

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

TERUMO BCT INC.,

Petitioner

v.

HAEMONETICS CORP.,

Patent Owner

IPR2025-01420
U.S. Patent No. 10,792,416

**PETITION FOR *INTER PARTES* REVIEW
UNDER 35 U.S.C. § 312 AND 37 C.F.R. § 42.104**

Mail Stop PATENT BOARD
Patent Trial and Appeal Board
U.S. Patent & Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

TABLE OF CONTENTS

I.	Mandatory Notices.....	1
A.	Real Parties-In-Interest.....	1
B.	Related Matters.....	1
C.	Counsel	1
D.	Service Information.....	2
II.	Fees	2
III.	Certification of Grounds of Good Standing	2
IV.	Identification Of Challenge And Relief Requested.....	2
A.	Identification Of Prior Art.....	2
B.	Statutory Grounds of Unpatentability	4
V.	'416 Patent Overview	4
A.	The '416 Patent is Related to Plasma Apheresis.....	4
B.	The '416 Patent's Purported Invention	6
C.	Prosecution History	10
VI.	Prior Art Overview	11
A.	Overview of Lavender.....	11
B.	Overview of Neyrinck.....	15
C.	Overview of Bainbridge	16
D.	Overview of Darashkevich.....	17
E.	Overview of Min	17
F.	Overview of Turgut.....	18
G.	Overview of Headley.....	18

H.	Overview of Barrett.....	19
VII.	Level Of Ordinary Skill.....	19
VIII.	Claim Construction.....	20
IX.	Detailed Grounds Explanation.....	20
A.	Ground I: Claims 1, 7, 9, 11, 14, and 15 are rendered obvious over Lavender in view of Neyrinck.....	20
1.	Reasons to Combine Lavender and Neyrinck.....	20
2.	Claim 1	23
3.	Claim 7: A method according to claim 1, further comprising: calculating the donor's body mass index based, at least in part on the weight and height of the donor, the donor plasma volume calculated based, at least in part, on the donor's body mass index.	34
4.	Claim 9: A method according to claim 1, further comprising: inserting a venous-access device into the donor prior to step (e).	35
5.	Claim 11: A method according claim 1, further comprising: determining a volume of anticoagulant introduced into the whole blood based on a number of rotations of an anticoagulant pump, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the number of rotations of the anticoagulant pump.....	35
6.	Claim 14: A method according to claim 1, further comprising: monitoring a volume of plasma component collected within the plasma collection container, the calculated volume of pure plasma collected within the plasma collection container based, at least in part, on the monitored volume of collected plasma component.....	37
7.	Claim 15: A method according to claim 1, further comprising: monitoring a weight of plasma component collected within the plasma collection container, the calculated volume of pure plasma collected within the plasma collection container based, at	

least in part, on the monitored weight of collected plasma
component.....37

- B. Ground II: Claims 2-6, 17-22, 24, 26, 28, and 29 are rendered obvious
over Lavender in view of Neyrinck and further in view of Bainbridge.
.....38
1. Reasons to Combine Lavender, Neyrinck, and Bainbridge.....38
 2. Claim 2: A method according to claim 1, further comprising:
returning, after collecting at least a portion of the target plasma
collection volume, the contents of the blood component
separation device to the donor through the first line.41
 3. Claim 3: A method according to claim 2, further comprising:
calculating an intravascular deficit based, at least in part on, the
volume of pure plasma collected and a volume of the contents of
the blood component separation device returned to the donor. 42
 4. Claim 4: A method according to claim 3, further comprising:
returning a volume of saline to the donor to obtain a target
intravascular deficit.....43
 5. Claim 5: A method according to claim 4, wherein the target
intravascular deficit is 0 milliliters.43
 6. Claim 6: A method according to claim 4, wherein the target
intravascular deficit is between –250 and 500 milliliters.....44
 7. Claim 1744
 8. Claim 18: A system according to claim 17, wherein the controller
is further configured to: return, after collecting at least a portion
of the target plasma collection volume, fluid remaining within
the blood component separation device via the first line.47
 9. Claim 19: A system according to claim 18, wherein the controller
is further configured to: calculate an intravascular deficit based,
at least in part on, the volume of pure plasma collected and a
volume of the contents of the blood component separation device
returned to the donor.47

10. Claim 20: A system according to claim 19, further comprising: a saline line configured to fluidly connect to a saline source and the blood component separation device, the controller configured to return a volume of saline to the donor to obtain a target intravascular deficit.....47
11. Claim 21: A system according to claim 20, wherein the target intravascular deficit is between –250 and 500 milliliters.....48
12. Claim 22: A system according to claim 17, wherein the controller is further configured to: calculate the donor's body mass index based, at least in part, on the weight and height of the donor, the donor plasma volume calculated based, at least in part, on the donor's body mass index.48
13. Claim 24: A system according to claim 17, wherein the volume of anticoagulant in the collected plasma component is based, at least in part, on a volume of anticoagulant added to the drawn whole blood and the donor's hematocrit.48
14. Claim 26: A system according to claim 17, wherein the controller is configured to monitor a number of rotations of an anticoagulant pump to determine a volume of anticoagulant introduced into the whole blood, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the number of rotations of the anticoagulant pump.....52
15. Claim 28: A system according to claim 17, further comprising: a plasma container weight sensor configured to monitor a volume of plasma component collected within the plasma container, the calculated volume of pure plasma collected within the plasma container based, at least in part, on the monitored volume of collected plasma component.52
16. Claim 29: A system according to claim 17, further comprising: a plasma container weight sensor configured to monitor a weight of plasma component collected within the plasma container, the calculated volume of pure plasma collected within the plasma container based, at least in part, on the monitored weight of collected plasma component.52

C.	Ground III: Claim 8 is rendered obvious over Lavender in view of Neyrinck and Darashkevich.	52
1.	Claim 8: A method according to claim 1, wherein the target percentage of plasma is between 26.5 and 29.5 percent of the donor's plasma volume.....	53
D.	Ground IV: Claim 23 is rendered obvious over Lavender in view of Neyrinck, Bainbridge and Darashkevich.	54
1.	Claim 23: A system according to claim 17, wherein the target percentage of plasma is between 26.5 and 29.5 percent of the donor's plasma volume.....	54
E.	Ground V: Claims 10 and 13 are obvious over Lavender in view of Neyrinck and Min.....	55
1.	Reasons to Combine Lavender, Neyrinck, and Min.....	55
F.	Ground VI: Claim 25 is obvious over Lavender in view of Neyrinck, Bainbridge and Min.....	61
1.	Claim 25: A system according to claim 17, further comprising: an anticoagulant source weight sensor configured to measure the weight of the anticoagulant source, the controller further configured to monitor a change in volume within the anticoagulant source based on the measured weight of the anticoagulant source, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the change in volume within the anticoagulant source.....	61
G.	Ground VII: Claim 12 is obvious over Lavender in view of Neyrinck, Min, and Turgut.....	63
1.	Claim 12: A method according to claim 1, further comprising: determining a volume of anticoagulant within the blood component separation device, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the volume of anticoagulant within the blood component separation device.....	63

- H. Ground VIII: Claim 27 is obvious over Lavender in view of Neyrinck, Bainbridge, Min, and Turgut.....65
1. Claim 27: A system according to claim 17, further comprising: an optical sensor located on the blood component separation device and configured to monitor the contents of the blood component separation device and determine if a volume of anticoagulant remains within the blood component separation device, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the volume of anticoagulant within the blood component separation device..65
- I. Ground IX: Claims 16 and 30 are obvious over Lavender in view of Neyrinck, Bainbridge, Headley, and Barrett.....66
1. Claim 16: A method according to claim 1, wherein step (b) includes monitoring a volume of red blood cells collected within the blood component separation device, the determined hematocrit of the donor based, at least in part, on the monitored volume of red blood cells collected within the blood component separation device and a volume of whole blood withdrawn from the donor.66
2. Claim 30: A system according to claim 17, further comprising: an optical sensor located on the blood component separation device and configured to monitor a volume of red blood cells collected within the blood component separation device, the controller configured to determine the donor's hematocrit based, at least in part, upon on the monitored volume of red blood cells collected within the blood component separation device and a volume of whole blood withdrawn from the donor.....69

TABLE OF AUTHORITIES

Cases	Page(s)
<i>Eli Lilly & Co. v. Teva Pharm. Int’l GmbH</i> , 8 F.4th 1331 (Fed. Cir. 2021)	57, 68
<i>Intel Corp. v. PACT XPP Schweiz AG</i> , 61 F.4th 1373 (Fed. Cir. 2023)	57, 65
<i>KSR Int’l Co. v. Teleflex Inc.</i> , 550 U.S. 398 (2007).....	56, 64
<i>Nidec Motor Corp. v. Zhongshan Broad Ocean Motor, Co.</i> , 868 F.3d 1013 (Fed. Cir. 2017)	20
<i>Par Pharmaceutical, Inc. v. TWI Pharmaceuticals, Inc.</i> , 773 F.3d 1186 (Fed. Cir. 2014)	57
<i>In re Peterson</i> , 315 F.3d 1325 (Fed. Cir. 2003)	44, 54
<i>Phillips v. AWH Corp.</i> , 415 F.3d 1303 (Fed. Cir. 2005) (<i>en banc</i>)	20
Statutes	
35 U.S.C. §102(a)(1).....	3
35 U.S.C. §103.....	3, 4
35 U.S.C. § 314(a)	4
Other Authorities	
37 C.F.R. 42.104(b)(4)-(5).....	20
37 C.F.R. § 42.100(b)	20

EXHIBIT LIST

Exhibit	Reference
1001	U.S. Patent No. 10,792,416 (“’416 patent”)
1002	File History of the ’416 patent
1003	Declaration of Dr. Gary Fletcher in Support of Petition
1004	U.S. Patent No. 4,898,675 (“Lavender”)
1005	“Calculations in Apheresis” (“Neyrinck”)
1006	U.S. Patent Publication No. 2002/0033370 (“Bainbridge”)
1007	U.S. Patent Publication No. 2011/0097344 (“Darashkevich”)
1008	U.S. Patent No. 8,075,468 (“Min”)
1009	U.S. Patent Publication No. 2017/0029762 (“Turgut”)
1010	U.S. Patent No. 6,296,602 (“Headley”)
1011	U.S. Patent No. 9,370,324 (“Barrett”)
1012	“Membrane versus centrifuge-based therapeutic plasma exchange: a randomized prospective crossover study,” Carsten Hafer et al., <i>Int. Urol. Nephrol</i> (2016) 48:133-138; Springer Science+Business Media Dordrecht 2015.
1013	“Volume Limits – Automated Collection of Source Plasma,” November 4, 1992, Memorandum issued by the FDA Center for Biologics Evaluation and Research, Docket Number FDA-2013-S-0613.
1014	Bruce C. McLeod, MD, et al., “Apheresis: Principles and Practice,” 3rd Edition, AABB Press 2010.
1015	Sergeant SR, Ashurst JV. Plasmapheresis. [Updated 2023 Jul 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560566/?report=printable
1016	Japanese Patent Publication No. JP 2002-282352 A and certified Japanese to English translation (“Takagi”)
1017	J. Klespitz and L. Kovács, “Identification and control of peristaltic pumps in hemodialysis machines,” 14th IEEE International Symposium on Computational Intelligence and Informatics 83-87 (2013)
1018	Curriculum Vitae (“CV”) of Dr. Gary D. Fletcher

Terumo BCT (“Petitioner”) requests *inter partes* review (“IPR”) of claims 1-30 of U.S. Patent No. 10,792,416 (the “’416 patent”) (EX1001).

I. Mandatory Notices

A. Real Parties-In-Interest

Petitioner identifies itself as the real party-in-interest (“RPI”).

B. Related Matters

The ’416 patent is currently asserted against Petitioner by Patent Owner in *Haemonetics Corp. v. Terumo BCT, Inc.*, No. 1:25-cv-1409 (D. Colo. filed May 5, 2025) Petitioner filed petitions requesting *inter partes* review of Patent Nos. 11,738,124 (IPR2025-01374) and 10,758,652 (IPR2025-01391) and post grant review of 12,186,474 (PGR2025-00077) and 12,171,916 (PGR2025-0078). Petitioner is concurrently filing several other petitions for *inter partes* review and post grant review.

C. Counsel

Petitioner is filing a Power of Attorney appointing the practitioners associated with Customer Number 53,065. Petitioner designates the following lead and back-up counsel:

Lead Counsel	Back-up Counsel
John M. Caracappa (Reg. No. 43,532) Steptoe LLP 1330 Connecticut Ave NW Washington, DC 20036 Telephone: (202) 429-3000 Email: jcaracappa@steptoe.com	Katherine D. Cappaert (Reg. No. 71,639) Matthew Y. Sim (Reg. No. 77,422) Daniel Scott Chappell (Reg. No. 76,333) Steptoe LLP 1330 Connecticut Ave NW Washington, DC 20036

	Telephone: (202) 429-3000 Email: kcappaert@step toe.com msim@step toe.com schappell@step toe.com
--	---

D. Service Information

Post and hand delivery: Steptoe LLP
1330 Connecticut Ave NW
Washington, DC 20036
Telephone: (202) 429-3000
Email: terumo_bct@step toe.com

Please address all correspondence to counsel identified above. Petitioner consents to electronic service by email at the above-identified email addresses and:
terumo_bct@step toe.com.

II. Fees

Petitioner is concurrently electronically submitting the required fees for this Petition. The Board is authorized to charge Steptoe LLP's deposit account, No. 53065, for any fee deficiency.

III. Certification of Grounds of Good Standing

Petitioner certifies that the '416 patent is available for IPR and that Petitioner is not estopped or barred from requesting this IPR.

IV. Identification Of Challenge And Relief Requested

Petitioner requests *inter partes* review and cancellation of claims 1-30 of the '416 Patent.

A. Identification Of Prior Art

The following references are pertinent to the grounds of unpatentability explained below:

- U.S. Patent No. 4,898,675, issued February 6, 1990 (“Lavender”), prior art under at least 35 U.S.C. §102(a)(1)¹.
- “Calculations in Apheresis,” *Journal of Clinical Apheresis* 30:38–42 (2015) (“Neyrinck”), prior art under at least 35 U.S.C. §102(a)(1).
- U.S. Patent Publication No. 2002/0033370, published March 21, 2002 (“Bainbridge”), prior art under at least 35 U.S.C. §102(a)(1).
- U.S. Patent Publication No. 2011/0097344, published April 28, 2011 (“Darashkevich”), prior art under at least 35 U.S.C. §102(a)(1).
- U.S. Patent No. 8,075,468, issued December 13, 2011 (“Min”), prior art under at least 35 U.S.C. §102(a)(1).
- U.S. Patent Publication No. 2017/0029762, published February 2, 2017 (“Turgut”), prior art under at least 35 U.S.C. §102(a)(1).
- U.S. Patent No. 6,296,602, issued October 2, 2001 (“Headley”), prior art under at least 35 U.S.C. §102(a)(1).
- U.S. Patent No. 9,370,324, issued June 21, 2016 (“Barrett”), prior art under at least 35 U.S.C. §102(a)(1).

¹ References to 35 U.S.C. §103 are to the post-AIA statutory framework.

B. Statutory Grounds of Unpatentability

Petitioner requests cancellation of '416 patent claims 1-30 under 35 U.S.C. §103 based on the following Grounds.

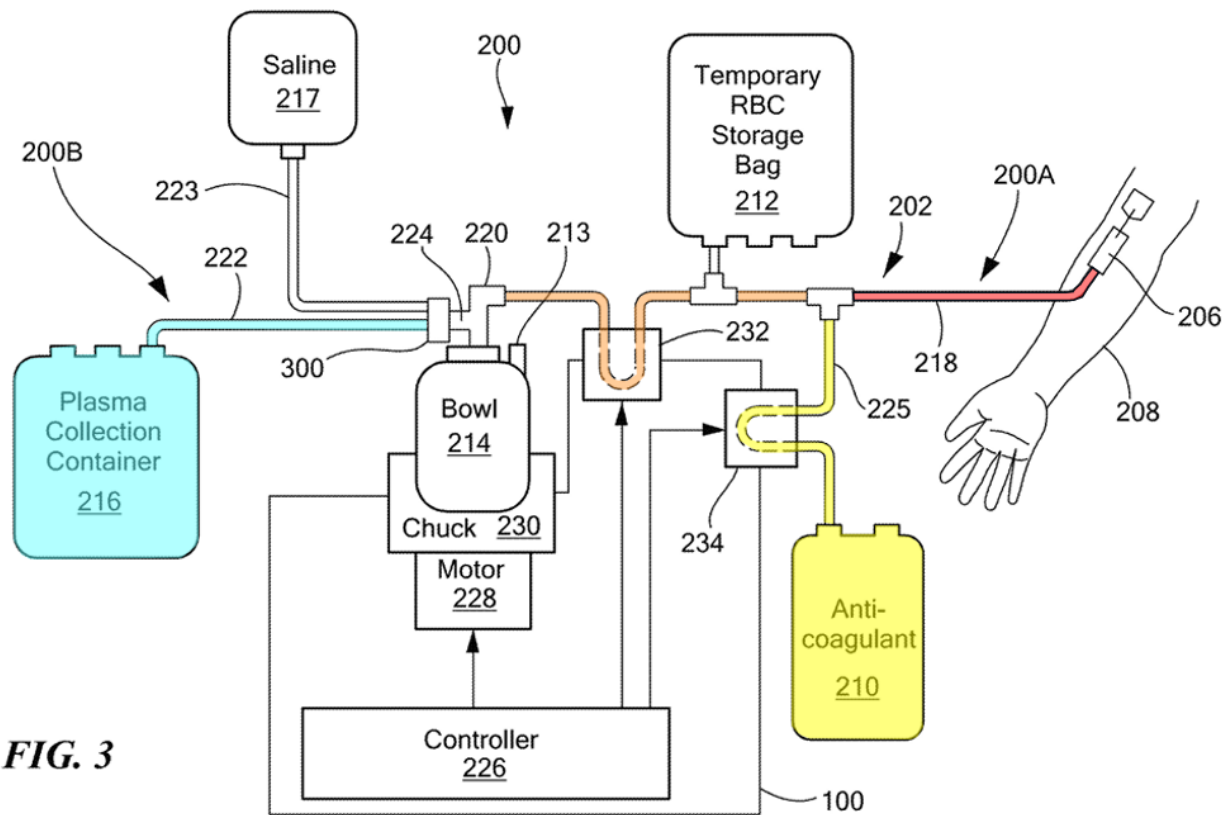
Ground	Claims	Basis
I	1, 7, 9, 11, 14, and 15	Obvious over Lavender in view of Neyrinck
II	2-6, 17-22, 24, 26, 28, and 29	Obvious over Lavender in view of Neyrinck, and Bainbridge
III	8	Obvious over Lavender in view of Neyrinck, and Darashkevich
IV	23	Obvious over Lavender in view of Neyrinck, Bainbridge, and Darashkevich
V	10 and 13	Obvious over Lavender in view of Neyrinck, and Min
VI	25	Obvious over Lavender in view of Neyrinck, Bainbridge, and Min
VII	12	Obvious over Lavender in view of Neyrinck, Min, and Turgut
VIII	27	Obvious over Lavender in view of Neyrinck, Bainbridge, Min, and Turgut
IX	16 and 30	Obvious over Lavender in view of Neyrinck, Bainbridge, Headley, and Barrett

This Petition demonstrates that there is a reasonable likelihood that Petitioner will prevail with respect to at least one of the challenged claims. *See* 35 U.S.C. § 314(a).

V. '416 Patent Overview

A. The '416 Patent is Related to Plasma Apheresis

The '416 patent, which recently issued on October 6, 2020, relates to a “system and method for collecting plasma” in blood apheresis systems. EX1001, Title, 1:13-15. “Apheresis is a procedure in which individual blood components,” *e.g.*, plasma and red blood cells, “can be separated and collected from whole blood.” EX1001, 1:18-20. The '416 patent relates to plasma apheresis (plasma collection). Figure 3 shows one embodiment of a plasma apheresis system. EX1003, ¶¶30-36.



EX1001, Fig. 3 (annotated); EX1003, ¶36.

Plasma apheresis involves withdrawing whole blood from a donor using venous access device 206. EX1001, 7:62-65. Pump 232 “causes the whole blood to be drawn from the donor” through an inlet line 218 (red) and pump 234 adds a fixed

amount of anticoagulant “into the whole blood” through “[a]n anticoagulant line” 225 (yellow) connected “to the inlet line.” EX1001, 8:60-65, 9:1-7. Anticoagulant is introduced in fixed proportions to the whole blood to prevent blood clotting See EX1013. “[T]he anticoagulant mixes with the plasma component” because “the osmolarity of the red blood cells prevents the anticoagulant . . . from entering/remaining with the red blood cells.” EX1001, 10:25-28; EX1003, ¶30-35, 37.

Then, the mixture (orange) of anticoagulant and “withdrawn whole blood ... enters a blood component separation device,” *e.g.*, centrifuge bowl 214, which “separates the whole blood into its constituent components,” *e.g.*, “plasma, platelets, red blood cells (“RBCs”) . . . [and] white blood cells.” EX1001, 7:32-7:43, 9:17-27. The donor’s plasma, *i.e.*, pure plasma, with anticoagulant introduced during collection, exits the blood component separation device and is collected and stored in a collection container (*e.g.*, a bag, in blue above). EX1001, 4:5-12, 7:62-8:6. The anticoagulant and pure plasma combination is known as anticoagulated plasma or plasma product. EX1001, 12:39-40; EX1003, ¶30-35, 38.

The FDA established guidelines regarding how much plasma any individual donor can donate considering donor parameters, like weight, hematocrit, and sex. See EX1013; EX1003, ¶30-35, 39.

B. The ’416 Patent’s Purported Invention

The '416 patent purports to solve problems associated with “determin[ing] the total volume of plasma that has been collected” from a donor after the withdrawn whole blood is mixed with anticoagulant by tailoring the volume of plasma collected based on the donor’s plasma volume and a target percentage of plasma to collect, and considering a donor’s hematocrit level and the amount of anticoagulant added into the system. EX1001, 1:44-50, 1:60-2:18, 6:54-67; EX1003, ¶40.

Donors have different hematocrit levels, which affect the donor’s plasma amount. EX1001, 10:37-39. The differing hematocrit levels also affect the volume of anticoagulant in a plasma collection container. EX1001, 10:46-49. The '416 patent thus discloses that controller 226 may determine the donor’s plasma volume based on hematocrit and then calculate the target volume of plasma to collect. EX1001, 13:43-46. Controller 226 may also use the % AC equation below, which uses a predetermined ratio of anticoagulant to anticoagulated whole-blood and the donor’s hematocrit to calculate the percentage of anticoagulant in the plasma container. EX1001, 10:58-11:28. In the % AC equation, “AC” is the inverse of the predetermined ratio of anticoagulant per unit of anticoagulated whole blood (*e.g.*, “AC” would be 16 if the ratio of anticoagulant to anticoagulated whole blood was 1:16) and Hct_D is the donor’s hematocrit. EX1001, 10:58-11:28. Anticoagulated whole blood is extracted blood mixed with anticoagulant. EX1003, ¶41.

$$\% AC = \frac{1}{1 + (AC - 1)(1 - Hct_D)}$$

Controller 226 also uses a weight sensor to monitor the collection container's weight and uses the weight to determine the total volume of liquid in the collection container. EX1001, 9:64-66, 10:32-36. The controller uses this total volume to calculate the anticoagulant and pure plasma volumes in the collection container. EX1001, 10:50-11:46. The '416 patent first calculates the anticoagulant volume. EX1001, 11:29-46. It then calculates the pure plasma volume by subtracting the anticoagulant volume from the total volume of liquid in the collection container. EX1001, 11:29-46; EX1003, ¶42.

The '416 patent also discloses two alternative methods of determining the amount of anticoagulant in the collection bag that do not consider a donor's hematocrit. These determine the anticoagulant in the collection bag by: (i) monitoring the volume of anticoagulant added to the system based on the number of rotations of the anticoagulant pump,² and (ii) measuring the change in weight of the

² The red blood cells' osmolarity prevents the anticoagulant from mixing with it, so essentially all the anticoagulant exits the bowl 214 and is collected within the plasma collection container 216. EX1001, 10:67-11:4. Thus, subtracting the anticoagulant

anticoagulant container. EX1001, 11:11-46. In both methods, the volume of added anticoagulant is used to calculate the volume of pure plasma collected in the plasma collection container by subtracting the added anticoagulant volume from the total volume in the collection container. EX1001, 10:67-11:4, 11:11-28, 12:7-22; EX1003, ¶43.

Of the three above methods, only the first, considers the donor's hematocrit. That method does not, however, use an amount of anticoagulant collected within the plasma collection container or supplied to the system to determine a percentage of anticoagulant within the collected plasma. EX1001, 12:50-54; EX1003, ¶44.

The '416 patent repeats each method to determine the pure plasma volume “until the calculated volume of pure plasma collected within the plasma collection container equals the target plasma collection volume,” *e.g.*, the volume determined by calculating “the total volume of plasma to collect on the individual donor (*e.g.*, based on their height, weight, hematocrit, blood volume and/or plasma volume).” EX1001, 12:61-65. When the system reaches a target volume of pure plasma, the controller “stops the draw of whole blood from the subject and reverses the direction

volume added to the system from the total volume in the collection container estimates the volume of pure plasma in the collection container. EX1001, 10:67-11:4, 12:7-22; EX1003, ¶43.

of the blood ... to draw the RBCs (and other components)” from the blood component separation device back to the donor. EX1001, 11:51-56; EX1003, ¶¶45-46.

C. Prosecution History

Application No. 15/793,339, which resulted in the ’416 patent, was filed on October 25, 2017. EX1001, Cover. The ’416 patent claims priority, as a continuation-in-part application, to U.S. Patent No. 10,758,652 (the “’652 patent”), which was filed on May 30, 2017. EX1001, 1:4-7. Accordingly, the effective filing date of the ’416 patent is May 30, 2017 for the disclosures overlapping with the ’652 patent. The effective filing date with respect to the new matter introduced in the ’416 patent is October 25, 2017.

On July 15, 2020, the Examiner issued a Notice of Allowance, as the first action on the merits, indicating claims 1-9 and 11-24 were allowed. EX1002, 07/15/2020-Allowance, PTOL-37. The reason for allowance was because the prior art failed to disclose that “a volume of anticoagulant in the collected plasma component is calculated in real-time, as the plasma is being collected.” EX1002, 07/15/2020-Allowance, p.2.

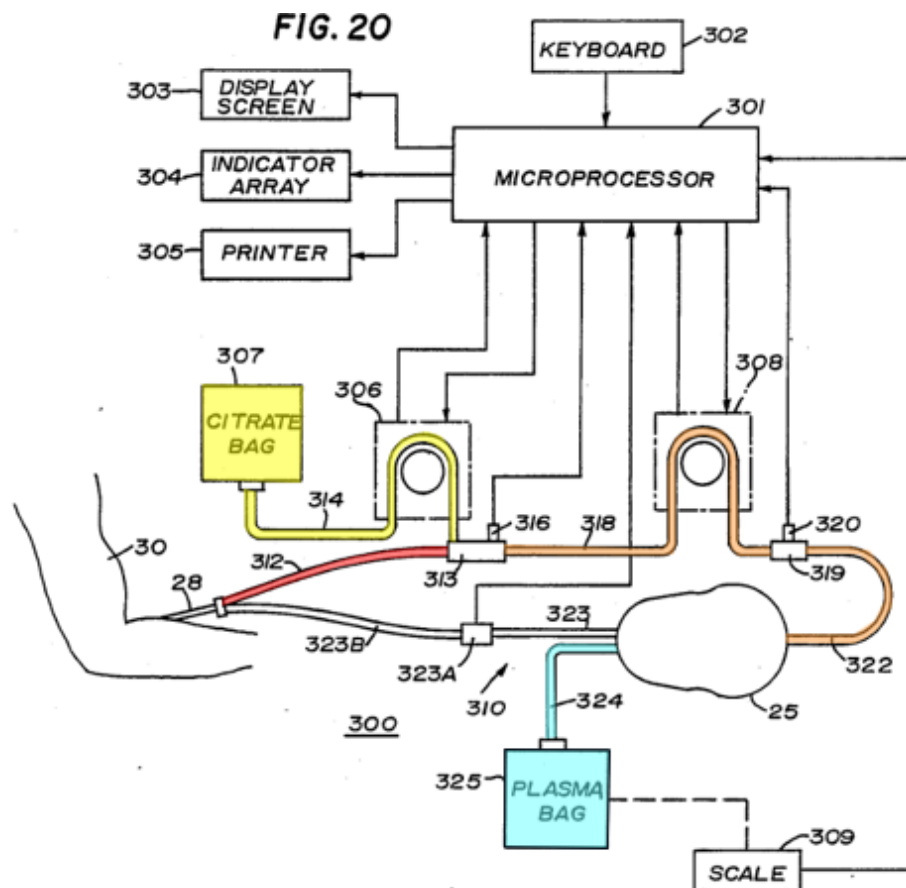
On July 22, 2020, the Examiner issued a Corrected Notice of Allowance, indicating claims 1-9, 11-24, and 26-32 were allowed. EX1002, 07/22/2020-Allowance, PTOL-37. The ’416 patent issued on October 6, 2020. EX1001, Cover.

VI. Prior Art Overview

A. Overview of Lavender

Lavender discloses “a system, method and device for continuously fractionating blood in situ.” EX1004, Abstract. Lavender recognized the need to track the anticoagulant volume collected during a plasma collection procedure to “accurately, safely and economically collect[] plasma from a source of blood.” EX1004, 3:26-28; EX1003, ¶47.

Figure 20 illustrates Lavender’s automatic system 300 for fractionating blood. EX1004, 16:34-53.



EX1004, Fig. 20 (annotated).

In Lavender's system 300, needle or catheter 28 is used to draw a donor's whole blood, which is then mixed with citrate (anticoagulant) pumped from citrate bag 307. EX1004, 16:57-17:2, 16:45-47. System 300 then pumps the whole blood and anticoagulant mixture to blood fractionator 25, which separates the anticoagulated whole blood into plasma and other blood fractions. EX1004, 5:42-52. The plasma and anticoagulant mixture exits the blood separation device through the plasma line and is collected in plasma bag 325. EX1004, 17:14-16; EX1003, ¶49.

Lavender's system performs real-time calculations during the collection process. These calculations account for donor parameters, like hematocrit, and a fixed anticoagulant to plasma ratio, which, in turn, relates to a fixed anticoagulant to anticoagulated whole blood ratio. See EX1004, 22:35-39, cols. 41, 42. They also account for the collected plasma and anticoagulant mixture weight during the collection process. These calculations are used in real-time calculations of the pure plasma and anticoagulant volumes in the plasma collection bag. EX1004, 20:55-68; EX1003, ¶50.

The table below shows several variables used and/or calculated in Lavender's system:

Variable	Description
----------	-------------

CF (conversion factor)	Predetermined ratio (or percentage) of anticoagulant to incoming plasma
QB	Blood flow from donor
TQB	Total blood flow
$HCTD$	Donor's hematocrit
QP	Plasma flow
TQP	Total plasma flow
QCP	Citrate pump rate
TQC	Total citrate (anticoagulant) flow
$TDPF$	Total dilute plasma (total fluid) in the collection container
TPF	Total plasma filtered (pure plasma) volume in the collection container
TCF	Total citrate (anticoagulant) volume in the collection container

These variables are used during the collection process to monitor the amount of plasma collected. For example, plasma flow (QP) is calculated based on the donor's blood flow (QB) and hematocrit ($HCTD$). EX1004, 41:4-44:42. QP is used to calculate the citrate pump rate (QCP) by multiplying QP by conversion factor (CF). QCP is used to calculate total citrate flow (TQC). See EX1004, 41:4-44:42.

The total plasma volume in the collection container is calculated in real time based on the total fluid volume in the collection container, determined by the container weight, and plasma dilution factor (*PDF*). See EX1004, 41:4-44:42. The total citrate volume in collection container (*TCF*) is then calculated in real time based on the total plasma volume in the collection container (*TPF*) and conversion factor (*CF*). See EX1004, 41:4-44:42; EX1003, ¶52.

Lavender's microprocessor repeatedly performs weight measurements and run-time calculations and displays updated values approximately every two seconds. EX1004, 20:55-68. Lavender's system determines the relationship (ratio) between the pure plasma volume and the anticoagulant volume in the collection container. See EX1004, 41:4-44:42. It uses this to determine the pure plasma volume. See EX1004, 41:4-44:42. Accordingly, Lavender discloses determining pure plasma volume based on anticoagulant volume. If any additional conversion or calculation is required, a POSITA would readily understand how to convert between the two volumes using the same relationship. EX1003, ¶53.

Lavender executes a main loop of the algorithm until the total plasma filtered (*TPF*) in plasma bag 325 is equal to or greater than a determined maximum total plasma volume to collect (*MAXPF*), as determined using a donor's weight. EX1004, cols. 43-44, claim 33; EX1003, ¶54. In Lavender, the total plasma volume to collect is 18% of the calculated donor circulating plasma volume. EX1004, 20:10-14, 22:35-

46, 41:1-44:42 (Table VI). And the donor circulating plasma volume is calculated based on 5% of donor weight. EX1004, 20:10-14, 22:35-46, 41:1-44:42 (Table VI); EX1003, 55.

B. Overview of Neyrinck

Neyrinck emphasizes the importance of accurately determining total blood volume (TBV) in apheresis procedures to ensure safety and efficacy. EX1005, pp.38-39. Because TBV varies significantly among individuals based on several physiological variables, Neyrinck outlines multiple methods for calculating TBV—incorporating height, weight, sex, age, and BMI. EX1005, pp.38-39. For example, Neyrinck identifies Nadler’s formula, widely used in apheresis machines, which calculates TBV based on gender, height, weight, and age. EX1005, p.39. Another method uses body mass index (BMI), calculated from weight and height, and assigns a blood volume per kilogram of body weight depending on the BMI category. EX1005, p.40; EX1003, ¶56.

Neyrinck explains that calculating TBV, extracorporeal volume, and total plasma volume of a donor (TPV) is needed to produce an optimal product while minimizing donor risk. EX1005, p.38. Determining TPV requires both TBV and hematocrit (Hct) values as hematocrit influences a donor’s TPV. EX1005, p.40. For example, where a donor has “a TBV of 5,000 ml and has an Hct of 50% there will be 2,500 mL of plasma, and in case of an Hct of 30% 3,500mL.” EX1005, pp.39-40.

This 1,000 mL difference could influence the duration of a plasma exchange procedure. EX1005, pp.39-40; EX1003, ¶57.

C. Overview of Bainbridge

Bainbridge relates to “a blood component separation device (*e.g.*, a centrifuge)” that separates whole blood into “various blood components” including “plasma and red blood cells.” EX1006, Abstract, ¶0003. Bainbridge’s apheresis system is designed to improve “collection efficiency” by maximizing “the amount of a particular blood component type” that is collected. EX1005, ¶0006; EX1003, ¶58.

Bainbridge improves collection efficiency by “continuously and instantaneously monitor[ing] the quantity of RBCs collected ... to determine the instantaneous hematocrit ... of the donor/patient.” EX1006, ¶0302. Bainbridge uses the change in hematocrit to provide “feed[back] adjustment control over certain flow rates” and achieve “the target amount of separated plasma.” EX1006, ¶0302-303. Bainbridge describes that “several advantages can be realized utilizing these procedures for... plasma collections. Such advantages include: ...reduced time requirements for... plasma collections.” EX1006, ¶0304; EX1003, ¶59.

Bainbridge’s system also administers replacement fluid, such as saline solution, “within the limited range of 80% to 120%” of the donor’s fluid balance

percentage to help maintain donor hydration and prevent hypovolemia. EX1006, ¶¶0278, 0282, 0286; EX1003, ¶60.

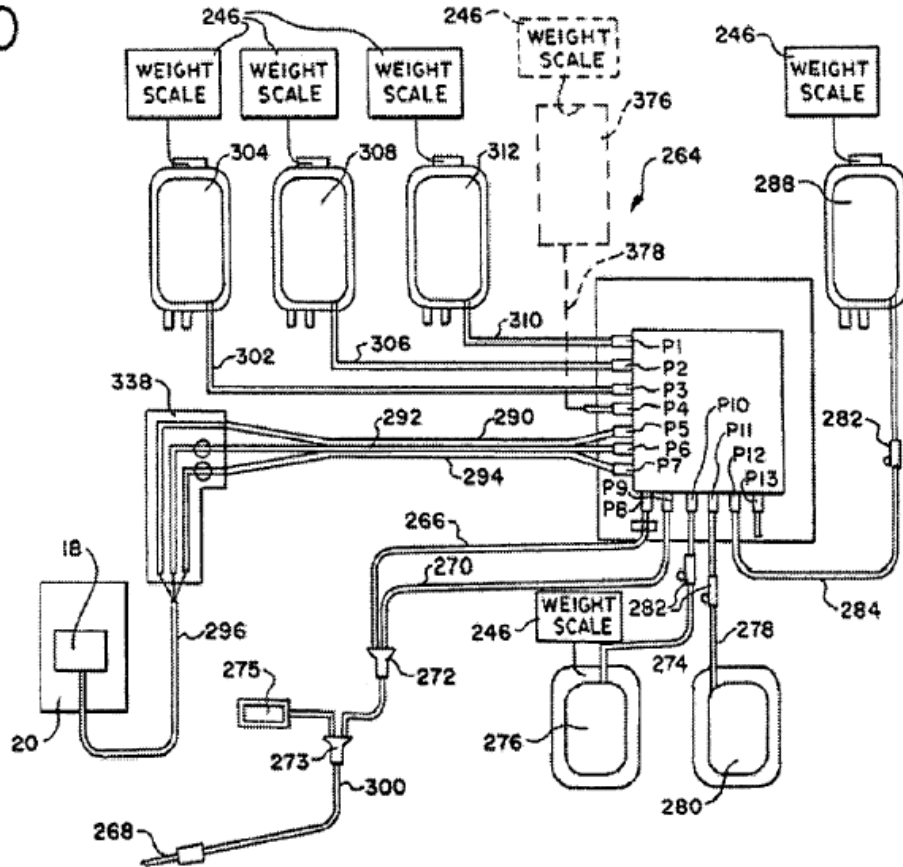
D. Overview of Darashkevich

Darashkevich discloses methods for removing pathogenic autoantibodies from a patient's circulation using apheresis. EX1007, ¶0083. In certain embodiments, plasmapheresis removes between approximately 15% to 30% of the patient's total circulating plasma, effectively reducing the concentration of harmful autoantibodies. EX1007, ¶0083. Darashkevich's procedure uses discontinuous flow centrifugation using a single venous catheter. EX1007, ¶0083; EX1003, ¶61.

E. Overview of Min

Min discloses blood processing systems for separating plasma from whole blood. EX1008, 7:4-8:5. Min's plasma collection procedures include a collection cycle, and pre- and post-collection cycles, where the system's tubing is primed by "convey[ing] a predetermined volume of anticoagulant . . . into the in-process container" during the pre-collection cycle. EX1008, 22:41-43, 32:16-18; EX1003, ¶62. Min's Figure 10 shows Min's system, which performs plasma collection.

FIG. 10



In Min, weight sensors 246 track weight changes and derive fluid processing volumes, including volume changes in anticoagulant container 276 and plasma collection container 304. EX1008, 11:52-55, 17:17-22; EX.1003, ¶63.

F. Overview of Turgut

Turgut discloses separation systems that effectively separate biological material, like blood components, using centrifugal force. EX1009, Abstract. Turgut uses a centrifuge to separate blood into components and a volume detector to determine a total volume of fluid within, for example, the centrifuge's separation chamber. EX1009, ¶0073; EX1003, ¶64.

G. Overview of Headley

Headley discloses systems and methods for collecting components from whole blood, including platelets suspended in plasma using a centrifuge. EX1010, Abstract; 2:3-7. Headley also uses an array of optical sensors with a control unit to determine red blood cell volume in a blood separation system. EX1010, 4:48-64; EX1003, ¶65.

H. Overview of Barrett

Barrett discloses a hemodialysis patient data acquisition and management system for monitoring blood separation procedures, like hemodialysis. EX1011, 4:14-67. Barrett describes several techniques to monitor hematocrit, including for real-time monitoring during hemodialysis. EX1011, 2:23-57. Barrett also discloses determining a patient's hematocrit by dividing a blood sample's calculated total red blood cell volume by the blood sample's total volume. EX1011, 2:45-49; EX1003, ¶66.

VII. Level Of Ordinary Skill

A person having ordinary skill in the art ("POSITA") would have had, as of the earliest claimed filing date of May 30, 2017, a bachelor's degree in biomedical engineering, or a related field, such as physical sciences, physics, computer engineering, electrical engineering, or the like, and a minimum of two to three years of experience related to blood separation devices or blood processing devices. A

higher level of education or specific skill might make up for less experience, and vice versa. EX1003, ¶29.

VIII. Claim Construction

The claims should be construed “in accordance with the ordinary and customary meaning of such claims as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent.” 37 C.F.R. § 42.100(b); *see also Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (*en banc*). Petitioner is unaware of any “prior claim construction determination” related to the ’416 patent. *See* 37 C.F.R. § 42.100(b). EX1003, ¶19.

Moreover, the Board “need only construe terms ‘that are in controversy, and only to the extent necessary to resolve the controversy.’” *Nidec Motor Corp. v. Zhongshan Broad Ocean Motor, Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)). Petitioner believes the Challenged Claims need no construction to demonstrate they are unpatentable.

IX. Detailed Grounds Explanation

The sections below, as supported by Dr. Fletcher’s Declaration, demonstrate how the claims are unpatentable. 37 C.F.R. 42.104(b)(4)-(5).

A. Ground I: Claims 1, 7, 9, 11, 14, and 15 are rendered obvious over Lavender in view of Neyrinck

1. Reasons to Combine Lavender and Neyrinck

A POSITA would have found it obvious and would have been motivated to combine Lavender's system with Neyrinck's teachings and would have had a reasonable expectation of success because 1) both relate to the same well-known technologies, 2) both apply substantially similar techniques to achieve similar results, and 3) the intended functionality of Lavender would remain substantially the same in the proposed combination. EX1003, ¶67.

First, a POSITA would have been motivated to combine Lavender and Neyrinck to improve the accuracy and donor-specific customization of Lavender's plasma collection volumes. EX1003, ¶68. Lavender calculates plasma collection volumes based on donor-specific data. For example, it calculates a donor's circulating plasma volume, which is 5% of the donor's weight, and then collects 18% of this volume. EX1004, 22:35-46; EX1003, ¶68.

Similarly, Neyrinck teaches calculating a donor's total plasma volume (TPV) based on donor-specific data when collecting a fixed volume of plasma. EX1005, pp.39-40. Neyrinck teaches how to calculate TPV using the donor's total blood volume (TBV)—calculated based on donor weight, height and hematocrit—and explains that hematocrit can affect the plasma volume being collected. EX1005, pp.39-40. *See also* §VI.B. A POSITA would readily recognize that incorporating Neyrinck's TPV calculation—based on TBV and hematocrit—into Lavender's system, would allow Lavender's system to calculate a more accurate and

individualized target plasma collection volume because it would consider individualized information like height and hematocrit. See §VI.B. EX1003, ¶69.

Second, Lavender and Neyrinck both relate to plasma apheresis and using donor-specific information to determine donor plasma volume. EX1003, ¶70. Lavender collects plasma based on a donor's circulating plasma volume; calculated using the donor's weight. EX1004, 1:12-13, 22:35-46. Similarly, Neyrinck teaches collecting plasma based on a donor's weight, height, and hematocrit. EX1005, p.39. Therefore, a POSITA would have had a reasonable expectation of success combining Lavender with Neyrinck because both relate to the same well-known technologies of using donor information to calculate donor plasma volume. EX1003, ¶70.

Third, Lavender and Neyrinck apply substantially similar techniques to achieve similar results. Lavender calculates the donor's circulating plasma volume as 5% of bodyweight and collects 18% of that volume. EX1004, 1:12-13, 22:35-46. Neyrinck similarly utilizes donor data like weight and height to calculate TBV and uses the calculated TBV and hematocrit to calculate TPV. EX1005, p.39-40. Both systems similarly use donor-specific information to determine a safe and effective plasma collection volume. EX1004, 3:26-28; EX1005, p.38. Thus, both references consider donor-specific input to determine how much plasma can be safely and efficiently collected. EX1003, ¶71. Because both systems are focused on achieving

similar results—determining the total plasma collection volume—and consider similar variables in determining that amount, a POSITA would have had a reasonable expectation of success in implementing Neyrinck’s TPV calculation in Lavender’s system. EX1003 ¶71.

Further, Lavender’s functionality would remain substantially the same in the proposed combination. As discussed above, Lavender calculates collection volumes based on donor-specific information like weight and hematocrit. EX1004, 20:10-21; 22:35-46. Neyrinck’s formulas determine TBV and TPV using similar donor inputs (*e.g.*, weight, height, and hematocrit). EX1005, p.39-40. Thus, Neyrinck’s plasma collection calculations could be readily implemented in Lavender’s computational framework. EX1003, ¶72. In one such example, Lavender’s system could implement Neyrinck’s TPV calculation, which considers donor hematocrit, to more accurately calculate a target plasma collection volume and improve collection yield. EX1003, ¶72. Additionally, Lavender recognizes that “various modifications and alterations may be made therein without departing from the true scope and spirit of the present invention.” EX1004, 45:1-7. Therefore, a POSITA would have had a reasonable expectation of success in combining Lavender with Neyrinck. EX1003, ¶72.

2. Claim 1

- a. 1[preamble] A method for collecting plasma comprising:**

To the extent the preamble is limiting, Lavender discloses a system, method and device for fractionating blood “to **collect blood substances, such as plasma.**” EX1004, Abstract, 1:12-13, claim 1 (“A method of collecting plasma...”), 5:42-49, 1:48-56; EX1003, ¶73.

b. 1[a] determining a weight and height of a donor;

Lavender determines a donor’s weight through “entry and validation of donor data, including ... **donor weight in pounds.**” EX1004, 20:10-14, Abstract; EX1003, ¶74.

Neyrinck calculates a donor’s TBV using the donor’s **weight** and **height**, according to Nadler’s formula. EX1005, pp.38-40.

As discussed in §IX.A.1, a POSITA would have been motivated to incorporate, and would have had a reasonable expectation of success incorporating, Neyrinck’s use of donor’s weight and height in Lavender’s system to calculate TBV and then more accurately calculate donor plasma volume. EX1003, ¶76.

c. 1[b] determining a hematocrit of the donor;

Lavender determines a hematocrit of the donor through “entry and validation of donor data, including ... **donor hematocrit in percent.**” EX1004, 20:10-14; EX1003, ¶77.

Neyrinck discloses calculating a donor’s TPV using a donor’s hematocrit and TBV. EX1005, pg. 39-40, Fig. 3.

d. 1[c] calculating a donor plasma volume based, at least in part, on the weight and height of the donor and the hematocrit of the donor;

Lavender in view of Neyrinck renders obvious limitation 1[c]. EX1003, ¶79.

Lavender calculates a **donor's circulating plasma volume** as 5% of donor **weight**. Lavender then collects 18% of that calculated volume. EX1004, 22:39-46; EX1005, 20:10-14, 22:35-46, 41:1-44:42 (Table VI).

Neyrinck discloses calculating TBV based on donor **height** and **weight** using either Nadler's formula or BMI. EX1005, p.39. EX1003, ¶81. After calculating the TBV, Neyrinck calculates a donor's total plasma volume (**TPV**) based on the donor's TBV and **hematocrit** (Hct) using the equation:

$$TPV = TBV * (1 - Hct)$$

EX1005, p.39-40, Fig. 3. Thus, Neyrinck's TPV calculation is based on the donor's weight and height (used to calculate TBV) and hematocrit. EX1003, ¶81.

As discussed in §IX.A.1, a POSITA would have been motivated to incorporate Neyrinck's TPV calculation into Lavender's system to more accurately calculate a donor's plasma volume. EX1003, ¶82. Neyrinck's method uses donor inputs already considered by Lavender (weight and hematocrit) and also uses the donor's height to yield a more individualized TBV. EX1005, p.38-40. Thus, a POSITA would recognize that replacing Lavender's simplified 5% body weight estimate for TPV with Neyrinck's TPV calculation based on both height and

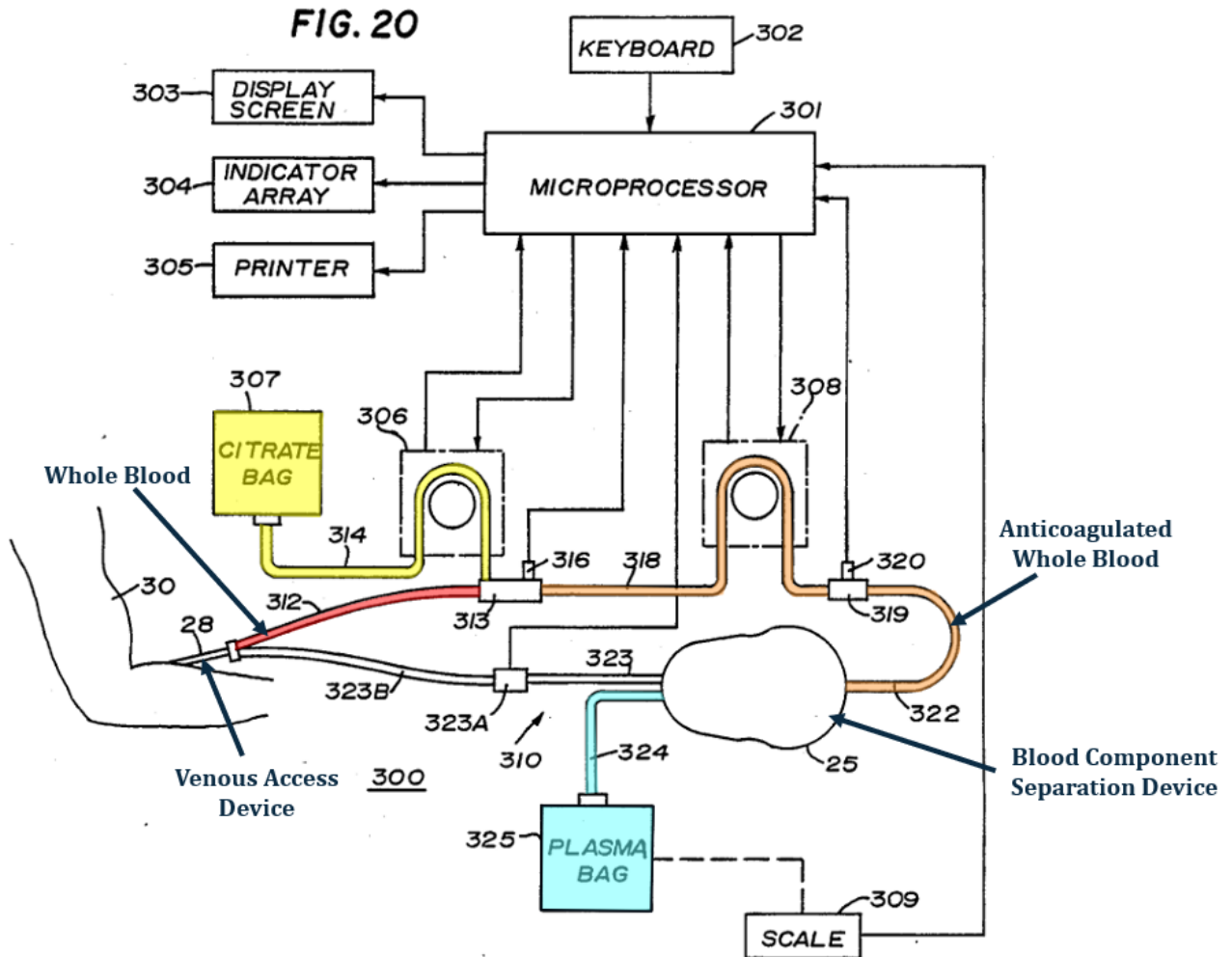
hematocrit would improve donor safety and product yield. EX1003, ¶82. Also, a POSITA would have had a reasonable expectation of success when incorporating Neyrinck's donor plasma volume into Lavender's system. See §IX.A.1; EX1003, ¶82.

- e. **1[d] calculating a target plasma collection volume based, at least in part, on the calculated donor plasma volume and a target percentage of plasma;**

Lavender calculates a target plasma collection volume that is 18% of a donor's circulating plasma volume. EX1004, 22:39-46. This target plasma collection volume is thus based, at least in part, on Neyrinck's TPV calculation and the 18% target percentage of plasma. EX1003, ¶83.

- f. **1[e] withdrawing whole blood from the donor through the venous-access device and a first line, the first line connected to a blood component separation device;**

Lavender withdraws whole blood through the venous-access device. A pump “pump[s] blood from the donor” through needle 28, tubes 312, 318, 322, and into fractionator 25, shown below in Figure 20. EX1004, 5:18-22, Fig. 20; EX1003, ¶84.



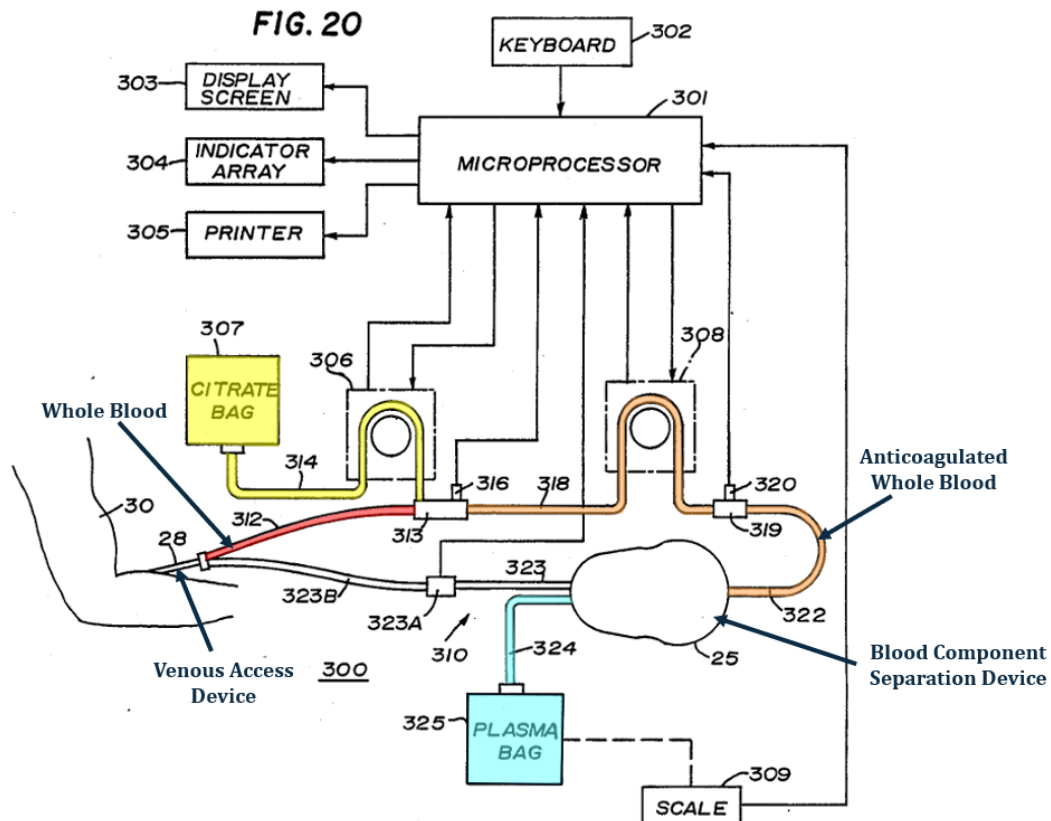
EX1004, Fig. 20 (annotated). The drawn blood is whole blood because it is a mixture of “a variety of blood fractions.” EX1004, 5:45; EX1003, ¶84.

The draw line is connected to blood fractionator 25, as “[t]he blood fractionator has an inlet ..., the inlet being connected to the donor by a blood tube.” EX1004, 5:13-16, Figs. 1, 20; EX1003, ¶85.

Blood fractionator 25 is a blood component separation device because “it produces a variety of blood fractions,” including plasma, from whole blood. EX1004, 5:42-45; EX1003, ¶86.

g. 1[f] introducing anticoagulant into the withdrawn whole blood through an anticoagulant line;

In Lavender, “[a] supply of anticoagulant 35 is connected to the tube 27” supplying withdrawn whole blood from the donor. EX1004, 5:22-28, Figs. 1, 20. “[A] second pump 31A ...provide[s] a predetermined flow rate ... of anticoagulant with the blood flowing from the donor 30 to the fractionator” via anticoagulant line 314. EX1004, 5:22-28, Figs. 1, 20 (tube 314); EX1003, ¶87.



EX1004, Fig. 20 (annotated).

- h. 1[g] separating the withdrawn whole blood into a plasma component and at least a second blood component using the blood component separation device;**

In Lavender, the withdrawn whole blood flows into Lavender's blood fractionator 25, which separates it into blood fractions (components), including a plasma component and a component containing red blood cells, white blood cells, and platelets (*i.e.*, at least a second blood component). EX1004, 1:21-25, 5:42-52, 10:58-11:6, Figs. 1, 20; EX1003, ¶88.

- i. 1[h] collecting the plasma component from the blood component separation device and into a plasma collection container;**

Lavender discloses that after the blood fractionator separates the components, “a plasma outlet port ... allows **plasma** to flow to a plasma collection bag” via tubing (*e.g.*, tubing 324 in Fig. 20). EX1004, 10:58-11:6, Figs. 1, 4, 15, 17, 20; EX1003, ¶89.

- j. 1[i] calculating a volume of anticoagulant in the collected plasma component as the plasma component is being collected in the plasma collection container;**

Lavender calculates a volume of anticoagulant collected in the collected plasma component as the plasma component is being collected in the plasma collection container. EX1003, ¶90. Lavender weighs the collected plasma and anticoagulant solution in plasma bag 325 (*TDPW* (total dilute plasma filtered in grams)), transmits the weight to microprocessor 301, and uses this weight to

calculate the volume of plasma and anticoagulant in plasma bag 325 (*TDPF*). EX1004, 16:34-53, 41:1-44:33 (Table VI, §5). *TDPF* is then multiplied by plasma factor *PDF*, determined using the predefined ratio of citrate added per milliliter of plasma to dilute incoming plasma to 68% of the initial concentration, to calculate the total amount of **filtered plasma (*TPF*)**. Then, *TPF* is multiplied by conversion factor (*CF*)³, which is determined using a predefined ratio of citrate added per milliliter of plasma, to calculate the volume of anticoagulant in plasma bag 325 (*i.e.*, **total citrate filtered (*TCF*)**). EX1004, 16:50-53, 22:35-46, 17:14-16, 41:1-44:33 (Table VI, §5(B)). These calculations are part of Lavender's main loop. EX1004, 41:1-44:33 (Table VI, §5(B)); EX1003, ¶90.

Lavender's microprocessor repeatedly measures *TDPW* in real-time and updates the above-identified calculated values. EX1004, 20:55-68, 41:1-44:33. Specifically, Lavender discloses "repeatedly performing the measurements and

³ Petitioner notes Table VI has two "CF" terms, (i) conversion factor (*CF*) and (ii) the rate citrate is pumped into the donor's whole blood (citrate filtered in ml/min (*CF*)). This appears to be a typographical error and a POSITA would understand that the "CF" in the total citrate filtered (*TCF*) equation is conversion factor (*CF*). EX1003, ¶90.

calculations . . . updating these values each time the program cycles through the main loop, and displaying the values in ‘Run’-message (Table V) which is updated approximately every two seconds.” EX1004, 20:55-68, 41:1-44:33; EX1003, ¶91.

Lavender thus calculates the anticoagulant volume as the plasma component is being collected in the plasma collection container by repeatedly performing the *TCF* calculation until the total plasma filtered is equal to or greater than the maximum total plasma filtered. EX1004, cols. 43-44; EX1003, ¶92.

k. 1[j] calculating a volume of pure plasma collected within the plasma collection container based, at least in part, on the calculated volume of anticoagulant in the collected plasma component; and

Lavender uses the amount of anticoagulant (citrate) added to the whole blood to calculate the total pure plasma volume collected. EX1004, 20:55-68, 41:1-44:33. As discussed with respect to claim limitation 1[i], *supra* §IX.A.2.j, Lavender calculates **total plasma filtered (*TPF*)** by multiplying the total amount of dilute plasma filtered (*TDPF*) by plasma dilution factor (*PDF*) (*i.e.*, $TPF = TDPF * PDF$). EX1004, 20:55-68, 22:35-46, 41:1-44:33. As discussed above, *PDF* is determined using the predefined ratio of citrate added per milliliter of plasma to dilute incoming plasma to 68% of the initial concentration. EX1004, 22:35-46. EX1003, ¶93.

Next, Lavender calculates the anticoagulant volume in the plasma container (*i.e.*, **total citrate filtered (*TCF*)**). See §IX.A.2.i.; EX1003, ¶94.

As shown in the annotated excerpt of §5(B) of Table VI below, the volume of pure plasma in the plasma collection bag (***TPF***) and the volume of anticoagulant in the plasma container (***TCF***) share a direct mathematical relationship. EX1004, 41:1-44:33 (Table VI, §5(B)); EX1003, ¶95.

$$\begin{array}{ll}\text{TPF}=\text{TDPF}*\text{PDF} & \text{(total plasma filtered, ml)} \\ \text{CF}=\text{PF}*\text{CF} & \text{(citrate filtered, ml/min)} \\ \text{TCF}=\text{TPF}*\text{CF} & \text{(total citrate filtered, ml/min)}\end{array}$$

That is, during collection, any change in the calculated value of the volume of anticoagulant (***TCF***) requires a corresponding change in the calculated value of the volume of pure plasma (***TPF***), and vice versa. EX1003, ¶96. Both ***TCF*** and ***TPF*** are based on the predefined ratio of citrate added per milliliter of plasma to dilute incoming plasma to 68% of the initial concentration. EX1004, 22:35-46. Accordingly, the volume of pure plasma collected in the plasma collection bag (***TPF***) is calculated in real-time based “at least in part” on the calculated volume of anticoagulant in the collected plasma component (***TCF***) because both ***TPF*** and ***TCF*** are dependent on the predefined ratio of citrate added per milliliter of plasma to dilute incoming plasma to 68% of the initial concentration and as one value changes, the other necessarily changes. EX1003, ¶96.

Lavender’s disclosure of the dependency of both ***TPF*** and ***TCF*** on the predefined ratio of citrate added per milliliter of plasma inherently discloses

calculating a volume of pure plasma collected in the plasma collection bag (***TPF***) based, at least in part, on a calculated volume of anticoagulant in the collected plasma component (***TCF***). EX1003, ¶97.⁴

Alternatively, a POSITA would have found this limitation obvious in view of Lavender’s disclosures because of (i) the interdependency between the predefined ratio of citrate added per milliliter of whole blood, *TPF* and *TCF*, and (ii) the understanding that the plasma volume in the collection bag is based, at least in part, on the volume of anticoagulant in the collection bag. EX1003, ¶¶98-99.

I. 1[k] continuing steps (e) through (i) until the calculated volume of pure plasma collected within the plasma collection container equals the target plasma collection volume.

As discussed above, Lavender performs steps (e)–(i). See §§IX.A.2.f-k. EX1003, ¶100.

When a blood separation procedure starts, Lavender’s system initializes the

⁴ The plain and ordinary meaning of the term “based, at least in part, upon” suggests that the calculation may rely on one or more methods and the ’416 patent does not disavow interpreting “based, at least in part, on” to encompass a direct relationship between the pure plasma volume in the collection container and the volume of anticoagulant in the collected plasma component. EX1003, ¶97.

system algorithm of Table VI. EX1004, 20:55-68, 41:1-44:33, Figs. 25A-25D. The Main Loop of the algorithm is repeated by “introducing anticoagulant to the blood from which the plasma is to be collected ... separating plasma from the extracted blood ... **until a predetermined ... volume of plasma has been collected.**”⁵ EX1004, 21:62-22:6, 46:14-22, claim 1; EX1003, ¶101.

3. **Claim 7: A method according to claim 1, further comprising: calculating the donor's body mass index based, at least in part on the weight and height of the donor, the donor plasma volume calculated based, at least in part, on the donor's body mass index.**

Lavender in view of Neyrinck renders obvious claim 7.

Neyrinck teaches calculating TBV based on a donor's **body mass index** (BMI), which is calculated using both **height** and **weight**. EX1005, pp.39–40. Specifically, Neyrinck explains that “based on the BMI the bodyweight of the person needs to be multiplied with a number as given in Table III to achieve the TBV.” EX1005, pp.39–40; EX1003, ¶103.

After calculating the TBV, Neyrinck calculates the **donor's total plasma volume** (TPV) using TBV and a donor's **hematocrit** (Hct) via equation:

$$TPV = TBV * (1 - Hct)$$

EX1005, p.39-40; EX1003, ¶104.

⁵ All emphasis added unless otherwise noted.

As discussed in §IX.A.1, a POSITA would have been motivated to incorporate Neyrinck's TPV equation (*e.g.*, using the **TBV based on BMI**) into Lavender's system to improve collection accuracy and donor safety. EX1003, ¶105.

4. **Claim 9: A method according to claim 1, further comprising: inserting a venous-access device into the donor prior to step (e).**

Lavender's needle is inserted in the donor's vein before the user presses the START button to initialize the system algorithm to turn on the blood pump to withdraw blood. EX1004, 5:13-22, 20:48-54, Figs. 1, 20; EX1003, ¶106.

5. **Claim 11: A method according claim 1, further comprising: determining a volume of anticoagulant introduced into the whole blood based on a number of rotations of an anticoagulant pump, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the number of rotations of the anticoagulant pump.**

Lavender determines a volume of anticoagulant introduced into the whole blood based on a number of rotations of the anticoagulant pump. EX1004, 41:27-30, 42:8-44:32. Lavender's system 300 uses anticoagulant pump 306 "for pumping anticoagulant from an associated source" into "the blood flowing from the donor 30 to the fractionator 25." EX1004, 15:47-53, 16:45-47, 16:54-17:2, claim 1, Fig. 20. Lavender introduces anticoagulant into the whole blood at "a predetermined flow rate," which Lavender expresses in its algorithm as QC . EX1004, 5:25-26. Lavender sets the citrate pump flow rate, QCP , to QC . EX1004, cols. 41, 42; EX1003, ¶107.

Lavender also calculates the volume of anticoagulant in the collected plasma component based on the number of rotations of the anticoagulant pump. EX1003, ¶108. Lavender discloses that “[t]he flow rate of the anti-coagulant and the blood are **fixed by the pumps** 31 and 31A used in conjunction with the supply 35 of anti-coagulant.” EX1004, 15:47-53. Further, as shown in §2 of Table VI, the rotations of citrate pump (**CRPM**) and blood pump (**BRPM**) are calculated based on the citrate pump flow rate (**QCP**) and blood pump flow rate (**QBP**). See Table VI, §2. As shown in the calculation below, the citrate and blood flow rates (**QCP** and **QBP**) both depend on **CF**. Thus, citrate and blood pump rotations (**CRPM** and **BRPM**) depend on **CF**.

$$QCP = QC = QP * CF = QB * (1 - HCTD) * CF, \text{ and}$$

$$\begin{aligned} QBP &= QB + QC = QB + QCP \\ &= QB + QP * CF \\ &= QB + QB * (1 - HCTD) * CF \end{aligned}$$

EX1003, ¶108.

Accordingly, as the calculations in the main loop (*e.g.*, volume of plasma filtered (**TPF**) and volume of citrate filtered (**TCF**)) depend on **CF** and **PDF**, whose values, along with predetermined blood flow rate **QB** and hematocrit **HCTD**, determine the citrate and blood pump rotations (**CRPM** and **BRPM**), the calculated volume of anticoagulant in the collected plasma component (**TCF**) is determined and

calculated based, at least in part, on the number of rotations of the anticoagulant pump (citrate pump **CRPM**). EX1003, ¶109.

6. **Claim 14: A method according to claim 1, further comprising: monitoring a volume of plasma component collected within the plasma collection container, the calculated volume of pure plasma collected within the plasma collection container based, at least in part, on the monitored volume of collected plasma component.**

Lavender monitors a volume of plasma component (*e.g.*, *TDPF* total dilute plasma filtered) collected within the plasma collection container. EX1004, 43:4-6. As discussed above in §IX.A.2.i., Lavender updates *TDPF* as the system withdraws blood. EX1003, ¶110.

Lavender uses the monitored volume of collected plasma component (*e.g.*, *TDPF*) to calculate a volume of pure plasma (*e.g.*, *TPF* total plasma filtered) in the plasma component (*e.g.*, *TPF* is the product of *TDPF* and *PDF*, the plasma dilution factor). EX1004, 41:1-44:40. Therefore, the volume of pure plasma collected within the plasma collection container is based, at least in part, on the monitored volume of the collected plasma component. EX1003, ¶111.

7. **Claim 15: A method according to claim 1, further comprising: monitoring a weight of plasma component collected within the plasma collection container, the calculated volume of pure plasma collected within the plasma collection container based, at least in part, on the monitored weight of collected plasma component**

Lavender monitors a weight of plasma component (*e.g.*, *TDPW* total weight

of dilute plasma filtered) collected within the plasma collection container. See EX1004, 41:1-44:40 (Table VI, §5(B)). Lavender discloses that the current total volume of pure plasma in the collection container (*TPF*) is based on the *TDPF* (“the monitored volume of collected plasma component”) which is based on the weight of the collected plasma component (*TDPW*). EX1004, 41:1-44:33. EX1003, ¶112.

B. Ground II: Claims 2-6, 17-22, 24, 26, 28, and 29 are rendered obvious over Lavender in view of Neyrinck and further in view of Bainbridge.

1. Reasons to Combine Lavender, Neyrinck, and Bainbridge.

As discussed above in §IX.A.1 (Ground I), a POSITA would have been motivated to modify Lavender’s system in view of Neyrinck. EX1003, ¶113. Additionally, a POSITA would have been motivated to modify the Lavender and Neyrinck system with Bainbridge and would have had a reasonable expectation of success in doing so because all relate to plasma apheresis, all apply substantially similar techniques to achieve similar results, and the functionality of the Lavender and Neyrinck system would not change with the addition of Bainbridge. EX1003, ¶113.

A POSITA would have been motivated to combine Lavender, Neyrinck, and Bainbridge to improve plasma collection efficiency and to ensure donor safety by avoiding dehydration. EX1003, ¶114. Lavender discloses a membrane-based blood fractionator. EX1004, 6:3-12. Bainbridge discloses a blood apheresis system

including a single needle and a single interconnect tubing 38 to draw and return the donor's blood. EX1006, ¶0091, Fig. 2a. Interconnect tubing 38 is connected to a centrifuge to separate blood into various blood components (*e.g.*, plasma, red blood cells). EX1006, ¶¶0086-87, Fig. 2a; EX1003, ¶113.

Lavender's system draws a donor's blood and pumps the blood into membrane-based blood fractionator 25 to separate the blood into blood components including plasma and red blood cells. EX1004, 1:21-25, 5:11-23. Bainbridge's system draws a donor's blood and pumps it into a centrifuge-type blood processing vessel to separate the blood into blood component types (*e.g.*, plasma, red blood cells). EX1006, ¶¶0086-87. It was generally known in the art that a centrifuge-based blood separation device, provided comparable treatment in less time than a membrane-based blood separation device. *See* EX1012, p.135. Therefore, a POSITA would have been motivated to modify the Lavender and Neyrinck system in view of Bainbridge's centrifuge-based collection device to more efficiently separate plasma from a donor's blood and reduce the overall procedure time. EX1003, ¶115.

Additionally, a POSITA would have been motivated to incorporate Bainbridge's centrifuge-based blood separation system with a single draw and return tubing into Lavender's system to administer appropriate amounts of replacement fluid during the plasma collection return cycle. EX1006, ¶¶0015, 0090, Figs. 2A-2D. Bainbridge's system administers replacement fluid, such as saline solution,

based on a donor's fluid balance percentage "within the limited range of 80% to 120%" during a return cycle to maintain donor hydration and prevent hypovolemia or related reactions. EX1006, ¶¶0278, 0282-286. Therefore, a POSITA would have been motivated to modify Lavender and Neyrinck in view of Bainbridge because incorporating Bainbridge's fluid balance feature in Lavender would ensure donor safety by avoiding dehydration and hypovolemia. EX1003, ¶0116.

Additionally, a POSITA would have had a reasonable expectation of success in making the proposed combination because Lavender, Neyrinck, and Bainbridge all relate to plasma apheresis. EX1003, ¶0117. Lavender collects plasma based on donor information. EX1004, 1:12-13, 22:35-46. Neyrinck also teaches using donor-specific information in plasma collection. EX1005, p.39. Similarly, Bainbridge relates to "a blood component separation device (*e.g.*, a centrifuge)" that separates whole blood into "various blood components" including "plasma." EX1006, ¶0003. Bainbridge also determines target collection volumes using donor data, like weight and height. EX1006, Figs. 33-35, ¶¶0071-73, 0303, 0336-340; EX1003, ¶0117.

Further, implementing Bainbridge's centrifuge blood processing system would not alter the core functionality of Lavender's system, as Lavender already separates plasma from whole blood like Bainbridge's system. EX1003, ¶0118. Additionally, Lavender recognizes that "various modifications and alterations may be made therein without departing from the true scope and spirit of the present

invention.” EX1004, 45:1-7. Therefore, a POSITA would have been motivated to incorporate Bainbridge’s centrifuge-type blood processing vessel system with a single draw and return tubing for administering replacement fluid to improve plasma separation efficiency and keep the donor hydrated and prevent hypovolemia, and would have had a reasonable expectation of success in doing so as the systems use substantially similar techniques to achieve similar results so the proposed modification would have achieved predictable results. EX1003, ¶118.

2. Claim 2: A method according to claim 1, further comprising: returning, after collecting at least a portion of the target plasma collection volume, the contents of the blood component separation device to the donor through the first line.

Lavender in view of Neyrinck and Bainbridge renders obvious claim 2.

Lavender **returns** contents (*e.g.*, red blood cells) of blood fractionator 25 to the donor through a blood outlet port during plasma collection. EX1004, 1:21-25, 10:58-63, Fig. 20; EX1003, ¶120.

Bainbridge discloses blood removal/return tubing assembly 20 that is configured to draw blood and **return** the contents of blood processing vessel 352 **through interconnect tubing** 38 after collecting plasma from a donor. EX1006, ¶¶0091, 0306, Fig. 2a; EX1003, ¶121.

As discussed in §IX.B.1, a POSITA would have been motivated to combine the Lavender-Neyrinck system with Bainbridge’s centrifuge-type components to

incorporate a single interconnect tubing for drawing and returning blood/components and would have had a reasonable expectation of success in doing so. EX1003, ¶122.

3. Claim 3: A method according to claim 2, further comprising: calculating an intravascular deficit based, at least in part on, the volume of pure plasma collected and a volume of the contents of the blood component separation device returned to the donor.

As discussed in §IX.B.2, (claim 2), Lavender in view of Neyrinck and Bainbridge discloses returning contents of the blood component separation device to the donor.

Bainbridge further discloses administering replacement fluid, such as saline solution, based on a donor's fluid balance percentage (target intravascular deficit) within the limited range of 80% to 120% (*e.g.*, “80% representing the lessened amount of fluid the donor/patient 4 is given back ... thus, if 80% is chosen for example, then the donor/patient 4 ends the procedure with 80% of the donated fluid volume.”) to maintain donor hydration and prevent hypovolemia or related reactions. EX1006, ¶¶0278, 0282, 0285-286. The amount of replacement fluid to return to the donor/patient is based on the **total collection flow rate** minus the flow rate of the anticoagulant inflow multiplied by the total fluid balance percentage. EX1006, ¶¶0278, 0282, 0285-286. Accordingly, Bainbridge's intravascular deficit is based on the total blood collection flow that includes both the volume of pure plasma collected

and the volume of the contents of the blood component separation device returned to the donor. EX1003, ¶124.

As discussed in §IX.B.1, a POSITA would have been motivated to incorporate Bainbridge's centrifuge-type components and use of fluid balance percentage for administering replacement fluid into Lavender's system to improve collection efficiency, maintain donor hydration, and prevent hypovolemia, and would have had a reasonable expectation of success in doing so. EX1003, ¶125.

4. Claim 4: A method according to claim 3, further comprising: returning a volume of saline to the donor to obtain a target intravascular deficit.

As discussed in §IX.B.3, (claim 3), Lavender in view of Neyrinck and Bainbridge discloses calculating an intravascular deficit.

Bainbridge further discloses administering **replacement fluid**, such as **saline solution**, based on a donor's **fluid balance percentage** (target intravascular deficit) within the limited range of 80% to 120% to maintain donor hydration and prevent hypovolemia or related reactions. EX1006, ¶¶0278, 0282, 0285-286. EX1003, ¶127.

5. Claim 5: A method according to claim 4, wherein the target intravascular deficit is 0 milliliters.

As discussed in §IX.B.4, (claim 4), Lavender in view of Neyrinck and Bainbridge discloses obtaining a target intravascular deficit.

As discussed above, Bainbridge discloses maintaining a donor's fluid balance within a range of 80% to 120%. EX1006, ¶¶0278, 0282, 0285-286. A POSITA

would understand that a fluid balance of 100% (between 80% and 120%) corresponds to an intravascular deficit of 0 milliliters. EX1003, ¶129. Choosing 100% (0 milliliters) from the limited range of 80% to 120% for the fluid balance percentage would have been an obvious design choice, as it is the natural and predictable result of operating within Bainbridge’s disclosed range. EX1006, ¶¶0278, 0282, 0285-286. Further, Bainbridge’s range encompasses the claimed value, establishing a prima facie case of obviousness. *In re Peterson*, 315 F.3d 1325, 1330 (Fed. Cir. 2003) (“a prior art reference that discloses a range encompassing a somewhat narrower claimed range is sufficient to establish a prima facie case of obviousness.”); EX1003, ¶129.

6. Claim 6: A method according to claim 4, wherein the target intravascular deficit is between –250 and 500 milliliters.

As discussed in §IX.B.4, (claim 4), Lavender in view of Neyrinck and Bainbridge discloses obtaining a target intravascular deficit.

As discussed above, it would have been obvious to a POSITA to choose 0 milliliter as the target intravascular deficit. See §IX.B.5 (claim 5). EX1003, ¶131. As 0 milliliters is between -250 and 500 milliliters, Lavender in view of Neyrinck and Bainbridge renders obvious this claim. See §IX.B.5 (claim 5). EX1003, ¶132.

7. Claim 17

a. 17[preamble] A system for collecting plasma comprising:

See §IX.A.2.a (1[preamble], Ground I). EX1003, ¶133.

- b. 17[a] a venous-access device for drawing whole blood from a donor and returning blood components to the donor;**

See §IX.A.2.f (1[e], Ground I). EX1003, ¶134.

- c. 17[b] a blood component separation device for separating the drawn blood into a plasma component and a second blood component, the blood component separation device having an outlet and being configured to send the plasma component to a plasma container;**

See §§IX.A.2.f, IX.A.2.h-i (Ground I: 1[e], 1[g], 1[h]). EX1003, ¶135.

- d. 17[c] a first line fluidly connected to the venous-access device and configured to transport drawn whole blood to the blood component separation device and return fluid within the blood component separation device to the donor, the flow through the first line being controlled by a first pump;**

See §§IX.A.2.f (1[e], Ground I), IX.B.2 (claim 2). EX1003, ¶136.

Lavender in view of Neyrinck and Bainbridge renders obvious returning fluid within the blood component separation device to the donor through the first line. See §IX.B.2 (claim 2). EX1003, ¶137.

- e. 17[d] an anticoagulant line connected to an anticoagulant source, the anticoagulant line configured to introduce anticoagulant into the drawn whole blood; and**

See §IX.A.2.g (1[f], Ground I). EX1003, ¶138.

- f. 17[e] a controller configured to control the operation of the blood component separation device and the first pump,**

See §IX.A.2.i, (1[h], Ground I). EX1003, ¶139.

Lavender discloses a microprocessor that “operates under program control to calculate, based on the donor data, the amount of plasma to be collected and the amount of anticoagulant to be added ... controls the operation of the extracorporeal devices, regulates the operating parameters, and stops the procedure when the predetermined amount of plasma has been obtained.” See EX1004, Abstract. The program thus controls the fractionator (blood component separation device) and the associated fluid pumps. EX1004, 18:27-64, claims 28, 29, 33, 35, 36, 38, and 40-41; EX1003, ¶140.

- g. 17[f] the controller configured to calculate (1) a donor plasma volume based, at least in part, on a weight and height of the donor and a hematocrit of the donor**

See §IX.A.2.d (1[c], Ground I). EX1003, ¶141.

- h. 17[g] (2) a target plasma collection volume based, at least in part, on the calculated donor plasma volume and a target percentage of plasma,**

See §IX.A.2.e (1[d], Ground I). EX1003, ¶142.

- i. 17[h] (3) a volume of anticoagulant in the collected plasma component as the plasma component is being collected in the plasma container, and**

See §IX.A.2.j (1[i], Ground I). EX1003, ¶143.

- j. 17[i] (4) a volume of pure plasma collected within the plasma container based, at least in part, upon the volume of anticoagulant in the collected plasma component,**

See §IX.A.2.k (1[j], Ground I). EX1003, ¶144.

- k. 17[j] the controller configured to stop the first pump when the calculated volume of pure plasma collected within the plasma container equals the target plasma collection volume.**

See §IX.A.2.l (1[k], Ground I). EX1003, ¶145.

- 8. Claim 18: A system according to claim 17, wherein the controller is further configured to: return, after collecting at least a portion of the target plasma collection volume, fluid remaining within the blood component separation device via the first line.**

See §§IX.B.7.a-k, IX.B.2 (claim 17, claim 2). EX1003, ¶146.

- 9. Claim 19: A system according to claim 18, wherein the controller is further configured to: calculate an intravascular deficit based, at least in part on, the volume of pure plasma collected and a volume of the contents of the blood component separation device returned to the donor.**

See §§IX.B.8, IX.B.3 (claim 18, claim 3). EX1003, ¶147.

- 10. Claim 20: A system according to claim 19, further comprising: a saline line configured to fluidly connect to a saline source and the blood component separation device, the controller configured to return a volume of saline to the donor to obtain a target intravascular deficit.**

See §§IX.B.9, IX.B.4 (claim 19, claim 4). EX1003, ¶148.

Bainbridge further discloses replacement fluid (*e.g.*, saline) tubing line 962 (blue) fluidly connected to a fluid source (not shown) and blood processing vessel 352a (red) via cassette member 115 (yellow). EX1006, ¶¶0278, 0282, 0285-286, Figs. 2C-D. EX1003, ¶149.

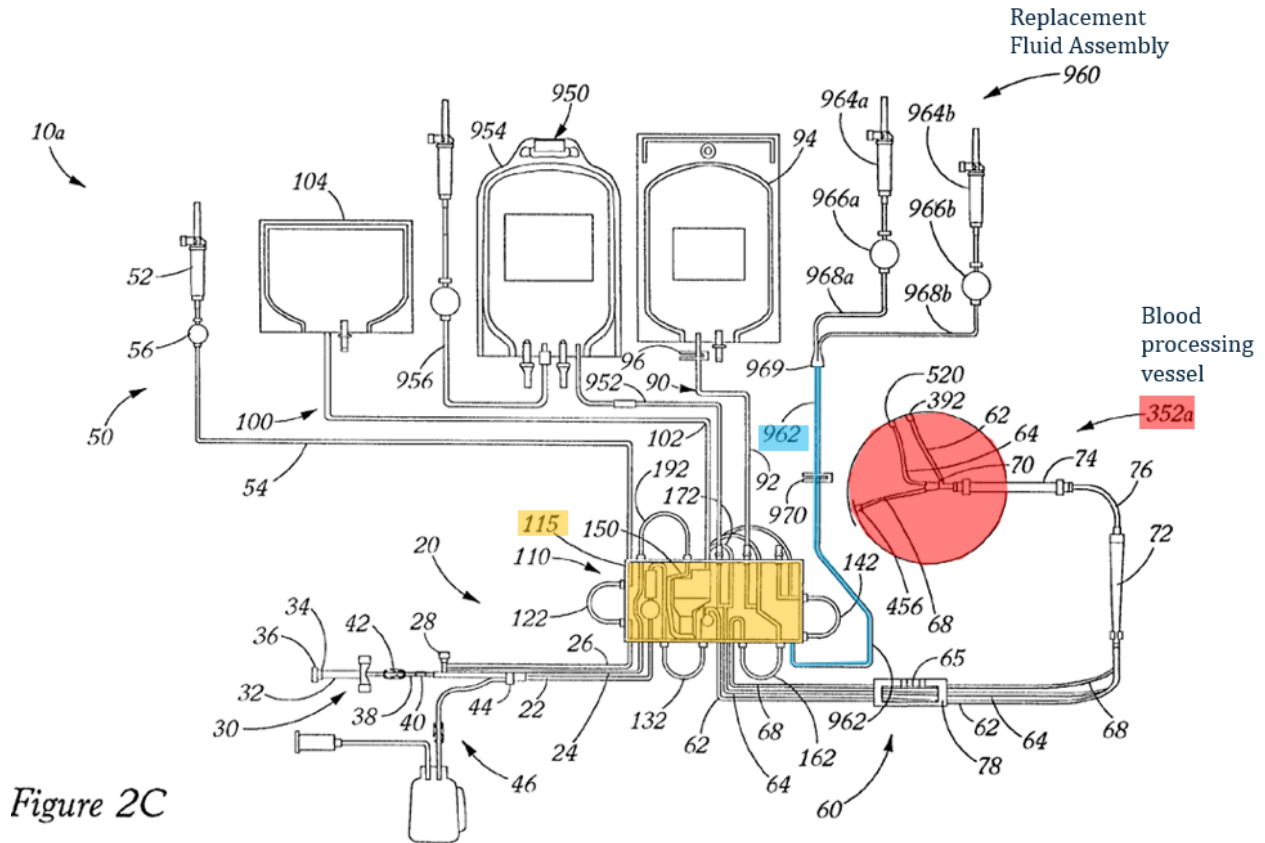


Figure 2C

EX1006, Fig. 2C (annotated).

11. **Claim 21:** A system according to claim 20, wherein the target intravascular deficit is between -250 and 500 milliliters.

See §§IX.B.10, IX.B.6 (claim 20, claim 6). EX1003, ¶150.

12. **Claim 22:** A system according to claim 17, wherein the controller is further configured to: calculate the donor's body mass index based, at least in part, on the weight and height of the donor, the donor plasma volume calculated based, at least in part, on the donor's body mass index.

See §§IX.B.7.a-k (claim 17), IX.A.3 (claim 7, Ground I). EX1003, ¶151.

13. **Claim 24:** A system according to claim 17, wherein the volume of anticoagulant in the collected plasma component is based, at least in part, on a volume of anticoagulant

**added to the drawn whole blood and the donor's
hematocrit.**

See §§IX.B.7.ak (claim 17). EX1003, ¶152.

The combination of Lavender, Neyrinck, and Bainbridge further discloses claim 24 under the plain and ordinary meaning of the term “based, at least in part, upon.” EX1003, ¶153. The claim language itself—“based, at least in part, upon”—suggests that the calculation may rely on interrelated methods and not just a single, exclusive approach. While the ’416 patent provides an equation for calculating the percentage of anticoagulant in the collected plasma (AC %) based on the donor’s hematocrit, it does not specify how the volume of anticoagulant in the collected plasma is calculated. The specification states that “[o]nce the technician/system 100 has calculated the percentage of anticoagulant within the plasma collection container 216 ... the technician/system 100 may determine the volume of anticoagulant within the container (based on the percentage of anticoagulant within the container 216).” EX1001, 11:29-36. As explained below, Lavender expressly discloses claim 24 under the plain and ordinary meaning of “based, at least in part, upon.” EX1003, ¶153.

In Lavender’s automatic system 300, the user enters donor data, including **hematocrit**, weight, and sex, before initializing the system algorithm. EX1004, 20:10-14, 20:55-67. The algorithms shown in Table VI use donor data, including hematocrit (**HCTD**), to calculate various interrelated equations. EX1004, 41:1-44:42

(Table VI). These equations determine collection volumes like the citrate (anticoagulant) volume (***TCF***) and the pure plasma volume (***TPF***). EX1004, 41:1-44:42 (Table VI); EX1003, ¶154.

Lavender's calculation of the volume of total citrate filtered (anticoagulant) in plasma bag 325 (***TCF***) is based, at least in part, upon the donor's **hematocrit** (***HCTD***). EX1003, ¶155. In Lavender, both the volume of anticoagulant (***TCF***) and the total plasma filtered (pure plasma) in plasma bag 325 (***TPF***) depend on total plasma flow volume (***TQP***), which is calculated based on the donor's hematocrit (***HCTD***) via equation $TQP = TQB * (1 - HCTD)$. EX1003, ¶155.

For example, ***TCF*** and ***TPF*** are both calculated based on the total volume of collected dilute plasma (***TDPF***), which is converted from the total dilute plasma filtered weight (***TDPW***), which is the measured total weight of the dilute plasma collected based on the amount of total plasma flow (***TQP***). EX1003, ¶156. ***TQP*** is a donor-specific amount based on hematocrit (***HCTD***). EX1003, ¶156. Thus, the values of ***TDPW*** and ***TDPF*** change based on ***TQP***. EX1004, 22:35-43, 41:4-44:42. Thus, any change in the donor's hematocrit value (***HCTD***) requires a corresponding change in the calculated value of the volume of anticoagulant (***TCF***), and vice versa so the volume of anticoagulant collected in the plasma collection bag (***TCF***) is calculated based, at least in part, on the donor's hematocrit (***HCTD***). EX1003, ¶156.

Additionally, Lavender calculates the volume of anticoagulant in plasma bag 325 based, at least in part, upon the donor's hematocrit because system 300 uses the plasma bag weight to calculate the volume of anticoagulant in plasma bag 325 (*i.e.*, **total citrate filtered (TCF)**) by multiplying a volume of the total amount of **filtered plasma (TPF)** by conversion factor (*CF*), where *CF* represents the volume of anticoagulant introduced into the incoming whole blood (V_{AC}) per incoming volume of plasma (V_P), or $CF = \frac{V_{AC}}{V_P}$. EX1004, 41:1-44:42 (Table VI, §5(B)); EX1003, ¶¶157. Total plasma in the collected plasma component (**TPF**) is calculated based on the total **volume of anticoagulant** and plasma mixture in the collection container (total dilute plasma filtered (**TDPF**)), which is determined using the collection container's weight, multiplied by dilution factor (**PDF**), which represents the ratio of incoming plasma volume (V_P) to the sum of incoming plasma volume and anticoagulant volume (V_{AC}). EX1004, 22:37-39, 41:10-44:57; EX1003, ¶¶158-61. A POSITA would understand that the volume of plasma introduced into the system (V_P) is related to the volume of whole blood introduced (V_B) as $V_P = V_B * (1 - HCTD)$, which is Lavender's equation for the plasma flow rate ($TQP = TQB * (1 - HCTD)$) converted to a volume equation. EX1003, ¶162.

Thus, the equation can also be written as $TCF = \frac{TDPF * V_{AC}}{[V_{AC} + V_B * (1 - HCTD)]}$, showing that Lavender determines the volume of anticoagulant in the collected plasma from

the volume of anticoagulant added to the whole blood and the subject's hematocrit. Therefore, the combination of Lavender, Neyrinck, and Bainbridge discloses this claim because a POSITA would understand that Lavender's volume of anticoagulant is directly calculated based on the donor's hematocrit. EX1003, ¶163.

14. **Claim 26: A system according to claim 17, wherein the controller is configured to monitor a number of rotations of an anticoagulant pump to determine a volume of anticoagulant introduced into the whole blood, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the number of rotations of the anticoagulant pump.**

See §§IX.B.7.a-k (claim 17), IX.A.5 (claim 5, Ground I). EX1003, ¶164.

15. **Claim 28: A system according to claim 17, further comprising: a plasma container weight sensor configured to monitor a volume of plasma component collected within the plasma container, the calculated volume of pure plasma collected within the plasma container based, at least in part, on the monitored volume of collected plasma component.**

See §§IX.B.7.a-k (claim 17), IX.A.5 (claim 5, Ground I). EX1003, ¶165.

16. **Claim 29: A system according to claim 17, further comprising: a plasma container weight sensor configured to monitor a weight of plasma component collected within the plasma container, the calculated volume of pure plasma collected within the plasma container based, at least in part, on the monitored weight of collected plasma component.**

See §§IX.B.7.a-k (claim 17), IX.A.7 (claim 15, Ground I). EX1003, ¶166.

- C. **Ground III: Claim 8 is rendered obvious over Lavender in view of Neyrinck and Darashkevich.**

1. Claim 8: A method according to claim 1, wherein the target percentage of plasma is between 26.5 and 29.5 percent of the donor's plasma volume.

Lavender calculates a target plasma collection volume that is 18% of the donor's circulating plasma volume. EX1004, 22:39-46.

Darashkevich discloses that “[i]n certain embodiments, plasmapheresis will remove between about 15% about 30% of the patient's total circulating plasma.” EX1007, ¶0083.

A POSITA would have found it obvious and would have been motivated to combine the Lavender-Neyrinck system with Darashkevich's teachings and would have had a reasonable expectation of success in doing so. EX1003, ¶169.

A POSITA would have been motivated to specify a percentage of donor's plasma to collect during plasma apheresis and would have turned to, and implemented, Darashkevich's target plasma collection amount—15-30% of donor's plasma volume—in the Lavender-Neyrinck system as all relate to the same well-known plasma apheresis technology. EX1004, 1:12-13, 22:35-46; EX1005, p.39; EX1007, ¶¶0029-30, 0083. Additionally, Lavender calculates a target plasma collection volume that is 18% of donor circulating plasma volume and Darashkevich discloses removing between about 15% [to] 30% of the patient's total circulating plasma.” EX1004, 22:39-46; EX1007, ¶0083. In view of these disclosures, choosing the target percentage of plasma between 26.5 and 29.5 percent of the donor's plasma

volume would have been an obvious design choice, because it is the natural and predictable result of operating within Darashkevich's disclosed range. EX1004, 22:39-46; EX1007, ¶0083.

Further, Lavender recognizes that "various modifications and alterations may be made therein without departing from the true scope and spirit of the present invention." EX1004, 45:1-7. Thus, incorporating Darashkevich's teachings would have been a routine, minor change that would have yielded the predictable result of collecting more plasma. EX1003, ¶171. Accordingly, the proposed combination discloses claim 8. *See In re Peterson*, 315 F.3d at 1330.

D. Ground IV: Claim 23 is rendered obvious over Lavender in view of Neyrinck, Bainbridge and Darashkevich.

1. Claim 23: A system according to claim 17, wherein the target percentage of plasma is between 26.5 and 29.5 percent of the donor's plasma volume.

See §§IX.B.7.a-k (claim 17, Ground II), IX.C.1 (claim 8, Ground III). EX1003, ¶172.

As discussed above in §IX.B.1, it would have been obvious to a POSITA to combine Lavender, Neyrinck, and Bainbridge. Additionally, and as discussed with respect to the Lavender, Neyrinck, and Darashkevich combination, (§IX.C.1) a POSITA would have been motivated to modify the Lavender-Neyrinck-Bainbridge system in view of Darashkevich to collect plasma in the range of 15-30% of a donor's plasma volume and would have had a reasonable expectation of success in

making the proposed combination because the systems are substantially the same, the modification is minor and routine, and it would have yielded the predictable result of collecting more plasma. EX1003, ¶173.

E. Ground V: Claims 10 and 13 are obvious over Lavender in view of Neyrinck and Min

1. Reasons to Combine Lavender, Neyrinck, and Min

A POSITA would have found it obvious and would have been motivated to combine Lavender and Neyrinck with Min's use of weigh sensors 246 to track weight changes to more accurately derive fluid processing volumes, including the volume changes of anticoagulant container 276 and plasma collection container 304. EX1008, 11:52-55, 17:17-22; EX1003, ¶174.

Additionally, a POSITA would have had a reasonable expectation of success in modifying the Lavender-Neyrinck system in view of Min because all relate to the same well-known technologies, all apply substantially similar techniques to achieve similar results, and the functionality of Lavender as modified by Neyrinck would not change when further modified in view of Min—that is, to monitor the weight of an anticoagulant bag during apheresis to determine a change in volume within the anticoagulant container. EX1008, 11:52-55, 17:17-22; EX1003, ¶175.

First, Lavender, Neyrinck, and Min are in the same field and all relate to the well-known technologies of separating blood components. EX1004, 1:12-13, 22:35-46; EX1005, p.39; EX1008, 7:51-55. Accordingly, a POSITA would have found it

obvious to combine the teachings of Lavender and Neyrinck with Min. Further, combining Lavender, Neyrinck, and Min entails the mere use of known solutions to improve similar systems and methods in the same way, *i.e.*, to use Min's technique of monitoring the weight of an anticoagulant bag to determine a volume of anticoagulant provided to whole blood prior to separation of blood components. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2007).

Second, Lavender, Neyrinck, and Min apply substantially similar techniques to achieve similar results. As discussed above, Lavender discloses fractionating blood "to **collect blood substances, such as plasma.**" EX1004, 1:12-13. Similarly, Neyrinck discloses separating plasma from a donor's blood cells and storing it in a plasma collection bag. EX1005, p.39. Further, Min discloses a system for "separating whole blood into plasma and red blood cells." EX1008, 4:26-29. A POSITA would have been motivated to add Min's weigh sensors into Lavender's blood fractionating system to gather and generate more detailed information for maximizing processing and separation efficiencies and reduce potential errors in determining the volume of anticoagulant due to errors in the blood and anticoagulant pump rates (*e.g.*, errors in pumps 306, 308 in Lavender). EX1004, Fig. 20; EX1008, 1:37-42, 11:52-55, 17:17-22; *see, e.g.*, EX1017; EX1003, ¶177.

Also, Min's systems for determining the amount of anticoagulant added to a blood separation system are similar to Lavender's monitoring of the added

anticoagulant. Indeed, Min's anticoagulant container and tube arrangement (*See* Fig. 10) is structurally similar to Lavender's (*See* Fig. 20). EX1008, 3:26-29. Therefore, it would have been obvious, and a POSITA would have been motivated, to modify Lavender's blood fractionating system to incorporate Min's weigh sensors. *See Intel Corp. v. PACT XPP Schweiz AG*, 61 F.4th 1373, 1380-81 (Fed. Cir. 2023). Additionally, it would have been an obvious design choice as it would have provided a more accurate anticoagulant volume amount and, in turn, lead to calculating a more accurate pure plasma volume. EX1003, ¶177.

Finally, the intended functionality of Lavender's blood fractionating system would not change by adding Min's weigh sensors as a POSITA would have expected Lavender's blood fractionating system to successfully determine the amount of anticoagulant added to the system when modified in view of Min. *Eli Lilly & Co. v. Teva Pharm. Int'l GmbH*, 8 F.4th 1331, 1345 (Fed. Cir. 2021).

Lavender also discloses converting weight changes to volume changes using a specific gravity. EX1003, ¶180. Accordingly, a POSITA would have had a reasonable expectation of success when modifying Lavender's algorithms for determining the volume of anticoagulant in the collected plasma component to incorporate Min's scale for monitoring the anticoagulant volume's weight change—each relate to the same well-known technologies and apply substantially similar

techniques to achieve similar results. *Par Pharmaceutical, Inc. v. TWI Pharmaceuticals, Inc.*, 773 F.3d 1186, 1198 (Fed. Cir. 2014).

2. **Claim 10: A method according to claim 1, further comprising: determining a change in volume within an anticoagulant container, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the change in volume within the anticoagulant container.**

Lavender in view of Neyrinck and Min discloses determining a change in volume within an anticoagulant container, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the change in volume within the anticoagulant container. EX1003, ¶181. As the '416 patent recognizes, a POSITA would understand that substantially all of the anticoagulant added to a centrifuge-based blood fractionating system would end up in the plasma collection container. *See* §V.B; EX1001, 10:67-11:4. As discussed above, it would have been obvious for a POSITA to replace Lavender's membrane-based fractionator with Min's centrifuge-based blood processing chamber 18. EX1004, 6:3-12; EX1008, 7:41-59. It was generally known in the art that a centrifuge-based blood separation device, provided comparable treatment faster than a membrane-based blood separation device. *See* EX1012, p.135. A POSITA would have been motivated to modify Lavender with Min's centrifuge-based collection device to separate plasma from a donor's blood more quickly. EX1003, ¶181.

A POSITA would have had a reasonable expectation of success in making this

modification as Min's centrifuge-based blood processing device is used for the same purpose as Lavender's system—separating whole blood into plasma—and implementing the centrifuge-based device in Lavender would have been a simple substitution that would have resulted in faster plasma separation and collection. EX1003, ¶182.

In the combined Lavender-Neyrinck-Min blood fractionating system, a POSITA would understand that the plasma collection container would contain substantially all of the added anticoagulant. EX1003, ¶183.

Further, as discussed above, it would have been obvious to a POSITA to incorporate Min's scale in Lavender/Neyrinck's system to monitor the change in volume of the anticoagulant container and calculate the volume of anticoagulant in the collected plasma component based, at least in part, on the change in volume within the anticoagulant container. Doing so would generate more detailed information for maximizing processing and separation efficiencies and reduce potential errors in determining the volume of anticoagulant due to errors in the blood and anticoagulant pump rates (*e.g.*, errors in pumps 306, 308 in Lavender). EX1004, Fig. 20; EX1008, 1:37-42; EX1003, ¶184.

3. **Claim 13: A method according to claim 1, wherein the volume of anticoagulant in the collected plasma component includes at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant added during a priming step.**

The volume of anticoagulant in the collected plasma component includes at least a portion of the anticoagulant introduced into the withdrawn whole blood. Lavender uses an anticoagulant pump in system 300 for pumping anticoagulant into the donor's whole blood before separating blood components. EX1004, 15:47-53, 16:54-17:2, claim 1, Figs. 1, 20. At least a portion of the anticoagulant introduced in the withdrawn whole blood is collected in the plasma collection bag because anticoagulant is pumped “at a rate sufficient to dilute incoming plasma to 68% of the initial concentration.” EX1004, 22:37-39. EX1003, ¶185.

The volume of anticoagulant in the collected plasma component also includes at least a portion of the anticoagulant added during a priming step. EX1003, ¶186. Lavender discloses a priming step, *e.g.*, “[t]he citrate bag 307 is then unclamped, and the system operates the citrate pump 306 to drive citrate to purge air from the tubes 312 and 314 [of system 300].” EX1004, 20:37-48. Min discloses that during the priming step, “anticoagulant pump PP4 conveys a predetermined volume of anticoagulant (*e.g.*, 10g) into the in-process container 312” where plasma is collected. EX1008, 22:40-42. Thus, at least a portion of the volume of anticoagulant in the collected plasma component (*e.g.*, plasma bag 325) would include at least a portion of the anticoagulant added during the priming step. EX1003, ¶186.

A POSITA would have been motivated to combine Lavender and Neyrinck's teachings with Min for the same reasons as discussed above. §IX.E.1. Additionally,

a POSITA would have looked to Min to calculate the total collection volume, including the volume of anticoagulant added during priming, to reduce errors caused by not accounting for all added anticoagulant when determining the anticoagulant volume in the plasma collection container. EX1003, ¶187.

F. Ground VI: Claim 25 is obvious over Lavender in view of Neyrinck, Bainbridge and Min.

- 1. Claim 25: A system according to claim 17, further comprising: an anticoagulant source weight sensor configured to measure the weight of the anticoagulant source, the controller further configured to monitor a change in volume within the anticoagulant source based on the measured weight of the anticoagulant source, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the change in volume within the anticoagulant source.**

See §IX.E.1. EX1003, ¶188.

As discussed in §IX.B.1, it would have been obvious to a POSITA to combine Lavender, Neyrinck, and Bainbridge, and a POSITA would have had a reasonable expectation of success in combining them. EX1003, ¶189. Additionally, and like with the combination of Lavender, Neyrinck, and Min, in §IX.F.1, a POSITA would have been motivated to modify the Lavender-Neyrinck-Bainbridge system in view of Min to track weight changes to more accurately derive fluid processing volumes, including the volume change of the anticoagulant and plasma collection containers. EX1008, 11:52-55, 17:17-22. Similarly, a POSITA would have had a reasonable expectation of success in making the proposed combination because the systems are

substantially the same, the modification is minor and routine, and would have yielded predictable results. EX1003, ¶189.

Lavender discloses a controller that monitors the change in volume within a collection container by converting a change in weight to a change in volume using specific gravity. §IX.E.1; EX1003, ¶190. Min uses weigh sensors 246 to track the anticoagulant container's weight changes and derive fluid processing volumes, including the volume change of anticoagulant container 276 and plasma collection container 304. EX1008, 11:52-55, 17:17-22. Each of Min's weigh sensors "provide output reflecting weight changes over time" and "[t]his output is conveyed to [a] controller. . . [for] process[ing] the incremental weight changes to derive fluid processing volumes." EX1008, 17:17-22. Thus, the combined system discloses an anticoagulant source weight sensor configured to measure the weight of the anticoagulant source (*i.e.*, Min's weigh sensors), and the controller further configured to monitor a change in volume within the anticoagulant source based on the measured weight of the anticoagulant source (*i.e.*, Min's controller). EX1008, 17:17-22. As discussed above, a POSITA would understand that substantially all of the anticoagulant added to Lavender's blood fractionating system, when modified to include Min's centrifuge-based device, would end up in the plasma collection container and that a POSITA would incorporate Min's monitoring of the anticoagulant source's volume into Lavender's algorithms to provide additional

measurements of the anticoagulant volume in the plasma collection container. See §§V.B, IX.E.1; EX1001, 10:67-11:4; EX1004, 43:28; EX1008, 17:17-22. Thus, Lavender in view of Neyrinck, Bainbridge, and Min teaches the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the change in volume within the anticoagulant source. EX1003, ¶190.

G. Ground VII: Claim 12 is obvious over Lavender in view of Neyrinck, Min, and Turgut

- 1. Claim 12: A method according to claim 1, further comprising: determining a volume of anticoagulant within the blood component separation device, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the volume of anticoagulant within the blood component separation device.**

Lavender calculates a volume of anticoagulant collected in the collected plasma component by weighing the collected plasma and anticoagulant solution in plasma bag 325. EX1004, 16:50-53, 17:14-16; See §IX.A.2.j. Min uses weigh sensors 246 to track the anticoagulant container's weight changes and derive fluid processing volumes, including the volume change of anticoagulant container 276 and plasma collection container 304. EX1008, 11:52-55, 17:17-22. However, a POSITA would have recognized that determining the total volume of anticoagulant in the collected plasma component based on the anticoagulant container's change in volume would not account for any anticoagulant remaining in the blood separation device. See §IX.E.1.; EX1003, ¶191. A POSITA would have also recognized that

the anticoagulant volume in the plasma collection container would be more accurately determined if the anticoagulant remaining in the blood separation device was accounted for. *See* EX1003, ¶191.

A POSITA would have found it obvious and would have been motivated to combine Lavender, Neyrinck, and Min with Turgut's teaching of a volume detector—a centrifuge separation chamber used to separate blood into components—to determine the volume of fluid within a blood separation system. EX1009, ¶0073. EX1003, ¶192.

Turgut's blood component separation system is structurally similar to Lavender's (*See* Fig. 20) and is used to separate blood into different components. EX1009, ¶¶0052-68, Fig. 1A; *KSR Int'l Co.*, 550 U.S. at 417. Therefore, it would have been obvious, and a POSITA would have been motivated, to modify the Lavender-Min blood fractionating system, which monitors the anticoagulant volume input into the system and includes Min's centrifuge (*see* §IX.E.1), to incorporate Turgut's volume detector to detect the fluid volume (plasma plus anticoagulant) remaining in the blood separation device. EX1003, ¶194.

A POSITA would have used Turgut's volume detector to determine the volume of fluid in the separation device and then have subtracted the volume of red blood cells (total volume of whole blood times hematocrit (**HCTD**)) to calculate the volume of anticoagulant and plasma in the device. A POSITA would then multiply

this volume times the plasma dilution factor times the conversion factor (*i.e.*, $PDF * CF$) to calculate the volume of anticoagulant remaining within the blood component separation device. EX1003, ¶195. This remaining anticoagulant volume would then be subtracted from the amount of anticoagulant added to the system to more accurately estimate the total amount of anticoagulant within the plasma collection container. *See Intel Corp. v. PACT XPP Schweiz AG*, 61 F.4th 1373, 1380-81 (Fed. Cir. 2023); EX1003, ¶195.

The combined system discloses determining a volume of anticoagulant within the blood component separation device, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the volume of anticoagulant within the blood component separation device. EX1003, ¶196.

H. Ground VIII: Claim 27 is obvious over Lavender in view of Neyrinck, Bainbridge, Min, and Turgut

- 1. Claim 27: A system according to claim 17, further comprising: an optical sensor located on the blood component separation device and configured to monitor the contents of the blood component separation device and determine if a volume of anticoagulant remains within the blood component separation device, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the volume of anticoagulant within the blood component separation device.**

See §IX.G.1 (claim 12, Ground VII). EX1003, ¶197.

As discussed above in §IX.F.1, it would have been obvious to a POSITA to combine Lavender, Neyrinck, Bainbridge, and Min, and a POSITA would have had

a reasonable expectation of success in doing so. Additionally, and as discussed with respect to the Lavender, Neyrinck, Min, and Turgut combination, (§IX.G.1) a POSITA would have been motivated to modify the Lavender-Neyrinck-Bainbridge-Min system in view of Turgut to use a volume detector to more accurately calculate the volume of anticoagulant within the plasma collection container by accounting for anticoagulant remaining in the blood separation device. EX1009, ¶0073. EX1003, ¶198. Similarly, a POSITA would have had a reasonable expectation of success in making the proposed combination because the systems are substantially the same, the modification was minor and routine, and it would have yielded predictable results. EX1003, ¶198.

A POSITA would recognize that Turgut's volume detector may be an optical sensor, like Headley's optical sensor, discussed below. EX1010, 1:10-24; 4:48-64. See §§IX.I.1-2. It was generally known by a POSITA at the time of the '416 patent's effective filing date that a volume detector may be an optical sensor. EX1003, ¶199.

I. Ground IX: Claims 16 and 30 are obvious over Lavender in view of Neyrinck, Bainbridge, Headley, and Barrett

- 1. Claim 16: A method according to claim 1, wherein step (b) includes monitoring a volume of red blood cells collected within the blood component separation device, the determined hematocrit of the donor based, at least in part, on the monitored volume of red blood cells collected within the blood component separation device and a volume of whole blood withdrawn from the donor.**

Lavender teaches determining a volume of whole blood withdrawn from the donor in the Main Loop algorithm, which calculates the total blood flow (**TQB**) as blood is withdrawn. EX1004, 43:7-16. Lavender's blood pump and citrate pump rates are based on the donor's hematocrit. EX1004, 41:21-26.

Bainbridge teaches separating red blood cells from incoming whole blood during a blood separation procedure. EX1006, ¶0087. Headley relates to systems and methods for separating platelets and other blood components from blood. EX1010, Abstract. Headley teaches using an array 97 of optical sensors within a blood separation system (*e.g.*, a centrifuge) to determine a volume of red blood cells within the blood separation system. EX1010, 1:10-24; 4:48-64. It would have been obvious for a POSITA to include Headley's optical sensor(s) in Lavender's blood separation device to determine the volume of red blood cells collected from the donor and allow for their immediate return to the donor. EX1003, ¶201.

Barrett teaches determining a donor's hematocrit by dividing a blood sample's red blood cell volume by the sample's total volume. EX1011, 2:45-49.

A POSITA would have been motivated to combine the teachings of Lavender, Neyrinck, Bainbridge, Headley with Barrett, each of which relate to blood-component separation and use similar systems, to determine a real-time hematocrit of a donor during a collection procedure. EX1004, 22:35-46; EX1006, ¶0086-87; EX1010, 1:10-24; 4:48-64; EX1011, 2:45-49; EX1003, ¶203.

A POSITA would have been motivated to incorporate Barrett's teaching of determining a donor's hematocrit in Lavender's calculated values to reduce system error. For example, Lavender's pump rates, which are determined based on the donor's hematocrit, would be more accurately regulated with real-time hematocrit updates. EX1004, 41:21-26.

Thus, a POSITA would use both (i) Headley's monitored volume of red blood cells and (ii) the volume of whole blood withdrawn from the donor, Lavender's total blood flow (**TQB**), to determine a donor's real-time hematocrit. EX1003, ¶205. This equation would be added into Lavender's Main Loop algorithm to increase the accuracy of Lavender's calculated estimates. EX1003, ¶205. Also, to more effectively separate the red blood cells in Lavender's system, a POSITA would be motivated to replace Lavender's membrane-based blood fractionator with Bainbridge's centrifuge-type blood processing vessel to separate the blood into blood components. §IX.E.1 and 3; EX1004, 6:3-12; EX1006, ¶0086-87. Further, the intended functionality of the Lavender-Neyrinck-Bainbridge system would not change when modified to includes Headley's optical sensor(s) and Barrett's hematocrit calculation. *Eli Lilly & Co. v. Teva Pharm. Int'l GmbH*, 8 F.4th 1331, 1345 (Fed. Cir. 2021).

Accordingly, Lavender in view of Neyrinck, Bainbridge, Headley, and Barrett teach monitoring a volume of red blood cells collected within the blood component

separation device, the determined hematocrit of the donor based, at least in part, on the monitored volume of red blood cells collected within the blood component separation device and a volume of whole blood withdrawn from the donor. EX1004, 41:8-44:32; EX1006, ¶0087; EX1010, 1:10-24; 2:45-49; 4:48-64, 17:19-24; EX1011, 2:45-49; EX1003, ¶207.

2. **Claim 30: A system according to claim 17, further comprising: an optical sensor located on the blood component separation device and configured to monitor a volume of red blood cells collected within the blood component separation device, the controller configured to determine the donor's hematocrit based, at least in part, upon on the monitored volume of red blood cells collected within the blood component separation device and a volume of whole blood withdrawn from the donor.**

See §IX.I.1 (Claim 16). EX1003, ¶208.

As discussed above, Headley teaches using an array 97 of optical sensors within a blood separation system (*e.g.*, a centrifuge) to determine a volume of red blood cells within the blood separation system. EX1010, 1:10-24; 4:48-64. Thus, Headley discloses an optical sensor located on the blood component separation device and configured to monitor a volume of red blood cells collected within the blood component separation device. See §IX.I.1.; EX1010, 1:10-24; 4:48-64.

Using Lavender's Main Loop algorithm, Headley's optical sensor, and Barrett's equation to determine hematocrit, Lavender, modified in view of Neyrinck, Bainbridge, Barrett, and Headley teaches an optical sensor configured to monitor a

volume of red blood cells and a controller configured to determine the subject's hematocrit based, at least in part, upon on the monitored volume of red blood cells collected within the blood component separation device and a volume of whole blood withdrawn from the subject. See §IX.I.1; EX1003, ¶209; EX1004, 41:8-44:32; EX1006, ¶0087; EX1010, 2:45-49.

Date: October 9, 2025

Respectfully submitted,
/ John M. Caracappa, Reg. No. 43,532/
John M. Caracappa, Reg. No. 43,532
Katherine D. Cappaert, Reg. No. 71,639
Matthew Y. Sim, Reg. No. 77,422
Scott Chappell, Reg. No. 76,333
STEPTOE LLP
1330 Connecticut Avenue N.W.
Washington, D.C. 20036
Tel: (202) 429-3000
Fax: (202) 429-3902

Counsel for Terumo BCT, Inc.

CERTIFICATE OF WORD COUNT UNDER 37 CFR §42.24(d)

Pursuant to 37 C.F.R. §42.24(a), Petitioner hereby certifies that portions of the above-captioned Petition for Inter Partes Review of U.S. Patent 10,792,416, in accordance with and reliance on the word count provided by the word-processing system used to prepare this Petition, that the number of words in this paper is 13,906. Pursuant to 37 C.F.R. §42.24(a), this word count is in compliance and excludes the table of contents, table of authorities, mandatory notices under §42.8, certificate of service, certificate of word count, appendix of exhibits, and any claim listing. This word count was prepared using Microsoft Word.

Date: October 9, 2025

Respectfully submitted,
/ John M. Caracappa, Reg. No. 43,532/
John M. Caracappa, Reg. No. 43,532
STEPTOE LLP
1330 Connecticut Avenue N.W.
Washington, D.C. 20036
Tel: (202) 429-3000
Fax: (202) 429-3902

Counsel for Terumo BCT, Inc.

CERTIFICATE OF SERVICE

The undersigned certifies service pursuant to 37 C.F.R. §§ 42.6(e) and 42.105(b) on the Patent Owner on October 9, 2025 by filing a copy of this Petition for IPR of U.S. Patent No. 10,792,416 and supporting materials through the Patent Trial and Appeal Case Tracking System and sending a copy of the same via pre-paid, overnight Federal Express at the correspondence address of record for U.S. Patent No. 10,792,416:

McCarter & English, LLP
c/o Jonathan C. Lovely
265 Franklin Street
Boston, MA 02110

With a courtesy copy to Patent Owner at the purported address according to the assignment records of the United States Patent and Trademark Office and according to Patent Owner's website, <https://www.haemonetics.com/contact-support>:

Haemonetics Corporation
125 Summer Street
Boston, MA 02110

Petition for *Inter Partes* Review of U.S. Patent No. 10,792,416
IPR2025-01420

With a courtesy copy to Patent Owner's counsel of record in Haemonetics Corporation v. Terumo BCT, Inc., Case No. 25-cv-1409-RMR-SBP (D. Colo.) by electronic mail:

Carolyn Juarez
NOD Law PC
726 Front St. Suite 220
Louisville, CO 80027-1881
(720) 536-4904
carolyn@nod-law.com

Erik B. Milch
Elizabeth Shrieves
Proskauer Rose LLP
1001 Pennsylvania Ave., NW
Suite 600 South
Washington, DC 20004-2533
(202) 416-6899
emilch@proskauer.com
eshrieves@proskauer.com

Joseph M. Drayton
Connor J. Villar
Proskauer Rose LLP
Eleven Times Square
New York, NY 10036-8299
(212) 969-2900
cvillar@proskauer.com

Alan S. Teran
Proskauer Rose LLP
2255 Glades Road
Suite 421 Atrium
Boca Raton, FL 33431-7360
(561) 995-4723
ateran@proskauer.com

Date: October 9, 2025

Respectfully submitted,

/ John M. Caracappa, Reg. No. 43,532/

John M. Caracappa, Reg. No. 43,532

STEPTOE LLP

1330 Connecticut Avenue N.W.

Washington, D.C. 20036

Tel: (202) 429-3000

Fax: (202) 429-3902

Counsel for Terumo BCT, Inc.