UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

TERUMO BCT INC.,

Petitioner

v.

HAEMONETICS CORP.,

Patent Owner

IPR2025-01374
U.S. Patent No. 11,738,124

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

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3. Claim 9: 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of anticoagulant in the collected plasma component includes at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant added during a priming step. 60

4. Claim 13: A system according to claim 11, 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

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EXHIBIT LIST

Exhibit	Reference
1001	U.S. Patent No. 11,738,124 ("'124 patent")
1002	File History of the '124 patent
1003	Declaration of Dr. Gary Fletcher in Support of Petition
1004	U.S. Patent No. 4,898,675 ("Lavender")
1005	U.S. Patent No. 7,072,769 ("Fletcher-Haynes")
1006	U.S. Patent No. 8,075,468 ("Min")
1007	U.S. Patent No. 9,370,324 ("Barrett")
1008	U.S. Patent No. 6,296,602 ("Headley")
1009	U.S. Patent Publication No. 2017/0029762 ("Turgut")
1010	"Membrane versus centrifuge-based therapeutic plasma exchange: a randomized prospective crossover study," Carsten Hafer et al., Int. Urol. Nephrol (2016) 48:133-138; Springer Science+Business Media Dordrecht 2015.
1011	"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.
1012	Curriculum Vitae ("CV") of Dr. Gary D. Fletcher
1013	Bruce C. McLeod, MD, et al., "Apheresis: Principles and Practice," 3rd Edition, AABB Press 2010.
1014	Japanese Patent Publication No. JP 2002-282352 A and English translation ("Takagi")
1015	Sergent 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

Terumo BCT ("Petitioner") requests *inter partes* review ("IPR") of claims 1-20 of U.S. Patent No. 11,738,124 (the "'124 patent") (EX1001).

I. Mandatory Notices

A. Real Parties-In-Interest

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

B. Related Matters

The '124 patent is currently asserted, along with seven other patents in the same patent family, against Petitioner by Patent Owner in *Haemonetics Corp. v. Terumo BCT, Inc.*, No. 1:25-cv-1409 (D. Colo. filed May 5, 2025) (the "District Court case'). Petitioner intends to challenge other patents asserted in the District Court case through *inter partes* review and post-grant review proceedings.

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:

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

IV. Identification Of Challenge And Relief Requested

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].
- U.S. Patent No. 7,072,769, issued July 4, 2006 ("Fletcher-Haynes"), 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 No. 9,370,324, issued June 21, 2016 ("Barrett"), 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 Publication No. 2017/0029762, published February 2, 2017 ("Turgut"), prior art under at least 35 U.S.C. §102(a)(1).

B. Statutory Grounds of Unpatentability

Petitioner requests cancellation of '124 patent claims 1-20 under 35 U.S.C. § 103 based on the following Grounds.

Ground	Claims	Basis
1	1, 3, 5, 6, 8, 10-12, 14, 16-17, and 19	Anticipated by or Obvious over Lavender

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

2	1, 3, 5, 6, 8, 10-12, 14, 16-17, and 19	Obvious over Lavender in view of Fletcher-Haynes
3	2, 9, 13, and 20	Obvious over Lavender in view of Fletcher-Haynes and Min
4	7 and 18	Obvious over Lavender in view of Fletcher-Haynes, Headley, and Barrett
5	4 and 15	Obvious over Lavender in view of Fletcher-Haynes, Min, and Turgut

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. ’124 Patent Overview

A. The ’124 Patent is Related to Plasma Apheresis

The ’124 patent, which recently issued on August 29, 2023, relates to a “system and method for collecting plasma” in blood apheresis systems. EX1001, Title, 1:26-28. “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, 1:32-34. The ’124 patent specifically relates to plasma apheresis, which is plasma collection. Figure 3 of the ’124 patent shows one embodiment of a plasma apheresis system. EX1003, ¶¶30-36.

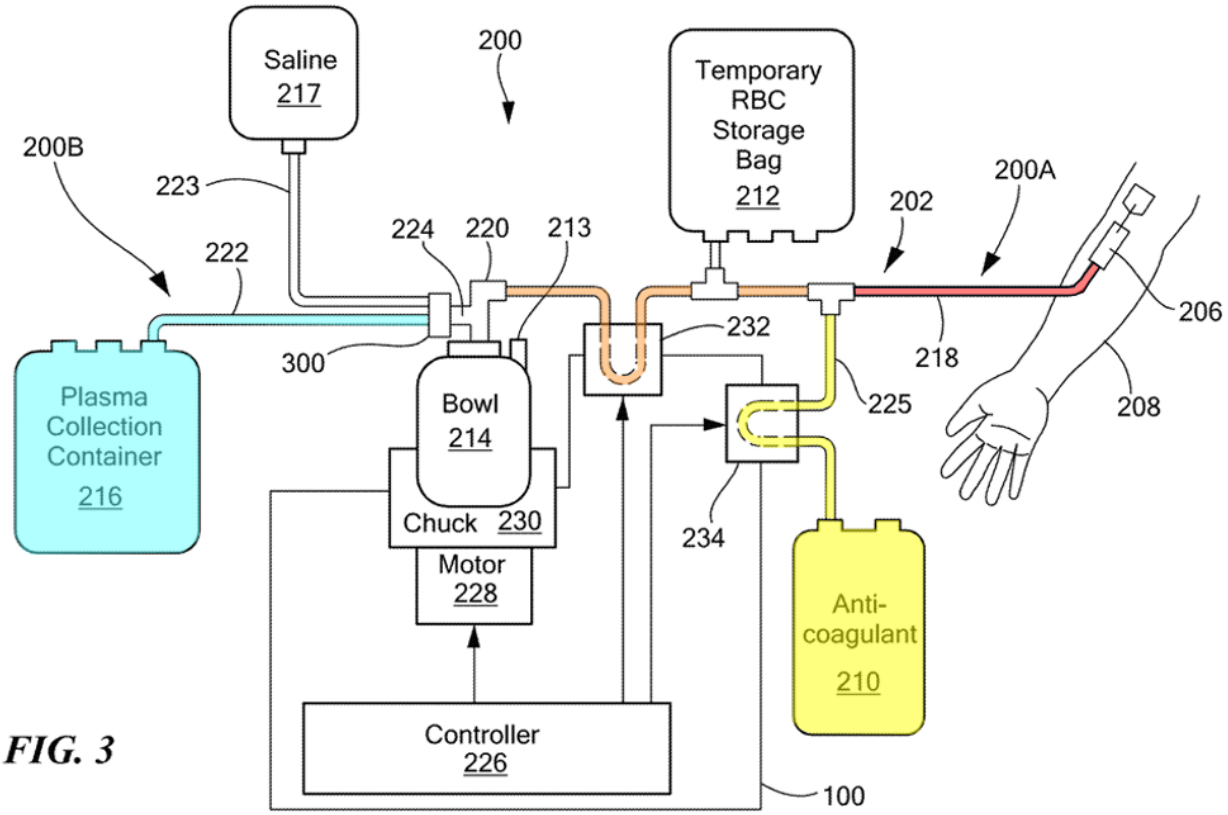


FIG. 3

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

Plasma apheresis involves withdrawing whole blood from a donor's arm using venous access device 206. EX1001, 5:28-31. 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, 6:26-31, 5:34-40. Anticoagulant is introduced in fixed proportions to the whole blood drawn from the donor to prevent blood clotting in the draw line. *See* EX1010. "[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, 7:58-61; 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, 4:65-5:9, 6:52-60. The donor's plasma, *i.e.*, pure plasma, along with anticoagulant introduced during the collection process, exits the blood component separation device and is collected and stored in a collection container (*e.g.*, a bag, shown in blue above). EX1001, 2:6-10, 5:28-38. The anticoagulant and pure plasma combination is known as anticoagulated plasma or plasma product. EX1001, 10:5-6; EX1003, ¶38.

The FDA established guidelines regarding how much plasma any individual donor can donate that consider donor parameters, like weight, hematocrit, and sex. *See* EX1011; EX1003, ¶39.

B. The '124 Patent's Purported Invention

The '124 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. EX1001, 1:56-62. The '124 patent purports to solve these problems by taking into consideration a donor's hematocrit

level and the amount of anticoagulant added into the system. EX1001, 1:66-2:24; 4:23-33; EX1003, ¶40.

Each donor has a different hematocrit level, which affects the amount of plasma in the donor's whole blood. EX1001, 8:3-5. The differing levels of hematocrit also affect the volume of anticoagulant in a plasma collection container ("anticoagulant volume"). EX1001, 8:12-15. Given this variability, the '124 patent discloses that controller 226 may 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, 8:24-61. In % 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, 8:24-61. 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, 7:30-32, 7:65-8:2. The controller uses the total volume of liquid

in the collection container to calculate the anticoagulant and pure plasma volumes in the collection container. EX1001, 8:17-9:55. The ’124 patent first calculates the anticoagulant volume. EX1001, 8:62-9:12. It then calculates the volume of pure plasma by subtracting the anticoagulant volume from the total volume of liquid in the collection container. EX1001, 8:62-9:12; EX1003, ¶42.

The ’124 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 anticoagulant container. EX1001, 8:44-9:12. 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

[2] “Because the osmolarity of the red blood cells prevents the anticoagulant from mixing with it, essentially all of the anticoagulant exits the bowl 214 and is collected within the plasma collection container 216 along with the plasma.” EX1001 at 8:34-38. Under this assumption, subtracting the anticoagulant volume added to the system from the total volume in the collection container estimates the volume of pure plasma in the collection container. EX1001 at 8:34-38; 9:40-55; EX1003, ¶43.

volume in the collection container. EX1001, 8:34-38, 8:44-62, 9:40-55; EX1003, ¶43.

Of the three above methods, only the first, which is based on the predetermined ratio of anticoagulant to anticoagulated whole blood, 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, 10:16-19; EX1003, ¶44.

The '124 patent repeats each method to determine the pure plasma volume "until a target volume of pure plasma is collected in the plasma collection container," *e.g.*, the volume set by FDA regulation. EX1001, 9:8-12. 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 of the blood … to draw the RBCs (and other components)" from the blood component separation device back to the donor. EX1001, 9:17-23; EX1003, ¶¶45-46.

B. Prosecution History

Application No. 17/943,410, which resulted in the '124 patent, was filed on September 13, 2022. EX1001, Cover. The '124 patent claims priority, through intervening continuation applications, to U.S. Patent No. 10,758,652 (the "'652

patent"), which was filed on May 30, 2017. EX1001, 1:6-21. Accordingly, the effective filing date of the '124 patent is May 30, 2017.

On December 14, 2022, the Examiner rejected pending claims 1-20 as unpatentable over the '652 patent due to non-statutory double patenting. EX1002, 12/14/2022 Non-Final Rejection at 2.

On March 14, 2023, the Applicant filed a terminal disclaimer and argued that it mooted the rejection. EX1002, 03/14/2022 Amendment at 7; 3/14/2022 Terminal Disclaimer.

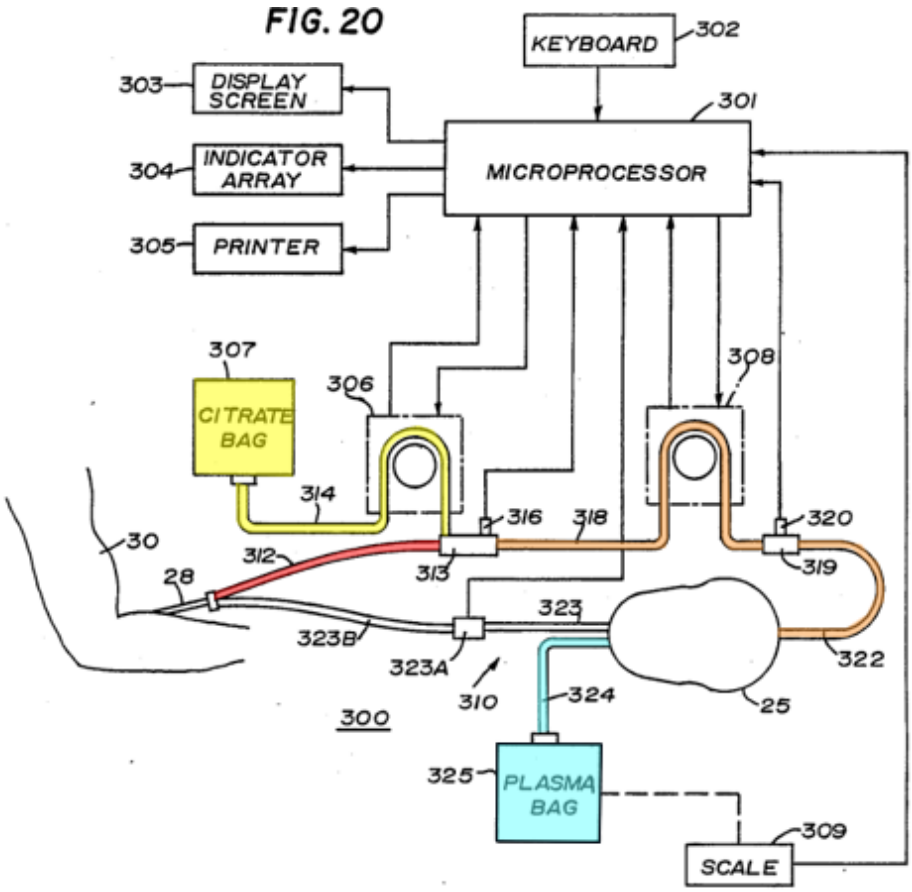
On May 8, 2020, the Examiner issued a Notice of Allowance. EX1002, Notice of Allowance. The '124 patent issued on August 29, 2023. EX1001, Cover.

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 volume of anticoagulant collected during a plasma collection procedure to, among other things, "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, a needle or catheter 28 is used to draw whole blood from a donor, which is then mixed with citrate (a blood 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 several 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 weight of the collected plasma and anticoagulant mixture during the collection process. These calculations are ultimately used to calculate the volume of pure plasma and anticoagulant in the plasma collection bag in real time. 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 volume of fluid in the collection container, determined by the weight of the container, 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 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. It uses this to determine the pure plasma volume. 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.

B. Overview of Fletcher-Haynes

Fletcher-Haynes discloses a blood collection system that maximizes blood component yield by maximizing at least one process parameter, based on either a target yield or a fixed procedure time. EX1005, Abstract. Fletcher-Haynes recognized the need to determine "the maximum amount of plasma which should be collected considering the medical and physical characteristics of the donor." EX1005, 48:29-31. For example, Fletcher-Haynes' prediction algorithms include donor's gender, height, weight, hematocrit, and platelet pre-count parameters. EX1005, 27:30-35; 49:19-52:36; EX1003, ¶55.

Figure 7A illustrates Fletcher-Haynes' collection assembly 10' for separating blood into components. EX1005, 45:14-16. Donor's blood is pumped through inlet line 22 (red), and anticoagulant is pumped from AC container 30 (yellow) into to the inlet line 22. EX1005, 45:22-37. The blood is mixed with anticoagulant and separated into components flowing into platelet collect bags 38 and plasma collect bag 54 (blue). EX1005, 45:22-37. The remaining blood is pumped back to the donor. EX1005, 45:22-37; EX1003, ¶56.

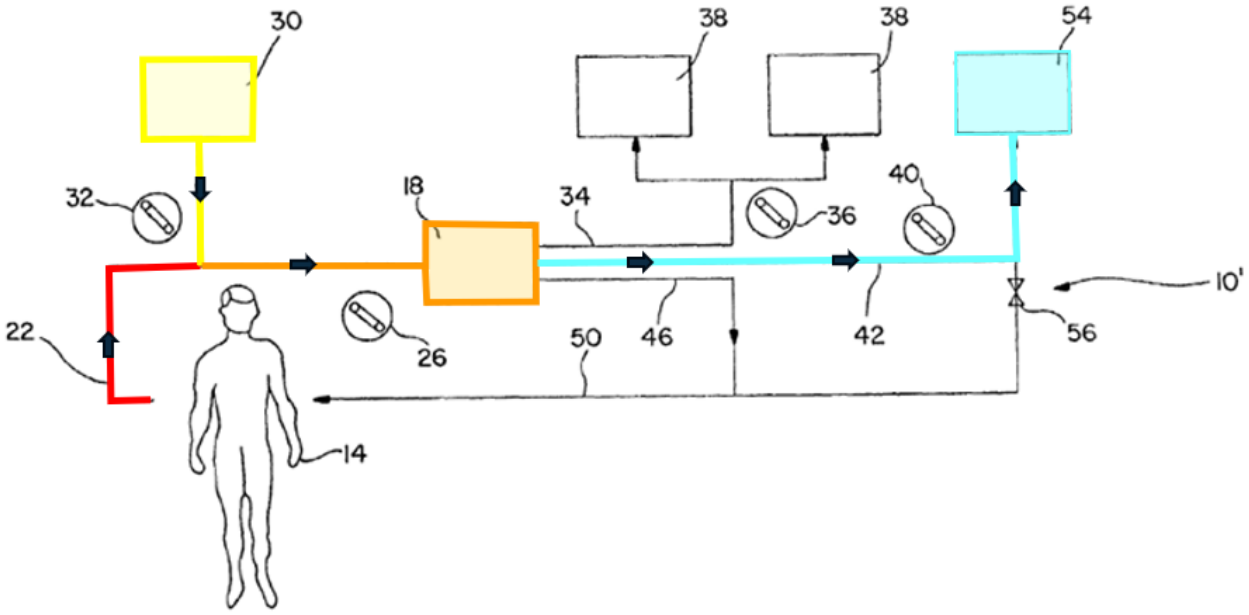


Figure 7A

EX1005, Fig. 7A (annotated).

Assembly 10' operates according to a collection procedure derived from procedure goal(s) and may include maximizing "at least one process control

parameter." EX1005, 7:38-43; 9:35-44. This maximization is determined by inputting donor-provided data, like height, weight, and blood processing machine type in optimization and prediction models. EX1005, 49:19-26; EX1003, ¶57.

Fletcher-Haynes' prediction model uses an initial parameter configuration that accounts for these factors (*i.e.*, height, weight, total blood volume, hematocrit, and platelet pre-count) to generate several target parameters, including: ". . . ; (2) inlet flow rate; **(3) AC ratio;** (4) procedure time; . . . ; (**7) source plasma volume; (8) AC in the platelet and plasma collect bags 38, 54;** . . . ; (10) AC infusion rate; and (11) output approval." EX1005, 49:22-26. When executed during a blood separation procedure, the prediction model determines any of parameters (1)-(11) in real-time. EX1005, 34:8-24; 48:66-49:19-25; EX1003, ¶58.

Fletcher-Haynes' prediction algorithms may be integrated with its optimization algorithms, and Fletcher-Haynes specifically recites "the optimizer model 172 may interface with the prediction model or actually integrally incorporate the prediction model" and refers to Eqs. 1-22. EX1005, 58:63-67. Stated differently, Fletcher-Haynes discloses 22 equations that can be incorporated into a prediction model to predict a particular blood component's yield. EX1005, 58:63-67. One is an equation for calculating total blood volume using a donor's height and weight, another is an equation for calculating anticoagulant (AC) ratio using a donor's hematocrit, and another is an equation for calculating source plasma volume or a

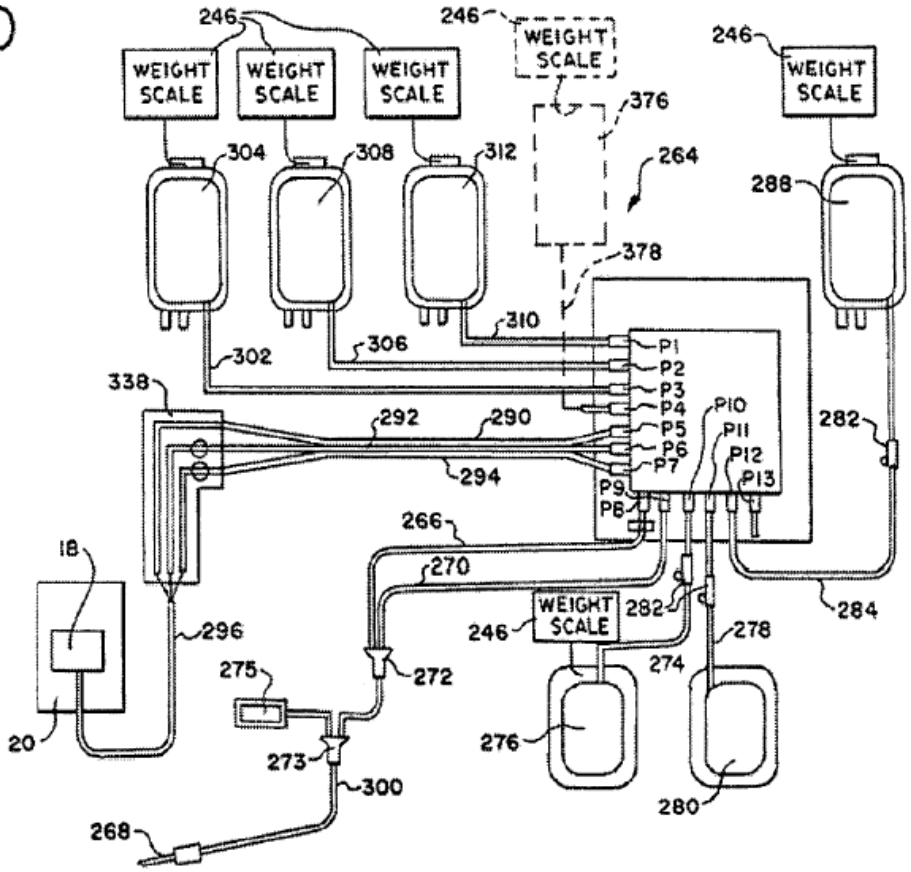
target pure plasma volume collected or to collect. EX1005, 49:40-52:17. Specifically, Equation 10 defines the total blood volume of a donor (V_B) using a donor's height and weight; Equation 9 determines the AC Ratio (R) using a donor's hematocrit; and Equation 22 defines the predicted total volume in the source plasma bag (V_{SPB}). EX1005, 49:40-52:17. These equations can be integrated with Fletcher-Haynes' optimization algorithms. EX1005, 58:63-67; EX1003, ¶59.

Fletcher-Haynes explains that it is preferable during procedures "to have computer/database system 140 exert control over apheresis machine functions, including process control manipulation and optimization." EX1005, 34:8-24, 49:40-52:17; EX1003, ¶60.

C. Overview of Min

Min discloses blood processing systems for separating plasma from whole blood. EX1006, 7:4-8:5. Min teaches plasma collection procedures that include a collection cycle, and pre- and post-collection cycles, which include priming the system's tubing by "convey[ing] a predetermined volume of anticoagulant . . . into the in-process container" during the pre-collection cycle. EX1006, 22:41-43; 32:16-18; EX.1003, ¶61. Figure 10 of Min shows Min's system for performing blood processing procedures, like plasma collection.

FIG. 10



In Min, weigh sensors 246 track weight changes and derive fluid processing volumes, including the volume change in anticoagulant container 276 and plasma collection container 304. EX1006, 11:52-55, 17:17-22. EX.1003, ¶62.

D. Overview of Barrett

Barrett discloses a hemodialysis patient data acquisition and management system for monitoring blood separation procedures, like hemodialysis. EX1007, 4:14-67. Barrett describes several techniques to monitor hematocrit, including ones used for real-time monitoring during hemodialysis. EX1007, 2:23-57. Barrett specifically discloses determining a patient's hematocrit by dividing a blood

sample's calculated total red blood cell volume by a total volume of the blood sample. EX1007, 2:45-49. EX1003, ¶63.

E. Overview of Headley

Headley discloses systems and methods for collecting, from whole blood, platelets suspended in plasma, among other blood components. EX1008, Abstract. Headley's blood separation systems use a centrifuge to separate blood into components and use of an array of optical sensors with a control unit to determine red blood cell volume in a blood separation system. EX1008, 4:48-64; EX1003, ¶64.

F. Overview of Turgut

U.S. Patent Publication No. 2017/0029762 A1 ("Turgut") discloses separation systems that effectively separate biological material, like blood components, with the help of centrifugal force. EX1009, Abstract. Turgut's blood separation systems use a centrifuge to separate blood into components and use a volume detector to determine a total volume of fluid within, for example, the centrifuge's separation chamber. EX1009, ¶73; EX1003, ¶65.

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 '124 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. Gary D. Fletcher's Declaration, demonstrate how the claims are unpatentable. 37 C.F.R. 42.104(b)(4)-(5). *See* EX1003, ¶¶66-203.

A. Ground 1: Claims 1, 3, 5, 6, 8, 10-12, 14, 16-17, and 19 are anticipated by or rendered obvious over Lavender

1. 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 continuously fractionating blood in situ." EX1004, Abstract. Lavender fractions blood "to **collect blood substances, such as plasma**." EX1004, 1:12-13; *see also id.* at claim 1 ("A method of collecting plasma…."), 5:42-49, 1:48-56; EX1003, ¶66.

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

Lavender determines a weight of a donor through "entry and validation of donor data, including ... **donor weight in pounds**." EX1004, 20:10-14; *see also* EX1004 Abstract. EX1003, ¶67.

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

Lavender determines a hematocrit of a donor through "entry and validation of donor data, including … **donor hematocrit in percent**." EX1004, 20:10-14. EX1003, ¶68.

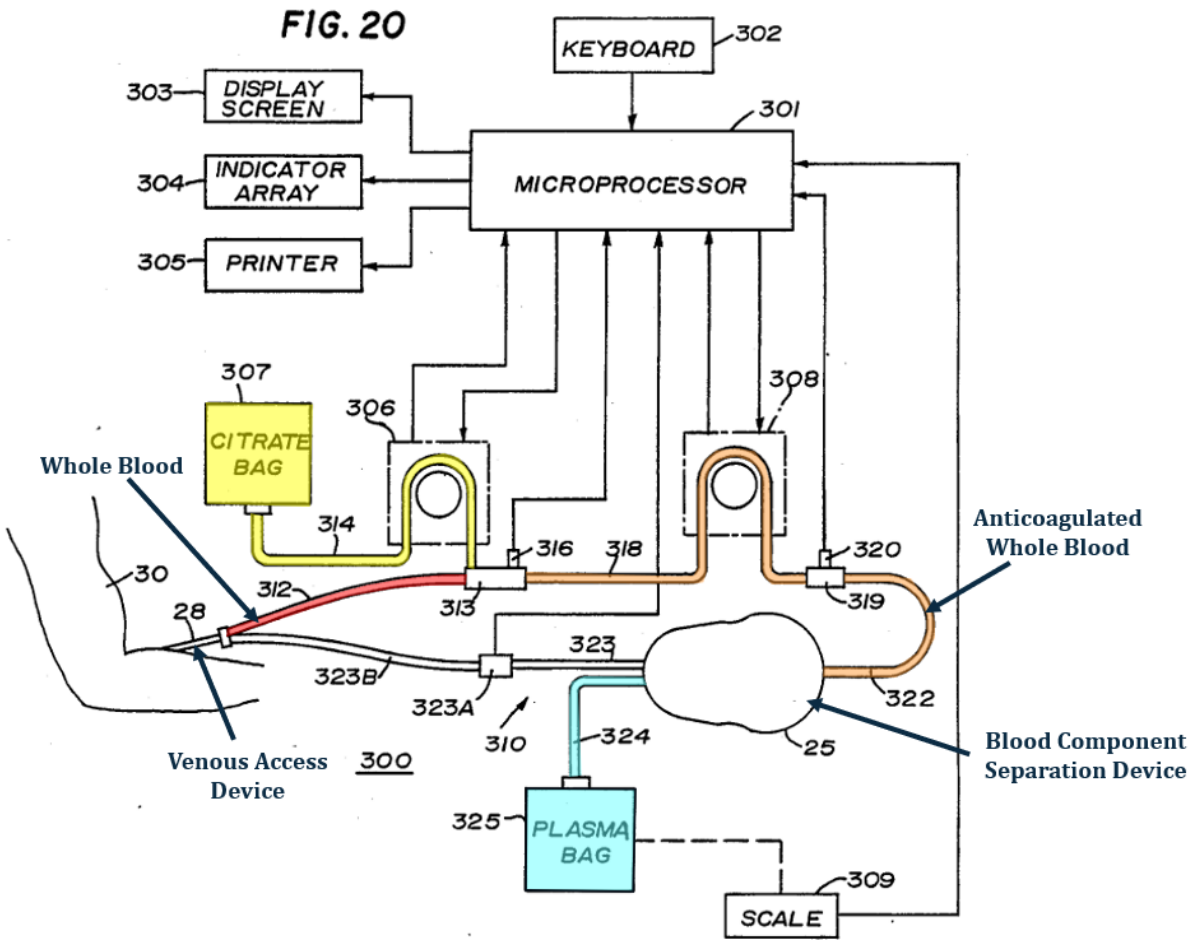
d. 1[c] inserting a venous-access device into the donor;

Lavender's blood fractionator uses a catheter, needle, or double lumen needle inserted into an appropriate vein or artery of the donor to draw blood from the donor for processing, allowing blood to flow from the catheter or needle through a blood

tube and into an inlet of the blood fractionator. EX1004, 5:13-22, FIGS. 1, 20; EX1003, ¶69.

e. 1[d] withdrawing whole blood from the donor through the venous-access device and a draw line, the draw 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 blood fractionator 25, shown below in FIG. 20. EX1004, 5:18-22, FIG. 20.



EX1004, FIG. 20 (annotated).

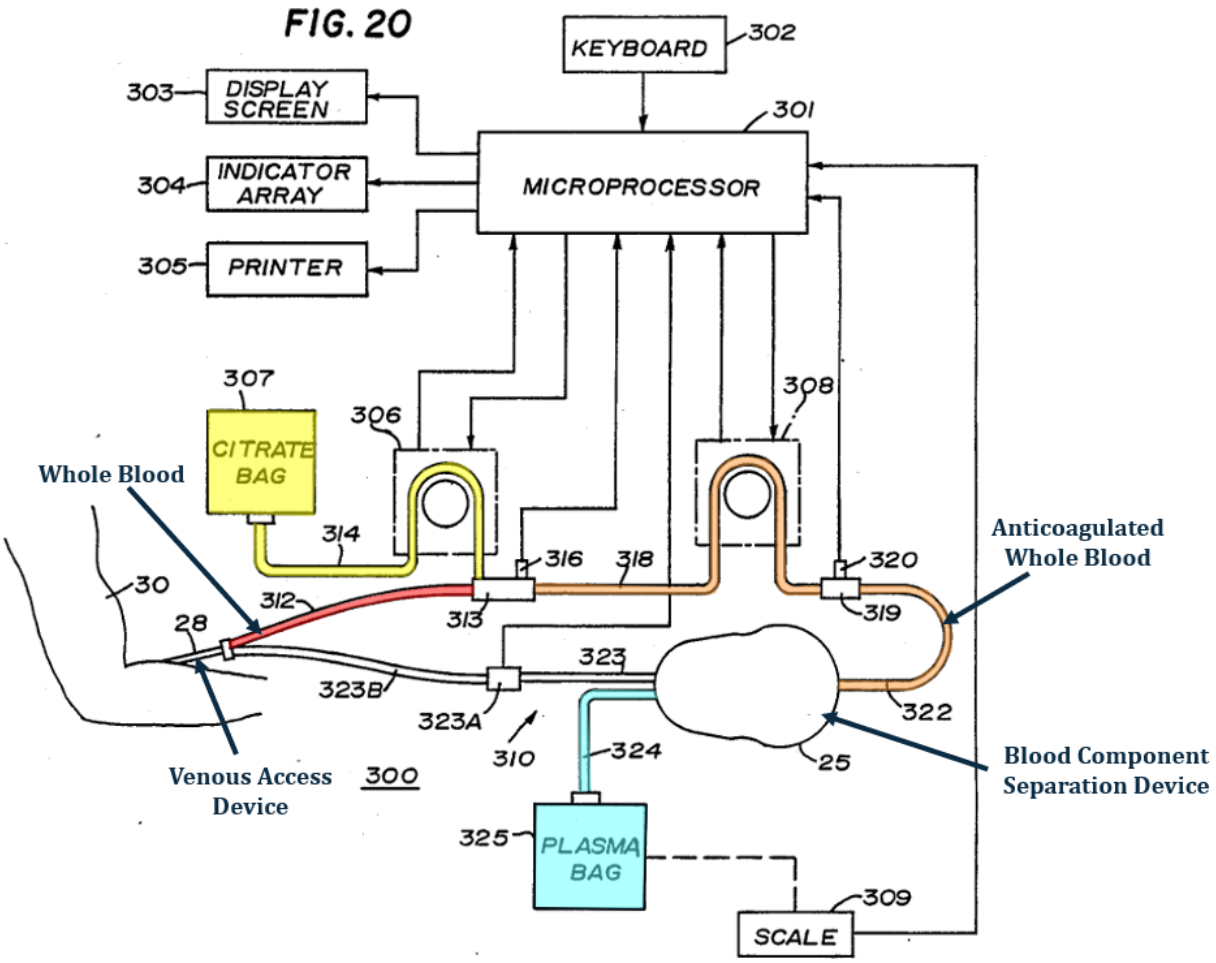
In Lavender, the blood drawn from needle 28 is whole blood because it is a mixture of "a variety of blood fractions." EX1004, 5:44. EX1003, ¶70.

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 and 20. EX1003, ¶71.

Blood fractionator 25 is a blood component separation device because "it produces a variety of blood fractions" from whole blood, "plasma [being] one of the most important blood fractions." EX1004, 5:42-45. EX1003, ¶72.

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

In Lavender's automated blood fractionation system, "[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, ¶73.



EX1004, FIG. 20 (annotated).

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

In Lavender, after whole blood is drawn from the donor, the whole blood flows into Lavender's blood fractionator 25, which separates the whole blood into blood fractions (components), including a plasma component and a component

containing red blood cells, white blood cells, and platelets. EX1004, 1:21-25, 5:42-52, 10:58-11:6, FIGS. 1, 20; EX1003, ¶74.

h. 1[g] 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, ¶75.

i. 1[h] calculating a volume of anticoagulant in the collected plasma component based, at least in part, upon the hematocrit of the donor;

Lavender discloses limitation 1[h] under the plain and ordinary meaning of the term "based, at least in part, upon." EX1003, ¶76. 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 '124 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, 8:62-9:2. As explained below, Lavender anticipates this limitation under the plain and ordinary meaning of "based, at least in part, upon." Alternatively, as discussed below, a POSITA would have understood that Lavender renders this limitation obvious. EX1003, ¶76.

Regardless of how "based, at least in part, upon," is interpreted, Lavender in view of Fletcher-Haynes renders obvious element 1[h], as discussed in Ground 2, below. EX1003, ¶77.

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, 55-67. EX1003, ¶79. 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***). *Id*.

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***). In Lavender, both the volume of anticoagulant (***TCF***) and the total plasma filtered (pure plasma) in plasma bag 325 (***TPF***) depend on the total plasma flow volume (***TQP***), which is calculated based on the donor's hematocrit **(*HCTD*)** via equation $TQP = TQB * (1 - HCTD)$. EX1003, ¶80.

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***). *Id*. ***TQP*** is a donor specific amount based on hematocrit (***HCTD***) that determines how much anticoagulant needs to be added to dilute the donor's blood to 68% of the original plasma concentration, which, in turn, changes ***TDPW*** and ***TDPF***. EX1004, 41:4-44:42; EX1004, 22:35-43. 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, ¶¶81-82.

A POSITA would understand that Lavender also directly calculates the volume of anticoagulant in plasma bag 325 based, at least in part, upon the hematocrit of the donor. System 300 uses the weight of the plasma bag 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)[3] (expressed as $TCF = TPF * CF$), where $\boldsymbol{CF}$ represents the volume of anticoagulant introduced into the incoming whole blood ($\boldsymbol{V_{AC}}$) per incoming volume of plasma ($\boldsymbol{V_P}$), or $CF = \frac{V_{AC}}{V_P}$.. EX1004, 41:1-44:42 (Table VI, §5(B)). Conversion factor (CF) is determined using a predefined ratio of citrate added per milliliter of whole blood to dilute incoming plasma to 68% of the initial concentration. EX1004, 22:35-46. EX1003, ¶83.

Lavender weighs the collected plasma and anticoagulant solution in plasma bag 325 and transmits the weight to microprocessor 301. EX1004, 16:50-53; 17:14-16. Total plasma in the collected plasma component ($\boldsymbol{TPF}$) is calculated based on the total **volume of anticoagulant** and plasma mixture in the collection container (total dilute plasma filtered ($\boldsymbol{TDPF}$)), which is determined using the collection container's weight. The $\boldsymbol{TPF}$ equation is $TPF = TDPF * PDF$. Plasma dilution

[3] Petitioner notes that two different terms are identified as "CF" in Table VI, the conversion factor (CF) and the rate that citrate is pumped into the donor's whole blood in system 300, or citrate filtered in ml/min (CF). This appears to be a typo and a POSITA would readily understand that the "CF" used in the equation to calculate the total citrate filtered (TCF) is the conversion factor (CF) and not the rate that citrate is pumped.

factor (***PDF***) 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. A POSITA would understand this would be expressed as: $PDF = \frac{V_P}{V_P+V_{AC}}$. EX1003, ¶¶83-84.

Lavender therefore determines the volume of anticoagulant in the collected plasma component, as follows:

$$TCF = TPF * CF = TDPF * PDF * CF = TDPF * \left(\frac{V_{AC}}{V_P}\right) * \left(\frac{V_P}{V_P+V_{AC}}\right) = TDPF * \frac{V_{AC}}{V_P+V_{AC}}$$

A POSITA would also understand that the volume of plasma introduced into the system ($\mathbf{V_P}$) is related to the volume of whole blood introduced ($\boldsymbol{V_B}$) 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, ¶85.

Lavender therefore determines the volume of anticoagulant in the collected plasma from $TCF = TDPF * \frac{V_{AC}}{[V_{AC}+V_B *(1-HCTD)]}$, 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, Lavender renders this limitation obvious because a POSITA would understand that Lavender's volume of anticoagulant is directly calculated based on the donor's hematocrit. EX1003, ¶86.

j. 1[i] 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 discloses limitation 1[i] under the plain and ordinary meaning of the term "based on." EX1003, ¶87. The claim language itself—"based, at least in part, on"—suggests that the calculation may rely on one or more methods, not just a single, exclusive method. Although the '124 patent provides an example where a technician determines the volume of collected pure plasma by calculating the volume of anticoagulant in the plasma component—specifically, by measuring the volume of anticoagulant in the container and subtracting this from the total fluid volume in the collection container—the patent does not expressly disavow other reasonable interpretations of "based, at least in part, on," including it encompassing a direct relationship between the pure plasma volume in the collection container and the volume of anticoagulant in the collected plasma component. As explained below, Lavender discloses this limitation under the plain and ordinary meaning of "based, at least in part, on." Alternatively, as discussed below, a POSITA would have understood that Lavender renders this limitation obvious under the broad interpretation. EX1003, ¶87.

Even if a narrower interpretation of "based, at least in part, on" is adopted in view of the '124 patent's exemplary calculation—Lavender in view of Fletcher-Haynes renders limitation 1[i] obvious, as discussed in Ground 2, below.

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. Lavender first calculates **total plasma filtered (*TPF*)**, representing the total amount of pure plasma in the plasma collection bag. EX1004, 20:55-68; 41:1-44:33. TPF is determined by multiplying the total amount of dilute plasma filtered ($TDPF$) by a plasma dilution factor (PDF) (*i.e.*, $\boldsymbol{TPF} = TDPF * PDF$). EX1004, 20:55-68; 41:1-44:33. 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. Thus, 32 ml of citrate is added to the incoming whole blood for every 68 ml of plasma to dilute the incoming plasma to 68% of its initial concentration; and PDF is defined at .68. EX1004, 20: 35-46; 41:1-44:33; EX1003, ¶89.

Lavender then calculates the anticoagulant volume in the plasma container (*i.e.*, **total citrate filtered (*TCF*)**). *See* §IX.A.1.i.; EX1003, ¶90.

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. EX1003, ¶91.

```
TPF=TDPF*PDF        (total plasma filtered, ml)
CF=PF*CF            (citrate filtered, ml/min)
TCF=TPF*CF          (total citrate filtered, ml/min)
```

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. 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, ¶92.

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, ¶93. If the Board, however, determines this is not inherent in Lavender, Lavender renders this limitation obvious because a POSITA would (i) recognize the interdependency between the predefined ratio of citrate added per milliliter of whole blood, TPF and TCF, and (ii) understand that the plasma volume in the collection bag is based, at least in part, on the volume of anticoagulant in the collection bag. EX1003, ¶93.

k. 1[j] continuing steps (d) through (i) until a target volume of pure plasma is collected within the plasma collection container.

As discussed above, Lavender performs steps (d) – (i). *See* §§IX.A.1.e-j. EX1003, ¶94.

In response to the start of a blood separation procedure using Lavender's automatic system, the system initializes the system algorithm of Table VI. EX1004, 20:55-68, 41:1-44:33, Figs. 25A-25D. The Main Loop of the algorithm repeats **until a desired amount of plasma has been collected**.[4] EX1004, 21:62-22:2; EX1003, ¶95.

For example, Lavender repeats step (d)-(i) 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**." EX1004, 21:62-22:6; 46:14-22; *see also* claim 1; EX1003, ¶96.

2. Claim 3: A method according to 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, at least in part, on a number of rotations of an anticoagulant pump.

[4] All emphasis is added unless otherwise noted.

EX1004, 41:27-30; 42:8-44:32. Lavender's anticoagulant pump 306 pumps "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, ¶97.

Lavender also calculates the volume of anticoagulant in the collected plasma component based on the number of rotations of the anticoagulant pump. 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." 15:47-53. Further, as shown in §2 of Table VI, the rotations of the 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. EX1003, ¶98.

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

$$QBP = QB + QC = QB + QCP$$

$$= QB + QP * CF$$

$$= QB + QB * (1 - HCTD) * CF$$

Accordingly, as all of 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 ***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***). For example, as discussed above, $QC = QP * CF$ and $QP = QB * (1 - HCTD)$, so

$$CF = \frac{QC}{QP} = \frac{QC}{[QB*(1-HCTD)]}$$

$$= \frac{QCP}{[(QBP-QCP)*(1-HCTD)]}$$

$$= CRPM * \frac{CMR}{[(BRPM*BMR-CRPM*CMR)*(1-HCTD)]}$$

and $PDF = \frac{1}{CF+1}$.

EX1003, ¶99.

3. Claim 5: 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.1.i., Lavender updates ***TDPF*** as the system withdraws blood. EX1003, ¶100.

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, in Lavender, 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, ¶101.

4. Claim 6: 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* Table VI, §5(B). Lavender discloses that the current total volume of pure plasma in the collection container (***TPF***) is based on ***TDPF***, which is "the monitored volume of collected plasma component" based on the monitored weight of collected plasma component (***TDPW***). EX1004, 41:1-44:33. EX1003, ¶102.

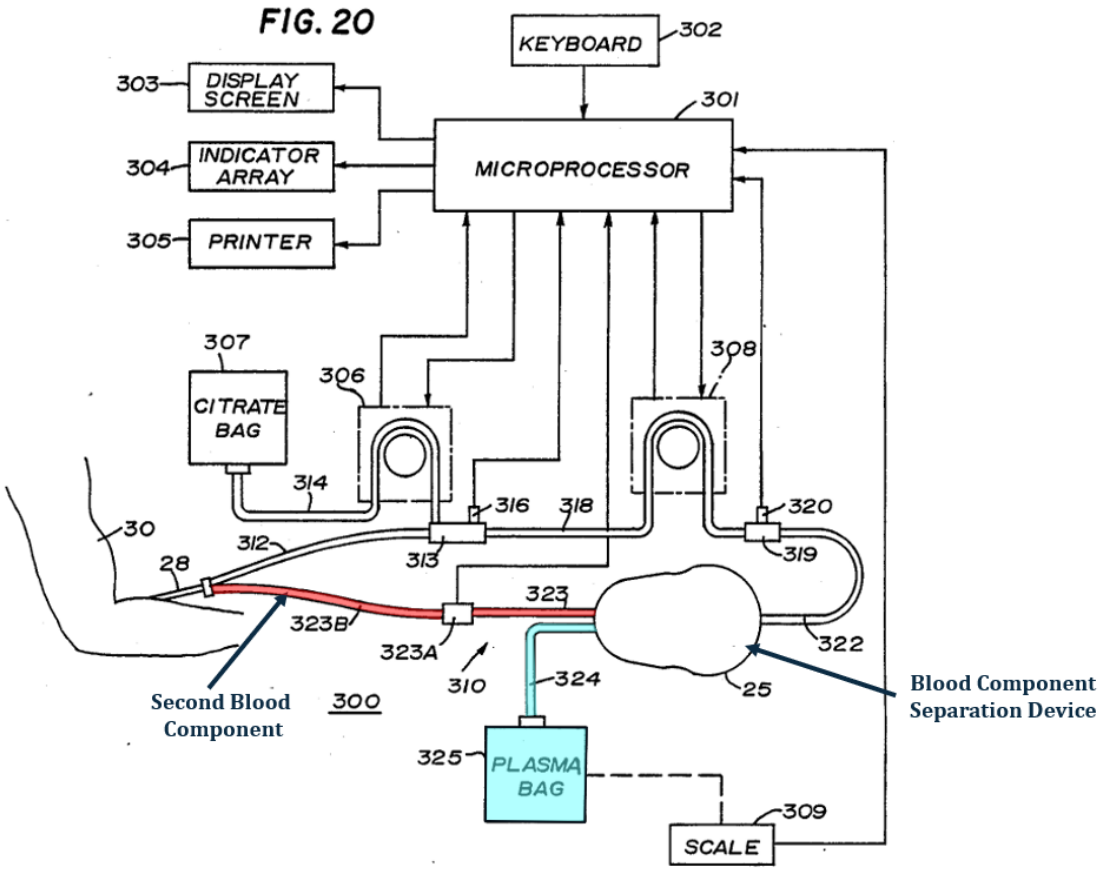
5. Claim 8: A method according to claim 1, wherein the target volume of pure plasma is based, at least in part, on the weight of the donor.

Lavender discloses directing "the user in entry and validation of donor data, including … **donor weight in pounds**." EX1004, 20:10-14. Then, Lavender determines a target volume of pure plasma, ***MAXPF***, which is based on the donor's

bodyweight (***BW***) and a predetermined constant ($C1$) of milliliters of plasma collected per pound of body weight. EX1004, Table VI, §2(g). EX1003, ¶103.

6. Claim 10: A method according to claim 1, further comprising: returning, after collecting at least a portion of the target volume of pure plasma, the second blood component to the donor through a return line.

Lavender collects a first blood component (*e.g.*, plasma) in a "blood fraction collection receptacle or bag." EX1004, 5:32-33. The second blood component (*e.g.*, RBC), is returned to donor 30 through tubing 323. EX1004, 10:58-63. EX1003, ¶104.



EX1003, FIG. 20 (annotated).

7. Claim 11

a. 11[preamble] A system for collecting plasma comprising:

Lavender discloses that its methods may be implemented in "a system for harvesting plasma." EX1004, Abstract, 1:15-17, 1:45-47, FIGS. 1, 20. EX1003, ¶105.

b. 11[a] a venous-access device for drawing whole blood from a subject and returning blood components to the subject;

See §IX.A.1.d, *supra*, EX1004, 5:13-22, Figs. 1, 20. 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 blood fractionator 25, and returns blood components to the donor through tube 323, shown above in FIG. 20. EX1004, 5:18-22, FIG. 20. EX1003, ¶106.

c. 11[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.1.g-h, *supra*, EX1004, 10:58-11:6; FIGS. 1, 4, 15, 17, 20. EX1003, ¶107.

d. 11[c] a blood draw line fluidly connected to the venous-access device and configured to transport drawn whole blood to the blood component separation device, the flow through the blood draw line being controlled by a blood draw pump;

See §IX.A.1.e, *supra*, EX1004, 5:13-22 and FIGS 1, 20. EX1003, ¶108.

e. 11[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.1.f, *supra*, EX1004, 5:22-28 and FIGS. 1, 20. EX1003, ¶109.

f. 11[e] a controller configured to control the operation of the blood component separation device and the blood draw pump,

See §IX.A.1.g, *supra*, EX1004, 10:58-11:6; and FIGS. 1, 20. EX1003, ¶110.

Lavender recites:

> The input and output pressures of the blood pump are sensed and inputted to a microprocessor, into which donor data including weight, sex, and hematocrit is also keyed by the user. The microprocessor 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. The program 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. This program control of the extracorporeal devices would include blood fractionator 25 (blood component separation device) and the associated fluid pumps. EX1004, 18:27-64; cls. 28, 29, 33, 35, 36, 38, 40-41. EX1003, ¶111.

g. 11[f] the controller configured to calculate (1) a volume of anticoagulant in the collected plasma component based, at least in part, upon the hematocrit of the subject, and

See §IX.A.1.i, *supra*, EX1004, 10:58-11:6; FIGS. 1, 20. EX1003, ¶112.

Petitioner notes that system 300's microprocessor executes the algorithms detailed in Table VI of Lavender. EX1004, 18:53-56.

h. 11[g] (2) 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.1.j, *supra*, EX1004, 8:29-64; 20:55-68; EX1004, 22:35-39; 41:1-44:33. Petitioner notes that system 300's microprocessor 301 executes the algorithms detailed in Table VI of Lavender. EX1004, 18:53-56; EX1003, ¶114.

i. 11[h] the controller configured to stop the blood draw pump when a target volume of pure plasma is collected within the plasma container.

Lavender's controller is configured to stop the blood draw pump when a target volume of pure plasma is collected within the plasma container. *See* §IX.A.1.k, *supra*. EX1004, 21:1-22:6; §5(C) of Table VI. EX1003, ¶115.

8. Claim 12: A system according to claim 11, 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.

In Lavender's automatic system 300, whole blood is drawn from a donor and mixed at mixer 313 with anticoagulant pumped from citrate bag 307. EX1004, 16:54-17:2; FIG. 20. The whole blood and anticoagulant mixture is pumped to blood fractionator 25, which separates the blood into components, and a plasma and anticoagulant mixture is collected in plasma bag 325. EX1004, 16:50-53; 17:14-16. EX1003, ¶116.

In Lavender's Main Loop algorithm of Table VI, a volume of anticoagulant in the collected plasma component (***TCF***) is calculated based on a volume of total plasma in the collected plasma component (***TPF***), via the equation $TCF = TPF * CF$, where ***CF*** is a conversion factor representing the volume of anticoagulant introduced into the incoming whole blood ($\boldsymbol{V_{AC}}$) per incoming volume of plasma ($\boldsymbol{V_P}$), or $CF = \frac{V_{AC}}{V_P}$. EX1004, 41:4-44:42. The total plasma in the collected plasma component (***TPF***) is calculated based on the total **volume of anticoagulant** and plasma solution in the collection container (total dilute plasma filtered (***TDPF***)), which is determined by the weight of the collection container. The equation for ***TPF*** is $TPF = TDPF * PDF$. The plasma dilution factor (***PDF***) represents the factor by which a volume of incoming plasma is diluted with a volume of anticoagulant. EX1004, 22:37-39; 41:10-44:57. As discussed above, POSITA would therefore understand that $PDF = \frac{V_P}{V_P + V_{AC}}$. EX1003, ¶¶ 84, 117.

Lavender therefore determines the volume of anticoagulant in the collected plasma component, as follows:

$$TCF = TPF * CF = TDPF * PDF * CF = TDPF * \left(\frac{V_{AC}}{V_P}\right) * \left(\frac{V_P}{V_P + V_{AC}}\right) = TDPF * \frac{VAC}{V_P + V_{AC}}$$

A POSITA would also understand that the volume of plasma introduced into the system ($\boldsymbol{V_P}$) is related to the volume of whole blood introduced ($\boldsymbol{V_B}$) as $V_P = V_B *$

$(1 - HCTD)$, which is simply Lavender's equation for the plasma flow rate ($TQP = TQB * (1 - HCTD)$) converted to a volume equation. EX1003, ¶118.

Lavender therefore determines the volume of anticoagulant in the collected plasma from $TCF = TDPF * \frac{V_{AC}}{[V_{AC}+V_B *(1-HCTD)]}$, showing that Lavender determines the volume of anticoagulant in the collected plasma from the volume of anticoagulant added to the whole blood and hematocrit. EX1003, ¶119.

Furthermore, because the dilute plasma filtered (***DPF***) in the collection container depends on the flow rate of dilute plasma filtered (***DPFW***), which depends on the volume of total citrate flow (***TQC***), representing a volume of anticoagulant added to the drawn whole blood, the ***DPF*** is based on the volume of anticoagulant added to the drawn whole blood (*i.e.*, ***TQC***). EX1004, 41:4-44:42. Accordingly, a volume of anticoagulant in the collected plasma component (*i.e.*, ***TCF***) is based at least in part on a volume of anticoagulant added to the drawn whole blood (*i.e.*, ***TQC***). EX1004, 41:4-44:42. EX1003, ¶120.

9. Claim 14: A system according to claim 11, 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.A.2, *supra,* EX1004, 41:27-30; 42:8-44:32; 15:47-53; 16:45-47; 16:54-17:2, claim 1; Fig. 20; cols. 41, 42. EX1003, ¶121.

10. Claim 16: A system according to claim 11, 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.A.3, *supra*, EX1004, 43:4-6; 41:1-44:40. EX1003, ¶122.

11. Claim 17: A system according to claim 11, 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.A.4, *supra*, EX1004, 41:1-44:33. EX1003, ¶123.

12. Claim 19: A system according to claim 11, wherein the target volume of pure plasma is based, at least in part, on the weight of the subject.

See §IX.A.5, *supra*, EX1004, 20:10-14; Table VI, §2(g). EX1003, ¶124.

B. Ground 2: Claims 1, 3, 5, 6, 8, 10, 11, 12, 14, 16, 17, and 19 are Obvious Over Lavender in view of Fletcher-Haynes

1. Reasons to Combine Lavender and Fletcher-Haynes

A POSITA would be motivated to combine the teachings of Lavender and Fletcher-Haynes to more accurately track and optimize the amount of plasma collected from the donor. EX1003, ¶125. For example, Fletcher-Haynes teaches using a donor's height, weight, and hematocrit to determine the total pure plasma amount to collect from the donor. EX1005, 20:9-15. By adding height to Lavender's data collection steps, Lavender's systems would more accurately determine the

optimal amount of pure plasma to collect. EX1003, ¶125.

A POSITA would have been motivated to combine Lavender's and Fletcher-Haynes' teachings, and would have had a reasonable expectation of success, because 1) each relate to plasma apheresis, 2) both apply substantially similar techniques to achieve similar results, and 3) Lavender's functionality would not change in the combination as Fletcher-Haynes is used for the same purpose as Lavender's system—using donor parameters to determine the total amount of pure plasma to collect. EX1003, ¶126.

For example, a POSITA would understand that Fletcher-Haynes' algorithms are essentially the same as Lavender's algorithms. EX1003, ¶127. Fletcher-Haynes calculates the collection volume using Equation 22, $V_{SPB} = V_{SP} * (1 + f_{ACP})$, which uses the following variables:

Variable	Description
V_{SPB}	Total volume in source plasma bag
V_{SP}	Volume of pure plasma in source plasma bag
f_{ACP}	Anticoagulant volume expressed as a fraction of pure plasma volume, or $f_{ACP} = \frac{V_{AC}}{V_P}$

EX1005, 51:14-27. EX1003, ¶127.

A POSITA would understand Fletcher-Haynes' anticoagulant volume expressed as a fraction of pure plasma volume (f_{ACP}) is equivalent to Lavender's

conversion factor (CF) for ml of citrate per ml of plasma. EX1003, ¶128.

Fletcher-Haynes' Equation 15 further defines $f_{ACP} = [(R-1) * (1-H)]^{-1}$. R is defined in Equation 3 as $\frac{Q_{IN}}{Q_{AC}}$, which is the ratio of flow of anticoagulated whole blood to flow of anticoagulant. EX1005, 46:48-50. A POSITA would understand that R is equivalent to the inverse of the predetermined ratio of anticoagulant per unit of anticoagulated whole blood, and H is the hematocrit of the donor. EX1005, 50:48-50; EX1003, ¶63. Fletcher-Haynes' Equation 22 may thus be rewritten as $V_{SP} = \frac{V_{SPB}}{1+f_{ACP}}$. EX1003, ¶129.

A POSITA would recognize the volume of anticoagulant in the source plasma bag (V_{ACB}) is the difference between the total volume in the source plasma bag V_{SPB} and the volume of pure plasma in the source plasma bag V_{SP}: $V_{ACB} = V_{SPB} - V_{SP}$. A POSITA could reduce the equation $V_{ACB} = V_{SPB} - V_{SP}$, using simple arithmetic, to $V_{ACB} = V_{SPB} * \frac{f_{ACP}}{1+f_{ACP}}$. EX. 1003, ¶130.

This equation is equivalent to Lavender's total citrate filtered equation ($TCF = TPF * CF$), which is based on the following variables:

Variable	Description
TCF (total citrate filtered)	Total citrate anticoagulant in plasma collection

	container (ml[5])
TPF (total plasma filtered)	Total plasma filtered (ml)
$TDPF$ (total dilute plasma filtered)	Total dilute plasma in plasma collection container
CF (conversion factor)	Ratio of volume of incoming citrate to incoming plasma (ml of citrate/ml of plasma)
PDF	Plasma dilution factor

EX1004, Table VI: 2.b; EX1003, ¶131.

A POSITA would understand that CF and PDF in Lavender are related. Lavender uses a predetermined ratio (or percentage) of anticoagulant to incoming whole blood (or incoming plasma, *e.g.*, conversion factor (CF)) to determine the volumes of anticoagulant and plasma in a collection container. EX1004, 41:4-44:42. CF is the conversion factor, it is the ratio of the volume of incoming citrate to the volume of incoming plasma. From EX1004, Table VI: 2.b. [41:50] conversion factor CF is also equal to $\frac{QC}{QP}$, or the ratio of incoming citrate flow to incoming plasma flow. A POSITA would understand that CF, being the ratio of the volume of incoming citrate to the volume of incoming plasma, would also be the ratio of the flow of

[5] Petitioner notes that the "TCF" units in Table VI are incorrectly listed as ml/min. A POSITA would understand that this is an error as the total citrate filtered, "TCF," would be in milliliters not in ml/min. EX1003, ¶131.

incoming citrate to the flow of incoming plasma, as the volumetric flow rates QC and QP are volumes per unit time (ml/min), and in the ratio of flow rates the unit time would cancel, leaving the ratio of volumes. EX1003, ¶132.

A POSITA would understand this equation is the same as Fletcher-Haynes' $V_{ACB} = V_{SPB} * \frac{f_{ACP}}{1+f_{ACP}}$ because V_{ACB} and TCF are both the volume of anticoagulant in the collection container, V_{SPB} and $TDPF$ are both the total volume of liquid in the collection container (*e.g.*, plasma and anticoagulant), and f_{ACP} and CF are both conversion factors denoting anticoagulant volume expressed as a fraction of pure plasma volume. EX1003, ¶¶133-134.

Thus, a POSITA would have understood and been motivated to implement Fletcher-Haynes' equations in Lavender's system to optimize the data tracking and donor parameter monitoring before, during, and after a blood draw procedure, and would have had a reasonable expectation of success in doing so. EX1003, ¶¶125-134.

2. Claim 1

a. 1[preamble]:

See §IX.A.1.a, EX1003, ¶135.

b. 1[a];

See §IX.A.1.b, EX1003, ¶136.

c. 1[b];

See §IX.A.1.c, EX1003, ¶137.

d. 1[c];

See §IX.A.1.d, EX1003, ¶138.

e. 1[d];

See §IX.A.1.e, EX1003, ¶139.

f. 1[e];

See §IX.A.1.f, EX1003, ¶140.

g. 1[f];

See §IX.A.1.g, EX1003, ¶141.

h. 1[g];

See §IX.A.1.h, EX1003, ¶142.

i. 1[h] calculating a volume of anticoagulant in the collected plasma component based, at least in part, upon the hematocrit of the donor;

See §IX.A.1.i, EX1003, ¶143.

Fletcher-Haynes expressly discloses calculating a volume of anticoagulant in the collected plasma component based, at least in part, upon the hematocrit of the donor. EX1005, 20:9-15; 50:48-50; 51:52. EX1003, ¶144.

Fletcher-Haynes teaches using a donor's height, weight, and hematocrit to determine the total amount of pure plasma to collect from the donor. EX1005, 20:9-15. Fletcher-Haynes also calculates anticoagulant volume expressed as a fraction of pure plasma volume ($\boldsymbol{f_{ACP}}$). EX1005, 51:52. As discussed above, a POSITA would

understand that Fletcher-Haynes' anticoagulant volume expressed as a fraction of pure plasma volume ($\boldsymbol{f_{ACP}}$) is equivalent to Lavender's conversion factor CF. In Fletcher-Haynes, the anticoagulant volume is calculated using the donor's hematocrit (H) from $f_{ACP} = [(R-1) * (1-H)]^{-1}$. As discussed above, a POSITA would be motivated to use Fletcher-Haynes' calculations in Lavender and would have understood that using Fletcher-Haynes' equation to calculate the volume of anticoagulant in the collection container would amount to no more than combining prior art elements according to known methods to yield predictable results. §IX.B.1; EX1005, 50:48-50. EX1003, ¶145.

j. 1[i] 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

Should the Board find that "based on" is narrowly limited to the calculation disclosed in the '124 patent, a POSITA would have found it obvious to implement Fletcher-Haynes' calculation of the volume of pure plasma in the collection container based, at least in part, on the volume of anticoagulant in the collection container in Lavender's system. EX1003, ¶146.

Fletcher-Haynes expressly discloses calculating the volume of pure plasma in the collection container based, at least in part, on the volume of anticoagulant. EX1005, 22:66-23:3. Fletcher-Haynes recites, "Product Plasma - The volume of plasma product collected during the procedure (total plasma volume less

anticoagulant volume)."[6] EX1005, 22:66-23:3. A POSITA would utilize this formula to determine the collected pure plasma volume in Lavender's systems and methods by inserting Fletcher-Haynes' equation for product plasma into Lavender's Main Loop Algorithm. EX1003, ¶147. Such a combination would have been no more than combining prior art elements according to known methods to yield predictable results.

Because both Lavender and Fletcher-Haynes teach methods for determining the amount of pure plasma collected in a plasma apheresis procedure, it would have been obvious to substitute one method for the other. Referring to the Main Loop algorithm of Lavender, a POSITA would replace the equation $TPF = TDPF * PDF$ with $TPF = TDPF - TCF$ and replace $TCF = TPF * CF$ with $TCF = TDPF * PDF * CF$. The revised equation for TCF simply substitutes TPF with $TDPF$ and adds an additional predetermined constant (PDF). Such substitutions would be routine algebraic calculations for a POSITA and would yield predictable results because the equations rely on the same conversion constants (*i.e.*, *PDF* and *CF*) and are essentially the same equations derived from a predetermined ratio of

[6] Petitioner notes determining product plasma by taking the total plasma volume (*i.e.*, total volume of plasma and anticoagulant in the collection bag) less the anticoagulant volume, was well known in the art long before the filing of the '124 patent. For example, Japanese Patent Publication No. JP 2002-282352A (EX1014) discloses determining a pure plasma volume in a collection container using a volume of anticoagulant in the collection container.

anticoagulant added to incoming whole blood but written differently. EX1003, ¶¶30-35, 148. A revised Main Loop algorithm of Lavender using the product plasma formula from Fletcher-Haynes is shown below, with additions underlined and deletions marked in red strikethrough.

5. Main Loop:

A. Measure weight change per unit time for each pass through the loop.

B. Calculate:

TQB=TQB+(△t*(QBP-QCP)*0.0167)

TQP=TQB*(1-HCTD)

TQC=TQC+(△t*QCP*0.0167)

TQ=TQB+TQC

TDPW=total weight (total dilute plasma filtered, gm)

DPFW=(△weight/△time)*60 (dilute plasma filtered, gm/min)

DPF=DPFW*RSG (dilute plasma filtered, ml/min)

TDPF=TDPW*RSG (total dilute plasma filtered, ml)

PF=DPF*PDF (plasma filtered, ml/min)

TPF = TDPF − TCF

~~TPF=TDPF*PDF (total plasma filtered, ml)~~

CF=PF*CF (citrate filtered, ml/min)

TCF = TDPF * PDF * CF

~~TCF=TDPF*CF (total citrate filtered, ml/min)~~

TRC=TQC-TCF (total citrate returned to donor, ml)

C. Compare TPF with MAXPF.
If TPF less than MAXPF, repeat the loop.
If equal or greater, stop the program.

As shown above, the modified Main Loop algorithm of Lavender with the

product plasma equation from Fletcher-Haynes directly calculates the pure plasma volume in the plasma collection container using the volume of anticoagulant in the plasma collection container in real time. Specifically, the proposed combination would calculate $TPF = TDPF - TCF$. Thus, Lavender in view of Fletcher-Haynes renders obvious limitation 1[i] under a narrow interpretation of "based, at least in part, on." EX.1003, ¶149.

k. 1[j]

See §IX.A.1.k. EX1003, ¶150.

3. Claim 3

See §IX.A.2, EX1003, ¶151.

4. Claim 5

See §IX.A.3, EX1003, ¶152.

5. Claim 6

See §IX.A.4, EX1003, ¶153.

6. Claim 8

See §IX.A.5, EX1003, ¶154.

7. Claim 10

See §IX.A.6, EX1003, ¶155.

8. Claim 11

a. 11[preamble]:

See §IX.A.7.a, EX1003, ¶156.

b. 11[a]

See §§IX.A.7.b and IX.B.1.d, EX1003, ¶157.

c. 11[b]

See §§IX.A.7.c and IX.B.1.g-h, EX1003, ¶158.

d. 11[c]

See §§IX.A.7.d and IX.B.1.e, EX1003, ¶159.

e. 11[d]

See §§IX.A.7.e and IX.B.1.f, EX1003, ¶160.

f. 11[e]

See §§IX.A.7.f and IX.B.1.g, EX1003, ¶161.

g. 11[f]

See §§IX.A.7.g and IX.B.1.i, EX1003, ¶162.

h. 11[g]

See §§IX.A.7.h and IX.B.1.j, EX1003, ¶163.

i. 11[i]

See §§IX.A.7.i and IX.B.1.k, EX1003, ¶164.

9. Claim 12

See §IX.A.8, EX1003, ¶165

10. Claim 14

See §IX.A.9, EX1003, ¶166.

11. Claim 16

See §IX.A.10, EX1003, ¶167.

12. Claim 17

See §IX.A.11, EX1003, ¶168.

13. Claim 19

See §IX.A.12, EX1003, ¶169.

C. Ground 3: Claims 2, 9, 13, and 20 are obvious over Lavender in view of Fletcher-Haynes and Min

1. Reasons to Combine Lavender and Fletcher-Haynes with Min

A POSITA would have been motivated to combine the teachings of Lavender and Fletcher-Haynes with Min, and a POSITA would understand that there is a reasonable expectation of success in making this modification. EX1006, 11:52-55, 17:17-22; EX1003, ¶170.

A POSITA would have found it obvious and would have been motivated to combine the combination of Lavender and Fletcher-Haynes with Min's use of weigh sensors 246 to track weight changes and derive fluid processing volumes, including the volume change of anticoagulant container 276 and plasma collection container 304. EX1006, 11:52-55, 17:17-22; EX1003, ¶171.

Additionally, a POSITA would have had a reasonable expectation of success in modifying the Lavender-Fletcher-Haynes system in view of Min because 1) each relate to the same well-known technologies, 2) both apply substantially similar techniques to achieve similar results, and 3) the functionality of Lavender would not change because Lavender is used for the same purpose as Min's system—that is,

monitoring the weight of an anticoagulant bag in an apheresis procedure to determine a change in volume within the anticoagulant container. EX1006, 11:52-55, 17:17-22. Min uses weigh sensors 246 to track weight changes and derive fluid processing volumes, including the volume change of anticoagulant container 276 and plasma collection container 304. EX1006, 11:52-55, 17:17-22. EX1003, ¶30-35, 172.

Lavender, Fletcher-Haynes, and Min all relate to separating blood components. Accordingly, a POSITA would have found it obvious to combine the teachings of Lavender and Fletcher-Haynes with Min because they are in the same field of endeavor with the same well-known technologies. That is, combining Lavender, Fletcher-Haynes, 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. EX1003, ¶173; *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2007).

Lavender, Fletcher-Haynes, and Min also 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, Min discloses a system for "separating whole blood into plasma and red blood cells." EX1006, 4:26-29. A POSITA would have been motivated to add

Min's system to monitor the weight (and volume) of an anticoagulant bag to Lavender's blood fractioning system to provide an additional way to determine the estimated amount of anticoagulant in the plasma collection container, and Min's disclosed systems for determining the amount of anticoagulant added to a system function substantially similar to Lavender's technique of adding and monitoring the anticoagulant added to a blood separation system. Indeed, Min's anticoagulant container and tube arrangement (*See* Fig. 10) is structurally similar to that of Lavender's (*See* Fig. 20). EX1006, 3:26-29. Therefore, it would have been obvious, and a POSITA would have been motivated, to modify Lavender's blood fractioning system to incorporate Min's monitoring of the change in the weight of the anticoagulant container. *See Intel Corp. v. PACT XPP Schweiz AG*, 61 F.4th 1373, 1380-81 (Fed. Cir. 2023) ("There is a motivation to combine when a known technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way using the 'prior art elements according to their established functions'") (internal citations omitted). Additionally, it would have been an obvious design choice to use Min's anticoagulant monitoring scale in Lavender's system to improve the accuracy of the anticoagulant volume added to the system for determining more accurate pure plasma volume based on the anticoagulant volume. EX1003, ¶174.

Finally, the intended functionality of Lavender's blood fractioning system would not change when used for monitoring the anticoagulant weight similarly to Min's apheresis system. That is, a POSITA would have expected Lavender´s blood fractionating system to successfully determine the amount of anticoagulant added to the system from the anticoagulant container similarly to Min. *Eli Lilly & Co. v. Teva Pharm. Int'l GmbH*, 8 F.4th 1331, 1345 (Fed. Cir. 2021) (reasonable expectation of success is about the expectation of success by a POSITA). Additionally, Lavender discloses converting a change in weight to a change in volume using a specific gravity. Accordingly, a POSITA would understand that there is a reasonable expectation of success when modifying the algorithms to determine the volume of anticoagulant in the collected plasma component in Lavender's system with the weight scale of Min for monitoring the change in the anticoagulant volume—each relate to the same well-known technologies and both apply substantially similar techniques to achieve similar results. EX1003, ¶30-35, 175; *Par Pharmaceutical, Inc. v. TWI Pharmaceuticals, Inc.*, 773 F.3d 1186, 1198 (Fed. Cir. 2014) (a "reasonable expectation of success" does not require absolute certainty of success).

2. Claim 2: 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 Fletcher-Haynes 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. Min uses weigh sensors 246 to track weight changes and derive fluid processing volumes, including the volume change of anticoagulant container 276 and plasma collection container 304. EX1006, 11:52-55, 17:17-22. A POSITA would recognize, and the '124 patent acknowledges that substantially all of the anticoagulant added to a centrifuge-based blood fractionating system would end up in the plasma collection container. *See* §V.A.; EX1001 at 8:18-23; EX1003, ¶176.

If Patent Owner argues that Lavender's fractionator 25, which comprises a series of membranes 75, is not as efficient at separating some blood components and that substantially all of the anticoagulant added to Lavender's blood fractionating system would not end up in the plasma collection container, it would have been obvious for a POSITA to replace the membrane-based fractionator in Lavender with a centrifuge-based blood component collection device 18, like the one disclosed in Fletcher-Haynes. EX1004, 6:3-12; EX1005, 46:16-43. It was generally known in the art that a centrifuge-based blood separation device, as compared to a membrane-based blood separation device, provided a comparable treatment quality in a shorter time period. *See* EX1010, p. 135. A POSITA would have been motivated to combine

Lavender's system with Fletcher-Haynes' centrifuge-based collection device to more efficiently separate plasma from a donor's blood and reduce the overall procedure time. EX1003, ¶176.

A POSITA would have been motivated to combine Lavender's and Fletcher-Haynes' teachings, and would have had a reasonable expectation of success, because 1) each relate to the same well-known technologies, 2) both apply substantially similar techniques to achieve similar results, and 3) Lavender's functionality would not change in the combination as Fletcher-Haynes' centrifuge-based blood component collection device is used for the same purpose as Lavender's system—using donor parameters to determine the total amount of pure plasma to collect and separating a donor's blood to collect pure plasma. EX1003, ¶177.

Therefore, a POSITA would understand that substantially all of the anticoagulant added to the Lavender-Fletcher-Haynes blood fractionating system would end up in the plasma collection container. It would have been obvious to a POSITA to incorporate Min's technique of monitoring the change in volume of the anticoagulant container using a scale into the blood fractionating system of Lavender and Fletcher-Haynes to calculate the volume of anticoagulant in the collected plasma component based, at least in part, on the change in volume within the anticoagulant container. By adding this additional technique to determine the volume of anticoagulant in the plasma collection container, the system would reduce potential

errors in determining the volume of anticoagulant due to blood and anticoagulant pump rate errors (*e.g.*, errors in pumps 306, 308 in Lavender). EX1004, FIG. 20. EX1003, ¶178.

3. Claim 9: 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 fluid into the donor's whole blood prior to separation of 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, ¶179.

The volume of anticoagulant in the collected plasma component also includes at least a portion of the anticoagulant added during a priming step. 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, "the anticoagulant pump PP4 conveys a predetermined volume of anticoagulant

(*e.g.*, 10g) into the in-process container 312" where plasma is collected. EX1006, 22:40-42. Thus, at least a portion of the volume of anticoagulant in the collected plasma component (*e.g.*, the plasma bag 325) would include at least a portion of the anticoagulant added during the priming step described above. EX1003, ¶180.

A POSITA would have been motivated to combine the teachings of Lavender and Fletcher-Haynes with Min for the same reasons as discussed above. §IX.C.1. Additionally, a POSITA would have looked to Min to calculate the volume of anticoagulant added during the priming step in the total collection volume, to reduce any errors that may occur by not accounting for such a priming step in determining the anticoagulant volume in the plasma collection container. EX1003, ¶181

4. Claim 13: A system according to claim 11, 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.C.1. EX1003, ¶182.

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.C.1; EX1003, ¶183. Min uses weigh sensors 246 to track weight changes of the anticoagulant container and derive fluid processing volumes,

including the volume change of anticoagulant container 276 and plasma collection container 304. EX1006, 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." EX1006, 17:17-22. Thus, the combined system discloses an anticoagulant source weight sensor configured to measure the weight of the anticoagulant source (*i.e.*, the weigh sensors of Min), 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.*, the controller of Min). EX1006, 17:17-22. As discussed above, a POSITA would understand that substantially all of the anticoagulant added to the blood fractionating system of Lavender, when modified in view of Fletcher-Haynes' centrifuge-based blood fractionating system, would end up in the plasma collection container and that a POSITA would incorporate Min's monitored volume of the anticoagulant source into Lavender's algorithms to provide an additional measure of the anticoagulant volume in the plasma collection container. *See* §V.A.; §IX.C.1; EX1001, 8:18-23; EX1004, 43:28; EX1006, 17:17-22. Thus, Lavender in view of Fletcher-Haynes 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, ¶183.

Furthermore, as discussed above in §IX.C.1, if Patent Owner argues that substantially all of the anticoagulant added to Lavender's blood fractionating system would not end up in the plasma collection container a POSITA would be motivated to replace the membrane-based blood fractionator in Lavender with the centrifuge-based blood component collection device 18. *See* §IX.C.1.; EX1004, 6:3-12; EX1005, 46:16-43; EX1003, ¶184.

5. Claim 20: A system according to claim 11, 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.

See §IX.C.2, EX1003, ¶185.

D. Ground 4: Claims 7 and 18 are obvious over Lavender in view of Fletcher-Haynes, Headley, and Barrett

1. Claim 7: 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**) in ml while blood is being drawn from the donor. EX1004, 43:7-16. The pump rates for Lavender's blood pump and citrate pump are determined based on the donor's hematocrit. EX1004, 41:21-26; EX1003, ¶186.

Fletcher-Haynes teaches separating red blood cells from incoming whole blood during a blood separation procedure. EX1005, 7:33-35; 9:35-44. Headley relates to systems and methods for separating platelets and other blood components from blood. EX1008, 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. EX1008, 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 the red blood cells to be immediately returned to the donor during the separation procedure. EX1003, ¶187.

Barrett teaches determining a donor's hematocrit by dividing the red blood cell volume of a blood sample over the total volume of the blood sample. EX1007, 2:45-49; EX1003, ¶188.

A POSITA would have been motivated to combine the teachings of Lavender, Fletcher-Haynes, and Headley with Barrett to determine a real-time hematocrit of a donor during a collection procedure. Each of Lavender, Fletcher-Haynes, Headley, and Barrett relate to the well-known technologies of separating blood components. Accordingly, a POSITA would have found it obvious to combine the teachings of Lavender, Fletcher-Haynes, Headley, and Barrett because they are in the same field of endeavor with the same well-known technologies. EX1003, ¶189.

Additionally, Lavender, Fletcher-Haynes, Headley, and Barrett, 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. Barrett also teaches patient blood data acquisition and management for hemodialysis patients in preparation for blood separation procedures. EX1007, 1:6-19; EX1003, ¶190.

In view of Barrett's teaching of determining a donor's hematocrit by dividing the total red blood cell volume of a blood sample over the total volume of a blood sample, a POSITA would want to incorporate this equation from Barrett into Lavender's Main Loop algorithm to determine the donor's hematocrit as blood is being drawn from the donor. A POSITA would recognize this would reduce error in the calculated values of Lavender and account for the change in the donor's hematocrit as blood is being drawn. For example, the pump rates of Lavender's system, which are determined based on hematocrit of the donor, may be more accurately regulated if the hematocrit is updated in real time during a procedure. EX1004, 41:21-26; EX1003, ¶191.

Thus, a POSITA would use both (i) the monitored volume of red blood cells collected during a blood separation procedure from Headley, and (ii) the volume of whole blood withdrawn from the donor, or total blood flow (**TQB**) in Lavender, to determine a donor's real-time hematocrit in Lavender's Main Loop algorithm. This

equation could simply be added into the Main Loop algorithm of Lavender and would increase the accuracy of Lavender's calculated estimates. Also, to more effectively separate the red blood cells in Lavender's system, a POSITA would be motivated to replace the membrane-based blood fractionator in Lavender with the centrifuge-based blood component collection device 18 including a centrifuge. §IX.C.1; EX1004, 6:3-12; EX1005, 46:16-43; EX1003, ¶192.

It would have been an obvious design choice to use Barrett's equation in the system of Lavender, Fletcher-Haynes, and Headley to determine the real-time hematocrit of the donor during a separation procedure. The intended functionality of the system of Lavender and Fletcher-Haynes would not change when including Headley's optical sensor(s) and Barrett's equation for hematocrit. That is, a POSITA would have expected the combined system to successfully determine the hematocrit of a donor using a red blood cell volume determined by Headley's optical sensor(s) and Barrett's equation for hematocrit. EX1003, ¶193; *Eli Lilly & Co.*, 8 F.4th at 1345.

Accordingly, Lavender in view of Fletcher-Haynes, Headley, and Barrett teaches monitoring a volume of red blood cells collected within the blood component separation device because Headley teaches monitoring the volume of collected red blood cells. EX1008, 1:10-24; 4:48-64; 17:19-24; EX1007, 2:45-49. 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 is taught by Barret's equation for hematocrit, which determines hematocrit by dividing the red blood cell volume of a blood sample (*e.g.*, the volume of red blood cells collected) by the total volume of the blood sample (*e.g.*, total blood flow into the system, Lavender's **TQB**). EX1004, 41:8-44:32; EX1006, 12:22-25; 17:19-24; EX1008, 1:10-24; 2:45-49; 4:48-64; EX1003, ¶194.

2. Claim 18: A system according to claim 11, 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 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.D.1. As discussed above, Headley teaches the 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. EX1008, 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.D.1.; EX1008, 1:10-24; 4:48-64; EX1003, ¶195.

Accordingly, Lavender in view of Fletcher-Haynes, Headley, and Barrett teaches 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 using Headley's optical sensor. EX1008, 4:48-64. Using Lavender's Main Loop algorithm and Barrett's equation to determine hematocrit, Lavender, modified in view of Fletcher-Haynes, Min, Barrett, and Headley teaches 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.D.1; EX1003, ¶196; EX1004, 41:8-44:32; EX1006, 12:22-25; 17:19-24; EX1007, 2:45-49.

E. Ground 5: Claims 4 and 15 are obvious over Lavender in view of Fletcher-Haynes, Min, and Turgut

1. Claim 4: 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.

A POSITA would have recognized that determining the total volume of anticoagulant in the collected plasma component based on the change in volume within the anticoagulant container would not account for any remaining anticoagulant within the blood separation device that has not yet flowed into the plasma collection container. *See* §IX.C.1.; EX1003, ¶197. A POSITA would have recognized a need to account for the remaining anticoagulant within the blood

separation device when determining the volume of anticoagulant in the collection container using the volume of anticoagulant supplied to the blood separation device. *See* EX1003, ¶197. By accounting for this remaining anticoagulant within the blood separation device, the system would reduce errors and increase the accuracy of the determined anticoagulant volume in the plasma collection container. *See* EX1003, ¶197.

A POSITA would have found it obvious and would have been motivated to combine Lavender, Fletcher-Haynes, and Min with Turgut's teaching of a volume detector to determine a total volume of fluid within a blood separation system, such as a separation chamber of a centrifuge used to separate blood into components. EX1009, ¶73; EX1003, ¶198.

A POSITA would have found it obvious to combine the teachings of Lavender, Fletcher-Haynes, and Min with Turgut because they are in the same field of endeavor with the same well-known technologies of separating blood components. EX1003, ¶199; *KSR Int'l Co.*, 550 U.S. at 417.

Turgut's separation system is structurally similar to that of Lavender's (*See* Fig. 20) and is used to separate blood into different components. EX1009, ¶¶52-68, Fig. 1A. Therefore, it would have been obvious, and a POSITA would have been motivated, to modify Lavender's blood fractioning system with Fletcher-Haynes' centrifugal separation device to incorporate Turgut's monitoring of the volume of

fluid within the blood separation device. *See Intel Corp.*, 61 F.4th at 1380-81. Additionally, it would have been an obvious design choice to use Turgut's volume detector in Lavender's system to improve the accuracy of the calculated volume of anticoagulant within the plasma collection container. EX1003, ¶200.

A POSITA would understand that the volume of plasma plus anticoagulant remaining within the separation device could be determined using Turgut's volume detector to ascertain the total volume remaining in the separation device and subtracting the volume of red blood cells within the separation device, which is equal to the total volume of whole blood introduced to the separation device multiplied by the hematocrit ($HCTD$). A POSITA would then determine the volume of anticoagulant remaining within the separation device by multiplying the volume of plasma plus anticoagulant by the plasma dilution factor times the conversion factor (*i.e.*, $PDF * CF$). A POSITA would recognize that the determined volume of anticoagulant remaining within the blood component separation device should be subtracted from the amount of anticoagulant supplied to the blood component separation device to more accurately estimate the total amount of anticoagulant within the plasma collection container. EX1003, ¶201.

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, ¶202.

2. Claim 15: A system according to claim 11, 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.E.1, EX1003, ¶203. A POSITA would recognize that Turgut's volume detector may be an optical sensor, like Headley's optical sensor, discussed above, to determine a volume of red blood cells within the blood separation system. EX1008, 1:10-24; 4:48-64. It was generally known by a POSITA at the time of the effective filing date of the '124 patent that a volume detector may be an optical sensor. EX1003, ¶203.

Respectfully submitted,

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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 11,738,124, 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 13,938. 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.

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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 August 1, 2025 by filing a copy of this Petition for IPR of U.S. Patent No. 11,738,124 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. 11,738,124:

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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:

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