

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

TERUMO BCT INC.,

Petitioner

v.

HAEMONETICS CORP.,

Patent Owner

IPR2026-00046

U.S. Patent No. 10,980,926

**DECLARATION OF GARY D. FLETCHER, PH.D. IN SUPPORT OF
PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO.
10,980,926**

Table of Contents

I.	INTRODUCTION	1
II.	QUALIFICATIONS	2
III.	MATERIALS AND OTHER INFORMATION CONSIDERED	6
IV.	SUMMARY OF MY OPINIONS.....	8
V.	LEGAL PRINCIPLES	8
	A. Claim Construction	9
	B. Anticipation.....	9
	C. Obviousness	10
VI.	Level Of Ordinary Skill	13
VII.	Background on Plasma Apheresis	13
VIII.	'926 Patent Overview	17
	A. The '926 Patent is Related to Plasma Apheresis	17
	B. The '926 Patent's Purported Invention	19
IX.	Prior Art Overview	23
	A. Overview of Lavender	23
	B. Overview of Fletcher-Haynes	28
	C. Overview of Min.....	32
X.	Identification of How the '926 Patent's Claims are Unpatentable	33
	A. Ground I: Claims 1-4, 6-11, 13-18, 20-28, and 30 are rendered obvious by Lavender in view of Fletcher-Haynes.....	33
	1. It would have been obvious to modify the Lavender system using the teachings of Fletcher-Haynes.....	33
	2. Independent Claim 1	37
	3. Claim 2: A method according to claim 1, wherein the target collection volume is the calculated volume of pure plasma.	54
	4. Claim 3: A method according to claim 1, wherein the target collection volume is the calculated volume of pure plasma plus the calculated volume of anticoagulant.....	56

Declaration of Dr. Gary Fletcher in Support of Petition for
Inter Partes Review of U.S. Patent No. 10,980,926
 IPR2026-00046

5.	Claim 4: A method according to claim 1, wherein the calculated volume of anticoagulant is further based, at least in part, on the predetermined ratio of anticoagulant.....	57
6.	Claim 6: A method according to claim 1, wherein calculating the volume of anticoagulant includes calculating the volume of anticoagulant before withdrawing whole blood.	59
7.	Claim 7: A method according to claim 1, wherein calculating the target volume of pure plasma includes calculating the target volume of pure plasma before withdrawing whole blood from the donor.	59
8.	Claim 8.....	60
9.	Claim 9: A system according to claim 8, wherein the target collection volume is the calculated volume of pure plasma.	65
10.	Claim 10: A system according to claim 8, wherein the target collection volume is the calculated volume of pure plasma plus the calculated volume of anticoagulant to be collected in the plasma container.	65
11.	Claim 11: A system according to claim 8, wherein the volume of anticoagulant to be collected within the plasma container is further based, in least in part, on the predetermined ratio of anticoagulant.....	66
12.	Claim 13: A system according to claim 8, wherein the controller is configured to calculate the volume of anticoagulant before withdrawing whole blood from the donor.....	66
13.	Claim 14: A system according to claim 8, wherein the controller is configured to calculate the target volume of pure plasma before withdrawing whole blood from the donor.	66
14.	Claim 15.....	66
15.	Claim 16: A method according to claim 15, wherein the target collection volume is the calculated volume of pure plasma.	70

Declaration of Dr. Gary Fletcher in Support of Petition for
Inter Partes Review of U.S. Patent No. 10,980,926
 IPR2026-00046

16. Claim 17: A method according to claim 15, wherein the target collection volume is the calculated volume of pure plasma plus the calculated volume of anticoagulant to be collected in the plasma collection container.
 70
17. Claim 18: A method according to claim 15, wherein the volume of anticoagulant to be collected within the plasma collection container is further based, in least in part, on a predetermined ratio of anticoagulant. 70
18. Claim 20: A method according to claim 15, the volume of anticoagulant to be collected with the plasma component in the plasma collection container is also based, at least in part, on a volume of anticoagulant to be added to the drawn whole blood..... 70
19. Claim 21: A method according to claim 15, wherein the blood processing end point is when the target collection volume has been collected within the plasma collection container..... 71
20. Claim 22: A method according to claim 15, wherein the control system includes the controller..... 71
21. Claim 23..... 72
22. Claim 24: The system according to claim 23, wherein the blood processing device is configured to stop the blood draw pump when the target collection volume is collected within the plasma container. 74
23. Claim 25: The system according to claim 23, wherein the controller is part of the blood processing device..... 74
24. Claim 26: The system according to 23, wherein the controller is further configured to program the blood processing device with an end point based, at least in part, on the target collection volume. 74
25. Claim 27: A system according to claim 23, wherein the target collection volume is the calculated volume of pure plasma and/or the calculated

Declaration of Dr. Gary Fletcher in Support of Petition for
Inter Partes Review of U.S. Patent No. 10,980,926
IPR2026-00046

	volume of pure plasma plus the calculated volume of anticoagulant to be collected in the plasma container.	74
26.	Claim 28: A system according to claim 23, wherein the volume of anticoagulant to be collected within the plasma container is further based, at least in part, on a predetermined ratio of anticoagulant.	75
27.	Claim 30: A system according to claim 26, wherein the end point is when the target collection volume has been collected within the plasma container.	75
B.	Ground II: Claims 5, 12, 19, and 29 are rendered obvious over Lavender in view of Fletcher-Haynes and Min	75
1.	Reasons to Combine Lavender and Fletcher-Haynes with Min	75
2.	Claim 5: A method according to claim 1, wherein the calculated volume of anticoagulant includes at least a portion of the anticoagulant to be introduced into the withdrawn blood and at least a portion of a volume of anticoagulant to be added during a priming step.	80
3.	Claim 12: A system according to claim 8, wherein the volume of anticoagulant to be collected in the collected plasma component includes at least a portion of the anticoagulant to be introduced into the withdrawn blood and at least a portion of a volume of anticoagulant to be added during a priming step.	81
4.	Claim 19: A method according to claim 15, wherein the volume of anticoagulant to be collected in the collected plasma component includes at least a portion of the anticoagulant to be introduced into the withdrawn blood and at least a portion of a volume of anticoagulant to be added during a priming step.	82
5.	Claim 29: A system according to claim 23, wherein the volume of anticoagulant to be collected in the collected plasma component includes at least a portion of the anticoagulant to be introduced into the withdrawn	

Declaration of Dr. Gary Fletcher in Support of Petition for
Inter Partes Review of U.S. Patent No. 10,980,926
IPR2026-00046

blood and at least a portion of a volume of anticoagulant to be added
during a priming step. 82

XI.	Availability for Cross-Examination.....	82
XII.	Right to Supplement	82
XIII.	Jurat.....	83

Declaration of Dr. Gary Fletcher in Support of Petition for
Inter Partes Review of U.S. Patent No. 10,980,926
 IPR2026-00046

EXHIBIT LIST

Exhibit	Reference
1001	U.S. Patent No. 10,980,926 (“’926 Patent”)
1002	File History of the ’926 Patent
1004	U.S. Patent No. 7,072,769 (“Fletcher-Haynes”)
1005	U.S. Patent No. 4,898,675 (“Lavender”)
1006	U.S. Patent No. 8,075,468 (“Min”)
1007	U.S. Patent Publication No. 2003/0125881 (“Ryan”)
1008	“Membrane versus centrifuge-based therapeutic plasma exchange: a randomized prospective crossover study,” Carsten Hafer et al., <i>Int. Urol. Nephrol</i> (2016) 48:133-138; Springer Science+Business Media Dordrecht 2015.
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	Bruce C. McLeod, MD, et al., “Apheresis: Principles and Practice,” 3rd Edition, AABB Press 2010.
1011	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
1012	Curriculum Vitae (“CV”) of Dr. Gary D. Fletcher
1013	U.S. Patent No. 9,283,316 (“Flexman”)
1014	Japanese Patent Publication No. JP 2002-282352 A and certified Japanese to English translation (“Takagi”)

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 an *Inter Partes* review (“IPR”) proceeding of U.S. Patent No. 10,980,926 (“’926 patent”).

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 1–30 (the “challenged claims”) of the ’926 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 IPR or other proceeding involving the '926 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 EX1012 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 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 EX1012.

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 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 space. 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.

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 EX1012.

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 ’926 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 '926 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 '926 Patent (EX1001), the prosecution history (EX1002) of the '926 Patent, and the following materials:

- U.S. Patent No. 7,072,769, issued July 4, 2006 (“Fletcher-Haynes,” EX1004);
- U.S. Patent No. 4,898,675, issued February 6, 1990 (“Lavender,” EX1005);
- U.S. Patent No. 8,075,468, issued December 13, 2011 (“Min,” EX1006);

Declaration of Dr. Gary Fletcher in Support of Petition for
Inter Partes Review of U.S. Patent No. 10,980,926
IPR2026-00046

- U.S. Patent Publication No. 2003/0125881, published July 3, 2003 (“Ryan,” EX1007);
- “Membrane versus centrifuge-based therapeutic plasma exchange: a randomized prospective crossover study,” Carsten Hafer et al., *Int. Urol. Nephrol* (2016) 48:133-138; Springer Science+Business Media Dordrecht 2015. (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. (EX1010);
- 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>
(EX1011);
- U.S. Patent No. 9,283,316, issued March 15, 2016 (“Flexman,” EX1013);
and

- Japanese Patent Publication No. JP 2002-282352 A, published October 2, 2002, and certified Japanese to English translation (“Takagi,” EX1014).

16. I have considered these materials through the lens of a POSITA, which is discussed further in §§V and VI (below) related to the '926 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 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 13, 14, 15, 16, 17, 18, 20, 21, 22, 23, 24, 25, 26, 27, 28, and 30 are obvious over Lavender in view of Fletcher-Haynes; and
- Claims 5, 12, 19, and 29, are obvious over Lavender in view of Fletcher-Haynes and Min.

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.

A. 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. 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.

22. 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

23. 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.

24. 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.

25. 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 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
- f. whether the innovation applies a known technique that had been used to improve a similar device or method in a similar way.

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

27. 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.

28. 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.

VI. Level Of Ordinary Skill

29. In my opinion, a POSITA would have had, as of what I understand to be 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

30. The '926 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.

31. Plasmapheresis, also known as plasma exchange or therapeutic plasma exchange, has been a clinical procedure since the 1960s. EX1010, Chapter 1: Development of Apheresis Instrumentation. It selectively removes plasma and returns cellular components along with replacement fluid using centrifugation or membrane filtration. EX1011. 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.

32. 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.

33. 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. EX1010, Chapter 4: Current Instrumentation of Apheresis.

34. 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.

35. At the time the '926 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. EX1010, 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. EX1010, 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

¹ See EX1010, p. 14, “Celltrifuge II [a blood-processing centrifuge] included an optical sensor for monitoring the collected product and automatically adjusting the

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 '926 patent. *See, e.g.*, EX1014.

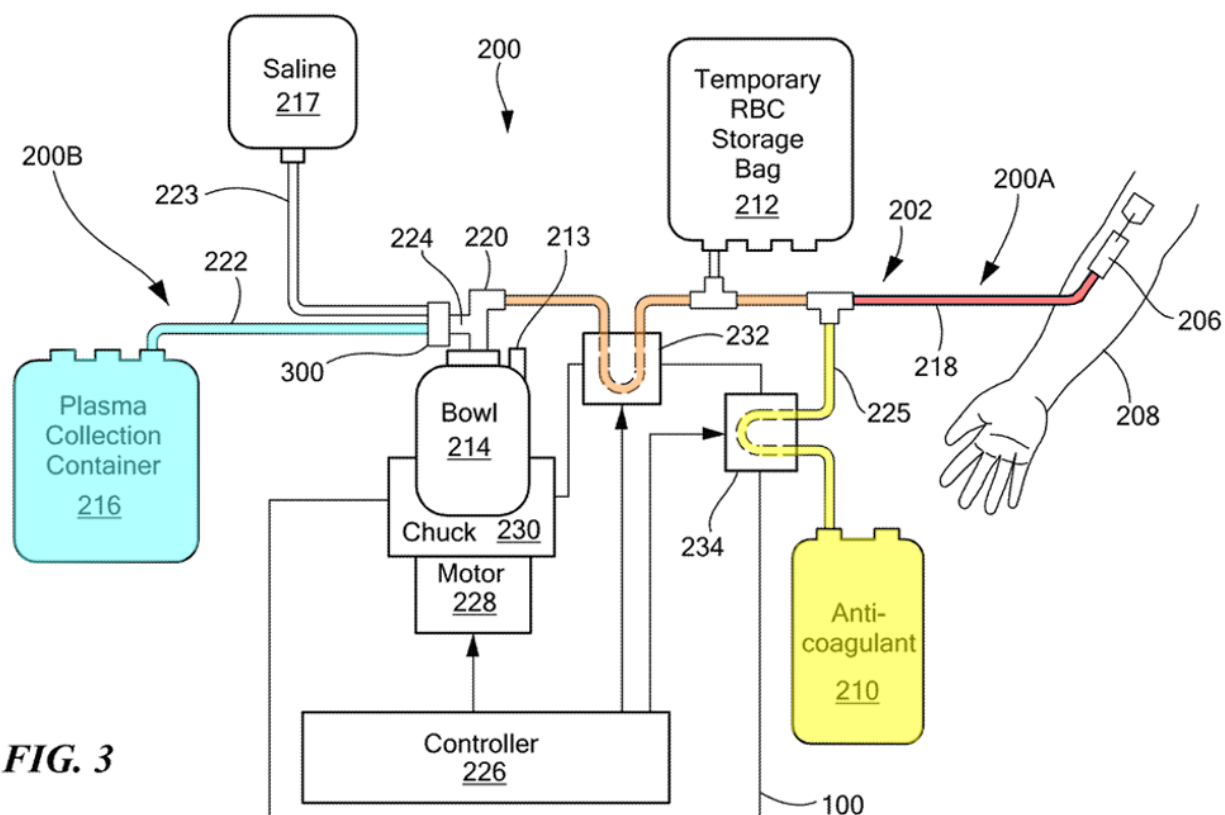
VIII. '926 Patent Overview

A. The '926 Patent is Related to Plasma Apheresis

36. The '926 patent, which I understand issued on April 20, 2021, relates to a “system and method for collecting plasma” in blood apheresis systems. EX1001, Title, 1:15-17. “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, 1:21-23. The '926 patent specifically relates to plasma apheresis, which is plasma collection. Figure 3 of the '926 patent shows one embodiment of a plasma apheresis system.

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.*, EX1014, p. 14, “The pump flow rates—and, thereby, the component collection—are controlled by the microprocessor in response to the optical monitor.”



EX1001, Fig. 3 (annotated).

37. Plasma apheresis involves withdrawing whole blood from a donor using venous access device 206. EX1001, 4:57-60. 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, 85:18-41, 6:21-41. Anticoagulant is introduced in fixed proportions to the whole blood drawn from the donor to prevent blood clotting in the draw line. See EX1011. “[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, 7:51-54.

38. Then, the mixture (orange) of anticoagulant and “withdrawn whole blood . . . enters a blood component separation device,” *e.g.*, centrifuge bowl 214, which “separates the whole blood into its constituent components,” *e.g.*, “plasma, platelets, red blood cells (“RBCs”) . . . [and] white blood cells.” EX1001, 4:56-67, 6:42-53. The donor’s plasma, *i.e.*, pure plasma, 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, in blue above). EX1001, 2:1-4, 5:27-34. The anticoagulant and pure plasma combination is known as anticoagulated plasma or plasma product. EX1001, 9:63-66.

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

B. The ’926 Patent’s Purported Invention

40. The ’926 patent purports to solve problems associated with “determin[ing] the total volume of plasma that has been collected” from a donor after the withdrawn whole blood is mixed with anticoagulant by tailoring the volume of plasma collected based on the donor’s plasma volume and a target percentage of

plasma to collect, and considering a donor's hematocrit level and the amount of anticoagulant added into the system. EX1001, 1:47-53; 1:56-2:15; 4:8-19.

41. Each donor has a different hematocrit level, which affects the amount of plasma in the donor's whole blood. EX1001, 7:63-64. The differing levels of hematocrit affect the volume of anticoagulant in a plasma collection bag ("anticoagulant volume"). EX1001, 7:67-8:5. Given this variability, the '926 patent discloses that controller 226 may determine the donor's plasma volume based on hematocrit and then calculate the target volume of plasma to collect. EX1001, 8:9-54. Controller 226 may also 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, 10:58-11:28. In % AC equation below, "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, 8:9-54. Anticoagulated whole blood is extracted blood mixed with anticoagulant.

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

42. The '926 patent discloses that the controller also monitors the weight

of the collection container using a weight sensor and uses it to determine the total volume of liquid in the collection container. EX1001, 7:23-25, 7:59-64. 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, 8:55-9:48. The '926 patent first calculates the anticoagulant volume. EX1001, 8:59-64. 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, 8:59-64. These calculations may occur in real time. EX1001, claims 1, 15.

43. The '926 patent also discloses two alternative methods of determining the amount of anticoagulant in the collection bag that do not consider a donor's hematocrit. These include determining the anticoagulant in the collection bag by: (i) monitoring the volume of anticoagulant added to the system based on the number of rotations of the anticoagulant pump, and (ii) measuring the change in weight of the anticoagulant container. EX1001, 8:45-54. Something to note is that "[b]ecause the osmolarity of the red blood cells prevents the anticoagulant from mixing with it, essentially all of the anticoagulant exits the bowl 214 and is collected within the plasma collection container 216 along with the plasma." EX1001, 8:26-31; 8:45-54; 9:30-46. Under this assumption, subtracting the volume of anticoagulant added to the system from the total volume in the collection container provides an estimate of the volume of pure plasma within the collection container. EX1001 at 8:26-31; 8:45-

54; 9:30-46. In both these methods disclosed in the '926 patent, the volume of anticoagulant that is added is then used to calculate the volume of pure plasma collected in the plasma collection container by subtracting the added anticoagulant volume from the total volume in the collection container. EX1001, 8:26-31; 8:45-54; 9:30-46.

44. Of the three methods I discussed above, only the first, which is based on the predetermined ratio of anticoagulant to anticoagulated whole blood, considers the donor's hematocrit. That method does not, however, use an amount of anticoagulant collected within the plasma collection container or supplied to the system to determine a percentage of anticoagulant within the collected plasma. EX1001, 10:9-15.

45. In the '926 patent, each method to determine the volume of pure plasma is repeated "until a target volume of pure plasma is collected in the plasma collection container," *e.g.*, the volume the volume determined by calculating "the total volume of plasma to collect on the individual donor (*e.g.*, based on their height, weight, hematocrit, blood volume and/or plasma volume)." EX1001, 8:9-14. When the system reaches a target volume of pure plasma, the controller "stops the draw of whole blood from the subject and reverses the direction of the blood ... to draw the RBCs (and other components)" from the blood component separation device back to the donor. EX1001, 9:10-16.

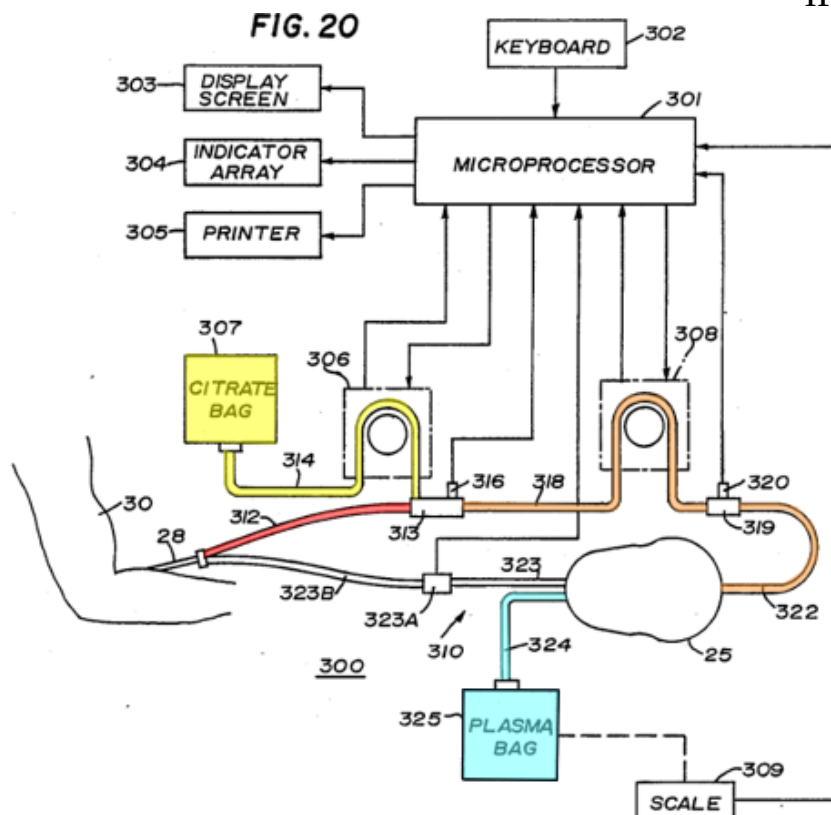
46. As I will explain below, these concepts were well known as of the priority date of the '926 patent.

IX. Prior Art Overview

A. Overview of Lavender

47. Lavender discloses “a system, method and device for continuously fractionating blood in situ.” EX1005, Abstract. Lavender recognized the need to track the volume of anticoagulant collected during a plasma collection procedure to, among other things, “accurately, safely and economically collect[] plasma from a source of blood.” EX1005, 3:26-28.

48. Figure 20 illustrates Lavender’s automatic system 300 for fractionating blood. EX1005, 16:34-53.



EX1005, Fig. 20 (annotated).

49. In Lavender's system 300, a needle or catheter 28 is used to draw whole blood from a donor, which is then mixed with citrate pumped from citrate bag 307. EX1005, 16:57-17:2. Citrate is a blood anticoagulant. EX1005, 16:45-47. The system then pumps the whole blood and anticoagulant mixture to blood fractionator 25, which separates the anticoagulated whole blood into plasma and other blood fractions. EX1005, 5:42-52. The plasma and anticoagulant mixture exits the blood separation device through the plasma line and is collected in plasma bag 325. EX1005, 17:14-16.

50. 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 EX1005, 22:35-39, cols. 41, 42. These calculations also account for the weight of the collected plasma and anticoagulant mixture during the collection process. Ultimately, these calculations are used to calculate the volume of pure plasma and anticoagulant in the plasma collection bag in real time. EX1005, 20:55-68.

51. Below are several of the variables used and/or calculated in Lavender's system:

Variable	Description
<i>CF</i> (conversion factor)	Predetermined ratio (or percentage) of anticoagulant to incoming plasma
<i>PDF</i>	Plasma dilution factor
<i>C1</i>	ml plasma collected/pound of <i>BW</i>
<i>C2</i>	ml dilute plasma collected/pound of <i>BW</i>
<i>C3</i>	ml citrate to be filtered/pound of <i>BW</i>
<i>QB</i>	Blood flow from donor
<i>TQB</i>	Total blood flow
<i>HCTD</i>	Donor's hematocrit

<i>BW</i>	Donor's body weight
<i>QP</i>	Plasma flow
<i>TQP</i>	Total plasma flow
<i>QC</i>	Citrate flow
<i>QCP</i>	Citrate pump rate
<i>TQC</i>	Total citrate (anticoagulant) flow
<i>TDPF</i>	Total dilute plasma (total fluid) in the collection container
<i>TPF</i>	Total plasma filtered (pure plasma) volume in the collection container
<i>TCF</i>	Total citrate (anticoagulant) volume in the collection container
<i>MAXPF</i>	Total plasma filtered (pure plasma) volume to collect
<i>MAXCF</i>	Total citrate (i.e. anticoagulant) volume to collect
<i>MAXDPF</i>	Total dilute plasma to collect (mixture of plasma and anticoagulant)

52. These variables are used both prior to and during the collection process to determine target volumes of pure plasma and anticoagulant to collect, and monitor the amount of plasma collected.

53. The total amount of pure plasma to collect (*MAXPF*) is determined by multiplying the donor's body weight (*BW*) by a first predetermined constant (*C1*),

which is derived from a calculated donor circulating plasma volume of 5% of body weight (*BW*), multiplied by a total pure plasma to collect of 18% of the donor circulating plasma volume, and further multiplied by the conversion between ml of plasma and pound of body weight of 453.6 ml/pound, i.e. $C1 = 0.05 * 0.18 * 453.6 = 4.0824$ ml/pound. EX1005, 22:35-43, 41:4-44:42. The total amount of citrate (i.e. anticoagulant) to collect (*MAXCF*) is determined by multiplying the donor's bodyweight (*BW*) by another predetermined constant (*C3*), which is derived from the first predetermined constant (*C1*) and the predetermined ratio of plasma to anticoagulant used to dilute incoming plasma to 68% of its initial concentration, i.e. $C3 = C1 * CF$. EX1005, 22:35-43, 41:4-44:42.

54. During an operation, the amount of plasma collected is monitored by the system. For example, plasma flow (*QP*) is calculated based on the donor's blood flow (*QB*) and hematocrit (*HCTD*). EX1005, 41:4-44:42. *QP* is then used to calculate the citrate pump rate (*QCP*) by multiplying it by the conversion factor (*CF*). *QCP* is used to calculate the total citrate flow (*TQC*). See EX1005, 41:4-44:42. The total plasma volume in the collection container is calculated in real time based on the total volume of fluid in the collection container, determined by the weight of the container, and the plasma dilution factor (*PDF*). The total citrate volume in the collection container (*TCF*) is then calculated in real time based on the total plasma volume in the collection container (*TPF*) and the conversion factor (*CF*).

55. The microprocessor repeatedly performs weight measurements and run-time calculations set forth in Lavender's algorithm and displays updated values approximately every two seconds. EX1005, 20:55-68. Lavender's system determines the relationship (or ratio) between the pure plasma volume and the anticoagulant volume in the collection container. The relationship is then used to determine the pure plasma volume. Accordingly, Lavender discloses a determination of pure plasma volume based on the volume of anticoagulant. If any additional conversion or calculation is required, a POSITA would readily understand how to convert between the two volumes using the same relationship.

56. Lavender executes a main loop of the algorithm until the total plasma filtered (*TPF*) in plasma bag 325 is equal to or greater than a determined maximum total plasma volume to collect (*MAXPF*), as determined using a donor's weight. EX1005, 43-44, claim 33.

B. Overview of Fletcher-Haynes

57. 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. EX1004, 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." EX1004, 48:29-31; 52:13. For example, Fletcher-Haynes' prediction algorithms include a

donor's gender, height, weight, hematocrit, and platelet pre-count parameters.

EX1004, 27:30-35; 49:19-52:36.

58. Figure 7A illustrates Fletcher-Haynes' collection assembly 10' for separating blood into components. EX1004, 45:14-16. Donor's blood is pumped through inlet line 22 (red), and anticoagulant is pumped from AC container 30 (yellow) into to the inlet line 22. EX1004, 45:22-37. Blood component separation device 18 separates anticoagulated whole blood into separate components flowing into platelet collect bags 38 and plasma collect bag 54. EX1004, 45:22-37. The remaining, uncollected blood is pumped back to the donor using return line 46. EX1004, 45:22-37.

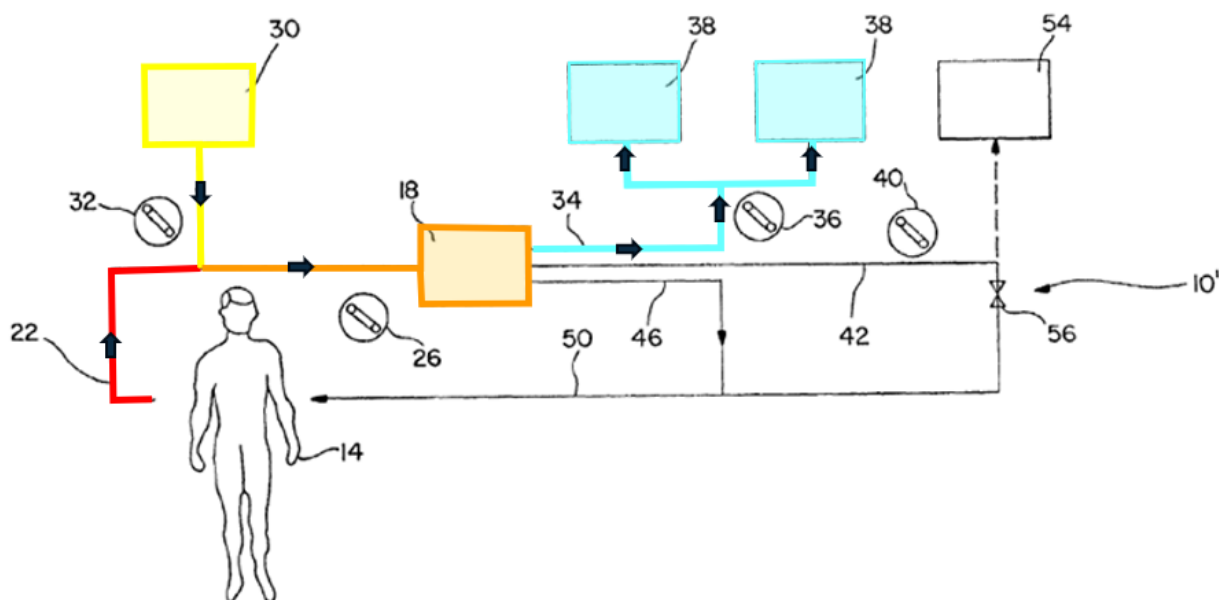


Figure 7A

EX1004, Fig. 7A (annotated).

59. Assembly 10' operates according to a collection procedure derived from procedure goal(s) and may include maximizing "at least one process control parameter." EX1004, 7:38-38; 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. EX1004, 49:19-26.

60. 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." EX1004, 49:22-26. When executed prior to a blood separation procedure, the prediction model determines target values of any of parameters (1)-(11). EX1005, 34:8-24; 48:66-49:19-25. When executed during a blood separation procedure, the prediction model determines any of parameters (1)-(11) in real-time. EX1004, 34:8-24; 48:66-49:19-25.

61. Fletcher-Haynes' prediction algorithms may be integrated with its optimization algorithms, and Fletcher-Haynes specifically recites "the optimizer model 172 may interface with the prediction model or actually integrally incorporate the prediction model," and refers to Eqs. 1-22. EX1004, 58:63-67. Stated

differently, Fletcher-Haynes discloses 22 equations that can be incorporated into a prediction model to predict a particular blood component's yield. EX1004, 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, another is an equation for the total volume in the source plasma bag or a target volume of diluted plasma (i.e. plasma and anticoagulant mixture) using the anticoagulant (AC) ratio, and another is an equation for calculating source plasma volume or a target pure plasma volume collected or to collect. EX1004, 49:40-52:17. Specifically, Equation 10 defines the total blood volume of a donor (VB) using a donor's height and weight; Equation 9 defines the AC Ratio (R) using a donor's hematocrit; Equation 22 defines the total volume in the source plasma bag or total volume of diluted plasma (V_{SPB}), and Equation 17 defines the predicted total volume of pure plasma in the source plasma bag (V_{SP}). EX1004, 49:40-52:17. These equations can be integrated with Fletcher-Haynes' optimization algorithms. EX1004, 58:63-67.

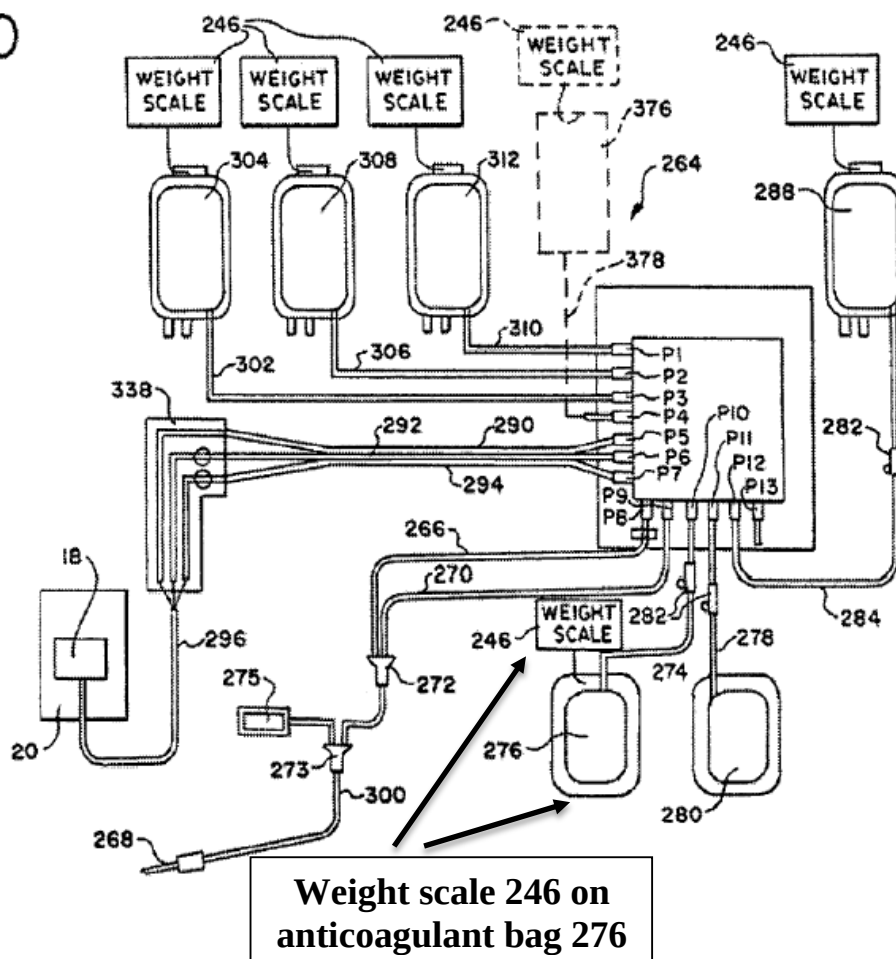
62. Fletcher-Haynes explains that it is preferable during procedures "to have computer/database system 140 exert control over apheresis machine functions, including process control manipulation and optimization." EX1004, 34:8-24, 49:40-52:17. Because computer/database system 140 can control apheresis 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 prior to or during those procedures. EX1004, 34:8-24, 49:40-52:17.

C. Overview of Min

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

FIG. 10



EX1006, FIG. 10 (annotated).

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

X. Identification of How the '926 Patent's Claims are Unpatentable

A. Ground I: Claims 1-4, 6-11, 13-18, 20-28, and 30 are rendered obvious by Lavender in view of Fletcher-Haynes

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

65. Lavender and Fletcher-Haynes are both directed to plasma apheresis systems. Moreover, both Lavender and Fletcher-Haynes disclose utilizing donor information to optimize the plasma collection process. Lavender discloses the use of donor parameters, like hematocrit, and a fixed anticoagulant to plasma ratio to calculate both a target and a real-time intra-operative volume of pure plasma and anticoagulant in the plasma collection bag. See EX1005, 22:35-39, cols. 41, 42. Fletcher-Haynes discloses determining a target amount of pure plasma to collect for a donor considering the medical and physical characteristics of the donor, such as a donor's gender, height, weight, hematocrit, and platelet pre-count parameters. EX1004, 27:30-35; 49:19-52:36.

66. In my opinion, a POSITA would be motivated to include Fletcher-Haynes' height parameter as one of the donor parameters to consider in Lavender's system when determining the total amount of pure plasma to collect from the donor (the target volume of pure plasma) because including additional donor-specific parameters would result in a more accurate determination of the optimal amount of pure plasma to collect. EX1005, 20:9-15.

67. Additionally, in my opinion, a POSITA would readily implement any of Fletcher-Haynes' calculations into Lavender's system to optimize determining target volumes. A POSITA would also incorporate any of Fletcher-Haynes'

calculations into Lavender's system to optimize the data tracking and donor parameter monitoring before, during, and after a blood draw procedure.

68. In my opinion, a POSITA would have been motivated to combine Lavender's and Fletcher-Haynes' teachings, and would have had a reasonable expectation of success, because, for example, and as discussed above, each relate to the same well-known technologies. Additionally, both apply substantially similar techniques to achieve similar results and Lavender's functionality would not change in the combination as Fletcher-Haynes is used for the same purpose as Lavender's system—using donor parameters to determine the total amount of pure plasma to collect.

69. In my opinion, the intended functionality of Lavender's blood component collection device would not change when implementing Fletcher-Haynes' calculations because Fletcher-Haynes' calculations would simply replace or be incorporated into the parameters calculated in Table VI of Lavender's algorithm. Additionally, both seek to optimize collecting blood components, like plasma, from a donor. That is, a POSITA would have expected Lavender's blood component collection device to successfully determine a target amount of anticoagulant to collect and/or a target amount of pure plasma to collect similarly to Fletcher-Haynes.

70. Additionally, incorporating Fletcher-Haynes' equations into Lavender's 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.

71. 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 $CF = \frac{Q_C}{Q_P} = \frac{Q_C}{Q_B} * \frac{Q_B}{Q_P} = \frac{1}{(R-1)} * \frac{1}{(1-HCTD)}$ 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). Similarly, Lavender's $MAXDPF = MAXPF + MAXCF = MAXPF * (1 + CF)$, which is equivalent to Fletcher-Haynes' Eq. 22.

72. In my opinion, incorporating Fletcher-Haynes' algorithms into Lavender's system would have been a known software modification that would have yielded predictable results. That is, incorporating Fletcher-Haynes' algorithms into Lavender's Main Loop entails the mere use of similar equations to improve similar systems and methods in the same way.

73. Thus, in my opinion, a POSITA would have been motivated to make, and would have had a reasonable expectation of success in making, these proposed modifications to Lavender's system in view of Fletcher-Haynes' disclosures because, for example, Fletcher-Haynes' disclosed calculations for target plasma volume can be implemented using minor software modifications in Lavender's main loop algorithm (e.g. as MAXPF in Table VI).

2. Independent Claim 1

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

74. In my opinion, to the extent the preamble is limiting, Lavender discloses "[a] system, method and device for continuously fractionating blood in situ." EX1005, Abstract. Lavender fractions blood "to collect blood substances, such

as plasma.” EX1005, 1:12-13; *see also id.* at claim 1 (“A method of collecting plasma...”), 5:42-49, 1:48-56.

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

75. Lavender determines a weight of a donor through “entry and validation of donor data, including ... donor weight in pounds.” EX1005, 20:10-14; *see also* EX1005 Abstract.

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

76. Lavender determines a hematocrit of a donor through “entry and validation of donor data, including ... donor hematocrit in percent.” EX1005, 20:10-14.

d. 1[c] calculating a volume of anticoagulant to be collected with a plasma component in a plasma collection container, the volume of anticoagulant to be collected with the plasma component based, at least in part on the hematocrit of the donor;

77. Lavender calculates a volume of anticoagulant to be collected in the collected plasma component. Specifically, Lavender’s system determines the total volume of citrate, an anticoagulant, to collect (*MAXCF*) before starting a procedure. EX1005, 20:46-54, 41:1-44:33 (Table VI, §2(i)). *MAXCF* is determined by multiplying the donor’s bodyweight (*BW*) by a predetermined constant (*C3*), which is also derived from a predetermined ratio of plasma to anticoagulant used to dilute incoming plasma to 68%, i.e. $C3 = C1 * CF$. EX1005, 22:35-41, 41:4-44:42. While

the donor's hematocrit is not explicitly used to determine *MAXCF*, Lavender's system determines the donor's hematocrit.

78. Fletcher-Haynes' system also determines the donor's hematocrit. EX1004, 20:9-15. Further, Fletcher-Haynes' system discloses calculating a volume of anticoagulant to be collected with a plasma component in a plasma collection container based, at least in part, on the donor's hematocrit. EX1004, 50:49-50, 50:61, 51:12-14. A POSITA would use Fletcher-Haynes' f_{ACP} and V_{SPB} equations in Lavender's Table VI calculations to determine a *MAXCF* value because doing so would allow Lavender to use both hematocrit and weight to determine *MAXCF*, resulting in a more accurate determination of the anticoagulant volume to collect during the plasma collection process.

79. Specifically, Fletcher-Haynes determines the fraction of AC in the collected plasma component f_{ACP} using an AC ratio and the donor's hematocrit in equation 15.

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

80. R is the ratio of the collective flow of anticoagulant and blood through the inlet line in relation to the flow of anticoagulant through the inlet line, and H is the donor's hematocrit. EX1004, 48:21-32, 50:16-52:14.

81. Equation 17 defines the target source plasma volume, i.e., the maximum volume of pure plasma to collect in the collection container. EX1004, 48:54-62, 50:16-52:14. Equation 22 recites:

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

where V_{SPB} is the total volume in the source plasma bag (including plasma and anticoagulant), V_{SP} is the volume of pure plasma in the source plasma bag. EX1004, 50:16-52:14. When the f_{ACP} equation is inserted into the V_{SPB} equation, it is clear that V_{SPB} is based on a donor's hematocrit:

$$V_{SPB} = V_{SP}(1 + [(R - 1)(H - 1)]^{-1})$$

82. In my opinion, a POSITA would look to Fletcher-Haynes' equations using hematocrit to determine target volumes in Lavender's system to better determine the volume of anticoagulant to be collected. Specifically, a POSITA would look to incorporate Fletcher-Haynes' Equations 15, 17, and 22 to determine Lavender's *MAXCF* based on the donor's hematocrit. As will be discussed below, in my opinion, a POSITA would recognize the following variables are equivalent in Lavender and Fletcher-Haynes:

Lavender's Variable	Fletcher-Haynes' Variable	Definition

<i>MAXPF</i>	V_{SP}	The target amount of pure plasma to collect in the collection container
<i>MAXDPF</i>	V_{SPB}	The target amount of dilute plasma (plasma and anticoagulant mixture) to collect in the collection container

83. In my opinion, a POSITA would have been motivated to plug Lavender's *MAXPF* into Fletcher-Haynes' equations to solve for a *new MAXPF* that is based on both the donor's weight and hematocrit, as doing so should provide a more accurate result.

84. First, Lavender determines *MAXPF* by using the donor's bodyweight:

$$MAXPF = BW * C1$$

where *C1* is a constant derived from a donor circulating plasma volume of 5% of bodyweight (BW), multiplied by a total pure plasma to collect of 18% of the donor circulating plasma volume. EX1005, 20:46-54, 41:1-44:33, Table VI: §2.g.

85. A POSITA would understand that in the Lavender-Fletcher-Haynes system incorporating Fletcher-Haynes' consideration of donor's hematocrit, Lavender's *MAXPF*, which, as shown above is equivalent to V_{SP} , would be used in Fletcher-Haynes' Equation 22 to determine V_{SPB} , the target total volume of dilute

plasma to be collected in a plasma collection bag, as shown in the below equations (showing substituted Equation 22 and with the expanded f_{ACP} equation):

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

$$V_{SPB} = MAXPF(1 + [(R - 1)(H - 1)]^{-1})$$

86. A POSITA, in my opinion, would also recognize that the target anticoagulant volume in the collection container may be determined by subtracting the target pure plasma volume from the target dilute plasma volume (e.g. $MAXCF = V_{SPB} - MAXPF$) because only plasma and anticoagulant are collected in the plasma collection container. See EX1004, 23:39-41. The determined V_{SPB} using Lavender's $MAXPF$ would then be used to determine a target volume of anticoagulant to be collected within the plasma collection bag, or *new MAXCF*, by subtracting $MAXPF$ from V_{SPB} :

$$new\ MAXCF = V_{SPB} - MAXPF$$

87. The *new MAXCF* calculated using Fletcher-Haynes' equations would replace Lavender's $MAXCF$, resulting in a more accurate anticoagulant target volume. Below is the *new MAXCF* equation with the above-derived equation for V_{SPB} plugged in:

$$new\ MAXCF = (MAXPF(1 + [(R - 1)(H - 1)]^{-1})) - MAXPF$$

or

$$\begin{aligned} \text{new } MAXCF &= MAXPF([(R - 1)(H - 1)]^{-1}) \\ &= MAXPF * f_{ACP} \end{aligned}$$

88. In other words, the *new MAXCF* equation shown above utilizes equations 15, 17, and 22 from Fletcher-Haynes, and a POSITA would simply solve for *new MAXCF* using Fletcher-Haynes' equations to determine *new MAXCF* using both the donor's weight and hematocrit. In my opinion, a POSITA would easily recognize that R is defined in Equation 3 of Fletcher-Haynes as $\frac{Q_{IN}}{Q_{AC}}$, which is the ratio of flow of anticoagulated whole blood to flow of anticoagulant, which are variables already calculated in Lavender (e.g., QB and QC). A POSITA would understand that in Lavender, $R = \frac{(QB + QC)}{QC} = \frac{QB}{QC} + 1$. This R may be used in the *new MAXCF* equation shown above.

89. This *new MAXCF* would replace Lavender's original *MAXCF*, and include a donor's hematocrit. Because V_{SPB} is determined using f_{ACP} , and f_{ACP} is based on the donor's hematocrit, this series of equations determines a target volume of anticoagulant to be collected within the plasma collection bag directly based on the donor's hematocrit.

- e. **1[d] calculating a target volume of pure plasma to collect in the plasma collection container based, at least in part, on the weight of the donor;**

90. Lavender calculates a target volume of pure plasma to collect in the plasma collection container based, at least in part, on the weight of the donor. Specifically, the total amount of pure plasma to collect (*MAXPF*) is determined by multiplying the donor's bodyweight (*BW*) by a first predetermined constant (*C1*), which is derived from a donor circulating plasma volume of 5% of bodyweight (*BW*), multiplied by a total pure plasma to collect of 18% of the donor circulating plasma volume. EX1005, 22:35-41, 41:4-44:42.

91. Fletcher-Haynes calculates a target volume of pure plasma based on a donor's height and weight. A POSITA would be motivated to incorporate Fletcher-Haynes' calculations into Lavender's system as it would result in a more accurate target volume of pure plasma. Further, after updating Lavender's *MAXCF* with *new MAXCF*, a POSITA would recognize the need to also update *MAXPF* to more accurately account for the total volume of fluid (*MAXDPF*) in the plasma collection container.

92. Lavender's *MAXDPF* is the total volume of fluid to collect in the plasma collection container, consisting of a mixture of pure plasma and anticoagulant. Lavender's *MAXDPF* is determined based on the donor's weight and a predetermined constant, $MAXDPF = BW * C2$. The predetermined constant *C2* is derived from a predetermined ratio of plasma to anticoagulant used to dilute incoming plasma by 68% of its initial concentration, i.e. $C2 = C1 / PDF$. As

discussed above, a POSITA would recognize that only plasma and anticoagulant are collected in the plasma collection container, and thus the determined *new MAXCF* plus the determined *MAXPF* should equal the determined *MAXDPF* (e.g. $MAXDPF = MAXCF + MAXPF$). See EX1004, 23:39-41.

93. In my opinion, a POSITA would understand that updating *MAXPF* would be accomplished by subtracting the *new MAXCF* (determined based on the donor's hematocrit) from the *MAXDPF* (determined based on the donor's weight) (e.g. $new MAXPF = MAXDPF - new MAXCF$). See §X.A.2.d; EX1005, 22:35-41, 41:4-44:42.

94. As can be seen from the following equations, through mathematical substitution Lavender in view of Fletcher-Haynes calculates a target volume of pure plasma to collect in the plasma collection container based, at least in part, on the weight of the donor.

95. Specifically, using Lavender's *MAXDPF* equation and the *new MAXCF* equation derived above, a POSITA would be able to derive the following new equation for *new MAXPF*:

$$new MAXPF = BW * C2 - new MAXCF$$

It is important to note that the *new MAXCF* value derived above is dependent on the *old MAXPF* value, which is calculated using Lavender's equation $MAXPF = BW *$

C1. The equation for *new MAXPF* shown immediately above utilizes both the donor's bodyweight, through the determination of *MAXDPF* disclosed in Lavender, and the donor's hematocrit through the calculation of *new MAXCF*.

f. 1[e] determining a target collection volume based, at least in part, on the calculated volume of anticoagulant and the calculated volume of pure plasma;³

96. As discussed above, in my opinion, it would have been obvious to a POSITA in view of Lavender and Fletcher-Haynes to determine (i) a volume of anticoagulant to be collected with a plasma component in a plasma collection container based, at least in part on the hematocrit of the donor, and (ii) a target volume of pure plasma to collect in the plasma collection container based, at least in part, on the weight of the donor. See §§X.A.2.d-e.

97. In response to the start of a blood separation procedure using Lavender's automatic system, the system initializes Table VI's system algorithm. EX1005, 20:55-68, 41:1-44:33, Figs. 25A-25D. The Main Loop of the algorithm repeats until a desired amount of plasma has been collected, such as the determined

³ The term "the calculated volume of pure plasma" in claim 1 lacks antecedent basis, and I assume this term should have read "the calculated target volume of pure plasma."

target pure plasma collection volume (*MAXPF*).⁴ EX1005, 21:62-22:2. Lavender's *MAXPF* is a target collection volume of pure plasma. *See id.*

98. As described in §X.A.2.e above, in my opinion, a POSITA would be motivated to incorporate Fletcher-Haynes' calculations into Lavender's system to more accurately determine a target volume of pure plasma. *See* §X.A.2.e. For example, when a POSITA utilizes Fletcher-Haynes' calculations in Lavender's system, a target volume of pure plasma may be determined based on a donor's hematocrit and a donor's weight, or *new MAXPF* as described above. *See* §X.A.2.d-e; EX1005, 22:35-41, 41:4-44:42. The equation for *new MAXPF* utilizes both the donor's bodyweight, through the determination of *MAXDPF* disclosed in Lavender, and the donor's hematocrit through the calculation of *new MAXCF*.

99. In my opinion, it would have been obvious to a POSITA to set this *new MAXPF* as a target collection volume in Lavender, and thus determine a target collection volume based on this *new MAXPF*. *See* §X.A.2.d-e, EX1005, Table VI, §5.C. By determining the target collection volume this way, the *new MAXCF* based on the donor's hematocrit is used to determine the target collection volume (i.e. *new MAXPF*), which increases the number of donor characteristics used to determine the target collection volume compared to the *MAXPF*, or target pure

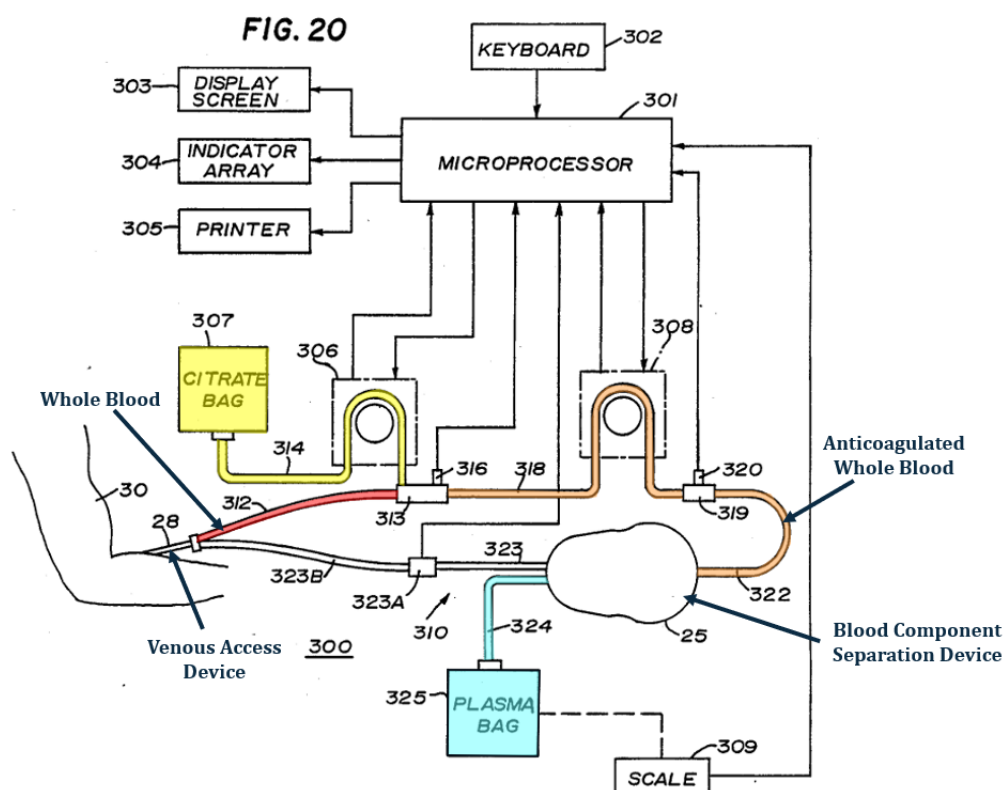
⁴ All emphasis added unless otherwise noted.

plasma volume, determined in Lavender. A POSITA would recognize that using *new MAXPF* as a target collection volume would result in a more accurate and patient specific target plasma volume.

100. By calculating the *new MAXPF* as the target collection volume, a POSITA would be utilizing both the calculated volume of anticoagulant and the calculated volume of pure plasma because *new MAXPF* is the calculated volume of pure plasma defined in claim 1 and is determined using the calculated volume of anticoagulant (i.e. *new MAXCF*). See §X.A.2.d-e.

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

101. Lavender withdraws whole blood through the venous-access device. A pump “pump[s] blood from the donor” through the needle 28, through the tubes 312, 318, 322 and into the fractionator 25, shown below in FIG. 20. EX1005, 5:18-22, Fig. 20.



EX1005, FIG. 20 (annotated).

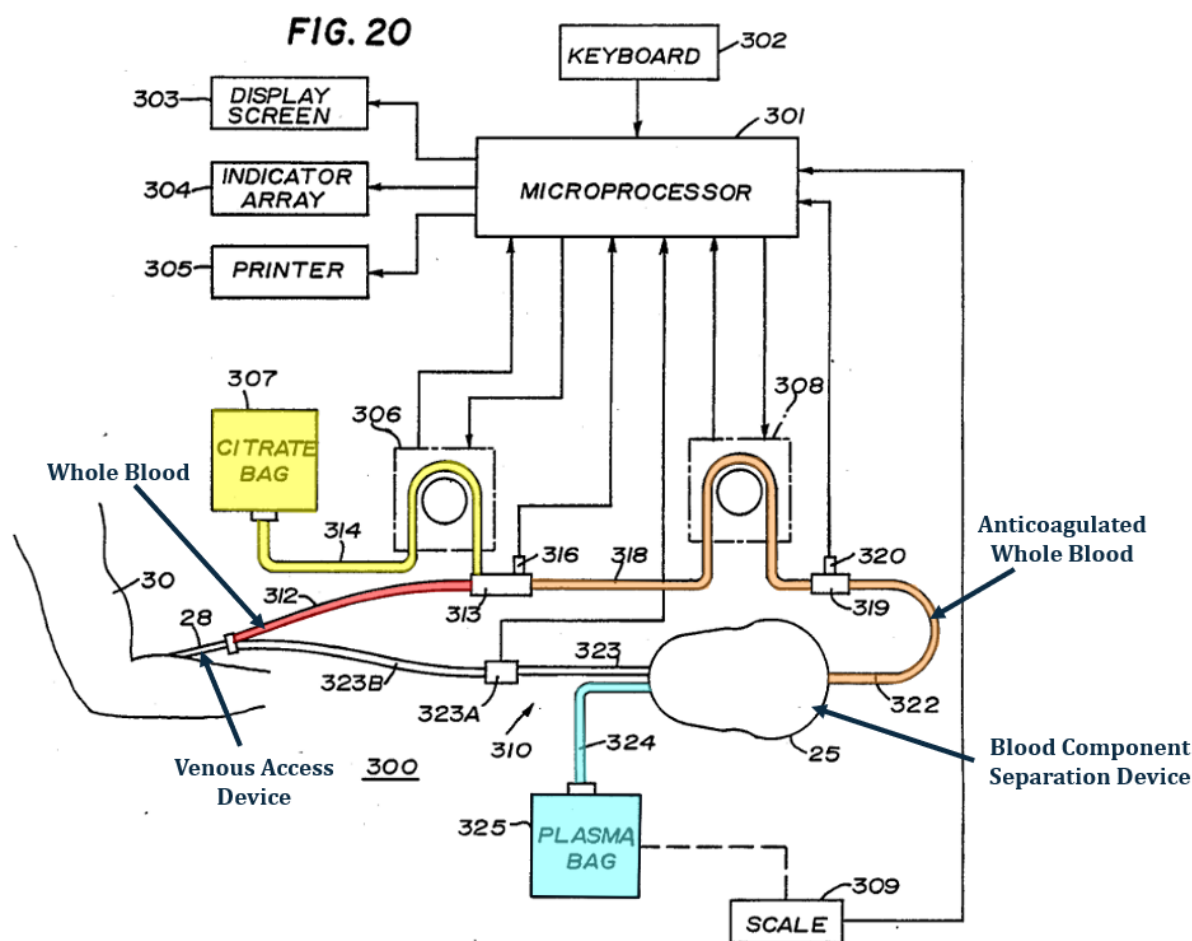
102. The drawn blood is whole blood because it is a mixture of “a variety of blood fractions.” EX1005, 5:45.

103. The draw line is connected to blood fractionator 25, as “[t]he blood fractionator has an inlet ..., the inlet being connected to the donor by a blood tube.” EX1005, 5:13-16, FIGS. 1, 20.

104. Blood fractionator 25 is a blood component separation device because “it produces a variety of blood fractions” from whole blood, “plasma [being] one of the most important blood fractions.” EX1005, 5:42-45.

h. 1[g] introducing anticoagulant into the withdrawn whole blood through an anticoagulant line at a predetermined ratio of anticoagulant to whole blood;

105. In Lavender’s automated blood fractionation system, “[a] supply of anticoagulant 35 is connected to the tube 27” supplying withdrawn whole blood from the donor. EX1005, 5:22-28, FIGS. 1, 20. “[A] second pump 31A ...provide[s] a predetermined flow rate ... of anticoagulant with the blood flowing from the donor 30 to the fractionator” via anticoagulant line 314. EX1005, 5:22-28, FIGS. 1, 20 (tube 314).



EX1004, FIG. 20 (annotated).

106. In Lavender's system, anticoagulant is added to the withdrawn whole blood at a predetermined ratio of anticoagulant to whole blood to achieve a predetermined ratio of plasma to anticoagulant to dilute incoming plasma to 68% of its initial concentration. EX1005, 22:35-41, 41:4-44:42. Specifically, the plasma flow (QP) is determined using the donor's hematocrit ($HCTD$) and the incoming blood flow (QB), and then the plasma flow (QP) is multiplied by a conversion factor (CF) to determine the citrate (an anticoagulant) flow (QC). EX1005, 22:35-41, 41:4-

44:42. Thus, the anticoagulant is provided to the incoming whole blood at a predetermined ratio of anticoagulant flow (QC) to incoming whole blood (QB) that dilutes the incoming plasma in the whole blood to 68% of its initial concentration. EX1005, 22:35-41, 41:4-44:42.

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

107. The whole blood drawn from the donor flows into Lavender's blood fractionator 25, which separates it into blood fractions (components), including a plasma component and a component containing red blood cells, white blood cells, and platelets. EX1005, 1:21-25, 5:42-52, 10:58-11:6, FIGS. 1, 20.

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

108. Lavender discloses that after the blood components are separated within the fractionator, "a plasma outlet port ... allows plasma to flow to a plasma collection bag" via tubing (e.g., tubing 324 in FIG. 20). EX1005, 10:58-11:6; FIGS. 1, 4, 15, 17, 20.

- k. **1[j] continuing steps (f) through (i) until the target collection volume is reached in the plasma collection container.**

109. As discussed above, Lavender performs steps (f) – (i). See §§X.A.2.g-j.

110. In response to the start of a blood separation procedure using Lavender's automatic system, the system initializes the system algorithm of Table VI. EX1005, 20:55-68, 41:1-44:33, Figs. 25A-25D. The Main Loop of the algorithm repeats until a desired amount of plasma has been collected, such as the determined target pure plasma collection volume (***MAXPF***).⁵ EX1005, 21:62-22:2.

111. For example, Lavender repeats step (f)-(i) by "introducing anticoagulant to the blood from which the plasma is to be collected ... separating plasma from the extracted blood ... until a predetermined ... volume of plasma has been collected." EX1005, 21:62-22:6; 46:14-22; *see also* claim 1.

112. Lavender's main loop algorithm repeats until the total plasma collected within the plasma collection container (*TPF*) is equal or greater than the target volume of pure plasma to collect (*MAXPF*). *See* EX1005, 22:35-41, 41:4-44:42, Table VI: §5.C.

113. With this understanding and as discussed in detail above, in my opinion, a POSITA would be motivated to incorporate calculations from Fletcher-Haynes into Lavender's system to determine a target volume of pure plasma (*new MAXPF*) based on a calculated volume of anticoagulant to collect (*new MAXCF*) to utilize

⁵ All emphasis added unless otherwise noted.

both (i) the donor's weight and (ii) the donor's hematocrit in determining the target volume of pure plasma. See §X.A.2.d-e.

114. Specifically, in my opinion, a POSITA would look to Fletcher-Haynes to improve the determination of the volume of anticoagulant to be collected in Lavender. After using Fletcher-Haynes' calculations to determine a target volume of anticoagulant to be collected within the plasma collection bag based on the donor's hematocrit, a POSITA would be motivated to determine a new target volume of pure plasma to collect (*new MAXPF*) by subtracting the *new MAXCF* (based on the donor's hematocrit) from Lavender's *MAXDPF* (based on the donor's weight) (e.g. $\text{new MAXPF} = \text{MAXDPF} - \text{new MAXCF}$). See §X.A.2.d-e; EX1005, 22:35-41, 41:4-44:42. This determination of *new MAXPF* is equivalent to the target collection, and Lavender's main loop algorithm may be repeated, and a plasma apheresis procedure continued, using Lavender's system 300 until *new MAXPF* is reached in the plasma collection container.

3. Claim 2: A method according to claim 1, wherein the target collection volume is the calculated volume of pure plasma.

115. I note that claim 2 requires, through its dependency from claim 1, the target collection volume be based, at least in part, on the calculated volume of anticoagulant and the calculated volume of pure plasma. Also, claim 2 requires the target collection volume be the calculated volume of pure plasma. I note "the

calculated volume of pure plasma” lacks antecedent basis in both claims 1 and 2.

For the purposes of this Declaration, I assume the calculated volume of pure plasma refers to the calculated target volume of pure plasma.

116. As discussed in §§X.A.2.d-e, in my opinion, a POSITA would be motivated to incorporate calculations from Fletcher-Haynes into Lavender’s system to determine a target volume of pure plasma, based on a calculated volume of anticoagulant to collect, to utilize the donor’s hematocrit and weight in determining the target volume of pure plasma. See §X.A.2.d-e.

117. Specifically, in my opinion, a POSITA would look to Fletcher-Haynes to improve both (i) the determination of the volume of anticoagulant to be collected in Lavender and (ii) the determination of the volume of pure plasma to be collected in Lavender. After utilizing the calculations from Fletcher-Haynes to determine a target volume of anticoagulant to be collected within the plasma collection bag based on the donor’s hematocrit, a POSITA would be motivated to determine a new target volume of pure plasma to collect (*new MAXPF*) by subtracting the *new MAXCF* determined based on the donor’s hematocrit from the *MAXDPF* in Lavender determined based on the donor’s weight (e.g. $new\ MAXPF = MAXDPF - new\ MAXCF$). See §X.A.2.d-e; EX1005, 22:35-41, 41:4-44:42. This determination of *new MAXPF* is equivalent to the target collection volume of claim 2, and utilizes

both the donor's hematocrit and weight, compared to utilizing just the donor's weight as described in Lavender.

4. Claim 3: A method according to claim 1, wherein the target collection volume is the calculated volume of pure plasma plus the calculated volume of anticoagulant.

118. Lavender's system monitors the total volume of dilute plasma (*TDPF*), a mixture of pure plasma and anticoagulant, collected during a procedure by measuring the weight of the plasma collection container with a scale and converting the weight using a specific gravity constant (*SGDP*). EX1005, 16:50-53, Table VI §§1.g., 1.i., and 5.B.

119. In my opinion, a POSITA would be motivated to set a target collection volume of dilute plasma compared to a target collection volume of pure plasma in Lavender's system to provide additional options to a user. For example, the FDA established guidelines regarding how much plasma any individual donor can donate which provides a maximum plasma volume to collect and a maximum dilute plasma volume (i.e. plasma and anticoagulant) to collect for specific donor weight ranges. See EX1009. To allow a user to select between these options for target collection volumes, a POSITA would be motivated to modify Lavender's main loop algorithm to set a target collection volume as a target dilute plasma volume instead of a target pure plasma volume.

120. Furthermore, Fletcher-Haynes defines a target collect volume (V_{SPB}) as

a target volume of dilute plasma for a procedure. See EX1004, 23:39-41; 48:32-65; 51:10-12; 52:14. Specifically, Fletcher-Haynes discusses establishing a plasma volume limit and defines plasma volume as “the volume of plasma collected during a procedure (plasma product volume plus anticoagulant volume).” See EX1004, 23:39-41; 48:32-65; 51:10-12; 52:14. Thus, a POSITA would be motivated to modify the Main Loop algorithm, specifically §5.C. of Table VI, in Lavender to compare *TDPF* with *MAXDPF* and stop the main loop algorithm when *TDPF* is equal to or greater than *MAXDPF*, setting the target collection volume to *MAXDPF*, the target volume of diluted plasma to collect. In my opinion, a POSITA would readily understand that *MAXDPF* is equal to *new MAXCF* plus *new MAXPF*.

5. Claim 4: A method according to claim 1, wherein the calculated volume of anticoagulant is further based, at least in part, on the predetermined ratio of anticoagulant.

121. Lavender calculates a volume of anticoagulant to be collected in the collected plasma component. See §X.A.2.d. Specifically, Lavender’s system determines the total volume of citrate, an anticoagulant, to collect (*MAXCF*) before starting a procedure based on the donor’s bodyweight and a predetermined constant (*C3*) derived from a predetermined ratio of plasma to anticoagulant used to dilute incoming plasma. EX1005, 20:46-54, 22:35-41, 41:1-44:42 (Table VI, §2(i)).

122. In my opinion, a POSITA would look to Fletcher-Haynes to improve Lavender’s determination of the anticoagulant volume of anticoagulant to collect.

See §X.A.2.d. Equation 15 in Fletcher-Haynes recites $f_{ACP} = [(R - 1)(H - 1)]^{-1}$ where f_{ACP} is anticoagulant expressed as a fraction of pure plasma volume, R is the ratio of the collective flow of anticoagulant and blood through the inlet line in relation to the flow of anticoagulant through the inlet line (i.e, the predetermined ratio of anticoagulant), and H is the donor's hematocrit. EX1005, 48:21-32, 50:16-52:14. Equation 17 in Fletcher-Haynes defines the target source plasma volume to collect in the collection container. EX1004, 48:54-62, 50:16-52:14. Equation 22 in Fletcher-Haynes recites $V_{SPB} = V_{SP}(1 + f_{ACP})$ where V_{SPB} is the total volume in the source plasma bag (including plasma and anticoagulant) and V_{SP} is the volume of pure plasma in the source plasma bag. EX1004, 50:16-52:14.

123. A POSITA would understand that the determined *MAXPF* in Lavender would be plugged in as V_{SP} into Fletcher-Haynes' Equation 22 to determine V_{SPB} , or a target total volume of dilute plasma to collect in a plasma collection bag (e.g., $V_{SPB} = MAXPF(1 + f_{ACP})$). The determined V_{SPB} using the *MAXPF* in Lavender would then be used to determine a target volume of anticoagulant to be collected within the plasma collection bag, or *new MAXCF*, by subtracting *MAXPF* from V_{SPB} (e.g., $new MAXCF = V_{SPB} - MAXPF$). Because V_{SPB} is determined using f_{ACP} and f_{ACP} is based on a predetermined ratio of anticoagulant (R), this series of Fletcher-Haynes equations, as implemented in Lavender, determines a target volume of anticoagulant to be collected within the plasma collection bag based, at least in

part, on a donor's hematocrit, as recited in claim 1, and further based, at least in part, on a predetermined ratio of anticoagulant, as required by claim 4.

6. Claim 6: A method according to claim 1, wherein calculating the volume of anticoagulant includes calculating the volume of anticoagulant before withdrawing whole blood.

124. Lavender calculates a volume of anticoagulant to be collected in the collected plasma component before withdrawing whole blood from a donor. Specifically, Lavender's system determines the total volume of citrate, an anticoagulant, to collect (*MAXCF*) before starting the collection procedure. See §X.A.2.d; EX1005, 20:46-54, 41:1-44:33 (Table VI, §2(i)). When equations from Fletcher-Haynes are used in Lavender's system, *new MAXCF* would be calculated before starting the collection procedure.

7. Claim 7: A method according to claim 1, wherein calculating the target volume of pure plasma includes calculating the target volume of pure plasma before withdrawing whole blood from the donor.

125. As discussed in §X.A.2.e, Lavender calculates a target volume of pure plasma to collect (*MAXPF*) when the system algorithm is initialized. This includes steps 2 and 3 set forth in Table VI, which relate to placing predetermined constants into the system algorithm and calculating pump rates for the blood and anticoagulant pumps. EX1005, 20:55-59, 41:4-44:42, Table VI, §2.g. This timing is also described in Message 43 in Table V that is displayed on Lavender's display as "PLEASE

WAIT FOR A FEW MOMENTS” while “variables are initialized.” EX1005, 35:37-40. When the internal calculations are finished, Message 44 is displayed instructing the user to insert a needle into the donor’s vein to start the procedure. EX1005, 35:35-45. When equations from Fletcher-Haynes are used in Lavender’s system, new MAXPF would be calculated before starting the collection procedure.

8. Claim 8

a. 8[preamble] A system for collecting plasma comprising:

126. Lavender discloses that its methods may be implemented in “a system for harvesting plasma.” EX1005, Abstract, 1:15-17, 1:45-47, FIGS. 1, 20.

b. 8[a] a venous-access device for drawing whole blood from a donor and returning blood components to the donor;

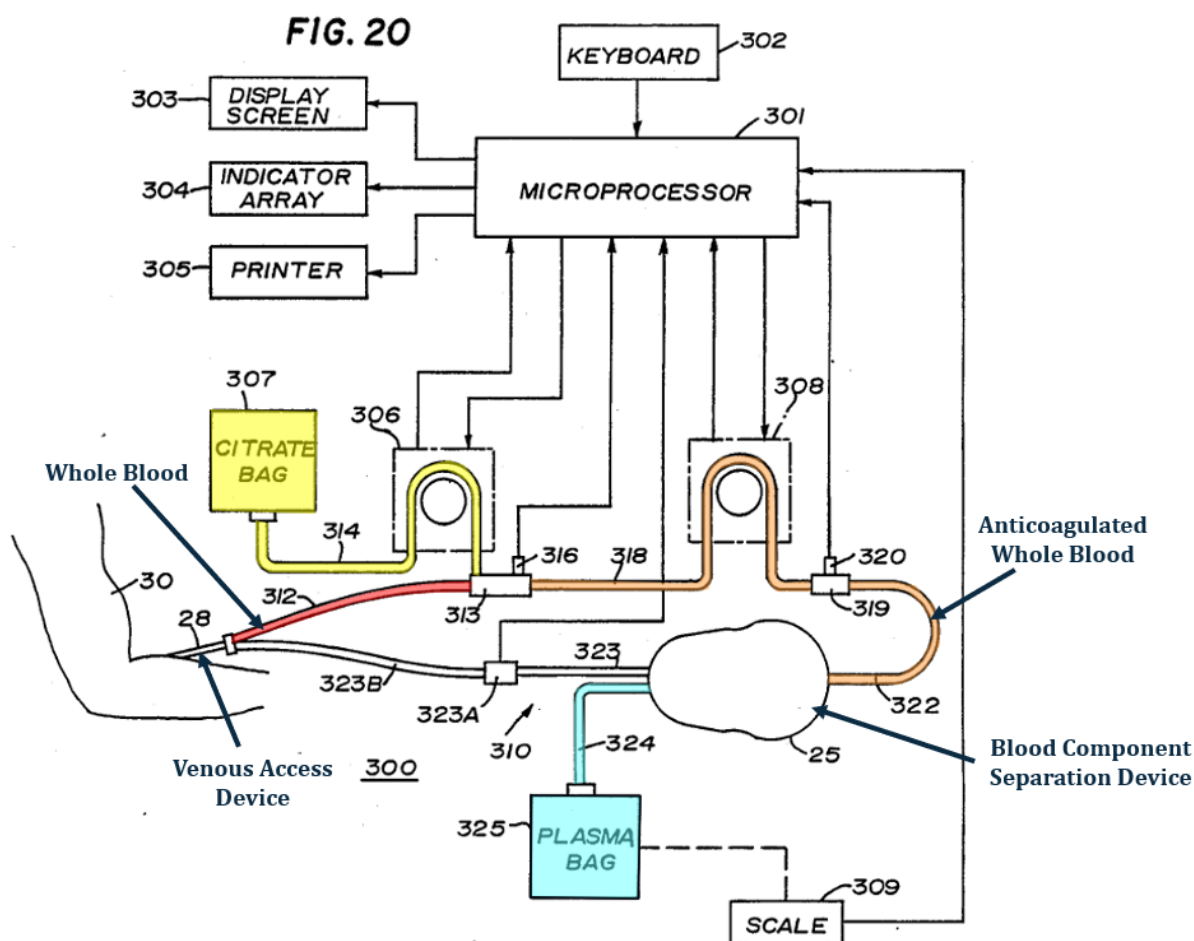
127. *See* §X.A.2.g, *supra*, EX1005, 5:13-22, Figs. 1, 20. Lavender withdraws whole blood through the venous-access device. A pump “pump[s] blood from the donor” through needle 28, tubes 312, 318, 322, and into blood fractionator 25, and returns blood components to the donor through tube 323, shown above in FIG. 20. EX1005, 5:18-22, FIG. 20.

c. 8[b] a blood component separation device for separating the drawn blood into a plasma component and a second blood component, the blood component separation device having an outlet and being configured to send the plasma component to a plasma container;

128. In Lavender, after whole blood is drawn from the donor, the whole blood flows into Lavender's blood fractionator 25, which separates the whole blood into blood fractions (components), including a plasma component and a component containing red blood cells, white blood cells, and platelets. EX1005, 1:21-25, 5:42-52, 10:58-11:6, FIGS. 1, 20. Lavender discloses that after the blood fractionator separates the components, "a plasma outlet port ... allows plasma to flow to a plasma collection bag" via tubing (e.g., tubing 324 in Fig. 20). EX1005, 10:58-11:6; FIGS. 1, 4, 15, 17, 20.

- d. 8[c] a blood draw line fluidly connected to the venous-access device and configured to transport drawn whole blood to the blood component separation device, the flow through the blood draw line being controlled by a blood draw pump;**

129. Lavender withdraws whole blood through the venous-access device. A pump "pump[s] blood from the donor" through needle 28, tubes 312, 318, 322, and into blood fractionator 25, shown below in FIG. 20. EX1005, 5:18-22, FIG. 20.



EX1005, FIG. 20 (annotated).

130. In Lavender, the blood drawn from needle 28 is whole blood because it is a mixture of “a variety of blood fractions.” EX1005, 5:44.

131. The draw line is connected to blood fractionator 25, as “[t]he blood fractionator has an inlet ..., the inlet being connected to the donor by a blood tube.” EX1005, 5:13-16, Figs. 1 and 20.

132. Blood fractionator 25 is a blood component separation device because “it produces a variety of blood fractions” from whole blood, “plasma [being] one of the most important blood fractions.” EX1005, 5:42-45.

- e. **8[d] an anticoagulant line connected to an anticoagulant source, the anticoagulant line configured to introduce anticoagulant into the drawn whole blood; and**

133. See §X.A.2.h, *supra*, EX1005, 5:22-28 and FIGS. 1, 20.

- f. **8[e] a controller configured to control the operation of the blood component separation device,**

134. See §X.A.1.d-f, *supra*, EX1005, 10:58-11:6; and FIGS. 1, 20. Lavender

recites:

The input and output pressures of the blood pump are sensed and inputted to a microprocessor, into which donor data including weight, sex, and hematocrit is also keyed by the user. The microprocessor operates under program control to calculate, based on the donor data, the amount of plasma to be collected and the amount of anticoagulant to be added. The program controls the operation of the extracorporeal devices, regulates the operating parameters, and stops the procedure when the predetermined amount of plasma has been obtained.

See EX1005, Abstract. This program control of the extracorporeal devices would include blood fractionator 25 (blood component separation device) and the associated fluid pumps. EX1005, 18:27-64; cls. 28, 29, 33, 35, 36, 38, 40-41. I note that “controller” and “control system” are used throughout the claims of the ’926 patent, and Lavender’s microprocessor 301 may correspond to the “controller” in the ’926 patent claims and system 300, and specifically display screen 303, indicator array 304, printer 305, keyboard 302, and microprocessor 301 together may correspond to the “control system” in the ’926 patent claims. EX1005, 16:34-17:28,

18:53-21:27, FIG. 20.

- g. 8[f] the controller configured to calculate (1) a volume of anticoagulant to be collected with plasma component in the plasma container, the volume of anticoagulant to be collected with the plasma component based, at least in part on the hematocrit of the donor,**

135. See §X.A.2.d, *supra*, EX1004, 48:21-62, 50:16-52:14; EX1005, 10:58-11:6; FIGS. 1, 20.

136. I note that system 300's microprocessor executes the algorithms detailed in Table VI of Lavender, which would include calculating the volume of anticoagulant to be collected in the plasma component, based, at least in part on the hematocrit of the donor. EX1005, 18:53-56.

- h. 8[g] (2) a target volume of pure plasma to collect in the plasma container based, at least in part, on the weight of the donor, and**

137. See §X.A.2.e, *supra*, EX1005, 22:35-41, 41:4-44:42.

- i. 8[h] (3) a target collection volume based, at least in part, on the calculated volume of anticoagulant and the calculated volume of pure plasma,**

138. See §X.A.2.f, *supra*, EX1005, 22:35-41, 41:4-44:42.

- j. 8[i] the system configured to stop the blood draw pump when the target collection volume is collected within the plasma container.**

139. See §X.A.2.k, *supra*, EX1005, 21:62-22:6; 46:14-22; *see also* claim 1.

9. Claim 9: A system according to claim 8, wherein the target collection volume is the calculated volume of pure plasma.

140. I note that claim 9 requires, through its dependency from claim 8, the target collection volume be based, at least in part, on the calculated volume of anticoagulant and the calculated volume of pure plasma. Also, claim 9 requires the target collection volume to be the calculated volume of pure plasma. I note “the calculated volume of pure plasma” lacks antecedent basis in both claims 1 and 9. I assume the calculated volume of pure plasma refers to the calculated target volume of pure plasma.

141. See §X.A.3, *supra*, EX1005, 22:35-41, 41:4-44:42. After utilizing Fletcher-Haynes’ calculations to determine a target volume of anticoagulant to be collected within the plasma collection bag based on the donor’s hematocrit, a POSITA would be motivated to determine a new target volume of pure plasma to collect (*new MAXPF*) by subtracting the *new MAXCF*, determined based on the donor’s hematocrit, from Lavender’s *MAXDPF*, determined based on the donor’s weight, (e.g. $new\ MAXPF = MAXDPF - new\ MAXCF$). See §X.A.2.d-e; EX1005, 22:35-41, 41:4-44:42. This calculation of *new MAXPF* utilizes an additional donor parameter, the donor’s hematocrit, compared to only using the donor’s weight to determine the target collection volume.

10. Claim 10: A system according to claim 8, wherein the target collection volume is the calculated volume of pure plasma

**plus the calculated volume of anticoagulant to be collected
in the plasma container.**

142. See §X.A.4, *supra*, EX1005, 16:50-53, Table VI §§1.g., 1.i., and 5.B;.

**11. Claim 11: A system according to claim 8, wherein the
volume of anticoagulant to be collected within the plasma
container is further based, in least in part, on the
predetermined ratio of anticoagulant.**

143. See §X.A.5, *supra*, EX1005, 20:46-54, 22:35-41, 41:1-44:42 (Table VI,
§2(i)).

**12. Claim 13: A system according to claim 8, wherein the
controller is configured to calculate the volume of
anticoagulant before withdrawing whole blood from the
donor.**

144. See §X.A.6, *supra*, EX1005, 20:46-54, 35:35-45; 41:1-44:33 (Table VI,
§2(i)).

**13. Claim 14: A system according to claim 8, wherein the
controller is configured to calculate the target volume of
pure plasma before withdrawing whole blood from the
donor.**

145. See §X.A.7, *supra*, EX1005, 20:46-54, 35:35-45; 41:1-44:33 (Table VI,
§2(i)).

14. Claim 15

**a. 15[preamble] A method for programming a blood
component processing device:**

146. Lavender discloses a method for programming blood component processing device (e.g., “automated system 300 including a blood fractionating system 20”). EX1005, 16:34-53, 18:53-20:68, Figs. 25A-25C. Microprocessor 301 of system 300 operates under stored program control, and the program is menu-driven with the menu messages appearing on a display screen 303, with “various display messages which appear during the operation of the program, the possible user replies and the response of the system 300 to these replies are all set forth in Table V.” EX1005, 18:53-62, Table V, Fig. 20. Microprocessor 301 is programmed to control automated system 300 including blood fractionating system 20. EX1005, 18:53-62, Table V, Fig. 20.

b. 15[a] receiving, in a control system, a weight of a donor;

147. Lavender’s system, and specifically Lavender’s “control system” (e.g. microprocessor 301, keyboard 302, display screen 303, indicator array 304), receives a weight of the donor through “entry and validation of donor data, including ... donor weight in pounds.” EX1005, 20:10-14; *see also* EX1005 Abstract. The system’s program displays messages 32-36, which direct the user in entry and validation of donor data, including . . . , donor weight in pounds. . .” EX1005, 20:10-14.

```
MESSAGE 35
*****
* User enters donor weight and
* presses ENTER.
* ENTER DONOR WEIGHT IN LBS: * Value checked for upper and lower
* acceptable limits. If out of range
* GOTO Low_weight_error or High_weight_error.
***** If value okay GOTO Message 36.
```

EX1005, Table V, Message 35.

c. 15[b] receiving, in the control system, a hematocrit of the donor;

148. Lavender's system, and specifically Lavender's "control system" (microprocessor 301), receives a hematocrit of the donor through "entry and validation of donor data, including ... donor hematocrit." EX1005, 20:10-14; *see also* EX1005 Abstract. The system's program displays messages 32-36, which direct the user in entry and validation of donor data, including . . . , donor hematocrit. . . ." EX1005, 20:10-14, Abstract.

```
MESSAGE 34
*****
* User enters donor's hematocrit value.
* When ENTER pressed check value for
* lower limits of male and female.
* ENTER DONOR HEMATOCRIT (PER CENT): * If less than 38 and female GOTO Crit_error_female.
* If less than 41 and male GOTO Crit_error_male.
***** If value okay GOTO Message 35.
```

EX1005, Table V, Message 34.

d. 15[c] calculating, using the control system, a volume of anticoagulant to be collected with a plasma component in a plasma collection container of the blood component processing device, the control system calculating the volume of anticoagulant to be collected with the plasma component based, at least in part on the hematocrit of the donor;

149. See §X.A.2.d, *supra*, EX1004, 48:21-62, 50:16-52:14; EX1005, 10:58-11:6; FIGS. 1, 20.

150. I note that system 300's microprocessor 301 executes the algorithms detailed in Table VI of Lavender. EX1005, 18:53-56. I note that "controller" is used throughout the claims of the '926 patent, and Lavender's microprocessor 301 may correspond to the "controller" in the '926 patent claims. EX1005, 16:34-17:28, 18:53-21:27, FIG. 20. I also note that "control system" is used throughout the claims of the '926 patent, and Lavender's system 300, and specifically display screen 303, indicator array 304, printer 305, keyboard 302, and microprocessor 301 together may correspond to the "control system" in the '926 patent claims. EX1005, 16:34-17:28, 18:53-21:27, FIG. 20.

- e. **15[d] calculating, using the control system, a target volume of pure plasma to collect in the plasma collection container, the control system calculating the target volume of pure plasma based, at least in part, on the weight of the donor;**

151. See §X.A.2.e, *supra*, EX1005, 22:35-41, 41:4-44:42.

- f. **15[e] determining a target collection volume based, at least in part, on the calculated volume of anticoagulant and the calculated volume of pure plasma; and**

152. See §X.A.2.f, *supra*, EX1005, 22:35-41, 41:4-44:42.

- g. **15[f] programming a controller of the blood component processing device with a blood processing**

**end point, the blood processing end point being based,
at least in part on the target collection volume.**

153. See §X.A.2.k, *supra*, EX1005, 21:62-22:6; 46:14-22; see also claim 1.

15. Claim 16: A method according to claim 15, wherein the target collection volume is the calculated volume of pure plasma.

154. See §X.A.3, *supra*, EX1005, 22:35-41, 41:4-44:42.

16. Claim 17: A method according to claim 15, wherein the target collection volume is the calculated volume of pure plasma plus the calculated volume of anticoagulant to be collected in the plasma collection container.

155. See §X.A.4, *supra*, EX1005, 16:50-53, Table VI §§1.g., 1.i., and 5.B.

17. Claim 18: A method according to claim 15, wherein the volume of anticoagulant to be collected within the plasma collection container is further based, in least in part, on a predetermined ratio of anticoagulant.

156. See §X.A.5, *supra*, EX1005, 20:46-54, 22:35-41, 41:1-44:42 (Table VI, §2(i)).

18. Claim 20: A method according to claim 15, the volume of anticoagulant to be collected with the plasma component in the plasma collection container is also based, at least in part, on a volume of anticoagulant to be added to the drawn whole blood.

157. See §X.A.5, *supra*, EX1005, 20:46-54, 22:35-41, 41:1-44:42 (Table VI, §2(i)). The constant *C3* in Lavender is defined as “ml citrate to be filtered/pound body weight” and is used to determine *MAXCF* by multiplying *C3* by the donor’s body weight *BW*. See EX1005, Table VI, §§1.l and 2.i. A POSITA would

understand from the definition of CF (conversion factor, ml citrate per ml plasma) that $C3 = C1 * CF$, i.e., (ml citrate to be filtered/pound of body weight) = (ml plasma collected/pound of body weight) * (conversion factor, ml citrate per ml plasma). A POSITA would therefore understand that $MAXCF = MAXPF * CF$. Lavender also determines the amount of anticoagulant to be added to the drawn whole blood, or citrate flow $QC = QP * CF$ from the plasma flow QP using the conversion factor CF , and the plasma flow $QP = QB * (1 - HCTD)$ is determined from the blood flow QB . Lavender therefore determines $MAXCF$, the volume of anticoagulant to be collected with the plasma component in the plasma collection container based, at least in part, on a volume of anticoagulant to be added to the drawn whole blood. See EX1005, Table VI, §§1.1.

19. Claim 21: A method according to claim 15, wherein the blood processing end point is when the target collection volume has been collected within the plasma collection container.

158. See §X.A.2.f-k, *supra*, EX1005, 22:35-41, 41:4-44:42.

20. Claim 22: A method according to claim 15, wherein the control system includes the controller.

159. See §X.A.14.b, *supra*, EX1005, 20:10-14.

160. Lavender's "control system" includes microprocessor 301, keyboard 302, display screen 303, indicator array 304, and potentially other components

shown in Fig. 20 or otherwise described. EX1005, 20:10-14. A POSITA would recognize that microprocessor 301 is equivalent to a controller.

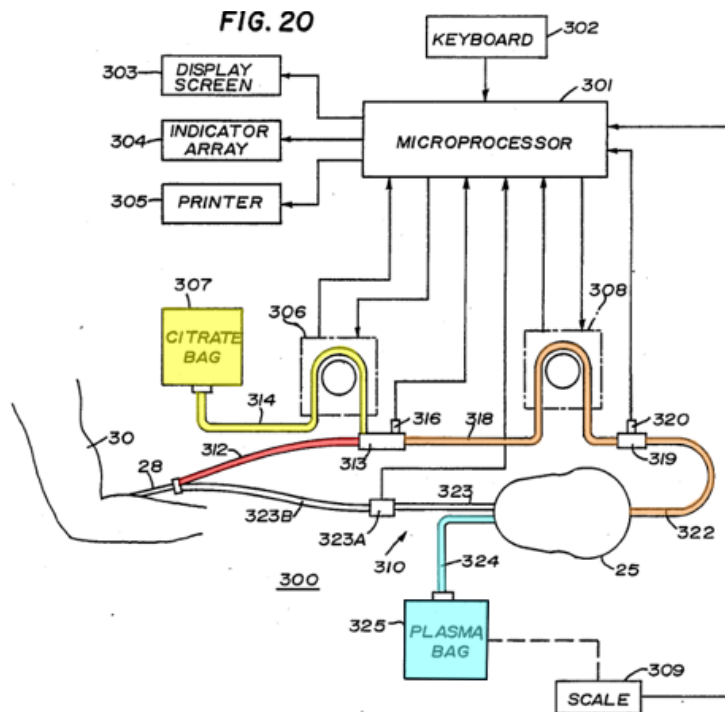
21. Claim 23

a. 23[preamble] A system for collecting plasma comprising:

161. See §X.A.8.a, *supra*, EX1005, Abstract, 1:15-17, 1:45-47, FIGS. 1, 20.

b. 23[a] a blood processing device including:

162. Lavender's system 300 is a blood processing device. EX1005, 16:34-53.



EX1005, Fig. 20 (annotated).

c. 23[b] a venous-access device for drawing whole blood from a donor and returning blood components to the donor,

163. See §X.A.8.b, *supra*, EX1005, 5:13-22, Figs. 1, 20.

- d. **23[c] a blood component separation device for separating the drawn blood into a plasma component and a second blood component, the blood component separation device having an outlet and being configured to send the plasma component to a plasma container,**

164. See §X.A.8.c, *supra*, EX1005, 1:21-25, 5:42-52, 10:58-11:6, FIGS. 1, 20.

- e. **23[d] a blood draw line fluidly connected to the venous-access device and configured to transport drawn whole blood to the blood component separation device, the flow through the blood draw line being controlled by a blood draw pump, and**

165. See §X.A.8.d, *supra*, EX1005, 5:18-22, FIG. 20.

- f. **23[e] an anticoagulant line connected to an anticoagulant source, the anticoagulant line configured to introduce anticoagulant into the drawn whole blood; and**

166. See §X.A.8.e, *supra*, EX1005, 5:22-28 and FIGS. 1, 20.

- g. **23[f] a controller configured to (1) calculate a volume of anticoagulant to be collected with plasma component in the plasma container, the volume of anticoagulant to be collected with the plasma component based, at least in part on a hematocrit of the donor,**

167. See §X.A.8.f-g, *supra*, EX1004, 48:21-62, 50:16-52:14; EX1005, 10:58-11:6; FIGS. 1, 20.

- h. 23[g] (2) calculate a target volume of pure plasma to collect in the plasma container based, at least in part, on a weight of the donor, and**

168. See §X.A.8.h, *supra*, EX1005, 22:35-41, 41:4-44:42.

- i. 23[h] (3) calculate a target collection volume based, at least in part, on the calculated volume of anticoagulant and the calculated volume of pure plasma.**

169. See §X.A.8.h, *supra*, EX1005, 22:35-41, 41:4-44:42.

- 22. Claim 24: The system according to claim 23, wherein the blood processing device is configured to stop the blood draw pump when the target collection volume is collected within the plasma container.**

170. See §X.A.8.j, *supra*, EX1005, 21:62-22:6; 46:14-22; *see also* claim 1.

- 23. Claim 25: The system according to claim 23, wherein the controller is part of the blood processing device.**

171. See §X.A.8.f, *supra*, EX1005, 10:58-11:6; and FIGS. 1, 20.

Microprocessor 301 in Lavender is part of system 300, a blood processing device.

EX1005, 16:34-53.

- 24. Claim 26: The system according to 23, wherein the controller is further configured to program the blood processing device with an end point based, at least in part, on the target collection volume.**

172. See §X.A.2.k, *supra*, EX1005, 21:62-22:6; 46:14-22; *see also* claim 1.

- 25. Claim 27: A system according to claim 23, wherein the target collection volume is the calculated volume of pure plasma and/or the calculated volume of pure plasma plus**

the calculated volume of anticoagulant to be collected in the plasma container.

173. See §X.A.3-4, *supra*, EX1005, 22:35-41, 41:4-44:42, 16:50-53, Table VI §§1.g., 1.i., and 5.B.

26. Claim 28: A system according to claim 23, wherein the volume of anticoagulant to be collected within the plasma container is further based, at least in part, on a predetermined ratio of anticoagulant.

174. See §X.A.5, *supra*, EX1005, 20:46-54, 22:35-41, 41:1-44:42 (Table VI, §2(i)).

27. Claim 30: A system according to claim 26, wherein the end point is when the target collection volume has been collected within the plasma container.

175. See §X.A.2.f-k, *supra*, EX1005, 22:35-41, 41:4-44:42.

B. Ground II: Claims 5, 12, 19, and 29 are rendered obvious over Lavender in view of Fletcher-Haynes and Min

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

176. In my opinion, a POSITA would have been motivated to combine the teachings of Lavender and Fletcher-Haynes with Min and a POSITA would understand that there is a reasonable expectation of success in making this modification because 1) all three relate to the same well-known technologies, 2) all three apply substantially similar techniques to achieve similar results, and 3) the

functionality of Lavender and Fletcher-Haynes would not change in the proposed combination. EX1006, 11:52-55, 17:17-22.

177. Lavender, Fletcher-Haynes, and Min all relate to separating blood components. Lavender, Fletcher-Haynes, and Min also apply substantially similar techniques to achieve similar results. As discussed above, Lavender discloses fractionating blood “to collect blood substances, such as plasma.” EX1005, 1:12-13. Fletcher-Haynes discloses a blood collection system for separating blood into components, such as plasma and other blood components. EX1004, 48:29-31; 52:13. Similarly, Min discloses a system for “separating whole blood into plasma and red blood cells.” EX1006, 4:26-29. Further, Lavender and Fletcher-Haynes disclose monitoring total citrate flow (*TQC* in Lavender and *QAC* in Fletcher-Haynes) from an anticoagulant bag. This is a similar purpose as Min’s system, which monitors both (i) blood and anticoagulant pump flow rates and (ii) the weight of an anticoagulant bag in an apheresis procedure to determine a change in volume within the anticoagulant container. EX1006, 11:52-55, 17:17-22. Specifically, Min uses weigh sensors 246 to track weight changes and derive fluid processing volumes, including the volume change of anticoagulant container 276 and plasma collection container 304. EX1006, 11:52-55, 17:17-22.

178. Thus, in my opinion, Lavender, Fletcher-Haynes, and Min all entail the mere use of known solutions to improve similar systems and methods in the same

way, i.e., to use Min's technique of monitoring the weight of an anticoagulant bag to determine a volume of anticoagulant provided to whole blood prior to separation of blood components.

179. A POSITA would have been motivated to add Min's system to monitor the weight (and volume) of an anticoagulant bag to Lavender's blood fractioning system to provide an additional way to determine the amount of anticoagulant in the plasma collection container, and Min's disclosed systems for determining the amount of anticoagulant added to a system function substantially similar to Lavender's blood separation system. Indeed, Min's anticoagulant container and tube arrangement (*See* Fig. 10) is structurally similar to that of Lavender's (*See* Fig. 20). EX1006, 3:26-29. Therefore, it would have been obvious, and a POSITA would have been motivated, to modify Lavender's blood fractioning system to incorporate Min's monitoring of the change in the weight of the anticoagulant container. Additionally, it would have been an obvious design choice to use Min's anticoagulant monitoring scale in Lavender's system to improve the accuracy of determining the anticoagulant volume added to the system.

180. In my opinion, if Patent Owner argues that Lavender's fractionator 25, which comprises a series of membranes 75, is not as efficient at separating some blood components and that substantially all of the anticoagulant added to Lavender's blood fractionating system would not end up in the plasma collection container, it

would have been obvious for a POSITA to replace the membrane-based fractionator in Lavender with a centrifuge-based blood component collection device 18, like the one disclosed in Fletcher-Haynes. EX1005, 6:3-12; EX1004, 46:16-43. It was generally known in the art that a centrifuge-based blood separation device, as compared to a membrane-based blood separation device, provided a comparable treatment quality in a shorter time period. *See* EX1008, p. 135. A POSITA would have been motivated to combine Lavender's system with Fletcher-Haynes' centrifuge-based collection device to more efficiently separate plasma from a donor's blood and reduce the overall procedure time.

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

182. Therefore, in my opinion, a POSITA would understand that substantially all of the anticoagulant added to the Lavender-Fletcher-Haynes blood fractionating system would end up in the plasma collection container. It would have

been obvious to a POSITA to incorporate Min's technique of monitoring the change in volume of the anticoagulant container using a scale into the blood fractionating system of Lavender and Fletcher-Haynes to calculate the volume of anticoagulant in the collected plasma component based, at least in part, on the change in volume within the anticoagulant container. By adding this additional technique to determine the volume of anticoagulant in the plasma collection container, the system would reduce potential errors in determining the volume of anticoagulant due to blood and anticoagulant pump rate errors (*e.g.*, errors in pumps 306, 308 in Lavender). EX1005, FIG. 20.

183. Finally, the intended functionality of Lavender's blood fractionating system would not change when used for monitoring the anticoagulant weight similarly to Min's apheresis system. That is, in my opinion, a POSITA would have had a reasonable expectation of success in modifying the Lavender-Fletcher-Haynes blood fractionating system in view of Min to successfully determine how much anticoagulant from the anticoagulant container is added to the system. Additionally, Lavender discloses converting a change in weight to a change in volume using a specific gravity. Accordingly, a POSITA would understand that there is a reasonable expectation of success when modifying Lavender's algorithms to determine the volume of anticoagulant in the collected plasma using Fletcher-Haynes' centrifuge and Min's weight scale to monitor the change in anticoagulant volume.

2. Claim 5: A method according to claim 1, wherein the calculated volume of anticoagulant includes at least a portion of the anticoagulant to be introduced into the withdrawn blood and at least a portion of a volume of anticoagulant to be added during a priming step.

184. The calculated volume of anticoagulant to be collected in the collected plasma component includes at least a portion of the anticoagulant introduced into the withdrawn whole blood. Lavender uses an anticoagulant pump in system 300 for pumping anticoagulant into the donor's whole blood before separating blood components. EX1005, 15:47-53, 16:54-17:2; claim 1; FIGS. 1, 20. At least a portion of the anticoagulant introduced in the withdrawn whole blood is collected in the plasma collection bag because anticoagulant is pumped "at a rate sufficient to dilute incoming plasma to 68% of the initial concentration," and this dilution rate is used to determine the volume of anticoagulant to be collected (e.g. *MAXCF*). See §X.A.2.d; EX1005, 22:37-39.

185. The calculated volume of anticoagulant to be collected in the collected plasma component also includes at least a portion of the anticoagulant added during a priming step. Lavender discloses a priming step, e.g., "[t]he citrate bag 307 is then unclamped, and the system operates the citrate pump 306 to drive citrate to purge air from the tubes 312 and 314 [of system 300]." EX1005, 20:37-48. Min discloses that during the priming step, "the anticoagulant pump PP4 conveys a predetermined volume of anticoagulant (e.g., 10g) into the in-process container 312" where plasma

is collected. EX1006, 22:40-42. Thus, at least a portion of the volume of anticoagulant in the collected plasma component (e.g., the plasma bag 325) would include at least a portion of the anticoagulant added during the priming step described above.

186. A POSITA, in my opinion, would have been motivated to combine the teachings of Lavender and Fletcher-Haynes with Min for the same reasons as discussed above. §X.B.1. Additionally, a POSITA would have looked to Min to calculate the volume of anticoagulant added during the priming step in the total collection volume and adjust to determination of *MAXCF* to include the anticoagulant added during the priming step, to reduce any errors that may occur by not accounting for such a priming step in determining the anticoagulant volume in the plasma collection container. A POSITA would recognize that the volume of anticoagulant added during the priming step would need to be added to the determined *MAXCF* in the centrifuge-based system of Lavender-Fletcher-Haynes, to account for this additional volume of anticoagulant in the plasma collection container.

3. **Claim 12: A system according to claim 8, wherein the volume of anticoagulant to be collected in the collected plasma component includes at least a portion of the anticoagulant to be introduced into the withdrawn blood and at least a portion of a volume of anticoagulant to be added during a priming step.**

187. See §X.B.1, *supra*, EX1005, 20:37-48; EX1006, 22:40-42.

4. **Claim 19: A method according to claim 15, wherein the volume of anticoagulant to be collected in the collected plasma component includes at least a portion of the anticoagulant to be introduced into the withdrawn blood and at least a portion of a volume of anticoagulant to be added during a priming step.**

188. See §X.B.1, *supra*, EX1005, 20:37-48; EX1006, 22:40-42.

5. **Claim 29: A system according to claim 23, wherein the volume of anticoagulant to be collected in the collected plasma component includes at least a portion of the anticoagulant to be introduced into the withdrawn blood and at least a portion of a volume of anticoagulant to be added during a priming step.**

189. See §X.B.1, *supra*, EX1005, 20:37-48; EX1006, 22:40-42.

XI. Availability for Cross-Examination

190. 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.

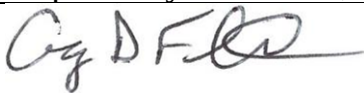
XII. Right to Supplement

191. 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.

XIII. Jurat

192. 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.

Dated:	Respectfully submitted,
October 17, 2025	
	Gary D. Fletcher, Ph.D.