

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

TERUMO BCT INC.,

Petitioner

v.

HAEMONETICS CORP.,

Patent Owner

PGR2025-00078

U.S. Patent No. 12,171,916

**DECLARATION OF GARY D. FLETCHER, PH.D. IN SUPPORT OF
PETITION FOR POST GRANT REVIEW OF U.S. PATENT NO. 12,171,916**

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EXHIBIT LIST

Exhibit	Reference
1001	U.S. Patent No. 12,171,916 (“’916 Patent”)
1002	File History of the ’916 Patent
1004	U.S. Patent No. 4,898,675 (“Lavender”)
1005	U.S. Patent No. 7,072,769 (“Fletcher-Haynes”)
1006	U.S. Publication No. 2002/0033370 (“Bainbridge”)
1007	U.S. Patent No. 10,195,319 (“Kimura”)
1008	U.S. Patent No. 6,743,192 (“Sakota”)
1009	“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.
1010	Curriculum Vitae (“CV”) of Dr. Gary D. Fletcher
1011	Bruce C. McLeod, MD, et al., “Apheresis: Principles and Practice,” 3rd Edition, AABB Press 2010.
1012	Japanese Patent Publication No. JP 2002-282352 A and certified Japanese to English translation (“Takagi”)
1013	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

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Terumo BCT, the “Petitioner,” requests post grant review of claims 1-22 of U.S. Patent No. 12,171,916 (the “’916 Patent”) (EX1001).

I. INTRODUCTION

1. I, Dr. Gary D. Fletcher, Ph.D., of Media, Pennsylvania, declare that:
2. I have been retained as a technical expert by counsel on behalf of Terumo BCT, Inc. (“Petitioner”). I understand that Petitioner is requesting that the Patent Trial and Appeal Board institute a post grant review (“PGR”) proceeding of U.S. Patent No. 12,171,916 (“the ’916 patent,” EX. 1001).
3. I have been asked by Petitioner’s counsel (“Counsel”) to provide my independent analysis and consideration of whether certain references teach or suggest the features recited in claims 1–22 (the “challenged claims”) of the ’916 patent. My opinions and the bases for my opinions are set forth below. My opinions are based on my education and experience.
4. In writing this Declaration, I have considered the following: my own knowledge and experience, including my teaching and work experience in the fields of blood sample collection and analysis, plasma apheresis equipment, and related technology; and my experience of working with others involved in those fields.
5. I am not, and never have been, an employee of Petitioner. I have no financial interest in either party or in the outcome of this proceeding. I am being

compensated for my work as an expert on an hourly basis, for all tasks involved. My compensation is not dependent on the outcome of these proceedings or on the content of my opinions. I will not receive any added compensation based on the outcome of any PGR, *inter partes* review, or other proceeding involving the '916 patent.

II. QUALIFICATIONS

6. My qualifications for forming the opinions in this report are summarized here and explained in more detail in my curriculum vitae (“CV”), which is provided as EX1010 appended hereto.

7. As detailed in my CV, I have extensive experience in the design, development, and manufacture of medical devices including blood processing technologies, with a career spanning over 30 years in this field. I have specific expertise in the design and development of blood fractionation technologies and have a sound understanding of the relevant technology and techniques used to separate plasma from a donor’s blood.

8. I am Founder and Principal Consultant at RnDDx Solutions LLC, a consulting firm founded in 2015, focused on industrial mechanical engineering, and research and product development, in medical devices, blood separation devices, point-of-care blood sample testing, diagnostics, optical devices, and on providing expert witness services, e.g., for patent litigation, including subject matter expertise

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in medical device engineering, and subject matter expertise in medical devices for blood collection and blood sample processing for diagnostics and therapeutics. I have particular expertise in mechanical engineering design and development of blood collection and stabilization systems, blood separation, and blood and cell preparation for both diagnostic and therapeutic applications. I have expertise in the development of blood separation devices, and have served as a consultant advisor to medical device companies developing blood separation devices. A complete list of my patents, publications, professional activities, and honors that I have received is set forth in my curriculum vitae, attached hereto as EX1010.

9. I am also co-Founder of a startup biotech company, Raven Biomaterials, developing novel patented immunomagnetic blood cell separation technology, with both diagnostic and cell therapy manufacturing applications.

10. I received my Bachelor of Arts in Physics and Mathematics from DePauw University, Greencastle, Indiana, in 1976, my Master of Philosophy degree in Physics from Yale University in 1978, and my Doctor of Philosophy degree in Physics, also from Yale University, in 1983. My doctoral research was in experimental atomic physics, where I gained experience in mechanical, electrical, and software engineering, optical physics, and vacuum engineering, developing and maintaining the experimental apparatus used in my research. I conducted

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postdoctoral research in experimental atomic and laser physics as a Postdoctoral Research Associate in Physics and Assistant Professor of Physics at the University of Virginia. At Lawrence Livermore National Laboratory I expanded my expertise in mechanical and optical engineering by developing x-ray spectroscopic and imaging instruments to measure x-rays emitted from laser-produced high-temperature plasmas. I have 23 years of senior industrial executive experience building new products and new businesses in the healthcare, life sciences, material sciences, medical device, imaging, and diagnostics spaces. That experience includes leading R&D and product development engineering teams of mechanical, electrical, optical, and software engineers. Among the positions described in my curriculum vitae, my industry experience includes engineering leadership role in 1996 in a company attempting to develop a noninvasive glucose measurement sensor. From 1996 to 2001, I led Engineering and Advanced Technology, including teams of optical, mechanical, electrical, software imaging, and clinical laboratory engineers, developing a noninvasive human complete blood count diagnostic device and diagnostic blood perfusion assessment tool, for a medical diagnostic startup company. As technical manager at Sarnoff Corporation from 2001 – 2004 I led a team developing and licensing a painless minimally invasive blood glucose monitor.

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11. As an R&D director at Becton Dickinson (“BD”) from 2004 to 2014, I developed blood collection and blood separation devices for diagnostic testing. I led a 5-member technology development group executing technology strategy to support medical device blood specimen collection and preservation business. I led research and development resolving manufacturing problems in core plastic blood collection products, and initiated a technology development stage-gate process to reduce technology risk in new product development. I also completed a “deep dive” technology assessment in blood fractionation technologies, leveraging and contacting academic experts in materials and fluidics, and led development effort assessing primary blood separation technologies. I also led product development in new business spaces, including the point of care blood collection and diagnostic testing space.

12. I have experience with the U.S. Patent system. I am co-inventor on fifteen issued U.S. Patents and ten issued European patents for devices and methods in the area of blood collection and processing including lancing devices and blood separation for diagnostic testing. A complete list of my patents is set forth in my curriculum vitae, attached hereto as EX1010.

13. Based on my experience and education, I believe that I am qualified to opine as to the knowledge and level of skill of one of ordinary skill in the art

(“POSITA”; refer to §VI, below) at the time of the alleged invention of the ’916 Patent and what such a person would have understood at that time, and the state of the art during that time. Based on my experiences, I understand and know of the capabilities of persons of ordinary skill in this field during the mid-2010s to the early 2020s and specifically during the time before the time of the alleged invention of the ’916 Patent. Indeed, I worked closely with many such persons in the medical device and blood processing field during that time frame.

III. MATERIALS AND OTHER INFORMATION CONSIDERED

14. All of the opinions contained in this declaration are based on the documents I have reviewed and my professional judgment, as well as my education, experience, and professional knowledge. I am not an attorney and I am not offering any legal opinions in this declaration.

15. In forming the opinions expressed in this declaration, I relied upon my education, knowledge, and experience in the relevant field of the art, and have considered the viewpoint of a POSITA as of May 30, 2017, which I have been informed is the earliest effective filing date of the claims for purposes of this analysis. I have considered the materials referenced herein, including the ’916 Patent (EX1001), the prosecution history (EX1002) of the ’916 Patent, and the following materials:

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- U.S. Patent No. 4,898,675 to Lavender (“Lavender,” EX1004);
- U.S. Patent No. 7,072,769 to Fletcher-Haynes *et al.* (“Fletcher-Haynes,” EX1005);
- U.S. Publication No. 2002/0033370 (“Bainbridge,” EX1006);
- U.S. Patent No. 10,195,319 (“Kimura,” EX1007);
- U.S. Patent No. 6,743,192 (“Sakota,” EX1008);
- “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. (EX1009)
- Bruce C. McLeod, MD, et al., “Apheresis: Principles and Practice,” 3rd Edition, AABB Press 2010. (EX1013)
- Japanese Patent Publication No. JP 2002-282352 A and English translation (“Takagi,” EX1014)
- In: 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>
(EX1015)

16. I have considered these materials through the lens of a POSITA, which is discussed further in §§V and VI (below) related to the '916 Patent as of the effective filing date, and I have done so during my review of these materials.

IV. SUMMARY OF MY OPINIONS

17. This Declaration explains the conclusions that I have formed based on my knowledge and experience and my review of the references (prior art) listed above. To summarize, I have concluded that:

- Claims 7-8, 14, and 16-21 are anticipated and/or obvious by Fletcher-Haynes alone;
- Claims 1-2, 5, 7-8, 10-12, and 14-22 are obvious over Fletcher-Haynes in view of Kimura and further in view of Lavender;
- Claims 3-4 are obvious over Fletcher-Haynes in view of Bainbridge and further in view of Lavender;
- Claims 6, 9 are obvious over Fletcher-Haynes in view of Bainbridge and further in view of Kimura;
- Claim 13 is obvious over Fletcher-Haynes in view of Bainbridge and further in view of Sakota; and
- Claims 1-4, 6-7, 10-21 lack an adequate written description.

V. LEGAL PRINCIPLES

18. In forming my analysis and conclusions expressed in this declaration, I have applied the legal principles described in the following paragraphs, which were provided to me by Terumo's counsel.

Claim Construction

19. I understand that a claim must be construed under the *Phillips* standard. Under that standard, words of a claim are given their plain and ordinary meaning as understood by a POSITA at the time of invention, in light of the specification and prosecution history, unless those sources show an intent to depart from such meaning, as well as pertinent evidence extrinsic to the patent. For purposes of this declaration, I applied the plain and ordinary meaning of each term as would have been understood by a person of ordinary skill in art at the time of the alleged invention unless explicitly stated otherwise.

B. Anticipation

20. I understand that a patent claim is invalid if it is anticipated by a single item of prior art. I understand that an anticipation analysis involves two steps. First, the patent claims are construed to ascertain their scope. Second, each construed asserted claim is compared to the prior art reference on an element-by-element basis.

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If the prior art reference discloses or contains each and every element of the claimed invention, either expressly or inherently, then it anticipates the claim.

21. I understand that anticipation by inherent disclosure is appropriate only when a prior art reference necessarily includes or discloses the unstated claim element. I also understand that the discovery of a new or previously unreported or unappreciated property of a prior art composition, or of a scientific explanation for how a prior art composition operates, does not make the prior art composition patentably new to the entity or person that discovered the new property or mode of operation. I further understand that there is no requirement that a POSITA would have recognized the inherent disclosure at the time of the invention.

(a) For anticipation by a prior art publication or document, I understand that the reference's description must enable a POSITA to practice the claimed invention without undue experimentation. I further understand that the following factors may be considered to determine whether any experimentation would have been undue:

- A) The quantity of experimentation necessary;
- B) The amount of direction or guidance presented;
- C) The presence or absence of working examples;
- D) The nature of the claimed invention;

- E) The state of the prior art;
- F) The relative skill of those in the art;
- G) The predictability or unpredictability of the art; and
- H) The breadth of the claims.

C. Obviousness

22. I understand that a patent claim can be considered to have been obvious to a POSITA at the time the application was filed. This means that, even if all of the elements of a claim are not found in a single prior art reference, the claim is not patentable if the differences between the subject matter in the prior art and the subject matter in the claim would have been obvious to a person of ordinary skill in the art at the time the application was filed.

23. I further understand that a determination of whether a claim would have been obvious must consider several factors, including, among others: (i) the level of ordinary skill in the art at the time the application was filed; (ii) the scope and content of the prior art; and (iii) what differences, if any, existed between the claimed invention and the prior art.

(b) I understand that the teachings of two or more references may be combined in the same way as disclosed in the claims, if such a combination would have been obvious to a person of ordinary skill

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in the art. In determining whether a combination based on either a single reference or multiple references would have been obvious, it is appropriate to consider at least the following factors:

- a. whether the teachings of the prior art references disclose known concepts combined in familiar ways, which, when combined, would yield predictable results;
- b. whether a POSITA could implement a predictable variation, and would see the benefit of doing so;
- c. whether the claimed elements represent one of a limited number of known design choices, and would have a reasonable expectation of success by a POSITA;
- d. whether a POSITA would have recognized a reason to combine known elements in the manner described in the claim;
- e. whether there is some teaching or suggestion in the prior art to make the modification or combination of elements claimed in the patent; and

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- f. whether the innovation applies a known technique that had been used to improve a similar device or method in a similar way.

24. I understand that a POSITA has ordinary creativity and is not an automaton.

25. I understand that in considering obviousness, it is important not to determine obviousness using the benefit of hindsight derived from the patent being considered, and I have not done that in regards to my opinions expressed herein.

26. I understand that certain factors—often called “secondary considerations”—may support or rebut an assertion of obviousness of a claim. I understand that such secondary considerations include, among other things, commercial success of the alleged invention, skepticism of those having ordinary skill in the art at the time of the alleged invention, unexpected results of the alleged invention, any long-felt but unsolved need in the art that was satisfied by the alleged invention, the failure of others to make the alleged invention, praise of the alleged invention by those having ordinary skill in the art, and copying of the alleged invention by others in the field. I further understand that there must be a nexus—a connection—between any such secondary considerations and the alleged invention.

I also understand that contemporaneous and independent invention by others is a secondary consideration tending to show obviousness.

D. Patent Eligible Subject Matter

27. I understand that a patent may be obtained for inventions of any new and useful process, machine, manufacture, or composition of matter, or any new or useful improvement to a process, machine, manufacture, or composition of matter.

28. I understand that patent claims that are directed to abstract ideas are not eligible for patenting. I understand that determining whether a claim recites patent eligible subject matter is a question of law.

E. Specification Requirements

29. I understand that a patent claim is invalid if the specification fails to meet the written description requirement. I understand that for a claim to be supported by a sufficient written description, the original disclosure in the application must reasonably convey to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date.

30. I understand that to satisfy the written description requirement, the specification must describe every claim limitation such that a person of ordinary skill, reading the specification, would inherently, necessarily, or immediately envisage the claimed invention.

31. I further understand that while no particular form of disclosure is required or that the specification recite the claimed invention in the exact same words, a description that merely renders the claimed invention obvious does not satisfy the written description requirement. In other words, it not sufficient for purposes of the written description requirement that the disclosure, when combined with the knowledge in the art, would lead one to speculate as to modifications that the inventor might have envisioned, but failed to disclose.

32. Further, I understand that mere textual support for each individual claim limitations without a description of the specifically claimed combination or actual functioning of the invention that the individual claim limitations together define is not a sufficient disclosure to meet the written description requirement.

33. I understand that dependent claims are supposed to further limit the scope of the independent claims, and if they do not, they are invalid.

VI. LEVEL OF ORDINARY SKILL

34. 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.

VII. BACKGROUND ON PLASMA APHERESIS

35. The '916 patent relates to apheresis systems, specifically apparatuses and methods for plasmapheresis, which is also called plasma apheresis—the extracorporeal separation and collection of plasma from whole blood, with cellular components returned to the donor.

36. Plasmapheresis, also known as plasma exchange or therapeutic plasma exchange, has been a clinical procedure since the 1960s. EX1013, Chapter 1: Development of Apheresis Instrumentation. It selectively removes plasma and returns cellular components along with replacement fluid using centrifugation or membrane filtration. EX1015. The earliest methodologies emerged from continuous centrifugation techniques in the 1960s, evolving to membrane-based and automated extraction systems. Early systems typically required large volumes of anticoagulants, continuous supervision by trained personnel, and bulky, non-portable equipment. Over time, manufacturers have introduced increasingly sophisticated machines that automate component separation, enhance flow control, monitor patient safety, and optimize plasma yield.

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37. In therapeutic plasmapheresis, plasma containing pathogenic substances (such as autoantibodies or toxins) is removed and replaced with a substitution fluid (e.g., saline, albumin, or donor plasma). In donor plasmapheresis, the plasma itself is collected for use in transfusion or further fractionation, and the remaining blood components (e.g., red blood cells, white blood cells, platelets) are reinfused into the donor.

38. In automated plasmapheresis, whole blood is drawn from the donor, mixed at a specified ratio with anticoagulant, and then separated into anticoagulated plasma and red blood cells and other cellular components. Once a target volume of anticoagulated plasma has been collected, the withdrawal of whole blood from the donor ceases, and the red blood cells and other cellular components are returned to the donor. EX1013, Chapter 4: Current Instrumentation of Apheresis.

39. The FDA issued guidelines for registered blood collection centers as to the volume of plasma that may be collected during plasmapheresis in order to improve the consistency of procedures for manufacturing source plasma, and to minimize the opportunity for staff error. EX1009. The FDA Memo noted inconsistencies due to the various types of anticoagulant solutions used, differing concentrations of the anticoagulant, and the range of anticoagulant to plasma ratios. The FDA Memo set forth a simplified plasma volume nomogram, in which the

volume (or weight) of plasma that may be collected from a particular donor is limited to ensure donor safety and comfort. The FDA nomogram limits the volume (or weight) of plasma based on the weight of the donor, and establishes the volume of anticoagulant that may be added to a 1:16 ratio of anticoagulant to anticoagulated blood, or 0.06 parts anticoagulant to 1 part anticoagulated blood, to determine a maximum collection volume for the total of the plasma plus the anticoagulant for a particular donor. EX1009.

40. At the time the '916 patent was filed, apheresis optimization techniques were well known in the art and routinely employed to improve donor safety, maximize plasma yield, and increase procedural efficiency. Clinicians and device manufacturers commonly utilized formulas based on donor-specific parameters—such as weight, height, body mass index, sex, and hematocrit—to estimate total blood volume and determine safe and effective plasma collection volumes. EX1013, p. 52 (“Some instruments limit both dose rate and total citrate infused based on an estimate of subject blood volume calculated from sex, height, and weight,” p. 55, “Nomograms based on height, weight, and hematocrit are used to predict the consequences of volume removal [of plasma],” p. 99, “Flow rates are controlled by donor-specific data entered,” and Table 6-8 on p. 135, showing maximum plasma collection volumes based on donor sex and weight.) Plasmapheresis systems often

incorporated fixed anticoagulant-to-anticoagulated-blood ratios (ACRs), typically between 1:8 and 1:16, and adjusted fluid flow rates accordingly to maintain proper anticoagulation while minimizing citrate-related adverse effects. EX1013, p. 129 (Table 6-3). Furthermore, advanced plasmapheresis systems used real-time sensor feedback (e.g., pressure, volume, optical detection) to dynamically monitor draw and return cycles¹, enabling adjustments to target volumes during the procedure.² Iterative recalculations of collection targets, particularly in multi-cycle procedures, were also recognized as necessary due to progressive changes in hematocrit and plasma composition. As such, individualized plasma volume estimation, anticoagulant adjustment, and cycle-by-cycle recalibration were part of the established technical knowledge in the field prior to the filing of the '916 patent. *See, e.g.*, EX1014.

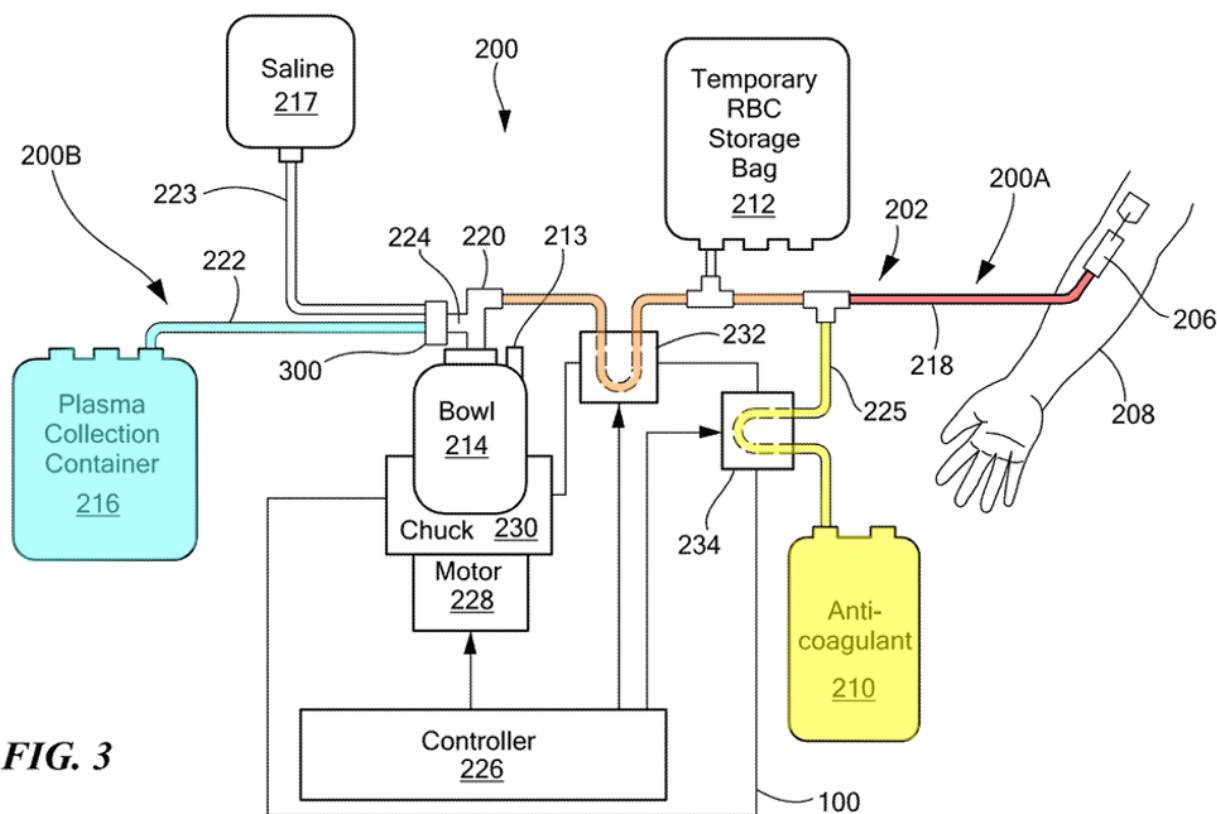
¹ *See* EX1013, p. 14, “Celltrifuge II [a blood-processing centrifuge] included an optical sensor for monitoring the collected product and automatically adjusting the pump speeds to maintain efficient separation without constant operator attention”; p. 78, “All reservoirs are monitored by electronic scales, and when specified maximum weights are reached, the instrument automatically switches from draw phase to return phase.”

² *See, e.g.*, EX1013, p. 14, “The pump flow rates—and, thereby, the component collection—are controlled by the microprocessor in response to the optical monitor.”

VIII. '916 PATENT OVERVIEW

A. The '916 Patent Relates To Plasma Apheresis

41. The '916 patent relates to a “system ... for collecting plasma” in blood apheresis systems. EX1001, Title, 1:8-9. “Apheresis is a procedure in which individual blood components,” e.g., plasma and red blood cells, “can be separated and collected from whole blood.” EX1001, 1:27-28. The '916 patent specifically relates to plasma apheresis, which is plasma collection.



EX1001, Fig. 3 (annotated).

42. Plasma apheresis involves withdrawing whole blood from a donor's arm using a venous access device 206. EX1001, 5:28-32. 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, 5:39-40, 6:28-33. Anticoagulant is introduced in fixed proportions to the whole blood drawn from the donor to prevent blood clotting in the draw line. See EX1009. "[T]he anticoagulant mixes with the plasma component" because "the osmolarity of the red blood cells prevents the anticoagulant ... from entering/remaining with the red blood cells." EX1001, 7:58-61.

43. The mixture (orange) of anticoagulant and "withdrawn whole blood ... enters a blood component separation device," *e.g.*, centrifuge bowl 214, which "separates the whole blood into its constituent components," *e.g.*, "plasma, platelets, red blood cells ("RBCs") ... [and] white blood cells." EX1001, 4:67-5:8, 6:53-60. The donor's plasma, *i.e.*, pure plasma, along with anticoagulant introduced during the collection process, exits the blood component separation device and is collected and stored in a collection container (*e.g.*, a bag, shown in blue above). EX1001, 2:3-10, 5:28-33. The anticoagulant and pure plasma combination is known as anticoagulated plasma or plasma product. EX1001, 10:5-6.

44. The FDA established guidelines regarding how much plasma any individual donor is able to donate. See EX1009 These guidelines consider donor parameters, like weight, hematocrit, and sex. *See* EX1009.

B. Purported Invention of the '916 Patent

45. The '916 patent purports to solve problems associated with “determin[ing] the total volume of plasma that has been collected” from a donor after the withdrawn whole blood is mixed with anticoagulant by considering a donor’s hematocrit level and the amount of anticoagulant added into the system. EX1001, 1:53-59, 1:63-2:21, 4:23-33.

46. Each donor has a different hematocrit level, which affects the amount of plasma in the donor’s whole blood. EX1001, 8:3-4. The differing hematocrit levels also affect the amount of anticoagulant volume in a plasma collection bag (“anticoagulant volume”). EX1001, 8:4-13. The '916 patent discusses three main volumes—target plasma collection volume, anticoagulant volume, and the total volume of plasma that has been collected.

47. With respect to 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, 2:52-53.

48. The technician begins collecting plasma after calculating the target plasma volume. EX1001, 6:23-33. Once the procedure starts, a technician can use an equation to calculate 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 plasma container. EX1001, 8:25-61.

49. 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, 8:25-61. Anticoagulated whole blood is extracted blood mixed with anticoagulant.

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

50. Alternatively, the technician can determine, without considering a donor's hematocrit, the amount of anticoagulant added to the system by using a "predetermined ratio of anticoagulant per unit anticoagulated whole blood," by monitoring "the number of rotations of the anticoagulant pump" introducing anticoagulant into this system, "and/or based on the change in weight of the anticoagulant container 210." EX1001, 8:45-61.

51. The '916 patent discloses that the controller also monitors the collection container's weight using a weight sensor and uses weight to determine the total volume of liquid in the collection container. EX1001, 7:30-32, 7:65-8:2. The controller uses the total volume of liquid in the collection container to calculate the volume of anticoagulant and pure plasma in the collection container. EX1001, 8:17-9:55. The '916 patent first calculates the anticoagulant volume. EX1001, 8:62-9:12. It then calculates the volume of pure plasma in the collection container by subtracting the anticoagulant volume from the total volume of liquid in the collection container. EX1001, 8:62-9:12.

52. The '916 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 collection container," e.g., the volume set by FDA regulation. EX1001, 9:4-12. When a target volume of pure plasma is collected, then the controller "stops the draw of whole blood from the subject and reverses the direction of the blood ... to draw the RBCs (and other components)" from the blood component separation device back to the donor. EX1001, 9:19-23.

IX. PRIOR ART OVERVIEW

A. Fletcher-Haynes

53. Fletcher-Haynes discloses a blood collection system that maximizes blood component yield by maximizing at least one process parameter, based on either a target yield or a fixed procedure time. EX1005, Abstract. Fletcher-Haynes recognized the need to determine 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.

54. 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.

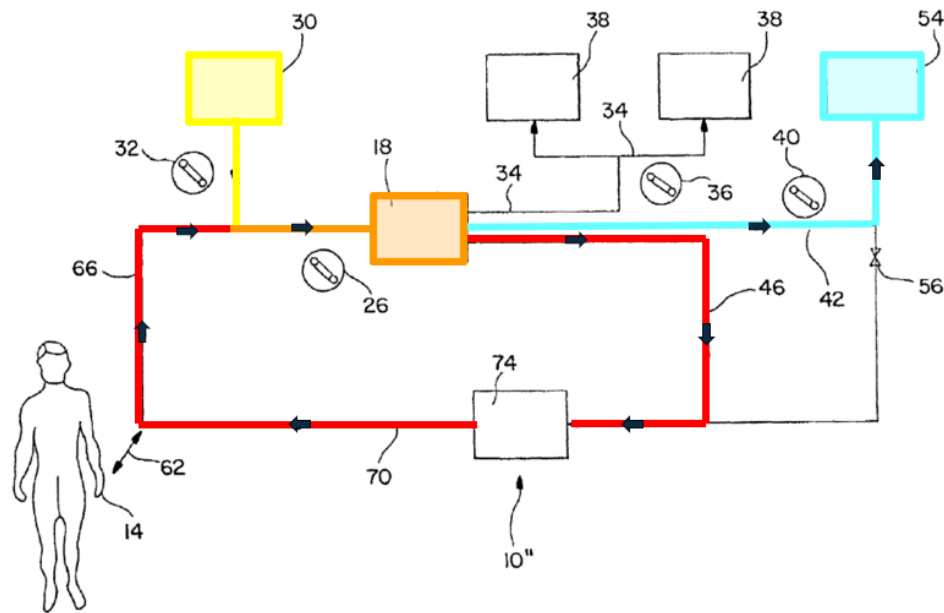


Figure 7B

EX1005, Fig. 7B (annotated).

55. Assembly 10'' operates according to a collection procedure derived from procedure goal(s) and may include maximizing "at least one process control parameter." EX1005, 7:38-43, 9:35-44. This maximization is determined by inputting donor-provided data, like height, weight, and blood processing machine type in optimization and prediction models. EX1005, 49:7-18.

56. 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.

57. 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.

58. 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.

B. Lavender

59. 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.

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

62. Lavender's system performs several real time calculations during the collection process. 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 take into account the weight of the collected plasma and anticoagulant solution during the collection process. These calculations are ultimately used to calculate the volume of pure plasma and anticoagulant in the plasma collection bag in real time. EX1004, 20:55-68.

63. 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 volume of anticoagulant.

64. 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.

C. Bainbridge

65. 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].

66. 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 describes that “several advantages can be realized utilizing these

procedures for... plasma collections. Such advantages include: ...reduced time requirements for... plasma collections.” EX1006, [0304].

D. Kimura

67. 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 identifies the current draw cycle as the final one, it stops drawing blood and initiates the final blood return step. EX1007, Fig. 4, 16:6-7.

68. 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 amount of anticoagulant introduced during the

priming step versus the draw and return cycles, Kimura can maintain constant the “selected ratio of” anticoagulant. EX1007, claim 4.

E. Sakota

69. 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.

70. 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.

X. DETAILED IDENTIFICATION HOW ALL CLAIMS OF THE '916 PATENT ARE UNPATENTABLE

71. The sections below, explain my reasoning why all claims of the '916 patent are unpatentable.

A. Ground I: Fletcher-Haynes anticipates or renders obvious claims 7-8, 14, 16-21.

1. Claim 7

i. 7[preamble] A system for collecting plasma, comprising:

72. 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.

ii. 7[a] a venipuncture needle configured to draw whole blood from a donor;

73. 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. Figs. 7A-7B.

iii. 7[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;

74. Fletcher-Haynes discloses a blood separator (*e.g.*, a blood component collection device 18) which is 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.

75. 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.

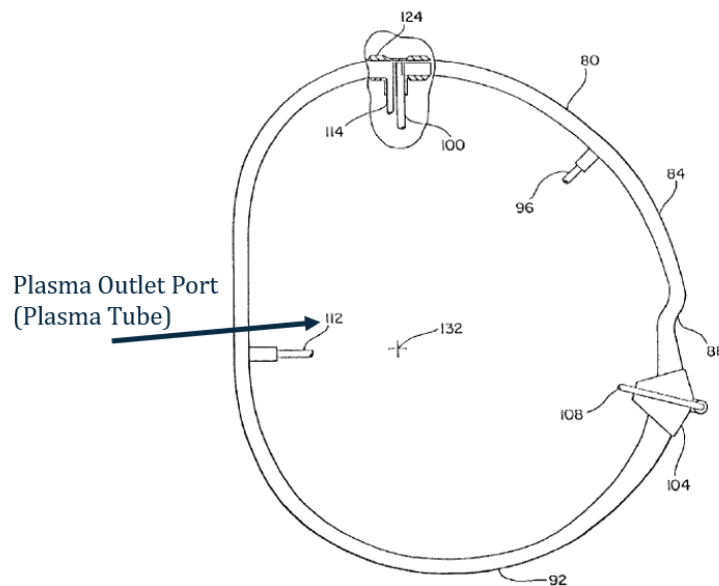


Figure 8B

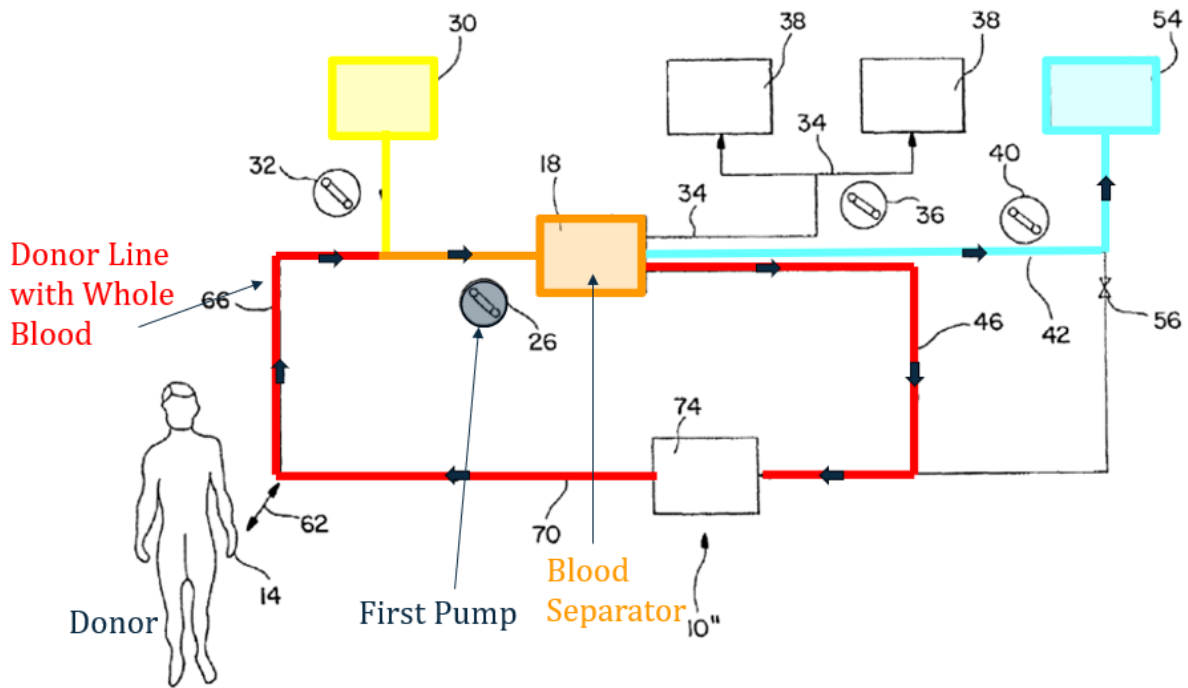


Figure 7B

77. 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.

- iv. **7[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;**

78. 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.

- v. **7[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;**

79. 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.

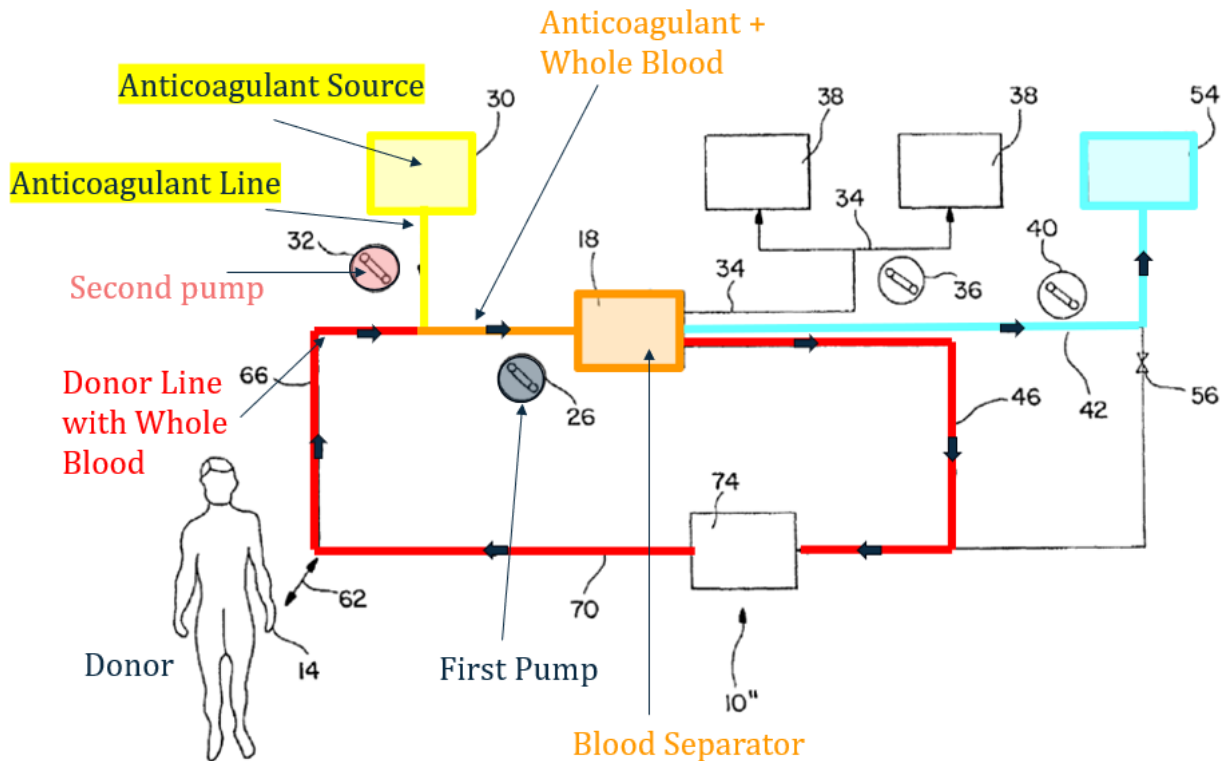


Figure 7B

- vi. **7[e] a touchscreen configured to receive input from an operator; and**

80. 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.

- vii. **7[f] a controller programmed to control operation of the system,**

81. Fletcher-Haynes discloses a controller (e.g., “the internal control of a blood component collection device 18”) that is 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.

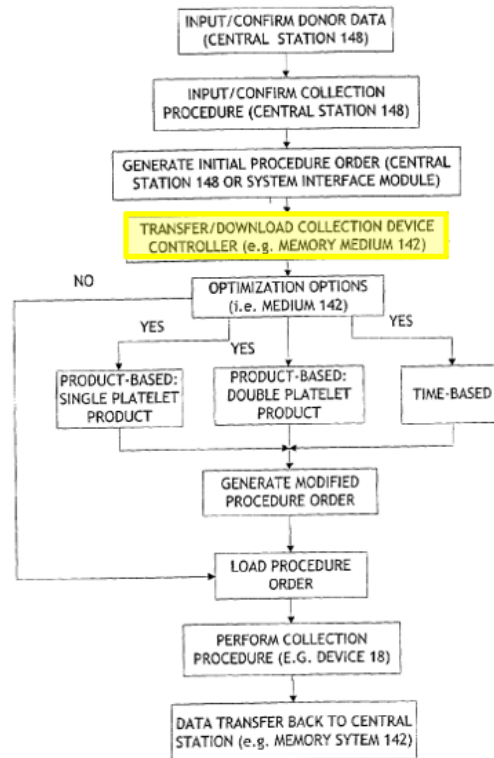


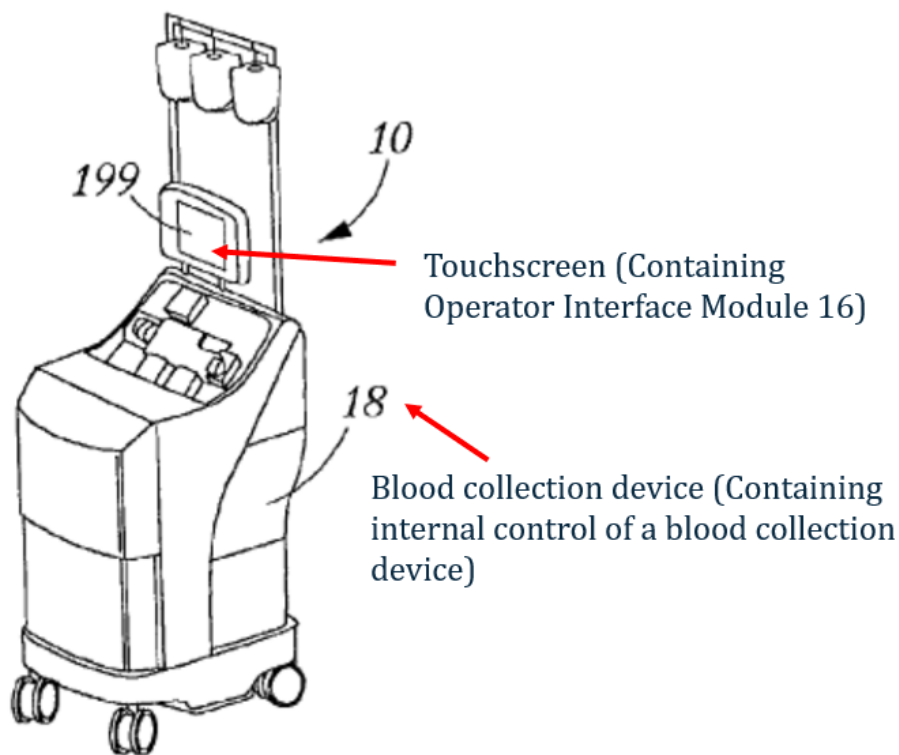
Figure 9A

EX1005, Fig. 9A (annotated).

viii. 7[g] the controller coupled to the touchscreen and programmed to receive at least a donor’s weight and hematocrit,

82. 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. 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 the donor’s weight and hematocrit. EX1005, Fig. 9A, 8:24-34.



EX1005, Fig. 1A (annotated).

- ix. 7[h] 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.**

83. 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 and controlled by the "internal control of a blood component collection device 18." EX1005, Fig. 9A, 53:17-18.

84. Fletcher-Haynes' "internal control of a blood component separation device" performs draw and return steps 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 7[a], 7[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, 45:24-39. 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 steps are distinct phases. EX1005, Fig. 7B, 46:10-15. Thus, Fletcher-Haynes anticipates limitation 7[h].

85. To the extent Patent Owner interprets that repeated draw and return phases are required by claim limitation 7[h], which is not required based on the plain and ordinary meaning of the claim. In my opinion it would have been obvious to a POSITA to perform repeated draw and return phases in a centrifugal, single-needle system like that of Fletcher-Haynes because current apheresis instruments already provided such capabilities; "uses intermittent flow via a single needle. In the draw cycle, anticoagulated whole blood is pumped into a blow-molded bowl from which separated plasma emerges and is directed into a plasma/air bag (Fig 4-25). When the cell-plasma interface is detected by an optical sensor, the return cycle is initiated. The blood pump is reversed and red cells from the bowl are directed to a collection bag while an appropriate volume of saline replacement is pumped back to the donor by a separate pump. Draw/return cycles continue until the targeted volumes of

plasma and red cells are collected, after which any residual plasma and red cells are returned to the donor.” EX1013, p91-92. EX1005, Fig. 7B, 46:16-28. Additionally, in my opinion, 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.

86. Additionally, repeated draw and return phases would have been obvious in view of Fletcher-Haynes and Bainbridge, as discussed in Ground II, below.

2. Claim 8

- i. **The system of claim 7, wherein the controller is further programmed to account for anticoagulant introduced into the plasma collection container separately from the plasma product.**

87. 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.³

3. Claim 14

i. 14[preamble] A system for collecting plasma, comprising:

88. *See* §X.A.1.i (limitation 7[preamble]).

ii. 14[a] a venipuncture needle configured to draw whole blood from a donor;

89. *See* §X.A.1.ii (limitation 7[a]).

iii. 14[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;

90. *See* §X.A.1.iii (limitation 7[b]).

³ I understand it is possible that Patent Owner could argue that this claim requires that anticoagulant be introduced into the container separate from the plasma product. That argument is illogical, however, as plasma product is a mixture of anticoagulant and pure plasma.

- iv. **14[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;**

91. See §X.A.1.iv (limitation 7[c]).

- v. **14[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;**

92. See §X.A.1.v (limitation 7[d]).

- vi. **14[e] a touchscreen configured to receive input from an operator; and**

93. See §X.A.1.vi (limitation 7[e]).

- vii. **14[f] a controller programmed to control operation of the system,**

94. See §X.A.1.vii (limitation 7[f]).

- viii. **14[g] the controller coupled to the touchscreen and programmed to receive donor parameters electronically from a control system,**

95. As I discuss in §X.A.1.viii (limitation 7[g]), Fletcher-Haynes discloses a controller coupled to the touchscreen and programmed to receive donor parameters, *e.g.*, at least a donor's weight and hematocrit.

96. Fletcher-Haynes further discloses that the controller may be *programmed* to receive these donor parameters electronically from a control system (*e.g.*, central computer database 140). Fletcher-Haynes discloses that a display

screen 331 on the control system directs an operator to enter donor parameters, *e.g.*, “gender, height, weight, [and] hematocrit ... before the system 140 may allow the operator or donation process to proceed.” EX1005, 27:30-38. Then, these values “may be transferred/downloaded onto the internal control of a blood component collection device” electronically from the control system, *e.g.*, “by a computer network system.” EX1005, 53:16-23.

ix. 14[h] to determine a target volume for plasma product and/or raw plasma based at least in part on the donor parameters and

97. Fletcher-Haynes further determines a target volume for plasma product comprising raw plasma and anticoagulant based at least in part on the donor parameters. 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 plasma product (*e.g.*, V_{SPB} , total volume in source plasma bag) and/or raw plasma (*e.g.*, V_{SP} , volume of pure plasma in the source plasma bag), using entered donor weight or hematocrit. EX1005, 48:1-3.

98. *First*, Fletcher-Haynes calculates an AC Ratio (R) using the donor’s hematocrit (H) in Equation 9.

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

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

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

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

100. **Second**, Fletcher-Haynes calculates total blood volume using a donor's weight (W), height (L), and gender in equation 10.

$$\begin{aligned} V_B &= 604 + 0.006012L^3 + 14.6W \text{ ml (male)} \\ &= 183 + 0.005835L^3 + 15.0W \text{ ml (female)} \end{aligned}$$

101. **Third**, in equation 17, reproduced below, Fletcher-Haynes provides four choices for determining a target volume of pure plasma (V_{SP}), with one choice calculated using the total blood volume V_B . The other three choices are a) no pure plasma is collected ($V_{SP} = 0$); b) a predetermined pure plasma volume constraint minus any plasma collected with platelets ($V_{CON} - V_C$); or c) specified as modified input. Note that from equation 19, f_{SP} is chosen from a range between 0.01 and 0.15, indicating that in Fletcher-Haynes the target volume of pure plasma (V_{SP}) is calculated to be between 1% and 15% of the total blood volume V_B .

$$\left\{ \begin{array}{l} V_{SP} = 0 \\ = V_{CON} - V_C \\ = f_{SP}V_B - V_C \\ = \text{specified as modified input} \end{array} \right. \geq 0$$

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

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

103. Expanding Equation 22 reveals that V_{SPB} is a sum of volume of pure plasma (V_{SP}) and volume of added anticoagulant ($V_{SP} * f_{ACP}$).

104. These values are target values because Fletcher-Haynes can run the prediction model “before the collection procedure is actually initiated.” EX1005, 53:36-38. Therefore, Fletcher-Haynes calculates a target volume for plasma product using donor weight and hematocrit.

- x. **14[i] 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.**

105. See §X.A.1.ix (limitation 7[h]).

4. Claim 16

- i. **The system of claim 14, further comprising the control system, wherein the control system is in electronic communication with the controller.**

106. 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 the blood component collection device) through “a computer network.” EX1005 53:16-19.

5. Claim 17

- i. The system of claim 16, 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.**

107. Fletcher-Haynes discloses a control system (*e.g.*, a central computer/database 140) that calculates the target volume for plasma product (*e.g.*, total volume in source plasma bag) and/or raw plasma (*e.g.*, volume of pure plasma in the plasma source 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.” EX1005, 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.

108. 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.

109. Fletcher-Haynes programs the controller on the blood component separation 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.

6. Claim 18

- i. A system of claim 14, 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.**

110. 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," such as 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 I discuss in §X.A.3.ix (limitation 14[h]), Fletcher-Haynes runs the prediction model using donor parameters to calculate a target volume for plasma product and/or raw plasma.

111. 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.

7. Claim 19

- i. The system of claim 14, wherein the donor parameters received electronically from the control system 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.**

112. As I discuss in §§X.A.1.viii, X.A.3.ix (limitations 7[g], 14[h]), Fletcher-Haynes' controller receives donor parameters that comprise a donor weight. Fletcher-Haynes further discloses that "information relating to a donor" may be 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 I discuss above in §X.A.3.ix (limitation 14[g]), the controller determines, *e.g.* calculates, the target volume for plasma product and/or raw plasma based at least in part on the donor weight. As I discuss above in §X.A.3.ix (limitation 14[g]), the controller is programmed to perform the calculations, *e.g.*, when the collection device controller is downloaded onto the internal control of the blood collection device from the control system. EX1005, Fig. 9A.

8. Claim 20

- i. The system of claim 19, wherein the donor parameters received electronically from the control system 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.**

113. As I discuss in §X.A.1.viii (limitation 7[g]), Fletcher-Haynes' controller receives donor parameters that comprise a donor hematocrit. Fletcher-Haynes further discloses that "information related to a donor" 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 I discuss above in §X.A.3.ix (limitation 14[h]), the controller determines, *e.g.* calculates, the target volume for plasma product and/or raw plasma based at least in part on the donor hematocrit.

9. Claim 21

- i. The system of claim 20, 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.**

114. As I discuss above in §X.A.3.ix (limitation 14[h]), Fletcher-Haynes determines, *e.g.*, calculates, the target volume for plasma product (V_{SPB}) comprising

raw plasma (V_{SP}) and anticoagulant ($V_{SP} * f_{ACP}$). As I discuss above in §X.A.5.i (claim 17), Fletcher-Haynes' controller is *programmed* to calculate the target volume of product plasma.

115. As I discuss above in §X.A.3.ix (limitation 14[h]), Fletcher-Haynes calculates the target volume for plasma product before withdrawing the whole blood, *e.g.*, by using a prediction model that runs before a collection procedure is initiated. Further, as discussed above in §X.A.3.ix (limitation 14[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).

B. Ground II: Fletcher-Haynes in view of Bainbridge renders obvious claims 1-2, 5, 7-8, 10-11, 14, 16-22.

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

116. 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.

117. 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 a “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.

118. One such aspect that 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” which “continue until a predetermined amount of” plasma “[has] been harvested.” EX1006, [0015], [0145]. Incorporating Bainbridge’s multiple draw and return cycles in a centrifugal apheresis system like Fletcher-Haynes’ system would have been obvious to a POSITA because performing multiple

draw and return cycles 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 have merely required a POSITA to reduce the amount of whole blood drawn per cycle. EX1006, [0016]; EX1005, 46:16-28.

119. 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, but its disclosed embodiments only show platelet bags and plasma bags. EX1005, 22:44-23:44, 61:62-62:3, Fig. 7B. In view of Fletcher-Haynes' disclosures related to red-blood-cell collection, a POSITA would have been motivated to also collect red blood cells in addition to platelets and plasma and would have turned to, and implemented, Bainbridge's red blood cell collection in Fletcher-Haynes' system. Incorporating Bainbridge's teachings would have been a routine, minor change to the Fletcher-Haynes' system that would have yielded predictable results.

120. Further, implementing Bainbridge's collection of red blood cells in "at least one RBC collection reservoir or bag" would not alter the functionality of Fletcher-Haynes 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.

121. Likewise, the incorporation of Bainbridge's real-time measurement of hematocrit 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 such as 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.

2. Claim 1

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

122. *See* §§X.A.1.i, X.A.3.i (limitations 7[preamble], 14[preamble]).

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

123. *See* §§X.A.1.ii, X.A.3.ii (limitations 7[a], 14[a]).

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;

124. *See* §§X.A.1.iii, X.A.3.iii (limitations 7[b], 14[b]).

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;

125. *See* §§X.A.1.iv, X.A.3.iv (limitations 7[c], 14[c]).

- 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;**

126. *See* §§X.A.1.v, X.A.3.v (limitations 7[d], 14[d]).

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

127. *See* §§X.A.1.vi, X.A.3.vi (limitations 7[e], 14[e]).

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

128. *See* §§X.A.1.vii, X.A.3.vii (limitations 7[f], 14[f]).

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

129. *See* §§X.A.1.viii, X.A.3.viii (limitations 7[g], 14[g]).

- ix. **1[h] to determine a target volume for plasma product and/or raw plasma,**

130. *See* §§X.A.3.viii (limitation, 14[h]).

- 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,**

131. *See* §§X.A.1.ix, X.A.3.x (limitations 7[h], 14[i]).

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

132. Fletcher-Haynes in view of Bainbridge renders obvious limitation 1[j].

133. *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].

134. *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.

135. *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 I discuss 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.

- 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.**

136. Fletcher-Haynes in view of Bainbridge renders obvious limitation 1[k].

137. *First*, Bainbridge performs repeated draw and return phases until “a predetermined amount of ... collected blood components,” *e.g.*, pure plasma, is collected and thus operates a subsequent draw and return cycle. EX1006, [0015], [0145].

138. *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]).

139. As further discussed in §X.B.1, a POSITA would have been motivated to incorporate Bainbridge's teaching of tracking the instantaneous hematocrit to use a more accurate value of hematocrit during successive applications of the prediction algorithm. A POSITA would have had a reasonable expectation of success when incorporating Bainbridge's teaching of real time hematocrit into Fletcher-Haynes' system. Therefore, Fletcher-Haynes in view of Bainbridge renders obvious limitation 1[k].

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.**

140. As I discuss above in §§X.A.3.ix, X.A.5.i (limitation 14[h], claim 17), 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.

4. Claim 5

i. The system of claim 1, wherein the user interface includes a touchscreen.

141. *See* §§X.B.2.vi., X.A.1.vi, X.A.2.vi (limitations 1[e], 7[e], 14[e]).

5. Claim 7

i. 7[preamble]

142. *See* §§X.B.2.i, X.A.1.i, X.A.3.i (limitations 1[preamble], 7[preamble], 14[preamble]).

ii. 7[a]

143. *See* §§X.B.2.ii, X.A.1.ii, X.A.3.ii (limitations 1[a], 7[a], 14[a]).

iii. 7[b]

144. *See* §§X.B.2.iii, X.A.1.iii, X.A.3.iii (limitations 1[b], 7[b], 14[b]).

iv. 7[c]

145. *See* §§X.B.2.iv, X.A.1.iv, X.A.3.iv (limitations 1[c], 7[c], 14[c]).

v. 7[d]

146. *See* §§X.B.2.v, X.A.1.v, X.A.3.v (limitations 1[d], 7[d], 14[d]).

vi. 7[e]

147. *See* §§X.B.2.vi, X.A.1.vi, X.A.3.vi (limitations 1[e], 7[e], 14[e]).

vii. 7[f]

148. *See* §§X.B.2.vii, X.A.1.vii, X.A.3.vii (limitations 1[f], 7[f], 14[f]).

viii. 7[g] the controller coupled to the touchscreen and programmed to receive at least a donor's weight and hematocrit,

149. *See* §§X.B.2.viii, X.A.1.viii, X.A.3.viii (limitations 1[g], 7[g], 14[g]).

ix. 7[h] 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.

150. 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.ix (limitation 7[h], Ground I).

151. To the extent Patent Owner interprets claim 7[h] to require repeated draw and return phases and asserts that Fletcher-Haynes does not disclose and/or render repeated phases obvious Bainbridge discloses an apheresis system that performs "removing and returning steps" that are "alternatively and repeatedly carried out during blood processing." EX1006, [0015], [0145]. As I discuss 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. Thus, the combination of Fletcher-Haynes and Bainbridge discloses this limitation.

6. Claim 8

152. *See* §X.A.2.i (claim 8).

7. Claim 10

i. 10[preamble] A system for collecting plasma, comprising:

153. *See* §§X.B.2.i, X.A.1.i, X.B.5.i, X.A.3.i (limitations 1[preamble], 7[preamble] Grounds I-II, 14[preamble]).

ii. 10[a] a venipuncture needle configured to draw whole blood from a donor;

154. *See* §§X.B.2.ii, X.A.1.ii, X.B.5.ii, X.A.3.ii (limitations 1[a], 7[a] Grounds I-II, 14[a]).

iii. 10[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;

155. *See* §§X.B.2.iii, X.A.1.iii, X.B.5.iii, X.A.3.iii (limitations 1[b], 7[b] Grounds I-II, 14[b]).

- iv. **10[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;**

156. *See* §§X.B.2.iv, X.A.1.iv, X.B.5.iv, X.A.3.iv (limitations 1[c], 7[c] Grounds I-II, 14[c]).

- v. **10[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;**

157. *See* §§X.B.2.v, X.A.1.v, X.B.5.v, X.A.3.v (limitations 1[d], 7[d] Grounds I-II, 14[d]).

- vi. **10[e] a touchscreen configured to receive input from an operator; and**

158. *See* §§X.B.2.vi, X.A.1.vi, X.B.5.vi, X.A.3.vi (limitations 1[e], 7[e] Grounds I-II, 14[e]).

- vii. **10[f] a controller programmed to control operation of the system,**

159. *See* §§X.B.2.vii, X.A.1.vii, X.B.5.vii, X.A.3.vii (limitations 1[f], 7[f] Grounds I-II, 14[f]).

- viii. **10[g] the controller coupled to the touchscreen and programmed to receive at least a donor's weight and hematocrit and**

160. *See* §§X.B.2.viii, X.A.1.viii, X.B.5.viii, X.A.3.viii (limitations 1[g], 7[g] Grounds I-II, 14[g]).

ix. 10[h] to determine a target volume for plasma product comprising raw plasma and anticoagulant,

161. Fletcher-Haynes further determines a target volume for plasma product comprising raw plasma and anticoagulant. 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 plasma product (*e.g.*, V_{SPB} , total volume in source plasma bag) and/or raw plasma (*e.g.*, V_{SP} , volume of pure plasma in the source plasma bag), using entered donor weight or hematocrit. EX1005, 48:1-3.

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

$$R = 1 + \frac{2.51}{H} \text{ (low), or } R = 1.33 \left(1 + \frac{2.51}{H}\right) \text{ (medium), or } R = 1.67 \left(1 + \frac{2.51}{H}\right) \text{ (high)}$$

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

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

164. **Second**, Fletcher-Haynes calculates total blood volume using a donor's weight (W), height (L), and gender in equation 10.

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

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

165. **Third**, in equation 17, Fletcher-Haynes calculates a target volume of pure plasma (V_{SP}) using the total blood volume.

$$\left\{ \begin{array}{l} V_{SP} = 0 \\ = V_{CON} - V_C \\ = f_{SP}V_B - V_C \\ = \text{specified as modified input} \end{array} \right. \geq 0$$

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

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

167. Expanding Equation 22 reveals that V_{SPB} is a sum of volume of pure plasma (V_{SP}) and volume of added anticoagulant ($V_{SP} * f_{ACP}$).

168. These values are target values because Fletcher-Haynes can run the prediction model “before the collection procedure is actually initiated.” EX1005, 53:36-38. Therefore, Fletcher-Haynes calculates a target volume for plasma product using donor weight and hematocrit.

- x. **10[i] 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,**

169. As I discuss in §X.B.7.ix (limitation 10[h]), Fletcher-Haynes determines a target volume for plasma product (*e.g.*, V_{SPB}) before withdrawing the donor's whole blood (*e.g.*, “before the collection procedure is actually initiated.”). As shown in §X.A.7.ix (limitation 10[h]), the target volume for plasma product (*e.g.*, V_{SPB} in equation 22) is based at least in part on an anticoagulant ratio (*e.g.*, R which is used to calculate the value of f_{ACP} in equation 15 and later used in equation 22), the donor's weight (*e.g.*, W in equation 10 used to calculate V_B), and the donor's hematocrit (*e.g.*, H used to calculate R in equation 9 and f_{ACP} in equation 15) because a change in one variable (*e.g.*, R , W , and H) would change the target volume for plasma product.

- xi. **10[j] 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.**

170. As I discuss in §§X.A.1.ix, X.B.5.ix (limitation 7[h], 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 I discuss above in §X.A.1.ix (limitation 7[h], 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.

8. Claim 11

- i. The system of claim 10, wherein the controller is configured to receive the donor’s weight and hematocrit electronically.**

171. In Fletcher-Haynes, “data entry” occurs at “respective interfaces” which include “touchscreen input/output devices 199.” EX1005, 10:12-15. As I discuss above in §X.A.1.vi (limitation 7[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 including weight and hematocrit. 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.

9. Claim 12

- i. The system of claim 10, 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.**

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

173. Bainbridge teaches that Fletcher-Haynes' controller may be programmed to control the plasma apheresis system until the plasma product in the plasma product collection container reaches the determined target volume. 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 is the target value of raw plasma (*e.g.*, V_{SP}) or plasma product (*e.g.*, V_{SPB}) calculated by Fletcher-Haynes' prediction model. Fletcher-Haynes' system "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. Therefore, Fletcher-Haynes in view of Bainbridge renders obvious repeating draw and return phases until the plasma product in the plasma product collection container reaches the determined target volume.

10. Claim 14

i. 14[preamble]

174. *See* §§X.B.2.i, X.A.1.i, X.B.5.i, X.B.7.i, X.A.3.i (limitations 1[preamble], 7[preamble] Grounds I-II, 10[preamble], 14[preamble] Ground I).

ii. 14[a]

175. *See* §§X.B.2.ii, X.A.1.ii, X.B.5.ii, X.B.7.ii, X.A.3.ii (limitations 1[a], 7[a] Grounds I-II, 10[a], 14[a] Ground I).

iii. 14[b]

176. *See* §§X.B.2.iii, X.A.1.iii, X.B.5.iii, X.B.7.iii, X.A.3.iii (limitations 1[b], 7[b] Grounds I-II, 10[a], 14[b] Ground I).

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iv. 14[c]

177. *See* §§X.B.2.iv, X.A.1.iv, X.B.5.iv, X.B.7.iv, X.A.3.iv (limitations 1[c], 7[c] Grounds I-II, 10[c], 14[c] Ground I).

v. 14[d]

178. *See* §§X.B.2.v, X.A.1.v, X.B.5.v, X.B.7.v, X.A.3.v (limitations 1[d], 7[d] Grounds I-II, 10[d], 14[d] Ground I).

vi. 14[e]

179. *See* §§X.B.2.vi, X.A.1.vi, X.B.5.vi, X.B.7.vi, X.A.3.vi (limitations 1[e], 7[e] Grounds I-II, 10[e], 14[e] Ground I).

vii. 14[f]

180. *See* §§ X.B.2.vii, X.A.1.vii, X.B.5.vii, X.B.7.vii, X.A.3.vii (limitations 1[f], 7[f] Grounds I-II, 10[f], 14[f] Ground I).

viii. 14[g]

181. *See* §X.A.3.viii (limitation 14[g], Ground I).

ix. 14[h]

182. *See* §X.A.3.ix (limitation 14[h], Ground I).

- x. **14[i] 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.**

183. As I discuss in §X.B.5.ix (limitation 7[h], Ground 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 I discuss above in §X.B.5.ix (limitation 7[h], Ground II), a POSITA would have been motivated to program Fletcher-Haynes’ controller to operate a plurality of draw and return phases as disclosed in Bainbridge.

11. Claim 15

- i. **The system of claim 14, 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.**

184. As I discuss above in §X.B.9.i (claim 12), 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 value of raw plasma

(*e.g.*, V_{SP}) or plasma product (*e.g.*, V_{SPB}) calculated by Fletcher-Haynes' prediction model.

12. Claim 16

185. *See* §X.A.4.i (claim 16, Ground I).

13. Claim 17

186. *See* §X.A.5.i (claim 17, Ground I).

14. Claim 18

187. *See* §X.A.6.i (claim 18, Ground I).

15. Claim 19

188. *See* §X.A.7.i (claim 19, Ground I).

16. Claim 20

189. *See* §X.A.8.i (claim 20, Ground I).

17. Claim 21

190. *See* §X.A.9.i (claim 21, Ground I).

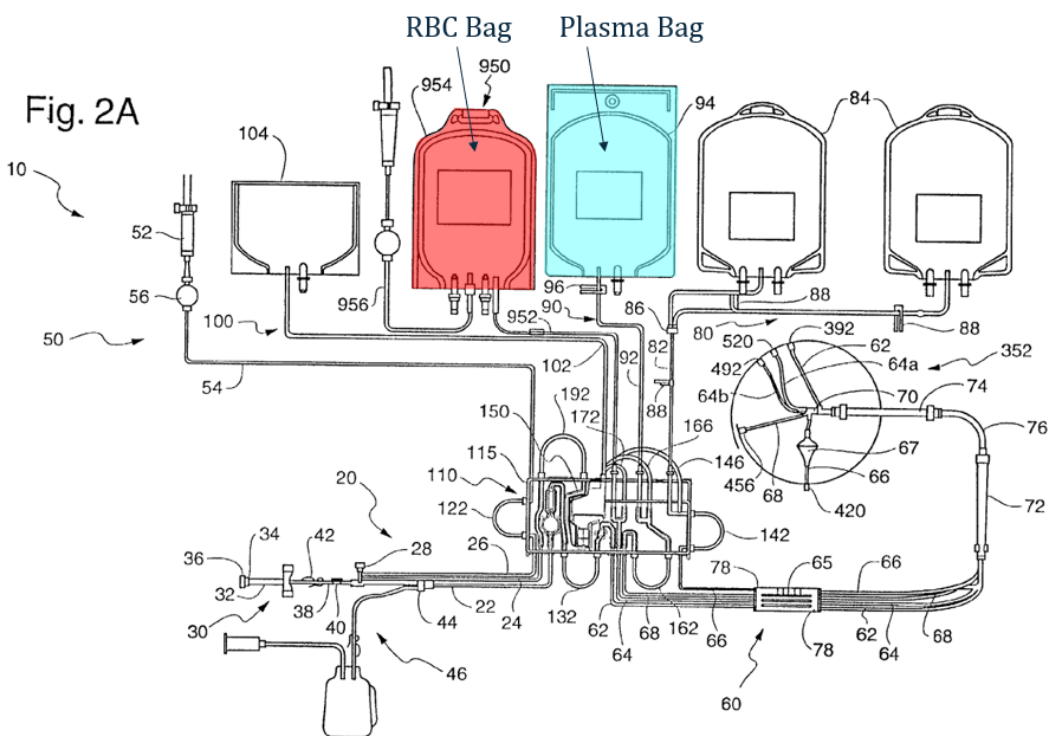
18. Claim 22

- i. The system of claim 14, further comprising a reservoir separate from the blood separator for receiving concentrated red blood cells.**

191. 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.

192. 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). EX1006, [0101], [0103], Fig. 2A.



193. As I discuss above in §X.B.1, it would have been obvious to a POSITA to incorporate the RBC tubing assembly as taught by Bainbridge into the blood

component separation system taught by Fletcher-Haynes, and a POSITA would have had a reasonable expectation of success when doing so.

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

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

194. As I discuss above in §X.B.1 (Ground II), a POSITA would have been motivated to modify the Fletcher-Haynes system in view of the teachings of Bainbridge. A POSITA would have further been motivated to modify the Fletcher-Haynes/Bainbridge system with Lavender and 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.

195. 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 procedures to improve the collection of blood components, resulting in “an easier, safer, and more economical method of harvesting plasma.” EX1004, 1:11-13, 1:20-26, 11:23-26.

196. 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 implement Fletcher-Haynes' procedure tracking. EX1004, cols. 41-44.

197. 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 $R = \frac{(Q_B + Q_C)}{Q_C} = \frac{Q_B}{Q_C} + 1$, so that $\frac{Q_B}{Q_C} = R - 1$. Lavender's equation TABLE VI, 2.a states that $\frac{Q_P}{Q_B} = 1 - HCTD$. Hence a POSITA would understand from Lavender's equation 2.b. that $CF = \frac{Q_C}{Q_P} = \frac{Q_C}{Q_B} *$

$\frac{QB}{QP} = \frac{1}{(R-1)} * \frac{1}{(1-HCTD)}$ or $CF = [(R - 1) * (1 - HCTD)]^{-1}$, 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.

198. 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 similar equations to improve similar systems and methods in the same way.

1. 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.**

199. Fletcher-Haynes, in view of Bainbridge and Lavender renders obvious the additional requirements of claim 3. As I discuss in §§X.A.1.ix, X.B.5.ix (limitation 7[h]), Fletcher-Haynes and Bainbridge operate a plasma apheresis procedure that performs draw and return phases.

200. Lavender collects plasma until a target volume of raw plasma is collected, e.g., until $TPF = MAXPF$. EX1004, Table VI, §5C. 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.

201. 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.

202. The Fletcher-Haynes/Bainbridge system, as modified by Lavender, renders obvious that the target volume for plasma product or raw plasma is determined prior to the start of each draw phase. As I discuss 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.

2. Claim 4

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

203. 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.

D. Ground IV: Fletcher-Haynes in view of Bainbridge and Further in view of Kimura

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

204. A POSITA would have found it obvious and would have been motivated to combine Fletcher-Haynes’ system, as modified by Bainbridge, with the teachings of Kimura 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.

205. Like Fletcher-Haynes and Bainbridge, Kimura relates to multiple product collections which include plasma. 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, is further directed to using donor-specific procedures 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.

206. Fletcher-Haynes’ system calculates an amount of anticoagulant in the plasma component using an AC ratio. EX1005, Eqs. 15, 17. 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 priming stages have a higher AC ratio than that 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 determine a more accurate collection volume of dilute plasma.

207. Fletcher-Haynes and Bainbridge perform return steps but do not explicitly disclose when the blood return occurs once the target volume is reached. EX1006, [0015]. Kimura discloses that a final blood returning step occurs once it is determined that it is the last cycle. EX1007, Fig. 4. A POSITA would have been motivated to perform a final return step in the last cycle as taught by Kimura, rather than stop the plasma apheresis system outright after reaching a target volume of pure plasma to minimize the blood loss of the donor. 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.

1. Claim 6

- 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.**

208. 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 returned cycles until a “predetermined amount of a first blood component,” *e.g.*, plasma, “is separated” and collected. 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 I discuss 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.

2. Claim 9

- i. **The system of claim 8, 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.**

209. 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 I discuss in §X.D.1, a POSITA designing the Fletcher-Haynes/Bainbridge plasma apheresis system would have

turned to Kimura's to account for anticoagulant introduced in a priming step and would have had a reasonable expectation of success when incorporating Kimura's teaching into Fletcher-Haynes' system. 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.

E. Ground V: Fletcher Haynes in View of Bainbridge and Further in view of Sakota

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

210. As I discuss 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 refer to Sakota to supply the teachings of determining how much blood to withdraw per cycle.

211. *First*, Fletcher-Haynes, Bainbridge, and Sakota are analogous pieces of art. For example, 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.

212. **Second**, Sakota teaches how much blood should be drawn 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 extra corporeal blood circulation will be decreased and thus the danger of causing anemia or dizziness will be minimized.” EX1008, 2:11-15, 4:17-23.

213. **Third**, 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. Accordingly, a POSITA would understand that there is expectation of success when the Fletcher-Haynes/Bainbridge system is further modified with Sakota—each relate to the same well-known technologies and both apply substantially similar techniques to achieve similar results.

1. Claim 13

- i. The system of claim 10, 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.**

214. Fletcher-Haynes in view of Bainbridge and in further view of Sakota renders obvious the additional requirements of claim 14.

215. Sakota performs draw and return cycles “successively ... three to five times.” EX1008, 2:11-15. As I discuss in §X.E.1 (Ground V), it would have been obvious to a POSITA to program Fletcher-Haynes’ controller to perform at least three draw and return cycles, as taught by Bainbridge, and a POSITA would have had a reasonable expectation of success operating Fletcher-Haynes’ system using a plurality of draw and return cycles.

216. Sakota further discloses that a volume of whole blood to be drawn in a final draw phase may be different than a volume drawn in a prior draw phase. Sakota teaches draw and return cycles with “decrease in the process volume of whole blood per cycle.” EX1008, 4:17-18. As described above in §X.E.1, a POSITA would have been motivated to design draw and return cycles with a volume of whole blood to be drawn in a final draw phase different than (less than) a volume drawn in a prior draw phase to avoid “the danger of causing anemia or dizziness” during a blood draw

procedure and would have had a reasonable expectation of success when making the proposed combination. EX1008 4:22-23.

XI. GROUND VI: LACK OF PATENT ELIGIBLE SUBJECT MATTER

217. Because patent eligibility is a question of law, I do not provide any opinions on patent eligibility. I have, however, been asked to provide my opinions as a POSITA regarding issues that may underlie the question of patent eligibility. Because many of these opinions relate to the conventionality of equipment, systems, and methods discussed in the '916 Patent, these opinions are discussed in my Background on Plasma Apheresis Section.

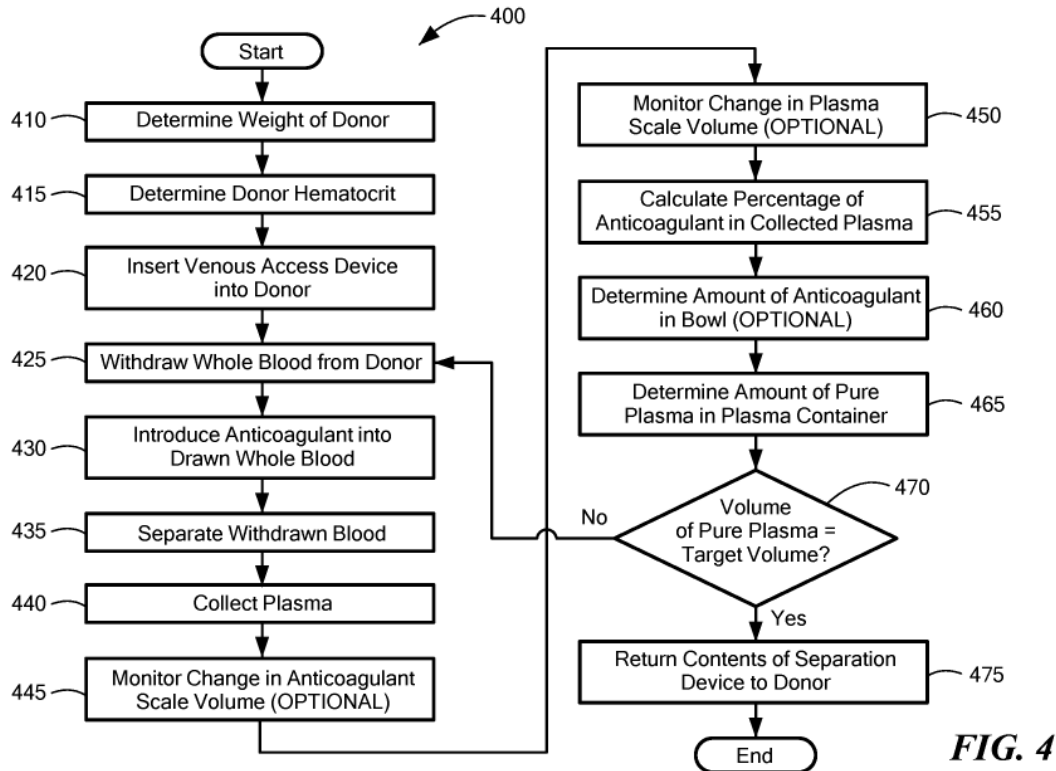
XII. GROUND VII: CLAIMS 1-4, 6-7, AND 10-21 LACK SUPPORT IN THE '916 PATENT SPECIFICATION

218. I understand that the '916 patent is a continuation of the '652 patent and shares the same specification and that all claims must have support in either the specification of the '652 patent or the specification of the '916 patent. But, the claims of the '916 patent barely resemble the specification it shares with the '652 patent.

2. Disclosure of the Purported Invention

219. As I discuss above, Haemonetics' purported invention is a blood processing system that continues collecting plasma until reaching a target volume of pure plasma. EX1001, 4:23-25. 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. 4. Figure 4 of the '916 patent illustrates the steps allegedly performed by Haemonetics' patented system.



220. As shown in Figure 4, the technician or the system determines the weight, height, and hematocrit of a donor to determine a total plasma volume to collect from a donor before inserting a venous access device into a donor. This is the only time that a target volume is determined according to the '916 patent.

221. Then, the method enters a loop (steps 425-470) that continues until “volume of pure plasma = target volume.” EX1001, Fig. 4. The technician or the

system withdraws whole blood from a donor, 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. EX1001, 8:24-29.

F. Argument

222. Claims 1-4, 6-7, and 10-21 recite limitations that lack written description support in the '916 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 **target volumes**, and has **a control system**. None of these categories have sufficient written description support in the '916 patent's specification.

1. There is no written description support for “programming a controller”

223. Claim 20, which requires programming the controller in Haemonetics' claimed apheresis system, lacks adequate written description support. Haemonetics discloses a system that has a controller that controls operation of the centrifuge bowl and can calculate (1) a percentage of anticoagulant in the collected plasma component, and (2) a volume of pure plasma collected within the plasma container. EX1001, 3:10-20. 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.

2. Limitations requiring a plasma product are unsupported.

224. Claims 1-3, 6-7, 10, 14-15, and 17-21 require measuring a plasma product and lack adequate written description support in the '916 patent.

225. Haemonetics uses the term “plasma product” sparsely in its specification: once to describe the technical field of the purported invention, later to distinguish the alleged invention to prior art systems, and finally in the context of discussing saline return in prior art systems. EX1001, 4:31, 10:5-6. Figure 4, which shows the purported invention of the '916 patent, does not reference plasma product.

226. As a threshold matter, Haemonetics' sparse disclosure that the field of the invention is collecting “a plasma product” does not tell a POSITA that the '916 patent recites measuring/calculating target or current plasma product volumes.

227. Further, the reason for these sparse disclosures is that the '916 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, 4:23-25. 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, 10:21-26. Thus, the focus of the patent is *pure plasma* collection, not plasma product collection.

228. Instead, a POSITA would understand that the purported invention tracks the amount of pure plasma collected. For example, as seen in Figure 4 of the ’916 patent, the specification focuses on tracking the amount of pure plasma collected. Thus, there is inadequate written description support for claim limitations related to tracking plasma product.

3. Draw and return cycle limitations lack adequate written description support.

229. Claims 1-4, 7, 10, and 13-14, which require collecting plasma from whole blood using a draw and return cycle, lack of written description support in the specification of the ’916 patent.

230. First, there’s no mention of draw and return cycles in the ’916 patent specification. While Haemonetics includes Fig. 4 to allegedly show that the ’916 patent discloses withdrawing whole blood, separating whole blood, collecting

plasma, determining an amount of pure plasma in the plasma container, and returning uncollected components. However, nowhere in the specification does Haemonetics disclose that these steps are performed in *a cycle*. In fact, the word “cycle” never appears anywhere outside of the claims. Thus, claims 1-2, 10, and 13, which all recite draw and return cycles, lack written description support.

231. Second, there’s no mention of controlling any aspects of such cycles in the specification. Claim 1 requires a controller to operate a draw and return cycle, and there is no disclosure in the specification about which part of the patented system controls a draw and return cycle. Similarly, claims 3-4 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 13), lack written description support.

232. Lastly, there’s no disclosure in the ’916 patent of repeating any cycles, yet claims 1, 3-4, 10, and 13 require repeated cycles. For example, claim 13 recites that such a cycle is repeated at least three times. Similarly, claim 10 recites a system that performs a plurality of cycles, and claim 1 recites a controller operating “a subsequent draw and return cycle.” But the ’916 patent includes no disclosures that would require multiple cycles, nor does the ’916 patent disclose a single needle configuration that would require performing draw and return steps in distinct phases.

4. Calculating a Target Volume is Unsupported

233. Claims 1-3, 7, 10-14, 17-21 require calculating a target volume and are invalid for lacking an adequate written description. As shown in Figure 4, the '916 patent purportedly measures pure plasma collected in the plasma container as an apheresis. But Figure 4 does not contain a step that determines target volume. The specification does not provide adequate written support either, as the specification's *only* guidance to calculate the target volume is that “[t]he target volume of pure plasma may be based, at least in part, on the weight of the donor.” EX1001, 2:52-53. The '916 patent claims, however, much more than basing a target volume of pure plasma on a donor's weight and thus these claims lack adequate written description support.

234. For example, claim 1 recites the target volume of pure plasma being determined using a donor's hematocrit. This is not in the specification. Likewise, the specification does not disclose that the target volume may be recalculated mid-donation procedure. Thus, the '916 patent also fails to provide written description support for updating the donor's hematocrit mid-procedure for use in the recalculated target volume. The specification also does not disclose when the new target is allegedly calculated as required by some dependent claims. *See, e.g.*, EX1001, cl. 3.

235. Haemonetics' claim 1 broadens the scope of its claims to include calculating a "plasma product" target volume. Haemonetics' claimed system does not calculate a target volume for plasma product, meaning that any "target volume for plasma product" lack support in the specification.

5. Control system limitations lack written description support

236. Claims 14, 16-17, 19, and 20, which require that the plasma apheresis system interacts with a control system, lack of adequate written description support in the specification of the '916 patent.

237. The only time that the words "control system" appear anywhere in the '916 patent is in claims 14, 16-17, 19, and 20. The specification of the '916 patent does not explain what the control system is, what it does, or where it is located. Figure 3, which shows the hardware and software components of Haemonetics' claimed system, does not show a control system. For example, claim 14 requires that "the controller is coupled to a touch screen and programmed to received donor parameters electronically from a control system," but 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. There is no disclosure that anything other than a controller or a human technician receives data or performs calculations.

XIII. AVAILABILITY FOR CROSS-EXAMINATION

238. In signing this declaration, I recognize that the declaration will be filed as evidence in a case before the Patent Trial and Appeal Board of the United States Patent and Trademark Office. I also recognize that I may be subject to cross examination in the case and that cross examination will take place within the United States. If cross examination is required of me, I will appear for cross examination within the United States during the time allotted for cross examination.

XIV. RIGHT TO SUPPLEMENT

239. I reserve the right to supplement my opinions in the future to respond to any arguments that the Patent Owner may raise and to take into account new information as it becomes available to me.

XV. JURAT

240. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

Declaration of Dr. Gary Fletcher in Support of Petition for
Post Grant Review of U.S. Patent No. 12,171,916
PGR2025-00078

Dated:	Respectfully submitted,
<u>September 5, 2025</u>	