

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

HEMOSONICS LLC,
Petitioner,

v.

C. A. CASYSO GMBH,
Patent Owner.

IPR2021-00293
Patent 10,746,750 B2

Before JON M. JURGOVAN, NORMAN H. BEAMER,
and AMANDA F. WIEKER, *Administrative Patent Judges*.

BEAMER, *Administrative Patent Judge*.

JUDGMENT
Final Written Decision
Determining All Challenged Claims Unpatentable
35 U.S.C. § 318(a)

I. INTRODUCTION

On December 14, 2020, HemoSonics LLC (“Petitioner”) filed a Petition (Paper 2, “Pet.”) pursuant to 35 U.S.C. §§ 311–319 to institute an *inter partes* review of claims 1–31 of U.S. Patent No. 10,746,750 B2 (Ex. 1001, “the ’750 patent”). On April 22, 2021, C. A. Casyso GmbH (“Patent Owner”) filed a Preliminary Response, indicating that claims 10–17, 20, 27, 29, and 31 were disclaimed. Paper 8. We instituted *inter partes* review on July 1, 2021. Paper 9. Patent Owner filed a Response to the Petition, Petitioner filed a Reply, and Patent Owner filed a Sur-Reply. Paper 11 (“PO Resp.”); Paper 12 (“Reply”); Paper 14 (“Sur-Reply”).

An oral hearing took place on March 31, 2022. The Hearing Transcript (“Tr.”) is included in the record as Paper 17. After considering the parties’ arguments and supporting evidence, we determine that Petitioner has demonstrated by a preponderance of the evidence that the remaining challenged claims 1–9, 18, 19, 21–26, 28, and 30 of the ’750 patent are unpatentable.

II. BACKGROUND

A. The ’750 Patent

The ’750 patent, titled in part “Cartridge Device For A Measuring System For Measuring Viscoelastic Characteristics Of A Sample Liquid, . . . ,” issued August 18, 2020, from an application filed September 28, 2018, which relates through several continuations to an original parent application filed December 17, 2009, and a provisional

application filed December 23, 2008.¹ Ex. 1001, codes [54], [45], [22], [63], [60].

The '750 patent describes a device for measuring “viscoelastic characteristics” of, for example, blood clots — *i.e.*, the firmness of a blood clot from its initial formation through dissolution. Ex. 1001, Abstr., 2:16–21. Blood clot formation, or “hemostasis,” is activated by injury or inflammation, which causes cells called “platelets,” also called “thrombocytes,” to change shape, and triggers enzymes forming “fibrin” fibers, which fibers knit together the platelets to form the clot. *Id.* at 1:52–67; Ex. 1002 ¶¶ 32–35, 66. Part of the clotting process includes a “coagulation cascade,” which can be activated via “intrinsic” or “extrinsic” channels. Ex. 1001, 1:52–59; Ex. 1002 ¶¶ 34–35. After activation of the clotting process, prior to actual formation of a blood clot, the viscosity of the blood increases. Ex. 1002 ¶ 39. Once the clot begins to form, the clot takes on both viscous and elastic characteristics, and is referred to as being “viscoelastic.” *Id.*; *see also* Ex. 1022, 270 (“[V]iscoelastic materials, such as fibrin, like rubber, plastic, and a great many polymers, have different degrees of both elastic and viscous properties.”). The progress of blood clot formation is illustrated in Figure 2 of the '750 patent, reproduced below.

¹ For purposes of this Decision, we accept Petitioner’s unchallenged assertion that the '750 patent’s priority date pre-dates the AIA. Pet. 7 n. 4. Based on that, the Petition is considered timely notwithstanding it was filed less than nine months after issuance of the '750 patent. 37 C.F.R. § 42.102.

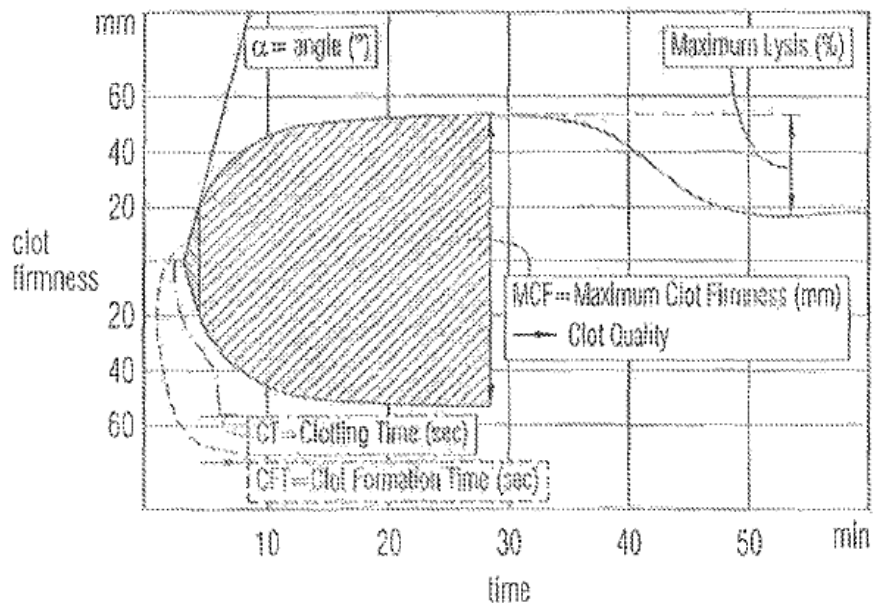


Figure 2 is a graph that depicts clot firmness as a function of time, including measurements of the diagnostic parameters: (i) “clotting time” (CT), when the clotting process of the blood transitions from viscous to viscoelastic behavior; (ii) “clot formation time” (CFT), when a clot reaches a predefined degree of firmness; (iii) “maximum clot firmness” (MCF), the maximum firmness that the clot reaches during the measurement; and (iv) “maximum lysis,” marking the dissolution of the clot. Ex. 1001, 2:20–21, 2:50–63. The ’750 patent refers to these parameters as “viscoelastic characteristics.” *Id.* at 1:45–47.

An embodiment of the device of the ’750 patent is illustrated in Figure 13c, reproduced below.

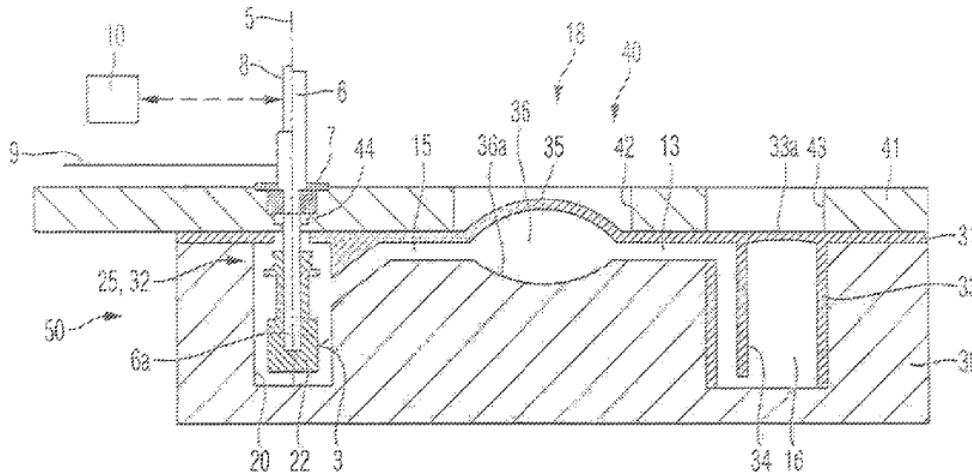


Figure 13c depicts a disposable cartridge (50) containing multiple measurement cavities (one of which is shown as item 20) into which blood samples are inserted via an inlet and ductwork (including items 33a, 16, 13, and 15), and mixed with various reagents to initiate the clot formation process in various ways. *Id.* at 8:18–25, 8:66–9:1, 9:26–28, 12:21–23, 12:54–57. The cartridge is attached at an interface (41) to a measuring system (40), which causes a shaft (6) to connect to a probe (22) within the cavity. *Id.* at 12:31–37, 12:60–67. During testing, the probe is immersed in blood in the cavity, the shaft rotates the probe, and as the blood clot forms, it couples to the probe, and the resulting resistance to the rotation is measured, determining the clotting parameters — this technique is generally referred to as “thromboelastometry.”² *Id.* at Fig. 3, 3:1–24, 12:37–45.

² Thromboelastometry is a type of “viscoelastic method” — methods that continuously determine the clotting parameters “from the formation of the first fibrin fibres until the dissolution of the blood clot by fibrinolysis.” *Id.* at 2:16–21, 3:1–2. Another type of viscoelastic method is “thromboelastography.” *Id.* at 2:36–37.

The various reagents that are mixed with the blood activate or suppress different parts of the coagulation cascade in order to test whether a patient has normal blood clotting capability and, if not, to diagnose the problem. *Id.* at 9:26–28, 9:33–49. Such reagents include “tissue factor,” which activates the extrinsic channel (called an “EXTEM” test), “Hageman factor” or “Factor XII,” which activates the intrinsic channel (called an “INTEM” test), and “cytochalasin D” which suppresses thrombocyte (*i.e.*, platelet) function (called a “FIBTEM” test). *Id.* at 1:52–55, 9:26–33. The ’750 patent states:

It is apparent to a person skilled in the art that in order to achieve a maximum benefit for a user different types of tests can be combined in one cartridge device. . . .

In a preferred embodiment the cartridge device 50 comprises four arrangements . . . having 4 measurement cavities. . . . Thus measurements can be done with different reagents on the same liquid sample or with [the] same reagents as well to check plausibility.

Id. at 9:18–25. An example of testing blood using different reagents in different cavities involves an EXTEM test in one cavity, an INTEM test in another cavity, and the combination of EXTEM and cytochalasin D in a third cavity. As the ’750 patent explains:

By comparison of the results on an EXTEM test of a pathologic sample to those of a FIBTEM test of the same sample it is possible to e.g. precisely determine if a coagulation disorder results from lack of fibrinogen or a malfunction of platelets.

Id. at 9:37–41. The ’750 patent cites the advantages of providing multiple measurement cavities in the disclosed cartridge arrangement:

Using such a cartridge the preparation of a measurement which provides almost overall information about the coagulation status of a patient merely requires the two steps of attaching the

cartridge device 50 to the measuring system 40 with the external control apparatus and injecting the blood sample as one sample liquid 1. Considering the significance of more complex and time consuming preparation of several thromboelastography or thromboelastometry tests, it is evident that the invention is of great advantage for easier, safer and more accurate [point of care] tests.

Id. at 9:53–63.

B. Illustrative Claim

Independent claim 1, which is the only independent claim of the '750 patent, is reproduced below.

1. A cartridge device for evaluation of hemostasis, comprising:
 - a plurality of cavities each configured to receive blood of a test sample, each cavity comprising a reagent or combination of reagents;
 - ductwork, including an inlet for receiving a test sample, wherein the ductwork is in communication with each of the plurality of cavities, whereby each of the plurality of cavities is configured to receive, via the ductwork, a portion of the test sample[;]
 - a first cavity of the plurality of cavities comprising a first reagent or a first combination of reagents that interact with the blood received therein, wherein the first reagent, or a reagent included in the first combination of reagents, is an activator of coagulation;
 - a second cavity of the plurality of cavities comprising a second combination of reagents that interact with blood of the test sample received therein, the second combination including an activator of coagulation and one or more reagents configured for suppressing thrombocyte function; and

a viscoelastic interrogation device that measures blood clot firmness of the test sample or other parameters dependent on measurement of blood clot firmness.

Ex. 1001, 14:42–65.

C. References

Petitioner relies upon the following prior art references (Pet. 4):

- U.S. Patent No. 5,629,209 (“Braun ’209”), “*Method and Apparatus for Detecting Viscosity Changes in Fluids*,” filed October 19, 1995, issued May 13, 1997. Ex. 1004.
- Lang T. and M. von Depka, “*Possibilities and limitations of thrombelastometry/-graphy*,” (“Lang 2006”) Hämostaseologie (2006) (certified English translation of the German version). Ex. 1006.
- U.S. Patent No. 5,204,525 (“Hillman ’525”), “*Capillary Flow Device*,” filed July 19, 1991, issued April 20, 1993. Ex. 1008.
- U.S. Patent No. 6,016,712 (“Warden ’712”), “*Device for Receiving and Processing a Sample*,” filed September 18, 1997, issued January 25, 2000. Ex. 1009.

Petitioner also filed the Declaration of Dr. Keith B. Neeves in support of the Petition. Ex. 1002 (“Neeves Decl.”). Patent Owner did not file declaratory testimony. *See generally* PO Resp.; Sur-reply.

D. Asserted Grounds of Unpatentability

Patent Owner has disclaimed claims 10–17, 20, 27, 29, and 31 of the ’750 patent. Ex. 2001. Therefore, claims 1–9, 18, 19, 21–26, 28, and 30 remain challenged on the following grounds of unpatentability (Pet. 4):

Claim(s) Challenged	Statutory Basis	References
1–4, 7–9, 18, 19, 21–26, 28, 30	§ 103(a)	Braun '209, Lang 2006
5	§ 103(a)	Braun '209, Lang 2006, Hillman '525
6	§ 103(a)	Braun '209, Lang 2006, Warden '712

E. Real Parties in Interest

Petitioner identifies Holding US POC, Inc. as the owner of 100% of the units of Petitioner; Holding POC (France) as the owner of 100% of the shares of Holding US POC, Inc.; Stago Healthcare SAS (France) as the owner of 100% of the shares of Holding POC (France); Holding Groupe Diagnostic (France) as the owner of 100% of the shares of Stago Healthcare SAS (France); and Stago International (France) as the owner of 100% of the shares of Holding Groupe Diagnostic (France). Pet. 65.

Patent Owner identifies itself as a real party in interest, which is owned by Instrumentation Laboratory Company, which is owned by Werfen Italy Investments Sr.I., which is owned by WerfenLife S.A. Paper 3, 2.

F. Related Proceedings

The '750 patent is a continuation of a continuation of U.S. Patent No. 9,915,671 (“the '671 patent”), which is the subject of *HemoSonics LLC v. C. A. Casyso GmbH*, IPR2018-00950. Pet. 65–66; Paper 3, 2. In IPR2018-00950, the Board held that all claims of the '671 patent were not patentable. Exs. 1011, 1014. Patent Owner appealed, and the appeal was pending as of the March 31, 2022 hearing. Paper 17, 14:5–7.³

³ We understand that the IPR2018-00950 Decision was affirmed per curiam on June 13, 2022.

III. ANALYSIS

A. Obviousness: Legal Standards

A claim is unpatentable for obviousness if, to one of ordinary skill in the pertinent art, “the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007) (quoting 35 U.S.C. § 103(a) (2000)).

The question of obviousness is resolved on the basis of underlying factual determinations, including (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of skill in the art; and (4) where in evidence, so-called secondary considerations, including commercial success, long-felt but unsolved needs, failure of others, and unexpected results. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).⁴

A patent claim “is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.” *KSR*, 550 U.S. at 418. Rather, an obviousness determination requires finding “both ‘that a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so.’” *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367–68 (Fed. Cir. 2016) (citation omitted); *see KSR*, 550 U.S. at 418 (for an obviousness analysis, “it can be important to identify a reason that

⁴ No evidence of secondary considerations appears in the record of this proceeding.

would have prompted a person of ordinary skill in the relevant field to combine the elements [in the way the claimed] new invention does”). “Although the *KSR* test is flexible, the Board ‘must still be careful not to allow hindsight reconstruction of references . . . without any explanation as to *how* or *why* the references would be combined to produce the claimed invention.’” *TriVascular, Inc. v. Samuels*, 812 F.3d 1056, 1066 (Fed. Cir. 2016) (citation omitted).

Further, an assertion of obviousness “cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *KSR*, 550 U.S. at 418 (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)); accord *In re NuVasive, Inc.*, 842 F.3d 1376, 1383 (Fed. Cir. 2016) (stating that “‘conclusory statements’” amount to an “insufficient articulation[] of motivation to combine”; “instead, the finding must be supported by a ‘reasoned explanation’” (citation omitted)); *In re Magnum Oil Tools Int’l, Ltd.*, 829 F.3d 1364, 1380 (Fed. Cir. 2016) (“To satisfy its burden of proving obviousness, a petitioner cannot employ mere conclusory statements. The petitioner must instead articulate specific reasoning, based on evidence of record, to support the legal conclusion of obviousness.”).

“[A] combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.” *KSR*, 550 U.S. at 416. “[I]n many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle. . . . A person of ordinary skill is also a person of ordinary creativity, not an automaton.” *Id.* at 420–421.

“The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art.” *In re Keller*, 642 F.2d 413, 425 (CCPA 1981). “Combining the *teachings* of references does not involve an ability to combine their specific structures.” *In re Nievelt*, 482 F.2d 965, 968 (CCPA 1973).

B. Level of Skill in the Art

Petitioner’s expert opines that a person of ordinary skill in the art (“POSITA”) of the ’750 patent as of the patent’s priority date would be as follows:

A POSITA would have a Bachelor of Science degree in a scientific and/or engineering related field plus four years of work experience in a relevant field, e.g., biology, chemical engineering, bioengineering or mechanical engineering related to medical devices. Alternatively, such a person would have an advanced degree. A person with an advanced degree in the relevant fields would require fewer years of work experience to be considered a POSITA.

Neeves Decl. ¶ 62.

Patent Owner does not offer an alternative. *See generally* PO Resp. Petitioner’s proposal is consistent with the level of ordinary skill in the art reflected by the prior art. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001); *In re GPAC Inc.*, 57 F.3d 1573, 1579 (Fed. Cir. 1995). On this record, the level of ordinary skill is neither in dispute nor dispositive of any challenge. For purposes of this Decision, we apply Petitioner’s articulation.

C. Claim Construction

The Petition was accorded a filing date of December 14, 2020. Paper 5, 1. In an *inter partes* review for a petition filed on or after November 13, 2018, a claim “shall be construed using 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). We apply the claim construction standard from *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (*en banc*).

Under that standard, claim terms are generally given their ordinary and customary meaning, as would be understood by one with ordinary skill in the art in the context of the specification, the prosecution history, other claims, and even extrinsic evidence including expert and inventor testimony, dictionaries and learned treatises, although extrinsic evidence is less significant than the intrinsic record. *Phillips*, 415 F.3d at 1312–17. Usually, the specification is dispositive, and it is the single best guide to the meaning of a disputed term. *Id.* at 1315.

Claim terms need only be construed to the extent necessary to resolve the controversy. *Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017).

Petitioner submits the following proposed constructions of claim terms:⁵

- “cavity” or “cavities” (claims 1–3, 6, 18, 19, 30): “space(s) within an object.”

⁵ We omit Petitioner’s proposed constructions that only pertain to claims that have been disclaimed.

- “one or more reagents configured for suppressing thrombocyte function” (claims 1, 4, 7, 8): “any reagent or reagents selected to inhibit platelet functionality.”
- “other parameters dependent on measurement of blood clot firmness” (claims 1, 24): “includ[ing] clotting time (CT), clot formation time (CFT), and maximum clot firmness (MCF).”
- “one or more reagents configured for testing platelet aggregometry” (claim 6): “selection of reagents that cause platelets to aggregate.”
- “configured to measure changing in elastic properties of the test sample” (claim 21): “require[s] configuration of the device so that over time it measures changes in any blood clot data point that relies in part on elastic properties, e.g., clot firmness.”
- “interrogated to determine a hemostatic parameter” (claim 22):
“Hemostatic means ‘of or caused by hemostasis’
A parameter is a property that describes characteristics or behavior.”
- “configured to perform a viscoelastic method of testing” (claim 23): “capable of performing a method to determine information about clot firmness.”

Pet. 12–20.

Patent Owner submits the following proposed constructions of claim terms:

- “viscoelastic interrogation device” (Claim 1): “a device that includes both a probe element and a measurement cavity that are used together to determine ‘blood clot firmness of the test

sample or other parameters dependent on measurement of blood clot firmness.”

- “test sample” (Claim 1): “construe the test sample that the viscoelastic interrogation device uses to measure blood clot firmness as being from one of the plurality of cavities.”
- “ductwork” (Claim 1): “to include one or more conduits that connect cavities and that are used to transport liquid between the cavities.”
- “cavity” or “cavities” (Claim 1): “to include a space in the cartridge that is distinct from the ductwork.”

PO Resp. 6–11.⁶

We determine that express construction of these terms is unnecessary for this Decision, except for any necessary explanations of the ordinary and undisputed meaning of pertinent medical terminology in the field of hemostasis, including, for example, that “thrombocyte” is synonymous with “platelet,” “tissue thromboplastin” is synonymous with “tissue factor,” and “viscoelastic” refers to having both viscous and elastic characteristics.

Neeves Decl. ¶¶ 30, 42, 66, 94.

With the exception of Patent Owner’s proposed construction of “cavity,” discussed below, the proposed constructions offered by the parties appear accurate, albeit limiting, as far as they go — in that they describe aspects of particular embodiments within the scope of the ’750 claims according to their plain meaning in the context of the claims as a whole and

⁶ In arguing that Petitioner has not proved obviousness, Patent Owner raises additional claim construction issues that it does not specifically denominate as such, which we discuss in the claim 1 section (III.D.4) below.

the '750 Specification. But we see no reason to limit the metes and bounds of the claims to specific disclosed embodiments by adopting the proposed articulations as a matter of claim construction. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co. Ltd.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (noting that “we need only construe terms ‘that are in controversy, and only to the extent necessary to resolve the controversy’”) (citing *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

Regarding “cavity,” Patent Owner’s proposal is not acceptable because it requires a cavity to be “distinct from the ductwork,” which is inconsistent with the '750 Specification: “[i]n a further embodiment the at least one reagent cavity is integrally formed with . . . one or more of the ductworks.” Ex. 1001, 6:40–43, *see also id.* at 8:66–9:1, 11:53–54; Reply 8–9.

D. Ground 1: Obviousness of Claims 1–4, 7–9, 18, 19, 21–26, 28, and 30 Over Braun '209 and Lang 2006

Petitioner challenges claims 1–4, 7–9, 18, 19, 21–26, 28, and 30 (and additional disclaimed claims that we do not address) as obvious over the combination of Braun '209 and Lang 2006. Pet. 32–57.

1. Braun '209

Braun '209 discloses a disposable multi-chamber cartridge with preloaded reagents used in conjunction with a measurement device to simultaneously conduct clot time tests using different reagents in different chambers. Ex. 1004, Fig. 1, 3:65–4:23, 6:51–7:6, 9:64–67. Petitioner relies, *inter alia*, on Figures 4 and 7 of Braun '209, reproduced below. Pet. 21–22.

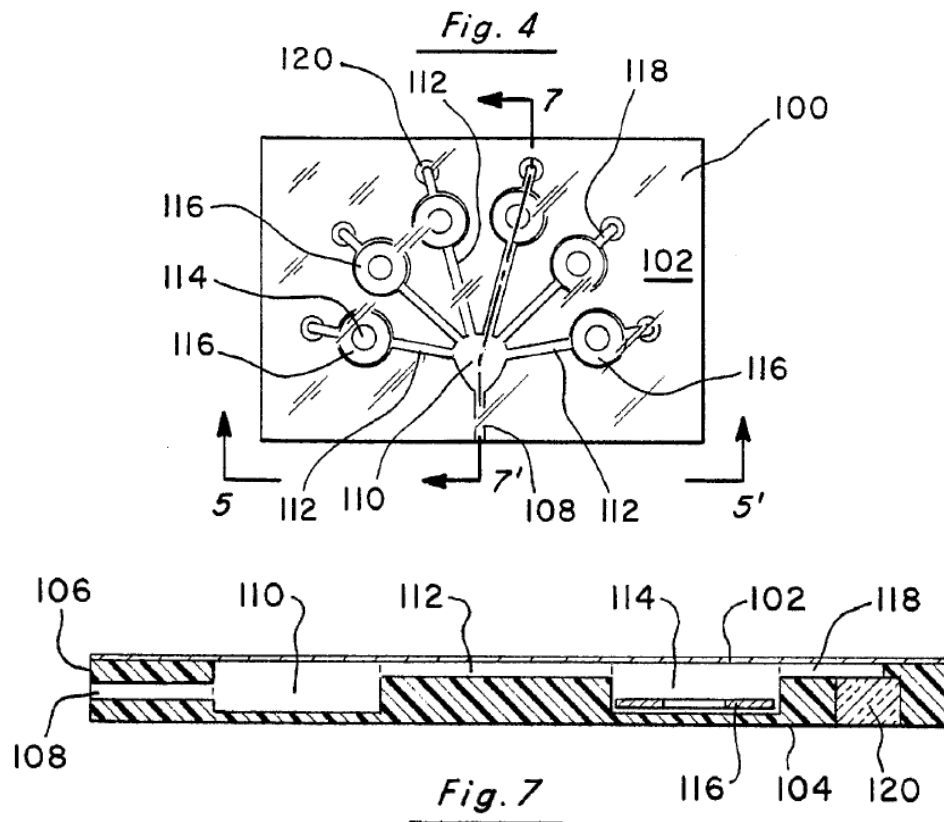


Figure 4 is a top view of a disposable cartridge (100), and Figure 7 is a cross-sectional view of the same. Ex. 1004, 6:8, 6:13–15. The cartridge has multiple fluid receiving chambers (114) into which blood samples are inserted via an injection port, fluid reservoir, and conduits (including items 108, 110, and 112), and mixed with various “viscosity-altering substances” to initiate the clot formation process in various ways. *Id.* at 7:26–54, 9:64–67. The cartridge is inserted into a testing device, which controls the test procedure and displays results. *Id.* at Fig. 1, 6:51–7:22. During testing, a ferromagnetic washer (116) that is placed inside each receiving chamber is magnetically raised and allowed to drop in the chamber via electromagnets in the testing device, and as the clot forms, the resulting resistance to motion of the washer is detected by inductively measuring the time it takes the washer to drop and determining the change in the viscosity

of the sample, including measuring the clotting time. *Id.* at Fig. 10, 4:20–21, 4:53–63, 7:7–16, 11:9–17.

The various viscosity-altering substances that are mixed with the blood include tissue thromboplastin, which activates the extrinsic channel, kaolin and diatomaceous earth, which activate the intrinsic channel, and aspirin, which suppresses thrombocyte function. *Id.* at 10:3–17; Ex. 1002 ¶¶ 90, 93.

Braun '209 describes the advantages of using the cartridge approach:

The apparatus of the present invention is able to detect changes in the viscosity of a fluid sample quickly, accurately, and repeatably. Each disposable cartridge of the apparatus of the present invention is capable of containing a large and variable number of test chambers, allowing several types of viscosity-related tests to be performed simultaneously using a single cartridge. Each type of analytical test is performed quickly, accurately, and reliably. The volume of the fluid samples used is minimal and the amount of fluid contained within each test chamber is automatically determined and thus varies little from test to test. Thus, discrepancies that may be introduced by individual procedures of technicians are eliminated. The disposable cartridges of the present invention are inexpensive to manufacture and small in size, thereby reducing the amount of storage space needed. Any viscosity-altering substances . . . placed within the cartridges may be, and preferably are, dried so that storage life is extended, even under less-than-ideal storage conditions. Moreover, because the operation of the herein-described apparatus is completely automatic, it is extremely simple to use and operator-caused errors and/or inconsistencies are virtually eliminated.

Ex. 1004, 3:65–4:18.

2. Lang 2006

For the Lang 2006 reference, Petitioner relies, *inter alia*, on Figure 2, reproduced below. Pet. 24.

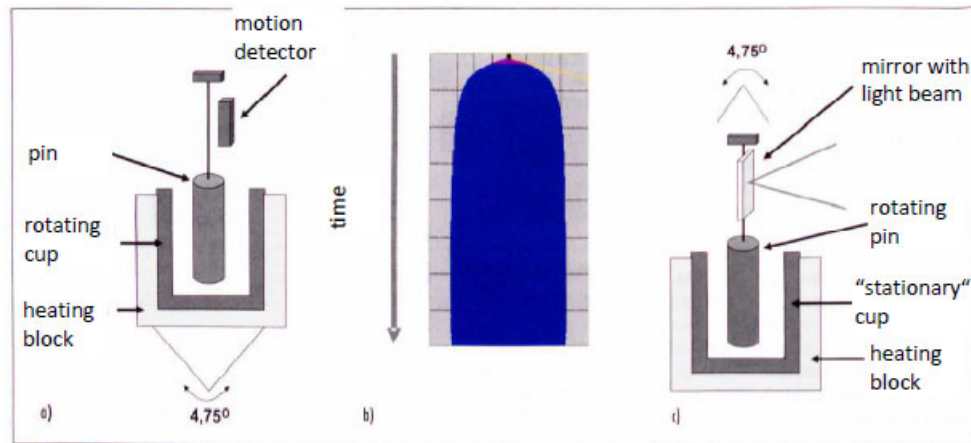


Fig. 2 Principle of TEG Haemoscope (a) and ROTEM (c) and thrombelastographic/-metric curve (b) as measurement result

The right-hand portion of Figure 2 depicts the measurement technique of thromboelastometry, embodied in the prior art “ROTEM” device, which is also referenced in the ’750 patent. Ex. 1006, 8–9;⁷ Ex. 1001, 2:60–62, 3:41–45. Thromboelastometry uses a rotating probe immersed in blood in a cavity, and as a blood clot forms, the clot couples to the probe, and the resulting resistance to the rotation is measured, determining the clotting parameters. Ex. 1006, Fig. 2, 8–9. As described in Lang 2006, the ROTEM device has four channels to perform four different blood clot tests in parallel. Ex. 1006, Table 1, 9; *see also* Ex. 1001, 3:45. Figure 4 of Lang 2006, reproduced below, depicts the resulting measurements:

⁷ Exhibit 1006 lacks page numbers. This decision identifies, e.g., page 1 as the first page of the exhibit, and so on.

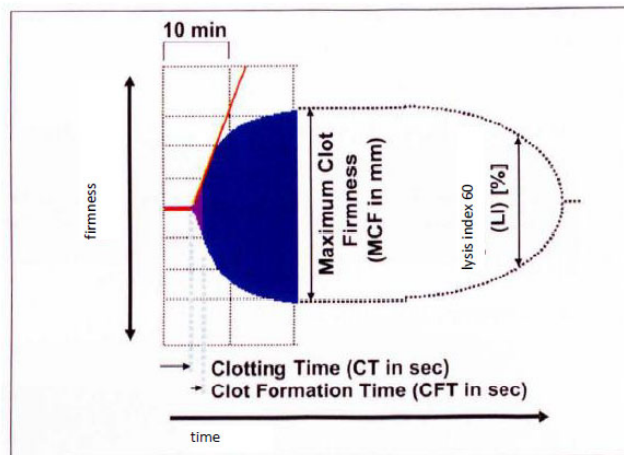


Fig. 4 Parameters of thrombelastometry (ROTEM)

As shown in Figure 4, the ROTEM tests measure clotting time, clot formation time, maximum clot firmness, and lysis, which are also measurements described in the '750 patent. Ex. 1006, Fig. 4, 12; Ex. 1001, Fig. 2, 2:16–21, 2:50–63. The reagents disclosed in Lang 2006, which are also referred to in the '750 patent as “available,” include those used in EXTEM tests, including “tissue factor,” which activates the extrinsic channel, those used in INTEM tests, such as kaolin, which activates the intrinsic channel, and “cytochalasin D,” which suppresses thrombocyte (i.e., platelet) function. Ex. 1006, 10–11, 14, 15; Ex. 1001, 9:26–41.

In particular, Lang 2006 discloses the same exemplary use of parallel testing as disclosed in the '750 patent — an EXTEM test in parallel with the combination of an EXTEM reagent and cytochalasin D (called a “FIBTEM” test) to determine if a coagulation disorder results from lack of fibrinogen or a malfunction of platelets. Ex. 1006, Fig. 6, 15–16; Ex. 1001, 9:30–41.

3. *The Combination of Braun '209 and Lang 2006*

In support of its challenges based on the combination of Braun '209 and Lang 2006, Petitioner relies on the Board's determination in *HemoSonics LLC v. C. A. Casyso GmbH*, IPR2018-00950, Paper 30 at 33

(PTAB Oct. 2, 2019) (final written decision), that one of ordinary skill would have appreciated the advantage of combining the cartridge technique of Braun '209 with the testing method of Lang 2006, and would have been motivated to do so. Pet. 26–27. Consistent with the Board's previous analysis in IPR2018-00950, Petitioner argues that one of ordinary skill would have recognized the benefits of the cartridge approach of Braun '209, including simultaneously and controllably testing a sample under different conditions, and improved storage of reagents. *Id.* at 27–28 (citing Neeves Decl. ¶ 77). Petitioner further argues that one of ordinary skill would have appreciated that Lang 2006 offers additional testing options based on the well-known thromboelastometry/thromboelastography techniques. *Id.* at 28–29 (citing Neeves Decl. ¶¶ 78–79). Both references measure the viscoelastic parameter of clotting time, describe point-of-care devices, provide rapid results, employ similar sample sizes, and allow for testing portions of a sample in parallel. *Id.* at 30–31 (citing Neeves Decl. ¶¶ 80–82).

Patent Owner argues against the combination, asserting that “[r]eplacing each of fluid-receiving cavities 114 of [Braun '209] with a cup and pin arrangement would be unduly complicated for the cartridge system described in [Braun '209],” and that the combination “would significantly increase the size of the Lang 2006 cartridge in direct contravention of one of the stated goals of [Braun '209]; that is, a reduction in size.” PO Resp. 16–17. This attorney argument is unavailing, because it incorrectly presumes one of ordinary skill would be forced to literally incorporate the specific structure disclosed in Lang 2006 into the cartridge approach of Braun '209. However, “[t]he test for obviousness is not whether the features of a

secondary reference may be bodily incorporated into the structure of the primary reference.” *Keller*, 642 F.2d at 425. Instead, the relevant issue is “what the combined teachings of the references would have suggested to those of ordinary skill in the art.” *Id.* “Combining the *teachings* of references does not involve an ability to combine their specific structures.” *In re Nievelt*, 482 F.2d at 968. *See also* Reply 21–23.

Accordingly, from our review of the record, we determine that Petitioner has articulated sufficient reasoning with rational underpinning supporting the combination of Braun ’209 and Lang 2006.

4. *Independent Claim 1*

Petitioner argues that the preamble of claim 1, “A cartridge device for evaluation of hemostasis,” is not limiting, but in the alternative argues that the combination of Braun ’209 and Lang 2006 would satisfy the limitation, given the cartridge of Braun ’209 and the measurement of clotting parameters taught by both references. Pet. 32 (citing Ex. 1004, Figs. 11a–11b, 1:15–22, 6:51–59; Ex. 1006, Figs. 4, 5, pp. 12–13; Neeves Decl. ¶¶ 86–88). We agree that the combination satisfies the preamble; therefore, there is no need at this time to determine whether the preamble is limiting. *See Vivid Techs.*, 200 F.3d at 803.

The first element of claim 1 requires, “a plurality of cavities each configured to receive blood of a test sample, each cavity comprising a reagent or combination of reagents.” Ex. 1001, 14:44–46. Petitioner relies on the fluid receiving chambers, into which reagents are placed, illustrated in Figure 4 of Braun ’209, and the multiple cavities containing reagents disclosed in Lang 2006. Pet. 33 (citing Ex. 1004, Figs. 4, 7, 4:63–5:3,

5:32–35, 6:62–63, 7:47–8:5, 9:42–48, 9:64–67; Ex. 1006, Tables 1, 2, 4, pp. 4, 5, 9, 11–13; Neeves Decl. ¶¶ 89–90).

The second element of claim 1 requires, “ductwork, including an inlet for receiving a test sample, wherein the ductwork is in communication with each of the plurality of cavities, whereby each of the plurality of cavities is configured to receive, via the ductwork, a portion of the test sample.”

Ex. 1001, 14:47–51. Petitioner relies on the conduits disclosed in Figures 4 and 7 of Braun ’209 that conduct the sample from the injection port, through the fluid receiving/dispensing reservoir and to the fluid receiving chambers. Pet. 33–34 (citing Ex. 1004, Figs. 4, 7, 4:63–5:3, 5:32–35, 6:62–63; 7:47–8:5, 9:42–48, 9:64–67; Neeves Decl. ¶¶ 91–93).

The third element of claim 1 requires, “a first cavity of the plurality of cavities comprising a first reagent or a first combination of reagents that interact with the blood received therein, wherein the first reagent, or a reagent included in the first combination of reagents, is an activator of coagulation.” Ex. 1001, 14:52–56. Petitioner relies on the provision in both references for including in the chambers or cavities extrinsic activators, such as tissue factor, and intrinsic activators, such as kaolin, which activate coagulation. Pet. 34–36 (citing Ex. 1004, 9:42–10:17; Ex. 1006, Tables 1, 2, 4, Fig. 6, pp. 9–11, 13, 16; Neeves Decl. ¶¶ 88–89, 94–95).

The fourth element of claim 1 requires, “a second cavity of the plurality of cavities comprising a second combination of reagents that interact with blood of the test sample received therein, the second combination including an activator of coagulation and one or more reagents configured for suppressing thrombocyte function.” Ex. 1001, 14:57–62. Petitioner relies on the provision in both references for including in the

chambers or cavities coagulation activators, as described for the third element, and in addition reagents that decrease the tendency of blood to coagulate, such as aspirin and cytochalasin D. Pet. 36–37 (citing Ex. 1004, Fig. 4, 9:43–10:17; Ex. 1006, Fig. 6, Tables 1, 2, pp. 9–11, 14–15; Neeves Decl. ¶¶ 96–98). In particular, Lang 2006 describes using the FIBTEM test to isolate contributions of platelets and fibrin to a clot, by comparing data from a chamber that includes an extrinsic activator with a chamber that includes an extrinsic activator and a suppressor of platelet function. *Id.*

The fifth element of claim 1 requires, “a viscoelastic interrogation device that measures blood clot firmness of the test sample or other parameters dependent on measurement of blood clot firmness.” Ex. 1001, 14:63–65. Petitioner relies on the thromboelastometry and thromboelastography devices disclosed in Lang 2006, such as ROTEM, as incorporated into the cartridge approach of Braun ’209, and the measurements of the various clot formation parameters using those devices as disclosed in Lang 2006. Pet. 38–39 (citing Ex. 1006, Figs. 2, 4, pp. 5, 8–9; Neeves Decl. ¶¶ 99–100).

Patent Owner argues that “[t]he [Braun ’209]-Lang 2006 combination is deficient because, taken together, these references do not disclose or suggest the claimed ‘plurality of cavities’ in combination with a ‘viscoelastic interrogation device’ (that is, a probe element and measurement cavity together).” PO Resp. 12. Patent Owner bases this argument on the premise that “claim 1 requires separate cavities for reagents and for viscoelastic interrogation.” *Id.* at 14. However, there is no such requirement in claim 1. The ’750 Specification specifically contemplates that a reagent cavity can be “integral[ly] formed” with a measurement cavity, including a provision in

one disclosed embodiment for passage holes to allow injection of reagents directly into a measurement cavity. Ex. 1001, 6:40–43, 8:66–9:1, 12:54–57; Reply 13–14.

Accordingly, having considered the record, we determine that Petitioner has proved by a preponderance of the evidence that claim 1 would have been obvious over the combination of Braun '209 and Lang 2006.

5. Dependent claims 2–4, 7–9, 18, 19, 21–26, 28, and 30

Claim 2 depends from claim 1, and additionally requires “the activator of coagulation of the first cavity and the activator of coagulation of the second cavity are one or more reagents configured for extrinsic activation of the coagulation cascade.” Ex. 1001, 14:66–15:2. Petitioner relies on the disclosure in both references of the use of tissue factor, which is an extrinsic activator of coagulation. Pet. 39–40 (citing Ex. 1004, 9:43–10:17; Ex. 1006, Table 2; Neeves Decl. ¶¶ 103–104).

Claim 3 depends from claim 2, and additionally requires “a third cavity of the plurality of cavities comprises one or more reagents configured for intrinsic activation of the coagulation cascade.” Ex. 1001, 15:3–5. Petitioner relies on the disclosure in both references of the use of intrinsic activators of coagulation, such as aspirin and the reagents used in the INTEM test. Pet. 40–41 (citing Ex. 1004, 9:64–10:16; Ex. 1006, Table 2; Neeves Decl. ¶¶ 106–107).

Claims 4, 7, and 8 depend from claims 3, 2, and 1, respectively, and additionally require “the one or more reagents configured for suppressing thrombocyte function include cytochalasin D.” Ex. 1001, 15:6–8, 15:15–20. Petitioner relies on the disclosure in Lang 2006 of the use of cytochalasin D

in the FIBTEM test. Pet. 41–42 (citing Ex. 1006, Table 2, Fig. 6, p. 15; Neeves Decl. ¶¶ 109–116).

Claim 9 depends from claim 1, and additionally requires “the device is a cartridge configured for use in conjunction with a measuring system.” Ex. 1001, 15:21–22. Petitioner relies on the disclosure in Braun ’209 of the use of a cartridge as described above. Pet. 42–43 (citing Ex. 1004, Figs. 1, 1A, 6:1–3, 51–59, 6:66–7:6; Neeves Decl. ¶¶ 118–119).

Claim 18 depends from claim 1, and additionally requires “the one or more reagents within each of the plurality of cavities are in a solid form.” Ex. 1001, 16:3–5. Petitioner relies on the disclosure in Braun ’209 of the use of reagents in dried form. Pet. 49–50 (citing Ex. 1004, 9:59–61; Neeves Decl. ¶¶ 142–143).

Claim 19 depends from claim 1, and additionally requires “a housing, wherein each of the plurality of cavities are at least partially defined by the housing.” Ex. 1001, 16:6–8. Petitioner relies on the disclosure in Braun ’209 of the use of a cartridge housing as described above. Pet. 50 (citing Ex. 1004, Fig. 7, 7:26–46, 8:15–28; Neeves Decl. ¶¶ 145–146).

Claims 21–26 and 28 depend from claim 1, and additionally require, respectively:

- the interrogation device is configured to measure changing in elastic properties of the test sample;

- the device is configured to be interrogated to determine a hemostatic parameter of the test sample;

- the interrogation device is configured to perform a viscoelastic method of testing;

- the interrogation device is configured to continuously measure the blood clot firmness or the other parameters

dependent thereon from the formation of the first fibrin fibers until the dissolution of the blood clot by fibrinolysis;

the interrogation device is configured to measure a maximum clot firmness;

the interrogation device is configured to measure a rate of clot formation[; and]

the interrogation device is configured for thromboelastometry or thromboelastography.

Ex. 1001, 16:13–30, 16:37–39. Petitioner relies on the disclosure in Lang 2006 of the measurement during clotting of clotting time, clot formation time, maximum clot firmness, and maximum lysis, in the context of both thromboelastometry and thromboelastography. Pet. 51–56 (citing Ex. 1006, Figs. 2, 3, 4, pp. 8–13; Neeves Decl. ¶¶ 151–167, 171–173).

Claim 30 depends from claim 1, and additionally requires “the ductwork defines a fluid pathway includes an inlet channel, a first channel, and a second channel, wherein the inlet channel is in communication with the inlet, wherein the first channel is in communication with the inlet channel and at least with the first cavity, and wherein the second channel is in communication with the inlet channel and at least with the second cavity.” Ex. 1001, 16:43–50. Petitioner relies on the duct arrangement disclosed in Braun ’209 discussed above. Pet. 56–57 (citing Ex. 1004, Figs. 4, 7; Neeves Decl. ¶¶ 178–179).

Patent Owner does not address Petitioner’s arguments regarding these claims. *See generally* PO Resp.

Having considered the record, we determine that Petitioner has proved by a preponderance of the evidence that claims 2–4, 7–9, 18, 19, 21–26, 28, and 30 would have been obvious over the combination of Braun ’209 and Lang 2006.

E. Ground 2: Obviousness of Claim 5 Over Braun '209, Lang 2006, and Hillman '525

Petitioner challenges claim 5 as obvious over the combination of Braun '209, Lang 2006, and Hillman '525. Pet. 58–60. Petitioner argues that one of ordinary skill would have been motivated to draw upon the teachings of Hillman '525 in regard to the disclosed reagents because that reference, like Braun '209 and Lang 2006, discloses an assay device for measurement of coagulation parameters, and the references discuss using the same types of reagents. *Id.* at 58–59 (citing Ex. 1008, Abstr., 4:52–56, 9:41–64; Ex. 1007, Table 2; Ex. 1004, 9:59–10:17; Neeves Decl. ¶ 180).

Claim 5 depends from claim 3, and additionally requires “the one or more reagents configured for intrinsic activation of the coagulation cascade include a Hagemann factor.” Ex. 1001, 15:9–11. Petitioner relies on the disclosure in Hillman '525 of the use of a Hagemann factor. Pet. 59–60 (citing Ex. 1008, 9:40–65; Neeves Decl. ¶¶ 182–183).

Patent Owner does not address Petitioner’s arguments regarding claim 5. *See generally* PO Resp.

Having considered the record, we determine that Petitioner has proved by a preponderance of the evidence that claim 5 would have been obvious over the combination of Braun '209, Lang 2006, and Hillman '525.

F. Ground 3: Obviousness of Claim 6 Over Braun '209, Lang 2006, and Warden '712

Petitioner challenges claim 6 as obvious over the combination of Braun '209, Lang 2006, and Warden '712. Pet. 60–63. Petitioner argues that one of ordinary skill would have been motivated to draw upon the teachings of Warden '712 in regard to processing blood samples because

that reference, like Braun '209, teaches use of a cartridge to assess components of the blood coagulation process. *Id.* at 60–61 (citing Ex. 1008, Abstr., 4:52–56, 9:41–64; Ex. 1007, Table 2; Ex. 1004, 9:59–10:17; Neeves Decl. ¶ 180).

Claim 6 depends from claim 2, and additionally requires “a fourth cavity of the plurality of cavities comprises one or more reagents configured for testing platelet aggregometry.” Ex. 1001, 15:12–14. Petitioner relies on the teachings in Warden '712 of devices and reagent compositions for testing platelet aggregometry. Pet. 61–63 (citing Ex. 1009, 2:16–49; 3:65–4:4, 4:16–37, 17:55–18:24; Neeves Decl. ¶¶ 187–188).

Patent Owner does not address Petitioner's arguments regarding claim 6. *See generally* PO Resp.

Having considered the record, we determine that Petitioner has proved by a preponderance of the evidence that claim 6 would have been obvious over the combination of Braun '209, Lang 2006, and Warden '712.

IV. CONCLUSION⁸

For the reasons above, Petitioner has shown by a preponderance of the evidence that the remaining challenged claims 1–9, 18, 19, 21–26, 28, and 30 of the '750 patent are unpatentable, as summarized in the following table.

Claims	35 U.S.C. §	References/ Basis	Claims Shown Unpatentable	Claims Not Shown Unpatentable
1–4, 7–9, 18, 19, 21–26, 28, 30	103(a)	Braun '209, Lang 2006	1–4, 7–9, 18, 19, 21–26, 28, 30	
5	103(a)	Braun '209, Lang 2006, Hillman '525	5	
6	103(a)	Braun '209, Lang 2006, Warden '712	6	
Overall Outcome			1–9, 18, 19, 21–26, 28, 30	

⁸ Should Patent Owner wish to pursue amendment of the challenged claims in a reissue or reexamination proceeding subsequent to the issuance of this decision, we draw Patent Owner's attention to the April 2019 *Notice Regarding Options for Amendments by Patent Owner Through Reissue or Reexamination During a Pending AIA Trial Proceeding*. See 84 Fed. Reg. 16,654 (Apr. 22, 2019). If Patent Owner chooses to file a reissue application or a request for reexamination of the challenged patent, we remind Patent Owner of its continuing obligation to notify the Board of any such related matters in updated mandatory notices. See 37 C.F.R. § 42.8(a)(3), (b)(2).

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, based on a preponderance of the evidence, claims 1–9, 18, 19, 21–26, 28, and 30 of U.S. Patent No. 10,746,750 B2 are held to be unpatentable; and

FURTHER ORDERED that, because this is a final written decision, parties to this proceeding seeking judicial review of our decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

For PETITIONER:

Brian Nolan
Ying-Zi Yang
MAYER BROWN LLP
bnolan@mayerbrown.com
yyang@mayerbrown.com

For PATENT OWNER:

W. Karl Renner
David Holt
Indranil Sarkar
FISH & RICHARDSON P.C.
axf-ptab@fr.com
holt2@fr.com
sarkar@fr.com

Christopher Schultz
Paul Pysher
BURNS & LEVINSON LLP
cschultz@burnslev.com
ppysher@burnslev.com