

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

TERUMO BCT INC.,

Petitioner

v.

HAEMONETICS CORP.,

Patent Owner

PGR2026-00009

U.S. Patent No. 12,324,873

**DECLARATION OF GARY D. FLETCHER, PH.D. IN SUPPORT OF
PETITION FOR POST GRANT REVIEW OF U.S. PATENT NO. 12,324,873**

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.....	9
	A. Claim Construction.....	9
	B. Anticipation	10
	C. Obviousness.....	11
	D. Patent Eligible Subject Matter.....	14
	E. Specification Requirements.....	14
	F. Indefiniteness.....	15
	G. Enablement Requirement	16
VI.	Level Of Ordinary Skill.....	17
VII.	BACKGROUND ON PLASMA APHERESIS	17
VIII.	'873 Patent Overview	21
	A. The '873 Patent is Directed to Plasma Apheresis	21
	B. The '873 Patent's Purported Invention	23
IX.	Prior Art Overview	26
	A. Overview of Lavender.....	26
	B. Overview of Fletcher-Haynes	32
	C. Overview of Min	35
	A. Overview of Barrett.....	36
	B. Overview of Headley.....	37
	C. Overview of Turgut	37
X.	Detailed Grounds Explanation.....	37
	A. Ground 1: Claims 1-5, 7, 8, 10-17, and 19-23 are anticipated and/or rendered obvious by Lavender.....	38
	1. Claim 1	38

Declaration of Dr. Gary Fletcher in Support of Petition for
Post Grant Review of U.S. Patent No. 12,324,873
PGR2026-00009

2. Claim 2: A method according to claim 1, further comprising calculating a percentage of anticoagulant in the collected plasma component.....45
3. Claim 3: A method according to claim 2, wherein the calculated percentage of anticoagulant in the collected plasma component is based, at least in part, on the ratio of anticoagulant added to the withdrawn whole blood, and the hematocrit of the donor.....47
4. Claim 4: A method according to claim 2, wherein the calculated volume of pure plasma collected within the plasma collection container is based, at least in part, on the calculated percentage of anticoagulant in the collected plasma component.....47
5. Claim 5: A method according to claim 1, further comprising: calculating a volume of anticoagulant in the collected plasma component based, at least in part, upon the hematocrit of the donor, the calculated volume of pure plasma collected within the plasma collection container based, at least in part, on the calculated volume of anticoagulant in the collected plasma component.48
6. Claim 7: A method according to claim 1, further comprising: monitoring the volume of plasma component collected within the plasma collection container.....56
7. Claim 8: A method according to claim 1, further comprising: monitoring a weight of plasma component collected within the plasma collection container, the calculated volume of pure plasma collected within the plasma collection container based, at least in part, on the monitored weight of collected plasma component.56
8. Claim 10: A method according to claim 1, further comprising: continuing steps (b) through (f) to collect a target volume of pure plasma and/or a target volume of plasma component within the plasma collection container.56
9. Claim 11: A method according to claim 10, wherein the target volume of pure plasma and/or the target volume of

Declaration of Dr. Gary Fletcher in Support of Petition for
Post Grant Review of U.S. Patent No. 12,324,873
PGR2026-00009

	plasma component is based, at least in part, on a weight of the donor.	57
10.	Claim 12: A method according to claim 10, further comprising: returning, after collecting at least a portion of the target volume of pure plasma and/or the target volume of plasma component, the second blood component to the donor through a return line.	57
11.	Claim 13.....	58
12.	Claim 14: A system according to claim 13, wherein the controller is further configured to calculate a percentage of anticoagulant in the collected plasma component.	60
13.	Claim 15: A system according to claim 14, wherein the calculated percentage of anticoagulant in the collected plasma component is based, at least in part, upon the ratio of anticoagulant added to the withdrawn whole blood, and the hematocrit of the donor.	60
14.	Claim 16: A system according to claim 14, wherein the calculated volume of pure plasma collected within the plasma collection container is based, at least in part, on the calculated percentage of anticoagulant in the collected plasma component.....	60
15.	Claim 17: A system according to claim 13, wherein the controller is further configured to calculate a volume of anticoagulant in the collected plasma component based, at least in part, upon the hematocrit of the subject, the volume of pure plasma collected within the plasma collection container based, at least in part, upon the volume of anticoagulant in the collected plasma component.	61
16.	Claim 19: A system according to claim 13, wherein the controller is configured to monitor the operation of an anticoagulant pump to determine a total volume of anticoagulant introduced into the system.....	61
17.	Claim 20: A system according to claim 13, further comprising: a plasma collection container weight sensor configured to monitor the volume of plasma component collected within the plasma collection container.....	62

Declaration of Dr. Gary Fletcher in Support of Petition for
Post Grant Review of U.S. Patent No. 12,324,873
PGR2026-00009

18.	Claim 21: A system according to claim 13, further comprising: a plasma collection container weight sensor configured to monitor a weight of plasma component collected within the plasma collection container, the calculated volume of pure plasma collected within the plasma collection container based, at least in part, on the monitored weight of collected plasma component.	62
19.	Claim 22: A system according to claim 13, wherein the controller is configured control the plasma collection process to collect a target volume of pure plasma and/or a target volume of plasma component within the plasma collection container.	63
20.	Claim 23: A system according to claim 22, wherein the target volume of pure plasma and/or the target volume of plasma component is based, at least in part, on a weight of the subject.	63
B.	Ground 2: Claims 1 and 24-30 are obvious over Lavender in view of Fletcher-Haynes	63
1.	Claim 1	63
2.	Claim 24	69
3.	Claim 25: A system according to claim 24, wherein the controller is configured to control the plasma collection process to collect a target volume of pure plasma and/or target volume of plasma component.	74
4.	Claim 26: A system according to claim 25, wherein the target volume of pure plasma and/or target volume of plasma component is based, at least in part, on a weight of the subject.	75
5.	Claim 27: A system according to claim 24, wherein the controller is configured to calculate a percentage of anticoagulant to be collected in the plasma component.	75
6.	Claim 28: A system according to claim 27, wherein the calculated percentage of anticoagulant to be collected in the plasma component is based, at least in part, upon the ratio	

Declaration of Dr. Gary Fletcher in Support of Petition for
Post Grant Review of U.S. Patent No. 12,324,873
PGR2026-00009

	of anticoagulant to be added to the withdrawn whole blood and the hematocrit of the donor.	75
7.	Claim 29: A system according to claim 27, wherein the calculated volume of pure plasma to be collected within the plasma collection container is based, at least in part, on the calculated percentage of anticoagulant to be collected in the plasma component.....	76
8.	Claim 30: A system according to claim 24, wherein the controller is further configured to calculate a volume of anticoagulant to be collected in the collected plasma component based, at least in part, upon the hematocrit of the subject, the volume of pure plasma to be collected within the plasma collection container based, at least in part, upon the volume of anticoagulant to be collected in the collected plasma component.....	76
C.	Ground 3: Claims 6 and 18 are obvious over Lavender in view of Fletcher-Haynes and Min.....	78
1.	Claim 6: A method according to claim 5, further comprising: determining a change in volume within an anticoagulant container, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the change in volume within the anticoagulant container.	78
2.	Claim 18: A system according to claim 17, further comprising: an anticoagulant source weight sensor configured to measure a weight of the anticoagulant source, the controller further configured to monitor a change in volume within the anticoagulant source based on the measured weight of the anticoagulant source, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the change in volume within the anticoagulant source.....	83
D.	Ground 4: Claims 9 and 18 are obvious over Lavender in view of Fletcher-Haynes, Headley, and Barrett.....	84
1.	Claim 9: A method according to claim 1, further comprising: monitoring a volume of red blood cells	

Declaration of Dr. Gary Fletcher in Support of Petition for
Post Grant Review of U.S. Patent No. 12,324,873
PGR2026-00009

	collected within the blood component separation device, the hematocrit of the donor being determined based, at least in part, on the monitored volume of red blood cells collected within the blood component separation device and a volume of whole blood withdrawn from the donor.	84
2.	Claim 18: A system according to claim 11, an optical sensor located on the blood component separation device and configured to monitor a volume of red blood cells collected within the blood component separation device, the controller configured to determine the subject's hematocrit based, at least in part, upon on the monitored volume of red blood cells collected within the blood component separation device and a volume of whole blood withdrawn from the subject.	88
E.	Ground 5: Claims 4 and 15 are obvious over Lavender in view of Fletcher-Haynes, Min, and Turgut.....	89
1.	Claim 4: A method according to claim 1, further comprising: determining a volume of anticoagulant within the blood component separation device, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the volume of anticoagulant within the blood component separation device.....	89
2.	Claim 15: A system according to claim 11, an optical sensor located on the blood component separation device and configured to monitor the contents of the blood component separation device and determine if a volume of anticoagulant remains within the blood component separation device, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the volume of anticoagulant within the blood component separation device.....	91
F.	Ground V: All Claims of the '873 Patent Are Ineligible Under Section 101	92
G.	Ground VI: Claims 10, 11, 12, 22, 23, and 25 Lack an Adequate Written Description in the '873 Patent Specification	93
2.	Disclosure of the Purported Invention	93

Declaration of Dr. Gary Fletcher in Support of Petition for
Post Grant Review of U.S. Patent No. 12,324,873
PGR2026-00009

3.	Argument	95
XI.	Availability for Cross-Examination	97
XII.	Right to Supplement	97
XIII.	Jurat.....	97

Declaration of Dr. Gary Fletcher in Support of Petition for
Post Grant Review of U.S. Patent No. 12,324,873
PGR2026-00009

EXHIBIT LIST

Exhibit	Reference
1001	U.S. Patent No. 12,324,873 (“’873 patent”)
1002	File History of the ’873 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	U.S. Patent No. 9,370,324 (“Barrett”)
1009	U.S. Patent No. 6,296,602 (“Headley”)
1010	“Membrane versus centrifuge-based therapeutic plasma exchange: a randomized prospective crossover study,” Carsten Hafer et al., Int. Urol. Nephrol (2016) 48:133-138; Springer Science+Business Media Dordrecht 2015.
1011	U.S. Patent Publication No. 2017/0029762 (“Turgut”)
1012	“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.
1013	Bruce C. McLeod, MD, et al., “Apheresis: Principles and Practice,” 3rd Edition, AABB Press 2010.
1014	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
1015	Curriculum Vitae (“CV”) of Dr. Gary D. Fletcher
1016	U.S. Patent Publication No. 2012/0175313 (“Barry”)
1017	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 a post grant review (“PGR”) proceeding of U.S. Patent No. 12,324,873 (“the ’873 patent,” EX. 1001).
3. I have been asked by Petitioner’s counsel (“Counsel”) to provide my independent analysis and consideration of whether certain references teach or suggest the features recited in claims 1–30 (the “challenged claims”) of the ’873 patent. My opinions and the bases for my opinions are set forth below. My opinions are based on my education and experience.
4. In writing this Declaration, I have considered the following: my own knowledge and experience, including my teaching and work experience in the fields of blood sample collection and analysis, plasma apheresis equipment, and related technology; and my experience of working with others involved in those fields.
5. I am not, and never have been, an employee of Petitioner. I have no financial interest in either party or in the outcome of this proceeding. I am being compensated for my work as an expert on an hourly basis, for all tasks involved. My compensation is not dependent on the outcome of these proceedings or on the content

of my opinions. I will not receive any added compensation based on the outcome of any PGR, *inter partes* review, or other proceeding involving the '873 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 EX1015 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 EX1015.

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 spaces. That experience includes leading R&D and product development engineering teams of mechanical, electrical, optical, and software engineers. Among the positions described in my curriculum vitae, my industry experience includes engineering leadership role in 1996 in a company attempting to develop a noninvasive glucose measurement sensor. From 1996 to 2001, I led Engineering and Advanced Technology, including teams of optical, mechanical, electrical, software imaging, and clinical laboratory engineers, developing a noninvasive human complete blood count diagnostic device and diagnostic blood perfusion assessment tool, for a medical diagnostic startup company. As technical manager at Sarnoff Corporation from 2001 – 2004 I led a team developing and licensing a painless minimally invasive blood glucose monitor.

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 EX1015.

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 ’873 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 '873 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 '873 Patent (EX1001), the prosecution history (EX1002) of the '873 Patent, and the following materials:

- U.S. Patent No. 7,072,769 to Fletcher-Haynes *et al.* ("Fletcher-Haynes," EX1004);
- U.S. Patent No. 4,898,675 to Lavender ("Lavender," EX1005);

Declaration of Dr. Gary Fletcher in Support of Petition for
Post Grant Review of U.S. Patent No. 12,324,873
PGR2026-00009

- U.S. Patent No. 8,075,468 to Min (“Min,” EX1006);
- U.S. Patent Publication No. 2003/0125881 to Ryan (“Ryan,” EX1007);
- U.S. Patent No. 9,370,324 to Barrett (“Barrett,” EX1008);
- U.S. Patent No. 6,296,602 to Headley (“Headley,” EX1009);
- “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 (EX1010);
- U.S. Patent Publication No. 2017/0029762 to Turgut (“Turgut,” EX1011);
- “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. (EX1012);
- Bruce C. McLeod, MD, et al., “Apheresis: Principles and Practice,” 3rd Edition, AABB Press 2010. (EX1013);
- 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>

(EX1012);

- U.S. Patent Publication No. 2012/0175313 to Barry (“Barry,” EX1016).

16. I have considered these materials through the lens of a POSITA, which is discussed further in §§V and VI (below) related to the ’873 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 1-5, 7, 8, 10-17, and 19-23 are anticipated by and/or rendered obvious by Lavender alone;
- Claims 1 and 24-30 are obvious over Lavender in view of Fletcher-Haynes;
- Claims 6 and 18 are obvious over Lavender in view of Fletcher-Haynes and Min;
- Claims 9 and 18 are obvious over Lavender in view of Fletcher-Haynes, Headley, and Barrett;

- Claims 4 and 15 are obvious over Lavender in view of Fletcher-Haynes, Min, and Turgut;
- Claims 1-30 are not drawn to patentable subject matter; and
- Claims 10, 11, 12, 22, 23, and 25 lack written description.

V. LEGAL PRINCIPLES

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

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.

D. Patent Eligible Subject Matter

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

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

E. Specification Requirements

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

32. I understand that to satisfy the written description requirement, the specification must describe every claim limitation such that a person of ordinary

skill, reading the specification, would inherently, necessarily, or immediately envisage the claimed invention.

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

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

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

F. Indefiniteness

36. I understand that that a claim is indefinite if the claim, when read in light of the specification and the prosecution history, fails to inform those skilled in the art about the scope of the invention with reasonable certainty. I have further been

informed that when a claim term can refer to various different methods for determining a measurement or threshold, such term is indefinite if those methods are calculated in different ways that may yield materially different results when the claims, the specification, and the prosecution history do not indicate which method the claims cover.

G. Enablement Requirement

37. It is my understanding that a claimed invention is enabled if the specification does not contain a sufficiently full and clear description of how to make and use the full scope of the claimed invention. To be enabled, the patent must permit one of skill in the art to make and use the full scope of the claimed invention at the time of original filing without having to conduct undue experimentation. In deciding whether a person having skill in the art would have to experiment unduly in order to make and use of the invention, I understand several factors, known as the *Wands* factors, may be considered: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. I understand that no one or more of these factors alone is dispositive. Rather, whether the degree of experimentation required is undue

requires weighing these factors in the context of the claimed invention and the state of the art at the time of the original application.

VI. LEVEL OF ORDINARY SKILL

38. A person having ordinary skill in the art (“POSITA”) would have had, as of the earliest claimed filing date of May 30, 2017, a bachelor’s degree in biomedical engineering or a related field, such as physical sciences, physics, computer engineering, electrical engineering, or the like, and a minimum of two to three years of experience related to blood separation devices or blood processing devices. A higher level of education or specific skill might make up for less experience, and vice versa.

VII. BACKGROUND ON PLASMA APHERESIS

39. The ’873 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.

40. Plasmapheresis, also known as plasma exchange or therapeutic plasma exchange, has been a clinical procedure since the 1960s. EX1013, Chapter 1: Development of Apheresis Instrumentation. It selectively removes plasma and returns cellular components along with replacement fluid using centrifugation or

membrane filtration. EX1013. 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.

41. 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.

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

43. 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. EX1007. 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. EX1012.

44. At the time the '873 patent was filed, apheresis optimization techniques were well known in the art and routinely employed to improve donor safety, maximize plasma yield, and increase procedural efficiency. Clinicians and device manufacturers commonly utilized formulas based on donor-specific parameters—such as weight, height, body mass index, sex, and hematocrit—to estimate total

blood volume and determine safe and effective plasma collection volumes. EX1013, p. 52 (“Some instruments limit both dose rate and total citrate infused based on an estimate of subject blood volume calculated from sex, height, and weight,” p. 55, “Nomograms based on height, weight, and hematocrit are used to predict the consequences of volume removal [of plasma],” p. 99, “Flow rates are controlled by donor-specific data entered,” and Table 6-8 on p. 135, showing maximum plasma collection volumes based on donor sex and weight.) Plasmapheresis systems often incorporated fixed anticoagulant-to-anticoagulated-blood ratios (ACRs), typically between 1:8 and 1:16, and adjusted fluid flow rates accordingly to maintain proper anticoagulation while minimizing citrate-related adverse effects. EX1013, p. 129 (Table 6-3). Furthermore, advanced plasmapheresis systems used real-time sensor feedback (e.g., pressure, volume, optical detection) to dynamically monitor draw and return cycles¹, enabling adjustments to target volumes during the procedure.² Iterative recalculations of collection targets, particularly in multi-cycle procedures,

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

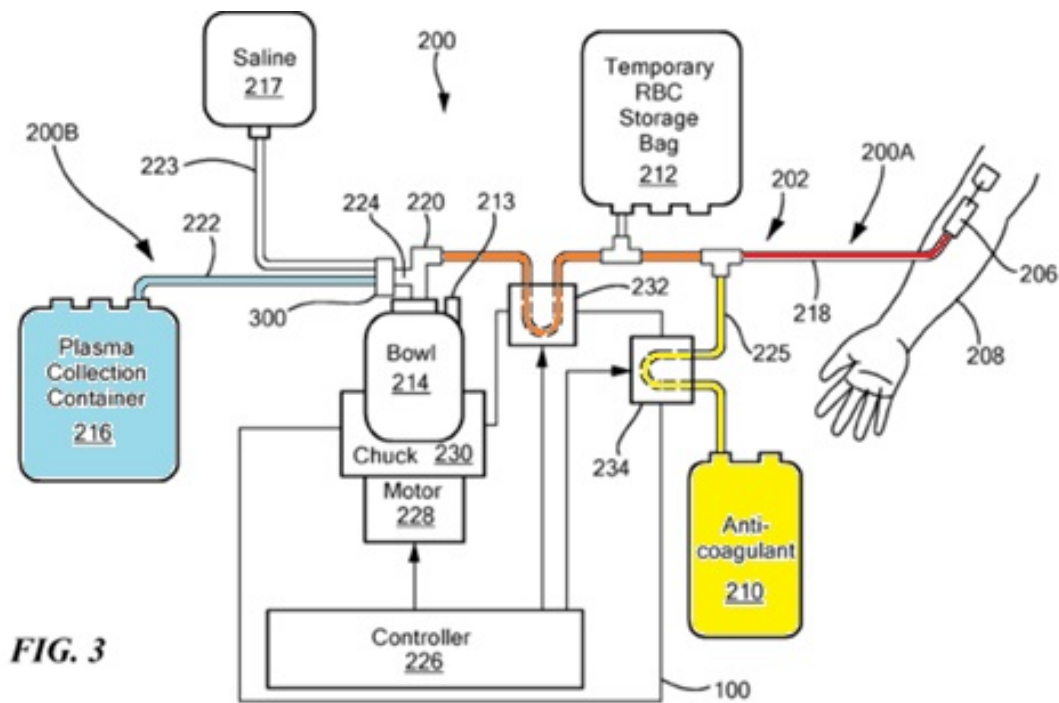
² See, e.g., EX1013, p. 14, “The pump flow rates—and, thereby, the component collection—are controlled by the microprocessor in response to the optical monitor.”

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 '873 patent. *See, e.g.*, EX1017.

VIII. '873 PATENT OVERVIEW

A. The '873 Patent is Directed to Plasma Apheresis

45. The '873 patent, which recently issued on June 10, 2025, relates to a “system and method for collecting plasma” in blood apheresis systems. EX1001, Title, 1:25-27. “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, 1:31-37. The '873 patent relates to plasma apheresis, which is plasma collection. EX1001, Abstract; 1:25-28. The '873 patent Figure 3 shows one embodiment of a plasma apheresis system.



EX1001, Fig. 3.

46. Plasma apheresis involves withdrawing whole blood from a donor's arm using venous access device 206. EX1001, 5:28-33. 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) into inlet line 218. EX1001, 4:46-47; 5:39-42; 6:26-33. Anticoagulant is introduced in fixed proportions to the whole blood drawn from the donor to prevent blood clotting in the draw line. See EX1012. "[T]he anticoagulant mixes with the plasma component" because "the osmolarity of the red blood cells prevents the anticoagulant . . . from entering/remaining with the red blood cells." EX1001, 7:58-63.

47. 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, 4:52-61, 4:66-5:5; 6:56-60. The donor’s plasma, i.e., pure plasma, along with anticoagulant introduced during the collection process, exits the blood component separation device and is collected and stored in a collection container (e.g., a bag, shown in blue above). EX1001, 7:33-39. The anticoagulant and pure plasma combination is called anticoagulated plasma or plasma product. EX1001, 1:26-28; 10:3-6.

48. The FDA established guidelines regarding how much plasma any individual donor can donate. *See* EX1012. These guidelines consider donor parameters, like weight, hematocrit, and sex. *See* EX1012.

B. The ’873 Patent’s Purported Invention

49. The ’873 patent purports to solve problems associated with “determin[ing] the total volume of plasma that has been collected” from a donor after the withdrawn whole blood is mixed with anticoagulant by considering a donor’s hematocrit level and the amount of anticoagulant added into the system. EX1001, 1:56-62; 1:66-3:66; 4:23-33.

50. Each donor's hematocrit level is different, which affects the amount of plasma in the donor's whole blood. EX1001, 8:3-4. The differing hematocrit levels also affect the volume of anticoagulant in a plasma collection bag ("anticoagulant volume"). EX1001, 8:7-13. Given this variability, the '873 patent discloses that controller 226 may use the % AC equation below, which includes a predetermined ratio of anticoagulant to anticoagulated whole-blood and the donor's hematocrit to calculate the percentage of anticoagulant in the plasma container. EX1001, 8:3-9:25. Specifically, in % AC 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, 8:3-61. Anticoagulated whole blood is extracted blood mixed with anticoagulant.

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

51. Controller 226 uses a weight sensor to monitor the collection container's weight and uses the weight to determine the total volume of liquid in the collection container. EX1001, 7:28-39; 7:65-8:2. The controller uses the total volume of liquid in the collection container to calculate the anticoagulant and pure plasma volumes in the collection container. EX1001, 8:3-9:55. The '873 patent first

calculates the anticoagulant volume. EX1001, 8:17-61. 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, 8:63-9:12. These calculations occur in real time. EX1001, claim 1.

52. The '873 patent also discloses two alternative methods of determining the amount of anticoagulant in the collection bag that do not consider a donor's hematocrit. These determine the anticoagulant in the collection bag by: (i) monitoring the volume of anticoagulant added to the system based on the number of rotations of the anticoagulant pump,³ and (ii) measuring the change in weight of the anticoagulant container. EX1001, 8:16-9:25. In both methods, the added anticoagulant volume is used to calculate the volume of pure plasma collected in the

³ “Because the osmolarity of the red blood cells prevents the anticoagulant from mixing with it, essentially all of the anticoagulant exits the bowl 214 and is collected within the plasma collection container 216 along with the plasma.” EX1001 at 8:34-38. Thus, subtracting the volume of anticoagulant added to the system from the total volume in the collection container estimates the volume of pure plasma within the collection container. EX1001 at 8:16-9:25.

plasma collection container by subtracting the added anticoagulant volume from the total volume in the collection container. EX1001, 8:16-9:25.

53. Of these three methods, only the first, which is based on the predetermined ratio of anticoagulant to anticoagulated whole blood, considers the donor's hematocrit. That method does not, however, use an amount of anticoagulant collected within the plasma collection container, or supplied to the system, to determine a percentage of anticoagulant within the collected plasma. EX1001 at 8:16-9:25; 10:16-26.

54. The '873 patent repeats each method to determine the pure plasma volume "until a target volume of pure plasma is collected in the plasma collection container," *e.g.*, the volume set by FDA regulation. EX1001, 8:17-22. When the system reaches a target volume of pure plasma, the controller "stops the draw of whole blood from the subject and reverses the direction of the blood ... to draw the RBCs (and other components)" from the blood component separation device back to the donor. EX1001, 9:17-23.

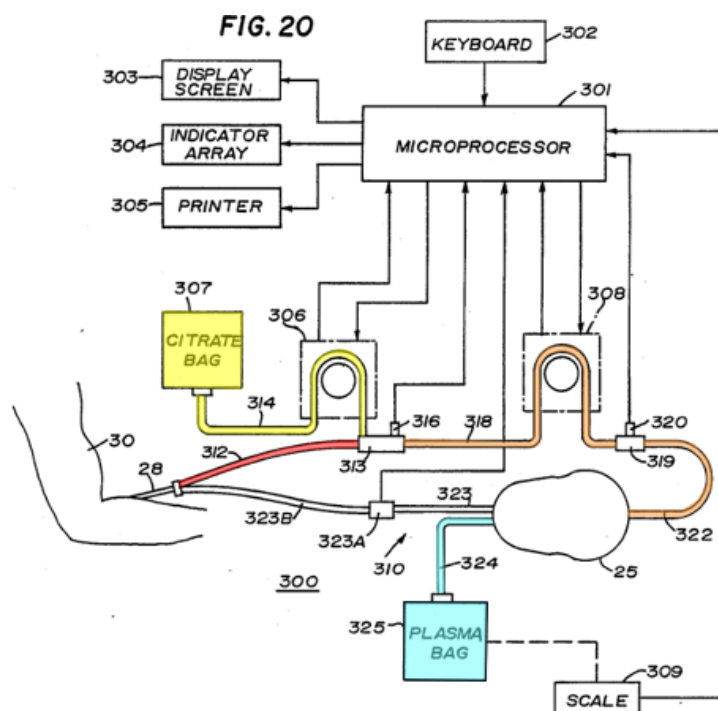
IX. PRIOR ART OVERVIEW

A. Overview of Lavender

55. Lavender discloses "a system, method and device for continuously fractionating blood in situ." Like the '873 patent, 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.

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



EX1005, Fig. 20 (annotated).

57. In Lavender’s system 300, a needle or catheter 28 is used to draw whole blood from a donor, which is then mixed with citrate (a blood anticoagulant) pumped from citrate bag 307. EX1005, 16:45-47, 16:60-17:2. System 300 then pumps the whole blood and anticoagulant mixture to blood fractionator 25, which separates the anticoagulated whole blood into plasma and other blood fractions. 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.

58. Lavender's system performs several real time calculations during the collection process. These calculations account for donor parameters, like hematocrit, and a fixed anticoagulant to plasma ratio, which, in turn, relates to a fixed anticoagulant to anticoagulated whole blood ratio. See EX1005, 22:35-39, cols. 41, 42. Lavender's Plasma Dilution Factor (PDF) defines how anticoagulant added to the withdrawn whole blood is added at a rate sufficient to dilute incoming plasma to 68% of the initial concentration. Thus, $PDF = .68$ because, after adding anticoagulant to the withdrawn whole blood at this rate, the amount of collected plasma and anticoagulant mixture is 68% plasma and 32% anticoagulant, and thus PDF defines a ratio of anticoagulant added to the withdrawn whole blood relative to incoming plasma from the donor's blood. The weight of the collected plasma and anticoagulant solution is measured during the collection process and PDF is used to determine a volume of anticoagulant and volume of pure plasma in the collection container.. EX1005, 20:55-68.

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

Variable	Description
CF (conversion factor) ⁴	Predetermined ratio (or percentage) of anticoagulant to incoming plasma
PDF	Plasma dilution factor
$C1$	ml plasma collected/pound of BW
$C2$	ml dilute plasma collected/pound of BW
$C3$	ml citrate to be filtered/pound of BW
QB	Blood flow from donor
TQB	Total blood flow
$HCTD$	Donor's hematocrit
BW	Donor's body weight
QP	Plasma flow
TQP	Total plasma flow

⁴ I note that Table VI has two different “ CF ” terms, (i) conversion factor (CF) and (ii) the rate citrate is filtered from the donor's whole blood in system 300, or citrate filtered in ml/min (CF). This appears to be a typographical error and a POSITA would understand that “ CF ” used in the total citrate filtered (TCF) equation is conversion factor (CF).

Declaration of Dr. Gary Fletcher in Support of Petition for
Post Grant Review of U.S. Patent No. 12,324,873
PGR2026-00009

<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 (pure plasma plus anticoagulant) volume to collect

60. These variables are used during the collection process to monitor the amount of plasma collected. For example, plasma flow (*QP*) is calculated based on the donor's blood flow (*QB*) and hematocrit (*HCTD*). 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*).

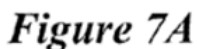
61. The microprocessor repeatedly performs weight measurements and run-time calculations set forth in Lavender's algorithm and displays updated values approximately every two seconds. EX1005, 20:55-68. Lavender's system determines the relationship (or ratio) between the pure plasma volume and the anticoagulant 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.

62. 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

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

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



65. Assembly 10' operates according to a collection procedure derived from procedure goal(s) and may include maximizing "at least one process control parameter." EX1005, 7:38-43; 9:35-44. This maximization is determined by inputting donor-provided data, like height, weight, and blood processing machine type in optimization and prediction models. EX1005, 49:19-26.

“...; (2) inlet flow rate; (3) AC ratio; (4) procedure time; ...; (7) source plasma

volume; (8) AC in the platelet and plasma collect bags 38, 54; . . . ; (10) AC infusion rate; and (11) output approval.” EX1005, 49:22-26. When executed during a blood separation procedure, the prediction model determines any of parameters (1)-(11) in real-time. EX1005, 34:8-24; 48:66-49:19-25;

67. Fletcher-Haynes’ prediction algorithms may be integrated with its optimization algorithms, and Fletcher-Haynes specifically recites “the optimizer model 172 may interface with the prediction model or actually integrally incorporate the prediction model” and refers to Eqs. 1-22. EX1005, 58:63-67. Stated differently, Fletcher-Haynes discloses 22 equations that can be incorporated into a prediction model to predict a particular blood component’s yield. EX1005, 58:63-67. One is an equation for calculating total blood volume using a donor’s height and weight, another is an equation for calculating anticoagulant (AC) ratio using a donor’s hematocrit, and another is an equation for calculating source plasma volume or a target pure plasma volume collected or to collect. EX1005, 49:40-52:17. Specifically, Equation 10 defines the total blood volume of a donor (VB) using a donor’s height and weight; Equation 9 determines the AC Ratio (R) using a donor’s hematocrit; and Equation 22 defines the predicted total volume in the source plasma bag (VSPB). EX1005, 49:40-52:17. These equations can be integrated with Fletcher-Haynes’ optimization algorithms. EX1005, 58:63-67.

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

C. Overview of Min

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

57. Barrett specifically discloses determining a patient's hematocrit by dividing a blood sample's calculated total red blood cell volume by a total volume of the blood sample. EX1007, 2:45-49.

E. Overview of Headley

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

F. Overview of Turgut

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

X. DETAILED GROUNDS EXPLANATION

74. The sections below explain my reasoning why all claims of the '873 patent are unpatentable.

A. Ground 1: Claims 1-5, 7, 8, 10-17, and 19-23 are anticipated and/or rendered obvious by Lavender

1. Claim 1

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

75. To the extent the preamble is limiting, Lavender discloses “[a] system, method and device for continuously fractionating blood in situ.” EX1004, Abstract. Lavender fractions blood “to collect blood substances, such as **plasma**.”⁵ EX1004, 1:12-13; See also id. at claim 1 (“A method of collecting plasma...”), 5:42-49, 1:48-56.

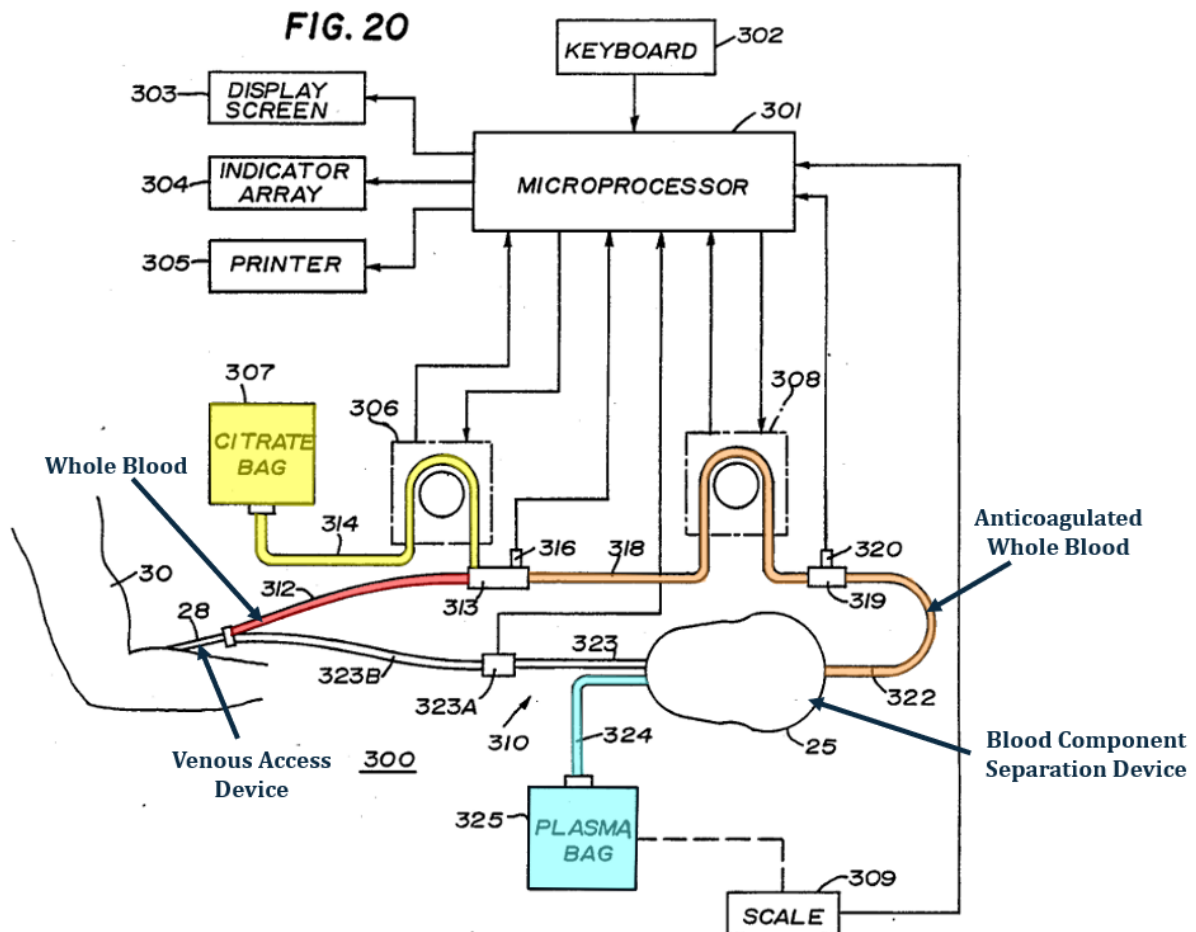
b. 1[a] inserting a venous-access device into a donor;

76. Lavender’s blood fractionator uses a catheter, needle, or double lumen needle inserted into an appropriate vein or artery of the donor to draw blood from the donor for processing, allowing blood to flow from the catheter or needle through a blood tube and into an inlet of the blood fractionator. EX1004, 5:13-22, Figs. 1 and 20.

⁵ All emphasis is added unless otherwise noted.

- c. 1[b] withdrawing whole blood from the donor through the venous-access device and a draw line, the draw line fluidly coupled to a blood component separation device;**

77. 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. EX1004, 5:18-22, Fig. 20.



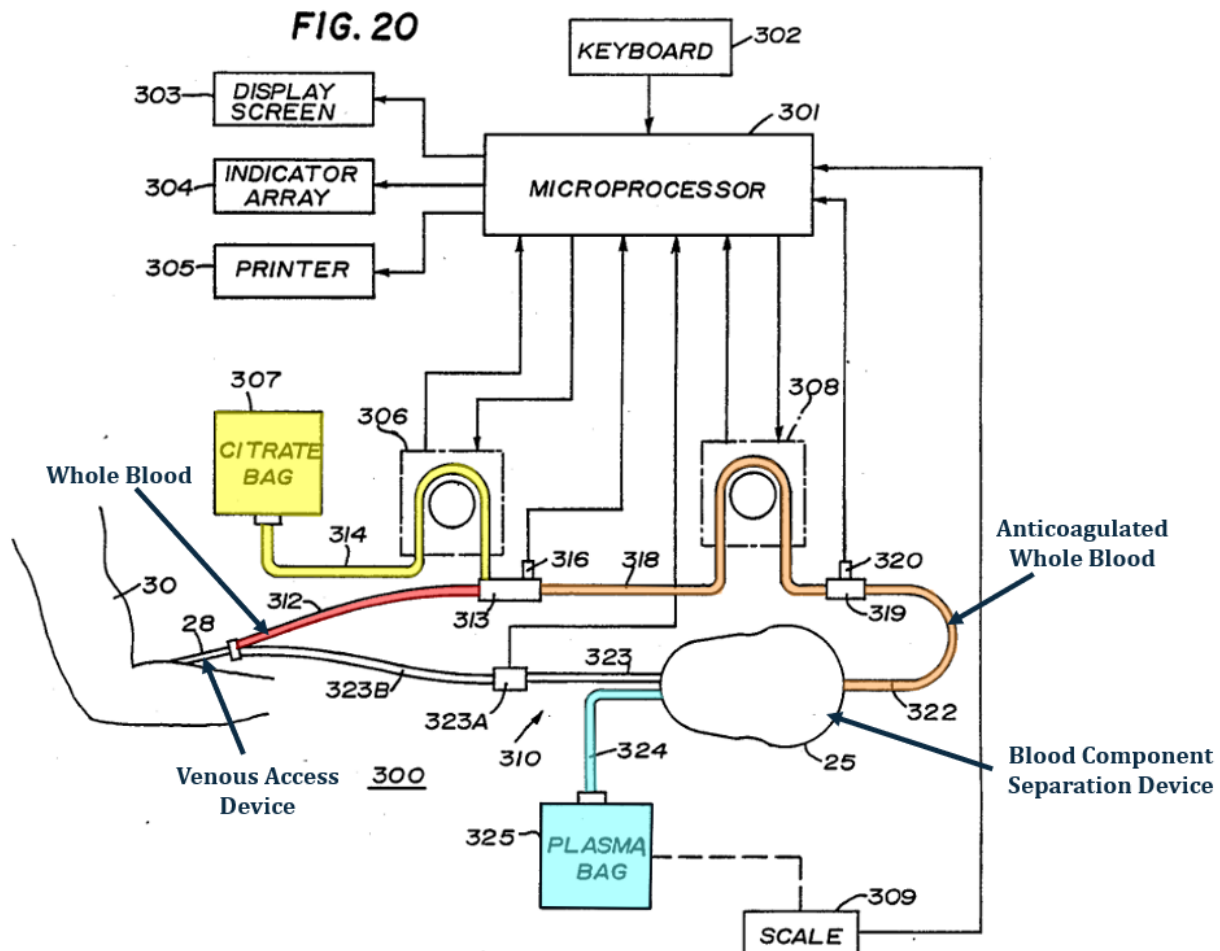
The drawn blood is whole blood because it is a mixture of “a variety of blood fractions.” EX1004, 5:45.

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

79. The fractionator is a blood component separation device because “it produces a variety of blood fractions” from whole blood, “plasma [being] one of the most important blood fractions.” EX1004, 5:42-45.

d. 1[c] introducing anticoagulant into the withdrawn whole blood through an anticoagulant line;

80. In Lavender’s automated system for separating blood into components, “[a] supply of anticoagulant 35 is connected to the tube 27” supplying withdrawn whole blood from the donor. EX1004, 5:22-28, Figs. 1 and 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 an anticoagulant line 314. EX1004, 5:22-28 and Figs. 1 and 20 (tube 314).



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

cells, white blood cells, and platelets. EX1004, 1:21-25, 5:42-52, 10:58-11:6, Figs. 1 and 20.

f. 1[e] collecting the plasma component from the blood component separation device and into a plasma collection container; and

82. 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). EX1004, 10:58-11:6; Figs. 1, 4, 15, 17, and 20.

g. 1[f] calculating a volume of pure plasma collected within the plasma collection container based, at least in part, on a volume of plasma component collected within the plasma collection container, a ratio of anticoagulant added to the withdrawn whole blood, and a hematocrit of the donor.

83. Lavender anticipates element 1[f] under the plain and ordinary meaning of the term “based on.” The claim language itself—“based, at least in part, on”—suggests that the calculation may rely on one or more methods and is not limited to a single, exclusive method. The patent does not expressly disavow other reasonable interpretations of “based, at least in part, on.” As explained below, in my opinion, Lavender discloses this limitation under the plain and ordinary meaning of “based, at least in part, on.” Alternatively, in my opinion and as discussed below, a POSITA would have understood that Lavender renders this limitation obvious.

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

85. Lavender uses the volume of plasma component collected within the plasma collection container, a ratio of anticoagulant added to the withdrawn whole blood, and the donor's hematocrit to calculate the total pure plasma volume collected. EX1004, 20:55-68; 41:1-44:33. As blood is being drawn from the donor, Lavender calculates total plasma filtered (*TPF*), representing the total amount of pure plasma in the plasma collection bag. EX1004, 20:55-68; 41:1-44:33. *TPF* is determined by multiplying the total amount of dilute plasma filtered (*TDPF*) by a plasma dilution factor (PDF) (i.e., ***TPF*** = *TDPF* * *PDF*). EX1004, 20:55-68; 41:1-44:33. *TDPF* is equivalent to the "volume of plasma component collected within the plasma collection container" in claim 1. The plasma dilution factor (PDF) is determined using the predefined ratio of citrate (anticoagulant) added per milliliter of plasma to dilute incoming plasma to 68% of the initial concentration. EX1004, 22:35-46. Thus, 32 ml of citrate is added to the incoming whole blood for every 68

ml of plasma to dilute the incoming plasma to 68% of its initial concentration; and *PDF* is defined at .68. EX1004, 20: 35-46; 41:1-44:33. Since *PDF* defines the amount of anticoagulant (citrate) added to the incoming whole blood to dilute the incoming plasma to 68% of the initial concentration, and is a ratio of “anticoagulant added to the withdrawn whole blood” relative to incoming plasma (e.g. withdrawn plasma from the donor). A POSITA would understand that *PDF* defines “a ratio of anticoagulant added to the withdrawn whole blood” relative to incoming plasma.

86. A POSITA would understand that *PDF* could thus be expressed as $PDF = \frac{V_P}{V_P + V_{AC}}$ where V_P is the volume of pure plasma and V_{AC} is the volume of anticoagulant.

87. A POSITA would understand that this equation, when inserted into the *TPF* equation shows that Lavender determines the volume of pure plasma in the collected plasma component, as follows:

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

A POSITA would also understand that the volume of plasma introduced into the system (V_P) is related to the volume of whole blood introduced (V_B) as $V_P = V_B * (1 - HCTD)$, which is Lavender’s equation for the plasma flow rate ($TQP = TQB * (1 - HCTD)$) converted to a volume equation.

88. Lavender therefore, in my opinion, determines the volume of pure plasma in the collection container from $TPF = TDPF * \frac{V_B * (1 - HCTD)}{[V_B * (1 - HCTD) + V_{AC}]}$, showing that Lavender determines the volume of pure plasma in the collection container (TPF) from the volume of plasma component collected within the plasma collection container ($TDPF$), a ratio of anticoagulant added to the withdrawn whole blood relative to incoming plasma through $PDF = \frac{V_P}{V_P + V_{AC}}$, and a hematocrit of the donor ($HCTD$).

89. If the Board, however, determines this is not inherent in Lavender, Lavender renders this limitation obvious, in my opinion, because a POSITA would (i) recognize the interdependency between the donor's hematocrit and the calculated TPF , which is based on PDF, which, in turn, is based on the volume of anticoagulant added to the whole blood, and (ii) understand that the plasma volume in the collection bag (TPF) is based, at least in part, on the donor's hematocrit ($HCTD$) and the volume of plasma component in the collection bag ($TDPF$).

2. Claim 2: A method according to claim 1, further comprising calculating a percentage of anticoagulant in the collected plasma component.

90. Lavender monitors a volume of anticoagulant (e.g., TCF total citrate filtered) collected within the plasma collection container and monitors a total volume of collected fluid (e.g. dilute plasma) in the plasma collection container (e.g., $TDPF$

total citrate filtered). EX1004, 43:27-28. Lavender updates **TDPF** as the system withdraws blood. In my opinion, a POSITA would readily understand how to calculate a percentage of anticoagulant in the collected plasma component by dividing **TCF** by **TDPF** (i.e., percentage of anticoagulant in the collected plasma component = $\left(\frac{TCF}{TDPF}\right) * 100$).

91. Furthermore, Lavender utilizes a predetermined plasma dilution factor (**PDF = 0.68**) that represents the percentage of pure plasma in the collected plasma component (**TDPF**), which is derived from the predefined ratio of citrate added per milliliter of plasma to dilute incoming plasma to 68% of the initial concentration. EX1004, 22:35-46. I note that **PDF** is not a percentage, but a fraction of 1, and a POSITA would readily understand that 0.68 represents the 68% dilution of incoming plasma and could easily convert such a decimal representation of 0.68 to a percentage of 68%. In my opinion, a POSITA would readily understand that only plasma and anticoagulant are collected within the collected plasma component, and the percentage of anticoagulant in the collected plasma component may be calculated simply by subtracting **PDF** from 1, or a percentage of anticoagulant in the collected plasma component is equal to $(1 - PDF)$ where the percentage is represented as a fraction of 1, or $(1 - PDF) * 100$ to determine a percentage represented out of 100.

3. **Claim 3: A method according to claim 2, wherein the calculated percentage of anticoagulant in the collected plasma component is based, at least in part, on the ratio of anticoagulant added to the withdrawn whole blood, and the hematocrit of the donor.**

92. As discussed hereinabove, Lavender calculates the volume of pure plasma collected in the plasma collection bag (**TPF**) based, at least in part, on the ratio of anticoagulant added to the withdrawn whole blood (**PDF**), and the donor's hematocrit (**HCTD**). See §X.A.1.g. Lavender's calculation of the volume of anticoagulant (e.g., **TCF** total citrate filtered) collected within the plasma collection container is based directly on **TPF** (i.e., $TCF = TPF * CF$). EX1004, 41:4-44:42. Thus, **TCF** is also calculated based, at least in part, on the ratio of anticoagulant added to the withdrawn whole blood (**PDF**), and the donor's hematocrit (**HCTD**). As discussed above in §X.A.2., in my opinion, a POSITA would readily understand how to calculate a percentage of anticoagulant in the collected plasma component by dividing **TCF** by **TDPF** (i.e., percentage of anticoagulant in the collected plasma component = $\left(\frac{TCF}{TDPF}\right) * 100$).

4. **Claim 4: A method according to claim 2, wherein the calculated volume of pure plasma collected within the plasma collection container is based, at least in part, on the**

calculated percentage of anticoagulant in the collected plasma component.

93. In Lavender's Main Loop algorithm of Table VI, the total plasma in the collected plasma component (*TPF*) is calculated based on the total volume of anticoagulant and plasma solution in the collection container (total dilute plasma filtered (*TDPF*)), which is determined by the weight of the collection container. As discussed above, the equation for *TPF* is $TPF = TDPF * PDF$. EX1004, 41:10-44:57. The plasma dilution factor (*PDF*) represents the factor by which a volume of incoming plasma is diluted with a volume of anticoagulant. EX1004, 22:37-39; 41:10-44:57. A POSITA, in my opinion, would therefore understand, using basic arithmetic, that $PDF = \frac{V_P}{V_P + V_{AC}}$, and thus *PDF* is a decimal representation of a percentage of pure plasma in the collected plasma component. In my opinion, a POSITA would also understand that the remaining percentage, or $1 - PDF$ is a decimal representation of the percentage of anticoagulant in the collected plasma component. Thus, a POSITA would understand that the calculation of *TPF* is based, at least in part, on the percentage of anticoagulant in the collected plasma component (e.g. indirectly through *PDF*).

5. **Claim 5: A method according to claim 1, further comprising: calculating a volume of anticoagulant in the collected plasma component based, at least in part, upon the hematocrit of the donor, the calculated volume of pure plasma collected within the plasma collection container based, at least in part, on the**

calculated volume of anticoagulant in the collected plasma component.

94. Lavender anticipates and/or renders obvious claim 5 under the plain and ordinary meaning of the term “based on.” The claim language itself—“based, at least in part, on”—suggests that the calculation may rely on one or more methods and is not limited to a single, exclusive method. Although the ’873 patent provides an example in which a technician determines the volume of collected pure plasma by calculating the volume of anticoagulant in the plasma component—specifically, by measuring the volume of anticoagulant in the container and subtracting this from the total fluid volume in the collection container—the patent does not expressly disavow other reasonable interpretations of “based, at least in part, on.” As explained below, Lavender discloses this limitation under the plain and ordinary meaning of “based, at least in part, on.” Alternatively, as discussed below, in my opinion, a POSITA would have understood that Lavender renders this limitation obvious.

95. In my opinion, even if a narrower interpretation of “based, at least in part, on” is adopted in view of the ’873 patent’s exemplary calculation—claim 5 is rendered obvious by Lavender in view of Fletcher-Haynes, as discussed in relation to claim 1 in Ground 2, below.

- a. **Lavender discloses calculating a volume of anticoagulant in the collected plasma component based, at least in part, upon the hematocrit of the donor.**

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

97. In Lavender's Main Loop algorithm of Table VI, a volume of anticoagulant in the collected plasma component (**TCF**) is calculated based on a volume of total plasma in the collected plasma component (**TPF**), via the equation $TCF = TPF * CF$, where **CF** is a conversion factor representing the volume of anticoagulant introduced into the incoming whole blood (V_{AC}) per incoming volume of plasma (V_P), or $CF = \frac{V_{AC}}{V_P}$. EX1004, 41:4-44:42. The total plasma in the collected plasma component (**TPF**) is calculated based on the total volume of anticoagulant and plasma solution in the collection container (total dilute plasma filtered (**TDPF**)), which is determined by the weight of the collection container. The equation for **TPF** is $TPF = TDPF * PDF$. The plasma dilution factor (**PDF**) represents the factor by which a volume of incoming plasma is diluted with a volume of anticoagulant.

EX1004, 22:37-39; 41:10-44:57. In my opinion, a POSITA would therefore understand, using basic arithmetic, that $PDF = \frac{V_P}{V_P + V_{AC}}$.

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

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

99. A POSITA, in my opinion, would also understand that the volume of plasma introduced into the system (V_P) is related to the volume of whole blood introduced (V_B) as $V_P = V_B * (1 - HCTD)$, which is simply Lavender's equation for the plasma flow rate ($TQP = TQB * (1 - HCTD)$) converted to a volume equation.

100. Lavender therefore determines the volume of anticoagulant in the collected plasma from $TCF = TDPF * \frac{V_{AC}}{[V_{AC} + V_B * (1 - HCTD)]}$, showing that Lavender determines the volume of anticoagulant in the collected plasma from the subject's hematocrit.

b. Lavender discloses calculating a volume of pure plasma collected within the plasma collection container based, at least in part, on the calculated volume of anticoagulant in the collected plasma component.

101. Lavender uses the amount of anticoagulant (citrate) added to the whole blood to calculate the total pure plasma volume collected. EX1004, 20:55-68; 41:1-44:33. Lavender first calculates total plasma filtered (**TPF**), representing the total amount of pure plasma in the plasma collection bag. EX1004, 20:55-68; 41:1-44:33. **TPF** is determined by multiplying the total amount of dilute plasma filtered (**TDPF**) by a plasma dilution factor (**PDF**) (i.e., **TPF** = **TDPF** * **PDF**). EX1004, 20:55-68; 41:1-44:33. As discussed above, the plasma dilution factor (**PDF**) is determined using the predefined ratio of citrate added per milliliter of plasma to dilute incoming plasma to 68% of the initial concentration. EX1004, 22:35-46. Thus, 32 ml of citrate is added to the incoming whole blood for every 68 ml of plasma to dilute the incoming plasma to 68% of its initial concentration; and **PDF** is defined at 0.68. EX1004, 20: 35-46; 41:1-44:33.

102. Next, Lavender calculates the volume of anticoagulant in the plasma container (i.e. total citrate filtered (**TCF**)). Lavender weighs the collected plasma and anticoagulant solution in plasma bag 325 and transmits the weight information to microprocessor 301. EX1004, 16:50-53; 17:14-16. Using the total weight in the plasma bag, system 300 calculates the volume of anticoagulant in the plasma bag

325 (i.e. total citrate filtered (**TCF**)) by multiplying the total amount of filtered plasma (**TPF**) by a conversion factor (**CF**) for milliliters of citrate per milliliter of plasma. EX1004, 41:1-44:33 (Table VI, §5(B)). The conversion factor (**CF**) is determined using a predefined ratio of citrate added per milliliter of plasma to dilute incoming plasma to 68% of the initial concentration. EX1004, 22:35-46.

103. Lavender's microprocessor repeatedly measures the weight change of the plasma bag ("**TDPW**", total dilute plasma filtered in grams) in real time and updates the calculated values using the updated total weight in the plasma bag. EX1004, 20:55-68; 41:1-44:33. Specifically, Lavender discloses "repeatedly performing the measurements and calculations . . . updating these values each time the program cycles through the main loop, and displaying the values in 'Run'-message (Table V) which is updated approximately every two seconds." EX1004, 20:55-68; 41:1-44:33.

104. Lavender thus calculates the anticoagulant volume as the plasma component is being collected in the plasma collection container by repeatedly performing the **TCF** calculation in the main loop of the algorithm in real-time, which continues until the total plasma filtered is equal to or greater than the maximum total plasma filtered. EX1004, cols. 43-44.

105. As shown in the annotated excerpt of §5(B) of Table VI below, the volume of pure plasma in the plasma collection bag (**TPF**) and the volume of anticoagulant in the plasma container (**TCF**) share a direct mathematical relationship.

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

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

107. Lavender's disclosure of the dependency of both **TPF** and **TCF** on the predefined ratio of citrate added per milliliter of plasma inherently discloses calculating a volume of pure plasma collected in the plasma collection bag (**TPF**) based, at least in part, on a calculated volume of anticoagulant in the collected plasma component (**TCF**). If the Board, however, determines this is not inherent in Lavender, Lavender renders this limitation obvious because a POSITA would (i) recognize the interdependency between the predefined ratio of citrate added per milliliter of plasma, **TPF** and **TCF**, and (ii) understand that the plasma volume in the collection bag is based, at least in part, on the volume of anticoagulant in the collection bag. **TCF** is based on the donor's hematocrit because the anticoagulant added to the system is dependent on the plasma flow, and plasma flow is determined based on the donor's hematocrit. Thus Lavender discloses calculating a volume of anticoagulant in the collected plasma component based, at least in part, upon the hematocrit of the donor, the calculated volume of pure plasma collected within the plasma collection container based, at least in part, on the calculated volume of anticoagulant in the collected plasma component.

6. Claim 7: A method according to claim 1, further comprising: monitoring the volume of plasma component collected within the plasma collection container.

108. Lavender monitors a volume of plasma component (e.g., ***TDPF*** total dilute plasma filtered) collected within the plasma collection container. EX1004, 43:4-6. As discussed above in §X.A.1.g., Lavender updates ***TDPF*** as the system withdraws blood.

7. Claim 8: A method according to claim 1, further comprising: monitoring a weight of plasma component collected within the plasma collection container, the calculated volume of pure plasma collected within the plasma collection container based, at least in part, on the monitored weight of collected plasma component.

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

8. Claim 10: A method according to claim 1, further comprising: continuing steps (b) through (f) to collect a target volume of pure plasma and/or a target volume of plasma component within the plasma collection container.

110. As discussed above, Lavender performs steps (b) – (f). See §§X.A.1.c-g.

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

112. For example, Lavender repeats step (d)-(i) by "introducing anticoagulant to the blood from which the plasma is to be collected ... separating plasma from the extracted blood ... until a predetermined ... volume of plasma has been collected." EX1004, 21:62-22:6; 46:14-22; See also claim 1.

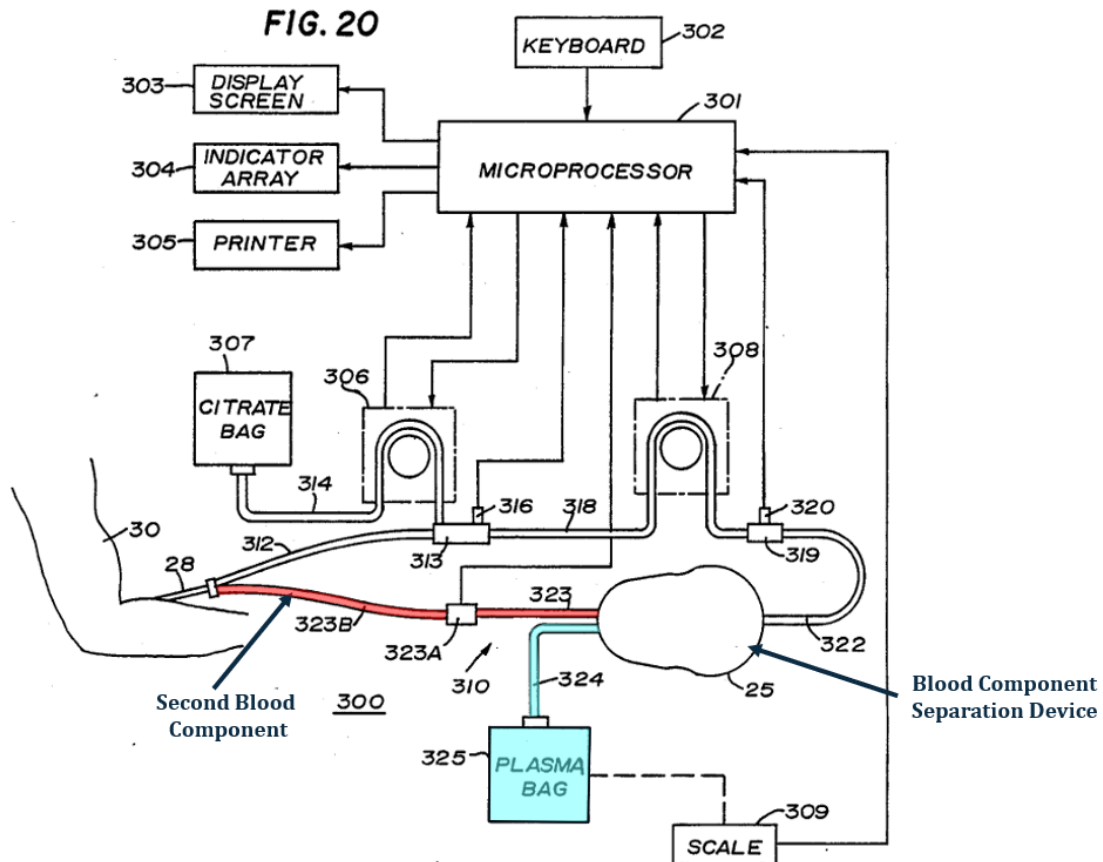
9. Claim 11: A method according to claim 10, wherein the target volume of pure plasma and/or the target volume of plasma component is based, at least in part, on a weight of the donor.

113. Lavender discloses directing "the user in entry and validation of donor data, including ... donor weight in pounds." EX1004, 20:10-14. Then, Lavender determines a target volume of pure plasma, **MAXPF**, which is based on the donor's bodyweight (**BW**) and a predetermined constant (C1) of milliliters of plasma collected per pound of body weight. EX1004, Table VI, §2(g).

10. Claim 12: A method according to claim 10, further comprising: returning, after collecting at least a portion of the target volume of pure plasma and/or the target volume of plasma component, the second blood component to the donor through a return line.

114. Lavender collects a first blood component (e.g., plasma) in a "blood fraction collection receptacle or bag." EX1004, 5:32-33. After collecting at least a

portion of the target volume of pure plasma, the second blood component (e.g., RBC), is returned to the donor 30 through the tubing 323. EX1004, 10:58-63.



EX1004, Fig. 20 (annotated)

11. Claim 13

a. 13[preamble] A system for collecting plasma comprising:

115. Lavender discloses that its methods may be implemented in “a system for harvesting plasma.” EX1004, Abstract, 1:15-17, 1:45-47, Figs. 1 & 20.

- b. **13[a] a venous-access device for drawing whole blood from a subject and returning blood components to the subject;**

116. See §§X.A.1.b-c, *supra*, EX1004, 5:13-22 and Figs 1 and 20.

- c. **13[b] a blood component separation device for separating the withdrawn blood into a plasma component and a second blood component, the blood component separation device having an outlet and being configured to convey the plasma component to a plasma collection container;**

117. See §§X.A.1.e-f, *supra*, EX1004, 10:58-11:6; FIGS. 1, 4, 15, 17, 20.

- d. **13[c] a blood draw line fluidly coupled to the venous-access device and configured to transport withdrawn whole blood to the blood component separation device, the flow through the blood draw line being controlled by a blood draw pump;**

118. See §X.A.1.c, *supra*, EX1004, 5:13-22 and FIGS 1, 20.

- e. **13[d] an anticoagulant line fluidly coupled to an anticoagulant source, the anticoagulant line configured to introduce anticoagulant into the withdrawn whole blood; and**

119. See §X.A.1.d, *supra*, EX1004, 5:22-28 and FIGS. 1, 20.

- f. **13[e] a controller configured to control the operation of the blood component separation device and the blood draw pump,**

120. See §X.A.1.g, *supra*, EX1004, 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 EX1004, Abstract. This program control of the extracorporeal devices would include blood fractionator 25 (blood component separation device) and the associated fluid pumps. EX1004, 18:27-64; cls. 28, 29, 33, 35, 36, 38, 40-41.

- g. 13[f] the controller configured to calculate a volume of pure plasma collected within the plasma collection container based, at least in part, on a volume of plasma component collected within the plasma collection container, a ratio of anticoagulant added to the withdrawn whole blood, and a hematocrit of the subject.**

121. See §X.A.1.g, *supra*. EX1004, 20:55-68; 41:1-44:33.

- 12. Claim 14: A system according to claim 13, wherein the controller is further configured to calculate a percentage of anticoagulant in the collected plasma component.**

122. See §X.A.2, *supra*.

- 13. Claim 15: A system according to claim 14, wherein the calculated percentage of anticoagulant in the collected plasma component is based, at least in part, upon the ratio of anticoagulant added to the withdrawn whole blood, and the hematocrit of the donor.**

123. See §X.A.3, *supra*.

- 14. Claim 16: A system according to claim 14, wherein the calculated volume of pure plasma collected within the plasma**

collection container is based, at least in part, on the calculated percentage of anticoagulant in the collected plasma component.

124. See §X.A.4, *supra*.

- 15. Claim 17: A system according to claim 13, wherein the controller is further configured to calculate a volume of anticoagulant in the collected plasma component based, at least in part, upon the hematocrit of the subject, the volume of pure plasma collected within the plasma collection container based, at least in part, upon the volume of anticoagulant in the collected plasma component.**

125. See §X.A.5, *supra*.

- 16. Claim 19: A system according to claim 13, wherein the controller is configured to monitor the operation of an anticoagulant pump to determine a total volume of anticoagulant introduced into the system.**

126. Lavender uses anticoagulant pump 306 in system 300 “for pumping anticoagulant from an associated source” into “the blood flowing from the donor 30 to the fractionator 25.” EX1004, 5:15:47-53, 16:45-47, 16:54-17:2, 41:27-30; 42:8-44:32, claim 1; Fig. 20. Lavender introduces anticoagulant into the whole blood at “a predetermined flow rate,” which Lavender expresses in its algorithm as QC . EX1004, 5:25-26. Lavender sets the citrate pump flow rate, QCP , to QC via a controller (i.e. microprocessor 301). EX1004, cols. 41 & 42, Fig. 20. The citrate pump flow rate, QCP , is used to determine TQC in Lavender’s Main Loop algorithm. EX1004, cols. 41 & 42, Fig. 20. The total volume of anticoagulant introduced into

Lavender's system is monitored by microprocessor 301 in the Main Loop algorithm, specifically tracking *TQC* or total citrate flow in ml, during a blood separation procedure. EX1004, 5:15:47-53, 16:45-47, 16:54-17:2, 41:27-30; 42:8-44:32; Fig. 20.

17. **Claim 20: A system according to claim 13, further comprising: a plasma collection container weight sensor configured to monitor the volume of plasma component collected within the plasma collection container.**

127. Lavender monitors a volume of plasma component (e.g., *TDPF* total dilute plasma filtered) collected within the plasma collection container using a scale 309 monitoring the weight of the plasma collection container (e.g. plasma bag 325). EX1004, 16:50-53, Fig. 20. As discussed above in §X.A.1.g, Lavender updates *TDPF* as the system withdraws blood.

18. **Claim 21: A system according to claim 13, further comprising: a plasma collection container weight sensor configured to monitor a weight of plasma component collected within the plasma collection container, the calculated volume of pure plasma collected within the plasma collection container based, at least in part, on the monitored weight of collected plasma component.**

128. See §X.A.7. As blood is being drawn from the donor, Lavender calculates total plasma filtered (*TPF*), representing the total amount of pure plasma in the plasma collection bag. EX1004, 20:55-68; 41:1-44:33. *TPF* is determined by

multiplying the total amount of dilute plasma filtered (**TDPF**) by a plasma dilution factor (**PDF**) (i.e., **TPF** = **TDPF** * **PDF**). EX1004, 20:55-68; 41:1-44:33.

19. **Claim 22: A system according to claim 13, wherein the controller is configured control the plasma collection process to collect a target volume of pure plasma and/or a target volume of plasma component within the plasma collection container.**

129. See §X.A.8, *supra*.

20. **Claim 23: A system according to claim 22, wherein the target volume of pure plasma and/or the target volume of plasma component is based, at least in part, on a weight of the subject.**

130. See §X.A.9, *supra*.

B. Ground 2: Claims 1 and 24-30 are obvious over Lavender in view of Fletcher-Haynes

1. Claim 1

a. 1[a]–1[e]

131. As discussed above, Lavender discloses claim limitations 1[preamble]-1[e]. See §§X.A.a-f.

- b. 1[f] calculating a volume of pure plasma collected within the plasma collection container based, at least in part, on a volume of plasma component collected within the plasma collection container, a ratio of anticoagulant added to the withdrawn whole blood, and a hematocrit of the donor.**

132. Should the Board find that “based on” is narrowly limited to the specific calculation disclosed in the ’873 patent, in my opinion, a POSITA would have found

it obvious to implement Fletcher-Haynes' calculation of the volume of pure plasma in the collection container based, at least in part, on a volume of plasma component collected within the plasma collection container, a ratio of anticoagulant added to the withdrawn whole blood, and a hematocrit of the donor into Lavender's system.

133. In my opinion, a POSITA would be motivated to combine the teachings of Lavender with Fletcher-Haynes's teachings to more accurately track and optimize the amount of plasma collected from the donor. For example, Fletcher-Haynes teaches using a donor's height, weight, and hematocrit to determine the total amount of pure plasma to collect from the donor. EX1005, 20:9-15. By adding the additional parameter of height to Lavender's data collection steps, Lavender's systems would more accurately determine the optimal amount of pure plasma to collect. A POSITA would readily implement 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.

134. A POSITA, in my opinion, 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

is used for the same purpose as Lavender's system—using donor parameters to determine the total amount of pure plasma to collect.

135. Fletcher-Haynes expressly discloses calculating the volume of pure plasma in the collection container based, at least in part, on (i) a volume of plasma component collected within the plasma collection container, (ii) a ratio of anticoagulant added to the withdrawn whole blood, and (iii) a hematocrit of the donor. EX1005, 22:66-23:3. Specifically, Fletcher-Haynes' Equation 15 recites $f_{ACP} = [(R - 1)(1 - H)]^{-1}$ 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 (e.g. a ratio of anticoagulant added to withdrawn whole blood), and H is the donor's hematocrit. EX1004, 48:21-32, 50:16-52:14. Equation 17 defines the target source plasma volume, or 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) and V_{SP} is the volume of pure plasma in the source plasma bag. EX1004, 50:16-52:14. A POSITA would look to Fletcher-Haynes' disclosures related to considering hematocrit when calculating real-time volumes in Lavender's system to better determine the volume of pure plasma. Specifically, in my opinion,

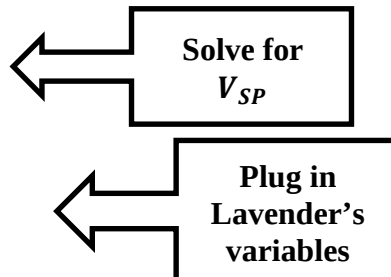
a POSITA would look to incorporate Equations 15, 17, and 22 to determine **TPF** based on the donor's hematocrit.

136. As discussed hereinabove, **TPF** is the total pure plasma collected in the plasma collection bag during a procedure. EX1005, Table VI §2.g. Lavender determines **TPF** by using the volume of dilute plasma collected: $TPF = TDPF * PDF$, where $TDPF$ is the volume of dilute plasma collected in the plasma collection bag determined using a weight sensor, and PDF is a constant derived from a predetermined ratio of plasma to anticoagulant used to dilute incoming plasma to 68%. EX1005, 20:46-54, 41:1-44:33, Table VI: §2.g. A POSITA would understand that the determined **TDPF** in Lavender could simply be plugged in as V_{SPB} , the dilute plasma volume in the source bag, into Equation 22 of Fletcher-Haynes to determine V_{SP} , the volume of pure plasma in a plasma collection bag (e.g., $TPF = TPF(1 + f_{ACP})$). When Fletcher-Hayne's equation for f_{ACP} is plugged into the equation for V_{SPB} (or **TDPF** in Lavender), a POSITA would readily derive an equation for V_{SP} (or **TPF**) to use in Lavender's system:

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

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

$$TPF = \frac{TDPF}{(1 + [(R - 1)(1 - H)]^{-1})}$$



137. Lavender's system already tracks $TDPF$ using a scale on the collection bag, so a POSITA could simply plug in the derived equation for V_{SP} above from Fletcher-Haynes to determine a real time pure plasma volume, or TPF , in the collection container. R in Fletcher-Haynes is 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 a POSITA would readily derive this R in Fletcher-Haynes by simply dividing the blood pump rate ($QBP = QB + QC$) by the citrate pump rate ($QCP = QC$), and Lavender is already calculating QBP and QCP prior to and during a procedure (i.e., $R = \frac{QBP}{QCP}$). Lavender's system also already receives the donor's hematocrit (H), and thus a POSITA can plug in the derived equation for TPF (or V_{SP}) from Fletcher-Haynes into Lavender's main loop algorithm to determine TPF during a procedure based on parameters the Lavender system is already calculating:

$$TPF = \frac{TDPF}{(1 + [(\frac{QBP}{QCP} - 1)(1 - H)]^{-1})}$$

138. By utilizing the above equation for TPF from Fletcher-Haynes in Lavender's main loop algorithm, Lavender's system calculates a volume of pure plasma collected within the plasma collection container based directly on (i) a volume of plasma component collected within the plasma collection container (e.g. $TDPF$), a ratio of anticoagulant added to the withdrawn whole blood (e.g. $\frac{QBP}{QCP}$), and

a hematocrit of the donor (e.g., H). This is reflected in the TPF equation shown immediately above.

139. Specifically, Fletcher-Haynes recites, “Product Plasma - The volume of plasma product collected during the procedure (total plasma volume less anticoagulant volume)”⁶, corresponding to the pure plasma collected in claim 1 of the '873 patent. EX1005, 22:66-23:3. In my opinion, a POSITA would easily utilize this formula in the systems and methods of Lavender to determine the collected pure plasma volume by inserting the equation for product plasma from Fletcher-Haynes into the Main Loop Algorithm of Lavender. Such a combination would have been no more than combining prior art elements according to known methods to yield predictable results.

140. In my opinion, a POSITA would understand, after utilizing Fletcher-Haynes' equations to determine a *new* TPF value based directly on (i) a volume of plasma component collected within the plasma collection container (e.g. $TDPF$), a ratio of anticoagulant added to the withdrawn whole blood (e.g. $\frac{QBP}{QCP}$), and a

⁶ I note that the equation to determine product plasma by taking the total plasma volume (i.e. total volume of plasma and anticoagulant in the collection bag) less the anticoagulant volume, was well know in the art long before the filing of the '873 patent. For example, Japanese Patent Publication No. JP 2002-282352A (EX1013) discloses determining a pure plasma volume in a collection container using a volume of anticoagulant in the collection container.

hematocrit of the donor (e.g., H), that the equation for TCF would need be updated to account for this *new TPF* value, i.e. $TCF = TDPF - TPF$. A POSITA would understand that $TCF = TDPF - TPF$, since the volume of fluid in the collection container only includes pure plasma and anticoagulant.

2. Claim 24

a. 24[preamble] A system for collecting plasma comprising:

141. See §X.A.11.a, *supra*.

b. 24[a] a venous-access device for drawing whole blood from a subject and returning blood components to the subject;

142. See §X.A.11.b, *supra*.

c. 24[b] a blood component separation device for separating the withdrawn blood into a plasma component and a second blood component, the blood component separation device having an outlet and being configured to convey the plasma component to a plasma collection container;

143. See §X.A.11.c, *supra*.

d. 24[c] a blood draw line fluidly coupled to the venous-access device and configured to transport withdrawn whole blood to the blood component separation device, the flow through the blood draw line being controlled by a blood draw pump;

144. See §X.A.11.d, *supra*.

- e. **24[d] an anticoagulant line fluidly coupled to an anticoagulant source, the anticoagulant line configured to introduce anticoagulant into the withdrawn whole blood; and**

145. See §X.A.11.e, *supra*.

- f. **24[e] a controller configured to control the operation of the blood component separation device and the blood draw pump,**

146. See §X.A.11.f, *supra*.

- g. **24[f] the controller configured to calculate a volume of pure plasma to be collected within the plasma collection container based, at least in part, on a volume of plasma component to be collected within the plasma collection container, a ratio of anticoagulant to be added to the withdrawn whole blood, and a hematocrit of the subject.**

147. In Lavender's system, the total amount of pure plasma to collect (*MAXPF*) within the plasma collection container is determined by multiplying the donor's bodyweight (*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, 22:35-41, 41:4-44:42. Lavender's system also determines a volume of dilute plasma to be collected (*MAXDPF*), or a "volume of plasma component to be

collected” in claim 24, by multiplying the donor’s bodyweight (*BW*) by a second predetermined constant (*C2*), which is derived from a predetermined ratio of plasma to anticoagulant used to dilute incoming plasma by 68% of its initial concentration, i.e. $C2 = C1 / PDF$.

148. A POSITA would be motivated to incorporate Fletcher-Haynes’ calculations into Lavender’s system as it would result in a more accurate determination of a target volume of pure plasma (*MAXPF*). 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 volume of plasma component to be collected within the plasma collection container (*MAXDPF*), a ratio of anticoagulant to be added to the withdrawn whole blood, and a hematocrit of the subject, compared to determining the target volume of pure plasma (*MAXPF*) based only on a donor’s weight and a predetermined constant.

149. Specifically, a POSITA would look to Fletcher-Haynes to better determine the volume of pure plasma to be collected using Lavender’s system.

150. Fletcher-Haynes determines a target volume for total plasma component comprising raw plasma and anticoagulant based at least in part on the donor’s parameters. Fletcher-Haynes’ controller runs a “prediction model for predicting a yield of a particular blood component to be collected before a collection

procedure is initiated using a compilation of algorithms” which determine, e.g., calculate, a target volume for plasma component (e.g., V_{SPB} , total volume in source plasma bag) and/or raw plasma (e.g., V_{SP} , volume of pure plasma in the source plasma bag), using entered donor weight, height, and hematocrit. EX1005, 48:1-3.

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

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

152. The AC Ratio (R) in Fletcher-Haynes is the ratio of the collective flow of anticoagulant and whole blood through the inlet line in relation to the flow of anticoagulant through the inlet line. EX1005, 48:23-26.

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

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

Fletcher-Haynes calculates a volume of total plasma (V_{SPB}) in equation 22.

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

154. In my opinion, a POSITA would be motivated to incorporate Fletcher-Haynes’ calculations of f_{ACP} and V_{SPB} into Lavender’s system as it would result in a more accurate determination of a target volume of pure plasma. 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 weight, compared to determining the target volume of pure plasma based only on a donor's weight.

155. Specifically, a POSITA would look to Fletcher-Haynes to better determine the volume of pure plasma to be collected using Lavender's system. After using Fletcher-Haynes' calculations to determine f_{ACP} based on the donor's hematocrit (H) and a ratio of anticoagulant to be added to the withdrawn whole blood (R), a POSITA would be motivated to determine a new target volume of pure plasma to collect (*new MAXPF*) by solving Fletcher-Haynes' equation for V_{SPB} using the volume of dilute plasma to be collected (*MAXDPF*) in Lavender. This equation is derived below:

$$V_{SPB} = V_{SP}(1 + f_{ACP})$$
$$\frac{V_{SPB}}{(1 + f_{ACP})} = V_{SP} \quad \leftarrow \text{Solve for } V_{SP}$$
$$\frac{MAXDPF}{(1 + [(R - 1)(1 - H)]^{-1})} = \text{new MAXPF} \quad \leftarrow \text{Plug in Lavender's variables}$$

See §X.A.1.g, *supra*; EX1005, 22:35-41, 41:4-44:42.

156. A POSITA would easily implement the above-derived equation for *new MAXPF* into the algorithms of Lavender, and specifically to set a new target

maximum volume of pure plasma to collect in Lavender's main loop algorithm in Table VI. In my opinion, a POSITA would also recognize that R in the equation for *new MAXPF* would be determined based on the equations disclosed in Fletcher-Haynes utilizing the donor's hematocrit. EX1005, 48:23-26. R in Fletcher-Haynes is 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 a POSITA would readily derive this R in Fletcher-Haynes by simply dividing the blood pump rate ($QBP = QB + QC$) by the citrate pump rate ($QCP = QC$), and Lavender is already calculating QBP and QCP prior to and during a procedure (i.e., $R = \frac{QBP}{QCP}$).

157. Thus, as illustrated in the above equation for *new MAXPF*, it would be obvious for a POSITA to modify Lavender in view of Fletcher-Haynes to configure Lavender's controller to calculate a volume of pure plasma to be collected within the plasma collection container based, at least in part, on a volume of plasma component to be collected within the plasma collection container, a ratio of anticoagulant to be added to the withdrawn whole blood, and a hematocrit of the subject.

3. **Claim 25: A system according to claim 24, wherein the controller is configured to control the plasma collection process to collect a target volume of pure plasma and/or target volume of plasma component.**

158. See §X.A.19, *supra*.

4. **Claim 26: A system according to claim 25, wherein the target volume of pure plasma and/or target volume of plasma component is based, at least in part, on a weight of the subject.**

159. See §X.A.20, *supra*.

5. **Claim 27: A system according to claim 24, wherein the controller is configured to calculate a percentage of anticoagulant to be collected in the plasma component.**

160. In the system of Lavender and Fletcher-Haynes described above, a *new MAXPF* is determined using a volume of plasma component to be collected within the plasma collection container (*MAXDPF*), a ratio of anticoagulant to be added to the withdrawn whole blood (*R*), and a hematocrit of the subject (*H*). See §X.B.2, *supra*. When utilizing this equation from Fletcher-Haynes in Lavender's system, in my opinion, a POSITA would recognize the need to recalculate the *MAXCF* by subtracting the *new MAXPF* from the calculated *MAXDPF* (e.g., $new\ MAXCF = MAXDPF - new\ MAXPF$). Accordingly, a POSITA would understand how the controller would calculate a percentage of anticoagulant to be collected in the plasma component by dividing *new MAXCF* by *MAXDPF* (i.e., percentage of anticoagulant to be collected in the plasma component $= \left(\frac{new\ MAXCF}{MAXDPF} \right) * 100$).

6. **Claim 28: A system according to claim 27, wherein the calculated percentage of anticoagulant to be collected in the plasma component is based, at least in part, upon the ratio of**

anticoagulant to be added to the withdrawn whole blood and the hematocrit of the donor.

161. See §X.B.3, *supra*.

7. **Claim 29: A system according to claim 27, wherein the calculated volume of pure plasma to be collected within the plasma collection container is based, at least in part, on the calculated percentage of anticoagulant to be collected in the plasma component.**

162. In the Lavender-Fletcher-Haynes combination described above, the total volume of pure plasma to be collected in the plasma collection container (*new MAXPF*) is calculated based on the following equation:

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

163. As described above, the equation for *new MAXPF* is derived by a POSITA using the equations provided in Fletcher-Haynes, including the equation for f_{ACP} , the anticoagulant expressed as a fraction of pure plasma volume. In my opinion, a POSITA would understand that f_{ACP} is a representation of the calculated percentage of anticoagulant to be collected in the plasma component, and is equivalent to a percentage written in a fraction form. Thus, through the use of f_{ACP} in Fletcher-Haynes, the calculation of *new MAXPF* is based, at least in part, on the calculated percentage of anticoagulant to be collected in the plasma component.

8. **Claim 30: A system according to claim 24, wherein the controller is further configured to calculate a volume of**

anticoagulant to be collected in the collected plasma component based, at least in part, upon the hematocrit of the subject, the volume of pure plasma to be collected within the plasma collection container based, at least in part, upon the volume of anticoagulant to be collected in the collected plasma component.

164. In the system of Lavender and Fletcher-Haynes described above, a *new MAXPF* is determined using a volume of plasma component to be collected within the plasma collection container (*MAXDPF*), a ratio of anticoagulant to be added to the withdrawn whole blood (*R*), and a hematocrit of the subject (*H*). See §X.B.2.g, *supra*. When utilizing this equation from Fletcher-Haynes in Lavender's system, a POSITA would recognize the need to recalculate the *MAXCF* by subtracting the *new MAXPF* from the calculated *MAXDPF* (e.g., *new MAXCF* = *MAXDPF* – *new MAXPF*). This *new MAXCF* is based, at least in part, on a volume of plasma component to be collected within the plasma collection container (*MAXDPF*), a ratio of anticoagulant to be added to the withdrawn whole blood (*R*), and a hematocrit of the subject (*H*). Due to the direct mathematical relationship between *new MAXCF* and *new MAXPF* (i.e., *new MAXCF* = *MAXDPF* – *new MAXPF*), a POSITA would readily understand that *new MAXPF* is based, at least in part, on *new MAXCF*.

165. Thus, it would be obvious for a POSITA to modify Lavender in view of Fletcher-Haynes to configure Lavender's controller to calculate a volume of

anticoagulant to be collected within the plasma collection container based, at least in part, on a hematocrit of the subject; and to calculate a volume of pure plasma to collect based, at least in part, on the calculated volume of anticoagulant to collect.

C. Ground 3: Claims 6 and 18 are obvious over Lavender in view of Fletcher-Haynes and Min

- 1. Claim 6: A method according to claim 5, further comprising: determining a change in volume within an anticoagulant container, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the change in volume within the anticoagulant container.**

166. 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. EX1006, 11:52-55, 17:17-22.

167. Specifically, a POSITA would have found it obvious and would have been motivated to combine the Lavender and Fletcher-Haynes disclosures with Min's teachings of using weigh sensors 246 to track weight changes and derive fluid processing volumes, including the volume change of anticoagulant container 276. EX1006, 11:52-55, 17:17-22.

168. Additionally, a POSITA would have had a reasonable expectation of success in modifying the Lavender-Fletcher-Haynes system in view of Min because 1) each relate to the same well-known technologies, 2) both apply substantially

similar techniques to achieve similar results, and 3) the functionality of Lavender would not change when Lavender is used for the same purpose as Min's system—that is, monitoring the weight of an anticoagulant bag in an apheresis procedure to determine a change in volume within the anticoagulant container. EX1006, 11:52-55, 17:17-22. Weigh sensors 246 in Min are utilized 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.

169. First, Lavender, Fletcher-Haynes, and Min all relate to the well-known technologies of separating blood components. Accordingly, a POSITA would have found it obvious to combine the teachings of Lavender and Fletcher-Haynes with Min because they are in the same field of endeavor with the same well-known technologies, e.g. technologies of separating blood components. That is, combining Lavender, Fletcher-Haynes, and Min entails the mere use of known solutions to improve similar systems and methods in the same way, i.e., to use Min's technique of monitoring the weight of an anticoagulant bag to determine a volume of anticoagulant provided to whole blood prior to separation of blood components.

170. Second, Lavender, Fletcher-Haynes, and Min apply substantially similar techniques to achieve similar results. As discussed above, Lavender discloses fractionating blood “to collect blood substances, such as plasma.” EX1004, 1:12-13.

Similarly, Min discloses a system for “separating whole blood into plasma and red blood cells.” EX1006, 4:26-29. A POSITA would have been motivated to add Min’s system to monitor the weight (and volume) of an anticoagulant bag into Lavender’s blood fractioning system to provide an additional way to determine the estimated amount of anticoagulant in the plasma collection container, and Min’s disclosed systems for determining the amount of anticoagulant added to a system function substantially similar to Lavender’s technique of adding and monitoring the anticoagulant added to a blood separation system. Indeed, Min’s anticoagulant container and tube arrangement (*See* Fig. 10) is structurally similar to that of Lavender’s (*See* Fig. 20). EX1006, 3:26-29. Therefore, it would have been obvious, and a POSITA would have been motivated, to modify Lavender’s blood fractioning system to incorporate Min’s monitoring of the change in the weight of the anticoagulant container. Additionally, it would have been an obvious design choice to use Min’s anticoagulant monitoring scale in Lavender’s system to improve the accuracy of the anticoagulant volume added to the system for determining more accurate pure plasma volume based on the anticoagulant volume.

171. Finally, the intended functionality of Lavender’s blood fractioning system would not change when used for monitoring the anticoagulant weight similarly to Min’s apheresis system. That is, in my opinion, a POSITA would have

expected Lavender's blood fractioning system to successfully determine the amount of anticoagulant added to the system from the anticoagulant container. Additionally, Lavender discloses converting a change in weight to a change in volume using a specific gravity. Accordingly, a POSITA would understand that there is a reasonable expectation of success when modifying the algorithms to determine the volume of anticoagulant in the collected plasma component in Lavender's system with the weight scale of Min for monitoring the change in the anticoagulant volume—each relate to the same well-known technologies and both apply substantially similar techniques to achieve similar results.

172. The combined system of Lavender in view of Fletcher-Haynes and Min discloses determining a change in volume within an anticoagulant container, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the change in volume within the anticoagulant container. Specifically, as acknowledged by the '873 patent, a POSITA would understand that substantially all of the anticoagulant added to a centrifuge-based blood fractionating system would end up in the plasma collection container. See §VIII.A-B; EX1001 at 7:58-65. To the extent 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 the blood

fractionating system of Lavender would not end up in the plasma collection container, it would have been obvious for a POSITA to replace the membrane-based fractionator in Lavender with a centrifuge-based blood component collection device 18, like the one disclosed in Fletcher-Haynes. EX1004, 6:3-12; EX1005, 46:16-43. It was generally known in the art that a centrifuge-based blood separation device, as compared to a membrane-based blood separation device, provided a comparable treatment quality in a shorter period of time. See EX1010, p. 135. In my opinion, a POSITA would have been motivated to combine the teachings of Lavender with Fletcher-Haynes' centrifuge-based collection device to more efficiently separate plasma from a donor's blood, and reduce the overall procedure time.

173. A POSITA, in my opinion, 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.

174. 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 may reduce potential errors in the determination of the volume of anticoagulant due to errors in the blood and anticoagulant pump rates (e.g., errors in pumps 306, 308 in Lavender). EX1004, Fig.20.

2. **Claim 18: A system according to claim 17, further comprising: an anticoagulant source weight sensor configured to measure a weight of the anticoagulant source, the controller further configured to monitor a change in volume within the anticoagulant source based on the measured weight of the anticoagulant source, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the change in volume within the anticoagulant source.**

175. See §X.C.1, *supra*.

D. Ground 4: Claims 9 and 18 are obvious over Lavender in view of Fletcher-Haynes, Headley, and Barrett

- 1. Claim 9: A method according to claim 1, further comprising: monitoring a volume of red blood cells collected within the blood component separation device, the hematocrit of the donor being determined based, at least in part, on the monitored volume of red blood cells collected within the blood component separation device and a volume of whole blood withdrawn from the donor.**

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

177. Fletcher-Haynes teaches separating red blood cells from incoming whole blood during a blood separation procedure. EX1005, 7:33-35; 9:35-44. Headley relates to systems and methods for separating platelets and other blood components from blood. EX1009, Abstract. Headley teaches the use of an array 97 of optical sensors within a blood separation system (e.g. a centrifuge), and the array 97 of optical sensors are used to determine a volume of red blood cells within the blood separation system. EX1009, 1:10-24; 4:48-64. It would have been obvious for a POSITA to include the optical sensor(s) of Headley in the blood separation device of Lavender to determine the volume of red blood cells collected from the donor and

allow the red blood cells to be immediately returned to the donor during the separation procedure.

178. Barrett teaches determining a donor's hematocrit by dividing the red blood cell volume of a blood sample over the total volume of the blood sample. EX1008, 2:45-49.

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

180. Additionally, Lavender, Fletcher-Haynes, Headley, and Barrett, apply substantially similar techniques to achieve similar results. As discussed above, Lavender discloses fractionating blood "to collect blood substances, such as plasma." EX1004, 1:12-13. Barrett also teaches patient blood data acquisition and management for hemodialysis patients in preparation for blood separation procedures. EX1008, 1:6-19.

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

182. Thus, a POSITA would use both (i) the monitored volume of red blood cells collected during a blood separation procedure from Headley, and (ii) the volume of whole blood withdrawn from the donor, or total blood flow (***TQB***) in Lavender, to determine a donor's real-time hematocrit in Lavender's Main Loop algorithm. This equation could simply be added into the Main Loop algorithm of Lavender and would increase the accuracy of Lavender's calculated estimates. Also, to more effectively separate the red blood cells in Lavender's system, a POSITA would be motivated to replace the membrane-based blood fractionator in Lavender

with the centrifuge-based blood component collection device 18 including a centrifuge. §IX.F.1; EX1004, 6:3-12; EX1005, 46:16-43.

183. In my opinion, it would have been an obvious design choice to use Barrett's equation in the system of Lavender-Fletcher-Haynes-Headley to determine the real-time hematocrit of the donor during a separation procedure. The intended functionality of the system of Lavender and Fletcher-Haynes would not change when including Headley's optical sensor(s) and Barrett's equation for hematocrit. That is, a POSITA would have expected the combined system to successfully determine the hematocrit of a donor using a red blood cell volume determined by Headley's optical sensor(s) and Barrett's equation for hematocrit.

184. Accordingly, Lavender in view of Fletcher-Haynes, Headley, and Barrett teach monitoring a volume of red blood cells collected within the blood component separation device because Headley teaches monitoring the volume of collected red blood cells. EX1009, 1:10-24; 4:48-64; 17:19-24; EX1008, 2:45-49. The determined hematocrit of the donor based, at least in part, on the monitored volume of red blood cells collected within the blood component separation device and a volume of whole blood withdrawn from the donor is taught by Barret's equation for hematocrit, which determines hematocrit by dividing the red blood cell volume of a blood sample (e.g. the volume of red blood cells collected) by the total

volume of the blood sample (e.g. total blood flow into the system, Lavender's **TQB**).

EX1004, 41:8-44:32; EX1006, 12:22-25; 17:19-24; EX1009, 1:10-24; 2:45-49;
4:48-64.

2. **Claim 18: A system according to claim 11, an optical sensor located on the blood component separation device and configured to monitor a volume of red blood cells collected within the blood component separation device, the controller configured to determine the subject's hematocrit based, at least in part, upon on the monitored volume of red blood cells collected within the blood component separation device and a volume of whole blood withdrawn from the subject.**

185. See §X.D.1, *supra*.. As discussed above, Headley teaches the use of an array 97 of optical sensors within a blood separation system (e.g. a centrifuge), and the array 97 of optical sensors are used to determine a volume of red blood cells within the blood separation system. EX1009, 1:10-24; 4:48-64. Thus, Headley discloses an optical sensor located on the blood component separation device and configured to monitor a volume of red blood cells collected within the blood component separation device. See §X.D.1; EX1009, 1:10-24; 4:48-64.

186. Accordingly, in my opinion, Lavender in view of Fletcher-Haynes, Headley, and Barrett teaches an optical sensor located on the blood component separation device and configured to monitor a volume of red blood cells collected within the blood component separation device using Headley's optical sensor. EX1009, 4:48-64. Using Lavender's Main Loop algorithm and Barrett's equation to

determine hematocrit, Lavender, modified in view of Fletcher-Haynes, Min, Barrett, and Headley teaches a controller configured to determine the subject's hematocrit based, at least in part, upon on the monitored volume of red blood cells collected within the blood component separation device and a volume of whole blood withdrawn from the subject. *See* §X.D.1, *supra.*; EX1004, 41:8-44:32; EX1006, 12:22-25; 17:19-24; EX1008, 2:45-49.

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

- 1. Claim 4: A method according to claim 1, further comprising: determining a volume of anticoagulant within the blood component separation device, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the volume of anticoagulant within the blood component separation device.**

187. In my opinion, a POSITA would have recognized that determining the total volume of anticoagulant in the collected plasma component based on the change in volume within the anticoagulant container would not account for any remaining anticoagulant within the blood separation device that has not yet flowed into the plasma collection container. *See* §X.C.1. In my opinion, a POSITA would have recognized a need to account for the remaining anticoagulant within the blood separation device when determining the volume of anticoagulant in the collection container using the volume of anticoagulant supplied to the blood separation device. By accounting for this remaining anticoagulant within the blood separation device,

the system would reduce errors and increase the accuracy of the determined anticoagulant volume in the plasma collection container.

188. A POSITA would have found it obvious and would have been motivated to combine Lavender, Fletcher-Haynes, and Min with Turgut's teaching of a volume detector to determine a total volume of fluid within a blood separation system, such as a separation chamber of a centrifuge used to separate blood into components. EX1011, [0073].

189. A POSITA would have found it obvious to combine the teachings of Lavender-Fletcher-Haynes-Min with Turgut because they are in the same field of endeavor with the same well-known technologies of separating blood components.

190. Turgut's separation system is structurally similar to that of Lavender's (*See* Fig. 20) and is used to separate blood into different components. EX1011, [0052]-[0068], Fig. 1A. Therefore, it would have been obvious, and a POSITA would have been motivated, to modify Lavender's blood fractioning system including Fletcher-Haynes' centrifugal separation device to incorporate Turgut's monitoring of the volume of fluid within the blood separation device. Additionally, it would have been an obvious design choice to use Turgut's volume detector in Lavender's system to improve the accuracy of the calculated volume of anticoagulant within the plasma collection container.

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

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

2. **Claim 15: A system according to claim 11, an optical sensor located on the blood component separation device and configured to monitor the contents of the blood component separation device and determine if a volume of anticoagulant**

remains within the blood component separation device, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the volume of anticoagulant within the blood component separation device.

193. See §X.E.1, *supra*. In my opinion, a POSITA would recognize that the volume detector of Turgut may be an optical sensor, similar to the optical sensor discussed above in Headley used to determine a volume of red blood cells within the blood separation system. EX1009, 1:10-24; 4:48-64. It was generally known by a POSITA at the time of the effective filing date of the '873 patent that a volume detector may be an optical sensor.

F. Ground V: All Claims of the '873 Patent Are Ineligible Under Section 101

194. Because patent eligibility is a question of law, I do not provide any opinions on patent eligibility. I have, however, been asked to provide my opinions as a POSITA regarding issues that may underlie the question of patent eligibility. Because many of these opinions relate to the conventionality of equipment, systems, and methods discussed in the '873 Patent, these opinions are discussed in my Background on Plasma Apheresis Section.

G. Ground VI: Claims 10, 11, 12, 22, 23, and 25 Lack an Adequate Written Description in the '873 Patent Specification

195. In my opinion, many of the '873 patent's claims barely resemble the patent's specification. Thus, Haemonetics' claims fail to meet the written description requirement.

2. Disclosure of the Purported Invention

196. As discussed above, Haemonetics' purported invention is a blood processing system that continues collecting plasma until reaching a target volume of pure plasma. EX1001, 7:33-36. To do that, Haemonetics purportedly tracks the amount of pure plasma in the container while blood is being drawn and checks whether the amount of pure plasma equals a target volume of pure plasma. See EX1001, Fig. 4. Figure 4 of the '873 patent illustrates the steps allegedly performed by Haemonetics' patented system.

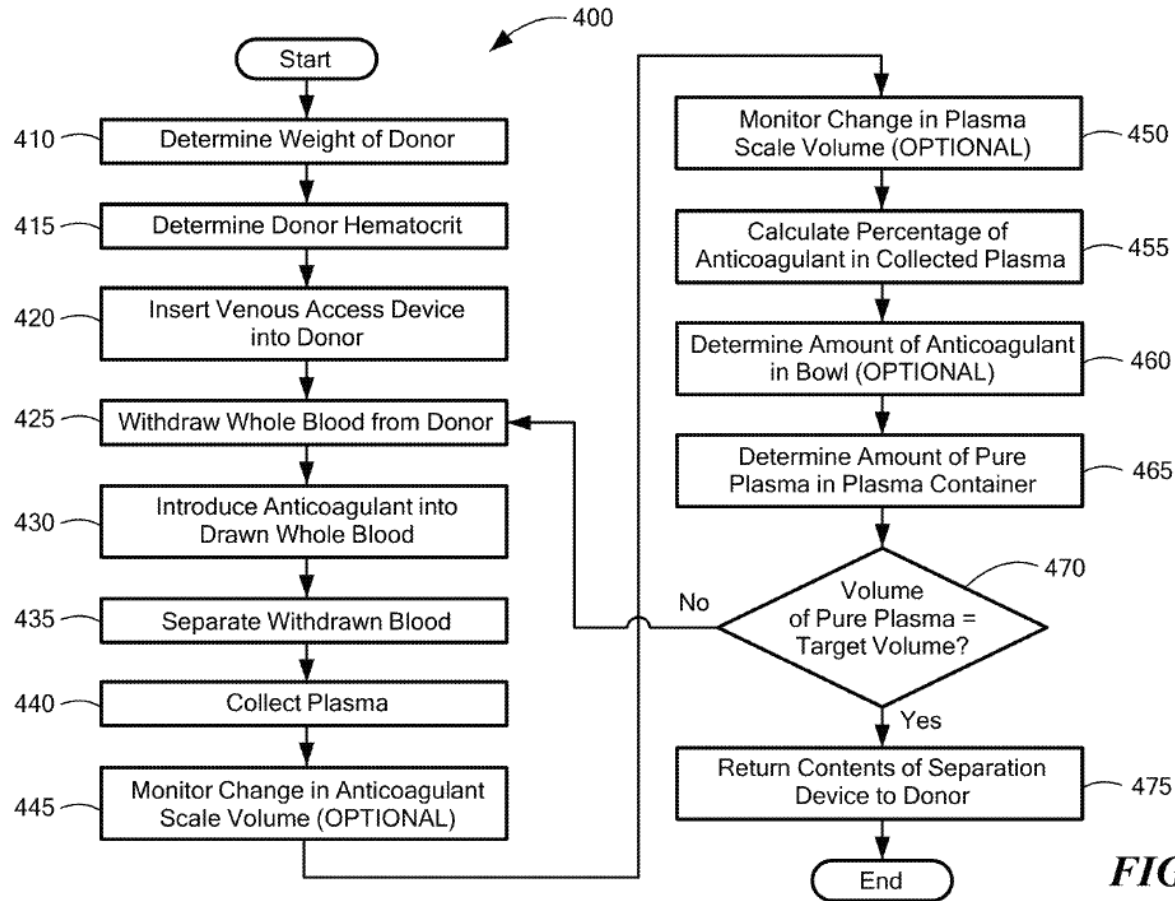


FIG. 4

197. As shown in Figure 4, the technician or system determines a donor's weight and hematocrit, inserts a venous access device into the donor, and then the method enters a loop (steps 425-470) that continues until "volume of pure plasma = target volume." EX1001, Fig. 4. The technician or the system withdraws whole blood, introduces anticoagulant into withdrawn blood, collects plasma, calculates the percentage of anticoagulant in collected plasma, and determines the amount of pure plasma in the plasma container. EX1001, 6:23-7:39. Once plasma collection is

complete, saline is returned to the donor to compensate for lost plasma. EX1001, 9:26-36.

3. Argument

198. In my opinion, claims 10, 11, 12, 22, 23, and 25 recite limitations that lack written description support in the '873 patent. For example, these claims, as discussed further below, include claim limitations that recite basic apheresis equipment that allegedly measures/calculates target volumes of **anticoagulated plasma**. This concept lacks sufficient written description support in the '873 patent's specification.

199. Claims 10, 11, 12, 22, 23, and 25, which require calculating a target volume of anticoagulated plasma, lack adequate written description support. Haemonetics uses the term "plasma component" sparsely in its specification, but does not refer to a target volume of plasma component anywhere in the specification except the claims. EX1001, 1:39-41, 17:4-8, 17:34-39. Figure 4, which shows the purported invention, does not reference plasma component.

200. First, Haemonetics' disclosure that the field of the invention is collecting "a plasma product" does not support claim limitations reciting measuring/calculating target or current plasma component volumes.

201. Further, the '873 patent teaches away from collecting a “plasma component” that is not “pure plasma.” “[I]llustrative embodiments of” Haemonetics’ purported invention include only a system for “collecting a target volume of pure plasma.” EX1001, 4:23-25. Haemonetics’ claimed system collects plasma until a collected volume reaches a target volume of pure plasma because doing so offers the purported improvement of “collect[ing] a greater volume of plasma as compared to prior art systems that stop based on a plasma/anticoagulant mixture.” EX1001, 10:23-26. Thus, the focus of the patent is ***pure plasma*** collection, not plasma component collection.

202. Additionally, in my opinion, Haemonetics’ claims 11, 23, and 26 broaden the scope of its claims to include calculating a “plasma component” target volume using “and/or” language. EX1001, claim 1. Specifically, each of claims 11, 23, and 26 recite “wherein the target volume of pure plasma and/or target volume of plasma component is based, at least in part, on a weight of the subject.” In doing so, Haemonetics claims what the '873 patent identifies as prior art (calculating a volume of plasma product) in addition to its purported invention (calculating a volume of pure plasma). EX1001, 10:1-6. Haemonetics’ disclosure of the prior art calculating a volume of plasma product is insufficient to provide written description support for

its claimed invention, which is focused on both calculating pure plasma volumes and calculating plasma component volumes.

203. Simply put, Haemonetics' claimed system does not calculate a target volume for plasma component, rendering any claims that calculate a target volume of anticoagulated plasma invalid for a lack of written description.

XI. AVAILABILITY FOR CROSS-EXAMINATION

204. 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

205. 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

206. 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

Declaration of Dr. Gary Fletcher in Support of Petition for
Post Grant Review of U.S. Patent No. 12,324,873
PGR2026-00009

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,
<u>November 2, 2025</u>	