UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INSTRUMENTATION LABORATORY COMPANY

Petitioner

v.

HEMOSONICS LLC

Patent Owner

Post-Grant Review Case No. Unassigned

Patent 9,977,039

PETITION FOR POST-GRANT REVIEW OF U.S. PATENT NO. 9,977,039

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I. INTRODUCTION:

Instrumentation Laboratory Company ("Petitioner") requests post-grant review ("PGR") of claims 1, 4, 26, 36, 51, 52 and 55 (the "Challenged Claims") of U.S. Patent No. 9,977,039, issued May 22, 2018 ("the '039 patent") (Ex. 1001), which public records indicate is assigned to HemoSonics LLC ("Patent Owner"). The '039 patent is based on the disclosure (same as U.S. Patents Nos. 9,272,280, 9,410,971, 10,031,144 and 10,161,944) of a single-sample cartridge with multiple test chambers in which distributed blood in hemostasis is interrogated by a specific acoustic technique. Although the patents claim priority from a pre-AIA[1] provisional application, the "transition" Challenged Claims are not enabled by any pre-AIA disclosure (Section VIII: Ground 2) and thus the '039 patent is subject to PGR under AIA §§ 3(n)(1) and 6(f)(2)(A). *U.S. Endodontics, LLC v. Gold Standard Instruments, LLC*, PGR2015-00019, Paper No. 54, at 7–8 (PTAB Dec. 28, 2016); *Schul International Company LLC v. Emseal Joint Systems Ltd.*, PGR2017-00053, Paper No. 10 (PTAB April 9, 2018); *Inguran LLC v. Premium Genetics (UK) Ltd.*, PGR2015-00017, Paper No. 8 (PTAB Dec. 22, 2015).

This Petition shows that it is more likely than not, under 35 U.S.C. § 324(a), that the Challenged Claims, which recite devices "designed to be interrogated to

[1] Leahy-Smith America Invents Act, Pub. L. 112-29, 125 Stat. 284, Sept. 22, 2011.

determine a hemostatic parameter," are indefinite under 35 U.S.C. § 112(b), and lacking in enablement and written description showing possession of invention under 35 U.S.C. § 112(a). If it is not settled under *LizardTech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1344 (Fed. Cir. 2005), that the Challenged Claims fail under section 112 because the only interrogation structure disclosed is recited in several claims dependent therefrom, this Petition also raises a 35 U.S.C. § 324(b) issue of whether facially broader claims supported by the same structure should be allowed, freely from PGR, to deceptively, facially preempt other, abstract interrogation implementations from using other cartridge features. It also shows that, more likely than not, independent Challenged Claims 1, 26, 51 and 52, impermissibly under 35 U.S.C. §§ 102 and 103, overreach prior art single-sample multi-chamber cartridges using other-than-acoustic interrogation techniques.

II. MANDATORY NOTICES UNDER 37 C.F.R. § 42.8(a)(1):

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

Petitioner, Instrumentation Laboratory Company is the real party-in-interest. Related entities, C A Casyso AG and Werfen USA, LLC, have interests represented by Petitioner.

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

Both claims of U.S. Patent No. 9,272,280 ("the '280 patent") were held unpatentable in *Instrumentation Laboratory Co. v. HemoSonics LLP*, IPR2017-

00852, Paper No. 47 (PTAB Feb. 13, 2019) ("'852 FWD," Ex. 1011), and claims 1, 2, 6–8, 15, and 16 of U.S. Patent No. 9,410,971 ("the '971 patent"), a continuation of the '280 patent, were held unpatentable in *Instrumentation Laboratory Co. v. HemoSonics LLP*, IPR2017-00855, Paper No. 55 (PTAB Feb. 13, 2019) ("'971 FWD," Ex. 1012). The claims were held unpatentable as anticipated by U.S. Pub. App. 2010/0154520 ("Schubert") (Ex. 1005), disclosing a rotationally-oscillating-pin interrogated cartridge device for multi-assay hemostasis evaluation explained at Section V(C)(2) and asserted in this Petition (Section XII: Ground 5 and Section XII: Ground 6). U.S. Patent No. 10,031,144 ("the '144 patent") is a continuation of the '971 patent, application for which was the direct parent of the '039 patent here requested for review. As each of these patents and U.S. Patent No. 10,161,944, all owned by Patent Owner, claim combinations of features disclosed in their common disclosure, they each may be affected by the requested review. Petitioner's U.S. Patent No. 9,915,671, based on the Schubert disclosure, but with claims in part copied from those at an earlier stage of the application for Patent Owner's '144 patent, is being reviewed in *HemoSonics LLC v. C.A. Casyso AG*, IPR2018-00950.

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

Pursuant to 37 C.F.R. § 42.8(b)(3), lead counsel for this Petition is Stephen Y. Chow (Reg. No. 31,338) and back-up counsel are Gabriel Goldman (Reg. No.

61,343) and Ronda Moore (Reg. No. 44,244). Pursuant to 37 C.F.R. § 42.10(b), Petitioner has filed a power of attorney designating the above-identified counsel.

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

Pursuant to 37 C.F.R. § 42.8(b)(4) service information for the Petition is as follows:

Lead Counsel	Back-Up Counsel
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Petitioner consents to electronic service at the above-identified email addresses.

III. ADDITIONAL REQUIREMENTS:

A. Payment of Fees Under 37 C.F.R. § 42.15:

The required fees are submitted herewith from Deposit Account No. 03-2410 (Order No. 51310-05007). If any additional fees are due at any time during this proceeding, the Office is authorized to charge such fees to Deposit Account No. Deposit Account No. 03-2410 (Order No. 51310-05007).

B. Timing Under 37 C.F.R. § 42.202:

The present petition for post-grant review is filed within nine months after the grant of the '039 patent.

C. Grounds for Standing Under 37 C.F.R. § 42.204(a):

Petitioner certifies that: (1) the '039 patent is eligible for post-grant review; and (2) Petitioner is not barred or estopped from requesting post-grant review of any claims of the '039 patent on the grounds identified herein.

IV. THE '039 PATENT:

A. The Specification:

The specification of the '039 patent is directed to "devices, systems and methods for evaluation of hemostasis" as well as "sound focusing assemblies" (Ex. 1001, Title and Abstract). It discloses a cartridge device (100) for use in evaluation of hemostasis (2:22-23; 2:51-64; 4:25-26; 18:30-19:15; Tables 2 and 3).

FIGS. 1A-G, 2-5, 8A-8D and 10B show a cartridge device (100) that includes a plurality of test chambers (110, 112, 114, 116), each chamber including a reagent or combination of reagents (2:25-29; 2:45-50, 5:65-6:3; Table 1).[2] The device (100) includes a fluid pathway including a plurality of channels (202, 204, 206, 208, 210, 212, 214) for distributing a blood sample from an inlet 102 to the plurality of test

[2] This summary and the annotated figure are supported by the Declaration of Frank M. LaDuca, Ph.D., FAHA, submitted as Ex. 1002, cited as "LaDuca," ¶¶ 48-53.

chambers (4:25-55) and a port (106) for applying a pressure gradient to move the sample through the cartridge (4:39-43), as shown in the following color-coded **annotated [‘039] FIG. 2**:

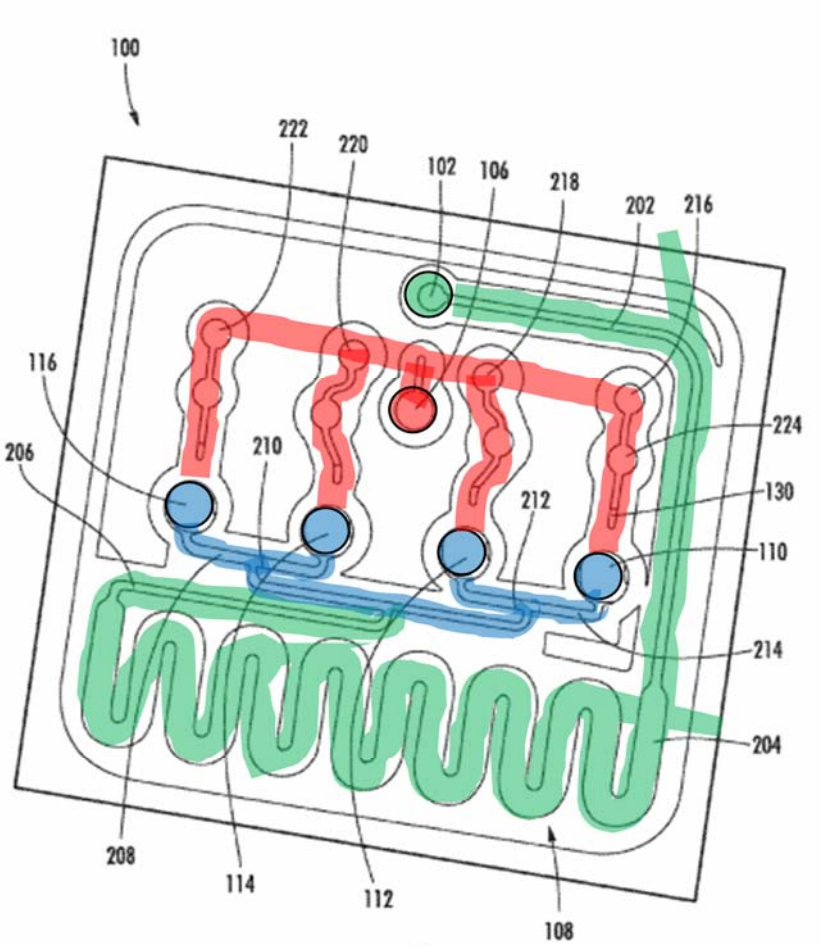
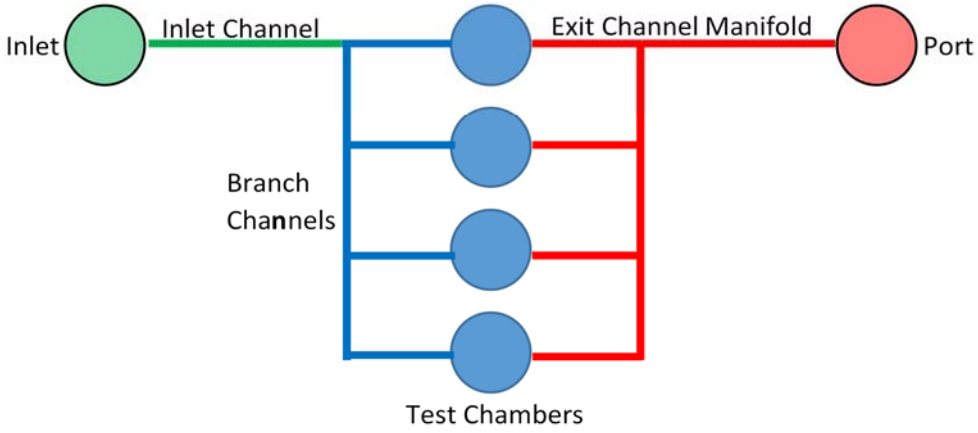


FIG. 2



The ‘039 patent specification describes a flow path of the cartridge device (100) that includes a serpentine heat exchanger channel (204) (FIGS. 2 and 10B; 7:38-42;

10:33-35), where a portion of the cartridge that defines the heat exchanger channel is held against a heating block (7:13-24; 8:5-30). That portion may have higher thermal conductivity than the remaining portion so as to achieve more rapid or efficient heating of the biological sample (*id*.). Also described is a hydrophobic filter (222, 220, 218 and 216) to prevent the blood sample from exiting the port (106) (5:11-18; 10:4-6).

In the depicted and described embodiments, the cartridge device (100) and test chambers (110, 112, 114, 116) are specifically structured for a particular type of acoustic interrogation (*e.g.*, 2:35-37; 2:43-44; 2:51-54; 3:3-6; 12:13-16; 15:50-53). Each test chamber includes a sound-focusing assembly (also referred to as a lens assembly or lens) that provides for dry ultrasonic coupling (test chamber cap (132) and lens (134) in FIGS. 1D and 1F; 11:52-12:16). The cartridge device (100) is positioned into a pocket (302) of an analysis system (300) to enable acoustic coupling with the test chambers (12:17-25; 13:29-45). Although the '039 patent specification details its purportedly novel acoustic interrogation (12:18-13:55), it does not disclose any cartridge or test chamber structure for any other interrogation technique or even suggest that an alternative interrogation technique may be used with the disclosed cartridge and test chamber structure.

B. Priority Date of the '039 Patent:

The ‘039 patent claims a priority date of Feb. 15, 2011 (Ex. 1001, 1:7-16); as shown here, however, especially in Section VIII, the Challenged Claims do not qualify for that date, but, at earliest, the filing date of the application.

C. File History of the ‘039 Patent:

Patent Owner filed Application No. 15/644,124 on July 7, 2017 as a continuation of an application that broadly claimed “A device for evaluation of hemostasis” comprising “a plurality of test chambers each configured to receive a test sample of blood,” wherein each of a first and second chamber comprises “[a] reagent or a combination of reagents that interact with the test sample of blood received therein” and “are configured to be interrogated to determine a hemostatic parameter of the test samples” (Ex. 1003 at 656 [emphasis added]). In a preliminary amendment filed a few days later, Patent Owner rewrote “configured” to “designed” so that the test chambers “are each designed to be interrogated to determine a hemostatic parameter of a test sample of blood that is received therein” (*id.* at 611, 615-16 [emphasis added], where the preliminarily amended claims 74, 88, 102 and 103 correspond to issued claims 1, 26, 51, and 52). This change aligned with Patent Owner’s IPR2016-00852 Preliminary Response, Paper No. 6, at 5 (June 6, 2017), that “the term ‘configured’ is used to mean ‘designed’ . . . a purposeful design to accommodate a function” (emphasis added). This subjective functional language was carried forward in Patent Owner’s prosecution and remains common to each of

the Challenged Claims (Ex. 1001, claim 1, 19:33-36; claim 26, 21:49-52; claim 51, 24:22-26; claim 52, 25:22-26).

The Examiner asserted that a POSA would view both the '039 patent claims and the Patent Owner's then co-pending Application No. 15/202,059 (issued as the '144 patent) as "designed for acoustic analysis" (Ex. 1003 at 502). The Examiner also stated as a reason for initial (but withdrawn) allowance of claim 103/52 considering a limitation that "each test chamber contain[] a specific combination of pre-loaded reagents that **are** designed to interrogate a hemostatic parameter of a test sample of blood that **is** received therein" (*id*. at 508-09 [emphases added]), confusing the reagents used in a test with the method or structure of interrogation. Ultimately, the Examiner agreed to allow the '039 patent with an amendment specifying distribution of the test sample along multiple channels (*id*. at 201, 203, and 206-07) to overcome rejections (*id*. at 269-78) based on Clague *et al.* (US 2005/0233460 Al, Ex. 1010), which disclosed interrogation with a vane inside its test chambers electromagnetically rotated to measure viscosity.

Although the Examiner remarked that a POSA would consider the claims addressed to "acoustic analysis," there is no textual or file history limitation of the Challenged Claims to that class of interrogation. Petitioner contends that, absent limitation to the disclosed structure for the disclosed acoustic interrogation, the Challenged Claims are indefinite and the written description fails to support the

Challenged Claims. Petitioner further contends that the Challenged Claims are anticipated by or obvious over the art asserted herein, including U.S. Patent No. 5,534,226 ("Gavin") (Ex. 1004), U.S. Pub. App. 2010/0154520 ("Schubert") (Ex. 1005) and U.S. Patent No. 6,016,712 ("Warden") (Ex. 1006). The art-based grounds raised herein were not considered by the Examiner during prosecution.

D. The Challenged Claims of the '039 Patent:

Challenged Claims 1, 26, 51 and 52 of the '039 patent are its only independent claims, each claiming a multi-test-chamber cartridge in which a test sample of blood is received and distributed by recited structure to test chambers "each designed to be interrogated to determine a hemostatic parameter of a test sample of blood that is received therein," with claim 52 claiming a system that acts with the cartridge. (LaDuca ¶ 54.)

Claim 1 is representative:

1. [1] A device comprising:

[1.1] a housing;

[1.2] a plurality of **test chambers**, wherein the plurality of test chambers includes [1.2.1] at least a first test chamber and a second test chamber that are each at least partially defined by the housing, [1.2.3] wherein the first test chamber and the second test chamber are **each designed to be interrogated to determine a hemostatic parameter of a test sample of blood that is received therein** and [1.3] a reagent

or combination of reagents, [1.3.1] wherein a first reagent or combination of reagents in the first test chamber is different than a second reagent or combination of reagents in the second test chamber; and

[1.4] a fluid pathway comprising a plurality of channels, each defined at least in part by the housing, [1.4.1] wherein the fluid pathway includes an inlet, defined at least in part by the housing, through which the test sample is introduced into the device, [1.4.2] wherein at least one channel of the plurality of channels is in communication with the inlet and with the first test chamber and the second test chamber to deliver a portion of the test sample to each of the first test chamber and the second test chamber, and [1.4.3] wherein the fluid pathway includes a first port, defined at least in part by the housing, in communication with a channel of the fluid pathway and from which a pressure gradient when applied from a source external to the first port draws the test sample through the at least one channel of the fluid pathway and into at least one of the test chambers, [1.4.2] wherein the at least one channel of the fluid pathway includes an inlet channel, a first channel, and a second channel, [1.4.2] 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 test chamber, and wherein the second channel is in communication with the inlet channel and at least with the second test chamber,

[1.1.1] wherein the housing includes a thermally conductive wall configured to allow the test sample to be heated, the thermally conductive wall having an outer surface area and an inner surface area;

[1.4.6] wherein the fluid pathway includes a portion at least partially defined by the inner surface area of the thermally conductive wall and the outer surface area of the thermally conductive wall is shaped to be held in at least partially conforming contact with or in close proximity to a heater to allow adjustment of a temperature of the test sample flowing through the portion at least partially defined by the inner surface area of the thermally conductive wall; and

[1.5] wherein the device can be used with an interrogation device to measure at least one viscoelastic property of the test sample.

(Ex. 1001, 19:28-20:13 [emphases added, bracketed numbers refer to elements tabulated in following **TABLE A** of Challenged Claims elements].)

Claim 1 can be summarized as requiring [at least] two test chambers "designed to be interrogated" for a "hemostatic parameter," each test chamber with different reagent(s), a fluid pathway for imputing, dividing and distributing a blood sample to each of the test chambers (i.e., inlet → [inlet] channel → [branch] channels → test chambers), a [first] port for interfacing with an external pump to move the sample along the fluid pathway, structural design elements for interfacing with a heater and structural design elements for interfacing with an interrogation device. (LaDuca ¶ 66.)

TABLE A – Claim Elements				
Limitation	Claim 1	Claim 26	Claim 51	Claim 52

1	"[cartridge] device"	(19:28)	(21:44)	(24:17)	(25:16)
1.1	"a housing"	(19:29)	(21:45)	(24:18)	(25:18)
1.1.1	at least a portion of the housing, such as a wall, is [or is designed to be] "**thermally conductive**"	(19:64)	(22:14-15)	(25:7-8, "to allow the test sample to reach about 37° C.")	N
1.2	"plurality of test chambers"	(19:30)	(21:46)	(24:19)	(25:19)
1.2.1	including "at least a first test chamber and a second test chamber that are each at least partially defined by the housing"	(19:31-32)	21:47-49)	24:20-22)	(25:19-22)
1.2.2	including a third test chamber so defined	N	N	(24:20-23)	N
1.2.3	wherein "each [chamber] is **designed to be interrogated** to determine a hemostatic parameter of a test sample of blood that is received therein"	(19:33-36)	(21:49-52)	(24:22-26)	(25:22-26)

1.3	including "a reagent or combination of reagents"	(19:36-37)	(21:53)	(24:26-27)	(25:26-27)
1.3.1	wherein different reagent(s) are in first and second test chambers	(19: 37-40)	(21:54-56)	(24:33-34)	(25:27-30)
1.3.2	reagent(s) in the first and second [and third] chambers activate coagulation via the intrinsic and/or extrinsic pathways	N	(22:16-23)	(24:27-33)	N
1.3.3	reagent(s) in at least one of the first or second chambers activate coagulation via the extrinsic pathway	N	(22:24-27)	N	N
1.3.4	reagent(s) in the second chamber include abciximab and/or cytochalasin D	N	(22:28-30)	N	N
1.4	"a fluid pathway comprising a plurality of channels defined at least in part by the [cartridge] housing"	(19:41-42)	(21:57-58)	(24:36-37)	(25:31-32)
1.4.1	wherein the test sample is "introduced" in an	(19:42-49)	(21:58-65)	(24:41-46)	(25:33-41)

	inlet "in communication with" channels" to deliver a portion" to each of the first and second [and third] test chambers				
1.4.2	wherein channels to each of the test chambers is in communication with an inlet channel in communication with the inlet (redundantly stated)	(19:45-49,56-63)	(22:5-13)	(24:52-60)	(implied by 25:33-41)
1.4.3	including "a **first port** at defined at least in part by the housing, in communication with a channel . . . from which a **pressure gradient** when applied **from a source external**. . . draws the test sample . . . into at least one of the test chambers"	(19:50-56)	(21:66-22:4)	(24:46-52)	(25:41-48)
1.4.4	includes "a second port . . . from which a **pressure gradient** when applied from a **source external** to the second port draws the test sample **from an**	N	N	(24:61-67)	N

	external vessel through the inlet and into the fluid pathway"				
1.4.5	"wherein the first port and/or the second port prevents the test sample from leaving the device"	N	N	(25:5-6)	N
1.4.6	wherein "the housing includes a **thermally conductive wall** configured to allow the test sample to be heated", wherein "the fluid pathway includes a portion at least partially defined by the inner surface area of the thermally conductive wall and the outer surface area of the thermally conductive wall is **shaped to be held in at least partially conforming contact with or in close proximity to a heater to allow adjustment of a temperature** of the test sample flowing through the portion at least partially defined by the inner	(19:64-20:9)	N	N	N

	surface area of the thermally conductive wall				
1.4.7	"wherein the fluid pathway includes a portion **designed to be held against a heater** to allow adjustment of a temperature of the test sample flowing through the portion"	N	N	(25:1-4)	N
1.5	"wherein the [cartridge] device can be used / is configured for use with an interrogation device to measure at least one viscoelastic property of the test sample"	(20:10-12)	(22:31-33)	(25:11-13)	N
1.6	"a consumable cartridge device configured to be positioned in an analysis system"	N	N	N	(25:16-17)
2	"a heat exchanger and a temperature control coupled thereto, designed to allow the temperature of the test sample before analysis in the test chamber"	N	N	N	(25:49-52)

3	"an interrogation device designed to measure a viscoelastic property of the test sample"	N	N	N	(25:53-54)
4	"a pressure control designed to apply the pressure gradient that causes the test sample to flow through the fluid pathway and into the test chambers"	N	N	N	(25:55-57)
5	an "analysis system" including "a pocket designed to receive the consumable cartridge . . . comprising an actuator system that allows the heat exchanger, the interrogation device and the pressure control to be positioned adjacent the cartridge"	N	N	N	(25:58-64)

Each of the Challenged Claims includes common elements of the [cartridge] device including [1.1] a housing, [1.2] at least two test chambers, [1.3] reagent(s) and [1.4] a fluid pathway for distributing a sample. The multi-chamber device is illustrated in FIG. 2 of the '039 patent (cartridge 100) which is annotated in Section IV.A. As claimed, the housing defines [1.2.1] test chambers (110, 112, 114, 116) as

well as [1.4] channels of a fluid pathway for [1.4.1] receiving and [1.4.2] distributing a sample from an inlet (102) to first and second test chambers. The test chambers (110, 112, 114, 116) each include [1.3] a reagent or combination of reagents, where [1.3.1] the reagent(s) in a first of the test chamber are different than the reagent(s) in a second of the test chambers. As shown in FIG. 2, the test chambers (110, 112, 114, 116) of the '039 patent are not fully enclosed spaces in the cartridge but rather part of the continuum of the fluid pathway (including, in depicted embodiments, channels flowing both in and out of the test chambers). The fluid pathway includes an inlet (102) flowing into an inlet channel (202, 204, 206) which then branches off into a plurality of branch channels (208, 210, 212, 214) each flowing into a respective test chamber (110, 112, 114, 116). The fluid pathway further [1.4.3] includes a port (102) defined by the housing and in communication with a channel of the fluid pathway for applying a pressure gradient from an external source[3] to the fluid pathway to move a sample into a test chamber. In the depicted embodiment of FIG. 2, the port (102) is at an end point of the fluid pathway and interfaces with a manifold of exit ports (130) from each of the test chambers (although the claims are not limited to this particular configuration). (LaDuca ¶ 55.)

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[3] An external pressure source is not a positively recited in the claims; only system claim 52 positively recites a pressure control for applying the pressure gradient.

The test chambers recited in each of Challenged Claims are structurally defined by being formed in part by the housing [1.2.1] and open to receiving sample fluid through the channels [1.4.1 and 1.4.2], and are expressly limited, functionally, but not structurally, as being [1.2.3] "designed to be interrogated to determine a hemostatic parameter of a test sample of blood that is received therein."[4]

In addition to the common elements, and thus distinguished by a "shape for contact or proximity," the basic cartridge **Claim 1** element [1.4.6] limits the claimed cartridge to one in which "the outer surface area of [a] thermally conductive wall [defining a sample fluid channel] is shaped to be held in at least partially conforming contact with or in close proximity to a heater to allow adjustment of a temperature of the test sample flowing [through the channel]" (Ex. 1001, 19:64-20:9 [emphases added]). Petitioner contends that this functional shape limitation is indefinite at least because no heater and no measure of "thermally conductive" [1.1.1] are specified and it is also unenabled. (LaDuca ¶ 60.)

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[4] Claims 1, 26 and 51 each also requires [1.5] that the cartridge "can be used with an interrogation device to measure at least one viscoelastic property of the test sample." This adds no definite structure. Nor does the system claim 52 element [3] of "an interrogation device designed to measure a viscoelastic property of the test sample" call for any definite structure.

Claim 26 is distinguished for its limitation requiring use of "abciximab /cytochalasin D":

> [1.3.2] wherein the first reagent or combination of reagents activates the test sample via an intrinsic pathway of coagulation, an extrinsic pathway of coagulation, or a combination thereof, wherein the second reagent or combination of reagents activates the test sample via an intrinsic pathway of coagulation, an extrinsic pathway of coagulation, or a combination thereof [*id*. 22:16-23], [1.3.3] wherein at least one of the first reagent or combination of reagents and the second reagent or combination of reagents activates the test sample via the extrinsic pathway of coagulation [*id*. 22:24-27], [1.3.4] wherein the second reagent or combination of reagents further includes one or both of abciximab and cytochalasin D [*id*. 22:28-30 (emphasis added)],

In contrast with the other claims, claim 26 recites limitations [1.3.3] that the reagent(s) in at least one of the first or second chambers activate coagulation via the extrinsic pathway and [1.3.4] that reagent(s) in the second chamber include abciximab and/or cytochalasin D. (LaDuca ¶¶ 59 and 66.)

Claim 26 also requires [1.1.1] that "at least a portion of the housing is thermally conductive to allow the test sample to be heated" (Ex. 1001, 22:14-15). (LaDuca ¶¶ 60 and 66.)

Claim 51 is distinguished in requiring [1.1.3] a third test chamber (Ex. 1001. 24:20-23). (LaDuca ¶¶ 57 and 67.) Like Claim 26, Claim 51 requires [1.3.2] that

the reagents in each required test chamber activate coagulation via the intrinsic and/or extrinsic pathways (Ex. 1001, 24:27-33). (LaDuca ¶¶ 59 and 67.)

Claim 51 recites [1.4.4]

> a second port, defined at least in part by the housing, in communication with a channel of the fluid pathway and from which a pressure gradient when applied from a source external to the second port draws the test sample to move from an external vessel through the inlet and the at least one channel of the fluid pathway into the housing.

(Ex. 1001, 24:61-67.) It further recites [1.4.5] that the "first and/or second port prevent the test sample from leaving the device" (Ex. 1001, 25:5-6), apparently supported by disclosure of a hydrophobic filter (222, 220, 218 and 216) to prevent the blood sample from exiting the port (106) (*id.* 5:11-18; 10:4-6). (LaDuca ¶¶ 58 and 67.) It requires [1.1.1] that "at least a portion of the housing is designed to be thermally conductive to allow the test sample to reach about 37° C in the test chamber" (*id.* 25:7-9). (LaDuca ¶¶ 57 and 67.)

Claim 52, claiming a system rather than only the cartridge, recites:

> [1.6] a consumable cartridge device configured to be positioned in an analysis system (*id.* 25:16-17)
>
> [2] a heat exchanger and a temperature control coupled thereto, designed to allow the temperature of the test sample before analysis in the test chamber (*id.* 25:49-52)

> [3] an interrogation device designed to measure a viscoelastic property of the test sample (*id.* 25:53-54)
>
> [4] a pressure control designed to apply the pressure gradient that causes the test sample to flow through the fluid pathway and into the test chambers (*id.* 25:55-57)
>
> [5] an analysis system [including] a pocket designed to receive the consumable cartridge . . . comprising an actuator system that allows the heat exchanger, the interrogation device and the pressure control to be positioned adjacent the cartridge (*id.* 25:58-64)

Claim 52's cartridge [1.6] is essentially that recited in Claim 1, including the challenged [1.2.3] interrogation design requirement of the test chambers, minus the Claim 1 statement of heating functionality [1.1.1] and [1.4.6]. (LaDuca ¶¶ 61-63 and 68.)

Claim 4 depends indirectly[5] from claim 1 (20:21), **claim 36** indirectly from claim 26 (23:30) and **claim 55** indirectly from (26:19), and each recites that a portion of a thermally conductive wall "comprises a thermally conductive polymer that has

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[5] The intervening dependent claims (claim 2, 3, 34, 35, 53 and 54) include subject duplicative of limitations 1.1.1, 1.4.6 and 1.4.7 of claims 1, 26, 51 and 52, already discussed *supra*.

a thermal conductivity that exceeds 0.123 W/m °K" (20:21-24, 23:30-33, 26:19-22). (LaDuca ¶¶ 64 and 69.)

V. 37 C.F.R. § 42.204(b)(1)-(2): IDENTIFICATION OF THE CHALLENGE

A. Statement of Requested Relief

Pursuant to 37 C.F.R. § 42.204(b), Petitioner respectfully requests post-grant review and cancellation of the Challenged Claims 1, 4, 26, 36, 51, 52 and 55 of the '039 patent under 35 U.S.C. §§ 321-328 and 37 C.F.R. §§ 42.200-42.224.

The overarching concern is that the Challenged Claims, unrestricted to any method (and structure) of "interrogat[ion] to determine a hemostatic parameter of a test sample of blood," are unenabled and indefinite and overclaim any invention disclosed in the '039 specification, Petitioner respectfully urges that these claims should not be allowed to remain as issued to be a cloud on present and future methods and structure of interrogation using a distribution of a single test sample in a cartridge device with multiple-assay test chambers. Defects in the Challenged Claims are exposed in Ground 1 (indefiniteness) and Ground 2 (written description and enablement). If the Challenged Claims survive these "formal" challenges, they should nonetheless be canceled as anticipated by and/or obvious over Gavin (Grounds 3 and 4 [in view or Warden]) and/or obvious over Schubert in view of Gavin (Grounds 5 and 6 [in further view of Warden]).

In view of the accompanying prior art references and supporting declaration of Dr. Frank LaDuca (Ex. 1002), Petitioner respectfully requests cancellation of the Challenged Claims as summarized in the following table.

Grounds	Exhibits
Ground 1: Claims 1, 4, 26, 36, 51, 52 and 55 are unpatentable under 35 U.S.C. § 112(b) for failing to particularly point out and distinctly claim the subject matter which the inventor regards as his or her invention.	1001, 1002, 1003
Ground 2: Claims 1, 4, 26, 36, 51, 52 and 55 are unpatentable under 35 U.S.C. § 112(a) because they are unsupported by the specification as to what structure was invented and enabled to the POSA.	1001, 1002, 1003

Ground 3: Claims 1 and 52 unpatentable under U.S.C. § 102 as anticipated by Gavin.	1001, 1002, 1004
Ground 4: Claim 51 unpatentable under U.S.C. § 103 as obvious over Gavin in view of Warden.	1001, 1002, 1004, 1006
Ground 5: Claims 1, 26 and 52 are unpatentable under 35 U.S.C. § 103 as obvious over Schubert in view of Gavin.	1001, 1002, 1004, 1005
Ground 6: Claim 51 is unpatentable under 35 U.S.C. § 103 as obvious over Schubert in view of Gavin and Warden.	1001, 1002, 1004, 1005, 1006
Ground 7: Claims 4 and 55 are unpatentable under 35 U.S.C. § 103 as obvious over Gavin (as in Ground	1001, 1002, 1004, 1005, 1013, 1014

3 in further consideration of the State of the Art and claims 4, 36 and 55 are unpatentable under 35 U.S.C. § 103 as obvious over Schubert in view of Gavin (as in Ground 5) in further consideration of the State of the Art	

B. Person of Ordinary Skill in the Art

The technical field of the '039 patent is "devices, systems and methods for evaluating hemostasis in a subject by analysis of a test sample from the subject to determine one or more indices of hemostasis." (Ex. 1001, 1:21-24.) The patent further states for the background of the technology that the "need is particularly acute during cardiac surgeries requiring cardiopulmonary bypass." (*Id.* at 1:36-37.) Thus the relevant field of art is centered on devices for evaluation of hemostasis for individuals near a clinical Point of Care ("POC"). (LaDuca ¶ 42.)

As explained by Dr. Frank LaDuca, an experienced developer of instruments for such hemostasis evaluation devices, including POC devices, who has managed teams for development of such instruments (LaDuca ¶ 41), the relevant POSA

> has a bachelor degree in a science discipline such as biology, chemistry, natural sciences, engineering or a biomedical engineering discipline

and at least 4 years of practical experience designing or creating devices for evaluating hemostasis.

(LaDuca ¶ 44) This POSA would have an understanding of the principles of blood coagulation and both POC and laboratory hemostasis diagnostics, including viscoelastic methods and a familiarity with a current landscape of tests and devices for evaluating hemostasis including comparative knowledge (both design and operational) of utility, features and limitations. (LaDuca ¶ 45).

C. State of the Art, Including References in this Challenge

The state of the art as of the claimed '039 priority date had included for some time various devices for hemostasis evaluation, including multi-channel (multi-assay) devices. (LaDuca ¶¶ 122, 123, 126 and 130) Interrogation of blood samples to measure properties of coagulating blood had been performed using viscoelastic methods of interrogating clot firmness since 1948 (including Thromboelastography (TEG) (Haemoscope Corp, Niles IL, USA) and thromboelastometry (TEM) (Pentapharm GmbH, Munich Germany) (sometimes also referred to as rotational thromboelastography (ROTEG), but more commonly, "TEG", and more commonly, rotational thromboelastometry (ROTEM)). (LaDuca ¶¶ 26-33.) Viscoelastic methods of interrogating clot firmness were first implemented in a cartridge-based system in Schubert, Ex. 1005. (LaDuca ¶ 88 and 91.) However, there are many other techniques of measuring viscoelastic properties (such as viscosity-based clotting

time tests for detecting fibrin formation) which also include cartridge-based implementations. (*id.* ¶¶ 22-25 and 34-36.) Thus, even before the claimed February 15, 2011 priority date of the '039 patent, there existed in the art numerous cartridge devices for multi-channel hemostasis evaluation. Many of these cartridge devices implemented different ways of controlling the temperature (*id.* ¶ 37) and flow (*id.* ¶¶ 124 and 131) of blood samples for evaluation. Following are the publications relied upon for this challenge:

1. U.S. Patent No. 5,534,226 ("Gavin") (Ex. 1004)

The following description of Gavin is supported by LaDuca ¶¶ 123-125.

U.S. Patent No. 5,534,226 ("Gavin") (Ex. 1004), issued in 1996, discloses interrogation by introduction of blood samples into multiple channels formed as elongated enclosures – chambers – in a cuvette or cartridge with different reagents in each channel, returning the results of the time to coagulation indicated by stoppage of flow in the channels. Gavin teaches a disposable cuvette (12) defining a plurality of conduits (30, 31, 32, 33, 34) where each conduit defines a region for blood coagulation analysis, *i.e.*, prothrombin time (PT) analysis. (FIG. 2; 6:2-3; 6:31-35.) Gavin teaches that a region of each of the conduits is designed to be interrogated to determine a hemostatic parameter. (6:13-22; 10:7-13; 10:60-11:3; 11:9-12.) Control channel conduits 30 and 34 include different reagent combinations than test channel conduits 31, 32 and 33. (Abstract, 6:20-30; 6:38-47; 7:22-32.)

As shown in **annotated [Gavin] Fig. 2**, below, the cuvette (12) in Gavin defines a fluid pathway which includes an inlet (supply reservoir 40, aperture 46 and opening 51) defined by the cuvette 12 through which the test sample is introduced (7:55-64; 8:5-11). Test regions for each of conduits (30, 31, 32, 33, 34) are in communication with the inlet via proximal portions of the conduits (30, 31, 32, 33, 34), common supply area (37) and supply conduit (38) whereby a portion of the test sample is distributed and delivered to the test regions. (*Id.*)

The fluid pathway in Gavin further includes a plurality of ports (drive apertures 35 in communication with terminal ends of conduits 30, 31, 32, 33, 34) where a pneumatic pressure can be applied from an external source (pneumatic source 87 via manifold assembly 60) to draw a test sample into at least one of the test chambers (into test regions for each of conduits 30, 31, 32, 33, 34) (9:10-17; 9:37-53). Gavin also teaches a configuration which prevents blood from being drawn into the manifold assembly 60 (9:12-15).

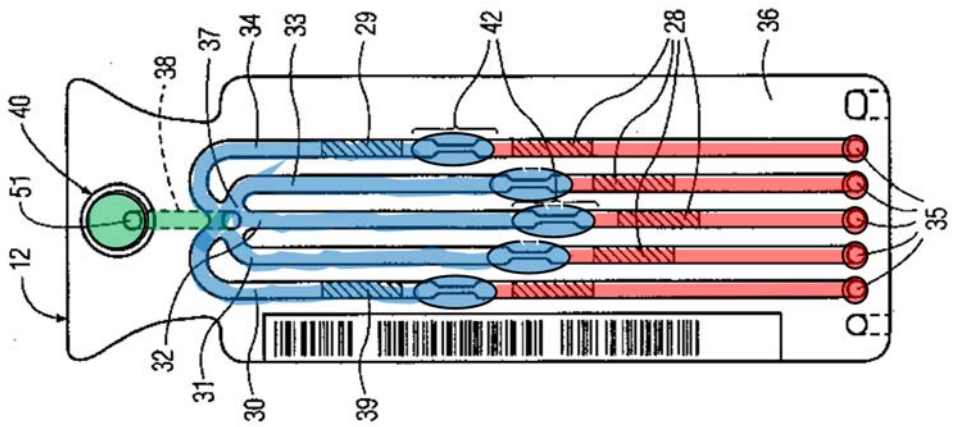
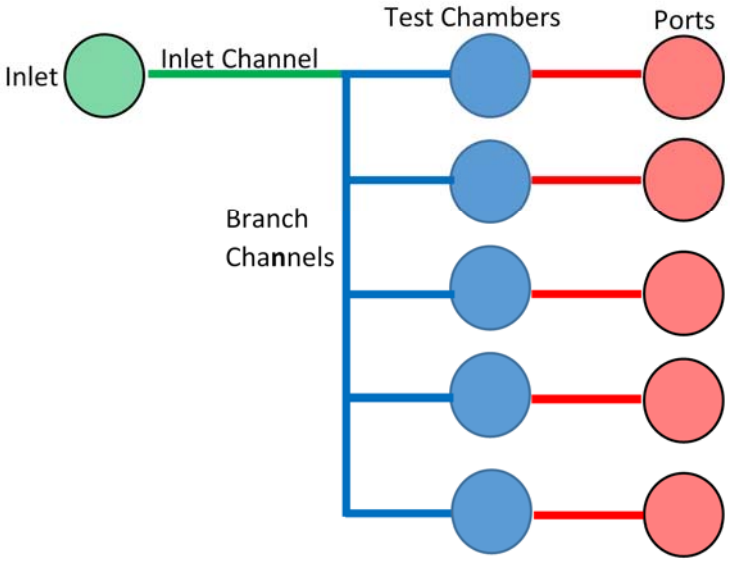


FIG. 2



The cuvette (12) is configured to be used with a testing device 14 to detect coagulation related activities including fibrin formation via photoelectric sensors 61. 10:7-13, 10:60-11:3. A cuvette (12) is placed within a channel (54) of the test device (14) via a slot (20) (FIGS. 1, 4A, 4B). A heating element (56) such as a foil heater is used to heat the cuvette (12) when it is within the channel (54) (8:24-32; 9:18-25). The test device (14) provides pneumatic pressure (pneumatic source 87 via manifold assembly 60) to the ports (drive apertures 35) to move the blood sample. The

pneumatic manifold assembly 60 rotates when the cuvette 12 is inserted into the cartridge thereby position the cuvette relative to an external pressure source (pneumatic manifold assembly 60), a heater (heating element 56) and an interrogation device (photoelectric sensors 61 and light sources 53 in testing interface unit 50) (Figs. 4a and 4b, 9:10-17; 9:37-53).

2. U.S. Pub. App. 2010/0154520 ("Schubert") (Ex. 1005)

The following description of Schubert is supported by LaDuca ¶¶ 126-129.

U.S. Pub. App. 2010/0154520 ("Schubert") (Ex. 1005), published in 2010, discloses a multi-chamber test cartridge for ROTEM type testing. (Fig. 6; ¶¶ 0029, 0081-0082.) The cartridge device (50) is used for evaluation of hemostasis (Abstract, ¶¶ 0002-0007; 0025). More particularly, the cartridge device (50) is configured to run different coagulation tests in parallel to isolate the effect of different components of the coagulation pathway. (¶¶ 0013, 0016, 0082, 0083. The cartridge device (50) includes a plurality of test chambers (¶¶ 0029; 0081-0082) where each chamber includes a different reagent or combination of reagents.

Schubert discloses a preferred four chamber embodiment where INTEM, EXTEM and FIBTEM tests are combined within one cartridge. (¶¶ 0082-0083.) These tests utilize different reagents which activate or suppress different parts of the coagulation cascade. INTEM includes a reagent for intrinsic activation (intrinsic activator), EXTEM includes a reagent for extrinsic activation (extrinsic activator)

and FIBTEM includes reagents for extrinsic activation and for suppressing thrombocyte function (extrinsic activator plus cytochalasin D) (*Id*.). The trademarked terms INTEM, EXTEM and FIBTEM are technical terms of art known at the time of the Schubert as determined by the panel in IPR2017-00852 and -00855 ('852 FWD [Ex. 1011] at 18-23, '971 FWD [Ex. 1012] at 12-16]). EXTEM includes an extrinsic activator (Tissue Factor), INTEM includes a contact activator (ellagic acid plus phospholipid) and FIBTEM combines extrinsic activation (using Tissue Factor) and cytochalasin D (an inhibitor of actin polymerization which neutralizes platelet contribution to the viscoelastic response, i.e., clot firmness). This is supported by literature contemporaneous with Schubert. (LaDuca, footnote 5.)

As shown in **annotated [Schubert] Fig. 6**, below, the cartridge device 50 includes a fluid pathway where branch channels (ducts 13, 14 and 15 and ducts 13' 14' and 15', respectively) connect respective measurement cavities 20 and 20' to a single inlet channel (receiving cavity 16) which in turn is in communication with an inlet (cavity cover 33a). (Ex. 1005, ¶¶ 0047-0048). While Fig. 6 shows an embodiment with two arrangements of FIG. 4 or 5, ¶¶ 0081-0082 of Schubert teaches that "[i]n a preferred embodiment the cartridge device 50 comprises four arrangements of FIG. 4 or 5 having 4 measurement cavities" where "measurements can be done with different reagents on the same liquid sample." A measurement cavity (20, 20') may be integrally formed with a reagent cavity (19, 19') (¶ 0040).

Schubert teaches an internal pump (18, 18') for moving the liquid sample 1 through the cartridge device 50. (Figs. 4-6, ¶¶ 0039; 0041; 0088.)

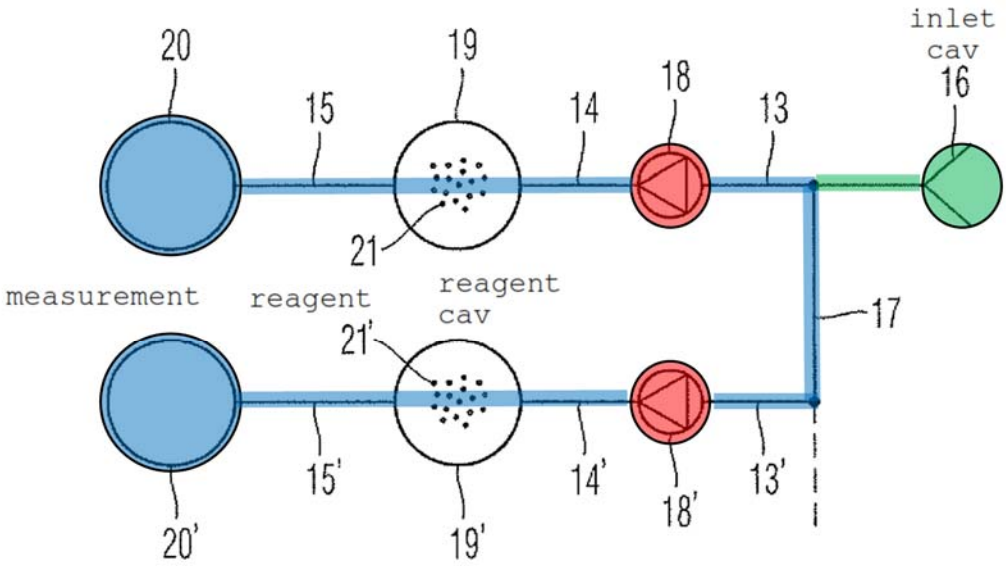
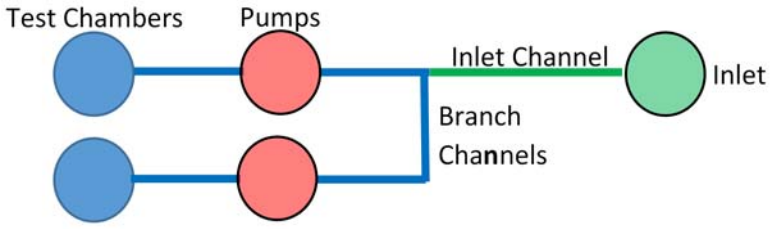


Fig. 6



Schubert further teaches interrogating (¶¶ 0029; 0031; 0011; 0083; 0088) each test chamber to measure changes in the viscoelastic property of the test sample (¶¶ 0006; 0009). Thus, Schubert teaches that cartridge device 50 can be used with a measuring system to measure a viscoelastic property of the test sample (¶¶ 0002, 0013-0018, 0025-0028 and 0098).

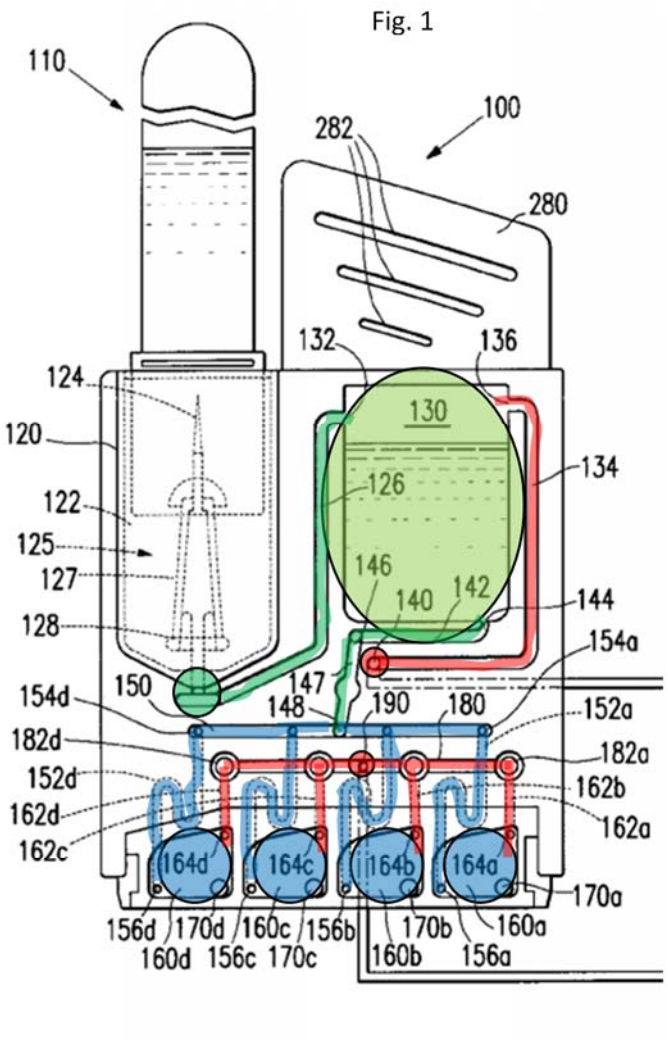
3. U.S. Patent No. 6,016,712 ("Warden") (Ex. 1006)

The following description of Warden is supported by LaDuca ¶¶ 130-133.

U.S. Patent No. 6,016,712 ("Warden") (Ex. 1006) discloses a multi-chamber coagulation testing cartridge for distributing and heating blood samples in different channels. The cartridge includes a plurality of test chambers (second chambers 160a-160d) (Ex. 1006, Fig. 1; 9:55-58; 11:8-9; 11:18-19; 11: 41-44; 11:57-59). Example assays which can be run using the cartridge include coagulation assays (16:61-67).

As depicted in **annotated [Warden] Fig. 1**, below, the cartridge includes a fluid path for distributing a sample from an inlet to the plurality of test chambers (Fig. 1; 14:49-15:2. An inlet (150) and inlet channel are in communication with a plurality of branch channels (152a-d), each of which flows into a respective test chamber 160a-d). An external pressure is applied via a port (140) along the flow path (downstream of the inlet but upstream of the test chambers). A negative pressure is applied to draw a sample into a loading chamber (130) followed by a positive pressure to move the sample into the test chambers (160a-d).

Fig. 1


110
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147
154d
148
190
180
152a
182d
182a
152d
162b
162d
162a
162c
164d
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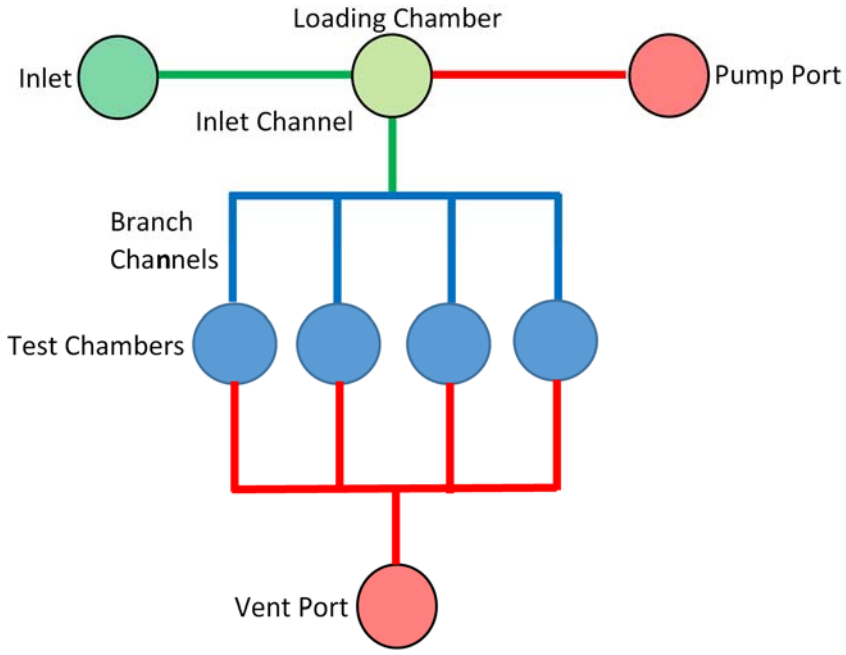
156a


Loading Chamber
Inlet
Pump Port
Inlet Channel
Branch
Channels
Test Chambers
Vent Port

Warden teaches that each of test chambers (160a-d) is in fluid communication with an exit port 190 via a manifold (vent plugs 182a-d and vent port 190). The vent plugs are configured to allow air to pass through while preventing the sample from reaching port 190. 7:6-10, 14:67-15:2, 13:31-49).

The cartridge in Warden is configured for insertion into a testing apparatus which provides, e.g., "for connection to a pressure varying apparatus and/or to read the results of an assay." (14:39-45).

VI. 37 C.F.R. § 42.204(b)(3): CLAIM CONSTRUCTION

Under 37 C.F.R. § 42.200(b), claims in a post grant review proceeding are construed using the same claim construction standard that is used to construe claims in a civil action. This includes "construing the claim in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent," *id*., consistent with *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005).

The terms of the Challenged Claims generally do not require construction and should be afforded their ordinary and customary, or "plain" meaning. Central limitations of the Challenged Claims, calling for "designed to be interrogated to determine a hemostatic parameter" [1.2.3] and can be used / is configured for use with an interrogation device to measure at least one viscoelastic property of the test sample [1.5] do not recite structure but only desired function. (LaDuca ¶¶ 73 and

77.) Although *Ex parte Rodriguez*, Appeal No. 2008-000693, op. at 20-23 (BPAI Oct. 1, 2009), construed certain "configured to" terms to require 35 U.S.C. § 112, para. 6 limitation to structure disclosed in the patent specification, as shown in Section VI(D),[6] the Challenged Claims have dependent claims that are limited to the particular structure for acoustic interrogation disclosed in the '039 patent specification. Under *LizardTech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1344 (Fed. Cir. 2005), the facially (and by virtue of claim differentiation) broader Challenged Claims should be stricken from offending the fundamental patent policy against abstract, innovation-preemptive, functional claiming based on limited disclosure long disallowed from *O'Reilly v. Morse,* 56 U.S. (15 How.) 62, 14 L. Ed. 601 (1853), as explained at *Ariad Pharmaceuticals, Inc. v. Eli Lilly and Co.*, 598 F.3d 1336, 1359 (Fed. Cir. 2010).

A. "test chamber" (claims 1, 26, 51, and 52)

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[6] The Office's recent request for comments on its proposed guidance for "Examining Computer-Implemented Functional Claim Limitations for Compliance with 35 U.S.C. 112," 84 Fed. Reg. 57 (Jan. 7, 2019) sets forth controlling law for consideration here including the application of *LizardTech*, 84 Fed. Reg. at 61 ("failure to demonstrate that the applicant possessed the full scope of the invention [or] to enable the full breadth of that claim").

No construction is necessary. The term's plain meaning to a POSA (or anyone else) standing alone or in the context of the Challenged Claims or the '039 specification is that it is a space for testing which is not necessarily fully, physically defined or enclosed. (LaDuca ¶ 71.) The '039 patent specification discloses a test chamber defined by walls, open to receive a quantity of a test sample (*i.e.*, blood), and open for venting and application of a pressure gradient (Ex. 1001, 4:56-5:3), and the claims recite this general distribution structure.[7] The claims require only that a "test chamber" be suitable for the purpose of running a test on blood. This use of the term "chamber" in the specification and claims is consistent with its dictionary definition:

> "a room or space used for a particular purpose"

American English definition of "chamber," Cambridge Academic Content Dictionary, https://dictionary.cambridge.org/us/dictionary/english/chamber.

[7] The '039 patent's use of the terms "channel" and "chamber" contrasts function rather than structure: a "channel" would be understood as a space for transport while a "test chamber" would be understood as a space for testing.

B. Interrogate, Interrogation (claims 1, 26, 51 and 52)

No construction is necessary. The plain meaning is to illicit a response to an inquiry, as corroborated in the dictionary meaning:

> 1 **:** to question formally and systematically
>
> 2 **:** to give or send out a signal to (a device, such as a transponder) for triggering an appropriate response

Merriam-Webster Online definition of "interrogate," https://www.merriam-webster.com/dictionary/interrogate.

C. "hemostatic parameter" (claims 1, 26, 51 and 52)

No construction is necessary. (LaDuca ¶ 72.) This is consistent with the panel reasoning in IPR2017-00852 and -00855 ('852 FWD [Ex. 1011] at 7-10, '971 FWD [Ex. 1012] at 9]). The plain meaning is a value characterizing some part of the hemostatic process, as consistent with the ordinary meaning of the term "parameter" exemplified in the dictionary definition:

> 2 : any of a set of physical properties whose values determine the characteristics or behavior of something - parameters of the atmosphere such as temperature, pressure, and density

Merriam-Webster Online definition of "parameter" at https://www.merriam-webster.com/dictionary/parameter. This is consistent with the non-exhaustive examples of hemostatic parameters in the '039 patent (Ex. 1001, Table 1; see also claim 18 of the '971 patent) and its statement that "in vitro diagnostics (IVD) are critically needed to quantify hemostatic dysfunction" (Ex. 1001, 1:34-35).

D. "[test chambers] designed to be interrogated to determine a hemostatic parameter of a blood sample received therein" (claims 1, 26, 51 and 52)

No construction is necessary – or allowed under *LizardTech*. This claim term (claim 1, 19:34-36; claim 26, 21:50-52; claim 51, 24:24-26; claim 52, 25:24-26) and limitation [1.2.3] does not recite structure,[8] but only subjectively intended function of "test chambers" to be interrogated. (LaDuca ¶ 73.) Although *Ex parte Rodriguez*, might otherwise be applied to limit the claims to the structure disclosed in the specification, that structure is already claimed in claims 15, 47 and 72, and under *LizardTech*, claims 1, 26, 51 and 52 should not be construed to cover the same subject matter.

Claims 14, 46 and 71, dependent from claims 1, 26 and 52, respectively, specify that at least one of the test chambers be "designed to be interrogated by acoustic pulses" (20:59; 23:67; 27:28). Being limited in this aspect only functionally, they too might be subject under *Ex parte Rodriguez* to 35 U.S.C. § 112(f) construction limiting them to the disclosed chamber structure, but they are also barred from such construction under *LizardTech*.

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[8] "[A]pparatus claims cover what a device is, not what a device does." *Hewlett-Packard Co. v. Bausch & Lomb Inc.*, 909 F.2d 1464, 1468 (Fed. Cir. 1990).

Claims 15, 47 and 72, indirectly dependent from claims 14, 46 and 71, respectively, specify the structure of a "sound focusing assembly" (20:61-65; 24:2-6; 28:2-6), which is the only structural limitation of the test chambers disclosed in the '039 patent specification. Reading this structure into independent Challenged Claims 1, 26, and 52 violates the doctrine of claim differentiation and would create a redundancy barred by the Federal Circuit in *LizardTech,* 424 F.3d at 1344. Allowing the Challenged Claims to survive by reading in limitations is deceptive to the public and innovators in the field, especially at this early part of the life of the patent subject to the post-grant review. Thus, the unlimited plain meaning of claims 1, 26, and 52 is that they claim a test chamber designed hold blood samples to be interrogated for hemostatic parameters, by any interrogation technique, past, present or future.

E. "thermally conductive" (claims 1, 26 and 51)

The plain meaning should apply: "able to conduct heat." (LaDuca ¶ 74)

F. "the outer surface of the thermally conductive wall is shaped to be held . . . in close proximity to a heater to allow adjustment of the temperature of the test sample flowing the portion at least partially defined by the inner surface of the thermally conductive wall" (claim 1)

The plain meaning of this language from claim 1 (20:3-9) should apply. (LaDuca ¶ 76.)

G. "at least one viscoelastic property" (claims 1, 26, 51 and 52)

No construction is necessary. This is consistent with the panel reasoning in IPR2017-00852 and -00855 ('852 FWD [Ex. 1011] at 18, '971 FWD [Ex. 1012] at 9]). Consistent with the specification, the plain meaning of "viscoelastic properties" are properties of a material that exhibits both elastic and viscous characteristics. Thus both viscosity and elasticity can be considered viscoelastic properties. (LaDuca ¶¶ 24 and 25.) Any interrogation device that is responsive to the coagulation process ("to determine a hemostatic parameter") can be said to be interrogating a viscoelastic property. Coagulating blood is a viscoelastic material having both fluid and solid components and coagulation including fibrin formation results in a change in the viscoelastic properties of the sample. (Ex. 1001, 16:16-26.) As blood coagulates and shifts from a predominately fluid state to a predominately solid state, its relative expression of viscous and elastic properties changes. Interrogation of a viscoelastic property does not have to include returning a specific parameter for a specific property or combination of properties (i.e. stiffness) but rather can be as simple as generally detecting a clotting process which is by definition indicative of a change in viscoelastic properties.

H. "the device [can be used/is configured for use] with an interrogation device to measure at least one viscoelastic property of the test sample" (claims 1 and 26/claim 51)

No construction is necessary – or allowed under *LizardTech*. As in Section VI(D) for the test chambers, this claim term (claim 1, 20:10-12 and claim 26, 22:31-33 ["can be used"]; claim 51, 25:11-13 ["is configured for use"]) recites an intended function of "the [entire] device" without specifying structure to achieve that function other than the very function of its use with an unspecified interrogation device. (LaDuca ¶ 77.) For the same reasons set forth in Section VI(D), because the only structure disclosed to achieve the function is claimed in claims 15, and 47 and 72, this limitation in claims 1, 26 and 51 may not be so limited, and applies broadly to interrogation for hemostatic parameters (associated in Section V(G) with "viscoelastic properties"), by any interrogation technique, past, present or future.

I. "first port" and "second port" (Claim 51)

No construction is necessary. The plain meaning of these claim terms (claim 51, 24:46-47; 24:61) as well the subsequent limitation reciting that the "first port and/or the second port prevents the test sample from leaving the device," is that the first and second ports are distinct claim elements. (LaDuca ¶ 78.)

J. "heat exchanger" (Claim 52)

Plain meaning should apply: something that exchanges heat. (LaDuca ¶ 79.)

K. "pressure control" (Claim 52)

Plain meaning should apply: a control for applying pressure, in the claim, the pressure gradient (25:44-45). (LaDuca ¶ 80.)

L. "actuator" (Claim 52)

This "nonce" word should be given plain meaning in the context of claim 52 with its required function "that allows the heat exchanger, the interrogation device, and the pressure control to be positioned adjacent to the consumable cartridge" (25:61-64). (LaDuca ¶ 81.)

* * * * * * *

Grounds for Review Under 37 C.F.R. § 42.204(b)(4)-(5)

VII. GROUND 1: IT IS MORE LIKELY THAN NOT THAT CLAIMS 1, 4, 26, 36 51, 52 and 55 OF THE '039 PATENT ARE UNPATENTABLE AS INDEFINITE UNDER 35 U.S.C. § 112(b).

Claims 1, 26, 51 and 52 are invalid for indefiniteness under 35. U.S.C. 112(b) (formerly para. 2), because they recite limitations that, under *Nautilus, Inc. v. Biosig Instruments*, 134 S. Ct. 2120 (2014), considering the claims as a whole and as informed by the extrinsic record, fail to inform a POSA with reasonable certainty about the scope of the claimed invention. A patent must be "precise enough to afford clear notice of what is claimed, thereby 'appris[ing] the public of what is still open to them.'" *Id.* at 2129. "Otherwise there would be a zone of uncertainty which

enterprise and experimentation may enter only at the risk of infringement claims." *Id.*

Here, Patent Owner has impermissibly expanded beyond its purported contribution of an acoustically-interrogated multiple-assay cartridge (*e.g.*, Ex. 1001, 2:35-37, 2:43-44. 2:51-54, 3:3-6; Ex. 1003 at 502), by introducing uncertainty as to what structure is claimed in its cartridge claims 1, 26 and 51 and its "system" claim 52 – all apparatus claims. (LaDuca ¶ 85.) These claims recite test chamber and overall device elements as merely "designed" for or "can be used with" or "configured for use with" unspecified methods of interrogation to return "hemostatic parameters" or "viscoelastic properties". But the '039 patent apparatus claims must recite structure, not merely functionality, *e.g., Hewlett-Packard Co. v. Bausch & Lomb Inc.,* 909 F.2d 1464, 1469 (Fed. Cir. 1990), and the only structure disclosed is for the disclosed acoustic interrogation. To allow Patent Owner's claim to function "tied" to an unspecified interrogation structure that otherwise might be part of future innovation with the policies underlying 35 U.S.C. § 112, including paragraph 6 (subsection (g)) jurisprudence, and the Supreme Court's continuing concerns about patent preemption of technical fields by claims to abstractions. As explained in the second paragraph of Section VI and at Section VI(D), limitation by construction to the disclosed structure for a particular kind of acoustic interrogation would leave in place the deceptively broad Challenged Claims as written. Post-grant review under

35 U.S.C. §§ 321-328 was provided by Congress to allow relatively early review of such formal issues as indefiniteness and failure to provide a supporting and enabling written description.

In addition there are multiple claim limitations in the Challenged Claims that are both vague and inconsistent with the specification (LaDuca ¶¶ 86-90) as further explained below.

A. Claims 1, 26, 51 and 52 Are Indefinite Under 35 U.S.C. § 112(b) for Failing to Provide Certainty of the Scope of the Invention in Cartridge Structure for Non-Acoustic Interrogation.

As explained in Section VI(D) on its construction, the claim limitation [1.2.3], "[test chambers] designed to be interrogated to determine a hemostatic parameter of a blood sample received therein" (claim 1, 19:34-36; claim 26, 21:50-52; claim 51, 24:24-26; claim 52, 25:24-26) and remainder of the claims specify no structure to achieve the recited function. Similarly, as explained in Section VI(H), the claim limitation [1.5], "the device [can be used/is configured for use] with an interrogation device to measure at least one viscoelastic property of the test sample" (claim 1, 20:10-12 and claim 26, 22:31-33 ["can be used"]; claim 51, 25:11-13 ["is configured for use"]) and the remainder of the term specify no structure to achieve the recited function.

The '039 patent does not provide any objective criteria for structurally differentiating between a chamber that is designed to be interrogated to determine a

hemostatic parameter and a chamber that does not meet this limitation or a device that can be used with an interrogation device to measure at least one viscoelastic property and a device that does not meet this limitation. The only disclosed structural characteristics of the test chambers or the claimed cartridge device generally which relate to interrogation to determine a hemostatic parameter or viscoelastic property are specific to acoustic interrogation, *e.g.,* sound focusing assemblies and the chambers being held in an orientation such that ultrasound can be focused into each testing chamber (11:52-13:55). (LaDuca ¶¶ 73, 77 and 85.) However, since these limitations are included in dependent claims 15, 47, and 72), claim differentiation and specifically *LizardTech* preclude such limitations from being read into the independent claims 1, 26, 51 and 52. Because the '039 patent fails to provide any guidance for the structural design of a chamber/device for any means of interrogation other than the disclosed acoustic method, the '039 patent fails to inform a POSA with reasonable certainty about the scope of the invention of claims 1, 26, 51 and 52, which are thus indefinite under 35 U.S.C. § 112(b).

B. Claims 1, 26 and 51 Are Indefinite Under 35 U.S.C. § 112(b) for Failing to Provide Certainty of the Scope of the Invention in Structure and Material to Heat the Samples.

Each of claims 1, 26 and 51 recite a portion of the housing being thermally conductive. (claim 1, 19:64; claim 26, 22:14-15; claim 51, 25:8-10.) Applying the

plain meaning and considering the claims as a whole as informed by the extrinsic record, this limitation is indefinite.

The "thermally conductive" limitation in the [1.1.1] limitation by itself does not specify structure: it is a property of conducting heat, which exists to some degree for all matter, e.g., such as plastics which comprise test cartridges. Although the '039 patent specification uses the term "thermally conductive" to indicate a classification (i.e. in classifying a polymer as a "thermally conductive polymer"), it fails to provide objective criteria for differentiating a thermally conductive element (*e.g.*, a thermally conductive wall or other portion of the housing) from a non-thermally conductive element. (LaDuca ¶¶ 86.)

The [1.1.1] limitation in claim 1 that "the housing includes a thermally conductive wall to allow the test sample to be heated" (19:64-65) does not limit the housing to any particular design or construction (other than having a wall), because all matter allows heat to be conducted at various rates and a heat source (which is not an element of this claim to a free-standing cartridge) providing an appropriate temperature gradient, would eventually reach the other side of the "thermally conductive wall" and enable heating of a test sample. (LaDuca ¶ 74.) Claim differentiation from claim 4 keeps the range of coverage in claim 1 to all materials of greater than zero conductivity. The [1.1.1] limitation in claim 26 that "at least a

portion of the housing is thermally conductive to allow the test sample to be heated" (22:14-15) suffers from the same indefiniteness.

The [1.4.7] limitation in claim 51 that "at least a portion of the housing is designed to be thermally conductive to allow the test sample to reach about 37° C. in the test chambers" (25:7-8) raises a question of what alternative design there might be to the wall being made of thermally conductive material. The '039 patent fails to provide any objective criteria for structurally differentiating between an element (*e.g.*, wall or portion of the housing) that allows the test sample to be heated or allow the test sample to reach about 37° C in the test chambers and an element that does not meet this limitation.

The claim [1.4.6] limitation in claim 1 that "the outer surface of the thermally conductive wall is shaped to be held . . . in close proximity to a heater to allow adjustment of the temperature of the test sample flowing the portion at least partially defined by the inner surface of the thermally conductive wall" (20:3-9) raises additional questions for determining the scope of the invention under claim 1. The term "close proximity" is impermissibly subjective[9] without any objective criteria provided by the '039 patent. (LaDuca ¶¶ 76 and 87.)

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[9]In *Abdou v. Alphatec Spine, Inc.*, No. 12-cv-1804 BEN (RBB), 2014 BL 328486, at 8-10 (S.D. Cal. Nov. 19, 2014), the court held the term of degree ''in proximity"

VIII. GROUND 2: IT IS MORE LIKELY THAN NOT THAT CLAIMS 1, 4, 26, 36, 51, 52 and 55 OF THE '039 PATENT ARE UNPATENTABLE AS UNSUPPORTED AND UNENABLED UNDER 35 U.S.C. § 112(a).

A. Claims 1, 4, 26, 36, 51, 52 and 55 Are Not Supported or Enabled Under 35 U.S.C. § 112(a) Because of the Lack of Disclosure of Any Structure for Interrogation Other than Echo-Acoustic.

Patent Owner's claims mix-and-match features which are not defined by structure but rather by the function of being interrogated by an arbitrary, unspecified interrogation device/method. This extension of the underlying disclosure (which is limited to a multi-assay cartridge specifically designed for acoustic interrogation) is impermissible.

A claim of a broad superset of wave transformation techniques was found unsupported by disclosure only of a particular technique and invalid under 35 U.S.C. § 112, para. 1, in *LizardTech*. The court specifically refused to read in the only disclosure because of duplication of claim scope. 424 F.3d at 1344.

LizardTech explained the requirements (*id*. at 1344-45):

> The "written description" clause of section 112 has been construed to mandate that the specification satisfy two closely related requirements.

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was indefinite since the relationship lacked any quantitative parameters or a range of distance.

> First, it must describe the manner and process of making and using the invention so as to enable a person of skill in the art to make and use the full scope of the invention without undue experimentation. . . . Second, it must describe the invention sufficiently to convey to a person of skill in the art that the patentee had possession of the claimed invention at the time of the application, i.e., that the patentee invented what is claimed. *See O'Reilly v. Morse*, 56 U.S. (15 How.) 62, 112–13, 14 L.Ed. 601 (1853) (denying a claim for use of "electro-magnetism, however developed for marking or printing intelligible characters ... at any distances" because others "may discover a mode of writing or printing at a distance ... without using any part of the process or combination set forth in the plaintiff's specification"); . . ..
>
> Those two requirements usually rise and fall together. That is, a recitation of how to make and use the invention across the full breadth of the claim is ordinarily sufficient to demonstrate that the inventor possesses the full scope of the invention, and vice versa. . . .

Both requirements are failed for the Challenged Claims.

For the first requirement, *In re Gosteli*, 872 F.2d 1008, 1012, (Fed. Cir. 1989), posed the question "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed"?

The clear answer is that '039 patent fails to disclosure of structural design of a chamber/device for any means of interrogation other than a sonar-like form of acoustic interrogation. (LaDuca ¶¶ 33, 53, 73, 85 and 93.) As reviewed at Section IV(A), the depicted and described embodiments, the cartridge device (100) and test

chambers (110, 112, 114, 116) are specifically designed for a particular type of acoustic interrogation (Ex. 1001, 2:35-37, 2:43-45, 2:51-54, 3:3-6, 12:13-16, 15:50-53; Ex. 1003 at 502). The '039 patent specification discloses for each test chamber in a sound-focusing assembly (also referred to as a lens assembly or lens) that provides for dry ultrasonic coupling (Ex. 1001, test chamber cap (132) and lens (134) in FIGS. 1D and 1F; 11:52-12:16). That is all. There is no invitation to adapt the cartridge features to any other form of interrogation.

The standard for determining whether the specification meets the second, enablement requirement is one where a patent is enabled if a POSA can make and use the invention without "undue experimentation" as set forth by the Supreme Court in *Minerals Separation Ltd. v. Hyde*, 242 U.S. 261, 270 (1916). *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988) set forth the factors that may be considered:

> . . . (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. . . .

Without specifying a particular interrogation technique, it is unknown what quantity of experimentation is necessary under factor (1). Dr. LaDuca, with extensive experience in developing POC hemostasis assay devices, testifies that:

93. The structure of the cartridge and test chambers disclosed in the specification – namely the inclusion of focusing assemblies and the coupling of acoustic transducers for focusing acoustic waves and receiving a response (like sonar) – is specialized for the type of acoustic interrogation described in the '039 patent. The specification does not suggest any adaptation or modification of the disclosed embodiments for any other interrogation technique. . . .

94. In view of the level of skill of the POSA, the breadth of the claims is so great as to require experimentation beyond routine experimentation for any given interrogation methods such that a POSA may consider the predictability of achieving reproducible test results when applied. Alternative methods of interrogation, may be unlimited in the imagination and limited only by the practicalities of available technology which can continue to evolve and change over the course of the lifetime of a patent. There are many other types of interrogation and interrogation devices implemented in the art for determining a hemostatic parameter and determining a viscoelastic property of a sample. By nature of the specific technical requirements for any interrogation method, virtually all of these techniques and devices require a different cartridge and/or test chamber structure than that disclosed in the '039 patent.

95. Such types of interrogation and interrogation devices may include, for example, other viscoelastic methods and devices for measuring clot firmness, such as the long-established TEG and TEM methods of interrogation by relative rotational oscillation of a cup and pin (first adapted for a cartridge structure in (Schubert (Ex. 1005)). Other

possible types of interrogation and interrogation devices which meet the claims include traditional clotting time measurement techniques and devices, such as for viscosity based interrogation. Gavin (Ex. 1004), uses an optical sensor to locate the position and rate of movement of a blood specimen in a test chamber which requires that it have an optically transparent enclosure (and its test chambers are relatively narrow with specified restricted areas 42 (Ex. 1004 6:17-19; 10:23-25) to form part of the interrogation), Warden (Ex. 1006) uses an optical transmission and light scattering system to identify the size and nature of clumping blood components, again which requires optical transparency of the chamber enclosure in the presence of an opaque blood sample.

96. . . . some technical features of interrogation of a disposable unit may be straightforward. However, once an interrogation method is selected, the design or adaptation of the cartridge and test chambers is specific for the interrogation method and requires development and experimentation beyond routine experimentation. In my experience, the design of a cartridge device and test chambers for a new interrogation technique requires multiple iterations, prototypes and refinements. Moreover, the design is likely to vary greatly depending on the type of interrogation applied and subjective choice.

97. At times, this means that the design of a cartridge device and test chambers for a particular interrogation technique may require experimentation and creativity beyond a POSAs abilities . . . evidenced, for example, by the complexities Patent Owner encountered in configuring the cartridge device and test chambers in the '039 Patent

> for acoustic interrogation . . . [and] by the complexities described in Schubert with respect to adapting a cartridge for viscoelastic methods of interrogating clot firmness . . . (Ex. 1005, 4:38-50).

The ’039 patent provided no guidance under *Wands* factor (2) or working examples under factor (3). The breadth of the claim under factor (8) – adaptation of a cartridge to all present and future methods of interrogating hemostatic parameter – offends patent policy established since at least *O'Reilly v. Morse*.

Challenged Claims 1, 26, 51 and 52 fail under both subsections (a) and (b) (formerly paragraphs 1 and 2) of 35 U.S.C. § 112.

B. Claims 4, 36 and 55 Are Not Supported or Enabled Under 35 U.S.C. § 112(a) Because Their Limitation of a Threshold Thermal Conductivity Fails To Provide Guidance to a POSA.

Claims 4, 36 and 55 are, on their faces, unsupported and unenabled because their requirement of “a thermally conductive polymer that has a thermal conductivity that exceeds 0.123 W/m °K” states a threshold nowhere stated in the ‘039 patent specification. These claims are unsupported by the specification and should never have been entered. See, *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244, (Fed. Cir. 2003) (when a range is claimed, there must be reasonable enablement of the scope of the range). Furthermore, similar to in *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320 (Fed. Cir. 2000), the ‘039 patent specification does not clearly disclose to a POSA that the inventors considered the claimed range to be part of their invention.

Dr. LaDuca testified:

> 92. . . . there is no mention of such a measure in the '039 patent specification, much less any disclosure of a specific value or range of thermal conductivity. Any given plastic, including those disclosed in the '039 patent specification, exhibits a wide variability of thermal conductivity in final form based on the injection molding or extrusion thereof. (Hansen D., Bernier G; Thermal conductivity of polyethylene: The effects of crystal size, density and orientation on thermal conductivity. Polymer Engineering and Science, 1972).

Thus, Challenged Claims 4, 36, and 55 fail under both subsections (a) and (b) (formerly paragraphs 1 and 2) of 35 U.S.C. § 112.

C. Claims 1, 4, 36 and 55 are not Supported or Enabled Under 35 U.S.C. § 112(a) Because of Inconsistencies with the Specification.

As Dr. LaDuca testifies (LaDuca ¶ 98), there are claim elements in the challenged claims that a POSA would recognize are inconsistent with the disclosure. With specific reference to limitation 1.4.6 relating to a wall of the housing being "shaped to be held in conforming contact with or in close proximity to a heater," nowhere, is "conforming contact" or wall "shape" mentioned in the specification of the '039 patent ("shape" is mentioned in the specification only with respect to the acoustic reflector and lens of the disclosed embodiment (Ex. 1001, 12:46-47; 12:59; 17:23-24)). (LaDuca ¶ 76.) Furthermore, "close proximity" is used only in the context of a heating block – which is a distinct element from the heater - and the

‘039 patent specification does not clarify what would constitute “close proximity.” ***Id.*** Thus, the specification fails to demonstrate possession of an invention where a wall of the housing is “shaped to be held in conforming contact with or in close proximity to a heater,” nor is such enabled.

IX. GROUND 3: IT IS MORE LIKELY THAN NOT THAT CLAIMS 1 AND 52 OF THE ‘039 PATENT ARE UNPATENTABLE AS ANTICIPATED BY GAVIN UNDER 35 U.S.C. § 102.

A. Claim 1 of the ‘039 Patent is Unpatentable as Anticipated by Gavin Under 35 U.S.C. § 102.

Claim 1 (basic cartridge) is invalid as anticipated by Gavin (Ex. 1004), disclosing a multi-chamber hemostatic assay (Section V(C)(1)) with each of limitations 1, 1.1, 1.1.1, 1.2, 1.2.1, 1.2.3, 1.3, 1.3.1, 1.4, 1.4.1, 1.4.2, 1.4.3, 1.4.6 and 1.5 in Table A.

1. Limitations 1 and 1.1: [Cartridge] Device Including a Housing:

Gavin teaches a disposable cuvette 12 that is a cartridge device for use with test device 14. A POSA would understand that a housing is disclosed by the plain and ordinary meaning of term “cuvette.” A POSA would understand that housing is depicted in Gavin, Fig. 2 and taught at 5:66-6:2 (“a substantially planar structure made from a transparent material”). (LaDuca ¶ 135.)

2. Limitation 1.1.1: Thermally Conductive Portion of the Housing:

A POSA would understand that all materials (i.e., plastic materials which constitute the disposable housing) have some degree of thermal conductivity. Thus, the walls of the cuvette 12 necessarily have some degree of thermal conductivity. Furthermore, Gavin explicitly teaches the cuvette 12 allowing the test sample to be heated. In particular, Gavin teaches a heater (heating element 56), where an outer surface (bottom surface) of the cuvette 12 is held in relation therewith to allow for heating of the sample (Ex. 1004, Figs 4a and 4b and 8:24-32, 9:18-25). Thus, a POSA would understand that the walls of the cuvette 12 are thermally conductive so as to allow the test sample to be heated. (LaDuca ¶ 136.)

3. Limitations 1.2 and 1.2.1: Plurality of Chambers, Including First and Second Chambers:

Gavin teaches a plurality of conduits (conduits 30, 31, 32, 33, 34) where each conduit defines a space (*i.e.,* chamber) for blood coagulation analysis, *i.e.*, prothrombin time (PT) analysis (Ex. 1004, Fig. 2 and 6:2-3, 6:31-35). The conduits (conduits 30, 31, 32, 33, 34) in Gavin are defined by the cuvette 12 housing. (LaDuca ¶ 137.)

4. Limitation 1.2.3: Chambers Designed to Be Interrogated:

A POSA would understand that each of the conduits is designed to be interrogated to determine a hemostatic parameter (Ex. 1004, 6:13-19, 6:20-22).

Gavin 10:7-13 teaches that "the pneumatic source cycles back and forth causing the blood sample in each of the conduits 30, 31, 32, 33, 34 to reciprocally flow pass the restricted region 42. As the blood sample in each of the conduits 30, 31, 32, 33, 34 begins to coagulate, fibrin forms and occludes the restricted regions 42 within the conduits 30, 31, 32, 33, 34. The occlusions eventually stop or substantially slow the flow of blood." (10:60-11:3.) The interrogation of the sample in the conduits is used to determine coagulation time (Ex. 1004, 11:9-12) which is a hemostatic parameter. (LaDuca ¶ 138.)

5. Limitations 1.3 and 1.3.1: Different Reagents in First and Second Chambers:

Gavin further teaches that control channel conduits 30 and 34 include different reagent combinations than test channel conduits 31, 32 and 33 (Ex. 1004, 6:38-47, 7:22-32). The Abstract teaches that each of the conduits contains a dried or lyophilized activation reagent and in at least one of the conduits a normalizing control agent is present which counteracts any effects of anticoagulants present in the blood sample, thereby allowing the blood sample to have generally normal coagulation characteristics. (LaDuca ¶ 139.)

6. Limitations 1.4, 1.41 and 1.42: Fluid Pathway Including an Inlet into an [Inlet] Channel into [Branch] Channels and into the First and Second Chambers:

The cuvette 12 in Gavin defines a plurality of conduits and channels forming a fluid pathway. The fluid pathway in Gavin includes an inlet (supply reservoir 40, aperture 46 and opening 51) defined by the cuvette 12 through which the test sample is introduced (Ex. 1004, Fig. 2 and 7:55-64 and 8:5-11). Each of the conduits (30, 31, 32, 33, 34) are in communication with the inlet via proximal portions of the conduits (branch channels) and a common supply area (37) and supply conduit (38) (inlet channel) whereby a portion of the test sample is delivered to the conduits for interrogation. See also **annotated Fig. 2 of Gavin** in Section V(C)(1) (LaDuca ¶ 140.)

7. Limitation 1.4.3: Fluid Pathway Including a First Port from Which a Pressure Gradient When Applied from a Source External Draws the Test Sample Into at Least One of the Test Chambers:

The fluid pathway in Gavin further includes a plurality of ports (drive apertures 35) defined by the cuvette 12 which are in communication with a channel (drive apertures 35 are in communication with terminal ends of conduits 30, 31, 32, 33, 34). Gavin teaches that a pneumatic pressure can be applied from an external source (pneumatic source 87 via manifold assembly 60) to each drive aperture 25 to draw a test sample through the inlet into the fluid pathway and at least one of the test

chambers (conduits 30, 31, 32, 33, 34) (Ex. 1004, Fig. 2 and 9:10-17, 9:37-53). (LaDuca ¶ 141.)

8. Limitation 1.4.6: Fluid Pathway Defined by a Thermally Conductive Wall Shaped To Be Held in Conforming Contact or Close Proximity to a Heater to Allow Adjustment of a Temperature of the Test Sample:

As stated above, all materials have some degree of thermal conductivity and Gavin explicitly teaches the cuvette 12 allowing the test sample to be heated. Thus, a POSA would understand the walls defining the fluid pathway in Gavin to be thermally conductive. Furthermore, as stated above, Gavin teaches a heater (heating element 56), where an outer surface (bottom surface) of the cuvette 12 is held in relation therewith to allow for heating of the sample (Ex. 1004, Figs 4a and 4b and 8:35-44, 9:30-36). (LaDuca ¶ 142.)

9. Limitation 1.5: Can Be Used with an Interrogation Device to Measure a Viscoelastic Property:

The cuvette 12 in Gavin is configured to be used with testing device 14 to detect fibrin strand formation in blood samples flowing through the conduits of the device (10:20-26), *i.e.*, measuring a "viscoelastic property" under Sections VI(G) and VI(H). Fibrin strand formation, which results in a change in viscosity of the blood, is the first recorded property of a viscoelastic measurement (Ex. 1001, 16:16-21 ["fibrin strands"], Ex. 1005 ¶0006 ["fibrin fibres"]). Thus, any measurement responsive to fibrin formation, and causing a change in viscosity, is a measurement

of a changing viscoelastic property. Measurement of fibrin formation recorded as a coagulation time in Gavin would therefore be understood by a POSA as interrogating changing the viscoelastic properties of the sample. (LaDuca ¶ 143.)

B. It Is More Likely than Not that Claim 52 of the '039 Patent is Unpatentable as Anticipated by Gavin with Inherency Under 35 U.S.C. § 102.

As detailed in Section IX(A), Gavin explicitly teaches each of limitations 1, 1.1, 1.2, 1.2.1, 1.2.3, 1.3, 1.3.1, 1.4, 1.4.1, 1.4.2 and 1.4.3 shared between claims 1 and 52. Gavin further teaches limitations 1.6, 2, 3, 4 and 5 of claim 52 (system).

1. Limitation 1.6: Cartridge Device Positioned in an Analysis System:

As stated above, disposable cuvette 12 is a cartridge device for use with a test device. Gavin 8:24-32 teaches that "[t]o use the present invention, a clean cuvette 12 is placed with the test device 14 (FIG. 1)." (*Also* Figs. 4a and 4b and 8:36-9:48.) (LaDuca ¶ 146.)

2. Limitation 2: Heat Exchanger and Temperature Control:

Gavin explicitly teaches a heater (heating element 56), where an outer surface (bottom surface) of the cuvette 12 designed to be held in relation therewith to allow for heating of the sample (Figs 4a and 4b and 8:24-32, 9:18-25). "The placement of the cuvette 12 fully within the testing interface unit 50 positions the restricted areas 42 and surrounding regions of the five conduits above the heating element 56.

Consequently, blood contained within the cuvette 12 can be raised to, and maintained at, a predetermined temperature for testing, despite variations in the surrounding ambient temperature or the original temperature of the cuvette 12." (9:30-37.) Thus, while not explicitly stated in Gavin, a POSA would understand that heating element 56 must be associated with a control which enables controlling the temperature of the sample. (LaDuca ¶ 147.)

3. Limitation 3: Use with an Interrogation Device to Measure a Viscoelastic Property:

The cuvette 12 in Gavin is configured to be used with testing device 14 to detect coagulation related activities including fibrin formation. (10:7-13, 10:60-11:3.) As explained in Sections VI(G), VI(H) and IX(A)(9), any measurement responsive to fibrin formation is a measurement interrogating changing viscoelastic property. Measurement of coagulation time in Gavin is responsive to fibrin formation and would therefore be understood by a POSA as interrogating changing viscoelastic properties of the sample. (LaDuca ¶ 148.)

4. Limitation 4: Pressure Control for Applying a Pressure Gradient:

In Gavin, pneumatic pressure can be applied from an external source (pneumatic source 87 via manifold assembly 60). "Each manifold member 62 is pneumatically coupled to a tube 64. The tubes 64 lead to pneumatic sources (not shown) capable of periodically supplying both positive and negative pressures

relevant to the ambient pressure." Ex. 1004, 8:49-52. Thus, while not explicitly stated in Gavin, a POSA would understand that pneumatic source must be associated with a control for varying the pressure relative to an ambient pressure for the conduits. Gavin further describes a preferred embodiment of a stepper motor 155 which enables uniformly controlling the pressure in each of the five conduits 30, 31, 32, 33, 34. (13:29-35.) (LaDuca ¶ 149.)

5. Limitation 5: Analysis System Including a Pocket with an Actuator:

Gavin teaches use of an external pressure source which is aligned and interfaces (via elastomeric seals 70) with the cartridge device (cuvette 12) when inserted into a pocket of a measurement system (device 14). Ex. 1004, Figs. 4a and 4b and 8:44-62, 9:15-31. Gavin also teaches a heater (heating element 56), where an outer surface (bottom surface) of the cuvette 12 is held in relation therewith to allow for heating of the sample when the cuvette 12 is inserted into the pocket. Ex. 1004, 8:35-44, 9:30-36. Gavin further teaches that the restricted areas 42 of the five conduits 30, 31, 32, 33, 34, are positioned relative to corresponding sets of photoelectric sensors 61. (Ex. 1004, Figs. 4a and 4b and 8:63-9:10, 9:36-44.) Gavin also teaches a rotating pneumatic manifold assembly 60 which functions as an actuator when the cuvette 12 is inserted into the cartridge to position the cuvette relative to an external pressure source (pneumatic manifold assembly 60), a heat exchange (heating element 56) and an interrogation device (photoelectric sensors 61

and light sources 53). (Ex. 1004, 9:15-44.) Thus, a POSA would understand Gavin to teach an actuator system to allow for proper positioning and alignment of such interfaced elements upon insertion of the cartridge into the measurement system. (LaDuca ¶ 150.)

X. GROUND 4: IT IS MORE LIKELY THAN NOT THAT CLAIM 51 OF THE '039 PATENT ARE UNPATENTABLE AS OBVIOUS OVER GAVIN IN VIEW OF WARDEN UNDER 35 U.S.C. § 103.

As detailed in Section IX(A), Gavin explicitly teaches each of limitations 1, 1.1, 11.1, 1.2, 1.2.1, 1.2.3, 1.3, 1.3.1., 1.4, 1.4.1, 1.4.2, 1.4.3 and 1.5 shared between claims 1 and 51. In addition, Gavin also teaches claim elements 1.2.2, 1.3.2, 1.4.4 and 1.4.7 and Warden teaches claim element 1.4.5 of claim 51 (three test chambers).

A. Limitation 1.2.2: Including a Third Test Chamber:

As stated above, Gavin teaches a plurality of conduits (conduits 30, 31, 32, 33, 34) where each conduit defines a space (i.e., chamber) for blood coagulation analysis, i.e. prothrombin time (PT) analysis (Fig. 2 and 6:2-3, 6:31-35). The conduits (conduits 30, 31, 32, 33, 34) in Gavin are defined by the cuvette 12 housing. (LaDuca ¶ 154.)

B. Limitation 1.3.2: First, Second and Third Chambers Activate Coagulation:

Gavin teaches that a clot promoting reagent 28 is disposed in each of the conduits 30, 31, 32, 33, 34 (6:20-30). The clot promoting reagent 28 can be a prothrombin time reagent such as dried rabbit brain thromboplastin or another clot

promoting reagent such as tissue factor. The Abstract teaches that each of the conduits contains a dried or lyophilized activation reagent and in at least one of the conduits a normalizing control agent is present which counteracts any effects of anticoagulants present in the blood sample, thereby allowing the blood sample to have generally normal coagulation characteristics. (LaDuca ¶ 155.)

C. Limitation 1.4.4: Fluid Pathway Including a Second Port from Which a Pressure Gradient When Applied from a Source External Draws the Test Sample from an External Vessel Through the Inlet and Into the Fluid Pathway:

As stated above, the fluid pathway in Gavin includes a plurality of ports (drive apertures 35) defined by the cuvette 12 which are in communication with a channel (drive apertures 35 are in communication with terminal ends of conduits 30, 31, 32, 33, 34). Gavin teaches that a pneumatic pressure can be applied from an external source (pneumatic source 87 via manifold assembly 60) to each drive aperture 25 to draw a test sample through the inlet into the fluid pathway and at least one of the test chambers (conduits 30, 31, 32, 33, 34) (Fig. 2 and 9:10-17, 9:37-53). (LaDuca ¶ 156.)

D. Limitation 1.4.7: Portion of the Fluid Pathway Designed to be Held Against a Heater to Allow Adjustment of a Temperature of the Test Sample:

As stated above, Gavin teaches a heater (heating element 56), where an outer surface (bottom surface) of the cuvette is held in relation therewith to allow for heating of the sample (Ex. 1004, Figs 4a and 4b and 8:24-32, 9:18-25). "The

placement of the cuvette 12 fully within the testing interface unit 50 positions the restricted areas 42 and surrounding regions of the five conduits above the heating element 56. Consequently, blood contained within the cuvette 12 can be raised to, and maintained at, a predetermined temperature for testing, despite variations in the surrounding ambient temperature or the original temperature of the cuvette 12." Ex. 1004, 9:30-37. (LaDuca ¶ 157.)

E. Limitation 1.4.5: Prevention of Sample Leaving the Device:

Gavin teaches each of the limitations of claim 51 except for limitation 1.4.5 involving the first and/or second ports preventing the test sample from leaving the device. However, Gavin does teach that the ports include a configuration which prevents blood from being drawn into the manifold assembly 60. In particular, Ex. 1004, 9:12-15 teaches "[a] photoelectric sensor 41 and light source 43 are disposed at the far end of the channel 54…[the] photoelectric sensor 41 and light source 43 serve as a fail-safe detector that prevents blood from being drawn into the manifold member 62." Thus, Gavin teaches preventing the test sample from leaving the device. (LaDuca ¶ 158.)

Warden (Ex. 1006) is in the same field as Gavin teaching a cartridge structure with an integrated fluid distribution flow-path and ports for interfacing with an external pump. (Section V(C)(3).) Warden teaches vent plugs which are configured for permitting air to vent from the one or more second chambers and sealing the one

or more second chambers when the sample reaches the vent plug" (Ex. 1006, 7:6-10, 14:67-15:2 and 13:31-49). Thus, it would have been obvious to a POSA, based on the teachings in Gavin on preventing external fluid flow and corresponding teachings in Warden, to modify the ports in Gavin to include vent plugs. For a POSA, this would be a simple and predictable extension and application of a known technique to achieve a same goal as the photoelectric sensor 41. (LaDuca ¶¶ 120 and 159.)

XI. GROUND 5: IT IS MORE LIKELY THAN NOT THAT CLAIMS 1, 26 AND 52 OF THE '039 PATENT ARE UNPATENTABLE AS OBVIOUS OVER SCHUBERT IN VIEW OF GAVIN UNDER 35 U.S.C. § 103.

Schubert (Ex. 2006), described at Section V(C)(2) as a prior art multi-chamber hemostatic assay using viscoelastic methods and the same reagents claimed in the Challenged Claims, most specifically in claim 26 (Abciximab/Cytochalasin D), explicitly discloses most of the limitations of those claims; the missing limitations for Claims 1, 26 and 52 are met by Gavin (Ex. 2004), *see* Section IX, to which a POSA would to combine with Schubert as both involve multi-chamber hemostatic assay cartridges.

A. Limitations of Claims 1, 26 and 52 Disclosed in Schubert

Following are limitations of claims 1, 26 and 52 disclosed in Schubert:

1. Limitations 1 and 1.1 (Claims 1, 26, and 52): [Cartridge] Device Including a Housing:

Ex. 1005, Abstract teaching "a cartridge device for a measuring system…" Also, Ex. 1005, FIG. 13c, ¶0029 ¶0077. A housing is disclosed by the plain and ordinary meaning of term "cartridge." See also, Ex. 1005, Fig. 13c and ¶0093 teaching that a cartridge body 30 and cover 31 form the cartridge device 50 and ¶0038 teaching that the cover can be "integrally formed with the cartridge body." (LaDuca ¶ 161.)

2. Limitation 1.1.1 (Claim 1 and 26): Thermally Conductive Portion of the Housing:

All materials have some degree of thermal conductivity. Ex. 1005, ¶0038 teaches that the cartridge device 50 may be made of plastic. Plastics, which are the essential structural composition of nearly all assay devices, have thermal or heat conductivity. (LaDuca ¶ 162.)

3. Limitations 1.2 and 1.2.1 (Claims 1, 26 and 52): Plurality of Chambers, Including First and Second Chambers:

Schubert, Ex. 1005, Fig. 6 depicts measurement cavities 20 and 20' and ¶¶0081-0082 teaches that FIG. 6 depicts "[t]wo arrangements of FIG. 4… arranged in parallel" and "In a preferred embodiment the cartridge device 50 comprises four arrangements of FIG. 4 or 5 having 4 measurement cavities." The measurement cavities are defined by the cartridge housing. See Ex. 1005, Fig. 13c where the

cartridge body 30 and cover 31 define measurement cavity 20. See also Ex. 1005, Abstract and ¶0093. (LaDuca ¶ 163.)

4. Limitation 1.2.3 (Claims 1, 26 and 52): Chambers Designed to Be Interrogated:

Schubert teaches carrying out a measurement in measurement cavity 20 on sample liquid 1 mixed with reagent 21. Ex. 1005, ¶¶0079 and 0080. Also, Ex. 1005, Abstract teaching "…at least one measurement cavity formed therein and having at least one probe element arranged in said at least one measurement cavity for performing a test on said sample liquid." Also, Ex. 1005, ¶0029. The tests in Schubert determine a hemostatic parameter. Ex. 1005, ¶0006 and ¶0009. (LaDuca ¶ 164.)

5. Limitations 1.3 and 1.3.1 (Claims 1, 26 and 52): Different Reagents in First and Second Chambers:

Schubert Ex. 1005, ¶0082 teaches: "In a preferred embodiment the cartridge device 50 comprises four arrangements of FIG. 4 or 5 having 4 measurement cavities 20, 20'." In some embodiments, the measurement cavity is integrally formed with the reagent cavity. Ex. 1005, ¶¶0039-0040 and ¶0080. Also, Ex. 1005, ¶0024 teaching that "different tests are required to get comprehensive information of a current bleeding status of a patient" and "[t]hese different tests require different reagents which have to be mixed with the blood sample;" Ex. 1005, ¶0083 teaching

combining INTEM, EXTEM and FIBTEM coagulation tests with a platelet aggregometry test within one cartridge. (LaDuca ¶ 165.)

6. Limitations 1.3.2, 1.3.3 and 1.3.4 (Claim 26): Reagents Activate Coagulation Via the Intrinsic and/or Extrinsic Pathway; Reagent In At Least One of the First or Second Chambers Activate Coagulation Via the Extrinsic Pathway and Reagent in the Second Chamber Include Abciximab and/or Cytochalasin D:

Schubert Ex. 1005, ¶0083 teaches combining INTEM, EXTEM and FIBTEM coagulation tests with a platelet aggregometry test within one cartridge. INTEM is disclosed as including a reagent for intrinsic activation (intrinsic activator), EXTEM is disclosed as including a reagent for extrinsic activation (extrinsic activator) and FIBTEM is disclosed as including reagents for extrinsic activation as well as for suppressing thrombocyte function (extrinsic activator plus cytochalasin D). This is consistent with the understood meanings of the trademark terms INTEM, EXTEM and FIBTEM at the time of Schubert (where a POSA would know that EXTEM includes Tissue Factor, INTEM includes ellagic acid plus phospholipid and FIBTEM includes Tissue Factor and cytochalasin D). (LaDuca ¶ 166.)

7. Limitations 1.4, 1.41 and 1.42 (Claims 1, 26 and 52): Fluid Pathway Including an Inlet into an [Inlet] Channel into [Branch] Channels and into the First and Second Chambers:

Schubert, Ex. 1005, Fig. 6 depicts a cartridge device 50 defining a fluid pathway comprising ductwork including a first set of ducts 13, 14 and 15 and a

second set of ducts 13' 14' and 15'. Ex. 1005, ¶0024 "the cartridge device further comprises at least one receiving cavity formed therein for receiving the sample liquid; at least one reagent cavity for holding at least one reagent; a ductwork connecting said cavities and the at least one measurement cavity…wherein the cover covers and at least partially forms said cavities and said ductwork." Ex. 1005, ¶0079 teaching: "receiving cavity 16 consists of a cavity within the cartridge device 50. The sample liquid 1 can be applied by means of a syringe, pipette etc, e.g. through a self-sealing cap shown as a receiving cavity cover 33a in FIG. 10 b." Also Ex. 1005, Fig. 6 depicting receiving cavity 16 connected to inlet ducts 13 and 13' via branch duct 17. Also Ex. 1005, ¶¶0047 and 0048. See also **annotated Fig. 6 of Schubert**, *supra.* (LaDuca ¶ 167.)

8. Limitations 1.5 (Claims 1 and 26) and 3 (Claim 52): Use with an Interrogation Device to Measure a Viscoelastic Property:

Schubert, Ex. 1005, ¶¶0025-0028 teaches "It is a problem underlying the presented invention to provide a cartridge device for a measuring system for measuring viscoelastic characteristics of a sample liquid, in particular a blood sample. Directly connected to this invention is the problem to provide a corresponding measuring system for measuring viscoelastic characteristics of a sample liquid, in particular the coagulation characteristics of a blood sample liquid." Also Ex. 1005, 0013, 0014, 0016-0018. (LaDuca ¶ 168.)

B. Schubert Fails To Disclose Explicitly the Following limitations:

Schubert teaches each and every element of claims 1, 26 and 52, except for failing to explicitly fully disclose the following:

- Limitation 1.4.3 (Claims 1, 26 and 52): Fluid Pathway Including a First Port From Which a Pressure Gradient When Applied From a Source External Draws the Test Sample Into at Least One of the Test Chambers;
- Limitation 1.4.6 (Claim 1): Fluid Pathway Defined by a Thermally Conductive Wall Shaped to be Held in Conforming Contact or Close Proximity to a Heater to Allow Adjustment of a Temperature of the Test Sample;
- Limitation 1.6 (Claim 52): Cartridge Device Positioned in an Analysis System;
- Limitation 2 (Claim 52): Heat Exchanger and Temperature Control;
- Limitation 4 (Claim 52): Pressure Control for Applying a Pressure Gradient;
- Limitation 5 (Claim 52): Analysis System Including a Pocket with an Actuator.

(LaDuca ¶¶ 117, and 169.)

C. A POSA Would Find It Obvious Modify Schubert with Features from Gavin To Meet the Limitations of Claims 1, 26 and 52 Not Expressly Taught by Schubert.

As detailed in Section IX, Gavin teaches each of limitations 1, 1.1, 1.2, 1.2.1, 1.2.3, 1.3, 1.3.1, 1.4, 1.4.1, 1.4.2 1.4.3 shared between claims 1, 26 and 52, limitation 1.1.1 shared between claims 1 and 26, limitation 1.4.6 of claim 1 and limitations 1.6, 2, 3, 4 and 5 of claim 52 (system). Gavin further teaches some aspects of the limitations of claim 26 relating to reagents (e.g., 1.3.2. as detailed in Section X). Gavin does not teach limitation 1.3.4 of claim 26, but Schubert does.

It would have been obvious to a POSA to start with the Schubert cartridge device 50 and measurement system in Schubert and add limitations 1.4.3, 1.4.6, 1.6, 2, 4 and 5 taught by Gavin[10] to meet all the limitations of claims 1, 26 and 52. (LaDuca ¶¶ 116 and 170.) Gavin teaches each of these limitations and is in a same field of coagulation testing cartridges with integrated fluid distribution fluidics which a POSA would have been motivated to combine as further described below.

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[10] Warden (as described in Section V(C)(3).) also teaches limitations 1.4.3, 1.4.6, 1.6, 2, 4 and 5 an could be substituted for Gavin and combined with Schubert for at least the same reasons noted with respect to Gavin. (LaDuca ¶¶ 170).

1. Limitation 1.4.3 (Claims 1, 26 and 52): Fluid Pathway Including a First Port From Which a Pressure Gradient When Applied From a Source External Draws the Test Sample Into at Least One of the Test Chambers:

It would have been obvious to a POSA to substitute the internal pump in Schubert with a port or a plurality of ports and an external pressure source (e.g., by substituting components of the fluidic design / flow path in Schubert with components of the fluidic design / flow path in Gavin. This represents simple substitutions of known elements to obtain predictable results. More particularly, the use of ports connected to a flow path of a device to apply a pressure gradient and thereby drive loading of a sample via an inlet and distribution of a sample to a plurality of test chambers was known in the art. Thus, a POSA could have substituted such teachings for the flow path configuration in Schubert and the results of such substitution would have been predictable. As evidenced by the teachings of Gavin (as well as Warden), a POSA would understand that a pressure gradient could be applied via a port in different ways and at different points along the fluid pathway with the same result as in Schubert being achieved. A POSA would have been motivated to modify Schubert to reduce the complexity and cost of the cartridge 50 by removing the internal pump. See, e.g., Ex. 1005, ¶ 0098 teaching keeping the total number of parts required for the cartridge device 50 at a minimum. Furthermore, Schubert contemplates modifications of its flow path configuration

including the positioning of its pump means 18. See, e.g., Ex. 1005, ¶ 0078 teaching that "[i]n a variation said cavities and ducts can be arranged in different ways one of which is shown in FIG. 5, wherein pump means 18 and reagent cavity 19 are changed." Thus, rather than teachings away, Schubert embraces modifications and changes to the example fluidic design described therein. (LaDuca ¶¶ 119 and 171.)

2. Limitation 1.4.6 (Claim 1): Fluid Pathway Defined by a Thermally Conductive Wall Shaped to be Held in Conforming Contact or Close Proximity to a Heater to Allow Adjustment of a Temperature of the Test Sample:

Schubert, Ex. 1005, Fig. 13c depicts cartridge body 30 and cartridge cover 31 forming walls of cartridge device 50. Ex. 1005, ¶0038 teaches that the cartridge device 50 may be made of plastic. Plastics, which are the essential structural composition of nearly all assay devices, have thermal or heat conductivity. Walls defined by cartridge device 50 of Schubert include inner and outer surface areas where at least a portion of the fluid pathway is defined by the inner surface area of the walls of cartridge device 50. See Fig. 13 c depicting an inner surface area of walls formed by cartridge body 30 and cartridge cover 31 cooperating to define ducts and cavities of the fluid pathway. The outer surface area of the walls of cartridge device 50 is shaped in a manner that would enable conforming contact or close proximity with a heater (e.g., to allow adjustment of a temperature of a test sample flowing through a flow path defined by an inner surface of the walls of cartridge

device 50). See Fig. 13c depicting an outer surface area of walls formed by cartridge body 30 and cartridge cover 31 defining a rectilinear shape which would facilitate holding the walls of the cartridge 50 in conforming contact or close proximity with a planer surface of a heater. It was also well known in the art to heat a sample to body temperature, during coagulation testing including for thromboelastography and thromboelastomety. Maintaining a test temperature of 37^{o}C for both laboratory testing (Scordato, R, Coagulation Instrument for Performing Clotting Tests, US 4,497,774) as well as point of care testing (Mintz M; US 3,836,333, System for Timing the Coagulation of Blood") is well established for coagulation, platelet function testing Aggregometer (Cardinal D, Flower R: Method of and Apparatus for Monitoring Platelet Aggregation and Test Cell for Use in Such Method and Apparatus. US 4,319,194) and thromboelastography (Lang T, Depka M; Possibilities and limitations of thrombelastometry/-graphy; Hamostaseologie 26:Suppl 1, S20-29, 2006 ("Lang 2006"), Ex. 1007) Certified Translation as Filed in IPR2018-00950). This provides for consistency and reproducibility of results and common basis for comparing ex vivo tests to in vivo conditions. Thus, to achieve this desired control of the reaction temperature a POSA would have been motivated to modify Schubert to include a heater such as disclosed in Gavin. Since both Gavin and Schubert involve cartridges for coagulation testing with integrated flow paths, it would have been obvious and predictable to apply the teachings in Gavin relating to

heating cuvette 12 in a similar manner to the cartridge in Schubert 50. (LaDuca ¶¶ 118 and 172.)

3. Limitation 1.6 (Claim 52): Cartridge Device Positioned in an Analysis System; Limitation 2 (Claim 52): Heat Exchanger and Temperature Control; Limitation 4 (Claim 52): Pressure Control for Applying a Pressure Gradient; Limitation 5 (Claim 52): Analysis System Including a Pocket with an Actuator:

Schubert already teaches that cartridge 50 interfaces with a separate measurement system for interrogation purposes. A POSA would have recognized that the cartridge in Schubert could be modified based on the teachings in Gavin to interface with a measurement system, as taught in Gavin. More particularly, as stated above, Gavin provides motivation to utilize an external pressure source and interface with a heater and enables such embodiments via its design of the cuvette 12 to fit within a measurement system (device 14). Gavin further provides teachings and motivation for coupling interfaced elements (such as a pneumatic assembly) via an actuator system (rotating pneumatic assembly 60). See Section IX(B). This would advantageously allow for proper positioning and alignment of such interfaced elements upon insertion of the cartridge into the measurement system. (LaDuca ¶ 173.)

XII. GROUND 6: IT IS MORE LIKELY THAN NOT THAT CLAIM 51 OF THE ‘039 PATENT ARE UNPATENTABLE AS OBVIOUS

OVER SCHUBERT IN VIEW OF GAVIN AND WARDEN UNDER 35 U.S.C. § 103.

As detailed in Section XI, Schubert in view of Gavin teaches each of claim elements 1, 1.1, 1.1.1, 1.2, 1.2.1, 1.2.3, 1.3, 1.3.1, 1.4, 1.4.1, 1.4.2, 1.4.3 and 1.5 which are included in claim 51 (three chambers). Further, as detailed in Section XI, a POSA would be motivated, starting with Schubert, to modify and combine Schubert with teachings from Gavin. In addition, Schubert in view of Gavin also teaches the following claim elements of claim 51:

A. Limitation 1.2.2 (Claim 51): Including a Third Test Chamber:

As stated above, Schubert teaches a preferred embodiment of a cartridge with four measurement chambers. ¶¶0081-0082 "In a preferred embodiment the cartridge device 50 comprises four arrangements of FIG. 4 or 5 having 4 measurement cavities." See also, Ex. 1005, ¶0083 teaching combining INTEM, EXTEM and FIBTEM coagulation tests with a platelet aggregometry test within one cartridge. (LaDuca ¶ 176.)

B. Limitation 1.3.2 (Claim 51): First, Second and Third Chambers Activate Coagulation:

As stated above, Ex. 1005, ¶0083 teaches combining INTEM, EXTEM and FIBTEM coagulation tests with a platelet aggregometry test within one cartridge. As stated above, INTEM, EXTEM and FIBTEM all include activators. (LaDuca ¶ 177.)

C. Limitation 1.4.4 (Claim 51): Fluid Pathway Including a Second Port from Which a Pressure Gradient When Applied from a Source External Draws the Test Sample from an External Vessel Through the Inlet and Into the Fluid Pathway:

As detailed in Section XI, it would have been obvious to a POSA to substitute the internal pump in Shubert with a port or a plurality of ports and an external pressure source (e.g., by substituting components of the fluidic design / flow path in Schubert with components of the fluidic design / flow path in Gavin). Gavin includes a plurality of ports (drive apertures 35) defined by the cuvette 12 which are in communication with a channel (drive apertures 35 are in communication with terminal ends of conduits 30, 31, 32, 33, 34). Gavin teaches that a pneumatic pressure can be applied from an external source (pneumatic source 87 via manifold assembly 60) to each drive aperture 25 to draw a test sample through the inlet into the fluid pathway and at least one of the test chambers (conduits 30, 31, 32, 33, 34) (Ex. 1004, Fig. 2 and 9:10-17, 9:37-53). (LaDuca ¶ 178.)

D. Limitation 1.4.7 (Claim 51): Portion of the Fluid Pathway Designed to be Held Against a Heater to Allow Adjustment of a Temperature of the Test Sample:

Gavin teaches a heater (heating element 56), where an outer surface (bottom surface) of the cuvette is held in relation therewith to allow for heating of the sample (Ex. 1004, Figs 4a and 4b and 8:24-32, 9:18-25). "The placement of the cuvette 12 fully within the testing interface unit 50 positions the restricted areas 42 and

surrounding regions of the five conduits above the heating element 56. Consequently, blood contained within the cuvette 12 can be raised to, and maintained at, a predetermined temperature for testing, despite variations in the surrounding ambient temperature or the original temperature of the cuvette 12." Ex. 1004, 9:30-37. A POSA would have been motivated to modify Schubert to include a heater and would seek a previously defined solution such as disclosed in Gavin. (LaDuca ¶ 179.)

E. Limitation 1.4.5 (Claim 51): Prevention of Sample Leaving the Device:

Schubert in view of Gavin teaches each of the limitations of claim 51 except for limitation 1.4.5 involving the first and/or second ports preventing the test sample from leaving the device. However, as explained in Section X(E), it would have been obvious to a POSA, based on the teachings in Gavin on preventing external fluid flow and corresponding teachings in Warden (Ex. 2006), to modify the ports in Gavin (as applied with respect to modifying flow path in Schubert) to include vent plugs. (LaDuca ¶ 180.)

XIII. Obviousness of claims 4 and 55 over Gavin (Ex. 1004) in view of the State of the Art and Obviousness of claims 4, 36 and 55 over Schubert in view of Gavin and in further view of the State of the Art.

As stated above, claims 1 and 52 are anticipated by Gavin (Section (IX)) and claims 1, 26 and 52 are obvious over Schubert in view of Gavin (Section (XI).

Claims 4, 36 and 55 depend indirectly[11] from claims 1, 26 and 52, respectively and further requires "a thermally conductive polymer that has a thermal conductivity that exceeds 0.123 W/m °K." Heating a blood sample to body temperature was a routine and standard practice as of the priority date of the '039 patent and it would have been desirable to a POSA to do so efficiently and quickly. A POSA would recognize that there are many polymers that may meet the open-ended range of thermal conductivity. High density polyethylene (HDPE) which is a commonly used plastic in disposable cartridge housings and has a stated thermal conductivity range of 0.288-.0480 W/m °K. See also, U.S. Publication No. 2003/0199082 ("Miller") which discloses the construction of blood assay trays from polymer compositions with a thermal conductivity greater than 3 W/m°K., and more preferably greater than 22 W/m°K) (Miller ¶¶ 19, 33) in order to provide a tray which can be rapidly heated and cooled to improve the efficiency of the assays (Miller¶¶ 14-15). (LaDuca ¶ 181.)

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11 Intervening dependent claims 2, 3, 34, 35, 53 and 54 involve subject matter included in limitations 1.1.1, 1.4.6 and 1.4.7 of claims 1, 26, 51 and 52 and are disclosed by Gavin by virtue of the same disclosure and for at least the same reasons as discussed with respect to those limitations.

Thus, while Gavin and/or Schubert do not explicitly disclose use of a polymer with a specific thermal conductivity greater than 0.123 W/m °K a POSA familiar with the State of the Art would have been motivated to use a polymer with greater thermal conductivity to improve the speed and efficiency of heating. Considering the use of different materials for construction is standard and routine and using a material with thermal conductivity in the disclosed range is both taught in the State of the Art and a predictable application for improving heating. ***Id.***

XIV. CONCLUSION

Petitioner submits that for the reasons set forth above, supported by the declaration of Dr. LaDuca and the Exhibits, it has been shown that more likely than not, Challenged Claims 1, 4, 26, 36, 51, 52 and 55 are invalid under all of 35 U.S.C. §§ 102, 103 and 112 and should reviewed by the Board and canceled.

Date: February 21, 2019

Respectfully submitted,
Attorney for Petitioner

/Stephen Y. Chow/
Stephen Y. Chow (Reg. No. 31,338)

CERTIFICATION OF SERVICE (37 C.F.R. § 42.6(e))

The undersigned hereby certifies that the above-captioned Petition for Post-Grant Review of U.S. Patent No. 9,977,039 (and accompanying exhibits), was served in its entirety on February 21, 2019, upon counsel for Patent Owner via overnight courier:

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CERTIFICATION OF WORD COUNT (37 C.F.R. § 42.6(e))

The undersigned hereby certifies that the attached Petition, including footnotes, but not the cover page, exhibit list, table of contents, mandatory notices, and certifications, contains 17,306 words, as measured by the Word Count function of Microsoft Word. This is less than the limit of 18,700 words as specified by 37 C.F.R. § 42.24(a)(ii).

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TABLE OF EXHIBITS

Exhibit	Citation	Author	Title
1001	U.S. Patent No. 9,977,039	Viola F, Walker W, Browne G, Magyar R, Hansen B, Denny C	Devices, Systems and Methods for Evaluation of Hemostasis
1002	Declaration of Dr. Frank M. LaDuca, Ph.D., FAHA		
1003	File history for '039 patent		
1004	U.S. Patent No. 5,534,226	Gavin M, Cimini C, Huang M, Kuklo A, Mawhirt J, Marcelino E	Portable Test Apparatus and Associated Method of Performing a Blood Coagulation Test
1005	U.S. Pat. App. Publ. 2010/0154520 A1	Schubert A, Romero-Galeano J, Kessler M	Cartridge Device for a Measuring System for Measuring Viscoelastic Characteristics for a Sample Liquid. A Corresponding Measuring System and Measuring Method
1006	U.S. Patent No. 6,016,712	Warden L, Kaplan E	Device for Receiving and Processing a Sample
1007	Hamostaseologie 26:Suppl 1, S20-29, 2006	Lang T, Depka M	Possibilities and limitations of thrombelastometry/-graphy

1008	Blood Coagulation and Fibrinolysis 18:3, 247-252, 2007	Nielson V	A Comparison of the Thrombelastograph and ROTEM"
1009	U.S. Patent No. 6,225,126	Cohen E, Delmonica P, Ravin G, George W, Lake J	Method and Apparatus for Measuring Hemostasis
1010	U.S. Patent Publication No. 2005/0233460	Clague C, Cheek, D, Nippoldt, D	Blood coagulation test cartridge, system, and method
1011	*Instrumentation Laboratory Co. v. HemoSonics LLP*, IPR2017-00852, Paper No. 47 (PTAB Feb. 13, 2019)		Final Written Decision
1012	*Instrumentation Laboratory Co. v. HemoSonics LLP*, IPR2017-00855, Paper No. 55 (PTAB Feb. 13, 2019)		Final Written Decision