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. 7,033,603
Issued: Apr. 25, 2006
Filed: May 2, 2003

Inter Partes Review No. IPR2019-00407

PETITION FOR *INTER PARTES* REVIEW

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Patent Trial and Appeal Board
US Patent and Trademark Office
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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, 2, 6, 11, 13, and 19 ("the challenged claims") of U.S. Patent No. 7,033,603 (Ex. 1001, "the '603 patent"). 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 '603 patent is directed to "fiber compositions comprising gels or hydrogels." Ex. 1001, Abstract. The challenged claims recite basic art-known combinations of biodegradable polymers, gels or hydrogels, and drugs. They are unpatentable over the prior art and should not have issued. This Petition identifies references that were not before the Patent Office during prosecution and anticipate the challenged claims. It also discusses critical developments in the prosecution of the European counterpart to the '603 patent, EP 1620038 B1 ("the '038 European patent," Ex. 1005), not previously brought to the Patent Office's attention, which demonstrate the unpatentability of the challenged claims issued in the United States.

Indeed, as recently as last year, the European counterpart to the '603 patent remained stuck in prosecution proceedings before the European Patent Office ("EPO") initiated by Patent Owner in 2004. *See generally* Ex. 1006. In those proceedings, the EPO concluded that the counterpart to challenged claim 1 lacks

novelty over U.S. Patent No. 5,186,936 ("Groves," Ex. 1007), a reference relied on in this Petition. Ex. 1006 at 370-71. In response, Patent Owner conceded that Groves discloses all limitations of challenged claim 1, but argued that an amendment could save claim 1 and its dependent claims from rejection. *Id.* at 379-381. Thus, in order to overcome Groves and eventually secure claims in Europe, Patent Owner was forced to add a significant limitation to the European equivalent of claim 1 requiring that "the concentration of the gel or the hydrogel varies as a function of distance along the long axis of the fiber." Ex. 1006 at 379-90; Ex. 1005 at 22:26-31 (claim 1). By Patent Owner's admission, the U.S. claims—which have no such limitation—are anticipated by Groves, a reference which the Patent Office never considered. As demonstrated below, the challenged claims are anticipated by Groves and other prior art.

Although the Patent Owner was on notice of Groves and had to narrow its European claims significantly to overcome it, Patent Owner asserted the '603 patent with its broader claims against Ethicon in U.S. district court. Those claims are challenged here. No discovery has been taken and no trial date has been set in the district court action. 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., allege that Ethicon's antibacterial sutures infringe the '603 patent and its parent, U.S. Patent No. 6,596,296 ("the '296 patent"). The '296 patent is the subject of a separate IPR petition that Ethicon is filing concurrently with this Petition. *See* IPR2019-00406. Ethicon, Inc. and Ethicon US, LLC were served with the complaint in the District Court Action on December 11, 2017. Ex. 1010; Ex. 1011. The court in the District Court Action has stayed all proceedings other than claim construction. *See* Ex. 1012 (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. 1013. 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 '603 and '296 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 Corporation's drug-eluting stents infringe the '603 and '296 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 '603 and '296 patents. That case was dismissed without prejudice on July 19, 2018.

On October 9, 2018, Medtronic filed IPR petitions regarding the '603 and '296 patents, assigned No. IPR2019-00038 and No. IPR2019-00037, respectively. Although Medtronic also challenges the claims of the '603 patent that are challenged in this Petition, Medtronic's petition also involves claims 4-5, 12, 15-18, 21-22, 24-26, and 31-33, which Ethicon does not challenge here. *Compare* IPR2019-00038, Paper 2 (Petition) at 6, *with* § V, *infra*. Further, with the exception of U.S. Patent No. 5,186,936 to Groves ("Groves," Ex. 1007), the Medtronic petition involves different art and does not discuss the prosecution of the European counterpart to the '603 patent, where Patent Owner concedes anticipation of the claims challenged by Ethicon. At this time, Patent Owner has not submitted preliminary responses to Medtronic's petitions and the Board has not issued an institution decision regarding 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 '603 patent is available for IPR and that Petitioner is not barred or estopped from requesting IPR of the '603 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 '603 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, 2, 6, 11, 13, and 19 of the '603 patent as unpatentable.

Claim 1 of the '603 patent recites:

> A drug delivery composition comprising at least one fiber having a bore and a wall, wherein said fiber comprises a first component and a second component, and wherein said first component is a biodegradable polymer and said second component is selected from the group consisting of a gel and a hydrogel.

In brief, the claim thus requires: (i) a bi-component fiber "having a bore and a wall," in which (ii) the "first component is a biodegradable polymer," and (iii) the "second component" is "a gel [or] a hydrogel."

Claims 2, 6, and 13 all depend directly from claim 1.

Claim 2 requires the biodegradable polymer component to be "present in the fiber bore" and the gel or hydrogel component to be "present in the fiber wall."

Claim 6 requires "a therapeutic agent [] loaded into the gel or hydrogel."

Claim 13 requires a "biodegradable polymer fiber" of claim 1 that "comprises a hydrophobic drug."

Claim 11 depends from claim 6 and requires that the therapeutic agent loaded into the gel or hydrogel be "selected from [a] group" that includes a broad range of therapeutic agents.

Claim 19 of the '603 patent is an independent claim. It recites: "A drug delivery composition comprising a fiber, wherein said fiber comprises an emulsion consisting essentially of a gel or hydrogel."

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, 2, 6, 11, 13, and 19 of the '603 patent be cancelled as unpatentable because they are anticipated under 35 U.S.C. § 102 or, at a minimum, obvious under 35 U.S.C. § 103 in view of the following prior art: U.S. Patent No. 5,186,936 to Groves (previously defined as "Groves," Ex. 1007); PCT International App. Pub. No. WO 95/23598 to Sirkar *et al.* ("Sirkar," Ex. 1008); and U.S. Patent No. 5,759,830 to Vacanti and Langer ("Vacanti," Ex. 1009). These references are prior art under pre-AIA § 102(b). The Patent Office did not consider any of these references during prosecution of the application for the '603 patent.

Petitioner presents the following grounds for trial:

Ground 1: Claims 1, 2, 6, 11, 13, and 19 are anticipated by Groves under 35 U.S.C. § 102 or, at a minimum, rendered obvious by Groves in view of the knowledge of a POSA under 35 U.S.C. § 103;

Ground 2: Claim 19 is anticipated by Sirkar under 35 U.S.C. § 102 or, at a minimum, rendered obvious by Sirkar in view of the knowledge of a POSA under 35 U.S.C. § 103;

Ground 3: Claims 1, 2, and 13 are anticipated by Vacanti under 35 U.S.C. § 102 or, at a minimum, rendered obvious by Vacanti in view of the knowledge of a POSA under 35 U.S.C. § 103.

VII. THE '603 PATENT

The '603 patent is entitled "Drug Releasing Biodegradable Fiber for Delivery of Therapeutics" and names Kevin D. Nelson and Brent B. Crow as inventors. Ex. 1001, Cover. The '603 patent issued on April 25, 2006 from App. No. 10/428,901, filed on May 2, 2003. *Id.* The earliest application to which it claims priority is Provisional Application No. 60/147,827, filed on August 6, 1999. *Id.*[1]

[1] Although it does not bear on this Petition, the '603 patent is entitled to a priority date no earlier than May 2, 2003, the filing date of the application that issued as the '603 patent. During prosecution of the European counterpart to the '603 patent, Patent Owner admitted that the European counterpart is not entitled to a priority date before May 2, 2003. *See* Ex. 1006 at 301-303 (arguing that Patent Owner's earlier PCT application, WO 01/10421 [D1], did not disclose the fibers recited in the '603 patent); *see also id.* at 396, 437 (striking claim to earlier priority date); *id.* at 618 (May 2, 2003 identified as claimed priority date in grant of European patent).

A. The State of the Art and the '603 Patent

The '603 patent is directed to "fiber compositions comprising gels or hydrogels" and their use in "tissue engineering and drug-delivery" applications. Ex. 1001, Abstract; Ex. 1002 ¶ 16. The fibers described in the patent are made of biodegradable polymers and gels or hydrogels. *See* Ex. 1001 at 2:64-3:33, 5:7-32. The fibers may also "contain one or more therapeutic agents," which can be "any drug incorporated in the biodegradable polymer fibers of the invention." *Id.* at 7:59-8:57.

The use of biodegradable polymers and gels or hydrogels in fibers for drug delivery was well known in the art by August 6, 1999, the claimed priority date of the '603 patent. Ex. 1002 ¶¶ 17-20. By that time, biodegradable polymers had been in use as drug delivery devices such as fibers for decades. *Id* ¶¶ 17-18. 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. 1016 (Lewis 1990) at 1.

The '603 patent provides general lists of known polymers and drugs to be used in its fibers. Ex. 1002 ¶¶ 18-19. With regard to polymers, the patent lists art-known biodegradable polymers, borrowing from a 1997 book chapter by Wai Hung Wong and David Mooney. Ex. 1001 at 15:55-16:29 (adapting Table 1 from Wong and

Mooney 1997); Ex. 1015 (Wong and Mooney 1997) at 55-56; Ex. 1002 ¶ 18. The '603 patent lists biodegradable polymers that had been used in drug delivery devices for decades, and acknowledges that "[t]hose of skill in the art will understand that these polymers are just examples of a class of biodegradable polymer matrices that can be used in this invention." *Id.* at 15:61-64; Ex. 1002 ¶ 18.

The '603 patent similarly provides a general, column-long list of therapeutic agents and drugs to incorporate in its fibers. Ex. 1001 at 7:59-8:57; Ex. 1002 ¶ 19. The patent states that "the present invention contemplates the use of any drug incorporated in the biodegradable polymer fibers," and incorporates by reference the U.S. Pharmacopeia. Ex. 1001 at 7:59-8:57. Although claim 13 requires a "hydrophobic drug," the '603 patent does not identify any particular therapeutic agent as a hydrophobic drug or explain how to identify such a drug. *See id.* However, many of the general classes of therapeutic agents listed in the patent were known to include hydrophobic drugs. Ex. 1002 ¶ 19.

Gels and hydrogels, the '603 patent explains, could be prepared "by a variety of methods well known to those of ordinary skill in the art." Ex. 1001 at 9:9-32. The use of gels and hydrogels in drug delivery devices was well known by the claimed priority date of the '603 patent. Ex. 1002 ¶¶ 20-21. As early as 1987, "the polymer and biomedical literature contain[ed] numerous publications on the preparation, structure, and applications of hydrogels." Ex. 1017 (Peppas 1987) at 4. By that

time, "hydrogels ha[d] become excellent carriers for release of drugs and bioactive macromolecules." *Id.* And by the 1990s, "biodegradable hydrogels ha[d] been used quite extensively in the controlled release drug delivery area." Ex. 1018 (Kamath 1993) at 60; Ex. 1002 ¶ 20.

The '603 patent uses these well-known polymer and gel materials to make "gel or hydrogel loaded biodegradable fiber[s]." Ex. 1001 at 2:65-67; Ex. 1002 ¶ 22. In challenged claim 1 and its dependent claims, the biodegradable polymer and the gel or hydrogel are simply layered to form a "bi-component fiber" in which the "first component is a biodegradable polymer and [the] second component is selected from the group consisting of a gel and a hydrogel." Ex. 1001 at 3:8-13, 5:33-36, 35:40-46 (claim 1). The gel or hydrogel component may be the "inner bore of the fiber," or "the inverse," "the outer wall" of the fiber:

Id. at Figs. 2A, 3B (text added from patent's description of figures), 3:58-60 (description of Fig. 2A), 4:4-5 (description of Fig. 3B), 5:33-36.

B. Prosecution History of the '603 Patent

U.S. Patent Application No. 10/428,901 ("the '901 application") was filed on May 2, 2003 as a continuation-in-part of Application No. 09/632,457 (now the '296 patent). Ex. 1001, Cover. The PTO initially rejected the proposed claims for obviousness-type double patenting over the claims of the '296 patent. Ex. 1004 at 105-09. After Patent Owner filed a terminal disclaimer against the '296 patent, claims 1-34 were allowed. *Id.* at 113, 145-46. During prosecution of the '603 patent (and prosecution of its parent, the '296 patent) the references relied upon in this Petition were not considered. *See generally* Ex. 1004. The '603 patent issued on April 25, 2006. Ex. 1001, Cover.

C. Claim Construction

In an *inter partes* review filed 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.*

The following terms were the subject of claim construction in the District Court Action: "**hydrogel**" and "**gel**" (recited in challenged claims 1, 6, and 19); and

"**an emulsion consisting essentially of a gel or hydrogel**" (recited in challenged claim 19). *See* Ex. 1013 at 5, 14-16. In the District Court Action, the court construed the relevant terms as follows:

- **"hydrogel"**: "a colloid in which a dispersed phase (colloid) is combined with a continuous phase (water) to produce a viscous jellylike product"
- **"gel"**: "a colloidal system with at least two phases, one of which forms a continuous three-dimensional network that acts as an elastic solid"
- "**an emulsion consisting essentially of a gel or hydrogel"**: "an emulsion having only the following material elements: a gel or hydrogel"

Ex. 1013 at 5, 14-17.

For purposes of this proceeding, Ethicon 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. "Hydrogel" and "Gel"

Both independent challenged claims of the '603 patent, claims 1 and 19, require a "hydrogel" or a "gel."

"Hydrogel" should be construed to mean "**a colloid in which a dispersed phase (colloid) is combined with a continuous phase (water) to produce a**

viscous jellylike product." This is the express definition of "hydrogel" in the '603 patent. Ex. 1001 at 5:39-42; 16:55-58 (restating definition). This construction was agreed upon by Ethicon and Patent Owner in the District Court Action (Ex. 1013 at 5), and was adopted by the district court. *Id.* at 16-17.

"Gel" should be construed to mean "**a colloidal system with at least two phases, one of which forms a continuous three-dimensional network that acts as an elastic solid**." This is the technical portion of the express definition of "gel" in the '603 patent. Ex. 1001 at 5:36-39; *id.* at 16:32-35.[2] This construction was advanced by Patent Owner and adopted by the district court. Ex. 1013 at 14-15.

Although Ethicon adopts the above constructions, construing the terms "hydrogel" and "gel" is not necessary to resolve this Petition. Patent Owner conceded that Groves meets each and every element of claim 1, including a "hydrogel," during prosecution before the EPO. *See* § IX.A.3, *infra*. Similarly, Sirkar and Vacanti disclose a "hydrogel" or a "gel" under the district court

[2] The second time the definition of "gel" is stated in the patent, it is provided in both "simple" and "[m]ore technical[]" terms: "In simple terms, a gel is a liquid system that acts like a solid. More technically defined, a gel is a colloidal system with at least two phases, one of which forms a continuous three-dimensional network that acts as an elastic solid." Ex. 1001 at 16:32-35.

constructions advanced by Patent Owner. *See* § IX.B.3, IX.C.3.a., *infra*. Thus, the challenged claims of the '603 patent are unpatentable over the prior art under the parties' agreed construction of "hydrogel" and the district court construction of "gel."

2. "An Emulsion Consisting Essentially of a Gel or Hydrogel"

Claim 19 of the '603 patent recites "[a] drug delivery composition comprising a fiber, wherein said fiber comprises an emulsion consisting essentially of a gel or hydrogel."

The phrase "an emulsion consisting essentially of a gel or hydrogel" should be construed to mean "**an emulsion having only the following material elements: a gel or hydrogel**." This construction was adopted in the District Court Action (Ex. 1013 at 15-16) and is consistent with the intrinsic record and the specific legal meaning of the transition phrase "consisting essentially of."

In the District Court Action, Patent Owner proposed construing "an emulsion consisting essentially of a gel or hydrogel" as "an emulsion consisting of essentially a **dispersed** gel or hydrogel **phase**." *Id.* at 15-16 (emphasis added). The district court correctly rejected this construction in view of the intrinsic record. *Id.*; Ex. 1002 ¶ 54. The court observed that "[t]he specification contemplates embodiments of the claimed drug-delivery fiber that include a gel or hydrogel, but not in a dispersed phase," and that "[t]hese embodiments are distinct from those incorporating a gel or hydrogel dispersed phase." *Id.* at 16 (citing Ex. 1001 at

6:17-20, 6:20-22). As a result, "the gel or hydrogel of Claim 19 **cannot be limited to a dispersed phase**." *Id.* (emphasis added). Further, the court "agree[d] with Ethicon" that "because 'gel' and 'hydrogel' have already been construed, the language added by [Patent Owner] is unnecessary." *Id.* at 15.

As the district court concluded, the proper construction of the disputed limitation instead applies the meaning of the transition phrase "consisting essentially of" that Patent Owners used in claim 19. The court explained: "The Federal Circuit has identified 'consisting essentially of' as a transition phrase that typically 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.'" Ex. 1013 at 16 (citing *PPG Indus. v. Guardian Indus. Corp.*, 156 F.3d 1351, 1354 (Fed. Cir. 1998)). Thus, "an emulsion consisting essentially of a gel or hydrogel" is properly construed to mean "an emulsion having only the following material elements: a gel or hydrogel." *Id.* Under the district court's construction, the "emulsion" of claim 19 is defined by the claim itself as a gel or hydrogel, with no other material elements. *See id.*

Under either the correct claim construction advanced by Ethicon and adopted by the district court, or the incorrect construction advanced by Patent Owner and rejected by the district court, claim 19 is unpatentable over the prior art.

VIII. LEVEL OF ORDINARY SKILL IN THE ART

For purposes of the '603 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. Ex. 1002 ¶ 34.

IX. THERE IS A REASONABLE LIKELIHOOD THAT AT LEAST ONE CLAIM OF THE '603 PATENT IS UNPATENTABLE

A. Ground 1: The Challenged Claims of the '603 Patent Are Anticipated or Obvious Over Groves

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

Groves issued as a U.S. patent on February 16, 1993, more than six years before the earliest claimed effective filing date of the '603 patent. Ex. 1007, Cover. Groves is therefore prior art under 35 U.S.C. § 102(b). The Patent Office did not consider Groves during prosecution of the '603 patent. It was not cited by the Patent Owner and it was not identified by the Patent Office.

2. Overview of Groves

Groves teaches and claims "[a] packing material for the treatment of infections, particularly in the teeth and gums." Ex 1007 at Abstract, 6:26-56 (claims 1-6). The packing material consists of a "biocompatible, polymeric carrier material" that contains "an antibiotic ester." *Id.* at Abstract. The "polymeric carrier" is "preferably" in a "string or fibrous form." *Id.* at 3:53-54. The carrier provides a

"continuous, controlled release" of antibiotic as the rate of release varies as a function of bacteria concentration. *Id.* at Abstract.

Groves, among other things, describes "the string or fiber" as "a hollow string or fiber having a lumen." *Id.* at 3:54-57. This fiber has two components: an "inner core" (or "lumen") and an "outer wall." *Id.* at 3:54-4:12, 6:44-56 (claims 5-6). The "inner core" of this bi-component fiber "contain[s] a hydrogel," such as "calcium alginate." *Id.* at 6:44-56 (claims 5-6); *see also id.* at 4:9-12. The "outer coating," contains "pectin, chitosan, [or] chitin," which are polymeric materials. *Id.* at 6:44-56 (claims 5-6); *see also id.* at 4:9-12. An "antibiotic ester [is] substantially carried in said inner core," and "said outer coating act[s] as a controlled release barrier to limit the generation of free antibiotic." *Id.* at 6:44-52 (claims 5-6); *see also id.* at 4:1-4.

Groves explains that its drug-loaded fibers, "which include an inner core and an outer coating," may also be used "for the controlled diffusion of free antibiotic without esterification, or for the controlled diffusion of other medicaments and nutrients such as vitamins, hormones, heparin, and the like at an implantation site." *Id.* at 4:56-64.

3. In European Prosecution, Patent Owner Conceded that Groves Anticipates Challenged Claims in the United States

After the '603 patent had issued, the EPO identified Groves as anticipatory prior art during ongoing prosecution of the European counterpart to the '603 patent. Specifically, in a June 2016 communication to Patent Owner, the EPO relied on

Groves for the first time, stating: "[**Groves**] **appears to take away novelty of at least claims 1 and 29 and discloses: a fiber comprising a drug-loaded hydrogel core (alginate) and an outer polymeric coating**, the combination of core and coating achieves a controlled drug release (see [Groves], column 1, lines 30-63, and claims 1-6)." Ex. 1006 at 370 (emphasis added).

The version of claim 1 pending at the time of the EPO communication contained all limitations in claim 1 of the '603 patent, as well as additional limitations. It recited as follows:

> A drug delivery composition comprising at least one fiber, wherein said fiber comprises a first component layer and a second component layer, and wherein said first component layer is a biodegradable polymer and said second component layer is selected from the group consisting of a gel or a hydrogel, wherein the first component layer is present in the outer wall of the fiber and the second component layer is present in the fiber bore, and in which a therapeutic agent is loaded into the gel or hydrogel.

Ex. 1006 at 340.[3]

[3] The European claim rejected over Groves included all of the limitations recited in the claim 1 of the '603 patent, and also required the "biodegradable polymer"

In its August 2016 response to the EPO, Patent Owner conceded that Groves discloses the elements of claim 1 (and therefore claim 1 as allowed in the United States). Specifically, Patent Owner acknowledged that Groves "discloses a system in which an antibiotic ester (serving as a prodrug) is provided in a biocompatible polymeric carrier material" for "antibiotic release." Ex. 1006 at 379. Patent Owner further acknowledged: "The biocompatible polymeric carrier material may be of 'string' or 'fibrous form' and may be hollow or have a lumen. The lumen may contain a relatively large supply of hydrogel and antibiotic ester, and an outer coating may be provided to act as a controlled release barrier to limit the generation of free antibiotic." *Id.*

Thus, Patent Owner conceded during European prosecution that Groves discloses: (i) a drug delivery composition (a "polymeric carrier material" for "antibiotic release"), (ii) comprising at least one fiber (in "string" or "fibrous form"), (iii) that is a bi-component fiber having a bore and a wall (a "lumen" and "outer coating"), (iv) in which the first component is a biodegradable polymer and the

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component to be "present in the outer wall of the fiber" and the "gel or [] hydrogel" component to be "present in the fiber bore," and further required "a therapeutic agent loaded into the gel or hydrogel." Ex. 1006 at 340. In the '603 patent, these additional limitations are recited in dependent claims 3 and 6.

second component is a gel or a hydrogel (a "polymeric carrier material" with a "hydrogel" lumen). *Id.* at 379-81.

To distinguish Groves during European prosecution, Patent Owner amended claim 1 to include the "limitation that '**the concentration of the gel or the hydrogel varies of as a function of distance along the long axis of the fiber**.'" *Id.* at 379; *see also id.* at 387. The challenged U.S. claims do not include this limitation or any similar limitation. Patent Owner argued to the EPO, however, that this amendment requiring a concentration gradient of gel or hydrogel overcame Groves, because Groves contains "no disclosure of the provision of a fibre in which the concentration of the gel or hydrogel varies as a function of distance along the long axis of the fibre as required by amended claims 1, 15 and 29." *Id.* at 380. Patent Owner argued that "[c]laims 1, 15 and 29 are therefore novel over [Groves]" as amended. *Id.* The '038 European Patent eventually issued with this limitation added to claim 1 and its dependent claims. *See* Ex. 1005 at 22:26-23:48 (claims).

Accordingly, by Patent Owner's own admissions, claim 1 of the '603 patent and its dependent claims are unpatentable over Groves absent an additional limitation requiring a concentration gradient of gel or hydrogel along the length of the claimed fiber. *Id.* The challenged claims contain no such limitation and are anticipated by Groves.

4. Claims 1, 2, 6, 11, 13, and 19 Are Unpatentable Over Groves

"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) (same).

A patent is obvious over the prior art if "the differences between the [patented] subject matter … and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a [POSA]." 35 U.S.C. § 103(a) (pre-AIA); *see also KSR Int'l Co. v. Tefeflex, Inc.*, 550 U.S. 398, 406-07 (2007).

As detailed below, Groves discloses each and every limitation of claims 1, 2, 6, 11, 13, and 19 of the '603 patent and therefore anticipates those claims under 35 U.S.C. § 102. At a minimum, Groves renders the challenged claims obvious in view of the knowledge of a POSA under 35 U.S.C. § 103.

a. Claim 1

Claim 1 of the '603 patent is directed to a "drug delivery composition" comprising at least one bi-component fiber "having a bore and a wall," in which the

"first component is a biodegradable polymer" and the "second component" is "a gel [or] a hydrogel." Groves discloses each and every element of this claim.

[1] "A drug delivery composition"

To the extent that the Board finds the preamble of claim 1 (a "drug delivery composition") limiting, it is disclosed by Groves. Ex. 1002 ¶ 71. The invention of Groves is a "controlled release vehicle for antibiotics." Ex. 1007 at 1:30-32, 1:45-46. The controlled release vehicle is in the form of a "packing material . . . for the treatment of infections." *Id.* at 1:66-67, 6:26-56 (claims 1-6). The "packing material" is a "biocompatible, polymeric carrier material carrying therein an antibiotic ester." *Id.* at 2:66-3:5; *see also id*. at 6:26-37 (claim 1) (reciting a "packing material for the treatment of infections" containing a "metronidazole ester"). Accordingly, Groves discloses and claims "a drug delivery composition."

[1.a.] "comprising at least one fiber"

The drug delivery composition disclosed and claimed by Groves comprises at least one fiber. Ex. 1002 ¶ 72. Specifically, Groves discloses that the "polymeric carrier may be of any desired shape, preferably being of string or fibrous form." Ex. 1007 at 3:53-54. Consistent with its disclosures, Groves claims a "packing material … in which [the] polymeric carrier comprises a fiber." *Id.* at 6:42-56 (claims 4-6).

[1.b.] "having a bore and a wall, wherein said fiber comprises a first component and a second component"

Groves discloses and claims bi-component fibers "having a bore and a wall." Ex. 1002 ¶¶ 73-74. Specifically, Groves teaches that the "[t]he string or fiber used as a polymeric carrier material" may contain an "inner core" and an "outer coating." Ex. 1007 at 3:54-4:1. Consistent with these disclosures, Claims 5 and 6 recite bi-component fibers containing "an inner core" and an "outer coating," with antibiotic ester "carried in said inner core." *Id.* at 6:44-56 (claims 5-6).

Groves' description of a fiber with an "inner core" and an "outer coating" is a disclosure of a bi-component fiber with a bore and a wall, as evidenced by the fact that the '603 patent uses the same terminology to describe its own bi-component fibers. Specifically, the '603 patent refers to the bore of its bi-component fibers as the "inner core" (Ex. 1001 at 10:40-41, 13:31-34), and describes a fiber with a hydrogel wall as a "Gel Coated Polymer Fiber." *Id.* at 26:25-29 (title of Example 2). Further, during prosecution of the European counterpart to the '603 patent, Patent Owner conceded that Groves discloses a bi-component fiber having a bore and a wall by stating to the EPO that Groves describes a composition in "fibrous form" that "may be hollow or have a lumen" and an "outer coating." Ex. 1006 at 380.

[1.c.] "and wherein said first component is a biodegradable polymer and said second component is selected from the group consisting of a gel and a hydrogel."

The bi-component fibers disclosed and claimed by Groves have "a biodegradable polymer" as their "first component" and "a gel [or] a hydrogel" as their "second component." Ex. 1002 ¶¶ 75-79. Specifically, Groves discloses bi-component fibers in which (i) the "outer coating" of the fiber contains "pectin, chitosan [or] chitin," and (ii) the "inner core" contains "a hydrogel." Ex. 1007 at 6:44-56 (claims 5-6); *see also id.* at 3:60-4:12.

The "outer coating" of the bi-component fibers of Groves contains "pectin, chitosan [or] chitin." *Id.* at 6:44-56 (claims 5-6); *see also id.* at 4:9-12. These materials are polysaccharides, a class of naturally derived biodegradable polymers. *See* Ex. 1001 at 9:56-61 (describing "polysaccharides" as "biodegradable polymer[s] used for fiber construction"); Ex. 1002 ¶ 77. The '603 patent specifically identifies "chitin" in its "non-exhaustive list of biodegradable polymers." Ex. 1001 at 16:1-29 (adapted from Wong and Mooney 1997); *see also* Ex. 1018 (Kamath 1993) at 76 (discussing "pectin" in review of biodegradable polymeric hydrogels for drug delivery); Ex. 1019 (Madihally 1999) at 1141 (describing "chitosan" as a biodegradable polymer); Ex. 1002 ¶ 77. Accordingly, Groves discloses a bi-component fiber with a biodegradable polymer component.

The same bi-component fiber disclosed and claimed by Groves also has "an inner core containing a hydrogel." Ex. 1001 at 6:44-56 (claims 5-6); *see also id.* at 3:60-4:12. Indeed, Groves expressly states that the inner core of its bi-component fibers contains "a hydrogel." *Id.* at 3:60-65, 6:44-56 (claims 5-6). The "second component" of Groves' bi-component fiber is therefore a gel or a hydrogel, as required by claim 1. Ex. 1002 ¶ 78. Patent Owner conceded this during European prosecution when it stated that Groves discloses a "polymeric carrier" in "fibrous form" that has a "lumen" containing "a relatively large supply of hydrogel." Ex. 1006 at 380.

Accordingly, Groves discloses a bi-component fiber having a biodegradable polymer as its first component and a gel or a hydrogel as its second component.

* * *

As demonstrated above, Groves discloses each and every element of claim 1 of the '603 patent.

b. Dependent Claim 2

Claim 2 depends from claim 1 and recites a bi-component fiber in which a biodegradable polymer is "present in the fiber bore" and a gel or a hydrogel is "present in the fiber wall." Groves discloses each and every element of this claim.

Groves discloses all limitations of claim 1 as demonstrated above. With regard to the further requirement that a biodegradable polymer component be

"present in the fiber bore," Groves discloses and claims fibers in which a biodegradable polymer, calcium alginate, is contained in the "inner core" of the fiber. Ex. 1007 at 4:9-10, 6:53-56 (claim 6). Alginates are biodegradable polymers. Ex. 1002 ¶ 82; Ex. 1015 (Wong and Mooney 1997) at 67-70 (discussing alginates in review of biodegradable polymers); Ex. 1020 (Barnett 1987) at 153 (describing alginates as "biodegradable"). Indeed, the '603 patent states that "[p]olysaccharides are the preferred polymers for this invention. Alginate, for example, is biocompatible, non-cytotoxic, non-carcinogenic, non-inflammatory, and non-immunogenic, and, therefore, a good candidate for use." Ex. 1001 at 17:64-67. Groves therefore discloses a bi-component fiber according to claim 1 in which a biodegradable polymer is "present in the fiber bore," as required by claim 2. Ex. 1002 ¶ 82.

The same bi-component fiber disclosed and claimed by Groves with a biodegradable polymer present in the inner bore also has "an outer coating which comprises a hydrogel." Ex. 1007 at 3:66-4:12; 6:44-56 (claims 5-6) (same). Accordingly, the bi-component fiber disclosed and claimed by Groves meets the additional limitation of claim 2 requiring a gel or a hydrogel to be "present in the fiber wall." Ex. 1002 ¶ 83.

Accordingly, Groves discloses each and every limitation of claim 2.

c. Dependent Claims 6 and 11

Claim 6 recites "a composition of claim 1 in which a therapeutic agent is loaded into the gel or hydrogel." Groves meets all limitations of claim 1 as described above. Groves also expressly discloses and claims a bi-component fiber in which "[t]he antibiotic ester is substantially carried in the inner core" containing a "hydrogel" as the "carrier" for the antibiotic ester. Ex. 1007 at 3:60-4:4, 6:44-52 (claim 5) (fiber with an "inner core containing a hydrogel" and "antibiotic ester being substantially carried in said inner core"). During European prosecution, Patent Owner conceded that, in the bi-component fibers of Groves, "[t]he lumen may contain a relatively large supply of hydrogel and an antibiotic ester." Ex. 1006 at 380. Accordingly, Groves discloses each and every limitation of claim 6. Ex. 1002 ¶ 86.

Claim 11 depends from claim 6 and requires that the "therapeutic agent [] loaded into the gel or hydrogel" be "selected from the group consisting of … antibiotics," among many other options. Groves discloses all limitations of claim 6 as described above. Groves further discloses a fiber composition where the therapeutic agent "loaded into the gel or hydrogel" is an "antibiotic." Specifically, Groves discloses and claims fibers with an "antibiotic ester [] substantially carried in said inner core." Ex. 1007 at 6:44-52 (claim 5). Groves further states that "[i]f desired, free antibiotic may also be added to the polymeric carrier to provide a bolus

of initial antibiotic release." *Id.* at 3:17-24; *see also id.* at 4:57-64. Accordingly, Groves discloses each and every limitation of claim 11. Ex. 1002 ¶ 87.

d. Dependent Claim 13

Claim 13 depends from claim 1 and recites: "[t]he composition of claim 1, wherein said biodegradable polymer fiber comprises a hydrophobic drug." Groves discloses all limitations of claim 1 as described above. Groves further discloses the use of a "hydrophobic drug" in its polymeric fibers. Groves, like the '603 patent, describes the use of an antibiotic in its bi-component fibers. Ex. 1007 at 1:66-2:5, 3:17-24, 4:57-64 (describing fibers loaded with "antibiotic ester" and/or "free antibiotic"); Ex. 1001 at 7:59-8:22 (listing "an antibiotic" in patent's general list of therapeutic agents).

Groves discloses loading an "antibiotic ester," with "at least one ester group of 10 to 18 carbon atoms per molecule," into the "polymeric carrier." Ex. 1007, Abstract; *see also* 2:1-16. The antibiotic esters disclosed in Groves contain long fatty acid chains, which are known to make drugs hydrophobic. Ex. 1002 ¶ 89; Ex. 1023 (MOLECULAR BIOLOGY OF THE CELL) at 48. Groves states that metronidazole palmitate containing 16 carbon atoms is a "preferred antibiotic ester." Ex. 1007 at 3:10-11. Metronidazole palmitate, with its long palmitic acid chain, is a hydrophobic drug. Ex. 1002 ¶ 90; Ex. 1023 (MOLECULAR BIOLOGY OF THE CELL) at 48.

Further, Groves discloses that its drug-loaded fibers also "may be used for the controlled diffusion of free antibiotic without esterification." Ex. 1007 at 4:57-64; *see also id.* at 3:17-24. In Groves, "metronidazole … is a preferred antibiotic for use in [the] invention." Ex. 1007 at 2:51-56. The antibiotic metronidazole is known to be a hydrophobic drug. Ex. 1002 ¶ 91; Ex. 1014 (Lacy 1997) at 10:52-11:52 (listing "metronidazole" among "the hydrophobic drugs which may be formulated in accordance with the present invention").

Accordingly, Groves discloses each and every limitation of claim 13.

At a minimum, it would have been obvious from Groves' disclosures that Groves teaches using a hydrophobic drug in its fibers. Groves teaches using antibiotic esters with 10 to 18 carbons atoms in its fibers, and identifies metronidazole palmitate (which has a palmitic acid chain) as a preferred antibiotic ester. Ex. 1007 at 2:1-16, 3:10-13; 6:26-56 (claims 1-6). A POSA would have understood that the fatty acid chains on the antibiotic esters taught by Groves render these molecules hydrophobic. Ex. 1002 ¶ 93; Ex. 1023 (MOLECULAR BIOLOGY OF THE CELL) at 48. Further, even without the addition of a palmitic acid chain, the preferred antibiotic of Groves, metronidazole, is a known hydrophobic drug. Ex. 1002 ¶ 93; Ex. 1023 (Lacy 1997) at 10:52-11:52. A POSA thus would have practiced Groves' teachings with the understanding that the fibers of Groves contain a hydrophobic drug. Ex. 1002 ¶ 93.

e. Independent Claim 19

Claim 19 of the '603 patent recites "[a] drug delivery composition comprising a fiber, wherein said fiber comprises an emulsion consisting essentially of a gel or hydrogel." Groves discloses each and every element of this claim.

As demonstrated above, to the extent the Board finds the "drug delivery composition" preamble limiting, it is disclosed by Groves. *See* § IX.A.4.a.[1.], *supra*. As further demonstrated above, Groves discloses "a fiber." *See* § IX.A.4.a.[1.a.], *supra*.

The balance of claim 19 requires that the "material elements" of the claimed fiber must be a gel or hydrogel. *See* § VII.C.2, *supra*; Ex. 1013 at 15-16. That is precisely what Groves discloses and claims: fibers made of hydrogels. Ex. 1007 at 3:5-9, 3:60-4:1, 6:26-56 (claims 1-6). Accordingly, Groves discloses all limitations of claim 19 and anticipates that claim under the correct construction adopted by the district court. Ex. 1002 ¶¶ 96-97.

Claim 19 of the '603 patent also would have been obvious under the incorrect construction proposed by Patent Owner and rejected by the court in the District Court Action. *See* Ex. 1013 at 15-16; § VII.C.2., *supra*. It would have been obvious to "disperse" the drug-loaded hydrogel of Groves, as required Patent Owner's incorrect construction. At the time of the '603 patent, drug-delivery fibers containing dispersions were routine. Ex. 1002 ¶ 98. Indeed, Groves discloses a

"polymeric carrier material" containing "dispersed" antibiotic ester, and teaches the preparation of fibers with "dispersed" drug in its examples. Ex. 1007, Abstract, 5:16-19. Groves explains that the antibiotic ester is "typically … distributed throughout the mass of the polymeric carrier" (*id.* at 2:29-37), and describes using a hydrogel as the "polymeric carrier" for the drug. *Id.* at 3:60-65. Further, Groves encourages a POSA to tailor its drug-delivery fibers to meet clinical needs. Ex. 1007 at 2:63-68 (the fiber carrier "can be tailored to an optimum clinical program for the treatment of chronic infections"); *id.* at 3:53-55 ("The polymeric carrier may be of any desired shape…"); *id.* at 4:4-8 ("[B]y control of the outer coating, the antibiotic release rates of the packing material of this invention may be controlled to conform to a large variety of desirable clinical programs."). A POSA would have been motivated by Groves' disclosures to disperse the drug-loaded hydrogel taught by Groves as an additional means of controlling drug release, with a reasonable expectation of success. Ex. 1002 ¶ 99.

* * *

For these reasons, Groves discloses each and every element of challenged claims 1, 2, 6, 11, 13, and 19 of the '603. Groves anticipates these claims or, at a minimum, renders these claims obvious in view of the knowledge of a POSA.

B. Ground 2: Claim 19 of the '603 Patent Is Anticipated or Obvious Over Sirkar

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

Sirkar was published on September 8, 1995, approximately four years before the earliest claimed effective filing date of the '603 patent. Ex. 1008, Cover. Sirkar is therefore prior art under 35 U.S.C. § 102(b). The Patent Office did not consider Sirkar during prosecution of the '603 patent. The Patent Owner did not cite Sirkar to the Patent Office and the Patent Office did not identify Sirkar.

2. Overview of Sirkar

Like Groves, Sirkar relates to the field of controlled release delivery systems. Ex. 1008 at Abstract, 2:1-11. Sirkar discloses a "controlled release device employing microporous membranes," in the form of "microporous hollow fibers." *Id.* at Abstract. The "porous hollow fiber" of Sirkar allows for "enormous flexibility in the rate of release of a selected agent." *Id.* at 4:3-10. The fibers are made of "polymeric" materials (*id.* at 8:13-14), and "may be used to deliver selected agents such as pharmaceuticals," among others. *Id.* at 4:12-21. In addition, the "membrane" of the porous hollow fiber may be a "hydrogel." *Id.* at 10:8-10, 19:20-21 (claim 7).

Sirkar further discloses "aqueous-organic partitioning of the selected agent to be delivered" within its porous hollow fibers. *Id.* at 4:12-15. As Sirkar explains, this means that if the "fiber lumen" is filled with "the selected agent in an **organic**

solvent," then "[t]he pores of the wall of the hollow fiber contain **water** or an appropriate aqueous solution." *Id.* at 6:9-13 (emphasis added). Inversely, if "the fiber contains the selected agent in **water**," then "[t]he pores of the wall of the fiber contain an **organic** solvent." *Id.* at 6:24-26 (emphasis added). Further, "[i]f the selected agent is to be delivered to ambient atmosphere having considerable potential for volatilizing the water in the pores of the hollow fiber wall, it is preferred that **water or organic solvent in the pore wall is gelled by the addition of appropriate gelling agents**." *Id.* at 7:19-23.

3. Independent Claim 19 Is Unpatentable Over Sirkar

Claim 19 of the '603 patent recites "[a] drug delivery composition comprising a fiber, wherein said fiber comprises an emulsion consisting essentially of a gel or hydrogel." Sirkar discloses each and every limitation of claim 19 of the '603 patent and therefore anticipates that claim under 35 U.S.C. § 102. At a minimum, Sirkar renders claim 19 obvious in view of the knowledge of a POSA under 35 U.S.C. § 103.

To the extent that the Board finds the preamble of claim 1 (a "drug delivery composition") limiting, it is disclosed by Sirkar. The invention of Sirkar is a "controlled release device" for the delivery of "pharmaceuticals," among other substances. Ex. 1008, Abstract; *see also id.* at 2:1-18.

Further, the drug delivery device taught by Sirkar "compris[es] a fiber." Specifically, Sirkar discloses and claims "microporous hollow fibers." *Id.* at Abstract; *see also id.* at 19:2-7 (claim 1).

The balance of claim 19 requires that the "material elements" of the claimed fiber must be a gel or hydrogel. *See* § VII.C.2, *supra*; Ex. 1013 at 15-16. Sirkar discloses this limitation. Specifically, Sirkar states that "[h]ydrogel hollow fibers … are equally useful for the present invention." Ex. 1008 at 10:8-10. Consistent with this disclosure, Sirkar claims "a microporous membrane comprising a hollow fiber" wherein "**the membrane is a hydrogel**." *Id.* at 19:1-7, 20-21 (claims 1 and 7) (emphasis added). In this "hydrogel" fiber claimed by Sirkar, the "membrane" (*i.e.*, the material that makes up the hollow fiber) is made entirely of "hydrogel," thus making "a hydrogel" the material element of the composition. Accordingly, Sirkar discloses each and every element of claim 19. Ex. 1002 ¶ 111.

Sirkar would also anticipate claim 19 under the incorrect construction proposed by Patent Owner, and rejected by the district court, requiring "an emulsion consisting essentially of a **dispersed** gel or a hydrogel **phase**." Ex. 1013 at 15 (emphasis added); § VII.C.2, *supra*. Sirkar describes a "porous hollow fiber" in which the "pores of the wall of the fiber contain water" or, alternatively, "an organic solvent." Ex. 1008 at 6:9-26. Sirkar further discloses that "[i]f the selected agent is to be delivered to ambient atmosphere having considerable potential for volatilizing

the water in the pores of the hollow fiber wall, **it is preferred that water or organic solvent in the pore wall is gelled by the addition of appropriate gelling agents**." *Id.* at 7:19-23 (emphasis added). Thus, Sirkar discloses a fiber with a gel or a hydrogel dispersed throughout the porous polymer wall of the fiber. Ex. 1002 ¶ 112. Sirkar therefore teaches a polymer fiber with a dispersed gel or hydrogel phase. *Id.*

To the extent Sirkar's disclosures alone do not anticipate claim 19 under Patent Owner's incorrect construction (*see* § VII.C.2, *supra*), they render the claim obvious in view of the knowledge of a POSA. It would have been obvious to a POSA that Sirkar describes fibers with a dispersed gel or hydrogel phase. Ex. 1002 ¶ 113. Sirkar explains that "[t]he pores of the wall of the fiber contain water," or "an organic solvent." Ex. 1008 at 6:9-26. Sirkar further discloses that, in some cases, "it is preferred" to have the "water or organic solvent in the pore wall [] gelled by the addition of appropriate gelling agents." *Id.* at 7:19-23. A POSA would have been very familiar with "appropriate gelling agents" to "gel[]" the water or organic solvent in "[t]he pores of the wall of the fiber." *Id.* at 6:9-26, 7:19-23; Ex. 1002 ¶ 113. A POSA also would have understood that the "gelled" water or organic solvent in the pores of the fiber wall would form a dispersed phase, because the resulting hydrogel or gel would be distributed throughout the wall of the polymer fiber. Ex. 1002 ¶ 114; Ex. 1008 at 6:9-26, 7:19-23. A POSA therefore would have applied Sirkar's teachings and a POSA's knowledge of gelling agents to prepare

fibers with a dispersed gel or hydrogel phase with a reasonable expectation of success. Ex. 1002 ¶ 114.

Accordingly, Sirkar anticipates claim 19 or, at a minimum, renders claim 19 obvious in view of the knowledge of a POSA under both the correct construction proposed by Ethicon and adopted by the district court and the incorrect construction proposed by Patent Owner and rejected by the district court.

C. Ground 3: Claims 1, 2, and 13 of the '603 Patent Are Anticipated or Obvious Over Vacanti

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

Vacanti issued as a U.S. patent on June 2, 1998, more than one year before the earliest claimed effective filing date of the '603 patent. Ex. 1009, Cover. Vacanti is therefore prior art under 35 U.S.C. § 102(b). The Patent Office did not consider Vacanti during prosecution of the '603 patent. Patent Owner did not cite Vacanti to the Patent Office and the Patent Office also did not identify Vacanti.

2. Overview of Vacanti

Vacanti teaches "[a] cell-scaffold composition [] prepared in vitro for implanting to produce functional organ tissue in vivo." Ex. 1009, Abstract. "The scaffold is three-dimensional and is composed of fibers of a biocompatible, biodegradable, synthetic polymer." *Id.* On these polymer "scaffolds" (also called "matrices"), "cells having a desired function are grown ... using cell culture techniques, followed by transfer of the polymer-cell scaffold into a patient at a site

appropriate for attachment, growth and function, after attachment and equilibration, to produce a functional organ equivalent." *Id.* at 5:36-42. In other words, Vacanti teaches the attachment of living cells to a synthetic polymer scaffold, followed by cell growth and proliferation, and eventually implantation in the patient. *Id.* at Abstract, 5:36-46, 10:43-49.

Vacanti discloses that "the fibers may have a coating which enhances cell attachment." *Id.* at Abstract. Specifically, Vacanti teaches that "attachment of the cells to the polymer is enhanced by coating the polymers with compounds such as basement membrane components, agar, agarose, gelatin, gum arabic, collagens types I, II, III, IV, and V, fibronectin, laminin, glycosaminoglycans, mixtures thereof, and other materials known to those skilled in the art of cell culture." *Id.* at 10:43-49. In its working examples, Vacanti describes coating biodegradable polymer fibers with such materials, followed by addition of cells for attachment studies. *Id.* at 18:45-63. Vacanti discloses that, "[a]fter 5 days, there was maximum attachment on polymer coated with crosslinked 11% gelatin." *Id.* at 19:50-52.

3. Claims 1, 2, and 13 are Unpatentable Over Vacanti

As detailed below, Vacanti discloses each and every limitation of claims 1, 2, and 13 of the '603 patent and therefore anticipates those claims under 35 U.S.C. § 102. At a minimum, Vacanti renders these claims obvious in view of the knowledge of a POSA under 35 U.S.C. § 103.

a. Claim 1

Claim 1 of the '603 patent is directed to a "drug delivery composition" comprising at least one bi-component fiber "having a bore and a wall," in which the "first component is a biodegradable polymer" and the "second component" is "a gel [or] a hydrogel." Vacanti discloses each and every element of claim 1.

[1] "A drug delivery composition"

To the extent that the Board finds the preamble of claim 1 (a "drug delivery composition") limiting, it is disclosed by Vacanti. Vacanti discloses biodegradable polymer matrices for growing cells, and further teaches that "nutrients, growth factors, inducers of differentiation or de-differentiation, products of secretion, immunomodulators, inhibitors of inflammation, regression factors, biologically active compounds which enhance or allow ingrowth of the lymphatic network or nerve fibers, and drugs can be incorporated into the matrix." Ex. 1009 at 6:13-18. Vacanti explains that "[o]ne of the advantages of a biodegradable polymeric matrix is that angiogenic and other bioactive compounds may be incorporated directly into the matrix so that they are slowly released as the matrix degrades in vivo." *Id.* at 10:30-33. Claim 8 recites cell-scaffold compositions further containing such active compounds. *Id.* at 24:65-25:2. Accordingly, Vacanti discloses and claims "a drug delivery composition." Ex. 1002 ¶ 122.

[1.a.] "comprising at least one fiber"

The drug delivery composition disclosed and claimed by Vacanti comprises at least one fiber. Ex. 1002 ¶ 123. Specifically, the invention of Vacanti is a "scaffold … composed of fibers of a biocompatible, biodegradable synthetic polymer." Ex. 1009, Abstract. Consistent with its disclosures, Vacanti claims "cell-scaffold composition[s]" that are "composed of fibers of a biocompatible, biodegradable, synthetic polymer." *Id.* at 24:23-46 (claim 1).

[1.b.] "having a bore and a wall, wherein said fiber comprises a first component and a second component"

Vacanti further discloses and claims bi-component fibers "having a bore and a wall." Ex. 1002 ¶¶ 124-125. Specifically, Vacanti discloses that "[i]n some embodiments, attachment of the cells to the polymer is enhanced by coating the polymers with compounds such as basement membrane components, agar, agarose, gelatin, gum arabic, collagens types I, II, III, IV, and V, fibronectin, laminin, glycosaminoglycans, mixtures thereof, and other materials known to those skilled in the art of cell culture." Ex. 1009 at 10:43-49. Vacanti further provides examples of coating biodegradable polymer fibers in this manner: "Polyglactin 910, polyorthoester, and polyanhydrides were treated with several different buffers in an effort to change the surface conformation of the polymer, and were coated with various materials thought to be important for cell attachment." *Id.* at 18:35-39. For

example, in one experiment, "polymer fibers [were] coated with 1% gelatin." *Id.* at 19:39-41.

Consistent with these disclosures, Vacanti claims a "cell-scaffold composition … further comprising a coating on said fibers which enhances cell attachment to the scaffold." *Id.* at 24:51-53 (claim 3). In another dependent claim, "the coating is a material selected from the group consisting of agar, agarose, gelatin, gum arabic, basement membrane material, collagens types I, II, III, IV, and V, fibronectin, laminin, glycosaminoglycans, and mixtures thereof." *Id.* at 25:54-59 (claim 4).

These coated polymer fibers disclosed and claimed by Vacanti are therefore bi-component fibers having a bore and a wall. Ex. 1002 ¶¶ 124-125. Indeed, the '603 patent later uses the same terminology ("coated" fiber) when discussing its own bi-component fibers. Ex. 1001 at 26:26-32 (describing a "biodegradable polymer fiber coated with a hydrogel").

[1.c.] "and wherein said first component is a biodegradable polymer and said second component is selected from the group consisting of a gel and a hydrogel."

The bi-component fibers disclosed and claimed by Vacanti have "a biodegradable polymer" as their "first component" and "a gel [or] a hydrogel" as their "second component." Ex. 1002 ¶¶ 126-128.

With regard to the "first component," the fibers disclosed and claimed by Vacanti are "fibers of a biocompatible, biodegradable synthetic polymer." Ex. 1009, Abstract. Vacanti teaches that "[t]he preferred material for forming the matrix or support structure is a biodegradable artificial polymer, for example, polyglycolic acid, polyorthoester, or polyanhydride, which is degraded by hydrolysis at a controlled rate and reabsorbed." *Id.* at 5:56-60. Polyglycolic acid and polyanhydride are also among the preferred biodegradable polymers of the '603 patent. Ex. 1001 at 15:56-59; *see also id.* at 16:5-29 (Table 1 adapted from Wong and Mooney 1997). Consistent with its disclosures, Vacanti claims cell-scaffold compositions made of fibers using these same biodegradable polymers. Ex. 1009 at 24:47-50 (claim 2).

With regard to the "second component," Vacanti discloses and claims biodegradable polymer fibers coated with gels. Specifically, Vacanti teaches biodegradable polymer fibers coated with materials including "[g]elatin [] cross-linked with a 50:50 solution of 2% gluteraldehyde:phosphate buffer." *Id.* at 18:53-54. A cross-linked gelatin is a gel. Ex. 1002 ¶ 128; Ex. 1021 (Heller 1987) at 142 (describing cross-linked gelatin hydrogels for delivery of mitomycin to bodily organs). Indeed, the '603 patent lists "gelatin" among the "materials that can form hydrogels" (Ex. 1001 at 17:36-46) and explains making gels using "chemical

crosslinkers like glutaraldehyde," the same substance used to make cross-linked gelatin in Vacanti. *Id.* at 9:21-24.

Accordingly, Vacanti discloses biodegradable polymer fibers coated with gel, and thus discloses bi-component fibers with a biodegradable polymer first component and a gel or hydrogel second component. Ex. 1002 ¶ 128.

* * *

For the reasons demonstrated above, Vacanti discloses each and every limitation of claim 1 of the '603 patent.

a. Dependent Claim 2

Claim 2 depends from claim 1 and requires the biodegradable polymer component "present in the fiber bore" and the gel or hydrogel component "present in the fiber wall." Vacanti discloses all limitations of claim 2.

Vacanti discloses each and every limitation of claim 1 as demonstrated above. As further explained above, Vacanti discloses biodegradable polymer fibers coated with a gel. § IX.C.3.a.[1.b.], *supra*. Vacanti therefore discloses bi-component fibers in which the biodegradable polymer makes up the "bore" and the gel makes up the "wall" of the fiber. Ex. 1002 ¶ 131. Indeed, the '603 patent describes its own bi-component fibers with a polymer bore and a gel wall as "Gel Coated Polymer Fibers." Ex. 1001 at 26:26-29 (heading of Example 2). Accordingly, Vacanti discloses each and every limitation of claim 2.

b. Dependent Claim 13

Claim 13 depends from claim 1 and recites a "biodegradable polymer fiber [that] comprises a hydrophobic drug." Vacanti discloses all limitations of claim 13.

As demonstrated above, Vacanti teaches a cell-scaffold matrix composed of biodegradable polymer fibers. § IX.C.3.a.[1]-[1.a.], *supra*. Vacanti further teaches that "drugs can be incorporated into the matrix," Ex. 1009 at 6:13-20, and that "[o]ne of the advantages of a biodegradable polymeric matrix is that angiogenic and other bioactive compounds may be incorporated directly into the matrix so that they are slowly released as the matrix degrades in vivo." *Id.* at 10:30-33. Like the '603 patent, Vacanti lists general classes of therapeutic agents that may be used. *Id.* at 6:10-20. Consistent with these disclosures, claim 8 of Vacanti recites cell-scaffolds composed of biodegradable polymers further containing "growth factors, compounds stimulating angiogenesis, immunomodulators, inhibitors of inflammation, and combinations thereof." *Id.* at 24:65-25:2 (claim 8). The classes of therapeutic agents listed in claim 8 of Vacanti were all later listed in the '603 patent. *Compare* Ex. 1009 at 24:65-25:2 (claim 8), *with* Ex. 1001 at 7:59-8:57 (listing "a growth factor, an immunomodulator, a compound that promotes angiogenesis, … [and] an anti-inflammatory compound," among others).

Although the '603 patent does not identify any drug as hydrophobic, it would have been well known that the general categories of therapeutic agents listed in

Vacanti and in the '603 patent include hydrophobic drugs. Ex. 1002 ¶¶ 133-134. For example, both Vacanti and the '603 patent list immunomodulators (medications used to help regulate or normalize the immune system) as drugs that may be incorporated. Ex. 1009 at 6:13-18, 24:65-25:2 (claim 8); Ex. 1001 at 7:59-8:57. It was well known that the class of immunomodulators includes hydrophobic compounds, such as muramyltripeptide cholesterol ("MDP-chol"), an immunomodulator known to activate white blood cells. Ex. 1002 ¶ 134; Ex. 1022 (Seyler 1997) at 376 (describing MDP-chol as "a very hydrophobic compound"). Accordingly, Vacanti discloses each and every limitation of claim 13. Ex. 1002 ¶¶ 133-134.

At a minimum, it would have been obvious from Vacanti's disclosures for a POSA to have selected a hydrophobic drug for use in Vacanti's fibers. A POSA would have been well aware of the hydrophobicity of different drug molecules, and would have been readily able to identify a hydrophobic drug. Ex. 1002 ¶ 135. The different drug classes disclosed in Vacanti (which were all later listed in the '603 patent) were known to include hydrophobic drugs, such as hydrophobic immunomodulators. Ex. 1009 at 6:13-18, 24:65-25:2 (claim 8); Ex. 1001 at 7:59-8:57; Ex. 1002 ¶ 135; Ex. 1022 (Seyler 1997) at 376. There would have been good reason to choose a hydrophobic drug, including that hydrogels generally provide for an extended release of hydrophobic drugs. Ex. 1002 ¶ 135. A POSA

thus would have practiced Vacanti's teachings to select a hydrophobic drug with a reasonable expectation of success. *Id.*

* * *

For these reasons, Vacanti discloses each and every element of claims 1, 2, and 13 of the '603 patent. Vacanti anticipates these claims or, at a minimum, renders these claims obvious in view of the knowledge of a POSA.

X. NO OBJECTIVE INDICIA OF NON-OBVIOUSNESS

To the extent obviousness is considered for any of the challenged claims, Ethicon 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 '603 patent. *See generally* Ex. 1004. Further, as demonstrated above, the '603 patent merely describes and claims what was already in the prior art. In addition, the '603 patent does not provide any working example of a drug delivery composition that is covered by its claims. Ethicon requests that the Board wait to undertake evaluation of secondary consideration evidence, if any, presented by Patent Owner until Ethicon 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).

XI. CONCLUSION

In view of the foregoing, Petitioner respectfully requests that Trial be instituted and that claims 1, 2, 6, 11, 13, and 19 of the '603 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 9,659. 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.

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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. 7,033,603:

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