wall material" and the dispersed "active agent" in the fibers of Song "must be immiscible with each other." *Id.* at 5:5-9. Figure 1 of Song illustrates a gradual release "fiber (11)" with an "active agent (13) [] dispersed throughout the support matrix [12]":



Id. at Figure 1, 3:44-56. As demonstrated below, Song discloses each and every element of claims 1, 11, 16-17, and 26 of the '296 patent.

3. Claim 1

Claim 1 of the '296 patent is directed to a composition that includes "at least one biodegradable polymer fiber" composed of two "immiscible" phases: the polymer portion of the fiber, and the discrete drug-containing regions dispersed throughout the fiber. *See* § VIII.C., *supra*. As shown below, Song meets each and every element of claim 1 and anticipates that claim under the constructions adopted by the district court or those proposed by Patent Owner in the District Court Action.

[1] "at least one biodegradable polymer fiber"

Song discloses a composition including at least one biodegradable polymer fiber. Specifically, Song describes a "delivery system … for the gradual release of an active agent," which "comprises an active agent and a wall material." Ex. 1005,

Abstract; *see also id.* at 1:52-65. This "delivery system" is in the form of a "fiber." Ex. 1005, Abstract; *see also id.* at 1:52-65, 11:20-14:35 (claims 1-29, all requiring a "fiber").

Song is "particularly directed to" fibers in which the wall material is made of "biodegradable polymers." *Id.* at 1:12-15. Song explains that "the use of biodegradable polymers is beneficial for many applications." *Id.* at 5:10-12. Song further provides that "[e]xamples of biodegradable polymers useful in [its] invention include copolymers of lactic and glycolic acid (PLGA)," among others. *Id.* at 5:12-18. These were among the most commonly used biodegradable polymers, and are identified as "[p]referred" in the '296 patent. *See* § VIII.A, *supra*; Ex. 1001 at 9:65-10:4. Thus, Song discloses a biodegradable polymer fiber as recited in claim 1 of the '296 patent. *See* Ex. 1002 ¶ 74.

[1.a.] "composed of a first phase and a second phase"

The biodegradable polymer fiber of Song contains a first phase (the polymer portion of the fiber) and a second phase (the discrete drug-containing regions dispersed throughout the fiber). *See* § VIII.C.1, *supra*.

Song's first phase is a biodegradable polymer, which makes up the "wall material" of its fibers. Ex. 1005, Abstract; *id.* at 1:10-15, 5:10-18. Song explains that "[t]he wall material can be any spinnable synthetic or natural **polymer**," and that "the use of **biodegradable polymers** is beneficial for many applications." *Id.* at

5:1-18 (emphasis added). Song is "particularly directed" to delivery systems "with biodegradable polymers." *Id.* at 1:10-15.

Song's second phase consists of discrete drug-containing regions dispersed throughout the fiber. The second phase is "an active agent [] **dispersed throughout** the support matrix." *Id.* at 2:38-42 (emphasis added); *see also id.* at 3:30-39, Figure 1. Claims 1 and 15 of Song recite "particles of active agent **dispersed throughout** the wall material" of the fiber, claim 2 recites "particles of active agent **dispersed throughout the fiber**," and claim 20 recites "crystalline active agent … **dispersed throughout the fiber**." *Id.* at 11:19-51, 12:15-27, 12:43-57 (claims 1, 2, 15, and 20) (emphasis added).

Song thus describes a biodegradable polymer fiber composed of a first phase (biodegradable polymer wall material) and a second phase (dispersed particles of active agent). *See* Ex. 1002 ¶¶ 75-78.

[1.b.] "the first and second phases being immiscible"

The first and second phases of Song's biodegradable polymer fiber are immiscible, meaning that they are incapable of dissolving into one another. *See* § VIII.C.2, *supra*. Song expressly states that the first phase (wall material of the fiber) and the second phase (dispersed active agent) "**must be immiscible with each other**." Ex. 1005 at 5:5-8 (emphasis added). Thus, Song explicitly discloses a fiber

containing "immiscible" first and second phases as required by claim 1 of the '296 patent. *See* Ex. 1002 ¶ 79.

[1.c.] "and wherein the second phase comprises one or more therapeutic agents"

The second phase of the biodegradable polymer fibers disclosed by Song "comprises one or more therapeutic agents." As discussed above, Song describes and claims fibers with "[a]n active agent [] dispersed throughout" the fiber (Ex. 1005 at 2:38-40), such as "anti-inflammatory substances" or "anti-coagulants," among others. *Id.* at 4:32-66; *see also* § X.A.3.[1.a], *supra*; Ex. 1002 ¶ 80.

* * *

For these reasons, Song discloses each and every limitation of claim 1 of the '296 patent and anticipates that claim.

[2] Patent Owner's Proposed Constructions

Song also anticipates claim 1 of the '296 patent under any of the (incorrect) claim constructions proposed by Patent Owner in the District Court Action.

In the District Court Action, Patent Owner proposed construing:

- "first phase" as "continuous phase comprising the polymer that makes up the fiber," or as "the first substance is made up of polymer"; and
- "second phase" as "dispersed phase containing one or more therapeutic agents," or as "the second substance [which] contains drug(s) and particles

> or droplets of the second substance are dispersed within the first substance."

Ex. 1018 at 8-9; § VIII.C.1, *supra*. Song discloses the "first phase" and "second phase" limitations so construed for the same reasons set forth above. In the fibers of Song, "an active agent is dispersed throughout" a polymer fiber. *See* § X.A.3.[1.a], *supra*.

Patent Owner argued in the District Court Action that the term "immiscible" means "not miscible," or "incapable of mutual solution at the proportions used." Ex. 1018 at 11; § VIII.C.2, *supra*. Song explicitly requires that that the polymer wall material of the fiber and the dispersed active agent "**must be immiscible with each other**." Ex. 1005 at 5:5-8 (emphasis added); *see also* § X.A.3.[1.b.], *supra*. Accordingly, the polymer and the dispersed drug of Song's fibers must be "not miscible," and they must be "incapable of mutual solution," regardless of "the proportions used." Ex. 1002 ¶ 84. Indeed, Song claims fibers in which the concentration of dispersed active agent may vary considerably. *See id.* at 11:38-51 (claim 2). Yet in any case, the dispersed active agent and the polymer portion of the fiber "must be immiscible with each other." *Id.* at 5:5-8.

4. Dependent Claim 11

Claim 11 depends from claim 1 and adds a limitation reciting that "said one or more therapeutic agents are selected from the group consisting of … anti-inflammatory compounds … [and] anti-coagulation agents," among others.

Song meets all the limitations of claim 1 as described above. *See* § X.A.3, *supra*. With regard to the therapeutic agents recited in claim 11, Song states that the "active agents may be … anti-inflammatory substances … [or] anti-coagulants," among others. Ex. 1005 at 4:40-66. Accordingly, Song discloses each and every limitation of claim 11 and anticipates that claim. *See* Ex. 1002 ¶ 87.

5. Dependent Claims 16-17

Claim 16 depends from claim 1 and adds a limitation reciting that "said biodegradable polymer is a single polymer, a co-polymer, or a mixture of polymers selected from the group consisting of … aliphatic polyesters," among others.

Claim 17 recites the biodegradable polymer fiber of claim 16 "wherein said aliphatic polyesters are selected from the group consisting of poly(glycolic acid), poly(lactic acid) … and copolymers, blends and mixtures thereof."

Song meets all the limitations of claim 1 as described above. *See* § X.A.3, *supra*. Song further discloses a fiber of claim 1 in which the biodegradable polymer is selected from the group of art-known polymers recited in claims 16 and 17.

The '296 patent identifies "Poly(glycolic acid)," "Poly(lactic acid)" and their "copolymers" as "Aliphatic polyesters." *See* Ex. 1001 at 10:13-38 (Table 1 adapted from Wong and Mooney 1997); *see also id.* at 28:49-54 (claim 17) ("said aliphatic polyesters are selected from the group consisting of poly(glycolic acid), poly(lactic acid) … and copolymers, blends and mixtures thereof"). Song discloses the use of the same aliphatic polyesters in its fibers: "biodegradable polymers useful in this invention include copolymers of lactic and glycolic acid … [and] polyglycolic acid." Ex. 1005 at 5:12-18. As stated in the '296 patent, "copolymers of lactic and glycolic acid" and "polyglycolic acid" are aliphatic polyesters. Ex. 1001 at 10:13-38; Ex. 1002 ¶ 90. Accordingly, Song discloses each and every limitation of claims 16-17 and anticipates those claims.

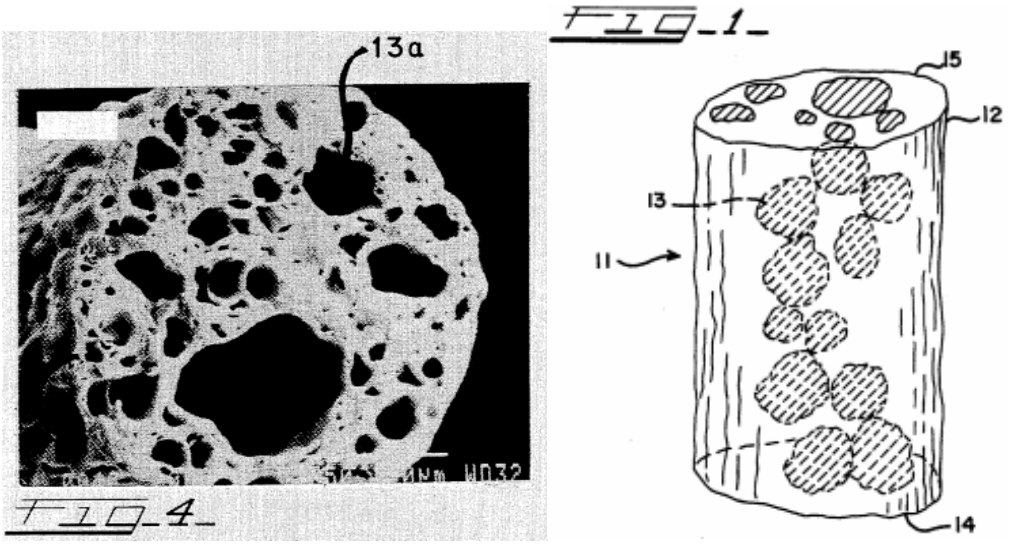
6. Dependent Claim 26

Claim 26 depends from claim 1 and adds a limitation reciting that "said one or more therapeutic agents are released at varying rates over time from said fiber."

Song meets all the limitations of claim 1 as described above. *See* § X.A.3, *supra*. Song also discloses varying rates of drug release over time. Song discloses and claims "[a] delivery system for the gradual release of an active agent" in the form of "a fiber." Ex. 1005 at 11:20-37 (claim 1). In the fibers of Song, "[t]he particles of active agent are dispersed through out the wall material such that the

particles of active agent are gradually released from the fiber when the fiber is contacted with a solvent for the active agent." Ex. 1005 at 1:61-65.

Drug is gradually released from the fiber as a solvent for the active agent "first dissolves the active agent in the openings at the ends … of the support matrix," then "fills these channels and begins to dissolve the newly exposed active agent." *Id.* at 3:63-4:3. As demonstrated in the figures, particles of dispersed drug are of varying size and random location within the fibers of Song:



Id. at Figures 1 and 4. The release rate from these fibers will vary over time. Ex. 1002 ¶¶ 92-93. Specifically, drug will be released at a varying rate as different dispersed drug regions of varying sizes and random locations within the fiber become "newly exposed" to solvent, dissolve, and are released from the fiber over time. *Id.* at 3:63-4:3; Ex. 1002 ¶¶ 92-93.

Accordingly, Song discloses each and every limitation of claim 26 and anticipates that claim.

At a minimum, Song renders claim 26 obvious in view of the knowledge of a POSA for the reasons above. A POSA would have understood from the design and release mechanism of Song's fibers that the active agent in Song's fibers will be released at varying rates over time. Ex. 1002 ¶¶ 95-96; Ex. 1005 at 2:62-68, 3:63-4:3. Indeed, it was well known that drug release from polymer matrix systems like those described in Song necessarily varies with time. *See* Ex. 1002 ¶ 95; Ex. 1020 (Dunn 1981) at 127. A POSA thus would have practiced Song's teachings to prepare a fiber that releases an active agent at varying rates over time with a reasonable expectation of success. Ex. 1002 ¶¶ 95-96.

* * *

For these reasons, Song discloses each and every element of claims 1, 11, 16-17, and 26 of the '296 patent. Song anticipates these claims or, at a minimum, renders these claims obvious in view of the knowledge of a POSA, under the claim constructions adopted by the court or those proposed by Patent Owner in the District Court Action.

B. Ground 2: Claims 4 and 20 Are Obvious Over Song Combined with the Knowledge of a POSA

1. Dependent Claim 4

Claim 4 recites "[t]he composition of claim 1, wherein said fiber is woven, braided or knitted in an assembly with other fibers, and at least one fiber in the assembly comprises one or more therapeutic agents." As demonstrated above, Song discloses each and every element of claim 1 and anticipates that claim. *See* § X.A.3, *supra*.

Using a "woven, braided or knitted" assembly of Song's fibers would have been obvious in view of Song and the knowledge of a POSA. Ex. 1002 ¶¶ 100-105. Song relates to polymer fibers. Ex. 1005 at 1:51-65, 5:10-18, 5:26-45. Although it does not state whether its polymer fibers are single strands or woven and braided, it was well known that polymer fibers could be either. Ex. 1002 ¶ 100; *see also* § VIII.A., *supra*. Indeed, Martin (the prior art reference over which the application resulting in the '296 patent was repeatedly rejected in prosecution, *see* § VIII.B., *supra*) explains that polymer fibers "are particularly useful" in "textile-based structure[s]," which include "**woven, knitted, braided** or non-woven constructions." Ex. 1013 (Martin) at 22:33-24:20 (emphasis added). Martin explains that these "structures and processes for their formation are **well known in the art as exemplified and described in textbooks** such as Textiles by N. Hollen and J. Saddler, The MacMillan Company (1973)." *Id.* at 23:25-28 (emphasis

added). Song also incorporates and cites references that discuss weaving, braiding, and knitting polymer fibers. Ex. 1005 at 5:28-33 (incorporating by reference Billmeyer); *id.* at References Cited (citing, *e.g.*, U.S. Patent No. 4,766,036 and European App. Pub. No. 0253554 (*i.e.*, Curatolo)).

A POSA would have known that the fibers of Song can be woven, braided or knitted. Ex. 1002 ¶¶ 100-103. Indeed, as discussed above, Song incorporates by reference portions of the *Fiber Technology* chapter of Billmeyer's TEXTBOOK OF POLYMER SCIENCE, which describes making "fabric" by "weaving" or "knitting" fibers together, or by using "[v]ariations of the weaving process [that] lead to … braids." Ex. 1008 (Billmeyer) at 525. In addition, Song cites U.S. Patent No. 4,766,036, which explains that polymer fibers may be "formed into … woven articles, knitted articles, ropes, braided articles, pile loops, and the like" (Ex. 1010 (Vaughn) at 8:3-6, 9:15-20), and Curatolo, which teaches that polymer fibers "can be … braided … to provide a greater overall surface area than that afforded by a straight elongated fiber." Ex. 1009 (Curatolo) at 4:20-23; *see also id.* at 7:1-4.

Woven, braided or knitted fibers offer well-known advantages for the use of polymer fibers in drug delivery. Ex. 1002 ¶ 104; *see also* Ex. 1013 (Martin) at 22:33-24:20. For example, it was well known that braided assemblies "provide a greater overall surface area than that afforded by a straight elongated fiber" (Ex. 1009 (Curatolo) at 4:20-23), which is advantageous for drug delivery. Ex. 1002

¶ 104. Further, a POSA would have had a reasonable expectation of success in weaving, braiding, or knitting Song's fibers. Ex. 1002 ¶ 105. Weaving, braiding, and knitting were simple, textbook techniques. *See* Billmeyer (Ex. 1008) at 525; Ex. 1013 (Martin) at 23:25-24:4. Indeed, the '296 patent does not provide any specific teachings of how to weave, braid, or knit fibers, as none were needed for a POSA. *See generally* Ex. 1001.

Accordingly, the combination of Song and the knowledge of a POSA renders claim 4 of the '296 patent obvious.

2. Dependent Claim 20

Dependent claim 20 recites "[t]he composition of claim 1, wherein said fiber comprises a plurality of polymer layers, wherein an outer layer circumscribes an adjacent inner layer." As demonstrated above, Song discloses each and every element of claim 1 and anticipates that claim. *See* § X.A.3, *supra*.

The addition of "a plurality of polymer layers" to the fibers of Song would have been obvious in view of Song's disclosures and the knowledge of a POSA. Ex. 1002 ¶¶ 107-111. Song is concerned with the "gradual release of active agents" from polymer fibers. Ex. 1005 at 1:8-15; *see also id.* at 1:51-65, 5:10-25. While Song does not expressly disclose adding multiple layers to its fibers, it would have been well known to a POSA that multiple polymer layers can be used to achieve a more gradual rate of drug release from a fiber over time. Ex. 1002 ¶¶ 108-109.

Indeed, Song's background discussion of the "the art of delivery systems for the gradual release of active agents" includes Dunn and Lewis's work with multilayered fibers. Ex. 1005 at 1:16-35 (discussing Dunn and Lewis 1981 (Ex. 1020) at 125-46). A POSA would have been well aware of the fact, as demonstrated in Dunn and Lewis, that additional layers are a means of controlling the rate of drug release from a fiber. Ex. 1020 (Dunn 1981) at 135-145; Ex. 1002 ¶ 109. The references cited in Song also include Dunn and Lewis's European App. Pub. No. 0126827, which describes achieving gradual drug release from polymer fibers by coating "active agent laden fibers with a coating of active agent free polymer." Ex. 1011 ('827 application) at 13:8-18.

A POSA thus would have been well aware of the benefits of multiple polymer layers for achieving a gradual rate of drug delivery from a fiber. Ex. 1002 ¶ 109. A POSA would have known, as Dunn and Lewis had shown in the paper cited by Song, that "release rates of the coaxial fibers are controlled by the polymer used as the rate-controlling sheath material…." Ex. 1020 (Dunn 1981) at 144.

Further, a POSA would have had a reasonable expectation of success in adding multiple polymer layers to the fibers of Song. Multilayered polymer fibers had been successfully prepared and used for gradual drug release since at least the early 1980s. Ex. 1020 (Dunn 1981) at 128-145. Indeed, the inventors of the '296 patent acknowledge that "core and sheath" fibers with coaxial polymer layers were

"**standard fiber structures well known to those familiar in the art**" at the time of the '296 patent. Ex. 1001 at 20:33-36 (emphasis added).

Accordingly, claim 20 of the '296 patent would have been obvious over Song and the knowledge of a POSA.

C. Ground 3: Claim 4 Is Obvious Over Song in View of Billmeyer or Curatolo

Claim 4 depends from claim 1 and recites "the composition of claim 1, wherein said fiber is woven, braided or knitted in an assembly with other fibers, and at least one fiber in the assembly comprises one or more therapeutic agents." Claim 4 is obvious over Song in view of Billmeyer or Curatolo.

1. Billmeyer and Curatolo Are Prior Art Not Considered by the Patent Office

Billmeyer was published in 1971, decades before the earliest claimed priority date of the '296 patent. Ex. 1008 at copyright page. Curatolo was published in 1988, eleven years before the earliest claimed priority date of the '296 patent. Ex. 1009, Cover. Billmeyer and Curatolo are prior art under 35 U.S.C. § 102(b). Neither reference was provided to or considered by the PTO during prosecution of the '296 patent.

2. Overview of Billmeyer

Billmeyer's TEXTBOOK OF POLYMER SCIENCE is a well-known textbook in the field of polymer science. Ex. 1002 ¶ 113. One of its chapters teaches "Fiber

Technology." *See* Ex. 1008 at 513-532. Portions of this chapter disclosing "spinning" techniques for forming polymer fibers are incorporated by reference in Song. Ex. 1005 at 5:28-33. In the same chapter, Billmeyer explains that fibers may be "transformed into a fabric," and that "[t]he most important method of doing this is weaving, in which a set of yarns running lengthwise [] is interlaced with a second set at right angles." Ex. 1008 at 525. Billmeyer also explains that "[o]ther methods of producing fabrics includ[e] knitting, in which a series of yarns is looped together" and "[v]ariations of the weaving process lead to … braids." *Id*.

3. Overview of Curatolo

Curatolo was cited in connection with prosecution of Song. *See* Ex. 1005, References Cited (listing European App. Pub. No. 0253554). Curatolo discloses "drug-containing fibers for the controlled release of said drug in the gastrointestinal tract of a mammal." Ex. 1009 at 2:1-4. The fibers of Curatolo "can be constructed of a variety of materials such as polymers and waxes, as carriers of the drug," and may be "bioerodible, erodible or biodegradable in [the] environment." *Id.* at 4:4-6. "[T]he use of fibers comprising bioerodible polymers: i.e., polymers which dissolve, disintegrate or degrade, is favored …." *Id.* at 5:10-11.

As discussed above (*see* § X.B.1, *supra*), Curatolo teaches that its fibers "can be … braided … to provide a greater overall surface area than that afforded by a straight elongated fiber." *Id.* at 4:20-23. Curatolo further explains that its polymer

fibers "can be made from extruded or woven fiber." *Id.* at 7:1-4; *see also id.* at 7:30-10:53 (Examples 1-4); § X.B.1, *supra*.

4. Motivation to Combine Song with Billmeyer or Curatolo and Reasonable Expectation of Success

A POSA would have had reason or motivation to combine Song with Billmeyer or Curatolo to create woven, braided, or knitted assemblies of Song's fibers. Ex. 1002 ¶¶ 116-117. While Song does not expressly state that its polymer fibers are woven, braided or knitted, a POSA would have been well aware of these textbook uses of polymer fibers as discussed above. Ex. 1002 ¶¶ 116-117; § X.B.1, *supra*. Indeed, Song would have directed a POSA to Billmeyer's discussion of woven, braided, or knitted fibers, because Song incorporates portions of the same chapter of Billmeyer in which these techniques are discussed. Ex. 1005 at 5:28-33; Ex. 1008 at 518-522, 525.

As discussed above, a POSA would have been motivated to make woven, braided or knitted assemblies of Song's fibers as taught by Billmeyer. § X.B.1, *supra*. Billmeyer also teaches that "tensile strength" is an important feature of polymer fibers (Ex. 1008 at 515), and braided fibers were known to have increased tensile strength over single strands. Ex. 1002 ¶ 116.

A POSA also would have been motivated to combine Song's drug-releasing fibers with Curatolo's teachings of braided drug-loaded fibers. Ex. 1002 ¶ 117. Curatolo relates to the release of active agents from polymer fibers, just as Song

does, and was cited in connection with the prosecution of Song. Ex. 1009 at 2:1-4, 3:44-49; Ex. 1005, References Cited. Song and Curatolo concern some of the same polymers and drugs for use in their fibers. Ex. 1005 at 4-40:66, 5:10-18; Ex. 1009 at 5:49-58, 6:49-7:4. Curatolo teaches that braided fibers "provide a greater overall surface area than that afforded by a straight elongated fiber" (Ex. 1009 at 4:20-23), a feature that a POSA would have recognized as advantageous for drug delivery using Song's fibers. Ex. 1002 ¶ 117.

A POSA would have had a reasonable expectation of success in combining Song with either Billmeyer or Curatolo to create woven, braided or knitted assemblies of Song's fibers. Weaving, braiding, and knitting are textbook techniques as discussed above. *See* § X.B.1., *supra*; Ex. 1002 ¶ 118.

5. Obviousness of Claim 4

As demonstrated above, claim 4 of the '296 patent is a straightforward combination of the anticipated fiber of claim 1 and art-known techniques of weaving, braiding, or knitting set forth in Billmeyer and Curatolo. *See* §§ X.B.1, X.C.1-3. Accordingly, the combination of Song with either Billmeyer or Curatolo renders claim 4 obvious.

D. Ground 4: Claim 20 Is Obvious Over Song in View Of Sidman

Claim 20 depends from claim 1 and recites "the composition of claim 1, wherein said fiber comprises a plurality of polymer layers, wherein an outer layer

circumscribes an adjacent inner layer." Claim 20 is obvious over Song in view Sidman.

1. Sidman is Prior Art Not Considered by the Patent Office

Sidman issued on September 28, 1982, over sixteen years before the earliest claimed priority date of the '296 patent. *See* Ex. 1006, Cover. Sidman is prior art under 35 U.S.C. § 102(b). Sidman was not provided to or considered by the PTO during prosecution of the '296 patent. Patent Owner did not cite Sidman to the Patent Office and the Patent Office did not identify Sidman.

2. Overview of Sidman

Sidman describes a "drug delivery device … formed of a poly-α-amino acid component having one or more drugs … contained therein." Ex. 1006, Abstract. "The poly-α-amino acid [] is a synthetic polymer" (*id.* at 5:29-30), which "must also possess … biodegradability." *Id.* at 9:19-21. The drug delivery device of Sidman may be "formed into such structures as … rods [and] fibers," among others. *Id.* at 9:11-15. The device contains a "drug to be delivered [] distributed throughout the [polymer]." *Id.* at 10:10-11. Potential drugs include "anticoagulants" and "antibiotics," among others. *Id.* at 9:44-56.

Sidman discloses that extrusion of a blend of polymer and drug "may be used to form fibers or rods such as shown in FIG. 2":

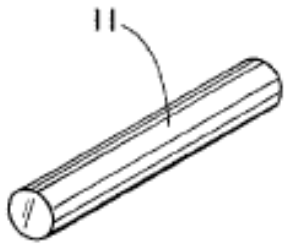


Fig. 2

Id. at Figure 2, 10:62-64; *see also id.* at 24:19-20 (claim 6). Sidman further explains that "it may be desirable to modify this implant configuration to obtain a drug release rate different from that obtained through the use of the unmodified rod structure of Fig. 2." *Id.* at 11:10-14. Thus, "[i]n the modification of FIG. 4," the fiber is formed of multiple polymer layers:

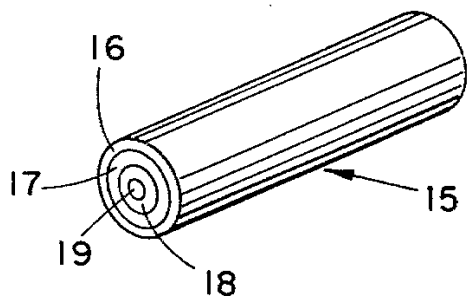


Fig. 4

Id. at Figure 4, 11:35-37 (implant device 15 formed of "layers" 16-19); *see also id.* at 24:21-25 (claim 7). Further, "each layer may have drug concentration different from that of an adjacent layer or layers." *Id.* at 11:38-39; *see also id.* at 24:21-25 (claim 7).

Sidman further explains that "it may be desirable to release two different substances in series" using its multilayered fibers with different drugs in different layers. *Id.* at 11:61-12:8.

Sidman teaches that fibers containing "multiple layers may be coextruded using well developed techniques." *Id.* at 11:43-45. Sidman also teaches making a multilayer polymer fiber by "form[ing] a core and coat[ing] it with successive layers of a polymeric matrix solution containing the drug dissolved or dispersed therein." *Id.* at 11:50-54. Sidman explains that a POSA can also use "a combination of techniques, e.g., extrusion and coating" to make multilayered polymer fibers. *Id.* at 11:54-60.

3. Motivation to Combine Song and Sidman and Reasonable Expectation of Success

A POSA would have been motivated to combine the teachings of Song and Sidman to make the drug-loaded fiber of Song with multiple polymer layers. Ex. 1002 ¶¶ 127-128. As discussed above, Song is concerned with "gradual release of active agents." Ex. 1005 at 1:16-26; § X.B.2, *supra*. And although Song does not expressly discuss the addition of multiple polymer layers to its fibers, a POSA would have been well aware that adding layers of polymer can lead to more gradual and sustained drug release from a fiber. Ex. 1002 ¶ 128; § X.B.2, *supra*.

A POSA would have been motivated to combine Song's drug-loaded fibers with Sidman's multiple polymer layers in order to achieve the objective of gradual

drug release. Ex. 1002 ¶ 128. Sidman teaches that "each layer may have a concentration different from that of an adjacent layer," leading to a more sustained rate of drug release from the fiber. Ex. 1006 at 11:14-17, 11:35-43.

A POSA also would have had a reasonable expectation of success in combining Song's fibers with Sidman's teaching of multiple polymer layers. Ex. 1002 ¶ 129. Making a fiber with multiple polymer layers would have been routine. *Id.*; *see also* § X.B.2, *supra*. As Sidman explains, "multiple layers may be coextruded using well developed techniques." Ex. 1006 at 11:43-54. Indeed, the inventors of the '296 patent acknowledged that multilayered "core and sheath" fibers were "standard fiber structures well known to those familiar in the art." Ex. 1001 at 20:33-36.

4. Obviousness of Claim 20

As demonstrated above, the combination of Song and Sidman discloses each and every limitation of claim 20 and renders the claim obvious. *See* §§ X.A.3, X.D.1-3, *supra*.

E. Ground 5: Claims 1, 4, 11, 16-17, 20, and 26 Are Anticipated or Obvious Over Choi In View of the Knowledge of a POSA

1. Choi is Prior Art Not Considered by the Patent Office

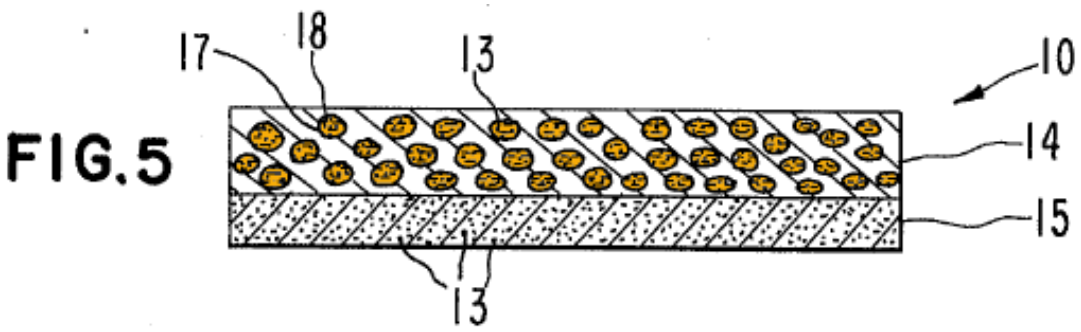
Choi issued on June 6, 1978, over twenty-one years before the earliest claimed priority date of the '296 patent. Choi is prior art under 35 U.S.C. § 102(b).

Choi was not provided to or considered by the PTO during prosecution of the '296 patent.

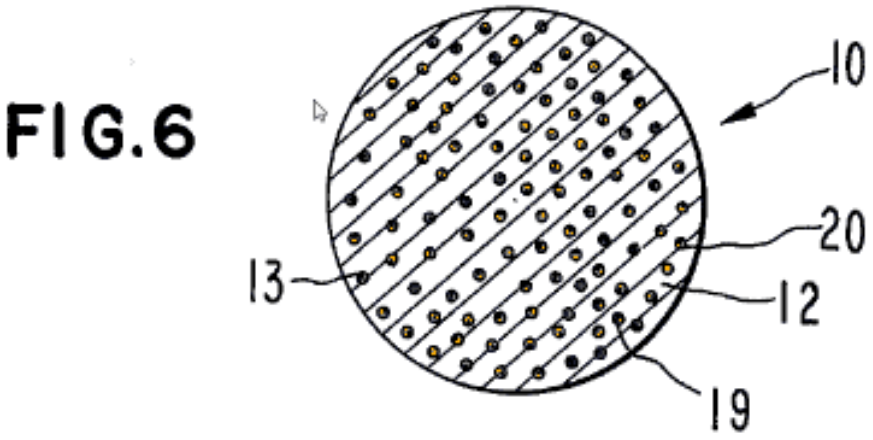
2. Overview of Choi

Choi discloses "polymers [] useful for making articles of manufacture, including devices and coatings for delivering beneficial agents." Ex. 1007, Abstract. "The polymers can be used for making devices and coatings for releasing a beneficial agent, as the polymers erode at a controlled rate, and thus can be used as carriers for drugs for releasing drug at a controlled rate to a drug receptor, especially where bioerosion is desired." *Id.* at 2:63-68. "[T]he polymers can be extruded into filaments, spun into fibers … and processed by like standard methods of manufacture." *Id.* at 28:22-28.

Choi describes various embodiments of a drug-delivery device made of its bioerodible polymers, referred to as "device 10" throughout. *Id.* at, *e.g.*, 33:1-4, 33:41-44. In the embodiment of Figure 5, an "active agent" (13) is "present in cells" (17), which are "dispersed throughout the matrix" of biodegradable polymer. *Id.* at 33:1-40. Within the cells (17), the active agent is "dissolved in a liquid 18 that is a solvent for the agent and a nonsolvent for the polymer." *Id.* at 33:8-11, Figure 5 (highlighting of dispersed drug-containing cells added):



In the embodiment of Figure 6, "device 10 [is] formed of a bioerodible polymer 12 comprising a multiplicity of microcapsules 19 with each microcapsule having a wall 20 made of an agent release rate controlling material. An agent 13 is housed within microcapsules 19." *Id.* at 33:41-45, Figure 6 (highlighting of drug-containing microcapsules added):



Both versions of device 10 are made of biodegradable polymers that can be "spun into fibers." *Id.* at 28:18-28; Ex. 1002 ¶¶ 131, 141. And both versions of device 10 contain discrete drug-containing regions dispersed throughout the fiber. *See id.* at 33:1-34:6, Figures 5-6; Ex. 1002 ¶¶ 139-140.

3. Claim 1

Claim 1 recites a composition that includes a "biodegradable polymer fiber" composed of two "immiscible" phases: "the polymer portion of the fiber," and "the discrete drug-containing regions dispersed throughout the fiber." *See* § VIII.C., *supra*. As shown below, Choi discloses every element of claim 1.

[1] "at least one biodegradable polymer fiber"

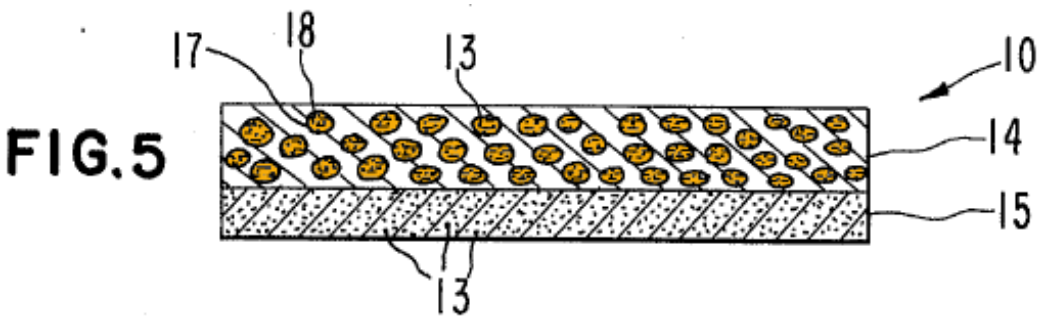
Choi describes biodegradable polymer fibers. Specifically, Choi discloses "polymers [] useful … for delivering beneficial agents." Ex. 1007, Abstract. The polymers "erode at a controlled rate, and thus can be used as carriers for drugs … especially where bioerosion is desired." *Id.* at 2:63-68. "[T]he polymers can be extruded into filaments [and] spun into fibers." *Id.* at 28:23-27.

[1.a.] "composed of a first phase and a second phase"

Choi discloses embodiments of biodegradable polymer fibers with a first phase (the polymer portion of the fiber) and a second phase (the discrete drug-containing regions dispersed throughout the fiber). Ex. 1007 at 33:1-40 (Figure 5 example); and 33:41-34:6 (Figure 6 example).

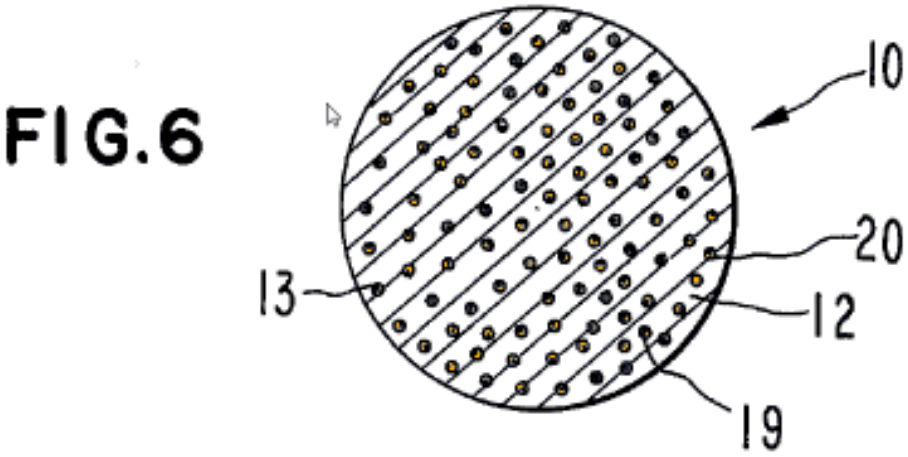
In the embodiment of Figure 5, "a plurality of cells 17 [is] **dispersed**" within a "polymeric matrix" (14). *Id.* at 33:7-8 (emphasis added). Within those dispersed cells, "[a]n agent 13 ... is dissolved in a liquid 18 that is a solvent for the agent and a nonsolvent for the polymer." *Id.* at 33:8-11. (In Choi, the term "agent" encompasses

"active agents," including "drugs." *Id.* at 29:18-29.) Thus, the drug-loaded "cells" in Figure 5 form "discrete drug-containing regions dispersed throughout the fiber" (Ex. 1018 at 10):



Ex. 1007 at Figure 5 (highlighting of dispersed "cells" added).

In the embodiment of Figure 6, "device 10 [is] formed of a bioerodible polymer 12 comprising a multiplicity of microcapsules 19," and "[a]n agent 13 is housed within microcapsules 19." *Id.* at 33:41-34:6. Thus, as in Figure 5, the drug-filled "microcapsules" of Figure 6 form "discrete drug-containing regions dispersed throughout the fiber" (Ex. 1018 at 10):



Ex. 1007 at Figure 6 (highlighting of microcapsules added).

Figures 5 and 6 both describe embodiments of polymer drug delivery device 10, which Choi discloses can be "spun into fibers." *Id.* at 28:18:28; Ex. 1002 ¶ 141. Thus, in Figure 10, device 10 is shown as a twisted fiber assembly. *Id.* at Figure 10. In Figure 10, device 10 is "**made of two fibers**, 26a and 26b, with one fiber 26a intertwisted with fiber 26b to provide a dual element device 10." *Id.* at 35:44-51 (emphasis added). The two fibers "are made of the like or unlike **bioerodible polymers** 12 containing **the same or different drugs** ...." *Id.* at 35:46-51.

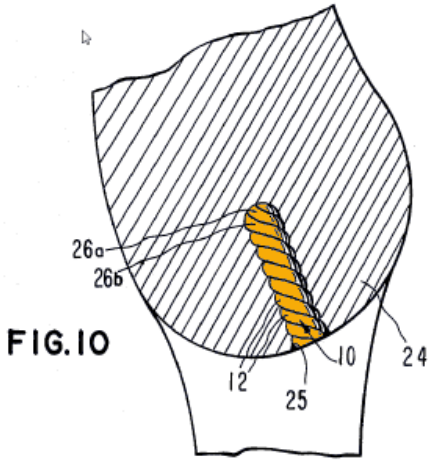


FIG. 10

Id. at Figure 10 (highlighting of fibers added).

Thus, Choi discloses drug delivery device 10 with dispersed drug-containing regions in the form of a biodegradable polymer fiber, and discloses these limitations of claim 1 of the '296 patent. Ex. 1002 ¶¶ 139-140.

Further, even if Choi did not explicitly disclose that the biodegradable polymers with dispersed drug-containing cells and microcapsule of Figures 5 and 6 could be formed into fibers, a POSA would have been motivated to do so and would

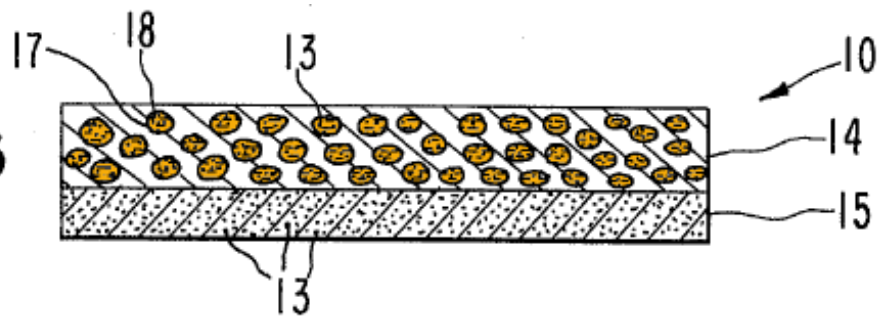
have had a reasonable expectation of success. Ex. 1002 ¶ 143. Choi teaches that a fiber format "provides the medical profession with a device for insertion into the natural cavities of the animal body," in order to "release[] a drug for promoting healing effects." *Id.* at 35:38-51. Choi further explains that the polymers of its "delivery devices" can be "spun into fibers" using "standard methods of manufacture." Ex. 1007 at 28:18-28; Ex. 1002 ¶ 143.

[1.b.] "the first and second phases being immiscible"

The first and second phases of Choi's Figure 5 and Figure 6 embodiments are "immiscible," meaning they are "incapable of dissolving into one another." § VIII.C., *supra*; Ex. 1018 at 14.

In Figure 5, "[a]n agent 13 is present in cells 17, which agent is dissolved in a liquid 18 that is a solvent for the agent and **a nonsolvent for the polymer**." Ex. 1007 at 33:7-11 (emphasis added).

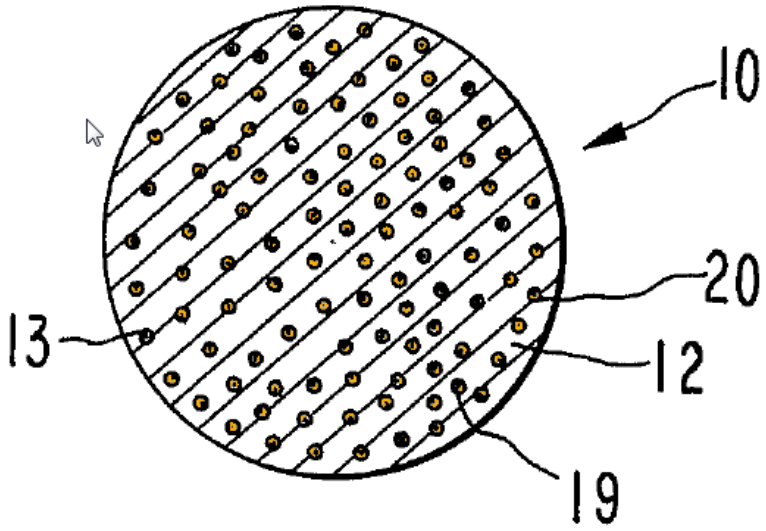
FIG.5



Id. at Figure 5 (highlighting of dispersed "cells" added). Because the drug-loaded cells are made of "**a nonsolvent for the polymer**," these dispersed drug-containing regions are incapable of dissolving into the surrounding polymer. Ex. 1002 ¶ 145.

Similarly, in Figure 6, device 10 is formed "of a bioerodible polymer 12 comprising a multiplicity of microcapsules 19 with each microcapsule having a wall 20 made of an agent release rate controlling material. An agent 13 is housed within microcapsules 19." Ex. 1007 at 33:41-45.

FIG.6



Id. at Figure 6 (highlighting of microcapsules added). Each microcapsule (19) is encapsulated by "wall" material (20), which acts as a barrier preventing the contents of the microcapsule from mixing into the surrounding biodegradable polymer. *Id.* at 33:41-34:6; Ex. 1002 ¶ 146. Indeed, Choi explains that the contents of the microcapsules are released only when device 10 "bioerodes," thus exposing the drug-filled microcapsules to the surrounding tissues. Ex. 1007 at 33:50-54. The drug-containing microcapsules therefore cannot dissolve in the surrounding polymer—rather, they are released only when that polymer bioerodes. Ex. 1002 ¶ 147.

[1.c] "and wherein the second phase comprises one or more therapeutic agents"

As discussed above, Choi describes fibers with dispersed drug-containing regions. *See* § X.E.3.[1]-[1.b.], *supra*. Accordingly, the second phase of Choi comprises one or more therapeutic agents.

* * *

For these reasons, Choi discloses each and every limitation of claim 1 of the '296 patent and anticipates that claim or, at a minimum, renders claim 1 obvious.

[2] Patent Owner's Proposed Constructions

Choi also anticipates or renders obvious claim 1 of the '296 patent under any of the (incorrect) claim constructions proposed by Patent Owner in the District Court Action.

As discussed above (*see* § VIII.C., *supra*), Patent Owner proposed construing "first phase" as "continuous phase comprising the polymer that makes up the fiber," or "the first substance is made up of polymer"; and "second phase" as "dispersed phase containing one or more therapeutic agents," or "the second substance [which] contains drug(s) and particles or droplets of the second substance are dispersed within the first substance." Ex. 1018 at 8-10. Choi discloses the "first phase" and "second phase" limitations under any of these constructions for the reasons discussed above. Choi discloses discrete drug-loaded cells or microcapsules dispersed throughout a polymer fiber. *See* § X.E.3.[1.a.], *supra*. Accordingly, the

fibers of Choi contain a first phase and a second phase under Patent Owner's proposed constructions in the District Court Action.

Further, the first and second phases of Choi's fibers are "immiscible" under either of Patent Owner's district court proposals. Patent Owner proposed construing the term "immiscible" as "not miscible," or "incapable of mutual solution at the proportions used." Ex. 1018 at 11-14. Choi requires its drug-loaded cells to be made of a "nonsolvent for the polymer." Ex. 1007 at 33:7-11. As a result, the drug-loaded cells must be "not miscible" with the polymer portion of the fiber. Ex. 1002 ¶ 152. They also must be "incapable of mutual solution," regardless of "the proportions used"—a nonsolvent for the polymer cannot form a solution with the polymer. *Id.* The drug-loaded microcapsules of Choi are "not miscible" with the polymer portion of the fiber, and they are "incapable of mutual solution" with the polymer portion of the fiber. Ex. 1002 ¶ 152. The microcapsules of Choi are encapsulated by a "rigid[]" material forming a "wall" between the contents of the microcapsule and the polymer. *Id.* at 33:41-61; Ex. 1002 ¶ 152.

4. Dependent Claim 4

Claim 4 requires the fiber of claim 1 to be "woven, braided or knitted in an assembly with other fibers." For the reasons described above, Choi anticipates claim 1 or, at a minimum, renders it obvious. *See* § X.E.3, *supra*. Choi also discloses

drug-loaded biodegradable polymer fibers that are "woven, braided or knitted" with other fibers.

As discussed above, Figure 10 of Choi is "made of two fibers *26a* and *26b*, with **one fiber *26a* intertwisted with fiber *26b* to provide a dual element device 10**." Ex. 1007 at 35:37-45 (emphasis added).

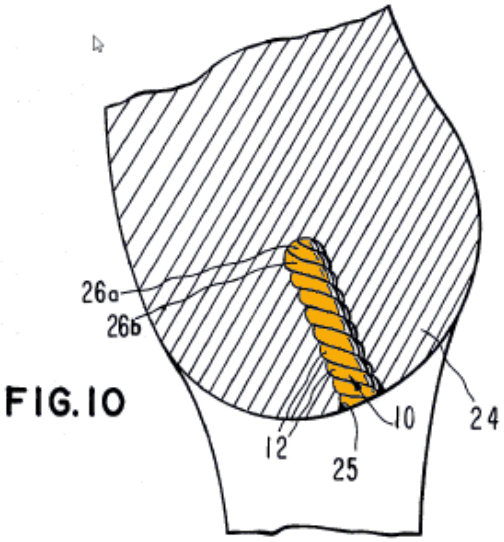


FIG. 10

Id. at Figure 10 (highlighting of fibers added); *see also id.* at 37:62-38:56, 38:64-68 (claims 1 and 4). Choi thus discloses the fiber of claim 1 "woven, braided or knitted in an assembly with other fibers" as required by claim 4 of the '296 patent.[1] Ex. 1002 ¶ 155.

[1] If claim 4 were deemed to require an assembly of more than two fibers, it would have been obvious to use additional fibers in Choi's "intertwisted" assembly. Ex.1002 ¶ 156. Choi teaches that its intertwisted fibers "contain[] the same or different drugs, thereby providing means for influencing drug release throughout the

5. Dependent Claim 11

Claim 11 recites "[t]he composition of claim 1 wherein said one or more therapeutic agents are selected from the group consisting of drugs … [and] anti-inflammatory compounds," among others.

Choi anticipates claim 1 or, at a minimum, renders claim 1 obvious as described above. *See* § X.E.3, *supra*. In addition, Choi discloses that the "'active agent' includes … **drugs**." Ex. 1007 at 29:22-29 (emphasis added). In Choi, "[t]he term 'drug' … broadly includes physiologically or pharmacologically active substances [including] … **anti-inflammatory agents**," among others. *Id.* at 29:30-30:37 (emphasis added). Accordingly, Choi anticipates claim 11 or, at a minimum, renders claim 11 obvious. Ex. 1002 ¶ 158.

6. Dependent Claims 16-17

Claim 16 recites "[t]he composition of claim 1, wherein said biodegradable polymer is a single polymer, a co-polymer, or a mixture of polymers selected from the group consisting of … aliphatic polyesters … [and] … **poly(ortho ester)**," among others. Choi anticipates claim 1 or, at a minimum, renders that claim obvious as described above. *See* § X.E.3, *supra*. With regard to the polymers recited in

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drug release period by varying the polymer and the drug." Ex. 1007 at 35:47-51. A POSA would have been motivated to braid more than two fibers to obtain further variation on drug release, and would expect success in doing so. Ex. 1002 ¶ 156.

claim 16, Choi is entitled "Drug Delivery Devices Manufactured from **Poly(orthoesters)** and Poly(orthocarbonates)," and its "invention concerns **orthoester** and orthocarbonate polymers." Ex. 1007, Abstract (emphasis added). Indeed, the numerous polymers described in Choi are all "ortho esters." *Id.* at 7:56-57; *see also id.* at 5:14-7:55; Ex. 1002 ¶ 160. Choi therefore discloses the additional elements of claim 16.

Claim 17 depends from claim 16. If "aliphatic polyesters" are selected as the biodegradable polymer in claim 16, claim 17 further requires that "said aliphatic polyesters are selected from the group consisting of **poly(glycolic acid)**, [and] **poly(lactic acid)**," among others, "and copolymers, blends and mixtures thereof."

Choi does not expressly disclose poly(glycolic acid) and poly(lactic acid), but these are two of the most well-known biodegradable polymers. It would have been obvious for a POSA to use poly(glycolic acid) or poly(lactic acid) as the biodegradable polymers in Choi. Ex. 1002 ¶ 163. A POSA would have been motivated to use poly(glycolic acid) or poly(lactic acid), because they were "[t]he **most widely investigated and advanced polymers** in regard to available toxicological and clinical data." Ex. 1019 (Lewis 1990) at 2 (emphasis added). They were also known to possess "biocompatibility, predictability of biodegradation kinetics [and] ease of fabrication," making them an optimal choice for the delivery fibers of Choi. *Id.* A POSA would have had a reasonable expectation of success in

using these polymers for the same reasons. *Id.* Accordingly, claim 17 is rendered obvious by Choi combined with the knowledge of a POSA at the time of the '296 patent.

7. Dependent Claim 20

Claim 20 recites "[t]he composition of claim 1, wherein said fiber comprises a plurality of polymer layers, wherein an outer layer circumscribes an adjacent inner layer."

Choi anticipates claim 1 or, at a minimum, renders that claim obvious as described above. *See* § X.E.3, *supra*. Choi also describes fibers with multiple polymer layers. As discussed above, Choi discloses that device 10 can be "spun into fibers … by like standard methods of manufacture." Ex. 1007 at 28:22-28. Choi further discloses that "[m]any variations of device 10 will be apparent to those skilled in the art. For example, a **greater number of layers can be used**." *Id.* at 33:20-22 (emphasis added); *see also id.* at 33:1-25. Choi further discloses embodiments in which device 10 "is a **multilayered structure** comprised of two outer layers." Ex. 1007 at 32:36-38 (emphasis added). Choi therefore anticipates claim 20 or, at a minimum, renders claim 20 obvious. Ex. 1002 ¶ 165.

8. Dependent Claim 26

Claim 26 depends from claim 1 and recites "[t]he composition of claim 1, wherein said one or more therapeutic agents are released at varying rates over time

from said fiber." Choi anticipates claim 1 or, at a minimum, renders that claim obvious as described above. *See* § X.E.3, *supra*. Choi also discloses that the described "polymers … are especially useful as bioerodible, agent-release, **rate controlling materials**." Ex. 1007 at 31:40-42 (emphasis added). Choi explains that its fibers can be made to release an agent "at a **variable rate**." *Id.* at 31:49-50 (emphasis added); *see also id.* at 40:62-42:2 (claim 26); Ex. 1002 ¶ 167.

Choi therefore anticipates claim 26 or, at a minimum, renders claim 26 obvious.

* * *

For these reasons, Choi anticipates claims 1, 4, 11, 16-17, 20, and 26 of the '296 patent or, at a minimum, renders those claims obvious in view of the knowledge of a POSA.

XI. NO OBJECTIVE INDICIA OF NON-OBVIOUSNESS

To the extent obviousness is considered for any of the challenged claims, Petitioner is not aware of any evidence of objective indicia of non-obviousness. Indeed, no evidence of objective indicia of non-obviousness, such as unexpected results or commercial success, was presented to the Patent Office during prosecution of the '296 patent. *See generally* Ex. 1004. Further, as demonstrated above, the '296 patent merely describes and claims what was already in the prior art. In addition, the '296 patent does not provide any working example of a drug delivery composition

that is covered by its claims. Petitioner requests that the Board wait to undertake evaluation of secondary consideration evidence, if any, presented by Patent Owner until Petitioner has been given an opportunity to test or respond to such evidence. *See Amneal Pharms., LLC v. Supernus Pharms., Inc.*, IPR2013-00368, slip op. at 12-13 (PTAB Dec. 17, 2013) (Paper 8).

XII. CONCLUSION

In view of the foregoing, Petitioner respectfully requests that Trial be instituted and that claims 1, 4, 11, 16-17, 20, and 26 of the '296 patent be cancelled.

Dated: December 7, 2018

Respectfully Submitted,

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CERTIFICATE OF COMPLIANCE
WITH TYPE-VOLUME LIMITATION

Pursuant to Rule 37 C.F.R. § 42.24(d), I hereby certify that, based upon the word count of the word-processing system used to prepare this petition, the number of words in this petition is 11,213. Pursuant to 37 C.F.R. § 42.24(a), this word count does not include a table of contents, a table of authorities, a certificate of service or word count, exhibits, appendix, or claim listing.

Dated: December 7, 2018

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CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e), I hereby certify that on December 7, 2018, I caused to be served a true and correct copy of the foregoing and any accompanying exhibits by: (1) Priority Mail Express upon the following correspondence address of record for U.S. Patent No. 6,596,296:

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Dallas, TX 75313-1851

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