**UNITED STATES PATENT AND TRADEMARK OFFICE**

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**BEFORE THE PATENT TRIAL AND APPEAL BOARD**

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TERUMO BCT INC.,

Petitioner

v.

HAEMONETICS CORP.,

Patent Owner

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PGR2025-00077

U.S. Patent No. 12,186,474

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# PETITION FOR POST-GRANT REVIEW OF U.S. PATENT NO. 12,186,474

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## EXHIBIT LIST

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| 1001 | U.S. Patent No. 12,186,474 ("'474 Patent") |
| 1002 | File History of the '474 Patent |
| 1003 | Declaration of Dr. Gary Fletcher in Support of Petition |
| 1004 | U.S. Patent No. 4,898,675 ("Lavender") |
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| 1007 | U.S. Patent No. 10,195,319 ("Kimura") |
| 1008 | U.S. Patent No. 6,743,192 ("Sakota") |
| 1009 | "Calculations in Apheresis" ("Neyrinck") |
| 1010 | "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. |
| 1011 | Curriculum Vitae ("CV") of Dr. Gary D. Fletcher |
| 1012 | 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 |
| 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 certified Japanese to 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 |
| 1016 | Samuel B. Nadler et al., Prediction of blood volume in normal human adults, 51 Journal of Investigative Surgery 224-232 (1962) ("Nadler") |

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Terumo BCT, the "Petitioner," requests post grant review of claims 1-26 of U.S. Patent No. 12,186,474 (the "'474 Patent") (EX1001).

# I. Mandatory Notices

## A. Real Parties-In-Interest

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

## B. Related Matters

The '474 Patent is currently asserted against Petitioner by Patent Owner in *Haemonetics Corp. v. Terumo BCT, Inc.*, No. 1:25-cv-1409 (D. Colo. filed May 5, 2025). Petitioner filed petitions requesting *inter partes* review of U.S. Patent Nos. 11,738,124 (IPR2025-01374) and 10,758,652 (IPR2025-01391), which are in the same patent family as the '474 patent. Petitioner intends to file several other petitions for *inter partes* review and post grant review of patents in the same family as the '474 patent.

## C. Counsel

Petitioner is filing a Power of Attorney appointing the practitioners associated with Customer Number 53065. 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. 50-53065, for any fee deficiency.

## III. Certification of Grounds of Good Standing

Petitioner certifies that the '474 Patent is available for post grant review ("PGR") and that Petitioner is not estopped or barred from requesting this PGR.

## IV. Timing

The ’474 patent issued January 7, 2025. Pursuant to 37 C.F.R. §§ 42.201-202, this Petition is being filed within nine months of the issue date of the ’474 patent. The earliest possible priority date is May 30, 2017.[1] EX1001, Page 2.

## V. Identification Of Challenge And Relief Requested

Petitioner requests post grant review and cancellation of claims 1-26 of the ’474 Patent.

### A. Identification Of Prior Art

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

[1] The May 30, 2017 earliest possible priority is for matter that was first disclosed in the application that led to U.S. Pat. No. 10,758,652, from which the ’474 patent is a continuation-in-part. However, several claims in the ’474 patent reference new matter first included in an application, filed Oct. 25, 2017, that later became U.S. Pat. No. 10,792,416. While Petitioner asserts that the’474 patent’s claims are not entitled to either priority date because they lack written description support, Petitioner applied the May 30, 2017 priority date in this Petition.

- U.S. Patent No. 4,898,675, issued February 6, 1990 ("Lavender"), prior art under at least 35 U.S.C. §102(a)(1).[2]
- 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. Publication No. 2002/0033370, published March 21, 2002 ("Bainbridge"), prior art under at least 35 U.S.C. §102(a)(1).
- U.S. Patent No. 10,195,319, issued February 5, 2019 ("Kimura"), prior art under at least 35 U.S.C. §102(a)(2).
- U.S. Patent No. 6,743,192, issued June 1, 2004 ("Sakota"), prior art under at least 35 U.S.C. §102(a)(1).
- "Calculations in Apheresis," published July 17, 2014 ("Neyrinck"), prior art under at least 35 U.S.C. §102(a)(1).

### B. Statutory Grounds of Unpatentability

Petitioner requests cancellation of claims 1-26 of the '474 Patent under 35 U.S.C. §§ 101-103, 112 based on the following Grounds.

| Ground | 35 U.S.C. | Claims | References |
|---|---|---|---|
| I | §102/§103 | 6, 7, 15, 17-21 | Fletcher-Haynes anticipates and/or renders obvious |
| II | §103 | 1,2, 6-7, 9-10, 12- | Fletcher-Haynes in view of Bainbridge |

[2] All references to 35 U.S.C. §§102, 103 are to the post-AIA statutory framework.

| | | | |
|---|---|---|---|
| | | 13, 15-21, 26 | |
| III | §103 | 3-4, 22-25 | Fletcher-Haynes in view of Bainbridge and further in view of Lavender |
| IV | §103 | 5, 8 | Fletcher-Haynes in view of Bainbridge and further in view of Kimura |
| V | §103 | 11 | Fletcher-Haynes in view of Bainbridge and further in view of Neyrinck |
| VI | §103 | 14 | Fletcher-Haynes in view of Bainbridge and further in view of Sakota |
| VII | §101 | 1-26 | Patent Ineligible Subject Matter |
| VIII | §112 | 1-11, 13-25 | Lack of Written Description |

This Petition demonstrates that it is more likely than not that at least one of the claims challenged in this petition is unpatentable. *See* 35 U.S.C. § 324(a).

## VI. ’474 Patent Overview

### A. The ’474 Patent Relates To Plasma Apheresis

The ’474 patent relates to a “system … for collecting plasma” in blood apheresis systems. EX1001, Title, 1:28-29. “Apheresis is a procedure in which individual blood components,” *e.g.*, plasma and red and white blood cells, “can be separated and collected from whole blood.” EX1001, 1:33-35. The ’474 patent relates to plasma apheresis, which is plasma collection. EX1003, ¶¶37-42. Figure 3 shows one embodiment of a plasma apheresis system. EX1003, ¶43.

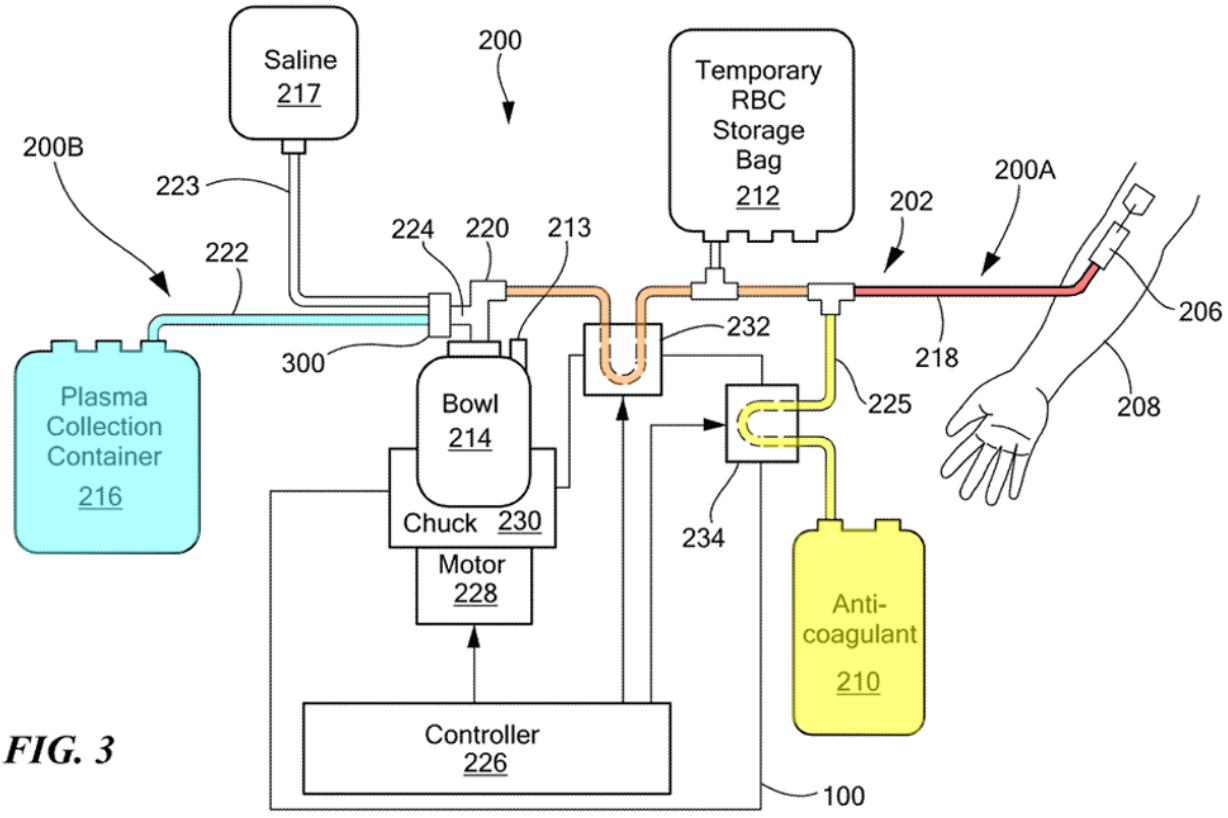



*FIG. 3*

EX1001, Fig. 3 (annotated); EX1003, ¶43.

Plasma apheresis involves withdrawing whole blood from a donor's arm using venous access device 206. EX1001, 7:47-50. Pump 232 "causes the whole blood to be drawn from the donor" through an inlet line 218 (red), and pump 234 adds a fixed amount of anticoagulant "into the whole blood" through "[a]n anticoagulant line" 225 (yellow) connected "to the inlet line." EX1001, 8:23-24, 9:11-14. 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, 10:41-45; EX1003, ¶44.

The mixture (orange) of anticoagulant and "withdrawn whole blood … enters a blood component separation device," *e.g.*, centrifuge bowl 214, which "separates the whole blood into its constituent components," *e.g.*, "plasma, platelets, red blood cells ("RBCs") … [and] white blood cells." EX1001, 7:50-53, 7:57-60. The donor's plasma, *i.e.*, pure plasma, along with anticoagulant introduced during collection, exits the separation device and is collected and stored in a collection container (*e.g.*, a bag, shown in blue above). EX1001, 8:18-21. The anticoagulant and pure plasma combination is called anticoagulated plasma or plasma product. EX1001, 17:20-21; EX1003, ¶45.

The FDA established plasma donation guidelines for individual donors. *See* EX1010. These guidelines consider donor parameters, like weight, hematocrit, and sex. *See* EX1010; EX1003, ¶46.

### B. Purported Invention of the '474 Patent

The '474 patent purports to solve problems associated with "determin[ing] the total volume of plasma that has been collected" after a donor's withdrawn whole blood is mixed with anticoagulant by considering a donor's hematocrit level and the amount of anticoagulant added into the system. EX1001, 1:59-65, 2:8-33, 7:4-17;

EX1003, ¶47. The '474 patent discusses three main volumes—target plasma collection volume, anticoagulant volume, and the total collected plasma volume.

For target plasma collection volume, the technician can calculate the target plasma collection volume "based, at least in part on the weight of the donor." EX1001, 2:64-65; EX1011; EX1003, ¶48.

Additionally, or alternatively, the technician or system may calculate a donor-specific target pure plasma volume using the donor's total blood volume. EX1001, 13:28-38. Lemmens' formula is used to estimate a donor's total blood volume (TBV) based on their body mass index (BMI). Lemmens' indexed blood volume (InBV) calculates mL of blood per kilogram using the equation:

$$lnBV = \frac{70}{\sqrt{\frac{BMIp}{22}}}$$

where 70 (mL/kg) is the assumed blood volume for an individual at ideal body weight (BMI = 22 kg/m²). EX1001, 13:47-52. InBV is multiplied by the donor's body weight in kg to calculate TBV in mL. The donor's plasma volume is then determined from the TBV and the donor's hematocrit. EX1001, 13:52-56. The system or technician multiplies this plasma volume by a target percentage—typically between 26.5% and 29.5%—to calculate the target pure plasma collection volume. EX1001, 13:57-14:7; EX1003, ¶49.

A technician begins collecting plasma after calculating the target plasma volume. EX1001, 13:59-14:3. Once the procedure starts, a technician can use an equation to calculate the volume of anticoagulant in a plasma collection bag ("anticoagulant volume"). Specifically, a technician can use the % AC equation below, which includes a predetermined ratio of anticoagulant to anticoagulated whole-blood and the donor's hematocrit, to calculate the percentage of anticoagulant in the collection bag. EX1001, 11:7-44. Donors have different hematocrit levels, which affects the amount of plasma in the donor's whole blood and the anticoagulant volume. EX1001, 10:57-63; EX1003, ¶50.

In the below 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, 11:7-44. Anticoagulated whole blood is extracted blood mixed with anticoagulant. EX1003, ¶51.

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

Alternatively, the technician can determine, without considering a donor's hematocrit, the amount of anticoagulant added to the system using a "predetermined ratio of anticoagulant per unit anticoagulated whole blood," by monitoring "the

number of rotations of the anticoagulant pump"[3] introducing anticoagulant into this system, "and/or based on the change in weight of the anticoagulant container 210." EX1001, 11:37-44; EX1003, ¶52.

The '474 patent discloses that the controller uses a weight sensor to monitor the collection container's weight and uses weight to determine the total volume of liquid in the collection container. EX1001, 10:13-15, 10:48-62, 12:20-38. The controller uses this total volume to calculate the anticoagulant and pure plasma volumes in the collection container. EX1001, 10:66-12:38. The '474 patent first calculates the anticoagulant volume. EX1001, 11:45-62. It then calculates the pure plasma volume by subtracting the anticoagulant volume from the total volume of liquid in the collection container. EX1001, 11:45-62; EX1003, ¶53.

The '474 patent repeats any of the above methods to determine the pure plasma volume "until a target volume of pure plasma is collected in the plasma

[3] Because red blood cells' osmolarity prevents anticoagulant from mixing with them, essentially all of the anticoagulant exits bowl 214 and is collected within plasma collection container 216. EX1001, 11:17-21. Thus, subtracting the anticoagulant volume added to the system from the total volume in the collection container estimates the pure plasma volume in the collection container. EX1001, 11:17-21, 11:49-54, 12:20-38; EX1003, ¶52.

collection container," *e.g.*, the volume set by FDA regulation. EX1001, 11:54-62. When a target volume of pure plasma is collected, 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, 12:2-6; EX1003, ¶54.

### C. Prosecution History

Application No. 17/205,234, which resulted in the '474 patent, was filed on March 18, 2021. EX1001, cover. The '474 patent was allowed on September 5, 2024 after Applicant filed a terminal disclaimer to moot the Examiner's non-final double-patenting rejection based on claim 11 of U.S. Patent No. 10,758,652 in view of U.S. Pub. No. 2012/0165685 to Weasler et al. EX1002, 18-22.

In the Notice of Allowance, the Examiner stated that "the prior art fails to disclose a method of collecting blood plasma wherein a volume of anticoagulant in the collected plasma component is calculated in real time, as the plasma is being collected (such as by counting anticoagulant pump revolutions), along with the other steps and limitations of the claims." EX1002, 21. The '474 patent issued on January 7, 2025. EX1001, cover.

## VII. Prior Art Overview

### A. Fletcher-Haynes

Fletcher-Haynes discloses a blood collection system that improves 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 a target amount of pure plasma to collect for a donor "considering the medical and physical characteristics of the donor." EX1005, 48:29-31; 52:13. For example, Fletcher-Haynes' prediction algorithms include a donor's gender, height, weight, hematocrit, and platelet pre-count parameters. EX1005, 27:30-34; 49:19-52:36; EX1003, ¶55.

Figure 7B illustrates Fletcher-Haynes' collection assembly 10" for separating blood into components. EX1005, 45:58-46:15. Donor's blood is pumped through donor access line 62 and into inlet line 66 (red), and anticoagulant is pumped from AC container 30 (yellow) into to the inlet line 66. EX1005, 45:22-37, 45:58-63. Blood component separation device 18 separates anticoagulated whole blood into separate components flowing into platelet collect bags 38 and plasma collect bag 54. EX1005,45:63-46:7. The remaining, uncollected blood is pumped back to the donor using return line 70. EX1005, 46:10-15; EX1003, ¶56.

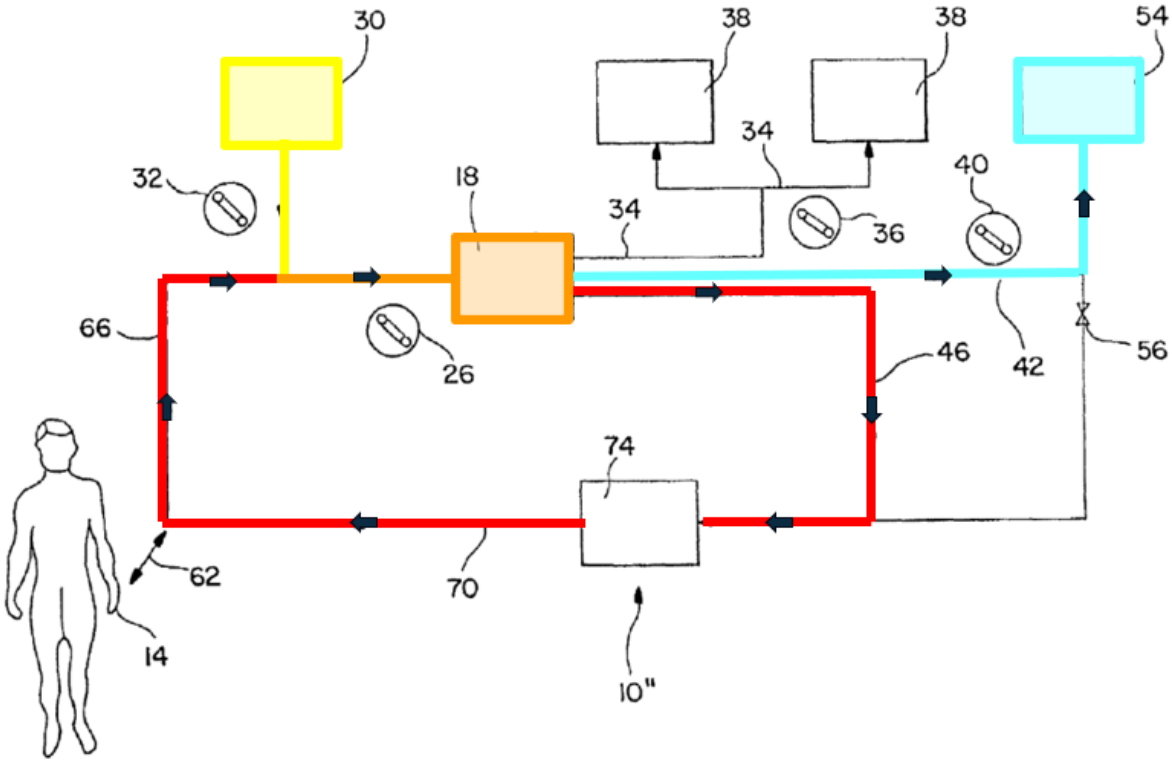



*Figure 7B*

EX1005, Fig. 7B (annotated); EX1003, ¶56.

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 and blood processing machine type in optimization and prediction models. EX1005, 49:7-18; 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, 48:66-49:26; EX1003, ¶58.

Fletcher-Haynes' prediction algorithms may be integrated with its optimization algorithms. Fletcher-Haynes discloses 22 equations that can be incorporated into a prediction model to predict a particular blood component's optimal 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 defines 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. Because computer/database system 140 can control apheresis machine functions, including process control manipulation and optimization, a POSITA would understand that optimizer and prediction models, and any of equations 1-22, would be executed during those procedures. EX1005, 34:8-24, 49:40-52:17; EX1003, ¶60.

**B. Bainbridge**

Bainbridge discloses "[m]ethods and apparatus[es] particularly involving the separation of blood into blood components" such as "plasma and red blood cells." EX1006, Abstract. Bainbridge designed its apheresis system to perform the steps of "removing blood from a donor" and "returning uncollected components of the blood to the donor … alternatively and repeatedly" until a predetermined amount of plasma or other blood components have been collected. EX1006, [0015], [0145]. Bainbridge further improves "collection efficiency" including by improving "the amount of a particular blood component type which is collected." EX1006, [0006]. EX1003, ¶61.

One way Bainbridge improves collection efficiency is by "continuously and instantaneously monitor[ing] the quantity of RBCs collected … to determine the instantaneous hematocrit … of the donor/patient." EX1006, [0302]. Bainbridge uses the change in hematocrit to provide "feed back adjustment control over certain flow rates" and achieve "the target amount of separated plasma." EX1006, [0302]-[0303].

Bainbridge explains "several advantages can be realized utilizing these procedures for… plasma collections" including "reduced time requirements for… plasma collections." EX1006, [0304]. EX1003, ¶62.

### C. Kimura

Kimura teaches "a blood component separation device for collecting a predetermined component from blood," including plasma. EX1007, 1:6-8, Fig. 4. Kimura collects plasma in cycles consisting of "a centrifugal separation step of introducing [the] whole blood withdrawn from [a] donor into a centrifugal separator" and "a blood returning step" repeated "a plurality of times." EX1007, 14:37-43, claim 2, Fig. 4, 16:6-7. Once Kimura determines that the present cycle is the last cycle, Kimura's system stops drawing blood, and performs a final return step. EX1007, Fig. 4, 16:6-7. EX1003, ¶63.

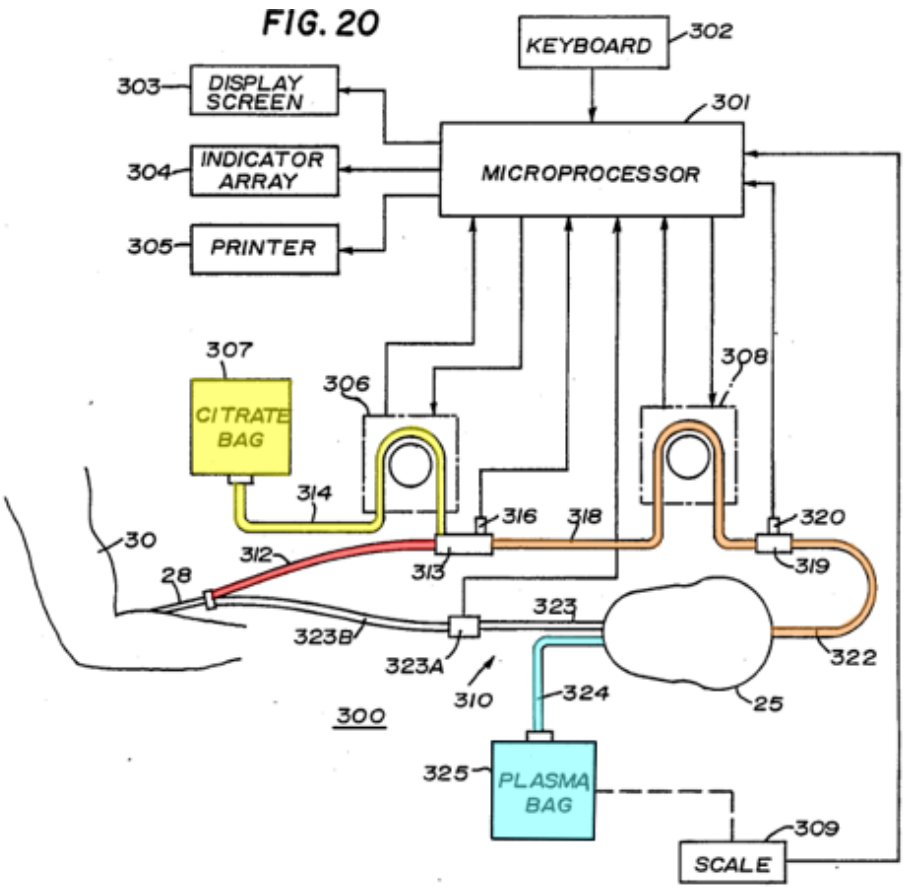
Kimura further teaches a method for setting a fixed "ratio of the amount of anticoagulant added in relation to the blood" for any blood donor. EX1007, 1:48-50. To achieve the proper anticoagulant ("ACD liquid") ratio "during the continuous supply of ACD liquid after the start of drawing of whole blood …, the amount of the ACD liquid to be supplied is determined by subtracting the amount of ACD liquid already supplied (for example, 30 ml) in the priming step … from the whole amount of ACD liquid to be supplied which is calculated from the ACD ratio." EX1007, 13:48-55. By separately tracking the anticoagulant amount introduced during the

priming step versus the draw and return phases, Kimura can maintain constant the "selected ratio of" anticoagulant. EX1007, claim 4; EX1003, ¶64.

### D. 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 in a collected plasma component during a plasma collection procedure, for example to "accurately, safely and economically collect[ ] plasma from a source of blood." EX1004, 3:26-28; EX1003, ¶65.

Figure 20 illustrates Lavender's automatic system 300 for fractionating blood. EX1004, 16:34-53; EX1003, ¶66.




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, 16:60-17:2, 16:45-47. System 300 pumps the whole blood and anticoagulant mixture to blood fractionator 25, which separates it 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, ¶67.

Lavender's system performs several real time calculations during the collection process. EX1003, ¶68. These calculations account for donor parameters, like hematocrit, as well as 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. These calculations also account for the weight of the collected plasma and anticoagulant solution during the collection process. These calculations are used to calculate the pure plasma and anticoagulant volumes in the plasma collection bag in real time. EX1004, 20:55-68; EX1003, ¶68.

The microprocessor repeatedly performs weight measurements and run-time calculations set forth in Lavender's algorithm and displays updated values approximately every two seconds. EX1004, 20:55-68. Because Lavender's system determines the relationship (or ratio) between the pure plasma volume and the anticoagulant volume in the collection container, a POSITA would readily understand how to convert between the two volumes. By utilizing this relationship, Lavender's determination of the pure plasma volume is based, at least in part, on the anticoagulant volume. EX1003, ¶69.

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 ($MAXPF$), which is determined using a donor's weight. EX1004, cols. 43-44, claim 33; EX1003, ¶70.

**E. Sakota**

Sakota teaches "an apheresis machine" and "a method for producing blood products using the same." EX1008, Abstract, 1:7-8. Sakota uses a "centrifuge … for separating whole blood into a lower density component," *e.g.*, plasma. EX1008, Abstract, 1:14-20; EX1003, ¶71.

Sakota's apheresis machine harvests plasma in "about 15 minute[]" cycles consisting of "draw, swell, surge, and return" steps that are "successively conducted at least three to five times." EX1008, 2:14-15, 10:29. Sakota "decrease[s] the process volume of whole blood per cycle" because "the amount of extracorporeal blood circulation will be decreased and thus the danger of causing anemia or dizziness can be minimized." EX1008. 4:17-23; EX1003, ¶72.

**F. Neyrinck**

Neyrinck emphasizes the importance of accurately determining total blood volume (TBV) in apheresis procedures to ensure safety and efficacy. EX1009, 38-39. Because physiological variables impact TBV, eyrinck discloses multiple methods for calculating TBV using height, weight, sex, age, morphology, and BMI. EX1009, pp.38-39. For example, Nadler's formula, widely used in apheresis machines, calculates TBV based on a person's gender, height, weight, and age. EX1009, p.39. Neyrinck's approaches include models for pediatric patients, based on gender and body type, and using body mass index (BMI) (calculated using weight and height)

as the primary variable. EX1009, pp.39-40. These methods assign a blood volume per kilogram of body weight depending on the BMI category. EX1009, 40; EX1003, ¶73.

## VIII. 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, ¶36.

## IX. 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 '474 Patent. *See* 37 C.F.R. § 42.100(b).

Moreover, the Board "need[s] 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. *See* EX1003, ¶19.

## X. Detailed Grounds Explanation

The sections below, as supported by Dr. Fletcher's Declaration, demonstrate how the claims are unpatentable. 37 C.F.R. §42.104(b)(4)-(5). EX1003, ¶¶74-247.

### A. Ground I: Fletcher-Haynes anticipates or renders obvious claims 6, 7, 15, 17-21

#### 1. Claim 6

##### i. 6[preamble] A system for collecting plasma, comprising:

To the extent the preamble is limiting, Fletcher-Haynes discloses a system for collecting plasma. Fletcher-Haynes discloses "an extracorporeal blood processing system[]" which utilizes "a method for **collecting** at least one predetermined blood component ("*e.g.*, a collection of platelets or red blood cells or **plasma**") from a source of whole blood **using a blood component collection system**." EX1005, 1:10-11, 7:33-38. EX1003, ¶75.

##### ii. 6[a] a venipuncture needle configured to draw whole blood from a donor;

Fletcher-Haynes "remove[s] [blood] from a donor through a needle assembly or other blood access device," *e.g.*, a venipuncture needle. EX1005, 1:27-31, Fig. 7B. EX1003, ¶76.

**iii. 6[b] a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;**

Fletcher-Haynes discloses a blood separator (*e.g.*, a blood component collection device 18) configured to "separate[] the whole blood … into three primary constituents" including a plasma product (*e.g.*, "plasma product volume plus anticoagulant volume") and a second blood component comprising red blood cells (*e.g.*, "a combination of red and white blood cells"). EX1005, 23:39-41, 45:38-57. EX1003, ¶77.

Fletcher-Haynes' blood separator contains a plasma output port coupled to a plasma line (*e.g.*, plasma tube 112 that "extend[s] externally of the rotatable device 18"). EX1005, 47:17-34; Figs. 8A & 8B. EX1003, ¶78.

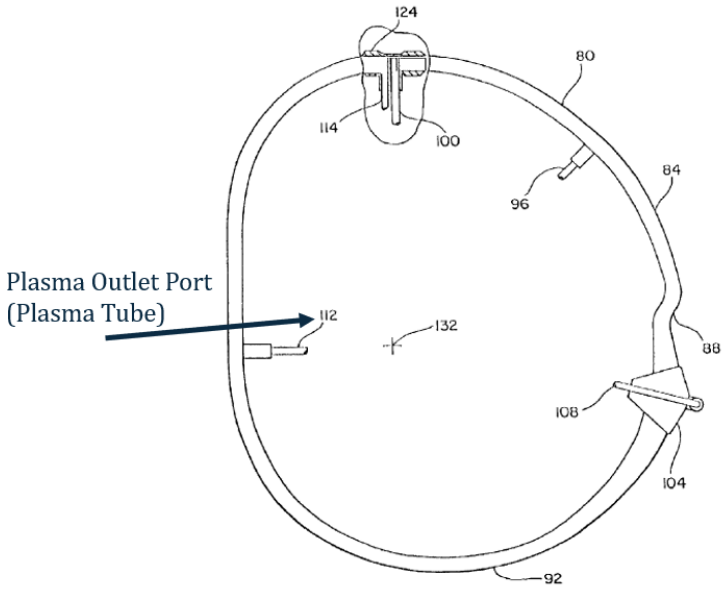
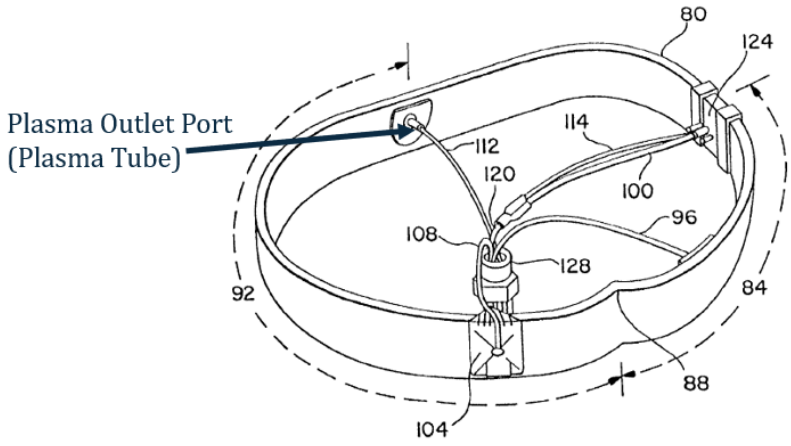



*Figure 8B*




The blood separator is configured to send the separated plasma through the plasma line to the plasma component collection container, as plasma collect bag 54 "is interconnected with the plasma line 42" and plasma tube 112 to "collect the separated plasma." EX1005, 45:51-56, 45:58-62. EX1003, ¶79.

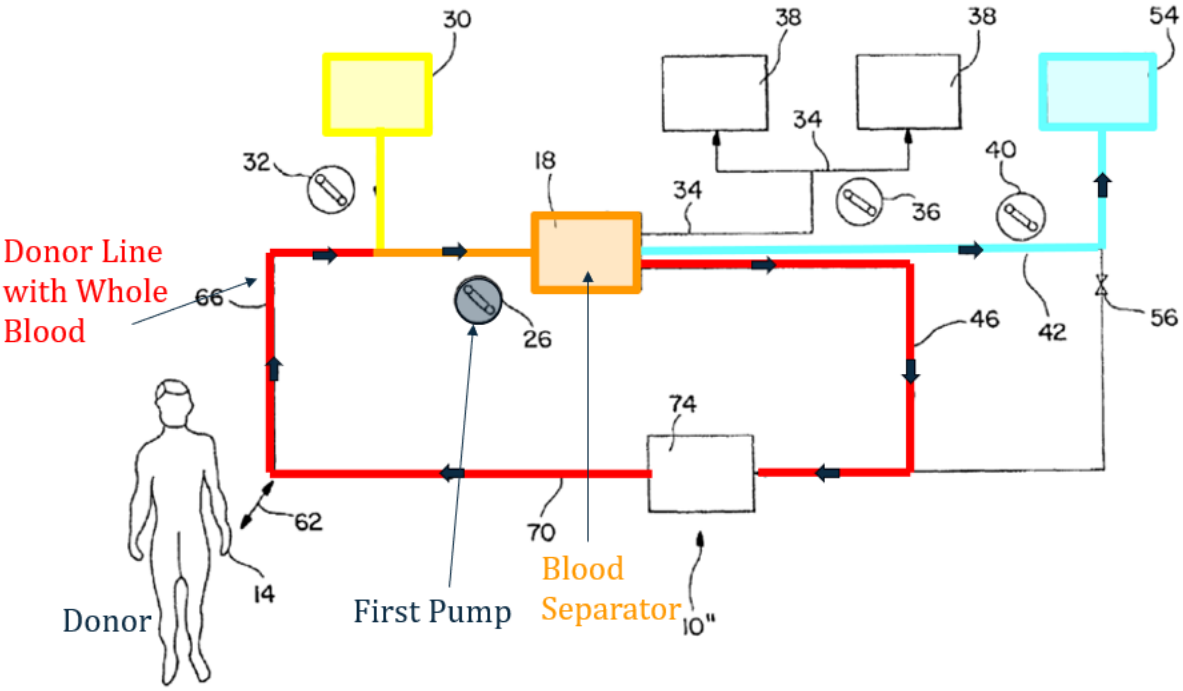



***Figure 7B***

Therefore, Fletcher-Haynes' blood component separation device has a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container. EX1003, ¶80.

**iv. 6[c] a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the blood separator, flow through the donor line being controlled by a first pump;**

Fletcher-Haynes discloses that "[t]he donor is fluidly connected to the blood component collection device," *e.g.*, the blood separator, "by an inlet line 22," or "through a donor access line 62 and into an inlet line 66," *e.g.*, the donor line, "and appropriate needle assembly," *e.g.*, the venipuncture needle. EX1005, 45:22-29. Further, "[w]hole blood from the donor 14 is continuously provided to the blood

component collection device 18 through the inlet line … utilizing an inlet pump 26," *e.g.*, a first pump, "to maintain this flow if desired/required." EX1005, 45:22-29, 45:58-67; Figs. 7A, 7B. EX1003, ¶81.

**v. 6[d] an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;**

As shown in Fig. 7B, Fletcher-Haynes discloses an anticoagulant line (*e.g.*, the line connecting draw line 66 with AC container 30) coupled to an anticoagulant source (*e.g.*, AC container 30). Fletcher-Haynes further discloses that the anticoagulant line combines anticoagulant with the whole blood, *e.g.*, by providing "anticoagulant from an anticoagulant ('AC') container 30" to the interconnected blood draw line. Whole blood and anticoagulant are combined "[p]rior to the blood of the donor 14 entering the blood component collection device 18." EX1005, 45:29-37. Fletcher-Haynes "utiliz[es] an AC pump 32," *e.g.*, a second pump, "to maintain … flow" of anticoagulant from the anticoagulant source. EX1005, 45:29-37; EX1003, ¶82.

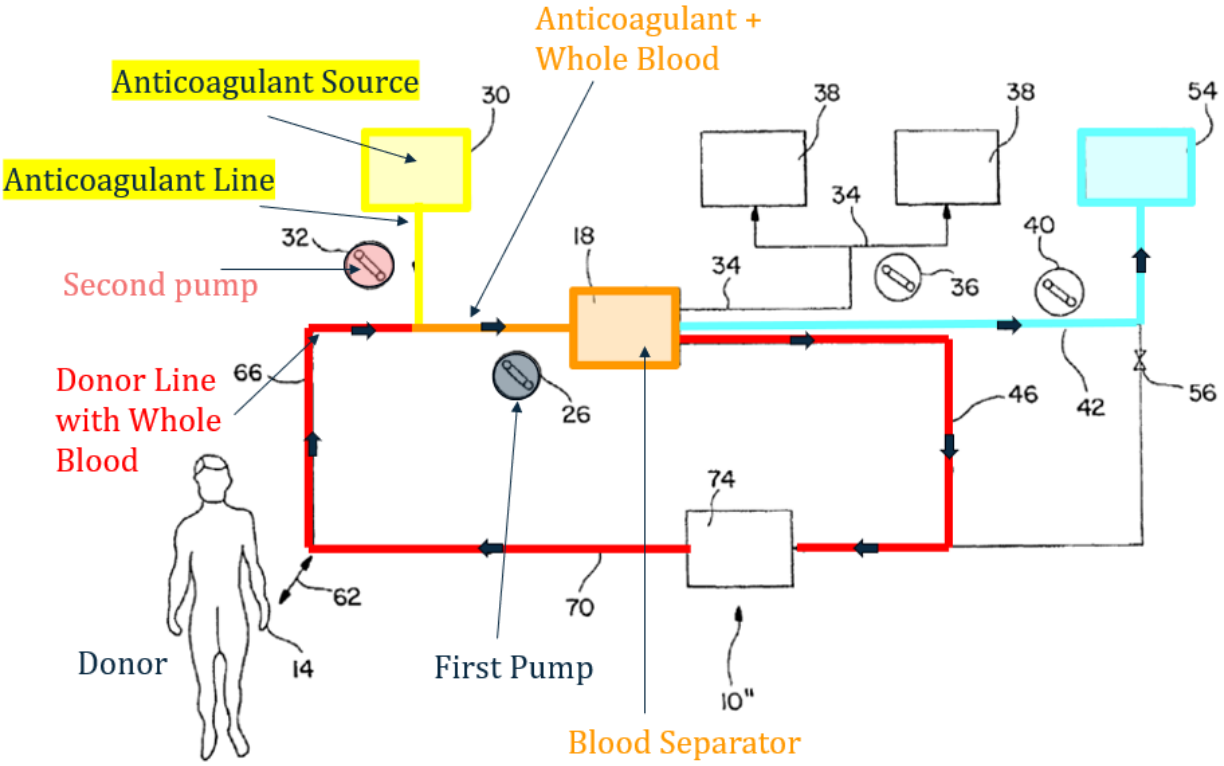



*Figure 7B*

**vi. 6[e] a touchscreen configured to receive input from an operator; and**

Fletcher-Haynes discloses "touchscreen input/output devices 199" configured to receive input from "the operator" (*e.g.*, "data entry, manipulation, and storage" or "[a]ll procedure interventions"). EX1005, 10:12-15, 34:21-24. EX1003, ¶83.

**vii. 6[f] a controller programmed to control operation of the system,**

Fletcher-Haynes discloses a controller (*e.g.*, "the internal control of a blood component collection device 18") programmed (*e.g.*, has the procedure order "transferred/downloaded onto the internal control of the blood component collection

device") to control operation of the system (*e.g.*, "derive[] process control parameters for achieving a predetermined yield of [a] blood component[]"). EX1005, 53:16-20, 53:47-52, Fig. 9A. EX1003, ¶84.

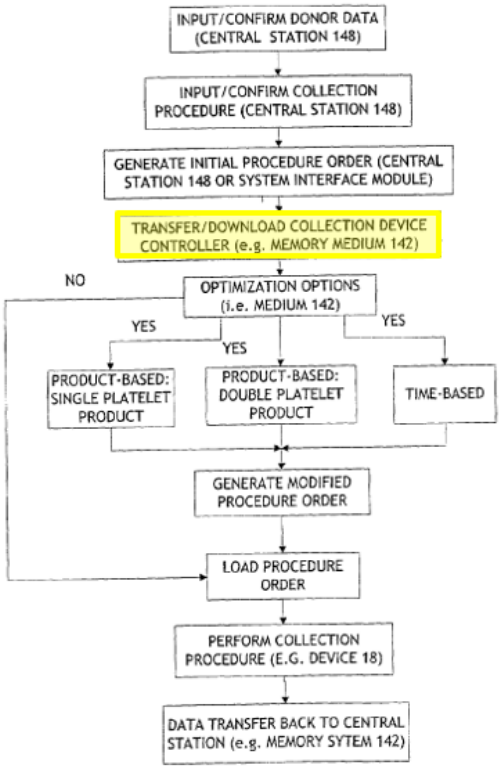


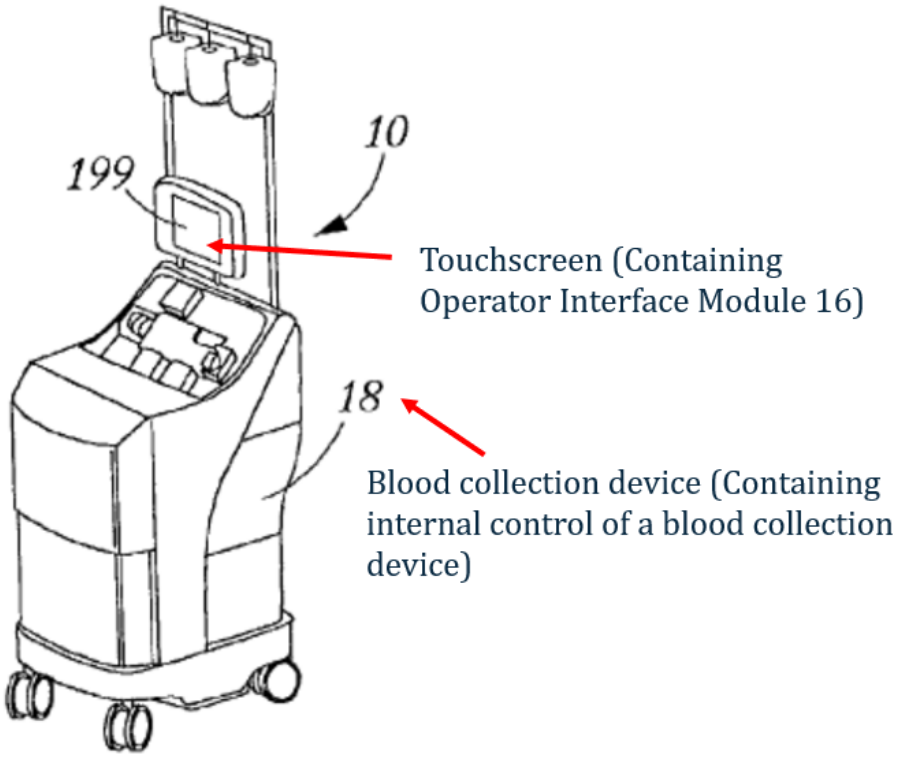

*Figure 9A*

EX1005, FIG. 9A (annotated).

**viii. 6[g] the controller coupled to the touchscreen and programmed to receive at least a donor's weight, height, sex and hematocrit,**

Fletcher-Haynes discloses that "data entry, manipulation and storage may [] be performed at/on each machine using, for example, respective interfaces, which here are … touchscreen input/output devices." EX1005, 10:12-15; 53:20-25, 52:43-

45, Fig. 1A. Fletcher-Haynes receives an input of "height, weight, gender, and platelet pre-count or hematocrit" via the touchscreen. EX1005, 1:48-52. EX1003, ¶85. These input values "are downloaded to the internal control of the blood collection device 18," *e.g.*, the controller. EX1005, 54:8-11. The process of downloading the input values "may include encoding of a computer program of instructions for executing [the] computer process," meaning that the controller is programmed to receive these values. EX1005, Fig. 9A, 8:24-34. EX1003, ¶85.




EX1005, FIG. 1A (annotated).

**ix. 6[h] to determine a target volume for plasma product and/or raw plasma based at least in part on the donor's total blood volume and/or the donor's plasma volume,**

Fletcher-Haynes' controller runs a "prediction model for predicting a yield of a particular blood component to be collected before a collection procedure is initiated using a compilation of algorithms" which determine, *e.g.*, calculate, a target volume for raw plasma (*e.g.*, $V_{SP}$, volume of pure plasma in the source plasma bag) and/or plasma product (*e.g.*, $V_{SPB}$ total volume in source plasma bag), using entered donor weight or hematocrit. EX1005, 48:1-3. EX1003, ¶86.

***First***, Fletcher-Haynes calculates an AC Ratio ($R$) (low, medium, or high) using the donor's hematocrit ($H$) in Equation 9. EX1003, ¶87.

$$R = 1 + \frac{2.51}{H}\,(\text{low}), or$$

$$R = 1.33\left(1 + \frac{2.51}{H}\right)\,(\text{medium}), \text{or}$$

$$R = 1.67\left(1 + \frac{2.51}{H}\right)\,(\text{high})$$

Fletcher-Haynes then, in equation 15, determines the fraction of AC in the collected plasma component $f_{ACP}$ using the AC ratio and hematocrit. EX1003, ¶88.

$$f_{ACP} = [(R-1)(1-H)]^{-1}$$

***Second***, in equation 10, Fletcher-Haynes calculates total blood volume $V_B$ using donor weight ($W$), height ($L$), and gender. EX1003, ¶89.

$$V_B = 604 + 0.006012L^3 + 14.6W \text{ ml (male)}$$

$$= 183 + 0.005835L^3 + 15.0W \text{ ml (female)}$$

***Third***, in equation 17, Fletcher-Haynes calculates a target volume of pure plasma ($V_{SP}$) using total blood volume $V_B$. EX1003, ¶90.

$$\begin{cases} V_{SP} = 0 \\ = V_{CON} - V_C \\ = f_{SP}V_B - V_C \\ = \text{specified as modified input} \end{cases} \geq 0$$

***Finally***, in equation 22, Fletcher-Haynes calculates a volume of plasma product ($V_{SPB}$). EX1003, ¶91.

$$V_{SPB} = V_{SP}(1 + f_{ACP})$$

Expanding equation 22 reveals that $V_{SPB}$ is a sum of volume of pure plasma ($V_{SP}$) and volume of added anticoagulant ($V_{SP} * f_{ACP}$). EX1003, ¶91.

These values are target values because Fletcher-Haynes can run the prediction model for a "product based optimization," *e.g.*, collecting the greatest amount of a blood component that is allowed during a donation session. EX1005, 59:36-38. The prediction model runs "before the collection procedure is actually initiated" and outputs a "desired yield" for the donation that is "provided to the device 18 for performing the collection procedure." EX1005, 53:36-38, 58:28-33, 59:36-38. Therefore, Fletcher-Haynes calculates a target volume for plasma product and/or raw plasma using a donor's total blood volume $V_B$. EX1003, ¶92.

**x. 6[i] to control the system to operate draw and return phases to withdraw whole blood from the donor and separate the whole blood into the plasma product and**

**the second blood component and to return the second blood component to the donor.**

Fletcher-Haynes anticipates and/or renders obvious element 6[i] under any meaning of the term "draw and return phases." EX1003, ¶93.

Fletcher-Haynes' controller (*e.g.*, "internal control of a blood component separation device") controls the system's operation. EX1005, 54:6-12. In Fletcher-Haynes' apheresis system, "all apheresis control during a procedure remains resident in the apheresis machine 10 itself." EX1005, 34:12-14. The collection procedure is performed on blood component separation device 18 and controlled by the "internal control of a blood component collection device 18." EX1005, Fig. 9A, 53:17-18. EX1003, ¶94.

Fletcher-Haynes' "internal control of a blood component separation device" performs draw and return phases which withdraw the whole blood from the donor, separate the whole blood into the plasma product and the second blood component, and return the second blood component to the donor, *e.g.*, "the uncollected components thereafter returned to the donor." *See* EX1005, 1:31-36, 52:37-47; §§X.A.1.ii, X.A.1.iii (limitations 6[a], 6[b]). Fletcher-Haynes' controller operates a draw phase where "[w]hole blood from the donor 14 is … continuously provided to the blood component collection device 18 through inlet line 22." EX1005, 45:24-26. Blood component separation device 18 then separates anticoagulated whole blood

into separate components flowing into platelet collect bags 38 and plasma collect bag 54. EX1005, 45:22-37. Then, Fletcher-Hayes' controller performs a return phase where any uncollected "plasma and RBC/WBC are provided back to the donor 14 through a plasma line 42 and RBC/WBC line 46." EX1005, 45:44-46. When "only a single line is connected to the donor," the draw and return phases are "effectively two-step versus continuous," *i.e.*, meaning the draw and return phases are distinct phases. EX1005, Fig. 7B, 46:10-15. Thus, Fletcher-Haynes anticipates limitation 6[i]. EX1003, ¶95.

If Patent Owner argues that claim limitation 6[i] requires repeated draw and return phases, which Petitioner submits the plain and ordinary meaning of the claim does not require, it would have been obvious to a POSITA to perform repeated draw and return phases in a centrifugal, single-needle system like Fletcher-Haynes'. EX1005, Fig. 7B, 46:16-28. A POSITA would have been motivated to repeat Fletcher-Haynes' draw and return phases to maximize donor comfort and/or accommodate a centrifugal separator whose total volume is less than that of the required amount of whole blood needed to collect a target amount of pure plasma. EX1003, ¶96.

Additionally, Petitioner submits repeated draw and return phases would have been obvious in view of Fletcher-Haynes and Bainbridge, as discussed in Ground II. EX1003, ¶97.

**2. Claim 7**

**i. The system of claim 6, wherein the controller is further programmed to account for anticoagulant introduced into the plasma collection container separately from the plasma product.**

Fletcher-Haynes' internal control of a blood component separation device generates 11 separate parameters during operation including "(7) source plasma volume" and "(8) AC in the platelet and plasma collect bags 38, 54." EX1005, 49:19-25. Additionally, Fletcher-Haynes displays an "estimated volume" for plasma product and the "AC volume in" the plasma product. EX1005, 40:54-56. Thus, a POSITA would understand that Fletcher-Haynes' internal control of its blood component separation device is programmed to account for the anticoagulant introduced in the system separately from the plasma product.[4] EX1003, ¶98.

**3. Claim 15**

**i. 15[preamble] A system for collecting plasma, comprising:**

*See* §X.A.1.i (limitation 6[preamble]). EX1003, ¶99.

[4] If Patent Owner argues anticoagulant needs to be introduced into the container separately from the plasma product, that argument is illogical because plasma product is a mixture of anticoagulant and pure plasma. EX1003, ¶98. If made, Petitioner reserves the right to respond.

**ii. 15[a] a venipuncture needle configured to draw whole blood from a donor;**

*See* §X.A.1.ii (limitation 6[a]). EX1003, ¶100.

**iii. 15[b] a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;**

*See* §X.A.1.iii (limitation 6[b]). EX1003, ¶101.

**iv. 15[c] a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the separator, flow through the donor line being controlled by a first pump;**

*See* §X.A.1.iv (limitation 6[c]). EX1003, ¶102.

**v. 15[d] an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;**

*See* §X.A.1.v (limitation 6[d]). EX1003, ¶103.

**vi. 15[e] a touchscreen configured to receive input from an operator; and**

*See* §X.A.1.vi (limitation 6[e]). EX1003, ¶104.

**vii. 15[f] a controller programmed to control operation of the system,**

*See* §X.A.1.vii (limitation 6[f]). EX1003, ¶105.

**viii. 15[g] the controller coupled to the touchscreen and programmed to receive donor parameters electronically,**

As discussed in §X.A.1.viii (limitation 6[g]), Fletcher-Haynes' controller is electronically coupled to a touchscreen and receives a donor's height, weight, and hematocrit (*e.g.*, donor parameters). EX1003, ¶106.

**ix. 15[h] to determine a target volume for plasma product and/or raw plasma based at least in part on the donor parameters and on the donor's total blood volume and/or the donor's plasma volume,**

As discussed in §X.A.1.ix (limitation 6[h]), Fletcher-Haynes calculates a target volume for plasma product (*e.g.*, $V_{SPB}$) based at least in part on donor parameters, *e.g.*, weight and hematocrit. EX1003, ¶107.

As discussed in §X.A.1.ix (limitation 6[h]), Fletcher-Haynes further calculates a donor's total blood volume (*e.g.*, $V_B = 604 + 0.006012L^3 + 14.6W$ ml for a male donor) and uses $V_B$ to calculate a target volume of pure plasma (*e.g.*, $V_{SP} = f_{SP}V_B - V_C$), and, in turn, $V_{SPB}$ ($V_{SPB} = V_{SP}(1 + f_{ACP})$). EX1003, ¶108.

Therefore, Fletcher-Haynes' target volume for plasma product is based at least in part on donor parameters and total blood volume. EX1003, ¶109.

**x. 15[i] the controller also configured to control the system to operate draw and return phases to withdraw whole blood from a donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor.**

*See* §X.A.1.x (limitation 6[i]). EX1003, ¶110.

**4. Claim 17**

**i. The system of claim 15, further comprising a control system, wherein the control system is in electronic communication with the controller.**

Fletcher-Haynes discloses a control system (*e.g.*, central computer/database 140) that "provides simplified donor data storage and control as well as communications with blood component collection machines to both ease and optimize" plasma collection procedures. EX1005, 2:59-64. The central computer/database 140 is in electronic communication with the controller (*e.g.*, "the internal control of a blood component collection device 18") through "a computer network system." EX1005 53:16-19; EX1003, ¶111.

**5. Claim 18**

**i. The system of claim 17, wherein the control system is programmed to calculate the target volume for plasma product and/or raw plasma and the controller is programmed to determine a target volume for plasma product and/or raw plasma by receiving the target volume for plasma product and/or raw plasma from the control system.**

Fletcher-Haynes discloses a control system (*e.g.*, a central computer/database 140) that calculates the target volume for plasma product (*e.g.*, volume of pure plasma in the plasma source bag) and/or raw plasma (*e.g.*, total volume in source plasma bag). For example, Fletcher-Haynes' central computer/database is

programmed, *e.g.*, using "various internal hardware and software elements … as known in the art," such as "an appropriate processor as used in a computer system." 9:53-63, 10:58-11:5. The programmed central computer/database "derives process control parameters for achieving a predetermined yield of blood components through a maximization of at least one parameter" including target volumes. EX1005, 53:47-52. EX1003, ¶112.

Fletcher-Haynes' controller (*e.g.*, the internal control of the blood component collection device 18) receives "various control parameters associated with the … collection procedure," including pure plasma and total volumes in the plasma source bag, through a "transfer[]/download[] onto the internal control of a blood component collection device by a computer system." EX1005, 53:9-20, 53:47-52. The internal control of the blood separator determines "the values for the various control parameters … as well as any ancillary/previously specified values" by receiving the target volume for plasma product and/or raw plasma from the control system, *e.g.*, by "download[ing]" these values "to the internal control of the blood collection device." EX1005, 54:6-12. Fletcher-Haynes' controller may also determine a volume of plasma product and/or raw plasma by performing "downstream optimization … in accordance with these values" received from the central computer/database. EX1005, 54:6-13; EX1003, ¶113.

Fletcher-Haynes programs the controller to determine a volume of pure plasma in the plasma source bag and/or a total volume in source plasma bag because in addition to downloading the control parameter values, Fletcher-Haynes "transfer[s]/download[s] collection device controller." EX1005, Fig. 9A; EX1003, ¶114.

**6. Claim 19**

**i. The system of claim 15, wherein the controller determines the target volume for plasma product and/or raw plasma by calculating the target volume for plasma product and/or raw plasma and wherein the controller is local to and coupled to the blood separator.**

Fletcher-Haynes' controller (*e.g.*, the internal control of a blood processing device) determines a target volume for plasma product and/or raw plasma by running a prediction model. Fletcher-Haynes' controller downloads "previously specified values," like donor parameters, "to the internal control of the blood collection device 18 such that the collection procedure may be initiated or reinitiated (downstream optimization) … in accordance with these values." EX1005, 54:6-13. As discussed in §X.A.1.ix (limitation 6[h]), Fletcher-Haynes runs the prediction model using donor parameters to calculate a target volume for plasma product and/or raw plasma. EX1003, ¶115.

Fletcher-Haynes' controller is local and coupled to the blood separator (*e.g.*, blood component collection device 18). Fletcher-Haynes teaches that "the values for

the various process control parameters as well [as] any ancillary/previously specified values," *e.g.*, the donor parameters used to calculate $V_{SP}$ and $V_{SPB}$, "are downloaded onto ***the internal control of a blood component collection device***." EX1005, 53:16-21. The internal control performs "optimization … on the individual blood processing machines 18," calculating run time parameters including the volume of pure plasma in the source plasma bag and total volume in the source plasma bag. EX1005, 52:13-14, 53:33-35, 54:6-13. EX1003, ¶116.

**7. Claim 20**

**i. The system of claim 15, wherein the donor parameters received electronically comprise a donor weight, wherein the controller is programmed to determine the target volume for plasma product and/or raw plasma based at least in part on the donor weight.**

As discussed above in §X.A.1.viii, (limitation 6[g]), Fletcher-Haynes renders obvious a controller which receives donor parameters from a control system comprising a donor weight. As discussed above in §X.A.1.ix (limitation 6[h]), Fletcher-Haynes determines a target volume for plasma product and/or raw plasma based at least in part on donor weight. EX1003, ¶117.

**8. Claim 21**

**i. The system of claim 20, wherein the donor parameters received electronically comprise a donor hematocrit, wherein the controller is programmed to determine the target volume for plasma product and/or raw plasma based at least in part on the donor hematocrit.**

As discussed in §X.A.1.viii (limitation 6[g]), Fletcher-Haynes' controller receives donor parameters that comprise a donor hematocrit. Fletcher-Haynes further discloses that "donor related data" is received from the control system, *e.g.*, "central/computer database 140," and transferred/downloaded onto the internal control of a blood component collection device." EX1005, 52:60-67, 53:16-20. As discussed in §X.A.1.ix (limitation 6[h]), the controller determines (calculates) the target volume for plasma product and/or raw plasma based at least in part on the donor hematocrit. EX1003, ¶118.

### B. Ground II: Fletcher-Haynes in view of Bainbridge renders obvious claims 1, 2, 6-7, 9-10, 12-13, 15-21, and 26.

#### 1. It would have been obvious for a POSITA to combine Fletcher-Haynes and Bainbridge.

A POSITA would have found it obvious and would have been motivated to combine Fletcher-Haynes' system with the teachings of Bainbridge and would have had a reasonable expectation of success because 1) both relate to the same well-known technologies, 2) both apply substantially similar techniques to achieve similar results, and 3) the intended functionality of Fletcher-Haynes would remain substantially the same in the proposed combination. EX1003, ¶119.

Both Fletcher-Haynes and Bainbridge relate to plasma apheresis. Fletcher-Haynes separates and collects a "selected blood component … includ[ing] platelets, red blood cells, white blood cells, stem cells, and plasma" and considers donor

parameters when determining target plasma collection volumes. EX1005, 1:20-26. Bainbridge similarly relates to "extracorporeal blood processing," such as an "apheresis procedure," that uses "a blood component separation device (*e.g.*, a centrifuge)" that separates whole blood into "various blood components" including "plasma." EX1006 [0003]. Bainbridge's apheresis procedure similarly determines target volumes using donor data, like weight. EX1006, Figs. 33-35, [0070]-[0072], [0336]-[0340]. Thus, a POSITA designing a system based on Fletcher-Haynes would have been motivated to turn to Bainbridge and incorporate its disclosures into Fletcher-Haynes' system. EX1003 ¶120.

One aspect a POSITA would have been motivated to incorporate is repeating draw and return phases during collection. Bainbridge's system performs "removing and returning steps … alternatively and repeatedly … during blood processing." EX1006, [0015]. Incorporating Bainbridge's multiple draw and return phases in a centrifugal apheresis system like Fletcher-Haynes' system would have been obvious to a POSITA because performing multiple draw and return phases minimizes the amount of blood withdrawn from a donor at once and maximizes donor comfort. Additionally, a POSITA would have had a reasonable expectation of success in making the proposed combination because both Fletcher-Haynes and Bainbridge perform substantially similar techniques to achieve similar results: Fletcher-Haynes already performs draw and return phases and thus repeating them, as disclosed in

Bainbridge, would just require reducing the amount of whole blood drawn per cycle. EX1006, [0016]; EX1005, 46:16-28; EX1003, ¶121.

Additionally, a POSITA would have been motivated to implement Bainbridge's red-blood-cell collection and real-time hematocrit monitoring in Fletcher-Haynes' system. Fletcher-Haynes discloses performing multiple blood product collections, including collecting red blood cells. EX1005, 22:44-23:44, 61:62-62:3, Fig. 7B. In view of these disclosures, a POSITA would have been motivated to implement Bainbridge's red blood cell collection in Fletcher-Haynes' system. Incorporating Bainbridge's teachings would have been a routine, minor change to Fletcher-Haynes' system that would have yielded predictable results. EX1003 ¶122.

Further, implementing Bainbridge's red blood cell collection in "at least one RBC collection reservoir or bag" would not alter Fletcher-Haynes' functionality as Fletcher-Haynes' system can perform red-blood-cell collection. EX1006, [0103]; EX1005, 31:1-5, Fig. 5A. Additionally, Fletcher-Haynes recognizes that "variations and modifications commensurate with [its] teachings, and skill and knowledge of the relevant art, are within the scope of the present invention." EX1005, 62:24-26. Thus, a POSITA would have been motivated to collect red blood cells in a collection reservoir or bag when performing multiple blood product collections and would have had a reasonable expectation of success in doing so. EX1003, ¶123.

Likewise, incorporating Bainbridge's real-time hematocrit measurements is consistent with Fletcher-Haynes' teachings. Bainbridge recognizes that there is "a drop of hematocrit during a procedure" which may "mean adjustments to certain flow rates such as the plasma pump rate to ensure that the target amount of separated plasma" is collected in a fixed-time procedure. EX1006, [0302]. Likewise, Fletcher-Haynes recognizes that "hematocrit...change[s] significantly from the values entered" before a procedure and uses hematocrit ($H$) in each iteration of its prediction model to calculate a target amount of pure plasma or plasma product. EX1005, 30:35-42, Eqs. 1-22. A POSITA would be motivated to incorporate Bainbridge to track instantaneous hematocrit in a system which tracks pump rates, like Fletcher-Haynes', to more accurately determine the amount of plasma collected. A POSITA incorporating Bainbridge's dynamic hematocrit teachings in Fletcher-Haynes would have used well-known and simple software modifications to Fletcher-Haynes' internal blood component code that would have provided predictable results. EX1003, ¶124.

### 2. Claim 1

#### i. 1[preamble] A system for collecting plasma, comprising:

*See* §§X.A.1.i, X.A.3.i (limitations 6[preamble], 15[preamble]). EX1003, ¶125.

**ii. 1[a] a venipuncture needle configured to draw whole blood from a donor;**

*See* §§X.A.1.ii, X.A.3.ii (limitations 6[a], 15[a]). EX1003, ¶126.

**iii. 1[b] a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;**

*See* §§X.A.1.iii, X.A.3.iii (limitations 6[b], 15[b]). EX1003, ¶127.

**iv. 1[c] a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the blood separator, flow through the donor line being controlled by a first pump;**

*See* §§X.A.1.iv, X.A.3.iv (limitations 6[c], 15[c]). EX1003, ¶128.

**v. 1[d] an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;**

*See* §§X.A.1.v, X.A.3.v (limitations 6[d], 15[d]).EX1003, ¶129.

**vi. 1[e] a touchscreen configured to receive input from an operator; and**

*See* §§X.A.1.vi, X.A.3.vi (limitations 6[e], 15[e]). EX1003, ¶130.

**vii. 1[f] a controller programmed to control operation of the system,**

*See* §§X.A.1.vii, X.A.3.vii (limitations 6[f], 15[f]). EX1003, ¶131.

**viii. 1[g] the controller coupled to the touchscreen and programmed to receive at least a donor's weight and hematocrit,**

As discussed in §§X.A.1.viii, X.A.3.viii (limitation 6[g], 15[g]), Fletcher-Haynes discloses a controller coupled to a touchscreen. Fletcher-Haynes' touchscreen receives a donor's "height, weight, [and] … hematocrit." EX1005, 1:48-52. EX1003, ¶132.

**ix. 1[h] to determine a target volume for plasma product and/or raw plasma based on the donor's total blood volume and/or the donor's plasma volume,**

*See* §§X.A.1.ix, X.A.3.ix (limitations 6[h], 15[h]). EX1003, ¶133.

**x. 1[i] to control the system to operate a draw and return cycle to withdraw the whole blood from the donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor,**

*See* §§X.A.1.x, X.A.3.x (limitations 6[i], 15[i]). EX1003, ¶134.

**xi. 1[j] to establish a current value of the hematocrit of the donor and a new target volume for plasma product and/or raw plasma, and**

Fletcher-Haynes in view of Bainbridge renders obvious limitation 1[j]. EX1003, ¶135.

***First***, "a beneficial feature of" Bainbridge is that its "system 2 [is] able to monitor or model the hematocrit … during the overall procedure … to determine the

instantaneous hematocrit," *e.g.*, the current value of hematocrit, "of the patient." EX1006, [0302]. EX1003, ¶136.

***Second,*** Fletcher-Haynes runs its prediction model "during a given collection procedure" through "downstream optimization" to maximize "at least one process parameter," *e.g.*, collection of plasma product or raw plasma. EX1005, 53:37-40. In Equation 15, Fletcher-Haynes' prediction model calculates a new donor hematocrit-dependent fraction of AC volume to pure plasma volume, $f_{ACP}$. Fletcher-Haynes then calculates a new target volume for plasma product (*e.g.*, $V_{SPB}$) and/or raw plasma (*e.g.*, $V_{SP}$), based at least in part, on a donor's hematocrit. Specifically, Fletcher-Haynes calculates $V_{SPB}$ using the donor hematocrit-dependent fraction of AC volume to pure plasma volume, $f_{ACP}$: $V_{SPB} = V_{SP}(1 + f_{ACP})$. EX1005, Eq. 22. The $f_{ACP}$ depends on hematocrit because $f_{ACP} = [(R - 1)(1 - H)]^{-1}$ where $H$ is the donor's hematocrit. EX1005, 51:53, Eq. 15. EX1003, ¶137.

***Third***, Fletcher-Haynes performs "downstream optimization" to calculate new target values of plasma product and raw plasma mid-procedure. EX1005, 12:16-20, 53:29-44, 54:6-13. As discussed above in §X.B.1, a POSITA would have been motivated to incorporate Bainbridge's teachings of updating hematocrit into Fletcher-Haynes' prediction model and would have had a reasonable expectation of success when doing so because Fletcher-Haynes already accounts for changing donor parameters when performing downstream optimization. EX1005, Eqs. 1-22.

Thus, using Bainbridge's instantaneous hematocrit during Fletcher-Haynes' downstream operation would establish a new target volume for plasma product and/or raw plasma. EX1003, ¶138.

**xii. 1[k] to control the system to operate a subsequent draw and return cycle, whereby the donor's changing hematocrit is taken into account in calculating the new target volume for plasma product and/or raw plasma.**

Fletcher-Haynes in view of Bainbridge renders obvious limitation 1[k]. EX1003, ¶139.

***First***, Bainbridge performs repeated draw and return cycles until "a predetermined amount of … collected blood components," *e.g.*, pure plasma, "have been harvested," and thus operates a subsequent draw and return cycle. EX1006, [0015], [0145]. EX1003, ¶140.

***Second***, Fletcher-Haynes in view of Bainbridge controls subsequent draw and return cycles, *e.g.*, by having a new modified plasma collection target, which accounts for the donor's changing hematocrit, *e.g.*, by using Bainbridge's current hematocrit calculations in Fletcher-Haynes' Equations 9 and 15. *See* §X.B.2.xi (limitation 1[j]); EX1003, ¶141.

As further discussed in §X.B.1, a POSITA would have been motivated to incorporate Bainbridge's teaching of tracking the instantaneous hematocrit to have a more accurate hematocrit value to use during successive applications of the

prediction algorithm and would have had a reasonable expectation of success in doing so. Therefore, Fletcher-Haynes in view of Bainbridge renders obvious limitation 1[k]. EX1003, ¶142.

**3. Claim 2**

**i. The system of claim 1, wherein the controller is programmed to determine the target volume for plasma product and/or raw plasma before a start of a first draw and return cycle.**

As discussed above in §X.A.1.ix (limitation 6[h]), Fletcher-Haynes' controller is programmed to determine the target volume for plasma product and/or raw plasma. Fletcher-Haynes further discloses determining the target volume for plasma product and/or raw plasma before a start of a first draw and return cycle, *e.g.*, through a prediction model "prior to running a donor on an apheresis machine." EX1005, 4:19-22. For example, Fletcher-Haynes uses a "prediction model … to allow operator input of various parameters … for predicting a yield of a particular blood component to be collected before a collection procedure is initiated." EX1005, 47:61-48:3. EX1003, ¶143.

**4. Claim 6**

**i. 6[preamble]**

*See* §§X.A.1.i, X.A.3.i, X.B.2.i (limitations 1[preamble], 6[preamble] Ground I, 15[preamble]). EX1003, ¶144.

**ii. 6[a]**

*See* §§X.A.1.ii, X.A.3.ii, X.B.2.ii (limitations 1[a], 6[a] Ground I, 15[a]). EX1003, ¶145.

**iii. 6[b]**

*See* §§X.A.1.iii, X.A.3.iii, X.B.2.iii (limitations 1[b], 6[b] Ground I, 15[b]). EX1003, ¶146.

**iv. 6[c]**

*See* §§X.A.1.iv, X.A.3.iv, X.B.2.iv (limitations 1[c], 6[c] Ground I, 15[c]). EX1003, ¶147.

**v. 6[d]**

*See* §§X.A.1.v, X.A.3.v, X.B.2.v (limitations 1[d], 6[d] Ground I, 15[d]). EX1003, ¶148.

**vi. 6[e]**

*See* §§X.A.1.vi, X.A.3.vi, X.B.2.vi (limitations 1[e], 6[e] Ground I, 15[e]). EX1003, ¶149.

**vii. 6[f]**

*See* §§X.A.1.vii, X.A.3.vii, X.B.2.vii (limitations 1[f], 6[f] Ground I, 15[f]). EX1003, ¶150.

**viii. 6[g]**

*See* §§X.A.1.viii, X.A.3.viii, X.B.2.viii (limitations 1[g], 6[g] Ground I, 15[g]). EX1003, ¶151.

**ix. 6[h]**

*See* §§X.A.1.ix, X.A.3.ix, X.B.2.ix (limitations 1[h], 6[h] Ground I, 15[h]). EX1003, ¶152.

**x. 6[i] to control the system to operate draw and return phases to withdraw whole blood from the donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor.**

Fletcher-Haynes' controller withdraws whole blood from the donor and separates it into the plasma product and the second blood component and returns the second blood component to the donor. *See* §X.A.1.x (limitation 6[i], Ground I). EX1003, ¶153.

If Patent Owner asserts that this limitation requires multiple draw and return phases and that Fletcher-Haynes does not disclose or render this limitation obvious, Bainbridge's apheresis system performs "removing and returning steps" that are "alternatively and repeatedly carried out during blood processing." EX1006, [0015], [0145]. As discussed in §X.B.1, a POSITA would have been motivated to incorporate Bainbridge's teaching of repeated draw and return phases into Fletcher-Haynes' apheresis system and would have had a reasonable expectation of success when performing the combination. EX1003, ¶154.

**5. Claim 7**

*See* §X.A.2.i (claim 7, Ground I). EX1003, ¶155.

**6. Claim 9**

**i. 9[preamble] A system for collecting plasma, comprising:**

*See* §§X.A.1.i, X.A.3.i, X.B.2.i, X.B.4.i (limitations 1[preamble], 6[preamble] Grounds I-II, 15[preamble]). EX1003, ¶156.

**ii. 9[a] a venipuncture needle configured to draw whole blood from a donor;**

*See* §§X.A.1.ii, X.A.3.ii, X.B.2.ii, X.B.4.ii (limitations 1[a], 6[a] Grounds I-II, 15[a]). EX1003, ¶157.

**iii. 9[b] a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;**

*See* §§X.A.1.iii, X.A.3.iii, X.B.2.iii, X.B.4.iii (limitations 1[b], 6[b] Grounds I-II, 15[b]). EX1003, ¶158.

**iv. 9[c] a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the blood separator, flow through the donor line being controlled by a first pump;**

*See* §§X.A.1.iv, X.A.3.iv, X.B.2.iv, X.B.4.iv (limitations 1[c], 6[c] Grounds I-II, 15[c]). EX1003, ¶159.

**v. 9[d] an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;**

*See* §§X.A.1.v, X.A.3.v, X.B.2.v, X.B.4.v (limitations 1[d], 6[d] Grounds I-II, 15[d]). EX1003, ¶160.

**vi. 9[e] a touchscreen configured to receive input from an operator; and**

*See* §§X.A.1.vi, X.A.3.vi, X.B.2.vi, X.B.4.vi (limitations 1[e], 6[e] Grounds I-II, 15[e]). EX1003, ¶161.

**vii. 9[f] a controller programmed to control operation of the system,**

*See* §§X.A.1.vii, X.A.3.vii, X.B.2.vii, X.B.4.vii (limitations 1[f], 6[f] Grounds I-II, 15[f]). EX1003, ¶162.

**viii. 9[g] the controller coupled to the touchscreen and programmed to receive at least a donor's weight, height and hematocrit and to determine a target volume for plasma product comprising raw plasma and anticoagulant,**

As discussed in §§X.A.1.viii (limitation 6[g]), Fletcher-Haynes discloses a controller coupled to a touchscreen. Fletcher-Haynes further discloses that "height, weight, gender, and platelet pre-count or hematocrit" are input using the touchscreen. EX1005, 1:48-52. EX1003, ¶163.

As discussed in §X.A.1.ix (limitation 6[h]), Fletcher-Haynes' controller (*e.g.*, the internal control on the blood component separation device) determines a target volume for plasma product comprising raw plasma and anticoagulant. EX1003, ¶164.

**ix. 9[h] wherein the target volume for plasma product is determined prior to withdrawing the whole blood from the donor based at least in part on the donor's total blood volume and/or the donor's plasma volume,**

As discussed in §X.A.1.ix (limitation 6[h]), Fletcher-Haynes determines the target volume for plasma product ($V_{SPB}$) based at least in part on the donor's total blood volume ($V_B$). $V_{SPB}$ may be determined before withdrawing a donor's whole blood, *e.g.*, through a prediction model "prior to running a donor on an apheresis machine." EX1005, 4:19-22. For example, Fletcher-Haynes uses a "prediction model … to allow operator input of various parameters … for predicting a yield of a particular blood component to be collected before a collection procedure is initiated." EX1005, 47:61-48:3. EX1003, ¶165.

**x. 9[i] the controller programmed to then control the system to operate a plurality of draw and return cycles to withdraw whole blood from the donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor.**

As discussed in §§X.A.1.x, X.B.4.x (limitation 6[i], Grounds I-II), Fletcher-Haynes and Bainbridge both disclose a system that withdraws whole blood from the donor, separates the whole blood into a plasma product and second blood component, and returns the second blood component to the donor. Bainbridge further performs the "removing and returning steps … alternatively and repeatedly," *i.e.*, a plurality of times. EX1006, [0015]. As discussed above in §X.B.4.x (limitation 6[i],

Ground II), a POSITA would have been motivated to program Fletcher-Haynes' controller to operate a plurality of draw and return cycles as disclosed in Bainbridge. EX1003, ¶166.

**7. Claim 10**

**i. The system of claim 9, wherein the controller is programmed to determine the target volume for plasma product based an anticoagulant ratio.**

Fletcher-Haynes' controller (*e.g.*, the internal control of the blood component separation device 18) is programmed (*e.g.*, receives a download of a collection device controller) to determine the target volume for plasma product (*e.g.*, $V_{SPB}$). As discussed above in §X.A.1.ix (limitation 6[h]), Fletcher-Haynes determines a target volume for plasma product (*e.g.*, $V_{SPB} = V_{SP}(1 + f_{ACP})$) based on the fraction of AC in the collected plasma component, $f_{ACP}$, using the anticoagulant ratio $R$ and hematocrit $H$ in equation 15: $f_{ACP} = [(R - 1)(1 - H)]^{-1}$. EX1003, ¶167.

**8. Claim 12**

**i. The system of claim 9, wherein the controller is configured to receive the donor's weight and hematocrit electronically.**

In Fletcher-Haynes, "data entry" occurs at "respective interfaces" which include "touchscreen input/output devices 199." EX1005, 10:12-15. As discussed above in §X.A.1.vi (limitation 6[e]), Fletcher-Haynes' touchscreen device is coupled with Fletcher-Haynes' controller (*e.g.*, the internal control of a blood component

collection device) to receive donor parameters. Fletcher-Haynes further discloses that the touchscreen and control are in "electronic or electromagnetic communication" which "make[s] broad use of multiple communication connections (including satellite and/or wide area networks (WAN's), for example)." EX1005, 10:1-7, 10:23-27; EX1003, ¶168.

**9. Claim 13**

**i. The system of claim 9, wherein the controller is programmed to control the system to collect the plasma product in the plasma product collection container until the plasma product in the plasma product collection container reaches the determined target volume.[5]**

Fletcher-Haynes discloses a controller that is programmed to control the system to collect the plasma product in the plasma collection container. Fletcher-Haynes' controller is programmed when the control system "transfer[s]/download[s] collection device controller" onto the internal control of a blood component collection device, at which point "all actual apheresis control during a procedure," *e.g.*, controlling draw and return phases, "remains resident in the apheresis machine

[5] Petitioner notes that this claim is invalid by Patent Owner's admission that "prior art plasmapheresis devices end plasma collection based on a total volume of anticoagulated plasma." EX1001, 12:53-56.

10 itself," including when to start and stop the plasma donation procedure. EX1005, Fig. 9A, 34:12-14, 53:9-20. EX1003, ¶169.

Fletcher-Haynes' system also "provides for the collection of … a 'maximum' quantity of at least one predetermined blood component," *e.g.*, plasma product or pure plasma and the internal control of Fletcher-Haynes' blood component separation device "achieve[s] the desired yield … required in the case of a product based optimization." EX1005, 3:2-10, 60:7-10. EX1003, ¶170.

Bainbridge teaches performing the plasma collection process until the plasma product in the plasma product collection container reaches the determined target volume. Specifically, Bainbridge repeats "[t]he cycle between blood removal and blood return/replacement … until a predetermined amount of … collected blood components have been harvested." EX1006, [0145]. A POSITA would have understood that the predetermined amount of collected blood component to which Bainbridge refers includes the target value of raw plasma. EX1003, ¶171.

Thus, Fletcher-Haynes' controller, as modified by Bainbridge, would repeat draw and return cycles until the plasma volume reaches the determined target value of raw plasma (*e.g.*, $V_{SP}$) or plasma product (*e.g.*, $V_{SPB}$) as calculated by Fletcher-Haynes' prediction model. EX1003, ¶172.

**10. Claim 15**

**i. 15[preamble]**

*See* §§X.A.1.vi, X.A.3.vi, X.B.2.vi, X.B.4.vi, X.B.6.i (limitations 1[preamble], 6[preamble] Grounds I-II, 9[preamble], 15[preamble] Ground I). EX1003, ¶173.

**ii. 15[a]**

*See* §§X.A.1.ii, X.A.3.ii, X.B.2.ii, X.B.4.ii, X.B.6.ii (limitations 1[a], 6[a] Grounds I-II, 9[a], 15[a] Ground I). EX1003, ¶174.

**iii. 15[b]**

*See* §§X.A.1.iii, X.A.3.iii, X.B.2.iii, X.B.4.iii, X.B.6.iii (limitations 1[b], 6[b] Grounds I-II, 9[b], 15[b] Ground I). EX1003, ¶175.

**iv. 15[c]**

*See* §§X.A.1.iv, X.A.3.iv, X.B.2.iv, X.B.4.iv, X.B.6.iv (limitations 1[c], 6[c] Grounds I-II, 9[c], 15[c] Ground I). EX1003, ¶176.

**v. 15[d]**

*See* §§X.A.1.v, X.A.3.v, X.B.2.v, X.B.4.v, X.B.6.v (limitations 1[d], 6[d] Grounds I-II, 9[d], 15[d] Ground I). EX1003, ¶177.

**vi. 15[e]**

*See* §§X.A.1.vi, X.A.3.vi, X.B.2.vi, X.B.4.vi, X.B.6.vi (limitations 1[e], 6[e] Grounds I-II, 9[e], 15[e] Ground I). EX1003, ¶178.

**vii. 15[f]**

*See* §§X.A.1.vii, X.A.3.vii, X.B.2.vii, X.B.4.vii, X.B.6.vii (limitations 1[f], 6[f] Grounds I-II, 9[f], 15[f] Ground I). EX1003, ¶179.

**viii. 15[g]**

*See* §§X.A.1.viii, X.A.3.viii, X.B.2.viii, X.B.4.viii, X.B.6.viii (limitations 1[g], 6[g] Grounds I-II, 9[g], 15[g] Ground I). EX1003, ¶180.

**ix. 15[h]**

*See* §§§X.A.1.ix, X.A.3.ix, X.B.2.ix, X.B.4.ix, X.B.6.ix (limitations 1[h], 6[h] Grounds I-II, 9[h], 15[h] Ground I). EX1003, ¶181.

**x. 15[i] the controller also configured to control the system to operate draw and return phases to withdraw whole blood from a donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor.**

*See* §§X.A.1.x, X.B.2.x, X.B.5.x (limitations 6[i] Grounds I-II, 9[i]). EX1003, ¶182.

If Patent Owner interprets this claim to require multiple draw and return cycles, which Petitioner asserts is not required under the plain and ordinary meaning of the claim language, and that Fletcher-Haynes does not disclose and/or render obvious multiple cycles, Bainbridge explicitly discloses an apheresis system that performs "removing and returning steps" that are "alternatively and repeatedly carried out during blood processing." EX1006, [0015]. As discussed in §X.B.1, a POSITA would have been motivated to incorporate Bainbridge's teaching of repeated draw and return cycles into Fletcher-Haynes' apheresis system and would

have had a reasonable expectation of success when performing the combination. EX1003, ¶182.

**11. Claim 16**

**i. The system of claim 15, wherein the controller is programmed to control the system to collect the plasma product in the plasma product collection container until a collected volume of plasma product reaches the target volume for plasma product and/or raw plasma.**

As discussed in §X.B.9.i (claim 13), Fletcher-Haynes in view of Bainbridge renders obvious a controller that is programmed to control the system to collect the plasma product in the plasma product collection container until the plasma product in the plasma product collection container reaches the determined target volume, where the determined target volume is the target volume of raw plasma (*e.g.*, $V_{SP}$) or plasma product (*e.g.*, $V_{SPB}$) calculated by Fletcher-Haynes' prediction model. EX1003, ¶183.

**12. Claim 17**

*See* §§X.A.4.i (claim 17). EX1003, ¶184.

**13. Claim 18**

*See* §§X.A.5.i (claim 18). EX1003, ¶185.

**14. Claim 19**

*See* §§X.A.6.i (claim 19). EX1003, ¶186.

**15. Claim 20**

*See* §§X.A.7.i (claim 20). EX1003, ¶187.

### 16. Claim 21

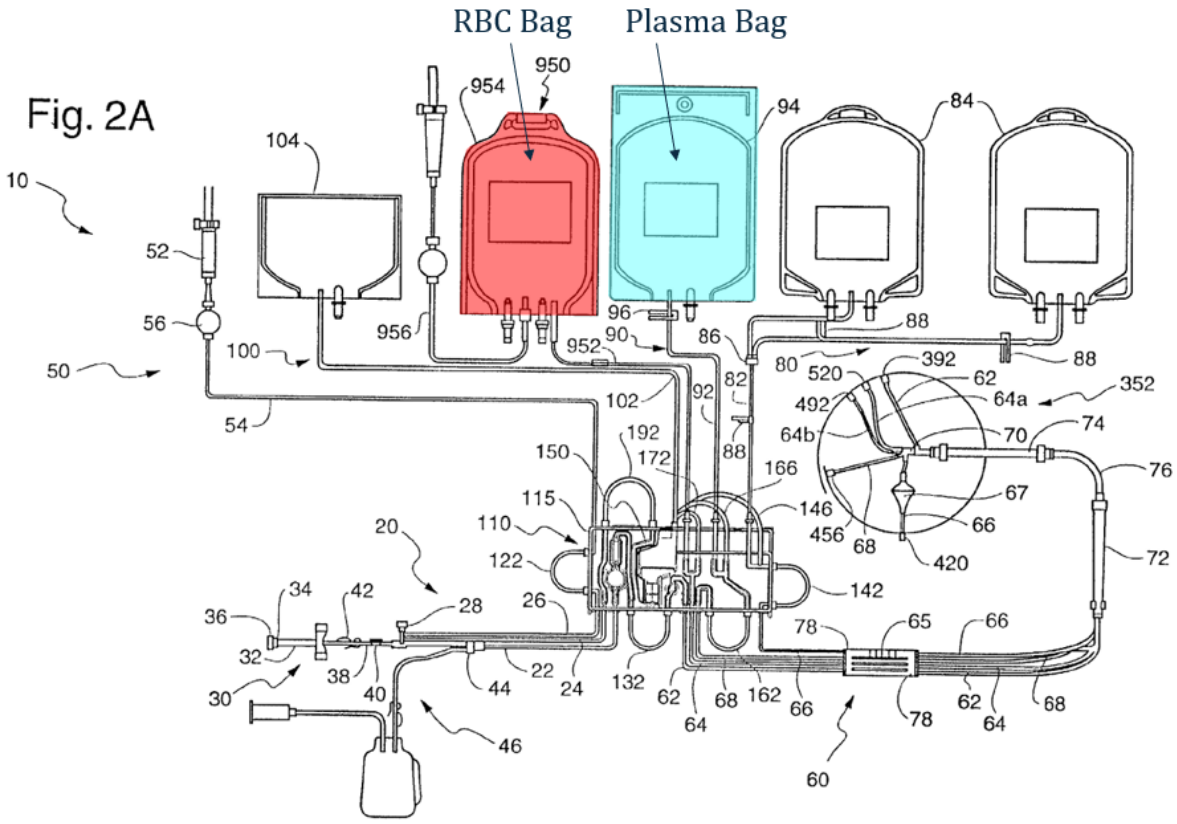
*See* §§X.A.8.i (claim 21). EX1003, ¶188.

### 17. Claim 26

#### i. The system of claim 15, further comprising a reservoir separate from the blood separator for receiving concentrated red blood cells.

Fletcher-Haynes discloses red blood cells are one "of the three blood product types … which may be … collected as part of a procedure." EX1005, 35:39-41. Fletcher-Haynes further discloses that red and white blood cells are directed through a "RBC/WBC line 46." EX1005, 45:46. EX1003, ¶189.

Bainbridge discloses that the blood separator "may be connected with an RBC… collection tubing assembly" which includes "at least one RBC collection reservoir, or bag." EX1006, [0103]. Bainbridge's RBC collection bag for receiving concentrated red blood cells (954) is separate from plasma collection bag (94). EX1005, [0101], [0103], Fig. 2A. EX1003, ¶190.




EX1008, Fig. 2A (annotated).

As discussed above in §X.B.1, it would have been obvious to a POSITA to incorporate Bainbridge's RBC tubing assembly into Fletcher-Haynes' blood component separation system, and a POSITA would have had a reasonable expectation of success when doing so. EX1003, ¶191.

### C. Ground III: Fletcher-Haynes in view of Bainbridge and Lavender renders obvious claims 3-4and 22-25.

#### 1. It would have been obvious to further modify the Fletcher-Haynes/Bainbridge system using the teachings of Lavender

As discussed above in §X.B.1 (Ground II), a POSITA would have been motivated to modify the Fletcher-Haynes system in view of Bainbridge. A POSITA would have further been motivated to modify the Fletcher-Haynes/Bainbridge system with Lavender because 1) each relates to plasma apheresis, 2) each applies substantially similar techniques to achieve similar results, and 3) the functionality of the Fletcher-Haynes/Bainbridge system would not change with the further addition of Lavender. EX1003, ¶192.

Like Fletcher-Haynes and Bainbridge, Lavender "relates to the collection of blood, and, in particular, to the fractioning of blood to collect blood substances, such as plasma" and also uses donor information to improve blood component collection, resulting in "an easier, safer, and more economical method of harvesting plasma." EX1004, 1:11-13, 1:20-26, 11:23-26. EX1003, ¶193.

Further, Fletcher-Haynes tracks "the current collection status" for the "blood product … which may be in the process of being collected as part of a procedure." EX1005, 35:38-41. Fletcher-Haynes repeatedly runs an optimization procedure to determine a target volume of pure and diluted plasma to collect, the same variables Lavender calculates before entering its Main Loop. EX1005, Eqs. 21-22. Thus, a

POSITA would have turned to Lavender to supply the requisite computer code related to implementing Fletcher-Haynes' procedure tracking. EX1004, cols. 41-44. EX1003, ¶194.

Additionally, incorporating Lavender's teachings of tracking collection into the Fletcher-Haynes/Bainbridge system would have been a routine, minor change to the system that would have yielded predictable results, as a POSITA would have understood that Fletcher-Haynes' algorithms are essentially the same as Lavender's algorithms. For example, a POSITA would have understood 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. As a second example, 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. A POSITA would understand that in Lavender $R = \frac{(QB+QC)}{QC} = \frac{QB}{QC} + 1$, so that $\frac{QB}{QC} = R - 1$. Lavender's equation TABLE VI, 2.a states that $\frac{QP}{QB} = 1 - \text{HCTD}$. Hence a POSITA would understand from Lavender's equation 2.b. that $\text{CF} = \frac{\text{QC}}{\text{QP}} = \frac{\text{QC}}{\text{QB}} * \frac{\text{QB}}{\text{QP}} = \frac{1}{(\text{R}-1)} * \frac{1}{(1-\text{HCTD})}$ or $\text{CF} = [(R-1)*(1-HCTD)]^{-1}$, which is the same equation as Fletcher-Haynes $f_{ACP}$. As a third example, a POSITA would understand that the sum

of Lavender's total plasma filtered ($TPF$) and total citrate filtered ($TCF$) is equal to Lavender's total dilute plasma filtered; $TDPF = TPF + TCF = TPF + TPF * CF = TPF * (1 + CF)$, or $TDPF = TPF * (1 + CF)$, which is equivalent to Fletcher-Haynes' Eq. 22. EX1003, ¶195.

Incorporating Lavender's loop code into Fletcher-Haynes' system would have been a known software modification that would have yielded predictable results. That is, incorporating Lavender's Main Loop into the Fletcher-Haynes/Bainbridge apheresis system entails the mere use of similar equations to improve similar systems and methods in the same way. "[W]hen a patent 'simply arranges old elements with each performing the same function it had been known to perform' and yields no more than one would expect from such an arrangement, the combination is obvious." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2007). EX1003, ¶196.

**2. Claim 3**

**i. The system of claim 2, wherein the controller is programmed to repeat draw and return phases until the target volume of plasma product and/or raw plasma is collected, wherein the target volume for plasma product and/or raw plasma is redetermined prior to the start of each draw phase.**

Fletcher-Haynes in view of Bainbridge and Lavender renders obvious claim 3. As discussed in §§X.A.1.x, X.B.4.x (limitation 6[i]), Fletcher-Haynes and Bainbridge disclose a plasma apheresis procedure that performs draw and return phases. EX1003, ¶197. Lavender collects plasma until a target volume of raw plasma

is collected, *e.g.*, until $TPF = MAXPF$. EX1004, Table VI, §5C. As discussed above in §X.C.1, it would have been obvious for a POSITA to combine Fletcher-Haynes, Bainbridge, and Lavender, and would have had a reasonable expectation of success when doing so. Therefore, Fletcher-Haynes in view of Bainbridge and Lavender renders obvious repeating draw and return phases until the target volume of raw plasma is collected. EX1003, ¶198.

Lavender's Main Loop "perform[s] the measurements and calculations" of $TPF$ "approximately every two seconds" and "stops the pumps" when "the desired weight of plasma has been collected … indicating that the plasma collection is complete." EX1004, 20:62-68; 21:61-22:2. EX1003, ¶199.

The Fletcher-Haynes/Bainbridge system, as modified by Lavender, renders obvious determining the target volume for plasma product or raw plasma prior to the start of each draw phase. As discussed above in §X.C.1, it would have been obvious to a POSITA to incorporate Fletcher-Haynes' prediction algorithm using a repeatable loop such as Lavender's Main Loop. Incorporating Fletcher-Haynes' prediction algorithm into a loop would repeat the prediction algorithm every two seconds. *See* EX1004, 20:60-68. Fletcher-Haynes' prediction model predicts a target volume of pure plasma ($V_{SP}$) and a target volume of plasma product ($V_{SPB}$). EX1005, Eqs. 21-22. Because a "normal apheresis" procedure "require[s] about 15 minutes," repeating the prediction model every two seconds would calculate the new target

volume of $V_{SP}$ and $V_{SPB}$ every two seconds, which is necessarily before the start of a new draw phase. EX1008, 2:13-14. EX1003, ¶200.

**3. Claim 4**

**i. The system of claim 3, wherein the controller is programmed to perform the draw and return phases at least three times.**

Fletcher-Haynes in view of Bainbridge and Lavender renders obvious claim 4 because Bainbridge performs draw and return phases "alternatively and repeatedly … during blood processing." EX1006, [0015]. It would have been well known to a POSITA to perform at least three draw and return phases using the teachings of Bainbridge. For example, Kimura discloses that the draw and return phase occurs "typically three or four times" during a blood donation procedure. EX1007, 12:24-25, Fig. 19, claim 2. Similarly, Sakota performs draw and return phases "successively … three to five times." EX1008, 2:11-15; EX1003, ¶201.

**4. Claim 22**

**i. The system of claim 21, wherein the controller is programmed to determine a target volume for plasma product based on the donor's total blood volume and the donor's plasma volume.**

As discussed in §X.A.1.ix (limitation 6[h]), Fletcher-Haynes' controller determines, *e.g.*, calculates a donor's total blood volume (*e.g.*, $V_B$, equation 10). As discussed above in §X.A.5.i (claim 18), Fletcher-Haynes' controller is programmed

to determine $V_B$, *e.g.*, when the central computer/database "transfer[s]/download[s] collection device controller 142." EX1005, Fig. 9A. EX1003, ¶202.

Lavender further discloses that the controller can be programmed to determine a target volume for plasma product based on the donor's plasma volume. Because "[i]t is generally accepted that the maximum percentage of total circulating plasma which can be safely donated in a single episode is 18%," Lavender's apheresis procedure collects "18% of the calculated donor circulating plasma volume." EX1004, 2:45-48, 22:39-41. EX1003, ¶203.

It would have been obvious to incorporate Lavender's collection of a target volume of pure plasma based on a percentage of the donor's total circulating plasma volume into the Fletcher-Haynes/Bainbridge system. Fletcher-Haynes calculates a target volume of pure plasma in Equation 17 as follows: $V_{SP} = f_{SP}V_B - V_C$, where $f_{SP}$ is $V_{CON}$ expressed as a fraction of total blood volume, $V_B$, and $V_{CON}$ is the volume constraint for total pure plasma collected. EX1005, Eq. 17, 51:55, 52:9-10. To set a target pure plasma collection volume of 18% of a donor's circulating plasma, a technician would (1) measure a donor's hematocrit (because a donor's plasma volume is proportional to a donor's total blood volume) and (2) select values of $V_{CON}$ and $f_{SP}$ such that $V_{SP}$ is 18% of the donor's total plasma volume. EX1004, 2:16-19. Accordingly, a POSITA would have had a reasonable expectation of success setting the volume constraints to achieve Lavender's collection of 18% of a donor's total

plasma volume because hematocrit was commonly measured before beginning apheresis procedures and values of $V_{CON}$ and $f_{SP}$ would have required simple arithmetic. EX1003, ¶204.

**5. Claim 23**

**i. The system of claim 22, wherein the controller is programmed to determine the donor's total blood volume based on the weight and height of the donor.**

As discussed in §X.A.1.ix (limitation 6[h]), Fletcher-Haynes' controller determines, *e.g.*, calculates a donor's total blood volume (*e.g.*, $V_B$, equation 10) based on the weight ($W$) and height ($L$) of a donor. As discussed in §X.A.5.i (claim 18), Fletcher-Haynes' controller is programmed to determine $V_B$, *e.g.*, when the central computer/database "transfer[s]/download[s] collection device controller 142." EX1005, Fig. 9A. EX1003, ¶205.

**6. Claim 24**

**i. The system of claim 23, wherein the controller is programmed to determine the donor's total blood volume before whole blood is withdrawn from the donor during a donation.**

As discussed in §X.A.1.ix (limitation 6[h]), Fletcher-Haynes calculates total blood volume using a donor's weight ($W$) and height ($L$) in equation 10. As discussed in §X.B.6.ix (limitation 9[h]), Fletcher-Haynes calculates the donor's total blood volume prior to blood being withdrawn during a donation. EX1003, ¶206.

### 7. Claim 25

#### i. The system of claim 24, wherein the controller is programmed to determine the target volume for plasma product comprising raw plasma and anticoagulant, wherein the target volume for plasma product is determined prior to withdrawing the whole blood from the donor based at least in part on an anticoagulant ratio, the donor's weight and the donor's hematocrit.

As discussed in §X.A.1.ix (limitation 6[h]), Fletcher-Haynes determines (calculates) the target volume for plasma product ($V_{SPB}$) comprising raw plasma ($V_{SP}$) and anticoagulant ($V_{SP} * f_{ACP}$). As discussed in §X.A.5.i (claim 18), Fletcher-Haynes' controller is programmed to calculate the target volume of product plasma. EX1003, ¶207.

As discussed in §X.B.6.ix (limitation 9[h]), Fletcher-Haynes calculates the target volume for plasma product by running a prediction model before initiating a collection procedure, *e.g.*, prior to withdrawing the whole blood from the donor. Further, as discussed in §X.A.1.ix (claim 6[h]), Fletcher-Haynes calculates the target volume for plasma product based at least in part on an anticoagulant ratio ($R$), the donor's weight ($W$) and the donor's hematocrit ($H$). EX1003, ¶208.

### D. Ground IV: Fletcher-Haynes in view of Bainbridge and further in view of Kimura renders obvious claims 5 and 8

#### 1. It would have been obvious to further modify the Fletcher-Haynes/Bainbridge system with the teachings of Kimura

A POSITA would have found it obvious and would have been motivated to combine Fletcher-Haynes' system, as modified by Bainbridge, with Kimura's teachings and would have had a reasonable expectation of success because 1) both relate to the same well-known technologies, 2) both apply substantially similar techniques to achieve similar results, and 3) the intended functionality of the Fletcher-Haynes/Bainbridge system would remain substantially the same in the proposed combination. EX1003, ¶209.

Like Fletcher-Haynes and Bainbridge, Kimura relates to blood product collections including plasma collection. Kimura collects "a blood component … from drawn blood and other blood components are returned into the blood donor." EX1007, 1:16-19. Kimura, like Fletcher-Haynes and Bainbridge, also uses donor-specific information to improve blood component collection procedures, meaning its teachings solve the same technical problem as Fletcher-Haynes and Bainbridge. Thus, a POSITA designing a system based on Fletcher-Haynes and Bainbridge would have turned to Kimura. EX1007, 1:50-52, 1:61-66. EX1003 ¶210.

Fletcher-Haynes' system calculates an anticoagulant amount in the plasma component using an AC ratio. EX1005, Eqs. 15, 17, 22. Bainbridge uses an

"anticoagulant peristaltic pump … to prime" the system to prevent coagulation in draw lines and the centrifuge. EX1006, [0138]. Bainbridge also notes that the AC ratio during priming stages differs from the ratio during normal operation. EX1006, [0305]. Kimura discloses that a POSITA can separately account for the anticoagulant added during a priming step. EX1007, 2:35-36, 13:48-55. Because Fletcher-Haynes calculates an amount of anticoagulant in the plasma component using AC ratios and Bainbridge calculates different AC ratios during priming steps and normal operation a POSITA would have been motivated to account for the anticoagulant introduced during the priming step, as disclosed in Kimura, to more accurately determine the dilute plasma collection volume. EX1003 ¶211.

Fletcher-Haynes and Bainbridge perform blood return steps but do not explicitly disclose when they occur after reaching the target volume. EX1006, [0015]. Kimura discloses that a final blood return step occurs once it is determined that it is the last cycle. EX1008, Fig. 4. A POSITA would have been motivated to perform a final return step in the last cycle as in Kimura to minimize the donor's blood loss. A POSITA would have had a reasonable expectation of success in incorporating a final return step in the Fletcher-Haynes/Bainbridge system because both systems already perform return cycles. EX1003 ¶212.

**2. Claim 5**

**i. The system of claim 1, wherein the controller is programmed to initiate a final return of the second blood component when (1) a measured volume of plasma product in the plasma collection container reaches the target volume for plasma product and/or (2) a volume of raw plasma in the plasma collection container reaches the target volume for raw plasma.**

Bainbridge repeats "[t]he cycle between blood removal and blood return" until a predetermined amount of plasma has been harvested. EX1006, [0145]. Kimura likewise repeats draw and return phases until a "predetermined amount of a first blood component," *e.g.*, plasma, "is separated." EX1008, 2:46-47, 12:25-26. Kimura performs a final blood returning step (S10) of an uncollected second blood component before stopping the blood donation program and after determining that "the present cycle is the last cycle," *e.g.*, when the collected volume of pure plasma equals the target volume of pure plasma. EX1007, Fig. 4, 9:65-66, 16:6-14. As discussed in §X.D.1, a POSITA would have been motivated to combine the Fletcher-Haynes/Bainbridge system with Kimura and would have had a reasonable expectation of success in doing so. EX1003, ¶213.

**3. Claim 8**

**i. The system of claim 7, wherein the controller is further programmed to account for anticoagulant introduced into the plasma collection container separate from the plasma product attributable to a priming or other pre-processing step.**

Kimura "performs a priming step of supplying anticoagulant, before blood drawing, to the [blood] separator, via a tube coupled to the blood draw needle." When Kimura introduces anticoagulant into the plasma collection component during the draw-and-return cycle, "the amount of anticoagulant supplied [] is determined by the anticoagulant ratio [and] ***preferably includes the amount of anticoagulant supplied in the priming step***." EX1007, 2:26-32. As discussed in §X.D.1, a POSITA designing the Fletcher-Haynes/Bainbridge plasma apheresis system would have turned to Kimura to account for anticoagulant introduced in a priming step and would have had a reasonable expectation of success incorporating Kimura's teaching. Thus, Fletcher-Haynes in view of Kimura renders obvious a controller that is further programmed to account for the anticoagulant introduced into the plasma collection container separate from the plasma product attributable to a priming step. EX1003, ¶214.

### E. Ground V: Fletcher-Haynes in view of Bainbridge and further in View of Neyrinck renders obvious claim 11

#### 1. It would have been obvious to a POSITA to combine the Fletcher-Haynes/ Bainbridge system with Neyrinck's teachings

As discussed in §X.B.1 (Ground II), a POSITA would have found it obvious and would have been motivated to modify Fletcher-Haynes' system with Bainbridge's mutiple draw and return cycles and red blood cell collection. EX1003, ¶215.

A POSITA designing Fletcher-Haynes' prediction algorithm would have been motivated to determine a more accurate equation to calculate total blood volume, *e.g.*, because people of the same weight or height may have different body morphologies or ages that influence their total blood volumes. A POSITA would have turned to Neyrinck for this as Neyrinck discloses calculating total blood volume based on the donor's weight, height, sex, age, morphology, and BMI. Such a modification would not change the intended functionality of Fletcher-Haynes' prediction algorithm and a POSITA would have had a reasonable expectation of success in adding the functionality as it only requires gathering additional donor information, which would have been straightforward as donor information was already being input, and modifying Fletcher-Haynes' total blood volume equation. EX1005, Fig. 9A; EX1003, ¶216.

**2. Claim 11**

**i. The system of claim 9, wherein the controller is programmed to determine the donor's total blood volume based on multiple parameters selected from the group consisting of the weight, height, sex, age, and morphology of the donor.**

Fletcher-Haynes in view of Bainbridge and Neyrinck discloses the additional requirements of claim 11. EX1003, ¶218.

Neyrinck discloses Nadler's formula to calculate the total blood volume of a male or female, *e.g.*, based on sex, using height and weight. EX1009, p.39. EX1003, ¶¶218-219.

$$For\ Males: (0.3669 \cdot Ht^3) + (0.03219 \cdot Wt) + 0.6041$$

$$For\ Females: (0.3561 \cdot Ht^3) + (0.03308 \cdot Wt) + 0.1833$$

$$\text{where } Ht = \text{Height (m)}, Wt = \text{Body weight (kg)}$$

Neyrinck also discloses that total blood volume, *e.g.*, approximate blood volume in mL/pound, is age dependent and that apheresis procedures "need to take into account the physics of the person," *e.g.*, the donor's morphology. EX1009, p.39, Table II. EX1003, ¶220. Neyrinck discloses that a person's BMI, *e.g.*, morphology, impacts the total blood volume of a donor. EX1009, p.39, Table III. EX1003, ¶220.

Additionally, Fletcher-Haynes discloses that a blood component separation device's internal controls may be programmed to determine the donor's total blood volume, *e.g.*, when the central computer/database "transfer[s]/download[s] collection device controller 142." EX1003, ¶221. As discussed above in §X.E.1, it would have been obvious to a POSITA to program Fletcher-Haynes' controller with Neyrinck's total blood volume formula. EX1003, ¶221.

### F. Ground VI: Fletcher-Haynes in view of Bainbridge and further in view of Sakota renders obvious claim 14.

#### 1. A POSITA would have been motivated to further modify the Fletcher-Haynes/ Bainbridge with Sakota

As discussed in §X.B.1 (Ground II), a POSITA would have modified Fletcher-Haynes' system with Bainbridge's teachings to design a plasma apheresis system that operates a plurality of draw and return cycles. However, such a system does not explicitly disclose how much blood to draw per cycle. A POSITA would have been motivated to look to Sakota's teachings fordetermining how much blood to withdraw per cycle. EX1003, ¶222.

Fletcher-Haynes, Bainbridge, and Sakota are analogous pieces of art. Like Fletcher-Haynes and Bainbridge, Sakota "relates to an apheresis machine and method for collecting blood products" including plasma. EX1008, 1:6-7, 14-20. Specifically, Sakota teaches "variable control" of an apheresis procedure for customized collection of blood products using a "[c]alculation of the [t]otal [a]mount of [b]lood" of a donor "based on the" donor's "sex, height, and weight." EX1008, 8:27-31. EX1003, ¶223.

Sakota also teaches how much blood to draw per cycle. For example, Sakota conducts three to five successive draw and return cycles each with a "decrease in the process of whole blood per cycle" so that "the danger of causing anemia or dizziness will be minimized." EX1008, 2:11-15, 4:17-23; EX1003, ¶224.

A POSITA would have had a reasonable expectation of success incorporating Sakota's teaching of decreasing blood draw volume per cycle into the Fletcher-Haynes/Bainbridge system. Incorporating Sakota's teachings would have required a simple software modification of Fletcher-Haynes' internal blood component code, which would have been well known to a POSITA and would have provided predictable results. EX1003, ¶225.

**2. Claim 14**

**i. The system of claim 9, wherein the controller is programmed to perform the draw and return cycles at least three times and the controller is programmed to determine a volume of whole blood to be drawn in a final draw phase which is different than a volume drawn in a prior draw phase.**

Fletcher-Haynes in view of Bainbridge and in further view of Sakota renders obvious claim 14. EX1003, ¶226.

Sakota performs draw and return cycles "successively … three to five times." EX1008, 2:11-15. As discussed in §X.F.1 (Ground VI) , it would have been obvious to a POSITA to program Fletcher-Haynes' controller to perform at least three draw and return cycles, and a POSITA would have had a reasonable expectation of success operating Fletcher-Haynes' system using a plurality of draw and return cycles. EX1003, ¶227.

Sakota further discloses that a volume of whole blood drawn in a final draw phase may differ from a volume drawn in a prior draw phase. Specifically, Sakota

teaches draw and return cycles with "decrease in the process volume of whole blood per cycle" to avoid "the danger of causing anemia or dizziness" during a blood draw procedure. EX1008, 4:17-18, 4:22-23; §X.F.1. EX1008 4:22-23. EX1003, ¶228.

## XI. §§101/112 GROUNDS

### A. Ground VII: All Claims of the '474 Patent Are Ineligible Under Section 101

Determining whether a patent claim is impermissibly directed to patent ineligible subject matter involves two steps. *Alice*, 573 U.S. at 217 (citing *Mayo Collaborative Servs. v. Prometheus Lab'ys, Inc.*, 566 U.S. 66, 75-77 (2012)).

The first step ("*Alice* Step One") determines whether the claims are directed to an abstract idea or other patent ineligible concept. *Alice*, 573 U.S. at 217. In applying *Alice* Step One, courts recognize that it is useful to "compare claims at issue to those claims already found to be directed to an abstract idea in previous cases." *Enfish, LLC v. Microsoft Corp.*, 822 F.3d 1327, 1334 (Fed. Cir. 2016).

The second step ("*Alice* Step Two") requires a search for an inventive concept, such as determining whether there are "additional elements [that] 'transform the nature of the claim' into a patent-eligible application." *Alice*, 573 U.S. at 217. Transformation into a patent-eligible application requires "more than simply stating the abstract idea while adding the words 'apply it.'" *Id.* at 221 (internal citation omitted). Implementing an abstract idea in a "particular technological environment" and using conventional technology does not make an abstract idea patent eligible.

*Atos, LLC v. Allstate Ins. Co.*, No. 20-CV-06224, 2021 WL 6063963, at *5-13 (N.D. Ill. Dec. 22, 2021) (citing *Intell. Ventures I LLC v. Symantec Corp.*, 838 F.3d 1307, 1314, 1319 (Fed. Cir. 2016)); *accord Bilski v. Kappos*, 561 U.S. 593, 610-11 (2010).

### 1. The Board Should Consider Representative Claim 6 to Assess the Patent Eligibility of the ’474 Patent

Claims can be treated as representative where the other claims do not “differ in any manner that is material to the patent-eligibility inquiry.” *Mortg. Grader, Inc. v. First Choice Loan Servs. Inc.*, 811 F.3d 1314, 1324 n.6 (Fed. Cir. 2016); *Content Extraction & Transmission LLC v. Wells Fargo Bank, Nat. Ass’n*, 776 F.3d 1343, 1348-49 (Fed. Cir. 2014).

Here, claim 6 is representative of all claims, as the claims recite generic computer processors that perform basic plasma collection procedures and automated volume calculations that can be done by a technician using generic computer components. Claim 6 is also representative because it also recites results-oriented calculations of anticoagulant and pure plasma volumes that can be performed on a controller as is found in the other challenged claims. Further, claim 6 recites fundamental plasma collection steps found in the challenged claims—drawing blood, introducing anticoagulant, separating blood into components, and collecting plasma. Lastly, like the other claims, representative claim 6 also recites the basic

plasma collection equipment used to perform the each of the fundamental apheresis steps.

Claim 6's limitations,with basic apheresis procedures in green and the abstract idea of automated calculations on a processor in purple, are reproduced below.

> A system for collecting plasma, comprising:
>
> a venipuncture needle configured to draw whole blood from a donor;
>
> a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;
>
> a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the blood separator, flow through the donor line being controlled by a first pump;
>
> an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;
>
> a touchscreen configured to receive input from an operator; and
>
> a controller programmed to control operation of the system, the controller coupled to the touchscreen and programmed to receive at least a donor's weight, height, sex and hematocrit, to determine a target volume for plasma product and/or raw plasma based at least in part on the donor's total blood volume and/or the donor's plasma volume, to control the system to operate draw and return phases to withdraw whole blood from the donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor.

As claim 6 is substantially similar and linked to the same abstract idea as the other claims of the ’474 patent, it is unnecessary for the Board to assess the patent eligibility of each claim. Instead, it can assess the patent eligibility of just claim 6 when rendering its determination. *See Content Extraction & Transmission*, 776 F.3d at 1348.

### 2. *Alice* Step One: The Challenged Patents Are Directed To Abstract Ideas

It is well-established that “methods which can be performed mentally, or which are the equivalent of human mental work,” “are unpatentable abstract ideas.” *See CyberSource Corp. v. Retail Decisions, Inc.*, 654 F.3d 1366, 1371 (Fed. Cir. 2011). That is because “[a] telltale sign of abstraction is when the claimed functions are mental processes that can be performed in the human mind or using a pencil and paper.” *Trinity Info Media, LLC v. Covalent, Inc.*, 72 F.4th 1355, 1361–62 (Fed. Cir. 2023) (quotation omitted).

Yet, such pen and paper calculations are at the heart of representative claim 6. Specifically, the ’474 patent performs a sequence of abstract calculations involving donor and system parameters. For example, claim 6 of the ’474 patent claims “the controller coupled to the touchscreen and programmed to receive at least a donor’s weight, height, sex and hematocrit, to determine a target volume for plasma product and/or raw plasma based at least in part on the donor's total blood volume and/or the

donor's plasma volume."

The '474 patent's specification further supports that the claims are "directed to" these mathematical calculations. For example, the specification explains that the goal of the invention is to determine the total collected volume of plasma. EX1001, 1:59-65. But equipment and steps common to all plasma apheresis procedures are used to gather the information needed to perform this calculation. EX1001, 1:35-51. The system uses well-known equipment to draw blood from the donor, introduce anticoagulant to prevent the drawn blood from clotting, separate the blood into plasma, and collect the anticoagulated plasma in a plasma collection container. *Id.* at Fig. 3, 3:28-29.

The '474 patent also explains that a technician can perform these calculations. Specifically, the '474 patent explains that "the technician . . . may calculate the percentage of anticoagulant within the collected plasma (step 455) (e.g., the plasma product contained within the plasma collection container 216) based on the amount of anticoagulant added/metered into the whole blood and the hematocrit of the donor." EX1001, 11:7-13. Similarly, the '474 Patent explains that the technician can determine the donor's weight and use this weight to determine "the volumes of blood components that may be withdrawn/collected (e.g., per the FDA guidelines)," *i.e.*, the target volume of pure plasma to collect. EX1001, 8:56-61. Further, the '474 patent explains that "[o]nce the technician/system 100 has calculated the percentage

of anticoagulant within the plasma collection container 216, the technician/system 100 may then use this information to calculate the volume of pure plasma within the plasma collection container 216 (Step 465).” EX1001, 11:45-49. The technician can calculate this by subtracting the volume of anticoagulant from “the total volume of fluid within the container 216” and that collection continues until “a target volume of pure plasma is collected within the plasma collection container.” EX1001, 11:49-62. In other words, the ’474 patent explains how a technician can gather basic donor and system parameters, which are known, to calculate the claimed volumes recited in the ’474 patent. *See Trinity Info Media*, 72 F.4th at 1361–62. And while the ’474 patent may require the technician to gather donor and system information used for the calculations, it does not change the fact that representative claim 6 is directed to mathematical calculations, not any improved system, and thus these elements do not make the claim patent eligible.

Additionally, while representative claim 6 recites that a “controller” and not a technician performs these calculations, this does not establish that the claims are not directed to an abstract idea. Simply put, “a claim does not satisfy Section 101’s eligible subject matter requirement by reciting generic computer implementation to ‘optimize’ an already-understood process.” *See, e.g.*, *Concaten*, 131 F. Supp. 3d at 1174; *accord Four Winds Interactive LLC v. 22 Miles, Inc.*, No. 16-cv-00704, 2017 WL 4334074, *6-8 (D. Colo. Mar. 28, 2017). Thus, the ’474 patent cannot be

accorded patentability by calculating the recited volumes using a generic computer processor instead of having a technician/user do them. "[Q]uintessential do it on a computer" claims are not patent eligible under *Alice* Step One. *Univ. of Fla. Rsch. Found., Inc. v. Gen. Elec. Co.*, 916 F.3d 1363, 1367 (Fed. Cir. 2019).

While sometimes using a computer to implement traditional pen and paper claims has been found to be patent eligible, those instances are inapposite to this case. For example, claims previously performed by pen and paper were found to be patent eligible when they encompassed specific sequences of rules that were used and applied to create desired results. *See, e.g.*, *McRO, Inc. v. Bandai Namco Games Am. Inc.*, 837 F.3d 1299, 1315 (Fed. Cir. 2016); In *McRO*, the Federal Circuit concluded that McRO's claims were directed to creating "a sequence of synchronized, animated characters" by utilizing an objective set of rules that had to be rendered in a specific way, with specific relationships between elements, which prevented broad preemption of all rules-based means of automating lip synchronization. *Id*. at 1304, 1315. In contrast, the '474 patent tries to encompass all known donor variables, as outlined in the FDA's 1992 guidance, that may be considered when collecting any blood product and then claim using a general-purpose processor to perform calculations a technician can do "based on" those variables.

Similarly, while in some situations *Alice* Step One can be satisfied if the

claims are directed to improving procedures, that is not the case here. *See CardioNet, LLC v. InfoBionic, Inc*, 955 F.3d 1358, 1368–69 (Fed. Cir. 2020). In *CardioNet*, the patented method was found to be patent eligible because it improved previous systems for detecting atrial fibrillation. *Id.* at 1366. Here, however, "the claims merely computerize pre-existing techniques" in apheresis, for example, by claiming a blood separator with a generic controller. *Id.* at 1370. Patent Owner may rely upon a single quote in its specification to allege that its patented system is "directed to" technical improvements in plasma collection. *See* EX1001, 1:59-2:4. But nowhere throughout the specification of the '474 patent does Patent Owner "explain[ ] how [the] particular arrangement of elements" such as its claimed processor, pump, and weight scale are "a technical improvement over prior art." *Amdocs (Israel) Ltd. v. Openet Telecom, Inc.*, 841 F.3d 1288, 1299 (Fed. Cir. 2016). Rather, it is the generic processor that calculates a pure plasma volume that supplies the alleged inventive aspect. Thus, the claims at issue here are different than the claims at issue in *CardioNet* because here "the claims merely computerize pre-existing techniques" in apheresis, for example, by claiming a blood separator with a generic controller. *CardioNet*, at 1370.

### 3. *Alice* Step Two: The Challenged Claims Do Not Contain An Inventive Concept

A concept may be patent-eligible despite being directed to an abstract idea

only if it recites "an inventive concept sufficient to transform the claimed abstract idea into a patent-eligible application." *Alice*, 573 U.S. at 221 (quotations and citation omitted). If it does not, it is patent ineligible. Similarly, if the computer functions claimed, individually and in combination, are "well-understood, routine, [and] conventional activities previously known to the industry," it is ineligible for patenting. *See Coop. Ent., Inc. v. Kollective Tech., Inc.*, 50 F.4th 127, 130 (Fed. Cir. 2022). Here, nothing in the claims of the '474 patent transforms the claimed abstract plasma collection calculations into patent eligible claims.

First, there is no inventive concept because the '474 patent's claims automate calculations previously performed by a technician using a general-purpose processor. The '474 patent's claimed controller does not provide "specific structural or inventive improvements in computer functionality related to this claimed system." *Customedia Techs., LLC v. Dish Network Corp.*, 951 F.3d 1359, 1366 (Fed. Cir. 2020). Instead, the controller is used to automate mathematical calculations that can be performed by a human using computers in the way that computers were meant to be used. *See, e.g.*, *Affinity Labs of Tex., LLC v. DIRECTV, LLC*, 838 F.3d 1253, 1264 (Fed. Cir. 2016). This does not establish an inventive concept.

Prforming math on a generic controller also does not provide an inventive concept under *Alice* Step Two because "simply implementing a mathematical principle on a physical machine, namely a computer, [is] not a patentable application

of that principle." *Mayo*, 566 U.S. at 84 (citing *Gottschalk v. Benson*, 409 U.S. 63, 71(1972)). "Given the ubiquity of computers, wholly generic computer implementation" of performing mathematics on a computer "is not generally the sort of additional feature" that makes an abstract idea patentable. *Alice*, 573 U.S. at 223-24.

Moreover, the'474 patent's specification, which must be looked at to assess whether an inventive concept exists in the claimed mathematical equations, establishes that there is no inventive concept. *See Arrhythmia Rsch. Tech., Inc. v. Corazonix Corp.*, 958 F.2d 1053, 1058–59 (Fed. Cir. 1992); *see also TecSec, Inc. v. Adobe Inc.*, 978 F.3d 1278, 1292 (Fed. Cir. 2020). The specification reveals that ***all*** calculations may be performed by a technician. EX1001, at 11:45-12:38. Replacing a technician with a computer does not supply an inventive concept under *Alice* Step Two. *See Trinity Info Media*, 72 F.4th at 1366-67.

Further, even if Patent Owner alleges it invented a new way to calculate a plasma product or anticoagulant volume, which it did not, "the novelty of the mathematical algorithm is not a determining factor at all" and "is treated as though it were a familiar part of the prior art." *See Parker v. Flook*, 437 U.S. 584 at 591–92 (1978). That is because "[t]he abstract idea itself," the mathematical principles behind calculating volumes, "cannot supply [an] inventive concept" no matter how groundbreaking the advance. *ChargePoint*, 920 F.3d at 775.

Patent Owner may allege that the claims supply an inventive concept because of the presence of mechanical components, *i.e.*, a weight sensor. But these are not specialized mechanical components, they are generic sensors and equipment. Moreover, their purpose is merely to provide information for the technician to perform abstract calculations. Use of generic equipment to improve the speed, accuracy, or efficiency of a known process does not provide a patent eligible improvement. *Recentive Analytics, Inc. v. Fox Corp.*, 134 F.4th 1205, 1214 (Fed. Cir. 2025); *OIP Technologies, Inc. v. Amazon.com, Inc.*, 788 F.3d 1359, 1363 (Fed. Cir. 2015). This is true even when "equipment can be 'vital' to an advance." *Yu v. Apple Inc.*, 1 F.4th 1040, 1045 (Fed. Cir. 2021).

Patent Owner may also claim that these tools allow for faster/more efficient calculations, but the Federal Circuit has rejected such arguments. For example, in *Trinity Info Media*, the Court found that the ability to perform faster calculations "merely reflect[ed] the improved speed inherent with applying the abstract idea using a computer" and did not render the claims patentable. *See Trinity Info Media*, 72 F.4th at 1363-64, 1366. The same applies here. Any alleged improvements are inherent to using standardized equipment with a general processor.

Simply put, reading the claims as a whole shows that they incorporate well-known plasma collection calculations that incorporate decades-old FDA guidance in an automated plasma collection system using basic plasma collection procedures

(drawing, separating, collecting, and returning blood) and equipment (needles, tubing, separation devices, pumps, weight sensors, and collection containers). Such purely "conventional or obvious" plasma collection equipment and/or steps are "not sufficient to transform an unpatentable" idea, like the claimed mathematical calculations, "into a patent-eligible application," especially here where "anyone who wants to make use" of a plasma collection system must perform these claimed on the claimed equipment. *Mayo*, 566 U.S. at 79.

Therefore, taken individually, as a whole, or as an ordered combination, the claim limitations of the '474 patent automate known apheresis procedures using well-known plasma collection equipment, and "neither improve the functions of the computer itself, nor provide specific programming, tailored software, or meaningful guidance for implementing the abstract concept." *Intell. Ventures I LLC v. Cap. One Fin. Corp.*, 850 F.3d 1332, 1342 (Fed. Cir. 2017). Accordingly, *Alice* Step Two is not satisfied.

### B. Ground VIII: Claims 1-11, and 13-25 Lack an Adequate Written Description Under Section 112[6]

Haemonetics overreached when filing its continuation applications. Despite the requirement that "the new claims" in a continuation "must find support in the original specification" the '474 patent's claims do not. *TurboCare Div. of Demag Delaval Turbomachinery Corp. v. GE*, 264 F.3d 1111, 1118 (Fed. Cir. 2001).

The '474 patent is a continuation-in-part of the '652 patent and a continuation of the '416 patent. But many of the '474 patent's claims barely resemble the specification it shares with these patents. Thus, Haemonetics' claims fail to meet the written description requirement of Section 112(a).

#### 1. Disclosure of the Purported Invention

As discussed above, Haemonetics' purported invention is a blood processing system that continues collecting plasma until reaching a target volume of pure plasma. EX1001, 7:4-6. To do that, Haemonetics purportedly tracks the amount of pure plasma in the container while blood is being drawn and checks whether the amount of pure plasma equals a target volume of pure plasma. *See* EX1001, Fig. 5.

[6] The Examiner never addressed the lack of written description or the support for the new matter. *See* §6C. The Prosecution History contained only a double patenting rejection, so the Board will address the lack of written description for the first time.

Figure 5 of the ’474 patent illustrates the steps allegedly performed by Haemonetics’ patented system. EX1003, ¶230.

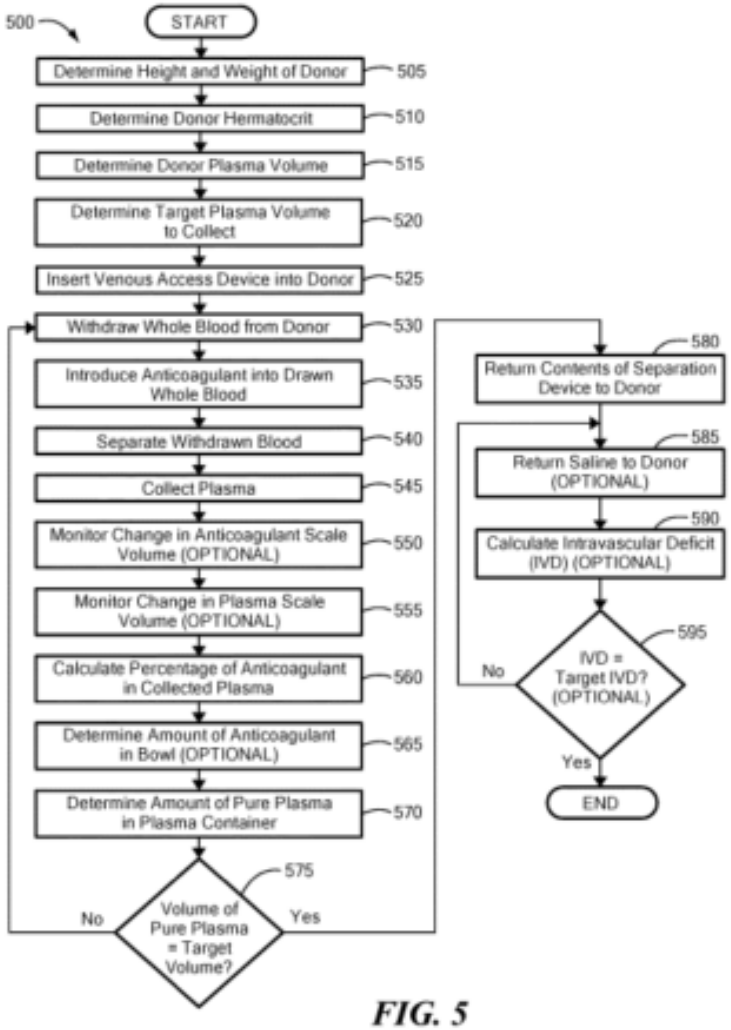



***FIG. 5***

As shown in Figure 5, the technician or system determines a donor’s weight, height, and hematocrit to calculate a total plasma volume to collect before withdrawing blood. According to the ’474 patent, this is the only time that a target plasma volume is determined. EX1003, ¶231.

Then, the method enters a loop (steps 530-570) that continues until "volume of pure plasma = target volume." EX1001, Fig. 5. The technician or the system withdraws whole blood, introduces anticoagulant into withdrawn blood, collects plasma, calculates the percentage of anticoagulant in collected plasma, and determines the amount of pure plasma in the plasma container. EX1005, 11:45-67. EX1003, ¶232.

The '474 patent does not show steps 530-570 occurring in a cycle (*i.e.*, they can occur simultaneously) nor does it explain how often the Figure 5 loop repeats. EX1003, ¶233.

**2. Argument**

Claims 1-11, 13-16, and 18-25 recite limitations that lack written description support in the '474 patent. For example, these claims, as discussed further below, include claim limitations that recite basic apheresis equipment that allegedly **programs a controller**, measures/calculates **plasma product**, performs **draw and return cycles**, calculates **new target volumes**, and has **a control system**. None of these categories have sufficient written description support in the '474 patent's specification. EX1003, ¶234.

**i. There is no written description support for "programming a controller"**

Claims 1-11, 13-16, 18, 20-25, which require programming the controller in Haemonetics' claimed apheresis system, lack adequate written description support.

The ’474 patent discloses “a controller that controls the operation of the centrifuge bowl and the first pump. The controller may calculate (1) a donor plasma volume, (2) a target plasma collection volume, and (3) a volume of pure plasma collected within the plasma container.” EX1001, 5:34-38. The specification never discusses the claimed controller being ***programmed*** to perform such calculations. For example, Haemonetics does not disclose when, how, or by whom the controller is programmed, *i.e.*, before being installed in the system or done by a technician during the operation of the plasma collection system. That is because the only time that the word “program” or “programmed” appears in the specification is in the claims. EX1003, ¶235.

**ii. Limitations requiring a plasma product are unsupported.**

Claims 1-3, 5, 6, 9-10, 13, 15, 16, 18-22, 25, require measuring a plasma product. EX1003, ¶236. Haemonetics uses the term “plasma product” sparsely in its specification: once to describe the technical field, later to distinguish the alleged invention over prior art systems, and finally in discussing saline return in prior art systems. EX1001, 1:26-28, 16:56-60, 17:15-24. Figure 5, which shows the purported invention, does not reference plasma product. EX1003, ¶237.

First, Haemonetics’ disclosure that the field of the invention is collecting “a plasma product” does not support claim limitations reciting measuring/calculating

target or current plasma product volumes. *See Biogen Int'l GMBH v. Mylan Pharms. Inc.*, 18 F.4th 1333, 1342-45 (Fed. Cir. 2021). EX1003, ¶238.

Further, the reason for these sparse disclosures is that the '474 patent teaches away from collecting a "plasma product" that is not "pure plasma." "[I]llustrative embodiments of" Haemonetics' purported invention include only a system for "collecting a target volume of pure plasma." EX1001, 7:4-6. Haemonetics' claimed system collects plasma until a collected volume reaches a target volume of pure plasma because doing so offers the purported improvement of "collect[ing] a greater volume of pure plasma collected as compared to prior art systems that collect based on the volume of the plasma product." EX1001, 10:16-18; 10:66-11:3. 17:19-20. Thus, the focus of the patent is ***pure plasma*** collection, not plasma product collection. EX1003, ¶238.

Additionally, Haemonetics' claim 1 broadens the scope of its claims to include calculating a "plasma product" target volume using "and/or" language. EX1001, claim 1. Specifically, it recites "to determine a target volume for plasma product and/or raw plasma." In doing so, Haemonetics claims what the '474 patent identifies as prior art (calculating a volume of plasma product) in addition to its purported invention (calculating a volume of pure plasma). EX1001, 12:51-56. Haemonetics' disclosure of the prior art calculating a volume of plasma product is insufficient to

provide written description support for its claimed invention, which is focused on calculating pure plasma volumes, also calculating plasma product volumes.

Simply put, Haemonetics' claimed system does not calculate a target volume for plasma product, rendering any "target volume for plasma product" claims invalid for a lack of written description. EX1003, ¶239.

**iii. Draw and return cycle limitations lack adequate written description support.**

Claims 1-4, 6, 9, 14, 15, which require collecting plasma from whole blood using draw and return cycles, are invalid for lack of written description support. EX1003, ¶240.

First, the '474 patent's specification does not mention draw and return cycles. Haemonetics includes Fig. 5 to allegedly show that the '474 patent discloses withdrawing whole blood, separating whole blood, collecting plasma, determining an amount of pure plasma in the plasma container, and returning uncollected components. But the specification does not disclose that these steps are performed in ***a cycle***. In fact, the word "cycle" does not appear outside of the claims. Thus, claims 1-4, 6, 9, 14, 15, which all recite draw and return cycles, lack written description support. EX1003, ¶241.

Second, the specification does not mention controlling any aspects of such cycles. Claim 1 requires a controller to operate a draw and return cycle but the

specification does not disclose which part of the patented system controls a draw and return cycle. Similarly, claims 2-3 and 14, which recite limitations related to the timing of calculating a target volume within a draw and return cycle (claims 2-3) or the amount of blood to draw per cycle (claim 14), lack written description support because these aspects of control are similarly not disclosed. EX1003, ¶242.

Lastly, the specification does not disclose repeating any cycles as required in yet claims 1, 4, 9, and 14. For example, claim 4 recites that such a cycle is repeated at least three times. Similarly, claim 9 recites a system that performs a plurality of cycles, and claim 1 recites a controller operating "a subsequent draw and return cycle." EX1003, ¶243.

But the '474 patent includes no disclosures that would require multiple cycles, nor does it disclose a single needle configuration that would require performing draw and return steps in distinct phases. *Contra* EX1005, 46:10-15; EX1003, ¶244.

Haemonetics may argue that performing repeated draw and return cycles using a centrifugal separator would have been obvious. However, "it is not sufficient for purposes of the written description requirement" to "combine[] with the knowledge in the art" what is in the specification to "speculate as to the modifications that the inventor" made. *Lockwood*, 107 F.3d at 1571-72. What matters is that the specification does not explain what a draw and return cycle is,

what happens during a draw and return cycle, and that the draw and return cycle is repeated.

#### iv. Calculating a new target volume mid-donation is Unsupported

Claims 1 and 3 require calculating a new target volume mid-donation and are invalid for lacking adequate written description support in the specification. As shown in Figure 5, the ’474 patent purportedly discloses calculating a target volume of pure plasma ***once*** before the system runs. The ’474 patent does not disclose re-calculating the target volume mid-donation. Nor does the specification disclose when the new target is allegedly calculated as required by claim 3. EX1001, cl. 3. Thus, any claims reciting repeated target volume calculations during operation cover “subject matter that is indisputably missing from the [’474] specification” and are invalid for a lack of written description. *Cisco Sys., Inc. v. Cirrex Sys., LLC*, 856 F.3d 997, 1009 (Fed. Cir. 2017). EX1003, ¶245.

#### v. Control system limitations lack written description support

Claims 17 and 18, which require that the plasma apheresis system interacts with a control system, are invalid for lack of adequate written description support. EX1003, ¶246.

The words “control system” only appear in claims 17 and 18 of the ’474 patent. The specification of the ’474 patent does not explain what the control system

is, what it does, or where it is located. For example, Claim 18 requires that "the controller" receives a target volume "electronically from a control system," yet the specification says that the calculations may be performed by a technician or a controller. Further, Figure 3, which shows the hardware and software components of Haemonetics' claimed system, discloses no hardware or software coupled to the controller of the blood separator that can be reasonably interpreted as a control system. EX1003, ¶247.

Dated: September 3, 2025

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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 12,186,474, 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 18,653. 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 September 3, 2025 by filing a copy of this Petition for IPR of U.S. Patent No. 12,186,474 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. 12,186,474:

McCarter & English, LLP
c/o Jonathan C. Lovely
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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:

Haemonetics Corporation
125 Summer Street
Boston, MA 02110

With a courtesy copy to Patent Owner's counsel of record in *Haemonetics Corporation v. Terumo BCT, Inc.*, Case No. 25-cv-1409-RMR-SBP (D. Colo. Filed May 5, 2025) by electronic mail:

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