

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

RESTEM, LLC.,
Petitioner,

v.

JADI CELL, LLC,
Patent Owner.

IPR2021-01535
Patent No. 9,803,176 B2

Before CHRISTOPHER G. PAULRAJ, ROBERT A. POLLOCK, and
DEVON ZASTROW NEWMAN, *Administrative Patent Judges*.

NEWMAN, *Administrative Patent Judge*.

DECISION
Granting Institution of *Inter Partes* Review
35 U.S.C. § 314, 37 C.F.R. § 42.4

I. INTRODUCTION

A. *Background and Summary*

RESTEM, LLC, (“Petitioner”) filed a Petition pursuant to 35 U.S.C. §§ 311–319 requesting an *inter partes* review of claims 1–15 “the Challenged Claims”) of U.S. Patent No. 9,803,176 (Ex. 1001, “the ’176 patent”). Paper 1 (“Pet.”). Jadi Cell, LLC, (“Patent Owner”) filed a Patent Owner Preliminary Response (“Prelim. Resp.”). Paper 7.

We have authority to determine whether to institute an *inter partes* review. 35 U.S.C. § 314(b) (2018); 37 C.F.R. § 42.4(a) (2019). An *inter partes* review may not be instituted “unless . . . the information presented in the petition . . . shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” 35 U.S.C. § 314(a). Upon consideration of the Petition, the Preliminary Response, and the evidence of record, we conclude that the information presented shows a reasonable likelihood that Petitioner would prevail in showing the unpatentability of at least one of the Challenged Claims. Accordingly, we authorize an *inter partes* review to be instituted as to the Challenged Claims of the ’176 patent on the grounds raised in the Petition. Our factual findings and conclusions at this stage of the proceeding are based on the evidentiary record developed thus far (prior to Patent Owner’s Response). This is not a final decision as to patentability of claims for which *inter partes* review is instituted. Any final decision will be based on the record, as fully developed during trial.

B. *Real Parties in Interest*

Petitioner identifies RESTEM LLC as the real party-in-interest for Petitioner. Pet. 1.

Patent Owner identifies Jadi Cell, LLC, as owner of the '176 patent. Paper 4, 2.

C. Related Matters

Petitioner states that no related litigation matter is pending and that the “application that matured into the '176 patent was used for a priority claim for pending U.S. Application No. 15/799,743, filed on October 31, 2017, which was used for a priority claim to pending U.S. Application No. 17/322,672, filed on May 17, 2021.” Pet. 1.

Patent Owner identifies no related matters. Paper 4, 2.¹

D. The '176 Patent

The '176 patent, titled “Methods and Compositions for the Clinical Derivation of An Allogenic² Cell and Therapeutic Uses” issued October 31, 2017, from Application No. 13/732,204 (“the '204 application), filed August 22, 2013. Ex. 1001, codes (21), (22), (45), (54).

The '176 patent discloses “an allogenic cell or stem cell³ population that can be used for treating a wide range of conditions” along with methods of “isolating, culturing, developing, or otherwise producing these cells.” *Id.*

¹ Paper 4 is not paginated. We cite to Paper 4 as if paginated beginning on the cover page.

² An “allogenic” cell is one that is “genetically different although belonging to or obtained from the same species.” *See* American Heritage Dictionary of Medicine, https://search.credoreference.com/content/entry/hmmedicaldict/allogeneic_also_allogenic/0 (accessed March 29, 2022). Ex. 3001.

³ “Stem cells” are cells with “the ability to differentiate along different lineages and the ability to self-renew.” Ding, Dah-Ching, et al., Mesenchymal Stem Cells, CELL TRANSPLANT 20(1):5–14 (2011). Ex. 3002. “Mesenchymal stem cells (MSCs) are stromal cells that have the ability to self-renew and also exhibit multilineage differentiation. MSCs can be isolated from a variety of tissues, such as umbilical cord, endometrial polyps, menses blood, bone marrow, adipose tissue, etc.”

at 7:23–30. The cells are obtained from the subepithelial layer (SL) of a mammalian umbilical cord using one of a “variety of techniques” so long as the technique “allows such extraction without significant damage to the cells.” *Id.* at 8:1–2, 8:34–38. Figure 1 of the ’176 patent, reproduced below, shows a section of umbilical cord.

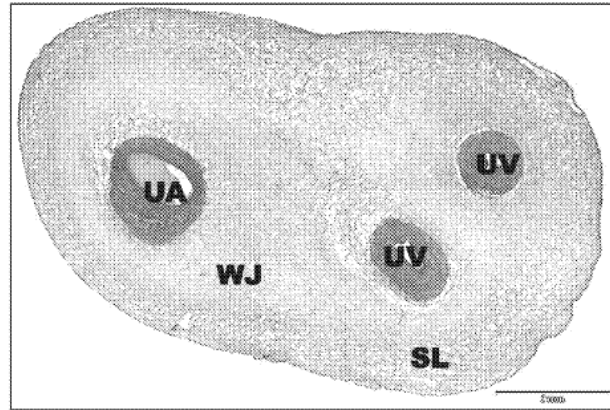


FIG. 1

“A cross section of a human umbilical cord is shown in FIG. 1, which shows the umbilical artery (UA), the umbilical veins (UV), the Wharton's Jelly (WJ), and the subepithelial layer (SL).” *Id.* at 3:27–29.

After extraction, the cells of the SL are placed on a substrate, which can be a solid or semi-solid material. *Id.* at 8:39–9:3. The SL is then “cultured in a suitable medium . . . for a period of time sufficient to establish primary cell cultures. (e.g. 3-7 days in some cases).” *Id.* at 9:16–18. The SL tissue is then removed and discarded, and the cells are further cultured and expanded in larger culture flasks in “either a normoxic or hypoxic culture conditions.” *Id.* at 9:19–22.

Example 2 of the ’176 patent describes one method of cell extraction and culturing:

Culturing Cells or Stem Cell from Umbilical Cord
for Clinical Use

Umbilical cord tissue is obtained and maternal blood is tested for infectious disease prior to derivation of cell and stem cell populations. A 1 cm piece of cord is washed 10 times in a solution of DPBS containing 10% PRP-Lysate or platelet lysate. The umbilical cord is then opened longitudinally to expose the interior of the umbilical cord. All tissue is removed that can give rise to endothelial cells. The umbilical cord is then place [sic, placed] directly into a cell culture dish containing Media Composition-1 with the interior of the umbilical cord in contact with the plastic and cultured in either normoxic or hypoxic culture environments.

On the third day the media is replaced with fresh Media Composition-1 and cultured until day seven when the explants are removed for primary cell expansion. The cells are fed every other day until approximately 500,000-1,000,000 cells can be harvested and further expanded. It is noted that the media used for subsequent examples is Media Composition-1 unless specifically noted otherwise.

Id. at 13:50–14:5 (Media Composition-1 is described at 13:31–48).

After culture is established, the cells can “be utilized as-is upon isolation from the SL tissue” or can be “differentiated into other cell types . . . by exposing the cells to chemicals, growth factors, supernatants, synthetic or naturally occurring compounds, or any other agent capable of transforming the cells.” *Id.* at 10:55–65.

The '176 patent discloses that cells isolated from the SL tissue “can have a variety of characteristic markers⁴ that distinguish them from cell[s]

⁴ A “genetic marker” or “cell marker” is “a readily recognizable genetic trait, gene, DNA segment, or gene product used for identification purposes especially when closely linked to a trait or to genetic material that is difficult to identify.” Merriam Webster dictionary: <https://www.merriam->

previously isolated from umbilical cord samples.” *Id.* at 7:65–68. Cells isolated from SL tissue are disclosed to have the following genetic characteristics as defined by cell markers: “are positive for SOX2 and OCT4, and are negative for NANOG as compared to control cells” and “are positive for CD44 . . . CD90 [and] CD 146.” *Id.* at 9:53–60. *See also* 8:3–33, providing “[v]arious cellular markers that are either present or absent [that] can be utilized in the identification of these SL-derived cells.”

E. Illustrative Claim

Petitioner challenges claims 1–15 of the ’176 patent. Pet. 7. Claim 1 is independent and claims 2–15 depend from claim 1. Ex. 1001, 19:5–20:28. Claim 1 is illustrative of the claimed subject matter and is reproduced below.

1. An isolated cell prepared by a process comprising:
placing a subepithelial layer of a mammalian umbilical
cord tissue in direct contact with a growth
substrate; and
culturing the subepithelial layer such that the isolated cell
from the subepithelial layer is capable of self-
renewal and culture expansion,
wherein the isolated cell expresses at least three cell
markers selected from the group consisting of
CD29, CD73, CD90, CD166, SSEA4, CD9, CD44,
CD146, or CD105, and
wherein the isolated cell does not express NANOG and at
least five cell markers selected from the group
consisting of CD45, CD34, CD14, CD79, CD106,
CD86, CD80, CD19, CD117, Stro-1, or HLA-DR.

webster.com/dictionary/genetic%20marker#medicalDictionary (accessed April 13, 2022). Ex. 3003.3001

Claims 1–9 and 11–15 recite isolated cells with various characteristics or culture environments, and claim 10 recites a culture of differentiated cells derived from the isolated cell of claim 1. *Id.* at 19:20–20:28.

F. Prior Art and Asserted Grounds

Petitioner asserts that the Challenged Claims are unpatentable based on the following grounds:

Ground	Claims Challenged	35 U.S.C. §	References
1	1–13, 15	102 ⁵	Majore ⁶
2	14	103	Majore, Mistry ⁷
3	1–13, 15	103	Majore, Pierantozzi, ⁸ Rojewski, ⁹ Meiron, ¹⁰

⁵ The Leahy-Smith America Invents Act (“AIA”), Pub. L. No. 112-29, 125 Stat. 284, 287–88 (2011), amended 35 U.S.C. §§ 102 and 103, effective March 16, 2013. Because the ’176 patent claims priority to a provisional application filed prior to the effective date of these AIA amendments, we apply the pre-AIA version of 35 U.S.C. § 102 and § 103.

⁶ Ingrida Majore, et al., *Growth and Differentiation Properties of Mesenchymal Stromal Cell Populations Derived from Whole Human Umbilical Cord*, STEM CELL REV AND REP 7:17–31 (2011) (Ex. 1011, “Majore”).

⁷ Sanjay Mistry, et al, U.S. Pat. No. US 7,510,873 B2, issued Mar. 31, 2009 (Ex. 1015, “Mistry”).

⁸ Enrico Pierantozzi, et al., *Pluripotency Regulators in Human Mesenchymal Stem Cells: Expression of NANOG But Not of OCT-4 and SOX-2*, STEM CELLS AND DEV. 20(5):915–923 (2011) (Ex. 1012, “Pierantozzi”).

⁹ Markus Thomas Rojewski, et al., *Phenotypic Characterization of Mesenchymal Stem Cells from Various Tissues*, TRANSFUS. MED. HEMOTHER., 35:168–184 (2008) (Ex. 1014, “Rojewski”).

¹⁰ Moran Meiron, et al., WO 2009/037690 A1, published March 26, 2009 (Ex. 1016, “Meiron”).

Ground	Claims Challenged	35 U.S.C. §	References
			Riekstina ¹¹
4	14	103	Majore, Pierantozzi, Rojewski, Meiron, Mistry
5	1–15	103	Phan, ¹² Pierantozzi, Rojewski, Meiron, Riekstina
6	1–8, 10–13, 15	103	Kita, ¹³ Pierantozzi, Rojewski, Meiron, Riekstina
7	14	103	Kita, Pierantozzi, Rojewski, Meiron, Riekstina, Mistry
8	9	103	Kita, Pierantozzi, Rojewski, Meiron, Majore

Pet. 7. Petitioner alleges “all of the cited references qualify as prior art even if the challenged claims were found to be entitled to the filing date of the first provisional application” and provides evidence of the public availability of these references. *Id.* at 3–6. Patent Owner does not challenge the prior art status of any asserted reference. *See generally* Prelim. Resp.

¹¹ Una Riekstina, et al., *Embryonic Stem Cell Marker Expression Pattern in Human Mesenchymal Stem Cells Derived from Bone Marrow, Adipose Tissue, Heart and Dermis*, STEM CELL REV AND REP 5:378–386 (2009) (Ex. 1013, “Riekstina”).

¹² Toan-Thang Phan and Ivor Jiun Lim, WO 2006/019357 A1, published February 23, 2006 *Ex. 1017, “Phan”).

¹³ Katsuhiko Kita, et al., *Isolation and Characterization of Mesenchymal Stem Cells From the Sub-Amniotic Human Umbilical Cord Lining Membrane*, STEM CELL REV AND REP 19(4):491–501 (2009) (Ex. 1013, “Riekstina”).

In support of its Petition, Petitioner relies on the supporting Declaration of Scott Olson, Ph.D., dated August 7, 2021. Ex. 1007 (“Olson Dec.”). In its Preliminary Response, Patent Owner relies on the supporting Declarations of Camillo Ricordi, M.D., (Ex. 2002), inventor Amit Patel, M.D., (Ex. 2009), Kristine Krafts, M.D., (Ex. 2017) and Scott Burger, M.D. (Ex. 2022).

II. ANALYSIS

A. Legal Standards

A patent claim is unpatentable under 35 U.S.C. § 102 if each and every element in a claim, arranged as recited in the claim, is found in a single prior art reference. *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008); *Karsten Mfg. Corp. v. Cleveland Golf Co.*, 242 F.3d 1376, 1383 (Fed. Cir. 2001).

A patent claim is unpatentable under 35 U.S.C. § 103 if the differences between the claimed 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 person having ordinary skill in the art to which said subject matter pertains. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). In *Graham v. John Deere Co.*, 383 U.S. 1 (1966), the Supreme Court set out a framework for assessing obviousness under § 103 that requires consideration of four factors: (1) the “level of ordinary skill in the pertinent art,” (2) the “scope and content of the prior art,” (3) the “differences between the prior art and the claims at issue,” and (4) “secondary considerations” of nonobviousness such as “commercial success, long felt but unsolved needs, failure of others, etc.” *Id.* at 17–18; *KSR*, 550 U.S. at 407.

Where the challenged claim is a product-by-process claim, analysis of patentability focuses on the product:

[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.

In re Thorpe, 777 F.2d 695, 698 (Fed. Cir. 1985) (citations omitted). *See also Amgen Inc. v. F. Hoffman-La Roche Ltd.*, 580 F.3d 1340, 1370 n 14 (Fed. Cir. 2009); *see also Purdue Pharma v. Epic Pharma*, 811 F.3d 1345 (Fed. Cir. 2016) (“Because validity is determined based on the requirements of patentability, a patent is invalid if a product made by the process recited in a product-by-process claim is anticipated by or obvious from prior art products, even if those prior art products are made by different processes.”).

B. Person of Ordinary Skill in the Art

“The level of skill in the art is a factual determination” that provides a primary guarantee of objectivity in an obviousness analysis. *Al-Site Corp. v. VSI Int’l Inc.*, 174 F.3d 1308, 1324 (Fed. Cir. 1999) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966); *Ryko Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714, 718 (Fed. Cir. 1991)).

Petitioner asserts that a person of ordinary skill in the art (“skilled artisan”) at the time of the invention would have had

at least a doctorate degree in cell biology, molecular biology, or a similar field with at least three years of experience in research relating to umbilical cord stem cells, or an Bachelor’s degree in cell biology, molecular biology, or a similar field, with approximately 10 years of experience relating to umbilical cord stem cells. . . . Additional education might substitute for experience, while significant experience in the field of

umbilical cord stem cell biology or post-natal tissue-derived stem cell biology might substitute for formal education.

Pet. 15 (citing Ex. 1007 ¶¶ 19–24). Patent Owner does not comment on the characterization offered by Petitioner or offer one of its own. *See generally* Prelim. Resp.

For purposes of this Decision, we adopt Petitioner’s characterization as it is consistent with the level of skill in the art at the time of the invention as reflected by the ’176 patent and the cited prior art. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that specific findings regarding ordinary skill level are not required “where the prior art itself reflects an appropriate level and a need for testimony is not shown” (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 163 (Fed. Cir. 1985))).

C. Claim Construction

We apply the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b). 37 C.F.R. § 42.100(b) (2019). Under that standard, claim terms “are generally given their ordinary and customary meaning” as understood by a person of ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc). “In determining the meaning of the disputed claim limitation, we look principally to the intrinsic evidence of record, examining the claim language itself, the written description, and the prosecution history, if in evidence.” *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 469 F.3d 1005, 1014 (Fed. Cir. 2006) (citing *Phillips*, 415 F.3d at 1312–17). Extrinsic evidence is “less significant than the intrinsic record in determining ‘the legally operative meaning of claim language.’” *Phillips*, 415 F.3d at 1317.

Petitioner offers constructions for multiple claim terms. Pet. 16–20. Patent Owner opposes Petitioner’s constructions and offers its own constructions along with argument why Petitioner’s proposed constructions should not be adopted. Prelim. Resp. 12–20.

It is not necessary to construe all proposed claim terms for purposes of rendering this Decision. *See Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011) (“[C]laim terms need only be construed ‘to the extent necessary to resolve the controversy.’”) (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)). In particular, because the patentability of a product-by-process claim focuses on the product, *In re Thorpe*, 777 F.2d at 698, it is not necessary to construe claim terms regarding steps of the recited process, e.g. “culturing the subepithelial layer.” For the purpose of institution, we construe only the following claim terms below:

I. “an isolated cell”

Petitioner proposes that “an isolated cell” means:

one or more cells present in a heterogeneous population of cells that expresses at least three cell markers selected from the group consisting of CD29, CD73, CD90, CD166, SSEA4, CD9, CD44, CD146, or CD105, and does not express NANOG and at least five cell markers selected from the group consisting of CD45, CD34, CD14, CD79, CD106, CD86, CD80, CD19, CD117, Stro-1, or HLA-DR.

Pet. 17. In support of its construction, Petitioner cites disclosures in the patent at Ex. 1001, 6:32–34, 8:35–39, 8:54–58, 8:62–64, 9:5, Dr. Olson’s testimony at Ex. 1007 ¶¶ 67–68, and *KCJ Corp. v. Kinetic Concepts, Inc.*, 223 F.3d 1351, 1356 (Fed. Cir. 2000). *Id.*

Patent Owner proposes that “an isolated cell” means “one or more cells isolated from the subepithelial layer of a mammalian umbilical cord.”

Prelim. Resp. 16. Patent Owner cites Ex. 1001 6:32–34, noting that the patent specification “expressly defines ‘isolated cell’ as ‘[referring] to a cell that has been isolated from the subepithelial layer of a mammalian umbilical cord.’” *Id.*

As neither party references any prosecution history related to interpretation of this claim term, we look only to the claim itself and the specification as intrinsic evidence. *DePuy Spine*, 469 F.3d at 1014. Claim 1 recites “an isolated cell prepared by a process comprising . . .” Ex. 1001 at 19:6. As Patent Owner notes, the patent specification states “the term ‘isolated cell’ refers to a cell that has been isolated from the subepithelial layer of a mammalian umbilical cord.” *Id.* at 6:32–34. The remainder of the citations Petitioner cites relate to additional steps for isolating the cell, or characteristics of the cell, such as the markers expressed or not expressed, but do not further elucidate the meaning of “an isolated cell” itself. Dr. Olsen’s testimony reiterates the content of these citations but does not add any additional information or explanation. Ex. 1007 ¶¶ 67–68. Given the definition provided in the specification, we interpret “an isolated cell,” consistent with Patent Owner’s definition, to mean “one or more cells isolated from the subepithelial layer of a mammalian umbilical cord.”

2. “subepithelial layer”

Petitioner proposes that the “subepithelial layer” means “the tissue of the umbilical cord inside and adjacent to the epithelial layer and part of the continuum of the Wharton’s jelly.” Pet. 18. Petitioner relies on Dr. Olson’s testimony that the subepithelial layer is not clearly defined in the ‘176 patent, but that “the protocol and figures disclosed in the ‘176 patent indicates that it considers the subepithelial layer to be the tissue inside and

adjacent to the epithelial layer and outside the vessels as part of the continuum of the Wharton's jelly.” Ex. 1007 ¶ 70.

Patent Owner proposes that the “subepithelial layer” means “the layer of tissue in umbilical cord that is located between—and distinct from—the amniotic membrane and Wharton's Jelly.” Prelim. Resp. 14. Patent Owner argues that Petitioner's proposed construction is anatomically incorrect because the specification “describes removing/dissecting the Wharton's Jelly from the subepithelial layer” and thus, the subepithelial layer cannot contain everything inside the whole amniotic membrane, including the Wharton's jelly. *Id.* at 14–15. Patent Owner argues that Petitioner “inaccurately equates ‘the subamniotic zone, the subamnion, the subepithelial layer, the amniotic membrane, and the umbilical cord lining’” when rather the components are different as well as the amniotic membrane and umbilical cord lining. *Id.* at 15.

On the present record, we consider Patent Owner's definition more consistent with the disclosure of the '176 patent. In particular, the specification discloses removal of Wharton's jelly from the umbilical cord prior to culturing the subepithelial layer. Ex. 1001 at 2:19–20. *See also* Ex. 2017 ¶ 21 (pathologist declaration stating “[t]he subepithelial layer and the Wharton's Jelly are morphologically distinctive and distinguishable”). We provisionally adopt Patent Owner's definition for purposes of this decision.

D. Ground I – Anticipation of Claims 1–13, and 15 by Majore

1. Summary of Majore (Ex. 1011)

Majore discloses isolating mesenchymal stem cells (MSC) from human umbilical cord (UC) tissue to create highly proliferative isolated cells. Ex. 1011 at 17. Majore discloses “cells isolated from whole UC

satisfies all requirements essential for the generation of stem cell banks containing permanently available cell material for applications in the field of regenerative medicine.” *Id.*

Majore describes a method for isolation of MSCs as follows:

For cell isolation from whole UC an explant culture approach was employed. Human UCs (MK 240707, HD 140509, NS 010408, NS 190109) were obtained from term delivery (38–40 weeks) by Cesarean section patients (n=4) . . . Blood from UC vessels was removed and the UC was placed in PBS (phosphate buffered saline) enriched with 5 g/l glucose (Sigma Aldrich), 50 µg/ml gentamicine (PAA Laboratories), 2.5 µg/ml amphotericin B (Sigma Aldrich), 100 U/ml penicillin and 100 µg/ml streptomycin (PAA Laboratories). At the laboratory UC was cut into approx. 10 cm large segments which further were minced in ca. 0.5 cm³ large pieces and placed in 175-cm² tissue culture flasks (Sarstedt). Then these pieces were incubated in αMEM (Invitrogen) enriched with 15% of allogeneic human serum . . . A beginning outgrowth of an adherent cell layer from single tissue pieces was observed after approx. 10 days. After 2 weeks, the tissue pieces were removed and the adherent cells were harvested . . . Cells were subcultured at the density of 4.000 cells/cm² in 175-cm² tissue culture flasks and grown until 80% of confluence. Subsequently cells were harvested as already described and used for immunophenotype analysis or cryopreserved.

Id. at 18. Majore discloses that immunophenotype analysis detected cell surface markers CD34, CD73, CD90, and CD105 in the isolated cells. *Id.* at 22 (Table 2). Majore further discloses that no “xenogenic¹⁴ media supplements during UC cell isolation, expansion and differentiation.” *Id.* at 28.

¹⁴ “Xenogenic” means “derived from, originating in, or being a member of another species.” Dictionary.com definition of “xenogenic,” found at: <https://www.merriam-webster.com/dictionary/xenogeneic#medical> Dictionary (accessed April 15, 2022). Ex. 3004.

2. Analysis of Claim 1

Petitioner asserts that Majore discloses the limitations of claim 1 either expressly or inherently, because its disclosed method of inducing stem cells to grow from umbilical cord tissue “necessarily includes the subepithelial layer of the umbilical cord recited by the ‘176 patent claims.” Pet. 21–28. Petitioner’s contentions are supported by the declaration testimony of Dr. Olsen (Ex. 1007 ¶¶ 92–122).

Patent Owner argues that Ground 1 should be denied because Petitioner’s inherency arguments are based on speculation that the disclosed method would result in the isolated cell of claim 1. Prelim. Resp. 21–29. Patent Owner’s arguments are supported by the declaration testimony of Dr. Burger (Ex. 2022 ¶¶ 101–106, 137–173).

For the reasons discussed below, we determine that Petitioner has demonstrated a reasonable likelihood that Petitioner will succeed in showing that Majore anticipates claim 1. We analyze Patent Owner’s opposing arguments as they apply to claim 1 below, using the subsections for claim 1 identified by the parties as shown in the following table:

[Pre]	An isolated cell prepared by a process comprising:
[A]	placing a subepithelial layer of a mammalian umbilical cord tissue in direct contact with a growth substrate; and
[B]	culturing the subepithelial layer such that the isolated cell from the subepithelial layer is capable of self-renewal and culture expansion,
[C]	wherein the isolated cell does not express NANOG...
[D]	wherein the isolated cell expresses at least three cell markers selected from the group consisting of CD29, CD73, CD90, CD166, SSEA4, CD9, CD44, CD146, or CD105;
[E]	wherein the isolated cell does not express...at least five cell markers selected from the group consisting of CD45, CD34, CD14, CD79, CD106, CD86, CD80, CD19, CD117, Stro-1, or

	HLA-DR.
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Pet. 12–13.

a) Petitioner’s Contentions

Petitioner asserts that every element of claim 1 is found in Majore, as follows:

([Pre] and [A]) “An isolated cell prepared by a process comprising placing a subepithelial layer of a mammalian umbilical cord tissue in direct contact with a growth substrate

Petitioner asserts that Majore discloses “isolating MSCs from umbilical cord tissue by placing pieces of whole umbilical cord onto the surface of a tissue culture flask.” Pet. 22 (citing Ex. 1007 ¶ 95). Petitioner asserts that because Majore minced the whole umbilical cord into 0.5 cm³ pieces, “the cubic dimensions of minced pieces necessarily results in at least some pieces with subepithelial layer exposed by the cut which would then be in contact with the tissue culture surface upon sinking to the bottom of the flask.” Pet. 22 (citing Ex. 1007 ¶ 96). Petitioner explains that through Majore’s “explant” method of isolating cells from tissues, the “cells that give rise to cultured MSCs, as defined by surface marker expression, migrate out of the umbilical cord tissue via intercellular communication to emulate a wound healing condition.” *Id.* Petitioner argues that the process “would result in MSCs from the subepithelial layer migrating to the periphery of the tissue and adhering to the tissue culture vessel” and thus the Majore protocol “produces cells that necessarily and inevitably comprise the cells of the subepithelial layer.” *Id.*

([B]) culturing the subepithelial layer such that the isolated cell from the subepithelial layer is capable of self-renewal and culture expansion

Petitioner asserts that Majore discloses an MSC isolation protocol and that MSCs were known to be highly proliferative somatic cells able to self-renew. Pet. 23 (citing Ex. 1007 ¶ 98).

([D]) wherein the isolated cell expresses at least three cell markers selected from the group consisting of CD29, CD73, CD90, CD166, SSEA4, CD9, CD44, CD146, or CD105

([C] and [E]) wherein the isolated cell does not express NANOG and at least five cell markers selected from the group consisting of CD45, CD34, CD14, CD79, CD106, CD86, CD80, CD19, CD117, Stro-1, or HLA-DR

Petitioner asserts that because the cells produced by Majore necessarily comprise the same cells of the '176 patent, Majore's cells would inherently possess these features and express or not express the markers recited in 1[C] and 1[D]. *Id.* at 23–24 (citing Ex. 1007 ¶ 101). Petitioner argues the markers themselves should not be given patentable weight as they merely describe a property of a known composition, but that, even if they are considered, the marker expression/non-expression evidence disclosed by Majore is consistent with the markers recited in 1[C] and 1[D]. *Id.* at 24 (citing Ex. 1007 ¶ 99).

b) Patent Owner's Contentions

Patent Owner argues that Majore does not disclose “placing a subepithelial layer of a mammalian umbilical cord tissue in direct contact with a growth substrate” because it is “silent” on how the umbilical cord pieces were placed within the flask. Prelim. Resp. 21–22. Patent Owner also argues that Petitioner has failed to provide evidence that Majore's process would have “*necessarily resulted*” in the recited elements, particularly without removal of the Wharton's jelly or strategic placement of the umbilical cord pieces. *Id.* at 22. Patent Owner argues that Majore's

protocol “involved adherent culturing,” which “does not involve the subepithelial layer facing and contacting the flask surface.” *Id.* at 24.

Patent Owner also argues that the umbilical cord segments would contain contaminants (non-subepithelial layer cells) that would not have the same genetic profile as the claimed isolated cell. *Id.* at 24–25. For example, Patent Owner argues that Majore does not disclose an “isolated cell [that] does not express NANOG” and, because the protocol used by Majore differs from that of the ’176 patent, that the cells are not the same as the claimed cells. *Id.* at 25–26. Patent Owner cites other “similar . . . processes” known to result in the expression of NANOG. *Id.* at 26 (citing Ex. 1007 ¶ 149).

Patent Owner further argues that Majore does not disclose the non-expression of at least five cell markers recited by 1[E]. *Id.* at 26. Patent Owner argues that Petitioner’s inherency case is insufficient without such evidence, and that “Majore provides no evidence that the cells expressing/not expressing particular markers were derived from any portion of the subepithelial layer of the tissue.” *Id.* at 26–28.

c) Discussion

As claim 1 is a product-by process claim, “determination of patentability is based on the product itself” and “does not depend on its method of production.” *In re Thorpe*, 777 F.2d at 697. Thus, we evaluate whether the evidence of record shows there is a reasonable likelihood that Petitioner would prevail in showing that the process of Majore would have resulted in “an isolated cell” having the marker characteristics of limitations [C], [D], and [E] recited in claim 1, despite any differences between Majore’s process and the process limitations of claim 1, i.e., limitations [A] and [B] referenced above. For this reason, we are not persuaded by Patent

Owner's arguments against anticipation based on the various differences in Majore's process from those recited in the claims. *See, e.g.*, Prelim. Resp. at 21–22 (Majore does not place a subepithelial layer in direct contact with a substrate); 23–24 (Majore does not remove Wharton's jelly); 24–25 (multiple cell types present would be “contaminant cells” that are “different from the claimed cells.”). Nor are we persuaded at this stage that Majore's lack of explicit recitation regarding the expression or non-expression of every claimed genetic marker is indicative that the isolated cells are not otherwise identical to what is claimed. Prelim. Resp. 25–26. That Majore did not disclose testing every marker recited by claim 1 does not mean that Majore fails to disclose a method to isolate *a cell* with a genetic marker profile that is nonetheless identical to the claimed cell.¹⁵

Setting aside the process limitation arguments, Patent Owner's sole remaining argument is that Petitioner did not provide evidence that Majore's experiments would have “*necessarily resulted*” in the recited elements. Patent Owner argues that “even if some small portion of subepithelial layer had adhered to the Majore flask (which is virtually impossible), Majore provides no evidence that the cells expressing/not expressing particular markers were derived from any portion of the subepithelial layer of the tissue.” Prelim. Resp. 29. Patent Owner, through Dr. Burger, argues that “the vast majority of surface area of any particular piece corresponds to tissue other than the subepithelial layer; thus, the cells expressing such markers were almost certainly derived from cells of other UC tissue such as

¹⁵ We find neither party's argument regarding the International Society for Cellular Therapy's (ISCT) criteria for MSCs and Majore's references to the criteria (Pet. 33; Prelim. Resp. 26–28) persuasive on this record, and therefore do not address them at this stage.

the Wharton’s Jelly, epithelium, etc.” and that, without evidence that the recited markers are expressed/not expressed as recited, there is no inherent disclosure. Prelim. Resp. 22, 25, 28–29 (citing Ex. 2022 ¶ 162). Patent Owner is correct that an ultimate finding of anticipation requires such confirmation, but, for purposes of institution, our standard is a reasonable likelihood. 35 U.S.C. § 314(a). Due to the breadth of claim 1, Majore’s method must produce *only one cell* having the recited limitations to anticipate. Petitioner’s expert testifies that production of such cells would be inherent by Majore. *See* Ex. 1007 ¶ 97 (“Majore’s protocol would produce a population of adherent cells that necessarily and inevitably comprise the cells of the subepithelial layer.”). And, although we recognize that the burden of persuasion does not rest on Patent Owner, Dr. Burger’s testimony, which focuses heavily on the differences in methodology between Majore and the ’176 patent disclosure and Petitioner’s alleged failure of proof, is not persuasive at this stage to overcome the evidence presented by Petitioner. *See* Ex. 2002 ¶¶ 137–163.

Indeed, both Majore and the ’176 patent disclose umbilical cord tissue cut into sections and placed into environments fostering cell culture and replication. Ex. 1011 at 18, Ex. 1001 at 13:57–14:5. Both methods encourage and result in adherent cells growing on a plastic growth surface awash in culture media. *Id.* On this record, Petitioner has provided sufficient factual basis to establish a reasonable likelihood that Majore’s explant method of dissecting umbilical cord, culturing cells, and growing adherent cells would have produced (or did produce) at least one cell with the recited limitations. In this regard, we credit the testimony of Dr. Olsen that the isolated cells disclosed in Majore are MSCs cultured from umbilical

cord tissues including the subepithelial layer, which have migrated to the periphery of the cut tissue and adhered to the tissue culture vessel. Ex. 1007 ¶¶ 95–97. That Majore discloses genetic markers with similar expression/non-expression to the markers recited in claim 1 is further evidence that at least some cells were cultured from the subepithelial layer. *Id.* ¶ 99. Moreover, even if we gave weight to the process limitations construed as requested by Patent Owner (Prelim. Resp. 13–20), the limitations are sufficiently broad as to read on Majore with the exception of the express/non-expressed markers. With regard to markers not examined by Majore, we credit Dr. Olson’s statement that “the cells obtained by Majore’s protocol necessarily and inevitably comprise the same cells produced by the process steps of claim 1[A] and 1[B]” and that the skilled artisan would have understood that the marker expression pattern would be identical for those cells. *Id.* ¶ 101.¹⁶ The evidence on this issue is subject to final determination on a more complete record developed through trial.

¹⁶ The parties are further invited to address in their post-institution briefing whether limitations [C] and [E] reciting the non-expression of certain markers should be treated as “negative limitations,” and the burden of proving that a negative limitation is satisfied by silence in the prior art. *See Almirall, LLC v. Amneal Pharms. LLC*, 28 F.4th 265 (Fed. Cir. 2022) (determining that “it was reasonable for the Board to find that, in the context of [the prior art reference], a skilled artisan would recognize that the reference discloses a complete formulation—excluding the possibility of an additional active ingredient”); *Novartis Pharms. Corp. v. Accord Healthcare, Inc.*, 21 F.4th 1362, 1373 (Fed. Cir. 2022) (recognizing that for negative limitations, “the disclosure must be read from the perspective of a person of skill in the art”).

3. *Analysis of Claims 2–8, 10–13, and 15*

Claims 2–8, 10–13, and 15 depend from claim 1. Claims 2 and 3 recite the expression or non-expression of additional markers not tested in Majore. Ex. 1001 at 20–26. Claims 4–6 recite that the cells are positive for SOX2, OCT4, or both. *Id.* at 19:27–20:2. Claim 7 recites an isolated cell of claim 1 with the ability to differentiate into one of a group of specified cell types and claims 11–14 recite isolated cells of claim 1 that have differentiated into individual of the enumerated cell types. *Id.* at 20:3–7, 20:19–26. Claim 8 recites the production of specified exosomes. *Id.* at 20:8–10. Claims 10 and 15 recite cultures of differentiated cells derived from a cell of claim 1. *Id.* at 20:14–18, 20:27–28.

For the same reasons explained above with regard to claim 1, we credit Dr. Olson’s testimony that cells produced by the method of Majore would have the same marker pattern, differentiation ability, exosome production ability, and ability to create the specified cultures as recited in claims 2–8, 10–13, and 15 because they would comprise the same cells produced by the process of claim 1. Ex. 1007 ¶¶ 102–122. As with claim 1, the evidence on this issue is subject to final determination on a more complete record developed through trial.

4. *Analysis of Claim 9*

Claim 9 recites culturing the cell of claim 1 in animal component-free media. Ex. 1001 at 20:11–13. For this claim, the evidence of record regarding some components of Majore containing animal components favors Patent Owner. *See* Prelim. Resp. 31, citing Ex. 2022 ¶ 173. As with claims 1–8 and 10–13, and 15 discussed above, we reserve a final determination as to the patentability of claim 9 to the conclusion of trial.

E. Ground II - Obviousness of Claim 14 over Majore and Mistry

1. Mistry (Ex. 1015)

Mistry is directed to methods for isolating cells from mammalian umbilical cord tissue that are “capable of self-renewal and expansion in culture” and “have the potential to differentiate into cells of other phenotypes.” Ex. 1015 at 3:18–22. Mistry teaches that culture media for cells is “known in the art for affecting differentiation of such potent cells [stem cells like MSCs] into specific types of cells or progenitors of specific cells.” *Id.* at 11:34–39. Mistry discloses that a need for therapy methods to “slow the progression of and/or cure heart disease, such as ischemic heart disease and congestive heart failure” means that “[c]ells that can differentiate into cardiomyocytes that can fully integrate into the patient’s cardiac muscle without arrhythmias are highly desirable.” *Id.* at 90:59–64. Mistry discloses that “umbilicus-derived cells were treated with 5-azacytidine alone or in combination with DMOS or chelerythrine chloride, and markers of cardiomyocytes measured by real-time PCR.” *Id.* at 91:9–13. Mistry confirmed that the treated cells expressed markers of cardiomyocytes relative to control cells. *Id.* at 91:60–92:3.

2. Analysis

Claim 14 recites an isolated cell of claim 1 that has differentiated into a cardiomyocyte cell. Petitioner argues that a skilled artisan “would have been motivated to combine the teachings of Mistry and Majore to produce MSC cell therapies for the treatment of disease,” in this case, to create a

cardiomyocyte therapeutic for cardiac disease. Pet. 29 (citing Ex. 1007 ¶¶ 85, 123).

Patent Owner argues that Mistry does not disclose differentiation into cardiomyocytes, but only the potential to do so. Prelim. Resp. 69–70. In addition, Patent Owner argues (regarding all claims) that objective evidence confirms nonobviousness of the claimed invention, and provides “(1) independent studies showing the advantages of the claimed cells satisfy a long felt need, a least to treat ARDS [acute respiratory distress syndrome]; (2) the failure of others to obtain a potency assay for stem cells or receive Phase III trial approval; and (3) commercial success shown by several licensees and related valuations.” *Id.* at 9–12.

For the same reasons explained in II.D.2. above with respect to claim 1, we credit Dr. Olson’s testimony that cells produced by the method of Majore would comprise cells having the same marker pattern, differentiation ability, exosome production ability, and ability to create the specified cultures as recited by these claims because the cells would comprise the same cells produced by the process of claim 1. Ex. 1007 ¶¶ 102–122. On this issue, the weight of evidence favors Petitioner that a skilled artisan would have been motivated to combine the teachings of Majore regarding isolation of MSCs for use in regenerative medicine and Mistry’s teachings regarding inducing MSCs to differentiate into cardiomyocytes using 5-azacytidine to seek to produce an isolated cell of claim 14 for the treatment of disease.

In addition, while we have considered Patent Owner’s objective indicia evidence, the question of whether such evidence supports a conclusion of non-obviousness is fact intensive and is best decided on a full

record. *Cf. Monark Knitting Mach, Corp. v. Sulzer Morat GmbH*, 139 F.3d 877, 886 (Fed. Cir. 1998) (determining that issues of fact concerning secondary considerations precluded grant of summary judgment). We reserve a final determination as to the patentability of claim 14 to the conclusion of trial.

F. Ground III – Obviousness of Claims 1–13, and 15 over Majore, Pierantozzi, Rojewski, Meiron, and Riekstina

1. Pierantozzi (Ex. 1012)

Pierantozzi discloses that because “MSCs from human adult tissues represent a promising source of cells for a wide range of cellular therapies, there is high interest in better understanding the mechanisms underlying proliferation, differentiation, and heterogeneity of these cells.” Ex. 1012, Abstract. Pierantozzi examined MSCs from human bone marrow, adipose tissue, and cardiac tissue that were isolated and cultured to 80% confluence. *Id.* at 916. Pierantozzi induced osteogenic and chondrogenic differentiation in the MSC populations using culture serum containing substances causing differentiation. *Id.* at 916–917. Expression of genetic markers in freshly isolated MSCs as compared to MSCs grown to 80% confluence was performed by reverse transcriptase-PCR to amplify extracted RNA, immunofluorescence, and immunoprecipitation assays. *Id.* at 917–918. Pierantozzi discloses that “NANOG was not expressed in freshly isolated MSCs, but was detected only after in vitro culture. NANOG was detected only in proliferating cells, but not in MSCs induced to differentiate.” *Id.* at Abstract. Pierantozzi states “we propose that activation of NANOG expression in MSCs is associated with, although cannot directly regulate, the transition from in vivo quiescence to adaptation to in vitro growth conditions.” *Id.*

2. Rojewski (Ex. 1014)

Rojewski discloses that MSCs are “candidates for several clinical applications” to treat injury and disease and that because “MSC isolated from different tissues do not represent a homogenous cell population,” it is necessary to characterize and perform quality control to understand the variations. Ex. 1014 at 173. Rojewski conducted a review to “summarize various different attempts to characterize mesenchymal stem cells based on surface protein expression by flow cytometry and to define multipotent subpopulations of mesenchymal stem cells for prospective isolation.” *Id.* at 168. Rojewski discloses a summary of phenotype data of the reviewed MSCs isolated from various tissues and provides a summary of data regarding expression of genetic markers. *Id.* at 169–173 (Table 1).

3. Meiron (Ex. 1016)

Merion is directed to “methods of treating diseases using adherent cells [MSCs] from adipose or placenta tissues, more specifically, to methods of treating ischemia and/or medical conditions requiring connective tissue regeneration and/or repair using the adherent cells.” Ex. 1016 at 1:6–9. Meiron discloses:

In recent years, considerable activity has focused on the therapeutic potential of mesenchymal stromal cells (MSCs) for various medical applications including tissue repair of damaged organs such as the brain, heart, bone and liver and in support of bone marrow transplantations (BMT). MSCs, a heterogeneous population of cells obtained from e.g. bone marrow, adipose tissue, placenta, and blood, is capable of differentiating into different types of mesenchymal mature cells (e.g. reticular endothelial cells, fibroblasts, adipocytes, osteogenic precursor cells) depending upon influences from various bioactive factors. *Id.* at 1:16–23.

Meiron analyzed the expression markers for its cells and discloses:

stromal stem cell surface markers (positive and negative) include but are not limited to CD105+, CD29+, CD44+, CD73+, CD90+, CD3-, CD4-, CD34-, CD45-, CD80-, CD19-, CD5-, CD20-, CD11B-, CD14-, CD19-, CD79-, FILA-DR-, and FMC7-. Other stromal stem cell markers include but are not limited to tyrosine hydroxylase, nestin and H-NF.

Id. at 20:23–28.

4. Riekstina (Ex. 1013)

Riekstina discloses a study of stem cell marker expression patterns in MSCs isolated from human bone marrow, adipose tissue, heart tissue, and dermal tissue. Ex. 1013, 379. Riekstina discloses that the “immunomodulatory and regenerative potential” of MSCs has shown “promising results in preclinical and clinical studies for a variety of conditions, such as graft versus host disease (GvHD), Crohn’s disease, osteogenesis imperfecta, cartilage damage and myocardial infarction.” *Id.* Riekstina discloses:

Our findings provide evidence that bone marrow MSCs express embryonic stem cell markers Oct4, Nanog, alkaline phosphatase and SSEA-4, adipose tissue and dermis MSCs express Oct4, Nanog, SOX2, alkaline phosphatase and SSEA-4, whereas heart MSCs express Oct4, Nanog, SOX2 and SSEA-4. Our results also indicate that human adult mesenchymal stem cells preserve tissue-specific differences under in vitro culture conditions during early passages, as shown by distinct germ layer and embryonic stem cell marker expression patterns.

Id. at 385.

5. Analysis

Petitioner argues, through Dr. Olson, that a skilled artisan would have understood that the teachings of references related to umbilical cord MSCs are relevant to teachings directed to MSCs derived from other tissues. Pet. 30–31 (citing Ex. 1007 ¶ 127). In addition, Petitioner argues that the skilled

artisan would have understood from the teachings of Pierantozzi and Majore that MSCs derived from various tissues could be useful alternatives (e.g., are interchangeable). *Id.* Petitioner argues that a skilled artisan would have had an expectation of success in combining Majore with Pierantozzi, Rojewski, Merion, and Reikstina to arrive at the subject matter of the Challenged Claims because “it would be completely unsurprising and, indeed, predictable for Majore’s MSCs to express markers previously observed as expressed on MSCs in the prior art.” *Id.* at 32 (citing Ex. 1007 ¶ 86). According to Petitioner, “a POSITA [person of ordinary skill in the art] would understand that expression patterns of MSCs from any tissue are informative of the biological properties of MSCs generally, and that MSCs from various tissues can often be used interchangeably for the proposed mechanisms of most cell therapies.” *Id.* For this reason, Petitioner argues, a skilled artisan would have been motivated to combine the cited prior art “for the purpose of improving MSC cellular therapies.” *Id.* at 32–33 (citing Ex. 1007 ¶¶ 86, 127–131).

Specific to claim 1, Petitioner argues that “Majore also renders 1[Pre], 1[A], 1[B], and 1[C] obvious because Majore discloses isolating cells from whole umbilical cord using an explant procedure.” *Id.* at 33 (citing Ex. 1007 ¶ 132). Petitioner argues that “a POSITA would have been able to predict that an isolated cell can be prepared by placing a subepithelial layer of mammalian umbilical cord tissue in direct contact with a substrate, and culturing the subepithelial layer such that the isolated cell is capable of self-renewal and culture expansion.” *Id.* Petitioner argues that Rojewski and Merion teach claim 1[C] and 1[D], and Pierantozzi discloses “the non-expression of NANOG in some fraction, or all, of the MSCs freshly isolated

from adult tissues.” *Id.* at 34–35 (citing Ex. 1007 § 136). Petitioner contends that “a POSITA would understand the detection of NANOG expression is exquisitely sensitive to the conditions used to culture the cells and the details of the detection method used.” *Id.* Petitioner further argues that the skilled artisan would have known that the isolated cells of Majore would include MSCs having identical genetic marker expression profiles to the cells of the Challenged Claims based on the ISCT criteria and the teachings of, Rowjewski, Merion, and Pierantozzi, rendering claim 1 obvious. *Id.* at 33–35 (citing Ex. 1007 ¶¶ 99, 133–139).

Patent Owner raises the same arguments with respect to Majore’s disclosure discussed with respect to Ground I, which we have addressed above. Prelim Resp. 32. Patent Owner argues that none of Pierantozzi, Rojewski, Meiron, or Riekstina cure the deficiencies in Majore’s failure to disclose the “placing” and “culturing” steps of claim 1 and that a skilled artisan could not have reasonably predicted success in combining the prior art teachings. *Id.* at 33.

Patent Owner argues that Majore is silent as to NANOG and Pierantozzi “teaches away from NANOG- negative cultured cells” because Pierantozzi discloses NANOG was “expressed in freshly isolated MSCs detected after in vitro culture,” which is when the Challenged Claims recite NANOG should not be expressed. *Id.* at 33–34. Patent Owner argues that Petitioner “tries to overcome that disclosure [by] referencing Pierantozzi’s pre-culture detection of NANOG,” which is incorrect as “[t]he claimed cells recite positive NANOG expression after culturing, not before.” (citing Ex. 2022 ¶ 178).

Patent Owner argues that Majore does not disclose the markers recited in 1[D] and 1[E] and its cells were not derived from the subepithelial layer of umbilical cord. *Id.* at 34–35. Patent Owner argues that Rojewski’s teachings do not teach the recited combinations because the cell populations discussed were not derived from the subepithelial layer of umbilical cord. *Id.* at 35. Patent Owner noted that Rojewski’s disclosures showed that “different tissues express different markers,” meaning that the teachings from one tissue would not necessarily apply to cells from different tissue origins. *Id.* at 35–36 (citing Ex. 2022 ¶¶ 123, 126).

For the reasons described in Ground I above, we presently understand, on this record, that the weight of evidence shows that cells produced by the method of Majore would comprise cells having the limitations recited in claims 1–13, and 15. The evidence on this issue is subject to final determination on a more complete record developed through trial.

However, to the extent that Majore is found at trial not to anticipate but rather only to disclose 1[Pre], 1[A], 1[B], and 1[C] as alleged in Ground III, we advise the parties that we presently view Patent Owner’s characterization of the evidence of the teachings of Rojewski, Pierantozzi, Meiron, and Riekstina to be more accurate. See Prelim. Resp. 34–37 (arguing that Rojewski teaches that a genetic marker’s expression profile is not necessarily the same across stem cells from various tissue sources; Pierantozzi teaches cells recite positive NANOG expression after in vivo culture, whereas the claimed cells do not recite NANOG when cultured; and Meiron’s teaching of genetic markers in stromal cells may not apply to the cells of Majore), 41–42 (further arguing that Riekstina teaches differing expression patterns of OCT4 and SOX2 from MSCs from different tissue

origins). On the record before us, the weight of evidence regarding the teachings of Rojewski, Pierantozzi, Meiron, and Riekstina does not favor Petitioner's case under Ground III.

As stated above, the question of whether the objective indicia evidence supports a conclusion that the subject matter of the claims is not obvious is best decided on a full record. We reserve a final determination as to the patentability of claims 1–13, and 15 to the conclusion of trial.

G. Ground IV – Obviousness of Claim 14 over Majore, Pierantozzi, Rojewski, Meiron, and Mistry

Claim 14 recites an isolated cell of claim 1 that has differentiated into a cardiomyocyte cell. Petitioner argues that Mistry teaches its “umbilical cord derived MSCs ‘are capable of self-renewal and expansion in culture and have the potential to differentiate into cells of other phenotypes; for example cardiomyocytes, or their progenitors’ (Mistry 18:9-13) via treatment with 5-azacytidine (Mistry at 90:56-91:30).” Pet. 40 (citing Ex. 1007 ¶ 166). Petitioner relies on its earlier arguments regarding the teachings of Majore, Pierantozzi, Rojewski, Merion, and Mistry to contend they render claim 14 obvious. *Id.*

For the same reasons explained in II.D.2. above, with respect to claim 1, the weight of evidence presently before us shows that cells produced by the method of Majore would comprise cells having the limitations recited in claims 1. On this issue, the weight of evidence favors Petitioner that a POSA would have been motivated to combine the teachings of Majore regarding isolation of MSCs for use in regenerative medicine and Mistry's teachings regarding inducing MSCs to seek to differentiate into cardiomyocytes using 5-azacytidine to produce an isolated cell of claim 14 for the treatment of disease. As stated above, the question of whether the

objective indicia evidence supports a conclusion that the subject matter of the claims is not obvious is best decided on a full record. We reserve a final determination as to the patentability of claim 14 to the conclusion of trial.

H. Ground V – Obviousness of Claims 1–15 over Phan, Pierantozzi, Rojewski, Meiron, and Riekstina

1. Phan (Ex. 1017)

Phan discloses a method for isolating “stem/progenitor cells from the amniotic membrane of umbilical cord” comprising “separating the amniotic membrane from the other components of the umbilical cord *in vitro*, culturing the amniotic membrane tissue under conditions allowing cell proliferation, and isolating the stem/progenitor cells from the tissue cultures.” Ex. 1017 ¶ 1. Phan discloses that its method includes “separating the cells from the amniotic membrane tissue before cultivation by a technique selected from the group consisting of enzymatic digestion and direct tissue explant.” *Id.* ¶ 9. Phan explains that the “term ‘direct tissue explant technique’ as used herein means that the tissue is first placed in media without enzymes. Then the cells separate from the main tissue mass and are harvested for collection.” *Id.* ¶ 40. Phan discloses an embodiment in which the method is used to isolate “epithelial and/or mesenchymal stem/progenitor cells.” *Id.* The cells are cultured under “conditions allowing the cells to undergo clonal expansion.” *Id.* ¶ 13. The cells “can ultimately be differentiated into, but not limited to, by morphology, epithelial or mesenchymal cells” which can include “skin fibroblasts, chondrocytes, osteoblasts, tenocytes, ligament fibroblasts, cardiomyocytes, smooth muscle cells, skeletal muscle cells, adipocytes, cells derived from endocrine glands, and all varieties and derivatives of neurectodermal cells.” *Id.* ¶¶ 42, 44.

2. *Analysis*

a) *Claim 1*

Petitioner argues that Phan discloses 1[Pre], 1[A], and 1[B] “including the process of contacting the amniotic membrane of umbilical cord with a growth substrate and culturing the tissue such that the isolated cells are capable of self-renewal and culture expansion.” Pet. 41–44 (citing Ex. 1007 ¶¶ 167, 169–172). Petitioner argues that “the umbilical cord tissue termed ‘amniotic membrane’ in Phan is the same tissue as the ‘subepithelial layer’ as disclosed in the ‘176 patent.” *Id.* Petitioner argues that Phan discloses the use of stem cell therapies for treating human and animal disease. *Id.* at 41.

With regard to 1[C] and 1[D], Petitioner argues these limitations have no patentable significance, and that Phan alone is sufficient to render the ‘176 claims obvious. *Id.* at 45 (citing *Atlas Powder Company v. Ireco Incorporated*, 190 F.3d 1342, 1347 (Fed. Cir. 1999); *In re Kubin*, 561 F.3d 1351, 1357 (Fed. Cir. 2009)). Notwithstanding, Petitioner argues that Pierantozzi, Rojewski, Merion, and Riekstina teach 1[C] and 1[D]. *Id.* at 46–48. Petitioner relies on its earlier characterizations of the teachings of Pierantozzi, Rojewski, Merion, and Riekstina as described above regarding “MSCs from various tissues [that] are known to express (or not express) the markers recited in the ‘176 patent claims.” Pet. 41. Petitioner argues that because the cited art is directed to use of MSCs to treat disease, a skilled artisan “would have been motivated to consult each of Pierantozzi, Rojewski, Merion and Riekstina to fill in any gaps with respect to the marker or differentiation potential of the MSCs made using the Phan methodology.” *Id.* at 42. Petitioner further argues that a skilled artisan

would have had an expectation of success as it would have been “completely unsurprising and predictable for Phan’s MSCs to express markers” previously reported in the prior art as expressed by MSCs. *Id.* Petitioner alleges the skilled artisan would have believed the “expression patterns of MSCs from any tissue are informative of the biological properties of MSCs generally, and MSCs from various tissues can often be used interchangeably in cell therapies,” and thus the skilled artisan would have been motivated to combine the art for the purpose of improving cellular therapies. *Id.* (citing Ex. 1007 ¶¶ 88, 168).

Patent Owner argues that Phan does not culture the subepithelial cell layer, but rather “discloses cutting up the amniotic membrane and then placing the amniotic membrane on culture dishes.” Prelim. Resp. 46–47. Patent Owner additionally argues that Phan discloses culturing amniotic membrane cells using collagenase treatment, but that this was not a cell growth medium, meaning Phan did not perform the step of culturing the subepithelial layer. *Id.* at 49–50.

Patent Owner argues Phan teaches that its cultured cells express NANOG, thereby not teaching the non-expression of the marker, and relies on its prior discussion of the defects of Pierantozzi with respect to this limitation. *Id.* at 50–51. Patent Owner reiterates its prior discussion of deficiencies in the teachings of Pierantozzi, Rojewski, Merion, and Rieckstina with respect to the claimed limitations.

As discussed with respect to Ground I above, obviousness of these product-by-process claims depends on whether the evidence of record shows that there is a reasonable likelihood that Petitioner would prevail in showing that the process of Phan would have resulted in “an isolated cell” having the

limitations recited in claim 1, despite that Phan's process differs from that disclosed in the '176 patent. For this reason, we are not persuaded by Patent Owner's arguments against obviousness based on the alleged differences in Phan's process. *See, e.g.*, Prelim. Resp. at 46–51 (addressing process differences). Nor are we persuaded that Phan's lack of evidence regarding expression or non-expression of every claimed genetic marker is persuasive of non-identity of the isolated cells (Prelim. Resp. at 25–26); Phan's method could render obvious a cell with every limitation of claim 1 without testing for each recited marker.

Phan discloses culture of umbilical cord-derived stem/progenitor cells under conditions allowing cell proliferation that can differentiate into specific cell types. Ex. 1017 ¶¶ 1, 45.

On this record, Petitioner has provided sufficient factual basis to establish a reasonable likelihood that Phan's disclosed method of dissecting umbilical cord, culturing cells, and growing adherent cells would have produced (or did produce) at least one cell with the limitations of claim 1. In this regard, we credit the testimony of Dr. Olsen that the cells produced by Phan would include the same produced by the '176 patent. Ex. 1007 ¶ 167. We acknowledge that Phan's disclosure of expression of NANOG in cultured cells does not support this conclusion; however, we are persuaded on this record by Dr. Olsen's testimony that "cells isolated via the explant method can comprise a heterogenous population of MSCs with different lineage commitment" that may result in "varying expression of NANOG." *Id.* ¶ 175. We encourage the parties to explore this issue further during trial.

Given Phan's teachings and the breadth of claim 1's isolated cell, we presently understand the weight of evidence favors institution on claim 1.

Even if we gave weight to the process limitations construed as requested by Patent Owner (Prelim. Resp. 46–51), the limitations of claim 1 are sufficiently broad as to read on Phan with the exception of the express/non-expressed markers.

b) Claims 2–15

To the extent that Phan is found at trial not to render claim 1 obvious but rather only to disclose 1[Pre], 1[A], and 1[B] as alleged in Ground V, we advise the parties that we presently understand Patent Owner’s characterization of the evidence of the teachings of Rojewski, Pierantozzi, Meiron, and Riekstina to be more accurate. *See* Prelim Resp. 50–58. As a result, the weight of the evidence of record regarding the contributions of Rojewski, Pierantozzi, Meiron, and Riekstina does not favor Petitioner’s case for the purposes of teaching limitations in the Challenged Claims not taught or rendered obvious by Phan.

As stated above, the question of whether the objective indicia evidence supports a conclusion that the subject matter of the claims is not obvious is best decided on a full record. We reserve a final determination as to the patentability of claims 1–15 to the conclusion of trial.

I. Ground VI – Obviousness of Claims 1–8, 10–13, and 15 by Kita, Pierantozzi, Rojewski, Meiron, and Riekstina

1. Kita (Ex. 1010)

Kita discloses a protocol to “isolate adult SCs from the cord lining membrane (subamniotic region of the umbilical cord), and characterize the isolated cells as a novel source for cell-based therapeutic approaches.” Ex. 1010, 492. Human umbilical cord was obtained, washed, and cut into 1-inch pieces and dissected to open the cord, then placed in petri dishes with growth medium and incubated. *Id.* Wharton’s jelly inside the cord was

dissected away, and pieces of “outer envelope membranes” were cultured in growth medium. *Id.*

Figure 1 C, reproduced below, shows the location of the subamniotic cells dissected out for study:

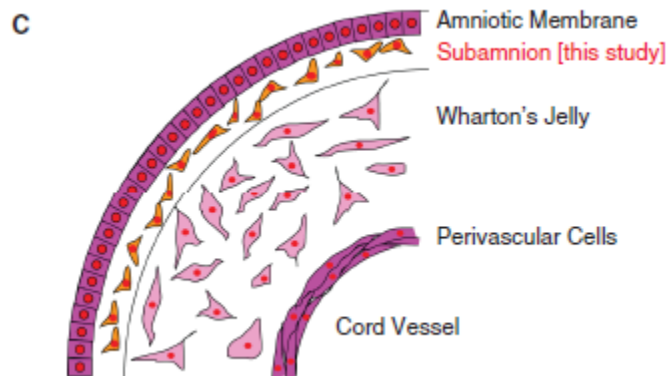


Figure 1 C is a “[d]iagram of the origin of cord lining membrane (CL)-mesenchymal stem cells (MSCs).” *Id.*

Kita discloses:

Approximately 10 to 14 days after starting the culture, a significant number of cells migrated from the implants into the petri dishes. Morphologically, most of cells appeared to be fibroblastoid (Fig. 1B, left), but we could also see a small population of epithelial-like cells when amniotic membrane was used as a source.

Id. at 494. Kita states that the minor population of epithelial-like cells were believed to be “subamniotic region-derived cells.” *Id.* at 493 (Fig. 1 legend). Osteogenic and adipogenic differentiation were successfully induced in the cell populations. *Id.* at 492.

2. Analysis of Claim 1

Petitioner claims Kita teaches 1[Pre], 1[A], and 1[B] of claim 1 of the '176 patent by isolating MSCs from umbilical cord, placing pieces of the separated subamniotic membrane onto the surface of a tissue culture

substrate, and culturing them. Pet. 55–57 (citing Ex. 1007 ¶¶ 203–207). Petitioner argues that a skilled artisan would have recognized Kita’s teachings to include the steps of 1[Pre], 1[A], and 1[B]. *Id.* at 57 (citing Ex. 1007 ¶ 208).

Petitioner alleges that steps 1[C] and 1[D] of claim 1 have no patentable weight, or, in the alternative, that Kita discloses that “MSCs isolated from the subamniotic express each of CD29, CD73, CD90, SSEA4, CD44, CD146 and CD105.” *Id.* at 57–58 (citing Ex. 1007 ¶ 209, Table 3). Petitioner also alleges that Rojewski and Merion disclose the “at least three” markers recited in 1[C]. *Id.* (citing Ex. 1007 ¶¶ 209, 210). Petitioner alleges that Kita discloses “MSCs isolated from the subamniotic do not express CD45, CD34, and Stro-1.” *Id.* at 59 (citing Ex. 1007 ¶ 209, Table 3). Petitioner alleges that Pierantozzi, Rojewski, and Meiron each teach non-expression of markers disclosed in 1[D]. *Id.* at 59 (citing Ex. 1007 ¶¶ 209, 211, Table 3).

Petitioner alleges that although “Kita discloses NANOG expression was detected by immunofluorescence and RT-PCR, it provides no data on the relative frequency of NANOG expressing cells,” which were cultured. *Id.* at 59 (citing Ex. 1007 ¶ 212). Petitioner alleges that a skilled artisan would have understood that “the freshly isolated cells of Kita do not express NANOG, notwithstanding Kita’s characterization of older, tissue culture-adapted MSCs” because freshly isolated MSCs do not express NANOG, as Pierantozzi teaches. *Id.* at 60 (citing Ex. 1007 ¶ 213).

Patent Owner alleges that the cells isolated by Kita cannot be the same as the cells in claim 1 because they are made by a different process, express NANOG and CD14 in culture, which the claimed cells do not, and the cells

do not express SOX or TERT. Prelim. Resp. at 60–63. Petitioner argues Kita’s protocol “involves a very different process,” and results in culture of the amniotic membrane, not the subepithelial membrane. *Id.* Patent Owner relies on its earlier characterization of the defects of the teachings of Pierantozzi, Rojewski, and Meiron. *Id.* at 63–64 (citing Ex. 2022 ¶ 309).

As discussed with respect to Ground I above, obviousness of these product-by-process claims depends on whether the evidence of record shows that there is a reasonable likelihood that Petitioner would prevail in showing that the process of Kita would have resulted in “an isolated cell” having the limitations recited in claim 1, despite that Kita’s process differs from that disclosed in the ’176 patent. For this reason, we are not persuaded by Patent Owner’s arguments against obviousness based on the alleged differences in Phan’s process. See, e.g., Prelim. Resp. at 60–70 (addressing process differences). Nor are we persuaded that Kita’s lack of evidence regarding expression or non-expression of every claimed genetic marker is persuasive of non-identity of the isolated cells (*id.* at 60–68); Kita’s method could render obvious a cell with every limitation of claim 1 without testing for each recited marker.

Kita discloses culture of umbilical cord-derived stem/progenitor cells under conditions allowing cell proliferation that can differentiate into specific cell types. *Id.* at 492.

On this record, Petitioner has provided sufficient factual basis to establish a reasonable likelihood that Phan’s disclosed method of dissecting umbilical cord, culturing cells, and growing adherent cells would have produced (or did produce) at least one cell with the limitations of claim 1. In this regard, we credit the testimony of Dr. Olsen that the cells produced by

Kita would include the same produced by the '176 patent. Ex. 1007 ¶¶ 201–213. We acknowledge that the evidence showing Kita's cells express NANOG and CD14 in culture, which the claimed cells do not, and that the cells do not express SOX or TERT makes this a closer case; however, we find persuasive Dr. Olsen's testimony that "cells isolated via the explant method can comprise a heterogeneous population of MSCs with different lineage commitment" that may result in "varying expression of NANOG." *Id.* ¶ 212. We encourage the parties to explore this issue further during trial.

Given Kita's teachings and the breadth of claim 1's isolated cell, we find the weight of evidence favors institution on claim 1. Even if we gave weight to the process limitations construed as requested by Patent Owner (Prelim. Resp. 60–64), the limitations of claim 1 are sufficiently broad as to read on Kita with the exception of the express/non-expressed markers. We reserve a final determination as to the patentability of claim 1 to the conclusion of trial.

3. *Dependent Claims 2–8, 10–13, and 15*

a) *Claims 7, 10–13, and 15*

Petitioner alleges that Kita discloses cells isolated from the subamnion that differentiate "into adipogenic, osteogenic, and chondrogenic lineages," meeting the limitations of claim 7 and rendering it and claims 10–13, which claim the individual cell types, obvious. Pet. 65 (citing Ex. 1007 ¶¶ 230, 231).

Petitioner alleges that Kita discloses MSCs isolated from the subamnion that grew into colonies and retained the ability to propagate, thus teaching claim 15 and rendering it obvious. *Id.* at 66 (citing Ex. 1007 ¶ 233).

Patent Owner alleges that Kita does not disclose isolated cells derived from the subepithelial layer, and therefore “does not satisfy all of the limitations of claims 7 and 10–15.”¹⁷ Prelim. Resp. 67.

For the reasons given above regarding claim 1, we find the weight of evidence favors Petitioner on these claims. We reserve a final determination as to the patentability of claims 7, 10–13, and 15 to the conclusion of trial.

b) Claims 2 and 3

Petitioner alleges that Kita discloses expression by its isolated MSCs of some of the recited genetic markers of claim 2, and that Rojewski and Meiron teach MSCs that express additional markers listed in claim 2. Pet. 61 (citing Ex. 1007 ¶ 209).

Petitioner alleges that Kita discloses isolated MSCs that do not express some of the recited genetic markers of claim 3, portions that do and do not express CD14, and that Pierantozzi, Rojewski, and Meiron teach MSCs that do not express additional markers listed in claim 3. *Id.* at 61–62 (citing Ex. 1007 ¶¶ 209, 215). Petitioner alleges these references together render claims 2 and 3 obvious. *Id.* at 63.

c) Claims 4–6

Petitioner alleges that although Kita did not express SOX2, Pierantozzi and Riekstina both report MSCs with expression of SOX2 and OCT4. *Id.* at 64 (citing Ex. 1007 ¶ 219). Petitioner alleges “a POSITA would understand detection of SOX-2 and OCT-4 is exquisitely sensitive to the conditions used to culture the cells and the details of the detection method” and would have understood these claims to be obvious based on

¹⁷ Claim 14 is not at issue in this ground. We construe this statement to regard claims 7, 10–13 and 15.

prior reports of MSCs from human umbilical cord expressing SOX2 and OCT4 and lack of specificity in culture conditions in the '176 patent. *Id.* at 63–64 (citing Ex. 1007 ¶¶ 220, 221). Petitioner alleges claims 4–6 would have been obvious based on the disclosures of Kita, Pierantozzi and Riekstina. *Id.* at 65 (citing Ex. 1007 ¶¶ 223–229).

Patent Owner incorporates its earlier arguments regarding Pierantozzi and Riekstina with respect to claim 4. Prelim. Resp. 66. For claims 5 and 6, Patent Owner argues that Kita's cells were not derived from the subepithelial layer and that Rojewski does not remedy Kita's deficiencies because its MSCs were derived from different tissue and their expression of OCT4 does not disclose the recited limitations. *Id.* at 67.

To the extent that Kita is found at trial not to render claim 1 obvious but rather only to disclose 1[Pre], 1[A], and 1[B] as alleged in Ground VI, we advise the parties that, on the present record, Patent Owner's characterization of the evidence of the teachings of Rojewski, Pierantozzi, Meiron, and Riekstina to be more accurate. *See* Prelim Resp. 62–67. As a result, we find the weight of evidence regarding the contributions of Rojewski, Pierantozzi, Meiron, and Riekstina does not favor Petitioner's case for the purposes of teaching limitations in the Challenged Claims not taught or rendered obvious by Kita.

As stated above, the question of whether the objective indicia evidence supports a conclusion that the subject matter of the claims is not obvious is best decided on a full record. We reserve a final determination as to the patentability of claims 4–6 to the conclusion of trial.

d) Claim 8

Petitioner alleges that although Kita does not disclose exosomes expressing CD63 and/or CD9, Rojewski discloses MSCs from other tissues that express these markers that are known exosome markers, and that MSCs were known to produce exosomes. Pet. 65–66 (citing Ex. 1007 ¶ 232). Petitioner alleges a skilled artisan would have expected Kita’s MSCs to produce exosomes expressing CD63 and/or CD9, rendering claim 8 obvious. *Id.*

Patent Owner incorporates its earlier argument that Rojewski does not disclose these features. Prelim. Resp. 68. As with regard to claims 4–6, we find that Patent Owner’s characterization of the evidence of the teachings of Rojewski appears to be more accurate and that the weight of evidence regarding the contributions of Rojewski does not favor Petitioner’s case for the purposes of teaching limitations of claim 8 that are not taught or rendered obvious by Kita.

As stated above, the question of whether the objective indicia evidence supports a conclusion that the subject matter of the claims is not obvious is best decided on a full record. We reserve a final determination as to the patentability of claim 8 to the conclusion of trial.

J. Ground VII – Obviousness of Claim 14 by Kita, Pierantozzi, Rojewski, Meiron, Riekstina, and Mistry

Claim 14 recites an isolated cell of claim 1 that has differentiated into a cardiomyocyte cell. Petitioner alleges the cited art “all disclose the value of MSCs as a therapeutic for diseases,” and that a skilled artisan would have been motivated to combine the teachings of the cited art “to produce cell therapies for treatment of disease.” Pet. 67 (citing Ex. 1007 ¶ 235).

Petitioner alleges that the teaching of obviousness of claim 1 in view of

Mistry's teaching of umbilical cord-derived cells made to differentiate into cells with cardiomyocyte markers via treatment with 5-azacytidine would have rendered claim 14 obvious. *Id.* (citing Ex. 1007 ¶ 236).

Patent Owner alleges Kita does not teach the claimed isolated cell and that Mistry does not teach differentiation into cardiomyocytes, only the expression of cardiac specific genes. Prelim. Resp. 69–70.

On this issue, we find the weight of evidence favors Petitioner that a POSA would have been motivated to combine the teachings of Majore regarding isolation of MSCs for use in regenerative medicine and Mistry's teachings regarding inducing MSCs to differentiate into cardiomyocytes using 5-azacytidine to seek to produce an isolated cell of claim 14 for the treatment of disease.

As stated above, the question of whether the objective indicia evidence supports a conclusion that the subject matter of the claims is not obvious is best decided on a full record. We reserve a final determination as to the patentability of claim 14 to the conclusion of trial.

K. Ground VIII – Obviousness of Claim 9 by Kita, Pierantozzi, Rojewski, Meiron, and Majore

Petitioner alleges that a skilled artisan would have been motivated to combine the teachings of Kita with Pierantozzi, Rojewski, Merion, and Majore “for the purpose of improving cellular therapies employing MSCs.” Pet. 67–68 (citing Ex. 1007 ¶ 237). Petitioner alleges the “use of chemically defined media or human only components was common in the field of MSC biology,” and would have been obvious over the cited art. *Id.*

Patent Owner alleges that Majore does not disclose the features of claim 9, and that Kita's culture medium includes 10% fetal bovine serum,

making the concept of use of non-animal components not obvious over the cited art.

For this claim, we find the evidence regarding some components of Majore containing animal components favors Patent Owner. *See* Prelim. Resp. 31, citing Ex. 2022 ¶ 173. We reserve a final determination as to the patentability of claim 9 to the conclusion of trial.

III. CONCLUSION

Based on the evidence before us, we determine Petitioner demonstrates a reasonable likelihood of prevailing in its assertions that the Challenged Claims of the '176 patent are unpatentable over the asserted prior art. Accordingly, *inter partes* review shall proceed in this case on all of the grounds raised in the Petition. *See SAS Inst.*, 138 S. Ct. 1348, 1359–60 (2018) (holding that a decision to institute under 35 U.S.C. § 314 may not institute on fewer than all claims challenged in the petition); *PGS Geophysical AS v. Iancu*, 891 F.3d 1354, 1360 (Fed. Cir. 2018) (stating the decision whether to institute *inter partes* review requires “a simple yes-or-no institution choice respecting a petition, embracing all challenges included in the petition”).

Our determination in this Decision is not a final determination on either the patentability of any challenged claims or the construction of any claim term and, thus, leaves undecided any remaining fact issues necessary to determine whether sufficient evidence supports Petitioner’s contentions by a preponderance of the evidence in the final written decision. *See Trivascular, Inc. v. Samuels*, 812 F.3d 1056, 1068 (Fed. Cir. 2016) (noting that “there is a significant difference between a petitioner’s burden to establish a ‘reasonable likelihood of success’ at institution, and actually

proving invalidity by a preponderance of the evidence at trial”) (quoting 35 U.S.C. § 314(a) and comparing *id.* § 316(e)).

IV. ORDER

Upon consideration of the record before us, it is:

ORDERED that, pursuant to 35 U.S.C. § 314(a), an *inter partes* review of claims 1–15 of U.S. Patent No. 9,803,176 B2 is instituted with respect to all grounds set forth in the Petition; and

FURTHER ORDERED that, pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4(b), *inter partes* review of U.S. Patent No. 9,803,176 B2 shall commence on the entry date of this Order, and notice is hereby given of the institution of a trial.

IPR2021-01535
Patent 9,803,176 B2

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