



# UNITED STATES PATENT AND TRADEMARK OFFICE

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|                                |             |                      |                     |                  |
|--------------------------------|-------------|----------------------|---------------------|------------------|
| APPLICATION NO.                | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
| 17/205,400                     | 03/18/2021  | Michael Ragusa       | 130670-80104        | 4686             |
| 86738                          | 7590        | 01/07/2025           | EXAMINER            |                  |
| MCCARTER & ENGLISH, LLP BOSTON |             |                      | DEAK, LESLIE R      |                  |
| 265 Franklin Street            |             |                      |                     |                  |
| Boston, MA 02110               |             |                      | ART UNIT            | PAPER NUMBER     |
|                                |             |                      | 3799                |                  |
|                                |             |                      | NOTIFICATION DATE   | DELIVERY MODE    |
|                                |             |                      | 01/07/2025          | ELECTRONIC       |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docket@mccarter.com

| APPLICATION NO. | ISSUE DATE  | PATENT NO. |
|-----------------|-------------|------------|
| 17/205,400      | 07-Jan-2025 | 12186474   |

MCCARTER & ENGLISH, LLP BOSTON  
265 Franklin Street  
Boston, MA 02110

## EGRANT NOTIFICATION

Your electronic patent grant (eGrant) is now available, which can be accessed via Patent Center at <https://patentcenter.uspto.gov>

The electronic patent grant is the official patent grant under 35 U.S.C. 153. For more information, please visit <https://www.uspto.gov/electronicgrants>



## UNITED STATES PATENT AND TRADEMARK OFFICE

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| APPLICATION NO. | ISSUE DATE | PATENT NO. | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|------------|------------|---------------------|------------------|
| 17/205,400      | 01/07/2025 | 12186474   | 130670-80104        | 4686             |

86738 7590 12/18/2024  
MCCARTER & ENGLISH, LLP BOSTON  
265 Franklin Street  
Boston, MA 02110

### ISSUE NOTIFICATION

The projected patent number and issue date are specified above. The patent will issue electronically. The electronically issued patent is the official patent grant pursuant to 35 U.S.C. § 153. The patent may be accessed on or after the issue date through Patent Center at <https://patentcenter.uspto.gov/>. The patent will be available in both the public and the private sides of Patent Center. Further assistance in electronically accessing the patent, or about Patent Center, is available by calling the Patent Electronic Business Center at 1-888-217-9197.

The USPTO is implementing electronic patent issuance with a transition period, during which period the USPTO will mail a ceremonial paper copy of the electronic patent grant to the correspondence address of record. Additional copies of the patent (i.e., certified and presentation copies) may be ordered for a fee from the USPTO's Certified Copy Center at <https://certifiedcopycenter.uspto.gov/index.html>. The Certified Copy Center may be reached at (800)972-6382.

#### **Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)**

(application filed on or after May 29, 2000)

The Patent Term Adjustment is 966 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Center (<https://patentcenter.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Patents Stakeholder Experience (OPSE), Stakeholder Support Division (SSD) at (571)-272-4200.

INVENTOR(s) (Please see PATENT CENTER site <https://patentcenter.uspto.gov> for additional inventors):

Michael Ragusa, Hingham, MA;

APPLICANT(s) (Please see PATENT CENTER site <https://patentcenter.uspto.gov> for additional applicants):

Haemonetics Corporation, Boston, MA;

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The USA offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to encourage and facilitate business investment. To learn more about why the USA is the best country in the world to develop technology, manufacture products, and grow your business, visit [SelectUSA.gov](https://selectusa.gov).





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## ISSUE FEE TRANSMITTAL FORM

|               |             |                      |                   |
|---------------|-------------|----------------------|-------------------|
| APPLICATION # | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET # |
| 17205400      | 03/18/2021  | Michael Ragusa       | 130670-80104      |

### Title of Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA

### Application Information

|                  |                                                |                 |            |
|------------------|------------------------------------------------|-----------------|------------|
| APPLICATION TYPE | Nonprovisional Application under 35 USC 111(a) | DATE DUE        | 12/05/2024 |
| CONFIRMATION #   | 4686                                           | ISSUE FEE DUE   | \$ 1200    |
| EXAMINER         | LESLIE DEAK                                    | PUBLICATION DUE | \$ 0       |
| GROUP ART UNIT   | 3799                                           | TOTAL FEES DUE  | \$1200     |
| CLASS - SUBCLASS | 604/006040                                     | PREV. PAID FEE  | \$ 0       |
| ENTITY STATUS    | Regular Undiscounted                           |                 |            |

### 1. CHANGE OF CORRESPONDENCE ADDRESS AND/OR INDICATION OF FEE ADDRESS (37 CFR 1.33 & 1.363)

#### Correspondence Address

CURRENT ADDRESS

#### Maintenance Fee Address

CURRENT ADDRESS



Change of correspondence address requested, system generated AIA/122-PC form attached



Fee address indication requested, system generated SB/47-PC form attached

## 2. ENTITY STATUS

### Change in Entity Status

#### NEW STATUS

## 3. THE FOLLOWING FEES ARE SUBMITTED



Issue Fee



Publication Fee

## 4. FEE AUTHORIZATION



I authorize USPTO to apply my previously paid issue fee to the current fees due



The Director is hereby authorized to apply my previously paid issue fee to the current fee due and to charge deficient fees to Deposit Account Number:



If in addition to the payment of the issue fee amount submitted with this form, there are any discrepancies in any amount(s) due, the Director is authorized to charge any deficiency, or credit any overpayment, to Deposit Account Number: 504876

## 5. FIRM AND/OR ATTORNEY NAMES TO BE PRINTED

#### NOTE: If no name is listed, no name will be printed

For printing on the patent front page, list to be displayed as entered

McCarter & English, LLP  
Jonathan C. Lovely

## 6. ASSIGNEE NAME(S) AND RESIDENCE DATA TO BE PRINTED

NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

**Haemonetics Corporation**

Boston, MA UNITED STATES

Corporation

**Signature**

I certify, in accordance with 37 CFR 1.4(d)(4) that I am an attorney or agent registered to practice before the Patent and Trademark Office who has filed and has been granted power of attorney in this application. I also certify that this Fee(s) Transmittal form is being transmitted to the USPTO via Patent Center on the date indicated below.

| <b>Signature</b>  | <b>Name</b>     | <b>Registration #</b> | <b>Date</b> |
|-------------------|-----------------|-----------------------|-------------|
| /Jonathan Lovely/ | Jonathan Lovely | 60821                 | 12/03/2024  |



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Page 1 of 2  
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## ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #  
**17/205,400**

RECEIPT DATE / TIME  
**12/03/2024 01:23:38 PM Z ET**

ATTORNEY DOCKET #  
**130670-80104**

### Title of Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA

### Application Information

|                        |                                                          |                      |                 |
|------------------------|----------------------------------------------------------|----------------------|-----------------|
| APPLICATION TYPE       | Utility - Nonprovisional Application under 35 USC 111(a) | PATENT #             | -               |
| CONFIRMATION #         | 4686                                                     | FILED BY             | Jonathan Lovely |
| PATENT CENTER #        | 68184466                                                 | FILING DATE          | 03/18/2021      |
| CUSTOMER #             | 86738                                                    | FIRST NAMED INVENTOR | Michael Ragusa  |
| CORRESPONDENCE ADDRESS | -                                                        | AUTHORIZED BY        | -               |

### Documents

**TOTAL DOCUMENTS: 1**

| DOCUMENT   | PAGES | DESCRIPTION                 | SIZE (KB) |
|------------|-------|-----------------------------|-----------|
| web85b.pdf | 3     | Issue Fee Payment (PTO-85B) | 58 KB     |

### Digest

| DOCUMENT   | MESSAGE DIGEST(SHA-512)                                                                                                                  |
|------------|------------------------------------------------------------------------------------------------------------------------------------------|
| web85b.pdf | 8FD7783DCC3968952F078E3A7FE4378A973AF8BDF456E3626<br>1FD03D3E76849218E7D7437F14A9D8501556DCD97679C8B78<br>6D820E57904E647FF2E2AC73243086 |

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

Terumo v. Haemonetics - PGR2025-00077  
Petitioner Terumo Exhibit 1002-0008

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

**National Stage of an International Application under 35 U.S.C. 371**

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

**New International Application Filed with the USPTO as a Receiving Office**

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.



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## ELECTRONIC PAYMENT RECEIPT

|                                    |                                                           |                                          |
|------------------------------------|-----------------------------------------------------------|------------------------------------------|
| APPLICATION #<br><b>17/205,400</b> | RECEIPT DATE / TIME<br><b>12/03/2024 01:23:38 PM Z ET</b> | ATTORNEY DOCKET #<br><b>130670-80104</b> |
|------------------------------------|-----------------------------------------------------------|------------------------------------------|

### Title of Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA

### Application Information

|                           |                                                             |                         |                 |
|---------------------------|-------------------------------------------------------------|-------------------------|-----------------|
| APPLICATION TYPE          | Utility - Nonprovisional Application<br>under 35 USC 111(a) | PATENT #                | -               |
| CONFIRMATION #            | 4686                                                        | FILED BY                | Jonathan Lovely |
| PATENT CENTER #           | 68184466                                                    | AUTHORIZED BY           | -               |
| CUSTOMER #                | 86738                                                       | FILING DATE             | 03/18/2021      |
| CORRESPONDENCE<br>ADDRESS | -                                                           | FIRST NAMED<br>INVENTOR | Michael Ragusa  |

### Payment Information

|                                      |                                                   |                                                 |
|--------------------------------------|---------------------------------------------------|-------------------------------------------------|
| PAYMENT METHOD<br><b>DA / 504876</b> | PAYMENT TRANSACTION ID<br><b>E2024B3D24105219</b> | PAYMENT AUTHORIZED BY<br><b>Jonathan Lovely</b> |
|--------------------------------------|---------------------------------------------------|-------------------------------------------------|

| FEE CODE                 | DESCRIPTION       | ITEM PRICE(\$) | QUANTITY | ITEM TOTAL(\$)    |
|--------------------------|-------------------|----------------|----------|-------------------|
| 1501                     | UTILITY ISSUE FEE | 1200.00        | 1        | 1200.00           |
| <b>TOTAL<br/>AMOUNT:</b> |                   |                |          | <b>\$1,200.00</b> |

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

#### New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

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Docket No.: 130670-80104  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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In re Utility Application of:  
Haemonetics Corporation

Application No.: 17/205,400

Confirmation No.: 4686

Filed: March 18, 2021

Art Unit: 3799

For: SYSTEM AND METHOD FOR COLLECTING  
PLASMA

---

Examiner: L. R. Deak

**COMMENTS ON STATEMENT OF REASONS**

**FOR ALLOWANCE**

MS Issue Fee  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Madam:

In response to the Examiner's statement of reasons for allowance contained in the Notice of Allowance mailed on September 5, 2024, please enter the following Comments. In accordance with MPEP 1302.14, these comments are submitted with the Issue Fee Transmittal.

Applicant believes that the claims of the present application are in condition for allowance. The Examiner's Statement of Reasons for Allowance, however, states that "...the prior art fails to disclose a method of collecting blood plasma wherein a volume of anticoagulant in the collected plasma component is calculated in real time, as the plasma is being collected (such as by counting anticoagulant pump revolutions)..." While the prior art fails to teach or suggest this limitation, the present claims do not include such a limitation and do not require real time calculation of the volume of anticoagulant in the collected plasma component.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 50-4876, under Order No. 130670-80104.

ME1 48844157v.1



Application No. 17/205,400  
Comments on Statement of Reason For Allowance

Docket No.: 130670-80104

Dated: December 3, 2024

Respectfully submitted,  
Electronic signature: /Jonathan C. Lovely, Reg.  
No. 60,821/  
Jonathan C. Lovely  
Registration No.: 60,821  
MCCARTER & ENGLISH, LLP  
265 Franklin Street  
Boston, Massachusetts 02110  
(617) 449-6500  
(617) 607-9200 (Fax)  
Attorney/Agent For Applicant



UNITED STATES  
PATENT AND TRADEMARK OFFICE

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www.uspto.gov

## ELECTRONIC ACKNOWLEDGEMENT RECEIPT

|                                    |                                                           |                                          |
|------------------------------------|-----------------------------------------------------------|------------------------------------------|
| APPLICATION #<br><b>17/205,400</b> | RECEIPT DATE / TIME<br><b>12/03/2024 01:18:57 PM Z ET</b> | ATTORNEY DOCKET #<br><b>130670-80104</b> |
|------------------------------------|-----------------------------------------------------------|------------------------------------------|

### Title of Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA

### Application Information

|                           |                                                             |                         |                 |
|---------------------------|-------------------------------------------------------------|-------------------------|-----------------|
| APPLICATION TYPE          | Utility - Nonprovisional Application<br>under 35 USC 111(a) | PATENT #                | -               |
| CONFIRMATION #            | 4686                                                        | FILED BY                | Tricia Troup    |
| PATENT CENTER #           | 68187451                                                    | FILING DATE             | 03/18/2021      |
| CUSTOMER #                | 86738                                                       | FIRST NAMED<br>INVENTOR | Michael Ragusa  |
| CORRESPONDENCE<br>ADDRESS | -                                                           | AUTHORIZED BY           | Jonathan Lovely |

### Documents

**TOTAL DOCUMENTS: 1**

| DOCUMENT                                                                  | PAGES | DESCRIPTION                                | SIZE<br>(KB) |
|---------------------------------------------------------------------------|-------|--------------------------------------------|--------------|
| Comments on Statement of<br>Reasons for<br>Allowance_130670-<br>80104.pdf | 2     | Post Allowance<br>Communication - Incoming | 20 KB        |

### Digest

| DOCUMENT                                                              | MESSAGE DIGEST(SHA-512)                                                                                                                  |
|-----------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| Comments on Statement of<br>Reasons for<br>Allowance_130670-80104.pdf | 87739CC98EA65D5B3AE73116A711EC7244EA0560B7EFADDF<br>7178427690A028959269BDB57846CC8A8AAD7D4CF8B98756C<br>E7768864D309069C2757242ADF93A3D |

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as

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**New Applications Under 35 U.S.C. 111**

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**New International Application Filed with the USPTO as a Receiving Office**

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## NOTICE OF ALLOWANCE AND FEE(S) DUE

86738 7590 09/05/2024  
MCCARTER & ENGLISH, LLP BOSTON  
265 Franklin Street  
Boston, MA 02110

EXAMINER

DEAK, LESLIE R

ART UNIT

PAPER NUMBER

3799

DATE MAILED: 09/05/2024

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 17/205,400      | 03/18/2021  | Michael Ragusa       | 130670-80104        | 4686             |

TITLE OF INVENTION: SYSTEM AND METHOD FOR COLLECTING PLASMA

| APPLN. TYPE    | ENTITY STATUS | ISSUE FEE DUE | PUBLICATION FEE DUE | PREV. PAID ISSUE FEE | TOTAL FEE(S) DUE | DATE DUE   |
|----------------|---------------|---------------|---------------------|----------------------|------------------|------------|
| nonprovisional | UNDISCOUNTED  | \$1200        | \$0.00              | \$0.00               | \$1200           | 12/05/2024 |

**THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.**

**THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.**

### HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 40% the amount of undiscounted fees, and micro entity fees are 20% the amount of undiscounted fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at [www.uspto.gov/PatentMaintenanceFees](http://www.uspto.gov/PatentMaintenanceFees).**

## PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via the USPTO patent electronic filing system.

By mail, send to: Mail Stop ISSUE FEE  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications. **Because electronic patent issuance may occur shortly after issue fee payment, any desired continuing application should preferably be filed prior to payment of this issue fee in order not to jeopardize copendency.**

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

86738 7590 09/05/2024  
MCCARTER & ENGLISH, LLP BOSTON  
265 Franklin Street  
Boston, MA 02110

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

### Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via the USPTO patent electronic filing system or by facsimile to (571) 273-2885, on the date below.

|                         |
|-------------------------|
| (Typed or printed name) |
| (Signature)             |
| (Date)                  |

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 17/205,400      | 03/18/2021  | Michael Ragusa       | 130670-80104        | 4686             |

TITLE OF INVENTION: SYSTEM AND METHOD FOR COLLECTING PLASMA

| APPLN. TYPE    | ENTITY STATUS | ISSUE FEE DUE | PUBLICATION FEE DUE | PREV. PAID ISSUE FEE | TOTAL FEE(S) DUE | DATE DUE   |
|----------------|---------------|---------------|---------------------|----------------------|------------------|------------|
| nonprovisional | UNDISCOUNTED  | \$1200        | \$0.00              | \$0.00               | \$1200           | 12/05/2024 |

| EXAMINER       | ART UNIT | CLASS-SUBCLASS |
|----------------|----------|----------------|
| DEAK, LESLIE R | 3799     | 604-006040     |

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 \_\_\_\_\_

2 \_\_\_\_\_

3 \_\_\_\_\_

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. Fees submitted: ☐ Issue Fee ☐ Publication Fee (if required)

4b. Method of Payment: (Please first reapply any previously paid fee shown above)

☐ Electronic Payment via the USPTO patent electronic filing system ☐ Enclosed check ☐ Non-electronic payment by credit card (Attach form PTO-2038)

☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. \_\_\_\_\_

5. Change in Entity Status (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29

☐ Applicant asserting small entity status. See 37 CFR 1.27

☐ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature \_\_\_\_\_

Date \_\_\_\_\_

Typed or printed name \_\_\_\_\_

Registration No. \_\_\_\_\_



# UNITED STATES PATENT AND TRADEMARK OFFICE

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| APPLICATION NO.                                                                                    | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.        | CONFIRMATION NO. |
|----------------------------------------------------------------------------------------------------|-------------|----------------------|----------------------------|------------------|
| 17/205,400                                                                                         | 03/18/2021  | Michael Ragusa       | 130670-80104               | 4686             |
| 86738 7590 09/05/2024<br>MCCARTER & ENGLISH, LLP BOSTON<br>265 Franklin Street<br>Boston, MA 02110 |             |                      | EXAMINER<br>DEAK, LESLIE R |                  |
|                                                                                                    |             |                      | ART UNIT<br>3799           | PAPER NUMBER     |
| DATE MAILED: 09/05/2024                                                                            |             |                      |                            |                  |

## Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

## OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.** Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

### Privacy Act Statement

**The Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. The United States Patent and Trademark Office (USPTO) collects the information in this record under authority of 35 U.S.C. 2. The USPTO's system of records is used to manage all applicant and owner information including name, citizenship, residence, post office address, and other information with respect to inventors and their legal representatives pertaining to the applicant's/owner's activities in connection with the invention for which a patent is sought or has been granted. The applicable Privacy Act System of Records Notice for the information collected in this form is COMMERCE/PAT-TM-7 Patent Application Files, available in the Federal Register at 78 FR 19243 (March 29, 2013).

<https://www.govinfo.gov/content/pkg/FR-2013-03-29/pdf/2013-07341.pdf>

Routine uses of the information in this record may include disclosure to:

- 1) law enforcement, in the event that the system of records indicates a violation or potential violation of law;
- 2) a federal, state, local, or international agency, in response to its request;
- 3) a contractor of the USPTO having need for the information in order to perform a contract;
- 4) the Department of Justice for determination of whether the Freedom of Information Act (FOIA) requires disclosure of the record;
- 5) a Member of Congress submitting a request involving an individual to whom the record pertains, when the individual has requested the Member's assistance with respect to the subject matter of the record;
- 6) a court, magistrate, or administrative tribunal, in the course of presenting evidence, including disclosures to opposing counsel in the course of settlement negotiations;
- 7) the Administrator, General Services Administration (GSA), or their designee, during an inspection of records conducted by GSA under authority of 44 U.S.C. 2904 and 2906, in accordance with the GSA regulations and any other relevant (i.e., GSA or Commerce) directive, where such disclosure shall not be used to make determinations about individuals;
- 8) another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c));
- 9) the Office of Personnel Management (OPM) for personnel research purposes; and
- 10) the Office of Management and Budget (OMB) for legislative coordination and clearance.

If you do not furnish the information requested on this form, the USPTO may not be able to process and/or examine your submission, which may result in termination of proceedings, abandonment of the application, and/or expiration of the patent.

|                               |                                      |                                        |                                 |
|-------------------------------|--------------------------------------|----------------------------------------|---------------------------------|
| <b>Notice of Allowability</b> | <b>Application No.</b><br>17/205,400 | <b>Applicant(s)</b><br>Ragusa, Michael |                                 |
|                               | <b>Examiner</b><br>LESLIE R DEAK     | <b>Art Unit</b><br>3799                | <b>AIA (FITF) Status</b><br>Yes |

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to TD and amendments filed 6 August 2024.  
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on \_\_\_\_\_.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on \_\_\_\_\_; the restriction requirement and election have been incorporated into this action.

3. ☒ The allowed claim(s) is/are 1-4 and 6-27. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see [http://www.uspto.gov/patents/init\\_events/pph/index.jsp](http://www.uspto.gov/patents/init_events/pph/index.jsp) or send an inquiry to [PPHfeedback@uspto.gov](mailto:PPHfeedback@uspto.gov).

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
**Certified copies:**  
a) ☐ All      b) ☐ Some\*      c) ☐ None of the:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).  
\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.  
**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.  
☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.  
**Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).**

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

|                                                                                                                   |                                                                                      |
|-------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892)                                                  | 5. <input type="checkbox"/> Examiner's Amendment/Comment                             |
| 2. <input type="checkbox"/> Information Disclosure Statements (PTO/SB/08),<br>Paper No./Mail Date _____.          | 6. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| 3. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit<br>of Biological Material _____. | 7. <input type="checkbox"/> Other _____.                                             |
| 4. <input type="checkbox"/> Interview Summary (PTO-413),<br>Paper No./Mail Date _____.                            |                                                                                      |

|                                                    |  |
|----------------------------------------------------|--|
| /LESLIE R DEAK/<br>Primary Examiner, Art Unit 3799 |  |
|----------------------------------------------------|--|



**DETAILED ACTION**

***Notice of Pre-AIA or AIA Status***

1. The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

***Terminal Disclaimer***

2. The terminal disclaimer filed on 6 August 2024 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of **US 10,758,652 and US 10,980,926** has been reviewed and is accepted. The terminal disclaimer has been recorded.

***Allowable Subject Matter***

3. Claims 1-4, 6-27 are allowed.

4. The following is an examiner's statement of reasons for allowance: The prior art fails to disclose or suggest the method and system as claimed by Applicant. In particular, the prior art fails to disclose a method of collecting blood plasma wherein a volume of anticoagulant in the collected plasma component is calculated in real time, as the plasma is being collected (such as by counting anticoagulant pump revolutions), along with the other steps and limitations of the claims. The prior art systems rely on calculations prepared in advance.

***Conclusion***

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LESLIE R DEAK whose telephone number is (571)272-4943. The examiner can normally be reached Monday-Friday, 9am to 5:30pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at <http://www.uspto.gov/interviewpractice>.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tom Sweet can be reached on 571-272-4761. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: <https://patentcenter.uspto.gov>. Visit <https://www.uspto.gov/patents/apply/patent-center> for more information about Patent Center and <https://www.uspto.gov/patents/docx> for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LESLIE R DEAK/  
Primary Examiner, Art Unit 3799  
27 August 2024

|                                                                                                                 |                                              |                                                                   |
|-----------------------------------------------------------------------------------------------------------------|----------------------------------------------|-------------------------------------------------------------------|
| <b><i>Search Notes</i></b><br> | <b>Application/Control No.</b><br>17/205,400 | <b>Applicant(s)/Patent Under Reexamination</b><br>Ragusa, Michael |
|                                                                                                                 | <b>Examiner</b><br>LESLIE R DEAK             | <b>Art Unit</b><br>3799                                           |

| CPC - Searched*                                                                                                                                                |            |          |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|----------|
| Symbol                                                                                                                                                         | Date       | Examiner |
| (A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC. | 10/28/2019 | LRD      |
| A61M1/029 A61M1/3672 A61M1/3693 A61M1/38 A61M2202/0415 A61M2230/207                                                                                            | 11/05/2020 | LRD      |

| CPC Combination Sets - Searched* |      |          |
|----------------------------------|------|----------|
| Symbol                           | Date | Examiner |
|                                  |      |          |

| US Classification - Searched* |          |      |          |
|-------------------------------|----------|------|----------|
| Class                         | Subclass | Date | Examiner |
|                               |          |      |          |

\* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

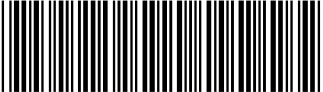
| Search Notes                                                           |            |          |
|------------------------------------------------------------------------|------------|----------|
| Search Notes                                                           | Date       | Examiner |
| inventor name search, EAST BRS search, consulted foreign search report | 10/28/2019 | LRD      |
| updated prior searches, consulted primary examiners                    | 02/27/2020 | LRD      |
| updated prior searches                                                 | 05/05/2020 | LRD      |
| consulted parent case, updated searches, ODP                           | 11/06/2020 | LRD      |
| consulted parent cases, updated searches, ODP                          | 04/30/2024 | LRD      |
| updated prior searches                                                 | 08/27/2024 | LRD      |

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|-----------------------------------------------------------------------------------------------------------------|----------------------------------------------|-------------------------------------------------------------------|
| <b><i>Search Notes</i></b><br> | <b>Application/Control No.</b><br>17/205,400 | <b>Applicant(s)/Patent Under Reexamination</b><br>Ragusa, Michael |
|                                                                                                                 | <b>Examiner</b><br>LESLIE R DEAK             | <b>Art Unit</b><br>3799                                           |

| Interference Search |                                                     |            |          |
|---------------------|-----------------------------------------------------|------------|----------|
| US Class/CPC Symbol | US Subclass/CPC Group                               | Date       | Examiner |
|                     | "current value of the hematocrit of the donor".clm. | 08/27/2024 | LRD      |

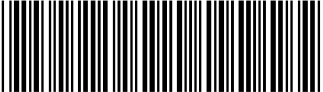
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|------------------------------------------------------------------------------------------------------------------|----------------------------------------------|-------------------------------------------------------------------|
| <b>Issue Classification</b><br> | <b>Application/Control No.</b><br>17/205,400 | <b>Applicant(s)/Patent Under Reexamination</b><br>Ragusa, Michael |
|                                                                                                                  | <b>Examiner</b><br>LESLIE R DEAK             | <b>Art Unit</b><br>3799                                           |

| CPC    |   |      |   |      |      |            |
|--------|---|------|---|------|------|------------|
| Symbol |   |      |   |      | Type | Version    |
| A61M   | / | 1    | / | 38   | F    | 2013-01-01 |
| A61M   | / | 1    | / | 385  | I    | 2013-01-01 |
| A61M   | / | 1    | / | 3644 | I    | 2014-02-04 |
| A61M   | / | 1    | / | 3672 | A    | 2013-01-01 |
| A61M   | / | 1    | / | 3693 | A    | 2013-01-01 |
| A61M   | / | 2202 | / | 0415 | A    | 2013-01-01 |
| A61M   | / | 1    | / | 3496 | A    | 2013-01-01 |
| A61M   | / | 2205 | / | 3379 | A    | 2013-01-01 |
| A61M   | / | 2205 | / | 3393 | A    | 2013-01-01 |
| A61M   | / | 2205 | / | 3306 | A    | 2013-01-01 |
| A61M   | / | 1    | / | 3626 | A    | 2013-01-01 |
| A61M   | / | 2230 | / | 207  | A    | 2013-01-01 |

| CPC Combination Sets |      |     |         |         |
|----------------------|------|-----|---------|---------|
| Symbol               | Type | Set | Ranking | Version |
| /                    |      |     |         |         |

|                                                                                                |  |                                    |                          |
|------------------------------------------------------------------------------------------------|--|------------------------------------|--------------------------|
| Use images from artifact folder? <input checked="" type="radio"/> Yes <input type="radio"/> No |  |                                    |                          |
| NONE<br>(Assistant Examiner)                                                                   |  | <b>Total Claims Allowed:</b><br>26 |                          |
| /LESLIE R DEAK/<br>Primary Examiner, Art Unit 3799<br>(Primary Examiner)                       |  | 27 August 2024<br>(Date)           | O.G. Print Claim(s)<br>1 |
|                                                                                                |  |                                    | O.G. Print Figure<br>4   |

|                                                                                                                  |                                              |                                                                   |
|------------------------------------------------------------------------------------------------------------------|----------------------------------------------|-------------------------------------------------------------------|
| <b>Issue Classification</b><br> | <b>Application/Control No.</b><br>17/205,400 | <b>Applicant(s)/Patent Under Reexamination</b><br>Ragusa, Michael |
|                                                                                                                  | <b>Examiner</b><br>LESLIE R DEAK             | <b>Art Unit</b><br>3799                                           |

|                                     |   |   |      |
|-------------------------------------|---|---|------|
| <b>INTERNATIONAL CLASSIFICATION</b> |   |   |      |
| <b>CLAIMED</b>                      |   |   |      |
| A61M1/38                            | / | 1 | / 38 |
| A61M1/36                            | / | 1 | / 36 |
| A61M1/34                            | / | 1 | / 34 |
| <b>NON-CLAIMED</b>                  |   |   |      |
|                                     | / |   | /    |

|                                   |                 |
|-----------------------------------|-----------------|
| <b>US ORIGINAL CLASSIFICATION</b> |                 |
| <b>CLASS</b>                      | <b>SUBCLASS</b> |
|                                   |                 |

|                            |                                          |  |  |  |  |  |
|----------------------------|------------------------------------------|--|--|--|--|--|
| <b>CROSS REFERENCES(S)</b> |                                          |  |  |  |  |  |
| <b>CLASS</b>               | <b>SUBCLASS (ONE SUBCLASS PER BLOCK)</b> |  |  |  |  |  |
|                            |                                          |  |  |  |  |  |

|                                                                                                |  |                                    |                          |
|------------------------------------------------------------------------------------------------|--|------------------------------------|--------------------------|
| Use images from artifact folder? <input checked="" type="radio"/> Yes <input type="radio"/> No |  |                                    |                          |
| NONE<br><br>(Assistant Examiner)                                                               |  | <b>Total Claims Allowed:</b><br>26 |                          |
| /LESLIE R DEAK/<br>Primary Examiner, Art Unit 3799<br>(Primary Examiner)                       |  | 27 August 2024<br>(Date)           | O.G. Print Claim(s)<br>1 |
|                                                                                                |  | (Date)                             | O.G. Print Figure<br>4   |

|                                                                                                                  |                                              |                                                                   |
|------------------------------------------------------------------------------------------------------------------|----------------------------------------------|-------------------------------------------------------------------|
| <b>Issue Classification</b><br> | <b>Application/Control No.</b><br>17/205,400 | <b>Applicant(s)/Patent Under Reexamination</b><br>Ragusa, Michael |
|                                                                                                                  | <b>Examiner</b><br>LESLIE R DEAK             | <b>Art Unit</b><br>3799                                           |

|                                                                                                                                                                                              |                 |              |                 |              |                 |              |                 |              |                 |              |                 |              |                 |              |                 |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|--------------|-----------------|--------------|-----------------|--------------|-----------------|--------------|-----------------|--------------|-----------------|--------------|-----------------|--------------|-----------------|
| <input type="checkbox"/> Claims renumbered in the same order as presented by applicant <input type="checkbox"/> CPA <input checked="" type="checkbox"/> T.D. <input type="checkbox"/> R.1.47 |                 |              |                 |              |                 |              |                 |              |                 |              |                 |              |                 |              |                 |
| <b>CLAIMS</b>                                                                                                                                                                                |                 |              |                 |              |                 |              |                 |              |                 |              |                 |              |                 |              |                 |
| <b>Final</b>                                                                                                                                                                                 | <b>Original</b> | <b>Final</b> | <b>Original</b> | <b>Final</b> | <b>Original</b> | <b>Final</b> | <b>Original</b> | <b>Final</b> | <b>Original</b> | <b>Final</b> | <b>Original</b> | <b>Final</b> | <b>Original</b> | <b>Final</b> | <b>Original</b> |
| 1                                                                                                                                                                                            | 1               | 10           | 11              | 19           | 20              |              |                 |              |                 |              |                 |              |                 |              |                 |
| 2                                                                                                                                                                                            | 2               | 11           | 12              | 20           | 21              |              |                 |              |                 |              |                 |              |                 |              |                 |
| 3                                                                                                                                                                                            | 3               | 12           | 13              | 21           | 22              |              |                 |              |                 |              |                 |              |                 |              |                 |
| 4                                                                                                                                                                                            | 4               | 13           | 14              | 22           | 23              |              |                 |              |                 |              |                 |              |                 |              |                 |
| 5                                                                                                                                                                                            | 6               | 14           | 15              | 23           | 24              |              |                 |              |                 |              |                 |              |                 |              |                 |
| 6                                                                                                                                                                                            | 7               | 15           | 16              | 24           | 25              |              |                 |              |                 |              |                 |              |                 |              |                 |
| 7                                                                                                                                                                                            | 8               | 16           | 17              | 25           | 26              |              |                 |              |                 |              |                 |              |                 |              |                 |
| 8                                                                                                                                                                                            | 9               | 17           | 18              | 26           | 27              |              |                 |              |                 |              |                 |              |                 |              |                 |
| 9                                                                                                                                                                                            | 10              | 18           | 19              |              |                 |              |                 |              |                 |              |                 |              |                 |              |                 |

|                                                                                                |                |                              |                   |
|------------------------------------------------------------------------------------------------|----------------|------------------------------|-------------------|
| Use images from artifact folder? <input checked="" type="radio"/> Yes <input type="radio"/> No |                |                              |                   |
| NONE                                                                                           |                | <b>Total Claims Allowed:</b> |                   |
| (Assistant Examiner)                                                                           | (Date)         | 26                           |                   |
| /LESLIE R DEAK/<br>Primary Examiner, Art Unit 3799                                             | 27 August 2024 | O.G. Print Claim(s)          | O.G. Print Figure |
| (Primary Examiner)                                                                             | (Date)         | 1                            | 4                 |

## Bibliographic Data

Application No: 17/205,400

Foreign Priority claimed: ☐ Yes ☒ No

35 USC 119 (a-d) conditions met: ☐ Yes ☒ No ☐ Met After Allowance

Verified and Acknowledged:

/LESLIE R DEAK/

Examiner's Signature

Initials

Title:

SYSTEM AND METHOD FOR COLLECTING PLASMA

---

| FILING or 371(c) DATE | CLASS | GROUP ART UNIT | ATTORNEY DOCKET NO. |
|-----------------------|-------|----------------|---------------------|
| 03/18/2021            | 604   | 3799           |                     |
| RULE                  |       |                |                     |

### APPLICANTS

Haemonetics Corporation, Boston, MA,

### INVENTORS

Michael Ragusa, Hingham, MA, UNITED STATES

### CONTINUING DATA

This application is a CON of 16931333 07/16/2020 PAT 10980934

16931333 is a CON of 15793339 10/25/2017 PAT 10792416

15793339 is a CIP of 15608183 05/30/2017 PAT 10758652

### FOREIGN APPLICATIONS

### IF REQUIRED, FOREIGN LICENSE GRANTED\*\*

03/29/2021

### STATE OR COUNTRY

UNITED STATES

### ADDRESS

### FILING FEE RECEIVED

\$3,000



# PE2E SEARCH - Search History (Prior Art)

| Ref # | Hits | Search Query                                                                                                                                                              | DBs                               | Default Operator | Plurals | British Equivalents | Time Stamp          |
|-------|------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------|------------------|---------|---------------------|---------------------|
| L1    | 2    | ("20180344910").PN.                                                                                                                                                       | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 11:36 AM |
| L2    | 1    | ( (A61M1/029 and A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415 and A61M2230/207).CPC. )                                                                        | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 11:37 AM |
| L3    | 1    | ( (A61M1/029 and A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415).CPC. )                                                                                         | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 11:37 AM |
| L4    | 20   | ( (A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415).CPC. )                                                                                                       | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 11:37 AM |
| L5    | 3    | "20120175313"                                                                                                                                                             | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 12:01 PM |
| L6    | 2    | "20030125881"                                                                                                                                                             | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 12:16 PM |
| L7    | 27   | 2009/0215602                                                                                                                                                              | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 12:17 PM |
| L8    | 3    | "20090215602"                                                                                                                                                             | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 12:18 PM |
| L9    | 2    | L1 AND ( (A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC. ) | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 12:25 PM |
| L10   | 8637 | ( (A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC. )        | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 12:25 PM |

|     |      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                             |    |     |     |                     |
|-----|------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------|----|-----|-----|---------------------|
| L11 | 1805 | L10 and hematocrit                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2019/10/28 12:26 PM |
| L12 | 1    | "I11" and (hematocrit with anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2019/10/28 12:26 PM |
| L13 | 1    | "I10" and (hematocrit with anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2019/10/28 12:30 PM |
| L14 | 2    | "I10" and (hematocrit same anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2019/10/28 12:30 PM |
| L15 | 44   | ((("RAGUSA") near3 ("Michael"))).INV.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | (US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT) | OR | OFF | OFF | 2019/10/28 12:31 PM |
| L16 | 2    | "I15" and (hematocrit same anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2019/10/28 12:31 PM |
| L17 | 183  | ("20010000185"  "20020062100"  "1025059"  "1611725"  "20010027156"  "20020043492"  "20020120227"  "20030055375"  "20030066807"  "20030125881"  "20030175150"  "20040186409"  "20050209522"  "20050235733"  "20060058167"  "20060155236"  "20070112289"  "20080146993"  "20120175313"  "20140039373"  "20140356851"  "20180344921"  "2087778"  "2661150"  "2750107"  "2792172"  "3096283"  "3145713"  "3239136"  "3244362"  "3244363"  "3409213"  "3456875"  "3489145"  "3565330"  "3655058"  "3737096"  "3774840"  "3987961"  "4007871"  "4010894"  "4014497"  "4040965"  "4056224"  "4082217"  "4086924"  "4140268"  "4142670"  "4151844"  "4197847"  "4285464"  "4300717"  "4303193"  "4321921"  "4387848"  "4425114"  "4430072"  "4447221"  "4457747"  "4464167"  "4466888"  "4482342"  "4490135"  "4530691"  "4534863"  "4643714"  "4647279"  "4655742"  "4680025"  "4684361"  "4692136"  "4708712"  "4713176"  "4734089"  "4740202"  "4740313"  "4755300"  "4767396"  "4795419"  "4795448"  "4806247"  "4806252"  "48 | (US-PGPUB; USPAT)                           | OR | OFF | OFF | 2019/10/28 12:37 PM |

|     |   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                      |    |     |     |                        |
|-----|---|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|----|-----|-----|------------------------|
|     |   | 08307" 4850995" 486<br>9812" 4871462" 4876<br>013" 4889524" 49118<br>33" 4934995" 494054<br>3" 4943273" 4968295"<br> 4983156" 4983158" <br>4985153" 4994188" 5<br>039401" 5045048" 50<br>98372" 5098373" 510<br>0372" 5100564" 5112<br>298" 5114396" 51356<br>67" 5141486" 514729<br>0" 5154716" 5174894"<br> 5194145" 5217426" <br>5217427" 5234403" 5<br>254248" 5273517" 52<br>77701" 5298016" 529<br>8171" 5300060" 5316<br>540" 5318511" 53185<br>12" 5348533" 536854<br>2" 5368555" 5386734"<br> 5387174" 5387187" <br>5403272" 5405308" 5<br>417650" 5431814" 54<br>37598" 5437624" 546<br>2667" 5470483" 5484<br>396" 5494592" 55056<br>85" 5514070" 554306<br>2" 5551941" 5585007"<br> 5607579" 5649903" <br>5651766" 5656163" 5<br>665061" 5712798" 57<br>28060" 5733253" 573<br>3446" 5733545" 5738<br>792" 5762791" 57796<br>60" 5783085" 579235<br>1" 5849203" 5882289"<br> 5906589" 5919125" <br>5964724" 5970432" 5<br>980760" 6007725" 60<br>59979" 6207063" 623<br>4989" 6296602" 6464<br>624" 6497676" 65583<br>07" 6623443" 674319<br>2" 7115205" 7186231"<br> 7270645" 7704454" <br>8628489" 8702637" 8<br>759094").PN. |                                      |    |     |     |                        |
| L18 | 2 | ("20180344910").PN.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2020/02/27<br>09:46 AM |
| L19 | 3 | "I15" and (hematocrit<br>same anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2020/05/05<br>01:39 PM |
| L20 | 1 | ("10758652").PN.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | (USPAT; USOCR)                       | OR | OFF | OFF | 2020/11/05<br>03:16 PM |
| L21 | 0 | ("20120175313").PN.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | (USPAT; USOCR)                       | OR | OFF | OFF | 2020/11/05<br>04:22 PM |

|     |     |                                                                                                                                                               |                                                                                                                                                                   |    |     |     |                        |
|-----|-----|---------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|-----|-----|------------------------|
| L22 | 1   | "20120175313"                                                                                                                                                 | (USPAT)                                                                                                                                                           | OR | OFF | OFF | 2020/11/05<br>04:22 PM |
| L23 | 10  | ("4713176"   "6348156"<br>  "6875191"   "7011761"<br>  "7087177"   "7297272"<br>  "7708710"  <br>"8075468").PN. OR<br>("8852140").URPN.                       | (US-PGPUB; USPAT;<br>USOCR)                                                                                                                                       | OR | OFF | OFF | 2020/11/05<br>04:22 PM |
| L24 | 8   | L23 and prim\$3                                                                                                                                               | (US-PGPUB; USPAT;<br>USOCR)                                                                                                                                       | OR | OFF | OFF | 2020/11/05<br>04:22 PM |
| L25 | 0   | (10/302682).APP.                                                                                                                                              | (USPAT; USOCR)                                                                                                                                                    | OR | OFF | OFF | 2020/11/05<br>04:26 PM |
| L26 | 1   | "20140100507"                                                                                                                                                 | (USPAT; USOCR)                                                                                                                                                    | OR | OFF | OFF | 2020/11/05<br>04:28 PM |
| L27 | 120 | A61M1/024.cpc.                                                                                                                                                | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                                              | OR | OFF | OFF | 2021/02/01<br>01:20 PM |
| L28 | 708 | G01n15/05.cpc.                                                                                                                                                | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                                              | OR | OFF | OFF | 2021/02/01<br>01:21 PM |
| L29 | 150 | G01n2015/055.cpc.                                                                                                                                             | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                                              | OR | OFF | OFF | 2021/02/01<br>01:21 PM |
| L30 | 3   | ((US-20030125881-<br>A1).did. AND<br>PGPB.dbnm.) OR ((US-<br>10758652-B2 OR US-<br>6348156-B1).did. AND<br>USPT.dbnm.)                                        | (US-PGPUB; USPAT;<br>USOCR; FIT (AU, AP,<br>AT, CA, CH, CN, DD,<br>DE, EA, EP, ES, FR,<br>GB, JP, KR, OA, RU,<br>SU, WO); FPRS; EPO;<br>JPO; DERWENT;<br>IBM_TDB) | OR | ON  | ON  | 2024/04/30<br>12:21 PM |
| L31 | 0   | L30 AND touchscreen                                                                                                                                           | (US-PGPUB; USPAT;<br>USOCR; FIT (AU, AP,<br>AT, CA, CH, CN, DD,<br>DE, EA, EP, ES, FR,<br>GB, JP, KR, OA, RU,<br>SU, WO); FPRS; EPO;<br>JPO; DERWENT;<br>IBM_TDB) | OR | ON  | ON  | 2024/04/30<br>12:21 PM |
| L32 | 0   | touchscreen WITH<br>plasmapheresis                                                                                                                            | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                                              | OR | OFF | OFF | 2024/04/30<br>12:22 PM |
| L33 | 4   | touchscreen SAME<br>plasmapheresis                                                                                                                            | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                                              | OR | OFF | OFF | 2024/04/30<br>12:22 PM |
| L34 | 16  | "10980926"                                                                                                                                                    | (US-PGPUB; USPAT;<br>USOCR; FIT (AU, AP,<br>AT, CA, CH, CN, DD,<br>DE, EA, EP, ES, FR,<br>GB, JP, KR, OA, RU,<br>SU, WO); EPO; JPO;<br>DERWENT)                   | OR | ON  | ON  | 2024/04/30<br>03:40 PM |
| L35 | 200 | ("1025059"   "1611725"<br>  "2087778"   "2661150"<br>  "2750107"   "2792172"<br>  "3096283"   "3145713"<br>  "3239136"   "3244362"<br>  "3244363"   "3409213" | (US-PGPUB; USPAT;<br>USOCR)                                                                                                                                       | OR | ON  | ON  | 2024/04/30<br>04:01 PM |

|  |  |                       |  |  |  |  |  |
|--|--|-----------------------|--|--|--|--|--|
|  |  | "3456875"   "3489145" |  |  |  |  |  |
|  |  | "3565330"   "3655058" |  |  |  |  |  |
|  |  | "3737096"   "3774840" |  |  |  |  |  |
|  |  | "3987961"   "4007871" |  |  |  |  |  |
|  |  | "4010894"   "4014497" |  |  |  |  |  |
|  |  | "4040965"   "4056224" |  |  |  |  |  |
|  |  | "4082217"   "4086924" |  |  |  |  |  |
|  |  | "4140268"   "4142670" |  |  |  |  |  |
|  |  | "4151844"   "4197847" |  |  |  |  |  |
|  |  | "4285464"   "4300717" |  |  |  |  |  |
|  |  | "4303193"   "4321921" |  |  |  |  |  |
|  |  | "4387848"   "4425114" |  |  |  |  |  |
|  |  | "4430072"   "4447221" |  |  |  |  |  |
|  |  | "4457747"   "4464167" |  |  |  |  |  |
|  |  | "4466888"   "4482342" |  |  |  |  |  |
|  |  | "4490135"   "4530691" |  |  |  |  |  |
|  |  | "4534863"   "4643714" |  |  |  |  |  |
|  |  | "4647279"   "4655742" |  |  |  |  |  |
|  |  | "4680025"   "4684361" |  |  |  |  |  |
|  |  | "4692136"   "4708712" |  |  |  |  |  |
|  |  | "4713176"   "4734089" |  |  |  |  |  |
|  |  | "4740202"   "4740313" |  |  |  |  |  |
|  |  | "4755300"   "4767396" |  |  |  |  |  |
|  |  | "4795419"   "4795448" |  |  |  |  |  |
|  |  | "4806247"   "4806252" |  |  |  |  |  |
|  |  | "4808307"   "4850995" |  |  |  |  |  |
|  |  | "4869812"   "4871462" |  |  |  |  |  |
|  |  | "4876013"   "4889524" |  |  |  |  |  |
|  |  | "4911833"   "4934995" |  |  |  |  |  |
|  |  | "4940543"   "4943273" |  |  |  |  |  |
|  |  | "4968295"   "4983156" |  |  |  |  |  |
|  |  | "4983158"   "4985153" |  |  |  |  |  |
|  |  | "4994188"   "5039401" |  |  |  |  |  |
|  |  | "5045048"   "5098372" |  |  |  |  |  |
|  |  | "5098373"   "5100372" |  |  |  |  |  |
|  |  | "5100564"   "5112298" |  |  |  |  |  |
|  |  | "5114396"   "5135667" |  |  |  |  |  |
|  |  | "5141486"   "5147290" |  |  |  |  |  |
|  |  | "5154716"   "5174894" |  |  |  |  |  |
|  |  | "5194145"   "5217426" |  |  |  |  |  |
|  |  | "5217427"   "5234403" |  |  |  |  |  |
|  |  | "5254248"   "5273517" |  |  |  |  |  |
|  |  | "5277701"   "5298016" |  |  |  |  |  |
|  |  | "5298171"   "5300060" |  |  |  |  |  |
|  |  | "5316540"   "5318511" |  |  |  |  |  |
|  |  | "5318512"   "5348533" |  |  |  |  |  |
|  |  | "5368542"   "5368555" |  |  |  |  |  |
|  |  | "5386734"   "5387174" |  |  |  |  |  |
|  |  | "5387187"   "5403272" |  |  |  |  |  |
|  |  | "5405308"   "5417650" |  |  |  |  |  |
|  |  | "5431814"   "5437598" |  |  |  |  |  |
|  |  | "5437624"   "5462667" |  |  |  |  |  |
|  |  | "5470483"   "5484396" |  |  |  |  |  |
|  |  | "5494592"   "5505685" |  |  |  |  |  |
|  |  | "5514070"   "5543062" |  |  |  |  |  |
|  |  | "5551941"   "5585007" |  |  |  |  |  |
|  |  | "5607579"   "5649903" |  |  |  |  |  |
|  |  | "5651766"   "5656163" |  |  |  |  |  |

|     |    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                      |    |     |     |                        |
|-----|----|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|----|-----|-----|------------------------|
|     |    | "5665061"   "5712798"<br>"5728060"   "5733253"<br>"5733446"   "5733545"<br>"5738792"   "5762791"<br>"5779660"   "5783085"<br>"5792351"   "5849203"<br>"5882289"   "5906589"<br>"5919125"   "5964724"<br>"5970432"   "5980760"<br>"6007725"   "6059979"<br>"6207063"   "6234989"<br>"6296602"   "6464624"<br>"6497676"   "6558307"<br>"6623443"   "6743192"<br>"7115205"   "7186231"<br>"7270645"   "7704454"<br>"8628489"   "8702637"<br>"8759094"   "9283316"<br>"10758652"  <br>"20010000185"  <br>"20010027156"  <br>"20020043492"  <br>"20020062100"  <br>"20020120227"  <br>"20030055375"  <br>"20030066807"  <br>"20030125881"  <br>"20030175150"  <br>"20040186409"  <br>"20050209522"  <br>"20050235733"  <br>"20060058167"  <br>"20060155236"  <br>"20070112289"  <br>"20080146993"  <br>"20120175313"  <br>"20140039373"  <br>"20140356851"  <br>"20180344910"  <br>"20180344921").pn.<br>AND (PGPB   USPT  <br>USOC).dbnm.<br>("20180344910").PN. |                                      |    |     |     |                        |
| L36 | 2  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L37 | 11 | ( (A61M1/029 and<br>A61M1/3672 and<br>A61M1/3693 and<br>A61M1/38 and<br>A61M2202/0415 and<br>A61M2230/207).CPC. )                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L38 | 11 | ( (A61M1/029 and<br>A61M1/3672 and<br>A61M1/3693 and<br>A61M1/38 and<br>A61M2202/0415).CPC.<br>)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/04/30<br>04:36 PM |

|     |       |                                                                                                                                                                           |                                             |    |     |     |                     |
|-----|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------|----|-----|-----|---------------------|
| L39 | 53    | ( ( A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415).CPC. )                                                                                                      | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L40 | 7     | "20120175313"                                                                                                                                                             | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L41 | 7     | "20030125881"                                                                                                                                                             | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L42 | 43    | 2009/0215602                                                                                                                                                              | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L43 | 13    | "20090215602"                                                                                                                                                             | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L44 | 2     | L1 AND ( (A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC. ) | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L45 | 12466 | ( (A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC. )        | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L46 | 2470  | L10 and hematocrit                                                                                                                                                        | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L47 | 7     | "I11" and (hematocrit with anticoagulant)                                                                                                                                 | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L48 | 6     | "I10" and (hematocrit with anticoagulant)                                                                                                                                 | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L49 | 16    | "I10" and (hematocrit same anticoagulant)                                                                                                                                 | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L50 | 59    | ((("RAGUSA") near3 ("Michael"))).INV.                                                                                                                                     | (US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT) | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L51 | 11    | "I15" and (hematocrit same anticoagulant)                                                                                                                                 | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L52 | 183   | ("20010000185" "20020062100" "1025059" "1611725" "20010027156" "20020043492" "20020120227" "20030055375                                                                   | (US-PGPUB; USPAT)                           | OR | OFF | OFF | 2024/04/30 04:36 PM |

|  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  |  |  |  |
|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|
|  |  | " 20030066807" 2003<br>0125881" 2003017515<br>0" 20040186409" 200<br>50209522" 200502357<br>33" 20060058167" 20<br>060155236" 20070112<br>289" 20080146993" 2<br>0120175313" 2014003<br>9373" 20140356851" <br>20180344921" 208777<br>8" 2661150" 2750107"<br> 2792172" 3096283" <br>3145713" 3239136" 3<br>244362" 3244363" 34<br>09213" 3456875" 348<br>9145" 3565330" 3655<br>058" 3737096" 37748<br>40" 3987961" 400787<br>1" 4010894" 4014497"<br> 4040965" 4056224" <br>4082217" 4086924" 4<br>140268" 4142670" 41<br>51844" 4197847" 428<br>5464" 4300717" 4303<br>193" 4321921" 43878<br>48" 4425114" 443007<br>2" 4447221" 4457747"<br> 4464167" 4466888" <br>4482342" 4490135" 4<br>530691" 4534863" 46<br>43714" 4647279" 465<br>5742" 4680025" 4684<br>361" 4692136" 47087<br>12" 4713176" 473408<br>9" 4740202" 4740313"<br> 4755300" 4767396" <br>4795419" 4795448" 4<br>806247" 4806252" 48<br>08307" 4850995" 486<br>9812" 4871462" 4876<br>013" 4889524" 49118<br>33" 4934995" 494054<br>3" 4943273" 4968295"<br> 4983156" 4983158" <br>4985153" 4994188" 5<br>039401" 5045048" 50<br>98372" 5098373" 510<br>0372" 5100564" 5112<br>298" 5114396" 51356<br>67" 5141486" 514729<br>0" 5154716" 5174894"<br> 5194145" 5217426" <br>5217427" 5234403" 5<br>254248" 5273517" 52<br>77701" 5298016" 529<br>8171" 5300060" 5316<br>540" 5318511" 53185<br>12" 5348533" 536854 |  |  |  |  |
|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|



|     |     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                      |    |     |     |                        |
|-----|-----|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|----|-----|-----|------------------------|
|     |     | 2" 5368555" 5386734"<br> 5387174" 5387187" <br>5403272" 5405308" 5<br>417650" 5431814" 54<br>37598" 5437624" 546<br>2667" 5470483" 5484<br>396" 5494592" 55056<br>85" 5514070" 554306<br>2" 5551941" 5585007"<br> 5607579" 5649903" <br>5651766" 5656163" 5<br>665061" 5712798" 57<br>28060" 5733253" 573<br>3446" 5733545" 5738<br>792" 5762791" 57796<br>60" 5783085" 579235<br>1" 5849203" 5882289"<br> 5906589" 5919125" <br>5964724" 5970432" 5<br>980760" 6007725" 60<br>59979" 6207063" 623<br>4989" 6296602" 6464<br>624" 6497676" 65583<br>07" 6623443" 674319<br>2" 7115205" 7186231"<br> 7270645" 7704454" <br>8628489" 8702637" 8<br>759094").PN. |                                      |    |     |     |                        |
| L53 | 2   | ("20180344910").PN.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L54 | 11  | "I15" and (hematocrit<br>same anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L55 | 1   | ("10758652").PN.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | (USPAT; USOCR)                       | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L56 | 0   | ("20120175313").PN.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | (USPAT; USOCR)                       | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L57 | 5   | "20120175313"                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | (USPAT)                              | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L58 | 13  | ("4713176"   "6348156"<br>  "6875191"   "7011761"<br>  "7087177"   "7297272"<br>  "7708710"  <br>"8075468").PN. OR<br>("8852140").URPN.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | (US-PGPUB; USPAT;<br>USOCR)          | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L59 | 9   | L23 and prim\$3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | (US-PGPUB; USPAT;<br>USOCR)          | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L60 | 0   | (10/302682).APP.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | (USPAT; USOCR)                       | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L61 | 2   | "20140100507"                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | (USPAT; USOCR)                       | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L62 | 190 | A61M1/024.cpc.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L63 | 987 | G01n15/05.cpc.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/04/30<br>04:36 PM |

|     |     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                              |    |     |     |                     |
|-----|-----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|----|-----|-----|---------------------|
| L64 | 220 | G01n2015/055.cpc.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | (US-PGPUB; USPAT; USOCR; DERWENT)                                                                                                            | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L65 | 3   | ((US-20030125881-A1).did. AND PGPB.dbnm.) OR ((US-10758652-B2 OR US-6348156-B1).did. AND USPT.dbnm.)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | (US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB) | OR | ON  | ON  | 2024/04/30 04:36 PM |
| L66 | 0   | L30 AND touchscreen                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | (US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB) | OR | ON  | ON  | 2024/04/30 04:36 PM |
| L67 | 0   | touchscreen WITH plasmapheresis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | (US-PGPUB; USPAT; USOCR; DERWENT)                                                                                                            | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L68 | 4   | touchscreen SAME plasmapheresis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | (US-PGPUB; USPAT; USOCR; DERWENT)                                                                                                            | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L69 | 16  | "10980926"                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | (US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); EPO; JPO; DERWENT)                | OR | ON  | ON  | 2024/04/30 04:36 PM |
| L70 | 200 | ("1025059"   "1611725"   "2087778"   "2661150"   "2750107"   "2792172"   "3096283"   "3145713"   "3239136"   "3244362"   "3244363"   "3409213"   "3456875"   "3489145"   "3565330"   "3655058"   "3737096"   "3774840"   "3987961"   "4007871"   "4010894"   "4014497"   "4040965"   "4056224"   "4082217"   "4086924"   "4140268"   "4142670"   "4151844"   "4197847"   "4285464"   "4300717"   "4303193"   "4321921"   "4387848"   "4425114"   "4430072"   "4447221"   "4457747"   "4464167"   "4466888"   "4482342"   "4490135"   "4530691"   "4534863"   "4643714"   "4647279"   "4655742"   "4680025"   "4684361"   "4692136"   "4708712"   "4713176"   "4734089" | (US-PGPUB; USPAT; USOCR)                                                                                                                     | OR | ON  | ON  | 2024/04/30 04:36 PM |

|  |  |                       |  |  |  |  |  |
|--|--|-----------------------|--|--|--|--|--|
|  |  | "4740202"   "4740313" |  |  |  |  |  |
|  |  | "4755300"   "4767396" |  |  |  |  |  |
|  |  | "4795419"   "4795448" |  |  |  |  |  |
|  |  | "4806247"   "4806252" |  |  |  |  |  |
|  |  | "4808307"   "4850995" |  |  |  |  |  |
|  |  | "4869812"   "4871462" |  |  |  |  |  |
|  |  | "4876013"   "4889524" |  |  |  |  |  |
|  |  | "4911833"   "4934995" |  |  |  |  |  |
|  |  | "4940543"   "4943273" |  |  |  |  |  |
|  |  | "4968295"   "4983156" |  |  |  |  |  |
|  |  | "4983158"   "4985153" |  |  |  |  |  |
|  |  | "4994188"   "5039401" |  |  |  |  |  |
|  |  | "5045048"   "5098372" |  |  |  |  |  |
|  |  | "5098373"   "5100372" |  |  |  |  |  |
|  |  | "5100564"   "5112298" |  |  |  |  |  |
|  |  | "5114396"   "5135667" |  |  |  |  |  |
|  |  | "5141486"   "5147290" |  |  |  |  |  |
|  |  | "5154716"   "5174894" |  |  |  |  |  |
|  |  | "5194145"   "5217426" |  |  |  |  |  |
|  |  | "5217427"   "5234403" |  |  |  |  |  |
|  |  | "5254248"   "5273517" |  |  |  |  |  |
|  |  | "5277701"   "5298016" |  |  |  |  |  |
|  |  | "5298171"   "5300060" |  |  |  |  |  |
|  |  | "5316540"   "5318511" |  |  |  |  |  |
|  |  | "5318512"   "5348533" |  |  |  |  |  |
|  |  | "5368542"   "5368555" |  |  |  |  |  |
|  |  | "5386734"   "5387174" |  |  |  |  |  |
|  |  | "5387187"   "5403272" |  |  |  |  |  |
|  |  | "5405308"   "5417650" |  |  |  |  |  |
|  |  | "5431814"   "5437598" |  |  |  |  |  |
|  |  | "5437624"   "5462667" |  |  |  |  |  |
|  |  | "5470483"   "5484396" |  |  |  |  |  |
|  |  | "5494592"   "5505685" |  |  |  |  |  |
|  |  | "5514070"   "5543062" |  |  |  |  |  |
|  |  | "5551941"   "5585007" |  |  |  |  |  |
|  |  | "5607579"   "5649903" |  |  |  |  |  |
|  |  | "5651766"   "5656163" |  |  |  |  |  |
|  |  | "5665061"   "5712798" |  |  |  |  |  |
|  |  | "5728060"   "5733253" |  |  |  |  |  |
|  |  | "5733446"   "5733545" |  |  |  |  |  |
|  |  | "5738792"   "5762791" |  |  |  |  |  |
|  |  | "5779660"   "5783085" |  |  |  |  |  |
|  |  | "5792351"   "5849203" |  |  |  |  |  |
|  |  | "5882289"   "5906589" |  |  |  |  |  |
|  |  | "5919125"   "5964724" |  |  |  |  |  |
|  |  | "5970432"   "5980760" |  |  |  |  |  |
|  |  | "6007725"   "6059979" |  |  |  |  |  |
|  |  | "6207063"   "6234989" |  |  |  |  |  |
|  |  | "6296602"   "6464624" |  |  |  |  |  |
|  |  | "6497676"   "6558307" |  |  |  |  |  |
|  |  | "6623443"   "6743192" |  |  |  |  |  |
|  |  | "7115205"   "7186231" |  |  |  |  |  |
|  |  | "7270645"   "7704454" |  |  |  |  |  |
|  |  | "8628489"   "8702637" |  |  |  |  |  |
|  |  | "8759094"   "9283316" |  |  |  |  |  |
|  |  | "10758652"            |  |  |  |  |  |
|  |  | "20010000185"         |  |  |  |  |  |
|  |  | "20010027156"         |  |  |  |  |  |

|     |    |                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                  |    |     |     |                        |
|-----|----|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|----|-----|-----|------------------------|
|     |    | "20020043492"  <br>"20020062100"  <br>"20020120227"  <br>"20030055375"  <br>"20030066807"  <br>"20030125881"  <br>"20030175150"  <br>"20040186409"  <br>"20050209522"  <br>"20050235733"  <br>"20060058167"  <br>"20060155236"  <br>"20070112289"  <br>"20080146993"  <br>"20120175313"  <br>"20140039373"  <br>"20140356851"  <br>"20180344910"  <br>"20180344921").pn.<br>AND (PGPB   USPT  <br>USOC).dbnm. |                                                                                                                                                  |    |     |     |                        |
| L71 | 0  | "current value of the<br>hematocrit of the<br>donor".clm.                                                                                                                                                                                                                                                                                                                                                     | (US-PGPUB; USPAT;<br>USOCR; FIT (AU, AP,<br>AT, CA, CH, CN, DD,<br>DE, EA, EP, ES, FR,<br>GB, JP, KR, OA, RU,<br>SU, WO)); EPO; JPO;<br>DERWENT) | OR | ON  | ON  | 2024/08/27<br>02:18 PM |
| L72 | 2  | ("20180344910").PN.                                                                                                                                                                                                                                                                                                                                                                                           | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                             | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L73 | 11 | ( (A61M1/029 and<br>A61M1/3672 and<br>A61M1/3693 and<br>A61M1/38 and<br>A61M2202/0415 and<br>A61M2230/207).CPC. )                                                                                                                                                                                                                                                                                             | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                             | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L74 | 11 | ( (A61M1/029 and<br>A61M1/3672 and<br>A61M1/3693 and<br>A61M1/38 and<br>A61M2202/0415).CPC.<br>)                                                                                                                                                                                                                                                                                                              | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                             | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L75 | 53 | ( (A61M1/3672 and<br>A61M1/3693 and<br>A61M1/38 and<br>A61M2202/0415).CPC.<br>)                                                                                                                                                                                                                                                                                                                               | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                             | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L76 | 8  | "20120175313"                                                                                                                                                                                                                                                                                                                                                                                                 | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                             | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L77 | 9  | "20030125881"                                                                                                                                                                                                                                                                                                                                                                                                 | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                             | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L78 | 44 | 2009/0215602                                                                                                                                                                                                                                                                                                                                                                                                  | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                             | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L79 | 15 | "20090215602"                                                                                                                                                                                                                                                                                                                                                                                                 | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                             | OR | OFF | OFF | 2024/08/27<br>02:19 PM |

|     |       |                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                             |    |     |     |                     |
|-----|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------|----|-----|-----|---------------------|
| L80 | 2     | L1 AND ( (A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC. )                                                                                                                                                                                                                                                       | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L81 | 12693 | ( (A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC. )                                                                                                                                                                                                                                                              | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L82 | 2513  | L10 and hematocrit                                                                                                                                                                                                                                                                                                                                                                                                              | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L83 | 7     | "I11" and (hematocrit with anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                       | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L84 | 6     | "I10" and (hematocrit with anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                       | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L85 | 16    | "I10" and (hematocrit same anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                       | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L86 | 60    | ((("RAGUSA") near3 ("Michael"))).INV.                                                                                                                                                                                                                                                                                                                                                                                           | (US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT) | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L87 | 11    | "I15" and (hematocrit same anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                       | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L88 | 183   | ("20010000185" "20020062100" "1025059" "1611725" "20010027156" "20020043492" "20020120227" "20030055375" "20030066807" "20030125881" "20030175150" "20040186409" "20050209522" "20050235733" "20060058167" "20060155236" "20070112289" "20080146993" "20120175313" "20140039373" "20140356851" "20180344921" "2087778" "2661150" "2750107" "2792172" "3096283" "3145713" "3239136" "3244362" "3244363" "3409213" "3456875" "348 | (US-PGPUB; USPAT)                           | OR | OFF | OFF | 2024/08/27 02:19 PM |

|  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |  |  |  |  |
|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|
|  |  | 9145" "3565330" "3655<br>058" "3737096" "37748<br>40" "3987961" "400787<br>1" "4010894" "4014497"<br> "4040965" "4056224" "<br>4082217" "4086924" "4<br>140268" "4142670" "41<br>51844" "4197847" "428<br>5464" "4300717" "4303<br>193" "4321921" "43878<br>48" "4425114" "443007<br>2" "4447221" "4457747"<br> "4464167" "4466888" "<br>4482342" "4490135" "4<br>530691" "4534863" "46<br>43714" "4647279" "465<br>5742" "4680025" "4684<br>361" "4692136" "47087<br>12" "4713176" "473408<br>9" "4740202" "4740313"<br> "4755300" "4767396" "<br>4795419" "4795448" "4<br>806247" "4806252" "48<br>08307" "4850995" "486<br>9812" "4871462" "4876<br>013" "4889524" "49118<br>33" "4934995" "494054<br>3" "4943273" "4968295"<br> "4983156" "4983158" "<br>4985153" "4994188" "5<br>039401" "5045048" "50<br>98372" "5098373" "510<br>0372" "5100564" "5112<br>298" "5114396" "51356<br>67" "5141486" "514729<br>0" "5154716" "5174894"<br> "5194145" "5217426" "<br>5217427" "5234403" "5<br>254248" "5273517" "52<br>77701" "5298016" "529<br>8171" "5300060" "5316<br>540" "5318511" "53185<br>12" "5348533" "536854<br>2" "5368555" "5386734"<br> "5387174" "5387187" "<br>5403272" "5405308" "5<br>417650" "5431814" "54<br>37598" "5437624" "546<br>2667" "5470483" "5484<br>396" "5494592" "55056<br>85" "5514070" "554306<br>2" "5551941" "5585007"<br> "5607579" "5649903" "<br>5651766" "5656163" "5<br>665061" "5712798" "57<br>28060" "5733253" "573<br>3446" "5733545" "5738<br>792" "5762791" "57796 |  |  |  |  |
|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|

|      |     |                                                                                                                                                                                                                                                                              |                                                                                                                                              |    |     |     |                     |
|------|-----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|----|-----|-----|---------------------|
|      |     | 60" "5783085" "5792351" "5849203" "5882289" "5906589" "5919125" "5964724" "5970432" "5980760" "6007725" "6059979" "6207063" "6234989" "6296602" "6464624" "6497676" "6558307" "6623443" "6743192" "7115205" "7186231" "7270645" "7704454" "8628489" "8702637" "8759094").PN. |                                                                                                                                              |    |     |     |                     |
| L89  | 2   | ("20180344910").PN.                                                                                                                                                                                                                                                          | (US-PGPUB; USPAT; USOCR; DERWENT)                                                                                                            | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L90  | 11  | "I15" and (hematocrit same anticoagulant)                                                                                                                                                                                                                                    | (US-PGPUB; USPAT; USOCR; DERWENT)                                                                                                            | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L91  | 1   | ("10758652").PN.                                                                                                                                                                                                                                                             | (USPAT; USOCR)                                                                                                                               | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L92  | 0   | ("20120175313").PN.                                                                                                                                                                                                                                                          | (USPAT; USOCR)                                                                                                                               | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L93  | 6   | "20120175313"                                                                                                                                                                                                                                                                | (USPAT)                                                                                                                                      | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L94  | 14  | ("4713176"   "6348156"   "6875191"   "7011761"   "7087177"   "7297272"   "7708710"   "8075468").PN. OR ("8852140").URPN.                                                                                                                                                     | (US-PGPUB; USPAT; USOCR)                                                                                                                     | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L95  | 9   | L23 and prim\$3                                                                                                                                                                                                                                                              | (US-PGPUB; USPAT; USOCR)                                                                                                                     | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L96  | 0   | (10/302682).APP.                                                                                                                                                                                                                                                             | (USPAT; USOCR)                                                                                                                               | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L97  | 2   | "20140100507"                                                                                                                                                                                                                                                                | (USPAT; USOCR)                                                                                                                               | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L98  | 195 | A61M1/024.cpc.                                                                                                                                                                                                                                                               | (US-PGPUB; USPAT; USOCR; DERWENT)                                                                                                            | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L99  | 996 | G01n15/05.cpc.                                                                                                                                                                                                                                                               | (US-PGPUB; USPAT; USOCR; DERWENT)                                                                                                            | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L100 | 225 | G01n2015/055.cpc.                                                                                                                                                                                                                                                            | (US-PGPUB; USPAT; USOCR; DERWENT)                                                                                                            | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L101 | 3   | ((US-20030125881-A1).did. AND PGPB.dbnm.) OR ((US-10758652-B2 OR US-6348156-B1).did. AND USPT.dbnm.)                                                                                                                                                                         | (US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB) | OR | ON  | ON  | 2024/08/27 02:19 PM |
| L102 | 0   | L30 AND touchscreen                                                                                                                                                                                                                                                          | (US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR,                                                                | OR | ON  | ON  | 2024/08/27 02:19 PM |

|      |     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                               |    |     |     |                     |
|------|-----|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|----|-----|-----|---------------------|
|      |     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | GB, JP, KR, OA, RU, SU, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)                                                                |    |     |     |                     |
| L103 | 0   | touchscreen WITH plasmapheresis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | (US-PGPUB; USPAT; USOCR; DERWENT)                                                                                             | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L104 | 4   | touchscreen SAME plasmapheresis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | (US-PGPUB; USPAT; USOCR; DERWENT)                                                                                             | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L105 | 16  | "10980926"                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | (US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); EPO; JPO; DERWENT) | OR | ON  | ON  | 2024/08/27 02:19 PM |
| L106 | 200 | ("1025059"   "1611725"   "2087778"   "2661150"   "2750107"   "2792172"   "3096283"   "3145713"   "3239136"   "3244362"   "3244363"   "3409213"   "3456875"   "3489145"   "3565330"   "3655058"   "3737096"   "3774840"   "3987961"   "4007871"   "4010894"   "4014497"   "4040965"   "4056224"   "4082217"   "4086924"   "4140268"   "4142670"   "4151844"   "4197847"   "4285464"   "4300717"   "4303193"   "4321921"   "4387848"   "4425114"   "4430072"   "4447221"   "4457747"   "4464167"   "4466888"   "4482342"   "4490135"   "4530691"   "4534863"   "4643714"   "4647279"   "4655742"   "4680025"   "4684361"   "4692136"   "4708712"   "4713176"   "4734089"   "4740202"   "4740313"   "4755300"   "4767396"   "4795419"   "4795448"   "4806247"   "4806252"   "4808307"   "4850995"   "4869812"   "4871462"   "4876013"   "4889524"   "4911833"   "4934995"   "4940543"   "4943273"   "4968295"   "4983156"   "4983158"   "4985153"   "4994188"   "5039401"   "5045048"   "5098372"   "5098373"   "5100372") | (US-PGPUB; USPAT; USOCR)                                                                                                      | OR | ON  | ON  | 2024/08/27 02:19 PM |



|  |  |                       |  |  |  |  |  |
|--|--|-----------------------|--|--|--|--|--|
|  |  | "5100564"   "5112298" |  |  |  |  |  |
|  |  | "5114396"   "5135667" |  |  |  |  |  |
|  |  | "5141486"   "5147290" |  |  |  |  |  |
|  |  | "5154716"   "5174894" |  |  |  |  |  |
|  |  | "5194145"   "5217426" |  |  |  |  |  |
|  |  | "5217427"   "5234403" |  |  |  |  |  |
|  |  | "5254248"   "5273517" |  |  |  |  |  |
|  |  | "5277701"   "5298016" |  |  |  |  |  |
|  |  | "5298171"   "5300060" |  |  |  |  |  |
|  |  | "5316540"   "5318511" |  |  |  |  |  |
|  |  | "5318512"   "5348533" |  |  |  |  |  |
|  |  | "5368542"   "5368555" |  |  |  |  |  |
|  |  | "5386734"   "5387174" |  |  |  |  |  |
|  |  | "5387187"   "5403272" |  |  |  |  |  |
|  |  | "5405308"   "5417650" |  |  |  |  |  |
|  |  | "5431814"   "5437598" |  |  |  |  |  |
|  |  | "5437624"   "5462667" |  |  |  |  |  |
|  |  | "5470483"   "5484396" |  |  |  |  |  |
|  |  | "5494592"   "5505685" |  |  |  |  |  |
|  |  | "5514070"   "5543062" |  |  |  |  |  |
|  |  | "5551941"   "5585007" |  |  |  |  |  |
|  |  | "5607579"   "5649903" |  |  |  |  |  |
|  |  | "5651766"   "5656163" |  |  |  |  |  |
|  |  | "5665061"   "5712798" |  |  |  |  |  |
|  |  | "5728060"   "5733253" |  |  |  |  |  |
|  |  | "5733446"   "5733545" |  |  |  |  |  |
|  |  | "5738792"   "5762791" |  |  |  |  |  |
|  |  | "5779660"   "5783085" |  |  |  |  |  |
|  |  | "5792351"   "5849203" |  |  |  |  |  |
|  |  | "5882289"   "5906589" |  |  |  |  |  |
|  |  | "5919125"   "5964724" |  |  |  |  |  |
|  |  | "5970432"   "5980760" |  |  |  |  |  |
|  |  | "6007725"   "6059979" |  |  |  |  |  |
|  |  | "6207063"   "6234989" |  |  |  |  |  |
|  |  | "6296602"   "6464624" |  |  |  |  |  |
|  |  | "6497676"   "6558307" |  |  |  |  |  |
|  |  | "6623443"   "6743192" |  |  |  |  |  |
|  |  | "7115205"   "7186231" |  |  |  |  |  |
|  |  | "7270645"   "7704454" |  |  |  |  |  |
|  |  | "8628489"   "8702637" |  |  |  |  |  |
|  |  | "8759094"   "9283316" |  |  |  |  |  |
|  |  | "10758652"            |  |  |  |  |  |
|  |  | "20010000185"         |  |  |  |  |  |
|  |  | "20010027156"         |  |  |  |  |  |
|  |  | "20020043492"         |  |  |  |  |  |
|  |  | "20020062100"         |  |  |  |  |  |
|  |  | "20020120227"         |  |  |  |  |  |
|  |  | "20030055375"         |  |  |  |  |  |
|  |  | "20030066807"         |  |  |  |  |  |
|  |  | "20030125881"         |  |  |  |  |  |
|  |  | "20030175150"         |  |  |  |  |  |
|  |  | "20040186409"         |  |  |  |  |  |
|  |  | "20050209522"         |  |  |  |  |  |
|  |  | "20050235733"         |  |  |  |  |  |
|  |  | "20060058167"         |  |  |  |  |  |
|  |  | "20060155236"         |  |  |  |  |  |
|  |  | "20070112289"         |  |  |  |  |  |
|  |  | "20080146993"         |  |  |  |  |  |

|      |       |                                                                                                                                                                                                         |                                      |    |     |     |                        |
|------|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|----|-----|-----|------------------------|
|      |       | "20120175313"  <br>"20140039373"  <br>"20140356851"  <br>"20180344910"  <br>"20180344921").pn.<br>AND (PGPB   USPT  <br>USOC).dbnm.                                                                     |                                      |    |     |     |                        |
| L107 | 2     | ("20180344910").PN.                                                                                                                                                                                     | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L108 | 11    | ( (A61M1/029 and<br>A61M1/3672 and<br>A61M1/3693 and<br>A61M1/38 and<br>A61M2202/0415 and<br>A61M2230/207).CPC. )                                                                                       | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L109 | 11    | ( (A61M1/029 and<br>A61M1/3672 and<br>A61M1/3693 and<br>A61M1/38 and<br>A61M2202/0415).CPC.<br>)                                                                                                        | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L110 | 53    | ( (A61M1/3672 and<br>A61M1/3693 and<br>A61M1/38 and<br>A61M2202/0415).CPC.<br>)                                                                                                                         | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L111 | 8     | "20120175313"                                                                                                                                                                                           | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L112 | 9     | "20030125881"                                                                                                                                                                                           | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L113 | 44    | 2009/0215602                                                                                                                                                                                            | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L114 | 15    | "20090215602"                                                                                                                                                                                           | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L115 | 2     | L1 AND ( (A61M1/024<br>OR A61M1/029 OR<br>A61M1/3672 OR<br>A61M1/3693 OR<br>A61M1/38 OR<br>A61M2202/0415 OR<br>A61M2230/207 OR<br>G01N15/05 OR<br>G01N2015/055 OR<br>G01N15/042 OR<br>G01N33/86).CPC. ) | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L116 | 12693 | ( (A61M1/024 OR<br>A61M1/029 OR<br>A61M1/3672 OR<br>A61M1/3693 OR<br>A61M1/38 OR<br>A61M2202/0415 OR<br>A61M2230/207 OR<br>G01N15/05 OR<br>G01N2015/055 OR                                              | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/08/27<br>02:19 PM |

|      |      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                   |    |     |     |                        |
|------|------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|----|-----|-----|------------------------|
| L117 | 2513 | G01N15/042 OR<br>G01N33/86).CPC. )<br>L10 and hematocrit                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | (US-PGPUB; USPAT;<br>USOCR; DERWENT)              | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L118 | 7    | "I11" and (hematocrit<br>with anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | (US-PGPUB; USPAT;<br>USOCR; DERWENT)              | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L119 | 6    | "I10" and (hematocrit<br>with anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | (US-PGPUB; USPAT;<br>USOCR; DERWENT)              | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L120 | 16   | "I10" and (hematocrit<br>same anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | (US-PGPUB; USPAT;<br>USOCR; DERWENT)              | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L121 | 60   | ((("RAGUSA") near3<br>("Michael"))).INV.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | (US-PGPUB; USPAT;<br>USOCR; EPO; JPO;<br>DERWENT) | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L122 | 11   | "I15" and (hematocrit<br>same anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | (US-PGPUB; USPAT;<br>USOCR; DERWENT)              | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L123 | 183  | ("20010000185" "20020<br>062100" "1025059" "16<br>11725" "20010027156" "<br>"20020043492" "20020<br>120227" "20030055375<br>" "20030066807" "2003<br>0125881" "2003017515<br>0" "20040186409" "200<br>50209522" "200502357<br>33" "20060058167" "20<br>060155236" "20070112<br>289" "20080146993" "2<br>0120175313" "2014003<br>9373" "20140356851" "2<br>20180344921" "208777<br>8" "2661150" "2750107"<br> "2792172" "3096283" "3<br>3145713" "3239136" "3<br>244362" "3244363" "34<br>09213" "3456875" "348<br>9145" "3565330" "3655<br>058" "3737096" "37748<br>40" "3987961" "400787<br>1" "4010894" "4014497"<br> "4040965" "4056224" "4<br>4082217" "4086924" "4<br>140268" "4142670" "41<br>51844" "4197847" "428<br>5464" "4300717" "4303<br>193" "4321921" "43878<br>48" "4425114" "443007<br>2" "4447221" "4457747"<br> "4464167" "4466888" "4<br>4482342" "4490135" "4<br>530691" "4534863" "46<br>43714" "4647279" "465<br>5742" "4680025" "4684<br>361" "4692136" "47087<br>12" "4713176" "473408<br>9" "4740202" "4740313" | (US-PGPUB; USPAT)                                 | OR | OFF | OFF | 2024/08/27<br>02:19 PM |

|      |    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                   |    |     |     |                     |
|------|----|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------|----|-----|-----|---------------------|
|      |    | "4755300" "4767396" "4795419" "4795448" "4806247" "4806252" "4808307" "4850995" "4869812" "4871462" "4876013" "4889524" "4911833" "4934995" "4940543" "4943273" "4968295" "4983156" "4983158" "4985153" "4994188" "5039401" "5045048" "5098372" "5098373" "5100372" "5100564" "5112298" "5114396" "5135667" "5141486" "5147290" "5154716" "5174894" "5194145" "5217426" "5217427" "5234403" "5254248" "5273517" "5277701" "5298016" "5298171" "5300060" "5316540" "5318511" "5318512" "5348533" "5368542" "5368555" "5386734" "5387174" "5387187" "5403272" "5405308" "5417650" "5431814" "5437598" "5437624" "5462667" "5470483" "5484396" "5494592" "5505685" "5514070" "5543062" "5551941" "5585007" "5607579" "5649903" "5651766" "5656163" "5665061" "5712798" "5728060" "5733253" "5733446" "5733545" "5738792" "5762791" "5779660" "5783085" "5792351" "5849203" "5882289" "5906589" "5919125" "5964724" "5970432" "5980760" "6007725" "6059979" "6207063" "6234989" "6296602" "6464624" "6497676" "6558307" "6623443" "6743192" "7115205" "7186231" "7270645" "7704454" "8628489" "8702637" "8759094").PN. |                                   |    |     |     |                     |
| L124 | 2  | ("20180344910").PN.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | (US-PGPUB; USPAT; USOCR; DERWENT) | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L125 | 11 | "I15" and (hematocrit same anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | (US-PGPUB; USPAT; USOCR; DERWENT) | OR | OFF | OFF | 2024/08/27 02:19 PM |
| L126 | 1  | ("10758652").PN.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | (USPAT; USOCR)                    | OR | OFF | OFF | 2024/08/27 02:19 PM |

|      |     |                                                                                                                                         |                                                                                                                                                                   |    |     |     |                        |
|------|-----|-----------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|-----|-----|------------------------|
| L127 | 0   | ("20120175313").PN.                                                                                                                     | (USPAT; USOCR)                                                                                                                                                    | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L128 | 6   | "20120175313"                                                                                                                           | (USPAT)                                                                                                                                                           | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L129 | 14  | ("4713176"   "6348156"<br>  "6875191"   "7011761"<br>  "7087177"   "7297272"<br>  "7708710"  <br>"8075468").PN. OR<br>("8852140").URPN. | (US-PGPUB; USPAT;<br>USOCR)                                                                                                                                       | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L130 | 9   | L23 and prim\$3                                                                                                                         | (US-PGPUB; USPAT;<br>USOCR)                                                                                                                                       | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L131 | 0   | (10/302682).APP.                                                                                                                        | (USPAT; USOCR)                                                                                                                                                    | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L132 | 2   | "20140100507"                                                                                                                           | (USPAT; USOCR)                                                                                                                                                    | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L133 | 195 | A61M1/024.cpc.                                                                                                                          | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                                              | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L134 | 996 | G01n15/05.cpc.                                                                                                                          | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                                              | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L135 | 225 | G01n2015/055.cpc.                                                                                                                       | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                                              | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L136 | 3   | ((US-20030125881-A1).did. AND<br>PGPB.dbnm.) OR ((US-<br>10758652-B2 OR US-<br>6348156-B1).did. AND<br>USPT.dbnm.)                      | (US-PGPUB; USPAT;<br>USOCR; FIT (AU, AP,<br>AT, CA, CH, CN, DD,<br>DE, EA, EP, ES, FR,<br>GB, JP, KR, OA, RU,<br>SU, WO); FPRS; EPO;<br>JPO; DERWENT;<br>IBM_TDB) | OR | ON  | ON  | 2024/08/27<br>02:19 PM |
| L137 | 0   | L30 AND touchscreen                                                                                                                     | (US-PGPUB; USPAT;<br>USOCR; FIT (AU, AP,<br>AT, CA, CH, CN, DD,<br>DE, EA, EP, ES, FR,<br>GB, JP, KR, OA, RU,<br>SU, WO); FPRS; EPO;<br>JPO; DERWENT;<br>IBM_TDB) | OR | ON  | ON  | 2024/08/27<br>02:19 PM |
| L138 | 0   | touchscreen WITH<br>plasmapheresis                                                                                                      | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                                              | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L139 | 4   | touchscreen SAME<br>plasmapheresis                                                                                                      | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                                              | OR | OFF | OFF | 2024/08/27<br>02:19 PM |
| L140 | 16  | "10980926"                                                                                                                              | (US-PGPUB; USPAT;<br>USOCR; FIT (AU, AP,<br>AT, CA, CH, CN, DD,<br>DE, EA, EP, ES, FR,<br>GB, JP, KR, OA, RU,<br>SU, WO); EPO; JPO;<br>DERWENT)                   | OR | ON  | ON  | 2024/08/27<br>02:19 PM |
| L141 | 200 | ("1025059"   "1611725"<br>  "2087778"   "2661150"<br>  "2750107"   "2792172"<br>  "3096283"   "3145713"                                 | (US-PGPUB; USPAT;<br>USOCR)                                                                                                                                       | OR | ON  | ON  | 2024/08/27<br>02:19 PM |

|  |  |                       |  |  |  |  |  |
|--|--|-----------------------|--|--|--|--|--|
|  |  | "3239136"   "3244362" |  |  |  |  |  |
|  |  | "3244363"   "3409213" |  |  |  |  |  |
|  |  | "3456875"   "3489145" |  |  |  |  |  |
|  |  | "3565330"   "3655058" |  |  |  |  |  |
|  |  | "3737096"   "3774840" |  |  |  |  |  |
|  |  | "3987961"   "4007871" |  |  |  |  |  |
|  |  | "4010894"   "4014497" |  |  |  |  |  |
|  |  | "4040965"   "4056224" |  |  |  |  |  |
|  |  | "4082217"   "4086924" |  |  |  |  |  |
|  |  | "4140268"   "4142670" |  |  |  |  |  |
|  |  | "4151844"   "4197847" |  |  |  |  |  |
|  |  | "4285464"   "4300717" |  |  |  |  |  |
|  |  | "4303193"   "4321921" |  |  |  |  |  |
|  |  | "4387848"   "4425114" |  |  |  |  |  |
|  |  | "4430072"   "4447221" |  |  |  |  |  |
|  |  | "4457747"   "4464167" |  |  |  |  |  |
|  |  | "4466888"   "4482342" |  |  |  |  |  |
|  |  | "4490135"   "4530691" |  |  |  |  |  |
|  |  | "4534863"   "4643714" |  |  |  |  |  |
|  |  | "4647279"   "4655742" |  |  |  |  |  |
|  |  | "4680025"   "4684361" |  |  |  |  |  |
|  |  | "4692136"   "4708712" |  |  |  |  |  |
|  |  | "4713176"   "4734089" |  |  |  |  |  |
|  |  | "4740202"   "4740313" |  |  |  |  |  |
|  |  | "4755300"   "4767396" |  |  |  |  |  |
|  |  | "4795419"   "4795448" |  |  |  |  |  |
|  |  | "4806247"   "4806252" |  |  |  |  |  |
|  |  | "4808307"   "4850995" |  |  |  |  |  |
|  |  | "4869812"   "4871462" |  |  |  |  |  |
|  |  | "4876013"   "4889524" |  |  |  |  |  |
|  |  | "4911833"   "4934995" |  |  |  |  |  |
|  |  | "4940543"   "4943273" |  |  |  |  |  |
|  |  | "4968295"   "4983156" |  |  |  |  |  |
|  |  | "4983158"   "4985153" |  |  |  |  |  |
|  |  | "4994188"   "5039401" |  |  |  |  |  |
|  |  | "5045048"   "5098372" |  |  |  |  |  |
|  |  | "5098373"   "5100372" |  |  |  |  |  |
|  |  | "5100564"   "5112298" |  |  |  |  |  |
|  |  | "5114396"   "5135667" |  |  |  |  |  |
|  |  | "5141486"   "5147290" |  |  |  |  |  |
|  |  | "5154716"   "5174894" |  |  |  |  |  |
|  |  | "5194145"   "5217426" |  |  |  |  |  |
|  |  | "5217427"   "5234403" |  |  |  |  |  |
|  |  | "5254248"   "5273517" |  |  |  |  |  |
|  |  | "5277701"   "5298016" |  |  |  |  |  |
|  |  | "5298171"   "5300060" |  |  |  |  |  |
|  |  | "5316540"   "5318511" |  |  |  |  |  |
|  |  | "5318512"   "5348533" |  |  |  |  |  |
|  |  | "5368542"   "5368555" |  |  |  |  |  |
|  |  | "5386734"   "5387174" |  |  |  |  |  |
|  |  | "5387187"   "5403272" |  |  |  |  |  |
|  |  | "5405308"   "5417650" |  |  |  |  |  |
|  |  | "5431814"   "5437598" |  |  |  |  |  |
|  |  | "5437624"   "5462667" |  |  |  |  |  |
|  |  | "5470483"   "5484396" |  |  |  |  |  |
|  |  | "5494592"   "5505685" |  |  |  |  |  |
|  |  | "5514070"   "5543062" |  |  |  |  |  |
|  |  | "5551941"   "5585007" |  |  |  |  |  |

|      |   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                 |    |    |    |                        |
|------|---|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|----|----|----|------------------------|
| L142 | 0 | "5607579"   "5649903"<br>"5651766"   "5656163"<br>"5665061"   "5712798"<br>"5728060"   "5733253"<br>"5733446"   "5733545"<br>"5738792"   "5762791"<br>"5779660"   "5783085"<br>"5792351"   "5849203"<br>"5882289"   "5906589"<br>"5919125"   "5964724"<br>"5970432"   "5980760"<br>"6007725"   "6059979"<br>"6207063"   "6234989"<br>"6296602"   "6464624"<br>"6497676"   "6558307"<br>"6623443"   "6743192"<br>"7115205"   "7186231"<br>"7270645"   "7704454"<br>"8628489"   "8702637"<br>"8759094"   "9283316"<br>"10758652"  <br>"20010000185"  <br>"20010027156"  <br>"20020043492"  <br>"20020062100"  <br>"20020120227"  <br>"20030055375"  <br>"20030066807"  <br>"20030125881"  <br>"20030175150"  <br>"20040186409"  <br>"20050209522"  <br>"20050235733"  <br>"20060058167"  <br>"20060155236"  <br>"20070112289"  <br>"20080146993"  <br>"20120175313"  <br>"20140039373"  <br>"20140356851"  <br>"20180344910"  <br>"20180344921").pn.<br>AND (PGPB   USPT  <br>USOC).dbnm.<br><br>"current value of the<br>hematocrit of the<br>donor".clm. | (US-PGPUB; USPAT;<br>USOCR; FIT (AU, AP,<br>AT, CA, CH, CN, DD,<br>DE, EA, EP, ES, FR,<br>GB, JP, KR, OA, RU,<br>SU, WO); EPO; JPO;<br>DERWENT) | OR | ON | ON | 2024/08/27<br>02:19 PM |
|------|---|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|----|----|----|------------------------|

## PE2E SEARCH - Search History (Interference)

There are no Interference searches to show.



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## ELECTRONIC PAYMENT RECEIPT

|                                    |                                                           |                                          |
|------------------------------------|-----------------------------------------------------------|------------------------------------------|
| APPLICATION #<br><b>17/205,400</b> | RECEIPT DATE / TIME<br><b>08/06/2024 12:52:17 PM Z ET</b> | ATTORNEY DOCKET #<br><b>130670-80104</b> |
|------------------------------------|-----------------------------------------------------------|------------------------------------------|

### Title of Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA

### Application Information

|                           |                                                             |                         |                 |
|---------------------------|-------------------------------------------------------------|-------------------------|-----------------|
| APPLICATION TYPE          | Utility - Nonprovisional Application<br>under 35 USC 111(a) | PATENT #                | -               |
| CONFIRMATION #            | 4686                                                        | FILED BY                | Tricia Troup    |
| PATENT CENTER #           | 66667806                                                    | AUTHORIZED BY           | Jonathan Lovely |
| CUSTOMER #                | 86738                                                       | FILING DATE             | 03/18/2021      |
| CORRESPONDENCE<br>ADDRESS | -                                                           | FIRST NAMED<br>INVENTOR | Michael Ragusa  |

### Payment Information

|                                      |                                                   |                                                 |
|--------------------------------------|---------------------------------------------------|-------------------------------------------------|
| PAYMENT METHOD<br><b>DA / 504876</b> | PAYMENT TRANSACTION ID<br><b>E202486C52389388</b> | PAYMENT AUTHORIZED BY<br><b>Jonathan Lovely</b> |
|--------------------------------------|---------------------------------------------------|-------------------------------------------------|

| FEE CODE                 | DESCRIPTION                                               | ITEM PRICE(\$) | QUANTITY | ITEM TOTAL(\$)  |
|--------------------------|-----------------------------------------------------------|----------------|----------|-----------------|
| 1814                     | STATUTORY DISCLAIMER,<br>INCLUDING TERMINAL<br>DISCLAIMER | 170.00         | 1        | 170.00          |
| <b>TOTAL<br/>AMOUNT:</b> |                                                           |                |          | <b>\$170.00</b> |

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

#### New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

#### National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C.

Terumo v. Haemonetics - PGR2025-00077  
Petitioner Terumo Exhibit 1002-0052



371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

**New International Application Filed with the USPTO as a Receiving Office**

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.



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## TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING REJECTION OVER A PRIOR PATENT

APPLICATION #  
**17205400**

FILING DATE  
**03/18/2021**

FIRST NAMED INVENTOR  
**Michael Ragusa**

ATTORNEY DOCKET #  
**130670-80104**

### Title of Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA



Filing of terminal disclaimer does not obviate requirement for response under 37 CFR 1.111 to outstanding Office Action



This electronic Terminal Disclaimer is not being used for a Joint Research Agreement.

| Owner                   | Percent interest |
|-------------------------|------------------|
| Haemonetics Corporation | 100%             |
| <b>Total</b>            | <b>100%</b>      |

The owner(s) of percent interest listed above in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of any patent granted on pending reference Application Number(s)

| Application # | Filing Date |
|---------------|-------------|
|---------------|-------------|

as the term of any patent granted on said reference application may be shortened by any terminal disclaimer filed prior to the grant of any patent on the pending reference application. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and any patent granted on the reference application are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, the owner does not disclaim the terminal part of any patent granted on the instant application that would extend to the expiration date of the full statutory term of any patent granted on said reference application, "as the term of any patent granted on said reference application may be shortened by any terminal disclaimer filed prior to the grant of any patent on the pending reference application," in the event that any such patent granted on the pending reference application: expires for failure to pay a maintenance fee, is held unenforceable, is found invalid by a court of competent jurisdiction, is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321, has all claims canceled by a reexamination certificate, is reissued, or is in any manner terminated prior to the expiration of its full statutory term as shortened by any terminal disclaimer filed prior to its grant.

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The owner(s) of percent interest listed above in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of prior patent number(s)

| Patent # |
|----------|
| 10758652 |
| 10980926 |

as the term of said prior patent is presently shortened by any terminal disclaimer. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the prior patent are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, the owner does not disclaim the terminal part of the term of any patent granted on the instant application that would extend to the expiration date of the full statutory term of the prior patent, "as the term of said prior patent is presently shortened by any terminal disclaimer," in the event that said prior patent later:

- expires for failure to pay a maintenance fee;
- is held unenforceable;
- is found invalid by a court of competent jurisdiction;
- is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321;
- has all claims canceled by a reexamination certificate;
- is reissued; or
- is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.



Terminal disclaimer fee under 37 CFR 1.20(d) included with Electronic Terminal Disclaimer request.

**Applicant claims the following entity status:**  
Regular Undiscounted

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I hereby declare that all statements made herein of my own knowledge are true and that all statemnts made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

---

I certify, in accordance with 37 CFR 1.4(d)(4) that I am: An attorney or agent registered to practice before the Patent and Trademark Office who is of record in this application

| Signature            | Name            | Registration # |
|----------------------|-----------------|----------------|
| /Jonathan C. Lovely/ | Jonathan Lovely | 60821          |

---

\* Statement under 37 CFR 3.73(b) is required if terminal disclaimer is signed by the assignee (owner). Form PTO/SB/96 may be used for making this certification. See MPEP 324.



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## ELECTRONIC ACKNOWLEDGEMENT RECEIPT

|                   |                                    |                     |
|-------------------|------------------------------------|---------------------|
| APPLICATION #     | RECEIPT DATE / TIME                | ATTORNEY DOCKET #   |
| <b>17/205,400</b> | <b>08/06/2024 12:52:17 PM Z ET</b> | <b>130670-80104</b> |

### Title of Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA

### Application Information

|                           |                                                             |                         |                 |
|---------------------------|-------------------------------------------------------------|-------------------------|-----------------|
| APPLICATION TYPE          | Utility - Nonprovisional Application<br>under 35 USC 111(a) | PATENT #                | -               |
| CONFIRMATION #            | 4686                                                        | FILED BY                | Tricia Troup    |
| PATENT CENTER #           | 66667806                                                    | FILING DATE             | 03/18/2021      |
| CUSTOMER #                | 86738                                                       | FIRST NAMED<br>INVENTOR | Michael Ragusa  |
| CORRESPONDENCE<br>ADDRESS | -                                                           | AUTHORIZED BY           | Jonathan Lovely |

### Documents

**TOTAL DOCUMENTS: 2**

| DOCUMENT             | PAGES | DESCRIPTION                                 | SIZE<br>(KB) |
|----------------------|-------|---------------------------------------------|--------------|
| petition-request.pdf | 3     | Terminal Disclaimer-Filed<br>(Electronic)   | 44 KB        |
| grantLetter.pdf      | 1     | Terminal Disclaimer-Electronic-<br>Approved | 18 KB        |

### Digest

| DOCUMENT             | MESSAGE DIGEST(SHA-512)                                                                                                                  |
|----------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| petition-request.pdf | E5C5BCAF4F41E80596C9CBE66FACFC3A63D5BFD773BF3597<br>CF436007A5A9C47F7466000491198C781C28EC70526CBB4FF<br>0FF9628D16001132A384C9EE4370ACD |
| grantLetter.pdf      | D7E53406D9D4BCDB07C33B2CA2C12495F378241CAE69BCA0                                                                                         |

2B6634C3D3F8ABB21D215332B86D431F768B47007687E7CBF  
CB371B5DB4E83D1FD939F607192074E

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

**New Applications Under 35 U.S.C. 111**

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

**National Stage of an International Application under 35 U.S.C. 371**

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

**New International Application Filed with the USPTO as a Receiving Office**

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.



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## APPROVAL LETTER

|                   |                   |                                      |
|-------------------|-------------------|--------------------------------------|
| APPLICATION #     | FILING DATE       | APPLICANT/PATENT UNDER REEXAMINATION |
| <b>17/205,400</b> | <b>03/18/2021</b> | <b>Michael Ragusa</b>                |

### Title of Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA

**Electronic terminal disclaimer filed on 08/06/2024**

 Approved

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UNITED STATES  
PATENT AND TRADEMARK OFFICE

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## ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #  
**17/205,400**

RECEIPT DATE / TIME  
**08/06/2024 12:48:43 PM Z ET**

ATTORNEY DOCKET #  
**130670-80104**

### Title of Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA

### Application Information

APPLICATION TYPE    Utility - Nonprovisional Application  
                                 under 35 USC 111(a)

PATENT #    -

CONFIRMATION #    4686

FILED BY    Tricia Troup

PATENT CENTER #    66668080

FILING DATE    03/18/2021

CUSTOMER #    86738

FIRST NAMED  
INVENTOR    Michael Ragusa

CORRESPONDENCE  
ADDRESS    -

AUTHORIZED BY    Jonathan Lovely

### Documents

**TOTAL DOCUMENTS: 4**

| DOCUMENT                                     |         | PAGES | DESCRIPTION                                                     | SIZE<br>(KB) |
|----------------------------------------------|---------|-------|-----------------------------------------------------------------|--------------|
| Response to Non-Final Office Action.pdf      |         | 12    | -                                                               | 55 KB        |
| Response to Non-Final Office Action-A....pdf | (1-1)   | 1     | Amendment/Request for Reconsideration-After Non-Final Rejection | 18 KB        |
| Response to Non-Final Office Action-SPEC.pdf | (2-2)   | 1     | Specification                                                   | 18 KB        |
| Response to Non-Final Office Action-CLM.pdf  | (3-9)   | 7     | Claims                                                          | 39 KB        |
| Response to Non-Final Office Action-REM.pdf  | (10-12) | 3     | Applicant Arguments/Remarks Made in an Amendment                | 25 KB        |



**Digest**

| <b>DOCUMENT</b>                              | <b>MESSAGE DIGEST(SHA-512)</b>                                                                                                    |
|----------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|
| Response to Non-Final Office Action.pdf      | D53CDD2B1D77574F5C9294DADA7F8E75E584A5596FC944B68BCCECFDF4B023837DA41864629D13FFE9673AE3B75AF183021A25219965D9B071219084C0B5EDDC  |
| Response to Non-Final Office Action-A....pdf | D5DC50E0231234142C5B296291446B55EAF0C2631E14DDAA626FAA18515D6203EF003EAF97F54ED497BBCF42CB8187AE199DF54FDD7118270DF6C71DA1C9642B  |
| Response to Non-Final Office Action-SPEC.pdf | F6947D406FE2B78A8D3F1A8C1DA9251C890057512270CBFC9EAD3B31F3F200E3026359DC4B775B9EBB1EF5C39CD9FE9ED ECB959B6F20CBEDA92D65A976449FDC |
| Response to Non-Final Office Action-CLM.pdf  | 1BAA9EC1934A703DACD08E2C2321A38300F9002026E7BF0B6DE0AFD75D2C8CEAA970272BA0C5C66B032EDA587B1DECF1524E5D221F85614EB86AA9711418FA0C  |
| Response to Non-Final Office Action-REM.pdf  | 6C1F325CBCD334569921CD4ABAABC24834F3C9F3A497286081BD6C0976D98A1661BE06528A67EF98937CCC0BCBD319A831C92C43F67DCD6F5E2F59208D925D68  |

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

**New Applications Under 35 U.S.C. 111**

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

**National Stage of an International Application under 35 U.S.C. 371**

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

**New International Application Filed with the USPTO as a Receiving Office**

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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In re Utility Application of:  
Haemonetics Corporation

Application No.: 17/205,400

Confirmation No.: 4686

Filed: March 18, 2021

Art Unit: 3799

For: SYSTEM AND METHOD FOR COLLECTING  
PLASMA

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Examiner: L. R. Deak

**AMENDMENT IN RESPONSE TO NON-FINAL OFFICE ACTION UNDER 37 C.F.R. § 1.111**

MS Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Commissioner:

**INTRODUCTORY COMMENTS**

In response to the Office Action dated May 8, 2024, please amend the above-identified U.S. patent application as follows:

**Amendments to the Specification** are reflected on page 2 of this paper.

**Amendments to the Claims** are reflected in the listing of claims which begins on page 3 of this paper.

**Remarks/Arguments** begin on page 10 of this paper.

**AMENDMENTS TO THE SPECIFICATION**

Please amend paragraph [0002] of the originally filed application as shown below:

[0002] U.S. Application No. 16/931,333, in turn, is a continuation of and claims priority from U.S. Application No. 15/793,339, entitled “System and Method for Collecting Plasma,” filed October 25, 2017, now U.S. Patent No. 10,792,416, attorney docket number 130670-80102 (formerly 1611/C86), and naming Michael Ragusa as inventor, the disclosure of which is incorporated herein, in its entirety, by reference.

### **AMENDMENTS TO THE CLAIMS**

The following **Listing of Claims** will replace all prior versions, and listing, of claims in the application.

#### **Listing of Claims**

1. (Currently Amended) A system for collecting plasma, comprising:

- a venipuncture needle configured to draw whole blood from a donor;
- a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;
- a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the blood separator, flow through the donor line being controlled by a first pump;
- an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;
- a touchscreen configured to receive input from an operator; and
- a controller programmed to control operation of the system, the controller coupled to the touchscreen and programmed to receive at least a donor's weight and hematocrit, to determine a target volume for plasma product and/or raw plasma based on the donor's total blood volume and/or the donor's plasma volume, to control the system to operate a draw and return cycle to withdraw the whole blood from the donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor, to establish a current value of the hematocrit of the donor and a new target volume for plasma product and/or raw plasma, and to control the system to operate a subsequent draw and return cycle, whereby the donor's changing hematocrit is taken into account in calculating the new target volume for plasma product and/or raw plasma.

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

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

4. (Original) The system of claim 3, wherein the controller is programmed to perform the draw and return phases at least three times.

5. (Canceled)

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

7. (Currently Amended) A system for collecting plasma, comprising:

a venipuncture needle configured to draw whole blood from a donor;

a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;

a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the blood separator, flow through the donor line being controlled by a first pump;

an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;

a touchscreen configured to receive input from an operator; and

a controller programmed to control operation of the system, the controller coupled to the touchscreen and programmed to receive at least a donor's weight, height, sex and hematocrit, to determine a target volume for plasma product and/or raw plasma based at least in part on ~~the weight, height, sex, and hematocrit~~ the donor's total blood volume and/or the donor's plasma volume, to control the system to operate draw and return phases to withdraw whole blood from the donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor.

8. (Original) The system of claim 7, wherein the controller is further programmed to account for anticoagulant introduced into the plasma collection container separately from the plasma product.

9. (Original) The system of claim 8, wherein the controller is further programmed to account for anticoagulant introduced into the plasma collection container separate from the plasma product attributable to a priming or other pre-processing step.

10. (Currently Amended) A system for collecting plasma, comprising:

a venipuncture needle configured to draw whole blood from a donor;

a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;

a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the blood separator, flow through the donor line being controlled by a first pump;

an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;

a touchscreen configured to receive input from an operator; and

a controller programmed to control operation of the system, the controller coupled to the touchscreen and programmed to receive at least a donor's weight, height and hematocrit and to determine a target volume for plasma product comprising raw plasma and anticoagulant, wherein the target volume for plasma product is determined prior to withdrawing the whole blood from the donor based at least in part on ~~an anticoagulant ratio, the donor's weight, height, and the donor's hematocrit~~ the donor's total blood volume and/or the donor's plasma volume, the controller programmed to then control the system to operate a plurality of draw and return cycles to withdraw whole blood from the donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor.

11. (Currently Amended) The system of claim 10, wherein the controller is programmed to determine the target volume for plasma product based an anticoagulant ratio ~~on the donor's total blood volume and the donor's plasma volume~~.

12. (Currently Amended) The system of claim 10 ~~11~~, wherein the controller is programmed to determine the donor's total blood volume based on multiple parameters selected from the group consisting of the weight, height, sex, age, and morphology of the donor.

13. (Original) The system of claim 10, wherein the controller is configured to receive the donor's weight and hematocrit electronically.

14. (Original) The system of claim 10, wherein the controller is programmed to control the system to collect the plasma product in the plasma product collection container until the plasma product in the plasma product collection container reaches the determined target volume.

15. (Original) The system of claim 10, wherein the controller is programmed to perform the draw and return cycles at least three times and the controller is programmed to determine a volume of whole blood to be drawn in a final draw phase which is different than a volume drawn in a prior draw phase.

16. (Currently Amended) A system for collecting plasma, comprising:

- a venipuncture needle configured to draw whole blood from a donor;
- a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;

- a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the separator, flow through the donor line being controlled by a first pump;

- an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;

- a touchscreen configured to receive input from an operator; and

- a controller programmed to control operation of the system, the controller coupled to the touchscreen and programmed to receive donor parameters electronically, to determine a target volume for plasma product and/or raw plasma based at least in part on the donor parameters and on the donor's total blood volume and/or the donor's plasma volume, the controller also configured and to control the system to operate draw and return phases to withdraw whole blood from a donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor.

17. (Original) The system of claim 16, wherein the controller is programmed to control the system to collect the plasma product in the plasma product collection container until a collected volume of plasma product reaches the target volume for plasma product and/or raw plasma.



18. (Original) The system of claim 16, further comprising a control system, wherein the control system is in electronic communication with the controller.

19. (Original) The system of claim 18, wherein the control system is programmed to calculate the target volume for plasma product and/or raw plasma and the controller is programmed to determine a target volume for plasma product and/or raw plasma by receiving the target volume for plasma product and/or raw plasma from the control system.

20. (Original) The system of claim 16, wherein the controller determines the target volume for plasma product and/or raw plasma by calculating the target volume for plasma product and/or raw plasma and wherein the controller is local to and coupled to the blood separator.

21. (Original) The system of claim 16, wherein the donor parameters received electronically comprise a donor weight, wherein the controller is programmed to determine the target volume for plasma product and/or raw plasma based at least in part on the donor weight.

22. (Original) The system of claim 21, wherein the donor parameters received electronically comprise a donor hematocrit, wherein the controller is programmed to determine the target volume for plasma product and/or raw plasma based at least in part on the donor hematocrit.

23. (Original) The system of claim 22, wherein the controller is programmed to determine a target volume for plasma product based on the donor's total blood volume and the donor's plasma volume.

24. (Original) The system of claim 23, wherein the controller is programmed to determine the donor's total blood volume based on the weight and height of the donor.

25. (Original) The system of claim 24, wherein the controller is programmed to determine the donor's total blood volume before whole blood is withdrawn from the donor during a donation.

26. (Original) The system of claim 25, wherein the controller is programmed to determine the target volume for plasma product comprising raw plasma and anticoagulant, wherein the target volume for plasma product is determined prior to withdrawing the whole blood from the donor based at least in part on an anticoagulant ratio, the donor's weight and the donor's hematocrit.

27. (Original) The system of claim 16, further comprising a reservoir separate from the blood separator for receiving concentrated red blood cells.

### **REMARKS**

Applicants would like to thank the examiner for the review of the present application. Applicants request reconsideration of the pending claims in view of the following remarks. Applicant has amended claims 1, 7, 10, 11, 12 and 16 and canceled claim 5 herewith. Claims 1-4, 6-27 are currently pending in the application.

#### **Amendment to the Specification**

Applicant has amended paragraph [0002], as outlined above, to correct a typographical error in the serial number for the priority application number for U.S. Application No. 16/931,333, filed on July 16, 2020. The Application Data Sheet as filed on March 18, 2021, the Filing Receipt dated March 30, 2021 and the Patent Center data for the present application is correct. Applicant believes that no petition is required to correct this typographical error. Therefore, Applicant respectfully requests that the specification be updated to reflect the correct application number.

#### **Double Patenting**

The office action suggests that claims 1-27 of the present application are patentably indistinct from claim 1-22 of application no. 17/205,374 and that the patentably indistinct claims must be canceled from all but one application or a clear line of demarcation must be maintained between the applications. To expedite prosecution of the present application, Applicant has amended independent claims 1, 7, 10, and 16 to include at least some of the subject matter of claims 5, 11 and 23. In particular, Applicant has amended claims 1, 7, 10 and 16 to specify that the controller determines a target volume for plasma product and/or raw plasma based on the donor's total blood volume and/or the donor's plasma volume. Applicant fails to see where any of claims 1-22 of application no. 17/205,374 teach such a limitation. Accordingly, Applicant believes that independent claims 1, 7, 10 and 16 (and dependent claims 2-4, 6, 7-27) are patentably distinct from claim 1-22 of application no. 17/205,374.

The office action rejected claims 1-27 on the grounds of nonstatutory double patenting as being unpatentable over claim 11 of U.S. Patent No. 10,758,652 in view of U.S. Publication No.

2012/0165685 to Weasler et al. (hereinafter “Weasler”). Additionally, the office action rejected claims 1-22 on the grounds of nonstatutory double patenting as being unpatentable over claims 8 and 23 of U.S. Patent No 10,980,926 in view of Weasler. To expedite prosecution, Applicant files herewith a terminal disclaimer with respect to U.S. Patent No. 10,758,652 and 10,980,926. Accordingly, Applicant believes that this rejection is now moot.

**CONCLUSION**

It is believed that the application is now in order for allowance and Applicant respectfully requests that a notice of allowance be issued. Applicant does not believe that any extension of time is required. However, if an extension of time is required, please charge the associated fee and any additional fees required by this paper or credit any overpayment to deposit account number 50-4876. Applicants also request that the examiner contact applicant's attorney, Jonathan C. Lovely, if it will assist in processing this application through issuance.

Dated: August 6, 2024

Respectfully submitted,  
Electronic signature: /Jonathan C. Lovely, Reg.  
No. 60,821/  
Jonathan C. Lovely  
Registration No.: 60,821  
MCCARTER & ENGLISH, LLP  
265 Franklin Street  
Boston, Massachusetts 02110  
(617) 449-6500  
(617) 607-9200 (Fax)  
Attorney/Agent For Applicant

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|                                                                                                                                 |                                                                                          |                                                                                                                                                                                                                               |              |                                            |               |                           |                 |                                       |                     |  |
|---------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|--------------------------------------------|---------------|---------------------------|-----------------|---------------------------------------|---------------------|--|
| <b>PATENT APPLICATION FEE DETERMINATION RECORD</b><br>Substitute for Form PTO-875                                               |                                                                                          |                                                                                                                                                                                                                               |              | Application or Docket Number<br>17/205,400 |               | Filing Date<br>03/18/2021 |                 | <input type="checkbox"/> To be Mailed |                     |  |
| ENTITY: <input checked="" type="checkbox"/> LARGE <input type="checkbox"/> SMALL <input type="checkbox"/> MICRO                 |                                                                                          |                                                                                                                                                                                                                               |              |                                            |               |                           |                 |                                       |                     |  |
| <b>APPLICATION AS FILED - PART I</b>                                                                                            |                                                                                          |                                                                                                                                                                                                                               |              |                                            |               |                           |                 |                                       |                     |  |
|                                                                                                                                 |                                                                                          | (Column 1)                                                                                                                                                                                                                    | (Column 2)   |                                            |               |                           |                 |                                       |                     |  |
| FOR                                                                                                                             |                                                                                          | NUMBER FILED                                                                                                                                                                                                                  | NUMBER EXTRA |                                            | RATE (\$)     |                           | FEE (\$)        |                                       |                     |  |
| <input type="checkbox"/> BASIC FEE<br>(37 CFR 1.16(a), (b), or (c))                                                             |                                                                                          | N/A                                                                                                                                                                                                                           | N/A          |                                            | N/A           |                           |                 |                                       |                     |  |
| <input type="checkbox"/> SEARCH FEE<br>(37 CFR 1.16(k), (l), or (m))                                                            |                                                                                          | N/A                                                                                                                                                                                                                           | N/A          |                                            | N/A           |                           |                 |                                       |                     |  |
| <input type="checkbox"/> EXAMINATION FEE<br>(37 CFR 1.16(o), (p), or (q))                                                       |                                                                                          | N/A                                                                                                                                                                                                                           | N/A          |                                            | N/A           |                           |                 |                                       |                     |  |
| TOTAL CLAIMS<br>(37 CFR 1.16(j))                                                                                                |                                                                                          | minus 20 =                                                                                                                                                                                                                    | *            |                                            | x \$100 =     |                           |                 |                                       |                     |  |
| INDEPENDENT CLAIMS<br>(37 CFR 1.16(h))                                                                                          |                                                                                          | minus 3 =                                                                                                                                                                                                                     | *            |                                            | x \$480 =     |                           |                 |                                       |                     |  |
| <input type="checkbox"/> APPLICATION SIZE FEE (37 CFR 1.16(s))                                                                  |                                                                                          | If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$310 (\$155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s). |              |                                            |               |                           |                 |                                       |                     |  |
| <input type="checkbox"/> MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))                                                      |                                                                                          |                                                                                                                                                                                                                               |              |                                            |               |                           |                 |                                       |                     |  |
| * If the difference in column 1 is less than zero, enter "0" in column 2.                                                       |                                                                                          |                                                                                                                                                                                                                               |              |                                            | TOTAL         |                           |                 |                                       |                     |  |
| <b>APPLICATION AS AMENDED - PART II</b>                                                                                         |                                                                                          |                                                                                                                                                                                                                               |              |                                            |               |                           |                 |                                       |                     |  |
|                                                                                                                                 |                                                                                          | (Column 1)                                                                                                                                                                                                                    | (Column 2)   |                                            | (Column 3)    |                           |                 |                                       |                     |  |
| AMENDMENT                                                                                                                       | 08/06/2024                                                                               | CLAIMS REMAINING AFTER AMENDMENT                                                                                                                                                                                              |              | HIGHEST NUMBER PREVIOUSLY PAID FOR         | PRESENT EXTRA |                           | RATE (\$)       |                                       | ADDITIONAL FEE (\$) |  |
|                                                                                                                                 | Total<br>(37 CFR 1.16(i))                                                                | * 26                                                                                                                                                                                                                          | Minus        | ** 27                                      | = 0           |                           | x \$100 =       |                                       | 0                   |  |
|                                                                                                                                 | Independent<br>(37 CFR 1.16(h))                                                          | * 4                                                                                                                                                                                                                           | Minus        | *** 4                                      | = 0           |                           | x \$480 =       |                                       | 0                   |  |
|                                                                                                                                 | <input type="checkbox"/> Application Size Fee (37 CFR 1.16(s))                           |                                                                                                                                                                                                                               |              |                                            |               |                           |                 |                                       |                     |  |
|                                                                                                                                 | <input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j)) |                                                                                                                                                                                                                               |              |                                            |               |                           |                 |                                       |                     |  |
|                                                                                                                                 |                                                                                          |                                                                                                                                                                                                                               |              |                                            |               |                           | TOTAL ADD'L FEE |                                       | 0                   |  |
| AMENDMENT                                                                                                                       |                                                                                          | (Column 1)                                                                                                                                                                                                                    | (Column 2)   |                                            | (Column 3)    |                           |                 |                                       |                     |  |
|                                                                                                                                 |                                                                                          | CLAIMS REMAINING AFTER AMENDMENT                                                                                                                                                                                              |              | HIGHEST NUMBER PREVIOUSLY PAID FOR         | PRESENT EXTRA |                           | RATE (\$)       |                                       | ADDITIONAL FEE (\$) |  |
|                                                                                                                                 | Total<br>(37 CFR 1.16(i))                                                                | *                                                                                                                                                                                                                             | Minus        | **                                         | =             |                           | x \$0 =         |                                       |                     |  |
|                                                                                                                                 | Independent<br>(37 CFR 1.16(h))                                                          | *                                                                                                                                                                                                                             | Minus        | ***                                        | =             |                           | x \$0 =         |                                       |                     |  |
|                                                                                                                                 | <input type="checkbox"/> Application Size Fee (37 CFR 1.16(s))                           |                                                                                                                                                                                                                               |              |                                            |               |                           |                 |                                       |                     |  |
| <input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))                                        |                                                                                          |                                                                                                                                                                                                                               |              |                                            |               |                           |                 |                                       |                     |  |
|                                                                                                                                 |                                                                                          |                                                                                                                                                                                                                               |              |                                            |               |                           | TOTAL ADD'L FEE |                                       |                     |  |
| * If the entry in column 1 is less than the entry in column 2, write "0" in column 3.                                           |                                                                                          |                                                                                                                                                                                                                               |              |                                            |               |                           | LIE             |                                       |                     |  |
| ** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".                                       |                                                                                          |                                                                                                                                                                                                                               |              |                                            |               |                           | /DAWN BREWER/   |                                       |                     |  |
| *** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".                                        |                                                                                          |                                                                                                                                                                                                                               |              |                                            |               |                           |                 |                                       |                     |  |
| The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1. |                                                                                          |                                                                                                                                                                                                                               |              |                                            |               |                           |                 |                                       |                     |  |

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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TO: docket@mccarter.com  
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SUBJECT: USPTO: Patent Electronic System - e-Postcard Notification for Customer Number 86738

Wed May 15 05:05:03 EDT 2024

Dear Patent Center Customer:

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265 Franklin Street  
Boston, MASSACHUSETTS, 02110  
UNITED STATES

An email notification regarding the correspondence was sent to the following email address(es) associated with customer number 86738:

docket@mccarter.com

This is a courtesy reminder that new correspondence is available for the application. If you have not done so already, please review the correspondence listed below. The official date of notification of the outgoing correspondence will be indicated on the form PTOL-90 accompanying the correspondence.

| Application | Document | Mailroom Date | Attorney Docket No. |
|-------------|----------|---------------|---------------------|
| 17205400    | CTNF     | 05/08/2024    | 130670-80104        |
| 17205400    | 892      | 05/08/2024    | 130670-80104        |
| 17205400    | 1449     | 05/08/2024    | 130670-80104        |
| 17205400    | 1449     | 05/08/2024    | 130670-80104        |
| 17205400    | 1449     | 05/08/2024    | 130670-80104        |
| 17205400    | 1449     | 05/08/2024    | 130670-80104        |
| 17205400    | 1449     | 05/08/2024    | 130670-80104        |
| 17205400    | 1449     | 05/08/2024    | 130670-80104        |
| 17205400    | 1449     | 05/08/2024    | 130670-80104        |
| 17205400    | 1449     | 05/08/2024    | 130670-80104        |
| 17205400    | 1449     | 05/08/2024    | 130670-80104        |
| 17205400    | 1449     | 05/08/2024    | 130670-80104        |
| 17205400    | 1449     | 05/08/2024    | 130670-80104        |

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You recently received an Office action from your examiner. Review of your patent application is under way! You can continue to advertise or mark any products covered by your application for your invention as "Patent Pending" for as long as this application is pending. This letter provides information about how to continue through the patent application process and the help available to you on your journey.

**Where are you in the patent application process?** Your patent application is now in step 3, Application Prosecution ([www.uspto.gov/UtilityPatentGuide](http://www.uspto.gov/UtilityPatentGuide).) Though the Office action includes a "rejection," that does not mean that you don't have a good idea you can patent. It means your examiner believes your application is not yet ready for allowance.

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2. file the Applicant Initiated Interview Request form (PTOL-413A) ([www.uspto.gov/sites/default/files/documents/PTOL413A.pdf](http://www.uspto.gov/sites/default/files/documents/PTOL413A.pdf)); or
3. contact your examiner directly via telephone (contact information is provided at the end of your Office action).

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|--------------------------------|-------------|----------------------|---------------------|------------------|
| APPLICATION NO.                | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
| 17/205,400                     | 03/18/2021  | Michael Ragusa       | 130670-80104        | 4686             |
| 86738                          | 7590        | 05/08/2024           | EXAMINER            |                  |
| MCCARTER & ENGLISH, LLP BOSTON |             |                      | DEAK, LESLIE R      |                  |
| 265 Franklin Street            |             |                      |                     |                  |
| Boston, MA 02110               |             |                      | ART UNIT            | PAPER NUMBER     |
|                                |             |                      | 3799                |                  |
|                                |             |                      | NOTIFICATION DATE   | DELIVERY MODE    |
|                                |             |                      | 05/08/2024          | ELECTRONIC       |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docket@mccarter.com



## **DETAILED ACTION**

### ***Notice of Pre-AIA or AIA Status***

1. The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

### ***Double Patenting***

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See

MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP § 2146 *et seq.* for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit [www.uspto.gov/patent/patents-forms](http://www.uspto.gov/patent/patents-forms). The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to [www.uspto.gov/patents/process/file/efs/guidance/eTD-info-1.jsp](http://www.uspto.gov/patents/process/file/efs/guidance/eTD-info-1.jsp).

3. Claims 1-27 of this application is patentably indistinct from claims 1-22 of Application No. 17/205,374. Pursuant to 37 CFR 1.78(f), when two or more applications filed by the same applicant or assignee contain patentably indistinct claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the patentably indistinct claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

4. Claims 1-27 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 11 of U.S. Patent No. 10,758,652 in view of US 2012/0165685

to Weasler et al. Although the claims at issue are not identical, they are not patentably distinct from each other.

With regard to instant claims 1, 7, 10, 16, patented claim 11 recites a venipuncture needle as an access device, a blood component separation device that separates plasma and sends it to a container, along with a container for red blood cells, a donor line with a pump, an anticoagulant line "configured to introduce anticoagulant" wherein the configuration comprises a pump, and a controller programmed to operate the device with various control schemes. Patented claim 11 does not recite a user interface or a touchscreen. However, Weasler discloses a plasmapheresis apparatus with venous access, containers, and pumps, coupled with a touchscreen user interface to enter patient parameters, enter control schemes, and relay information (see Weasler ¶¶0020-0023).

Where a claimed improvement on a device or apparatus is no more than "the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for improvement," the claim is unpatentable under 35 U.S.C. 103(a). *Ex Parte Smith*, 83 USPQ.2d 1509, 1518-19 (BPAI, 2007) (citing *KSR v. Teleflex*, 127 S.Ct. 1727, 1740, 82 USPQ2d 1385, 1396 (2007)). Applicant claims a combination that only unites old elements with no change in the respective functions of those old elements, and the combination of those elements yields predictable results; absent evidence that the modifications necessary to effect the combination of elements is uniquely challenging or difficult for one of ordinary skill in the art, the claim is unpatentable as obvious under 35 U.S.C. 103(a). *Ex Parte Smith*, 83 USPQ.2d at 1518-19 (BPAI, 2007) (citing *KSR*, 127 S.Ct. at 1740, 82 USPQ2d at 1396).

Accordingly, since the applicant[s] have submitted no persuasive evidence that the combination of the above elements is uniquely challenging or difficult for one of ordinary skill in the art, the claim is unpatentable as obvious under 35 U.S.C. 103(a) because it is no more than the predictable use of prior art elements according to their established functions resulting in the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for improvement. In the instant case, it is within the skill of a worker in the art to provide a plasmapheresis apparatus with a user interface in the form of a touchscreen in order to program desired control schemes since such elements are known in the art.

With regard to claims 2-6, 8, 9, 11-15, 17-26, Applicant is reciting different control schemes that the controller uses to operate the plasmapheresis machine. It is within the skill of a worker in the art to program a controller to generate the desired outcome. Accordingly, the instantly presented claims are unpatentable over the prior art of record.

With regard to claim 27, Applicant is claiming an additional container. It has been held that the mere duplication of the parts of an apparatus found in the prior art is not patentably significant unless a new and unexpected result is produced. See MPEP § 2144.04 (VI)(B).

5. Claims 1-22 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 8 and 23 of U.S. Patent No. 10,980,926 in view of US 2012/0165685 to Weasler et al. Although the claims at issue are not identical, they are not patentably distinct from each other.

With regard to instant claims 1, 7, 10, 16, patented claims 8 and 23 recite a venipuncture needle as an access device, a blood component separation device that separates plasma and sends it to a container, along with a container for red blood cells, a donor line with a pump, an anticoagulant line "configured to introduce anticoagulant" wherein the configuration comprises a pump, and a controller programmed to operate the device with various control schemes. Patented claim 11 does not recite a user interface or a touchscreen. However, Weasler discloses a plasmapheresis apparatus with venous access, containers, and pumps, coupled with a touchscreen user interface to enter patient parameters, enter control schemes, and relay information (see Weasler ¶¶0020-0023).

Where a claimed improvement on a device or apparatus is no more than "the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for improvement," the claim is unpatentable under 35 U.S.C. 103(a). Ex Parte Smith, 83 USPQ.2d 1509, 1518-19 (BPAI, 2007) (citing KSR v. Teleflex, 127 S.Ct. 1727, 1740, 82 USPQ2d 1385, 1396 (2007)). Applicant claims a combination that only unites old elements with no change in the respective functions of those old elements, and the combination of those elements yields predictable results; absent evidence that the modifications necessary to effect the combination of elements is uniquely challenging or difficult for one of ordinary skill in the art, the claim is unpatentable as obvious under 35 U.S.C. 103(a). Ex Parte Smith, 83 USPQ.2d at 1518-19 (BPAI, 2007) (citing KSR, 127 S.Ct. at 1740, 82 USPQ2d at 1396. Accordingly, since the applicant[s] have submitted no persuasive evidence that the combination of the above elements is uniquely challenging or difficult for one of ordinary

skill in the art, the claim is unpatentable as obvious under 35 U.S.C. 103(a) because it is no more than the predictable use of prior art elements according to their established functions resulting in the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for improvement. In the instant case, it is within the skill of a worker in the art to provide a plasmapheresis apparatus with a user interface in the form of a touchscreen in order to program desired control schemes since such elements are known in the art.

With regard to claims 2-6, 8, 9, 11-15, 17-26, Applicant is reciting different control schemes that the controller uses to operate the plasmapheresis machine. It is within the skill of a worker in the art to program a controller to generate the desired outcome. Accordingly, the instantly presented claims are unpatentable over the prior art of record.

With regard to claim 27, Applicant is claiming an additional container. It has been held that the mere duplication of the parts of an apparatus found in the prior art is not patentably significant unless a new and unexpected result is produced. See MPEP § 2144.04 (VI)(B).

### ***Conclusion***

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LESLIE R DEAK whose telephone number is (571)272-4943. The examiner can normally be reached on Monday-Friday, 9am to 5:30pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an



interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at <http://www.uspto.gov/interviewpractice>.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tom Sweet can be reached on 571-272-4761. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <https://ppair-my.uspto.gov/pair/PrivatePair>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

**/LESLIE R DEAK/  
Primary Examiner, Art Unit 3799  
3 May 2024**

|                                   |                                       |  |                                                               |             |
|-----------------------------------|---------------------------------------|--|---------------------------------------------------------------|-------------|
| <b>Notice of References Cited</b> | Application/Control No.<br>17/205,400 |  | Applicant(s)/Patent Under<br>Reexamination<br>Ragusa, Michael |             |
|                                   | Examiner<br>LESLIE R DEAK             |  | Art Unit<br>3799                                              | Page 1 of 1 |

**U.S. PATENT DOCUMENTS**

| * |   | Document Number<br>Country Code-Number-Kind Code | Date<br>YYYY-MM-DD | Name             | CPC Classification | US Classification |
|---|---|--------------------------------------------------|--------------------|------------------|--------------------|-------------------|
| * | A | US-10758652-B2                                   | 2020-09-01         | Ragusa; Michael  | A61M1/024          | 1/1               |
| * | B | US-10980926-B2                                   | 2021-04-20         | Ragusa; Michael  | A61M1/029          | 1/1               |
| * | C | US-20120165685-A1                                | 2012-06-28         | Weasler; Marc N. | A61B5/02042        | 600/595           |
|   | D |                                                  |                    |                  |                    |                   |
|   | E |                                                  |                    |                  |                    |                   |
|   | F |                                                  |                    |                  |                    |                   |
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**Notice of References Cited**

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|-----------------------------------------------------------------------------------------------------------------|----------------------------------------------|-------------------------------------------------------------------|
| <b><i>Search Notes</i></b><br> | <b>Application/Control No.</b><br>17/205,400 | <b>Applicant(s)/Patent Under Reexamination</b><br>Ragusa, Michael |
|                                                                                                                 | <b>Examiner</b><br>LESLIE R DEAK             | <b>Art Unit</b><br>3799                                           |

| CPC - Searched*                                                                                                                                                |            |          |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|----------|
| Symbol                                                                                                                                                         | Date       | Examiner |
| (A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC. | 10/28/2019 | LRD      |
| A61M1/029 A61M1/3672 A61M1/3693 A61M1/38 A61M2202/0415 A61M2230/207                                                                                            | 11/05/2020 | LRD      |

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|------------------------------------------------------------------------|------------|----------|
| Search Notes                                                           | Date       | Examiner |
| inventor name search, EAST BRS search, consulted foreign search report | 10/28/2019 | LRD      |
| updated prior searches, consulted primary examiners                    | 02/27/2020 | LRD      |
| updated prior searches                                                 | 05/05/2020 | LRD      |
| consulted parent case, updated searches, ODP                           | 11/06/2020 | LRD      |
| consulted parent cases, updated searches, ODP                          | 04/30/2024 | LRD      |

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| <b><i>Search Notes</i></b><br> | <b>Application/Control No.</b><br>17/205,400 | <b>Applicant(s)/Patent Under Reexamination</b><br>Ragusa, Michael |
|                                                                                                                 | <b>Examiner</b><br>LESLIE R DEAK             | <b>Art Unit</b><br>3799                                           |

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|                     | N/A                   | 05/05/2020 | LRD      |

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| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | N/A              |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

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|                                                                                                            | 1       | 2002-282352                                                                                                                                                                                                                                                     | JP                         | A                      | 2002-10-02                                      | Terumo Corp                                                              |                                                                          | ×              |
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| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | N/A              |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

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|--------------------|------------------------------|-----------------|--|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> See Kind Codes of USPTO Patent Documents at [www.USPTO.GOV](http://www.USPTO.GOV) or MPEP 901.04. <sup>2</sup> Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>3</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>4</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>5</sup> Applicant is to place a check mark here if English language translation is attached.

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

|                        |                  |
|------------------------|------------------|
| Application Number     | 17205400         |
| Filing Date            | 2021-03-18       |
| First Named Inventor   | Michael Ragusa   |
| Art Unit               | N/A              |
| Examiner Name          | Not Yet Assigned |
| Attorney Docket Number | 130670-80104     |

**CERTIFICATION STATEMENT**

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

**OR**

That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

**SIGNATURE**

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

|            |                                       |                     |            |
|------------|---------------------------------------|---------------------|------------|
| Signature  | /Jonathan C. Lovely, Reg. No. 60,821/ | Date (YYYY-MM-DD)   | 2022-04-04 |
| Name/Print | Jonathan C. Lovely                    | Registration Number | 60,821     |

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

## Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
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6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.



I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: November 18, 2021  
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104

Docket No.: 130670-80104  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Utility Application of:  
Michael Ragusa

Application No.: 17/205,400

Confirmation No.: 4686

Filed: March 18, 2021

Art Unit: N/A

For: SYSTEM AND METHOD FOR COLLECTING  
PLASMA

Examiner: Not Yet Assigned

**INFORMATION DISCLOSURE STATEMENT (IDS)**

MS Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR 1.97, Applicant hereby makes of record the following additional documents. A PTO Form SB/08 and a full copy of each of the documents required under 37 CFR 1.98(a)(2) accompany this statement.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 C.F.R. § 1.97(b)(3)).

In accordance with 37 C.F.R. § 1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patents. Applicant submits herewith copies of foreign patents in accordance with 37 C.F.R. § 1.98(a)(2).

Application No.: 17/205,400

Docket No.: 130670-80104

The Examiner is advised that the following applications contain subject matter that may be related to the present application:

| U.S. Application | Filing Date      | Publication No. / Patent No. | Status    | Atty. Docket No. |
|------------------|------------------|------------------------------|-----------|------------------|
| 15/608,183       | May 30, 2017     | 10,758,652                   | Issued    | 130670-08002     |
| 16/866,078       | May 4, 2020      | 10,980,926                   | Issued    | 130670-08005     |
| 17/205,374       | March 18, 2021   | 2021-0205509                 | Published | 130670-08006     |
| 15/793,339       | October 25, 2017 | 10,792,416                   | Issued    | 130670-80102     |
| 16/931,333       | July 16, 2020    | 10,980,934                   | Issued    | 130670-80103     |

/LESLIE R DEAK/ (05/02/2024)

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed references.

Applicant believes no fee is due with this response.

Dated: November 18, 2021

Respectfully submitted,  
 Electronic signature: /Jonathan C. Lovely, Reg.  
 No. 60,821/  
 Jonathan C. Lovely  
 Registration No.: 60,821  
 MCCARTER & ENGLISH, LLP  
 265 Franklin Street  
 Boston, Massachusetts 02110  
 (617) 449-6556  
 (617) 607-9200 (Fax)  
 Attorney/Agent For Applicant

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: April 4, 2022  
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Utility Application of:  
Michael Ragusa

Application No.: 17/205,400

Confirmation No.: 4686

Filed: March 18, 2021

Art Unit: N/A

For: SYSTEM AND METHOD FOR COLLECTING  
PLASMA

Examiner: Not Yet Assigned

**INFORMATION DISCLOSURE STATEMENT (IDS)**

MS Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR 1.97, Applicant hereby makes of record the following additional document. A PTO Form SB/08 and a full copy of the document required under 37 CFR 1.98(a)(2) accompany this statement.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 C.F.R. § 1.97(b)(3)).

Applicant submits herewith a copy of the cited foreign patent in accordance with 37 C.F.R. § 1.98(a)(2).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D/

Terumo v. Haemonetics - PGR2025-00077  
Petitioner Terumo Exhibit 1002-0095

Application No.: 17/205,400

Docket No.: 130670-80104

The Examiner is advised that the following applications contain subject matter that may be related to the present application:

| U.S. Application | Filing Date      | Publication No. / Patent No. | Status    | Atty. Docket No. |
|------------------|------------------|------------------------------|-----------|------------------|
| 15/608,183       | May 30, 2017     | 10,758,652                   | Issued    | 130670-08002     |
| 16/866,078       | May 4, 2020      | 10,980,926                   | Issued    | 130670-08005     |
| 17/205,374       | March 18, 2021   | 2021-0205509                 | Published | 130670-08006     |
| 15/793,339       | October 25, 2017 | 10,792,416                   | Issued    | 130670-80102     |
| 16/931,333       | July 16, 2020    | 10,980,934                   | Issued    | 130670-80103     |

/LESLIE R DEAK/ (05/02/2024)

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed reference.

Applicant believes no fee is due with this response.

Dated: April 4, 2022

Respectfully submitted,  
Electronic signature: /Jonathan C. Lovely, Reg.  
No. 60,821/  
Jonathan C. Lovely  
Registration No.: 60,821  
MCCARTER & ENGLISH, LLP  
265 Franklin Street  
Boston, Massachusetts 02110  
(617) 449-6556  
(617) 607-9200 (Fax)  
Attorney/Agent For Applicant

Doc code: IDS

PTO/SB/08a (01-22)

Doc description: Information Disclosure Statement (IDS) Filed

Approved for use through 05/31/2024. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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|                                                                                                     |                        |                  |
|-----------------------------------------------------------------------------------------------------|------------------------|------------------|
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | N/A              |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

| U.S. PATENTS                                                                                               |         |                                      |                            |                        |                                                 |                                                                          | Remove                                                                   |                |
|------------------------------------------------------------------------------------------------------------|---------|--------------------------------------|----------------------------|------------------------|-------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|----------------|
| Examiner Initial*                                                                                          | Cite No | Patent Number                        | Kind Code <sup>1</sup>     | Issue Date             | Name of Patentee or Applicant of cited Document | Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear |                                                                          |                |
|                                                                                                            | 1       | 6200287                              | B1                         | 2001-03-13             | Keller et al.                                   |                                                                          |                                                                          |                |
| If you wish to add additional U.S. Patent citation information please click the Add button.                |         |                                      |                            |                        |                                                 |                                                                          | Add                                                                      |                |
| U.S. PATENT APPLICATION PUBLICATIONS                                                                       |         |                                      |                            |                        |                                                 |                                                                          | Remove                                                                   |                |
| Examiner Initial*                                                                                          | Cite No | Publication Number                   | Kind Code <sup>1</sup>     | Publication Date       | Name of Patentee or Applicant of cited Document | Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear |                                                                          |                |
|                                                                                                            | 1       | 20050131334                          | A1                         | 2005-06-16             | Langley et al.                                  |                                                                          |                                                                          |                |
|                                                                                                            | 2       | 20140100507                          | A1                         | 2014-04-10             | Flexman, Greg                                   |                                                                          |                                                                          |                |
| If you wish to add additional U.S. Published Application citation information please click the Add button. |         |                                      |                            |                        |                                                 |                                                                          | Add                                                                      |                |
| FOREIGN PATENT DOCUMENTS                                                                                   |         |                                      |                            |                        |                                                 |                                                                          | Remove                                                                   |                |
| Examiner Initial*                                                                                          | Cite No | Foreign Document Number <sup>3</sup> | Country Code <sup>2i</sup> | Kind Code <sup>4</sup> | Publication Date                                | Name of Patentee or Applicant of cited Document                          | Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear | T <sup>5</sup> |
|                                                                                                            | 1       | 103354755                            | CN                         | A                      | 2013-10-16                                      | Haemonetics Corp                                                         |                                                                          | ×              |
|                                                                                                            | 2       | 69434848                             | DE                         |                        | 2007-04-12                                      | Gambro Inc                                                               |                                                                          | ☒              |

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

|                        |                  |
|------------------------|------------------|
| Application Number     | 17205400         |
| Filing Date            | 2021-03-18       |
| First Named Inventor   | Michael Ragusa   |
| Art Unit               | N/A              |
| Examiner Name          | Not Yet Assigned |
| Attorney Docket Number | 130670-80104     |

|   |             |    |    |            |                            |                                     |
|---|-------------|----|----|------------|----------------------------|-------------------------------------|
| 3 | 2003-516175 | JP | A  | 2003-05-13 | Baxter International, Inc. | <input checked="" type="checkbox"/> |
| 4 | 2012/091720 | WO | A1 | 2012-07-05 | Haemonetics Corp           | <input type="checkbox"/>            |
| 5 | 2019/084278 | WO | A1 | 2019-05-02 | Haemonetics Corp           | <input type="checkbox"/>            |

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**NON-PATENT LITERATURE DOCUMENTS**

Remove

| Examiner Initials* | Cite No | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>5</sup> |
|--------------------|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|
|                    | 1       |                                                                                                                                                                                                                                                                 |                |

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**EXAMINER SIGNATURE**

|                    |                              |                 |  |
|--------------------|------------------------------|-----------------|--|
| Examiner Signature | /LESLIE R DEAK/ {05/02/2024} | Date Considered |  |
|--------------------|------------------------------|-----------------|--|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> See Kind Codes of USPTO Patent Documents at [www.USPTO.GOV](http://www.USPTO.GOV) or MPEP 901.04. <sup>2</sup> Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>3</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>4</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>5</sup> Applicant is to place a check mark here if English language translation is attached.

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STATEMENT BY APPLICANT**  
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|                        |                  |
|------------------------|------------------|
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| First Named Inventor   | Michael Ragusa   |
| Art Unit               | N/A              |
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| Attorney Docket Number | 130670-80104     |

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☒ A certification statement is not submitted herewith.

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|            |                                       |                     |            |
|------------|---------------------------------------|---------------------|------------|
| Signature  | /Jonathan C. Lovely, Reg. No. 60,821/ | Date (YYYY-MM-DD)   | 2022-12-08 |
| Name/Print | Jonathan C. Lovely                    | Registration Number | 60,821     |

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
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Doc code: IDS

Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (01-22)

Approved for use through 05/31/2024. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

|                                                                                                     |                        |                  |
|-----------------------------------------------------------------------------------------------------|------------------------|------------------|
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | N/A              |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

| U.S.PATENTS                                                                                                |         |                                      |                            |                        |                                                 |                                                                        | Remove                                                                 |                |
|------------------------------------------------------------------------------------------------------------|---------|--------------------------------------|----------------------------|------------------------|-------------------------------------------------|------------------------------------------------------------------------|------------------------------------------------------------------------|----------------|
| Examiner Initial*                                                                                          | Cite No | Patent Number                        | Kind Code <sup>1</sup>     | Issue Date             | Name of Patentee or Applicant of cited Document | Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear |                                                                        |                |
|                                                                                                            | 1       | 8075468                              | B2                         | 2011-12-13             | Min et al.                                      |                                                                        |                                                                        |                |
| If you wish to add additional U.S. Patent citation information please click the Add button.                |         |                                      |                            |                        |                                                 |                                                                        | Add                                                                    |                |
| U.S.PATENT APPLICATION PUBLICATIONS                                                                        |         |                                      |                            |                        |                                                 |                                                                        | Remove                                                                 |                |
| Examiner Initial*                                                                                          | Cite No | Publication Number                   | Kind Code <sup>1</sup>     | Publication Date       | Name of Patentee or Applicant of cited Document | Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear |                                                                        |                |
|                                                                                                            | 1       | 20090215602                          | A1                         | 2009-08-27             | Min et al.                                      |                                                                        |                                                                        |                |
|                                                                                                            | 2       | 20230001059                          | A1                         | 2023-01-05             | Ragusa, Michael                                 |                                                                        |                                                                        |                |
| If you wish to add additional U.S. Published Application citation information please click the Add button. |         |                                      |                            |                        |                                                 |                                                                        | Add                                                                    |                |
| FOREIGN PATENT DOCUMENTS                                                                                   |         |                                      |                            |                        |                                                 |                                                                        | Remove                                                                 |                |
| Examiner Initial*                                                                                          | Cite No | Foreign Document Number <sup>3</sup> | Country Code <sup>2i</sup> | Kind Code <sup>4</sup> | Publication Date                                | Name of Patentee or Applicant of cited Document                        | Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear | T <sup>5</sup> |
|                                                                                                            | 1       |                                      |                            |                        |                                                 |                                                                        |                                                                        |                |
| If you wish to add additional Foreign Patent Document citation information please click the Add button.    |         |                                      |                            |                        |                                                 |                                                                        | Add                                                                    |                |
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| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | N/A              |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

| Examiner Initials* | Cite No | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>5</sup> |
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| Examiner Signature | /LESLIE R DEAK/ (05/02/2024) | Date Considered |  |
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<sup>1</sup> See Kind Codes of USPTO Patent Documents at [www.USPTO.GOV](http://www.USPTO.GOV) or MPEP 901.04. <sup>2</sup> Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>3</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>4</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>5</sup> Applicant is to place a check mark here if English language translation is attached.

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

|                        |                  |
|------------------------|------------------|
| Application Number     | 17205400         |
| Filing Date            | 2021-03-18       |
| First Named Inventor   | Michael Ragusa   |
| Art Unit               | N/A              |
| Examiner Name          | Not Yet Assigned |
| Attorney Docket Number | 130670-80104     |

**CERTIFICATION STATEMENT**

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

**OR**

That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

**SIGNATURE**

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

|            |                                       |                     |            |
|------------|---------------------------------------|---------------------|------------|
| Signature  | /Jonathan C. Lovely, Reg. No. 60,821/ | Date (YYYY-MM-DD)   | 2023-01-17 |
| Name/Print | Jonathan C. Lovely                    | Registration Number | 60,821     |

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Receipt date: 11/18/2021

17/205,400 - GAU: 3799

Doc code: IDS

Doc description: Information Disclosure Statement (IDS) Filed

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| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | N/A              |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

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|                                                                                                            | 1       | 5681273                              |                            | 1997-10-28             | Brown                                           |                                                                        |                                                                        |                |
|                                                                                                            | 2       | 8454548                              | B2                         | 2013-06-04             | Ohashi et al.                                   |                                                                        |                                                                        |                |
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|                                                                                                            | 1       | 2252788                              | RU                         | C1                     | 2005-05-27                                      | Mepotex                                                                |                                                                        | ×              |
|                                                                                                            | 2       | 2601449                              | RU                         | C2                     | 2016-11-10                                      | Fenval Ink                                                             |                                                                        | ☒              |

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|-----------------------------------------------------------------------------------------------------|------------------------|------------------|------------|
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     |                  | 17205400   |
|                                                                                                     | Filing Date            |                  | 2021-03-18 |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |            |
|                                                                                                     | Art Unit               | N/A              |            |
|                                                                                                     | Examiner Name          | Not Yet Assigned |            |
|                                                                                                     | Attorney Docket Number | 130670-80104     |            |

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| Examiner Signature                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | /LESLIE R DEAK/ {05/02/2024} |                                                                                                                                                                                                                                                                 | Date Considered |
| *EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.                                                                                                                                                                                                                                                                                                                                                                         |                              |                                                                                                                                                                                                                                                                 |                 |
| <sup>1</sup> See Kind Codes of USPTO Patent Documents at <a href="http://www.USPTO.GOV">www.USPTO.GOV</a> or MPEP 901.04. <sup>2</sup> Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>3</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>4</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>5</sup> Applicant is to place a check mark here if English language translation is attached. |                              |                                                                                                                                                                                                                                                                 |                 |

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

|                        |                  |
|------------------------|------------------|
| Application Number     | 17205400         |
| Filing Date            | 2021-03-18       |
| First Named Inventor   | Michael Ragusa   |
| Art Unit               | N/A              |
| Examiner Name          | Not Yet Assigned |
| Attorney Docket Number | 130670-80104     |

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|            |                                       |                     |            |
|------------|---------------------------------------|---------------------|------------|
| Signature  | /Jonathan C. Lovely, Reg. No. 60,821/ | Date (YYYY-MM-DD)   | 2021-11-18 |
| Name/Print | Jonathan C. Lovely                    | Registration Number | 60,821     |

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7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
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|                                                                                                                                              |   |    |   | Application Number       | Not Yet Assigned      |
|                                                                                                                                              |   |    |   | Filing Date              | Concurrently Herewith |
|                                                                                                                                              |   |    |   | First Named Inventor     | Michael Ragusa        |
|                                                                                                                                              |   |    |   | Art Unit                 | 3781                  |
|                                                                                                                                              |   |    |   | Examiner Name            | Not Yet Assigned      |
| Sheet                                                                                                                                        | 1 | of | 6 | Attorney Docket Number   | 130670-80104          |

| U.S. PATENT DOCUMENTS |                          |                                           |                                |                                                    |                                                                                 |
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| Examiner<br>Initials* | Cite<br>No. <sup>1</sup> | Document Number                           | Publication Date<br>MM-DD-YYYY | Name of Patentee or<br>Applicant of Cited Document | Pages, Columns, Lines, Where<br>Relevant Passages or Relevant<br>Figures Appear |
|                       |                          | Number-Kind Code <sup>2</sup> ( if known) |                                |                                                    |                                                                                 |
|                       | AA                       | US-1,025,059                              | 04-30-1912                     | Hatton et al.                                      |                                                                                 |
|                       | AB                       | US-1,611,725                              | 12-21-1926                     | Degerth et al.                                     |                                                                                 |
|                       | AC                       | US-2,087,778                              | 07-20-1937                     | Nelin                                              |                                                                                 |
|                       | AD                       | US-2,661,150                              | 12-01-1953                     | Abbott, Jr.                                        |                                                                                 |
|                       | AE                       | US-2,750,107                              | 06-12-1956                     | More                                               |                                                                                 |
|                       | AF                       | US-2,792,172                              | 05-14-1957                     | Tait                                               |                                                                                 |
|                       | AG                       | US-3,096,283                              | 07-02-1963                     | Hein                                               |                                                                                 |
|                       | AH                       | US-3,145,713                              | 08-25-1964                     | Latham, Jr.                                        |                                                                                 |
|                       | AI                       | US-3,239,136                              | 03-08-1966                     | Hein                                               |                                                                                 |
|                       | AJ                       | US-3,244,362                              | 04-05-1966                     | Hein                                               |                                                                                 |
|                       | AK                       | US-3,244,363                              | 04-05-1966                     | Hein                                               |                                                                                 |
|                       | AL                       | US-3,409,213                              | 11-05-1968                     | Latham, Jr.                                        |                                                                                 |
|                       | AM                       | US-3,456,875                              | 07-22-1969                     | Hein                                               |                                                                                 |
|                       | AN                       | US-3,489,145                              | 01-13-1970                     | Judson et al.                                      |                                                                                 |
|                       | AO                       | US-3,565,330                              | 02-23-1971                     | Latham, Jr.                                        |                                                                                 |
|                       | AP                       | US-3,655,058                              | 04-11-1972                     | Novak                                              |                                                                                 |
|                       | AQ                       | US-3,737,096                              | 06-05-1973                     | Jones et al.                                       |                                                                                 |
|                       | AR                       | US-3,774,840                              | 11-27-1973                     | Boatright                                          |                                                                                 |
|                       | AS                       | US-3,987,961                              | 10-26-1976                     | Sinn et al.                                        |                                                                                 |
|                       | AT                       | US-4,007,871                              | 02-15-1977                     | Jones et al.                                       |                                                                                 |
|                       | AU                       | US-4,010,894                              | 03-08-1977                     | Kellogg et al.                                     |                                                                                 |
|                       | AV                       | US-4,014,497                              | 03-29-1977                     | Spiewok et al.                                     |                                                                                 |
|                       | AW                       | US-4,040,965                              | 08-09-1977                     | Kohlheb                                            |                                                                                 |
|                       | AX                       | US-4,056,224                              | 11-01-1977                     | Lolachi                                            |                                                                                 |
|                       | AY                       | US-4,082,217                              | 04-04-1978                     | Westberg                                           |                                                                                 |
|                       | AZ                       | US-4,086,924                              | 05-02-1978                     | Latham, Jr.                                        |                                                                                 |
|                       | AA1                      | US-4,140,268                              | 02-20-1979                     | Lacour                                             |                                                                                 |
|                       | AB1                      | US-4,142,670                              | 03-06-1979                     | Ishimaru et al.                                    |                                                                                 |
|                       | AC1                      | US-4,151,844                              | 05-01-1979                     | Cullis et al.                                      |                                                                                 |
|                       | AD1                      | US-4,197,847                              | 04-15-1980                     | Djerassi                                           |                                                                                 |
|                       | AE1                      | US-4,285,464                              | 08-25-1981                     | Latham, Jr.                                        |                                                                                 |
|                       | AF1                      | US-4,300,717                              | 11-17-1981                     | Latham, Jr.                                        |                                                                                 |
|                       | AG1                      | US-4,303,193                              | 12-01-1981                     | Latham, Jr.                                        |                                                                                 |
|                       | AH1                      | US-4,321,921                              | 03-30-1982                     | Laszczower                                         |                                                                                 |
|                       | AI1                      | US-4,387,848                              | 06-14-1983                     | Kellogg et al.                                     |                                                                                 |
|                       | AJ1                      | US-4,425,114                              | 01-10-1984                     | Schoendorfer et al.                                |                                                                                 |
|                       | AK1                      | US-4,430,072                              | 02-07-1984                     | Kellogg et al.                                     |                                                                                 |
|                       | AL1                      | US-4,447,221                              | 05-08-1984                     | Mulzet                                             |                                                                                 |
|                       | AM1                      | US-4,457,747                              | 07-03-1984                     | Tu                                                 |                                                                                 |
|                       | AN1                      | US-4,464,167                              | 08-07-1984                     | Schoendorfer et al.                                |                                                                                 |
|                       | AO1                      | US-4,466,888                              | 08-21-1984                     | Verkaart                                           |                                                                                 |
|                       | AP1                      | US-4,482,342                              | 11-13-1984                     | Lueptow et al.                                     |                                                                                 |
|                       | AQ1                      | US-4,490,135                              | 12-25-1984                     | Troutner                                           |                                                                                 |
|                       | AR1                      | US-4,530,691                              | 07-23-1985                     | Brown                                              |                                                                                 |
|                       | AS1                      | US-4,534,863                              | 08-13-1985                     | Bacon et al.                                       |                                                                                 |

|                       |                              |                    |  |
|-----------------------|------------------------------|--------------------|--|
| Examiner<br>Signature | /LESLIE R DEAK/ (05/02/2024) | Date<br>Considered |  |
|-----------------------|------------------------------|--------------------|--|

ME1 36057896v.1

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D/

Terumo v. Haemonetics - PGR2025-00077  
 Petitioner Terumo Exhibit 1002-0109

Used in Lieu of PTO/SB/08A/B  
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|                                                                                                                                              |   |    |   |                          |                       |
|----------------------------------------------------------------------------------------------------------------------------------------------|---|----|---|--------------------------|-----------------------|
| Substitute for form 1449/PTO<br><br><b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><br><i>(Use as many sheets as necessary)</i> |   |    |   | <b>Complete if Known</b> |                       |
|                                                                                                                                              |   |    |   | Application Number       | Not Yet Assigned      |
|                                                                                                                                              |   |    |   | Filing Date              | Concurrently Herewith |
|                                                                                                                                              |   |    |   | First Named Inventor     | Michael Ragusa        |
|                                                                                                                                              |   |    |   | Art Unit                 | 3781                  |
|                                                                                                                                              |   |    |   | Examiner Name            | Not Yet Assigned      |
| Sheet                                                                                                                                        | 2 | of | 6 | Attorney Docket Number   | 130670-80104          |

|  |     |              |            |                     |  |
|--|-----|--------------|------------|---------------------|--|
|  | AT1 | US-4,643,714 | 02-17-1987 | Brose               |  |
|  | AU1 | US-4,647,279 | 03-03-1987 | Mulzet et al.       |  |
|  | AV1 | US-4,655,742 | 04-07-1987 | Vantard             |  |
|  | AW1 | US-4,680,025 | 07-14-1987 | Kruger et al.       |  |
|  | AX1 | US-4,684,361 | 08-04-1987 | Feldman et al.      |  |
|  | AY1 | US-4,692,136 | 09-08-1987 | Feldman et al.      |  |
|  | AZ1 | US-4,708,712 | 11-24-1987 | Mulzet              |  |
|  | AA2 | US-4,713,176 | 12-15-1987 | Schoendorfer et al. |  |
|  | AB2 | US-4,734,089 | 03-29-1988 | Cullis              |  |
|  | AC2 | US-4,740,202 | 04-26-1988 | Stacey et al.       |  |
|  | AD2 | US-4,740,313 | 04-26-1988 | Schoendorfer et al. |  |
|  | AE2 | US-4,755,300 | 07-05-1988 | Fischel et al.      |  |
|  | AF2 | US-4,767,396 | 08-30-1988 | Powers              |  |
|  | AG2 | US-4,795,419 | 01-03-1989 | Yawn et al.         |  |
|  | AH2 | US-4,795,448 | 01-03-1989 | Stacey et al.       |  |
|  | AI2 | US-4,806,247 | 02-21-1989 | Schoendorfer et al. |  |
|  | AJ2 | US-4,806,252 | 02-21-1989 | Brown et al.        |  |
|  | AK2 | US-4,808,307 | 02-28-1989 | Fischel et al.      |  |
|  | AL2 | US-4,850,995 | 07-25-1989 | Tie et al.          |  |
|  | AM2 | US-4,869,812 | 09-26-1989 | Schoendorfer et al. |  |
|  | AN2 | US-4,871,462 | 10-03-1989 | Fischel et al.      |  |
|  | AO2 | US-4,876,013 | 10-24-1989 | Shmidt et al.       |  |
|  | AP2 | US-4,889,524 | 12-26-1989 | Fell et al.         |  |
|  | AQ2 | US-4,911,833 | 03-27-1990 | Schoendorfer et al. |  |
|  | AR2 | US-4,934,995 | 06-19-1990 | Cullis              |  |
|  | AS2 | US-4,940,543 | 07-10-1990 | Brown et al.        |  |
|  | AT2 | US-4,943,273 | 07-24-1990 | Pages               |  |
|  | AU2 | US-4,968,295 | 11-06-1990 | Neumann             |  |
|  | AV2 | US-4,983,156 | 01-08-1991 | Knelson             |  |
|  | AW2 | US-4,983,158 | 01-08-1991 | Headley             |  |
|  | AX2 | US-4,985,153 | 01-15-1991 | Kuroda et al.       |  |
|  | AY2 | US-4,994,188 | 02-19-1991 | Prince              |  |
|  | AZ2 | US-5,039,401 | 08-13-1991 | Columbus et al.     |  |
|  | AA3 | US-5,045,048 | 09-03-1991 | Kaleskas et al.     |  |
|  | AB3 | US-5,098,372 | 03-24-1992 | Jonsson             |  |
|  | AC3 | US-5,098,373 | 03-24-1992 | Polaschegg          |  |
|  | AD3 | US-5,100,372 | 03-31-1992 | Headley             |  |
|  | AE3 | US-5,100,564 | 03-31-1992 | Pall et al.         |  |
|  | AF3 | US-5,112,298 | 05-12-1992 | Prince et al.       |  |
|  | AG3 | US-5,114,396 | 05-19-1992 | Unger et al.        |  |
|  | AH3 | US-5,135,667 | 08-04-1992 | Schoendorfer        |  |
|  | AI3 | US-5,141,486 | 08-25-1992 | Antwiler            |  |
|  | AJ3 | US-5,147,290 | 09-15-1992 | Jonsson             |  |
|  | AK3 | US-5,154,716 | 10-13-1992 | Bauman et al.       |  |
|  | AL3 | US-5,174,894 | 12-29-1992 | Ohsawa et al.       |  |
|  | AM3 | US-5,194,145 | 03-16-1993 | Schoendorfer        |  |
|  | AN3 | US-5,217,426 | 06-08-1993 | Bacehowski et al.   |  |
|  | AO3 | US-5,217,427 | 06-08-1993 | Cullis              |  |
|  | AP3 | US-5,234,403 | 08-10-1993 | Yoda et al.         |  |

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|--------------------|------------------------------|-----------------|--|
| Examiner Signature | /LESLIE R DEAK/ (05/02/2024) | Date Considered |  |
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Terumo v. Haemonetics - PGR2025-00077  
 Petitioner Terumo Exhibit 1002-0110

Used in Lieu of PTO/SB/08A/B  
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|                                                                                                                                              |   |    |   |                          |                       |
|----------------------------------------------------------------------------------------------------------------------------------------------|---|----|---|--------------------------|-----------------------|
| Substitute for form 1449/PTO<br><br><b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><br><i>(Use as many sheets as necessary)</i> |   |    |   | <b>Complete if Known</b> |                       |
|                                                                                                                                              |   |    |   | Application Number       | Not Yet Assigned      |
|                                                                                                                                              |   |    |   | Filing Date              | Concurrently Herewith |
|                                                                                                                                              |   |    |   | First Named Inventor     | Michael Ragusa        |
|                                                                                                                                              |   |    |   | Art Unit                 | 3781                  |
|                                                                                                                                              |   |    |   | Examiner Name            | Not Yet Assigned      |
| Sheet                                                                                                                                        | 3 | of | 6 | Attorney Docket Number   | 130670-80104          |

|  |     |              |            |                    |  |
|--|-----|--------------|------------|--------------------|--|
|  | AQ3 | US-5,254,248 | 10-19-1993 | Nakamura           |  |
|  | AR3 | US-5,273,517 | 12-28-1993 | Barone et al.      |  |
|  | AS3 | US-5,277,701 | 01-11-1994 | Christie et al.    |  |
|  | AT3 | US-5,298,016 | 03-29-1994 | Gordon             |  |
|  | AU3 | US-5,298,171 | 03-29-1994 | Biesel             |  |
|  | AV3 | US-5,300,060 | 04-05-1994 | Nelson             |  |
|  | AW3 | US-5,316,540 | 05-31-1994 | McMannis et al.    |  |
|  | AX3 | US-5,318,511 | 06-07-1994 | Riquier et al.     |  |
|  | AY3 | US-5,318,512 | 06-07-1994 | Neumann            |  |
|  | AZ3 | US-5,348,533 | 09-20-1994 | Papillon et al.    |  |
|  | AA4 | US-5,368,542 | 11-29-1994 | McMannis et al.    |  |
|  | AB4 | US-5,368,555 | 11-29-1994 | Sussman et al.     |  |
|  | AC4 | US-5,386,734 | 02-07-1995 | Pusinelli          |  |
|  | AD4 | US-5,387,174 | 02-07-1995 | Rochat             |  |
|  | AE4 | US-5,387,187 | 02-07-1995 | Fell et al.        |  |
|  | AF4 | US-5,403,272 | 04-04-1995 | Deniega et al.     |  |
|  | AG4 | US-5,405,308 | 04-11-1995 | Headley et al.     |  |
|  | AH4 | US-5,417,650 | 05-23-1995 | Gordon             |  |
|  | AI4 | US-5,431,814 | 07-11-1995 | Jorgensen          |  |
|  | AJ4 | US-5,437,598 | 08-01-1995 | Antwiler           |  |
|  | AK4 | US-5,437,624 | 08-01-1995 | Langley            |  |
|  | AL4 | US-5,462,667 | 10-31-1995 | Wollinsky et al.   |  |
|  | AM4 | US-5,470,483 | 11-28-1995 | Bene et al.        |  |
|  | AN4 | US-5,484,396 | 01-16-1996 | Naficy             |  |
|  | AO4 | US-5,494,592 | 02-27-1996 | Latham, Jr. et al. |  |
|  | AP4 | US-5,505,685 | 04-09-1996 | Antwiler           |  |
|  | AQ4 | US-5,514,070 | 05-07-1996 | Pages              |  |
|  | AR4 | US-5,543,062 | 08-06-1996 | Nishimura          |  |
|  | AS4 | US-5,551,941 | 09-03-1996 | Howell             |  |
|  | AT4 | US-5,585,007 | 12-17-1996 | Antanavich et al.  |  |
|  | AU4 | US-5,607,579 | 03-04-1997 | Latham, Jr. et al. |  |
|  | AV4 | US-5,649,903 | 07-22-1997 | Deniega et al.     |  |
|  | AW4 | US-5,651,766 | 07-29-1997 | Kingsley et al.    |  |
|  | AX4 | US-5,656,163 | 08-12-1997 | Brown              |  |
|  | AY4 | US-5,665,061 | 09-09-1997 | Antwiler           |  |
|  | AZ4 | US-5,712,798 | 01-27-1998 | Langley et al.     |  |
|  | AA5 | US-5,728,060 | 03-17-1998 | Kingsley et al.    |  |
|  | AB5 | US-5,733,253 | 03-31-1998 | Headley et al.     |  |
|  | AC5 | US-5,733,446 | 03-31-1998 | Holm               |  |
|  | AD5 | US-5,733,545 | 03-31-1998 | Hood, III          |  |
|  | AE5 | US-5,738,792 | 04-14-1998 | Schoendorfer       |  |
|  | AF5 | US-5,762,791 | 06-09-1998 | Deniega et al.     |  |
|  | AG5 | US-5,779,660 | 07-14-1998 | Kingsley et al.    |  |
|  | AH5 | US-5,783,085 | 07-21-1998 | Fischel            |  |
|  | AI5 | US-5,792,351 | 08-11-1998 | Wehrle et al.      |  |
|  | AJ5 | US-5,849,203 | 12-15-1998 | Brown et al.       |  |
|  | AK5 | US-5,882,289 | 03-16-1999 | Sakota et al.      |  |
|  | AL5 | US-5,906,589 | 05-25-1999 | Gordon et al.      |  |
|  | AM5 | US-5,919,125 | 07-06-1999 | Berch              |  |

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| Examiner Signature | /LESLIE R DEAK/ (05/02/2024) | Date Considered |  |
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Terumo v. Haemonetics - PGR2025-00077  
 Petitioner Terumo Exhibit 1002-0111

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|                                                                                                                                              |   |    |   |                          |                       |
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|                                                                                                                                              |   |    |   | Application Number       | Not Yet Assigned      |
|                                                                                                                                              |   |    |   | Filing Date              | Concurrently Herewith |
|                                                                                                                                              |   |    |   | First Named Inventor     | Michael Ragusa        |
|                                                                                                                                              |   |    |   | Art Unit                 | 3781                  |
|                                                                                                                                              |   |    |   | Examiner Name            | Not Yet Assigned      |
| Sheet                                                                                                                                        | 4 | of | 6 | Attorney Docket Number   | 130670-80104          |

|  |     |                   |            |                   |  |
|--|-----|-------------------|------------|-------------------|--|
|  | AN5 | US-5,964,724      | 10-12-1999 | Rivera et al.     |  |
|  | AO5 | US-5,970,432      | 10-19-1999 | Ishimoto et al.   |  |
|  | AP5 | US-5,980,760      | 11-09-1999 | Min et al.        |  |
|  | AQ5 | US-6,007,725      | 12-28-1999 | Brown             |  |
|  | AR5 | US-6,059,979      | 05-09-2000 | Brown             |  |
|  | AS5 | US-6,207,063-B1   | 03-27-2001 | Brown             |  |
|  | AT5 | US-6,234,989-B1   | 05-22-2001 | Brierton et al.   |  |
|  | AU5 | US-6,296,602-B1   | 10-02-2001 | Headley           |  |
|  | AV5 | US-6,464,624-B2   | 10-15-2002 | Pages             |  |
|  | AW5 | US-6,497,676-B1   | 12-24-2002 | Childers et al.   |  |
|  | AX5 | US-6,558,307-B2   | 05-06-2003 | Headley           |  |
|  | AY5 | US-6,623,443-B1   | 09-23-2003 | Polaschegg        |  |
|  | AZ5 | US-6,743,192-B1   | 06-01-2004 | Sakota et al.     |  |
|  | AA6 | US-7,115,205-B2   | 10-03-2006 | Robinson et al.   |  |
|  | AB6 | US-7,186,231-B2   | 03-06-2007 | Takagi et al.     |  |
|  | AC6 | US-7,270,645-B2   | 09-18-2007 | Langley et al.    |  |
|  | AD6 | US-7,704,454-B1   | 04-27-2010 | Langley et al.    |  |
|  | AE6 | US-8,628,489-B2   | 01-14-2014 | Pages et al.      |  |
|  | AF6 | US-8,702,637-B2   | 04-22-2014 | Pages et al.      |  |
|  | AG6 | US-8,759,094-B2   | 06-24-2014 | Ranby             |  |
|  | AH6 | US-9,283,316-B2   | 03-15-2016 | Flexman           |  |
|  | AI6 | US-10,758,652-B2  | 09-01-2020 | Ragusa            |  |
|  | AJ6 | US-10,792,416-B2  | 10-06-2020 | Ragusa            |  |
|  | AK6 | US-20010000185-A1 | 04-05-2001 | Keller et al.     |  |
|  | AL6 | US-20010027156-A1 | 10-04-2001 | Egozy et al.      |  |
|  | AM6 | US-20020043492-A1 | 04-18-2002 | Bischof           |  |
|  | AN6 | US-20020062100-A1 | 05-23-2002 | Pierce et al.     |  |
|  | AO6 | US-20020120227-A1 | 08-29-2002 | Childers et al.   |  |
|  | AP6 | US-20030055375-A1 | 03-20-2003 | Holst et al.      |  |
|  | AQ6 | US-20030066807-A1 | 04-10-2003 | Suzuki            |  |
|  | AR6 | US-20030125881-A1 | 07-03-2003 | Ryan              |  |
|  | AS6 | US-20030175150-A1 | 09-18-2003 | Grimm             |  |
|  | AT6 | US-20040186409-A1 | 09-23-2004 | Cavalcanti et al. |  |
|  | AU6 | US-20050209522-A1 | 09-22-2005 | Tadokoro et al.   |  |
|  | AV6 | US-20050235733-A1 | 10-27-2005 | Holst et al.      |  |
|  | AW6 | US-20060058167-A1 | 03-16-2006 | Ragusa et al.     |  |
|  | AX6 | US-20060155236-A1 | 07-13-2006 | Gara et al.       |  |
|  | AY6 | US-20070112289-A1 | 05-17-2007 | Cavalcanti et al. |  |
|  | AZ6 | US-20080146993-A1 | 06-19-2008 | Krishna           |  |
|  | AA7 | US-20120175313-A1 | 07-12-2012 | Barry, JR. et al. |  |
|  | AB7 | US-20140039373-A1 | 02-06-2014 | Ragusa et al.     |  |
|  | AC7 | US-20140356851-A1 | 12-04-2014 | Pages et al.      |  |
|  | AD7 | US-20180344910-A1 | 12-06-2018 | Ragusa            |  |
|  | AE7 | US-20200345924-A1 | 11-05-2020 | Ragusa            |  |
|  | AF7 | US-20200261630-A1 | 08-20-2020 | Ragusa            |  |

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| Examiner Signature | /LESLIE R DEAK/ (05/02/2024) | Date Considered |  |
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Terumo v. Haemonetics - PGR2025-00077  
 Petitioner Terumo Exhibit 1002-0112

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|                                                                                                                                              |   |    |   | Application Number       | Not Yet Assigned      |
|                                                                                                                                              |   |    |   | Filing Date              | Concurrently Herewith |
|                                                                                                                                              |   |    |   | First Named Inventor     | Michael Ragusa        |
|                                                                                                                                              |   |    |   | Art Unit                 | 3781                  |
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| Sheet                                                                                                                                        | 5 | of | 6 | Attorney Docket Number   | 130670-80104          |

| FOREIGN PATENT DOCUMENTS |                          |                                                                                      |  |                                   |                                                    |                                                                                 |
|--------------------------|--------------------------|--------------------------------------------------------------------------------------|--|-----------------------------------|----------------------------------------------------|---------------------------------------------------------------------------------|
| Examiner<br>Initials*    | Cite<br>No. <sup>1</sup> | Foreign Patent Document                                                              |  | Publication<br>Date<br>MM-DD-YYYY | Name of Patentee or<br>Applicant of Cited Document | Pages, Columns, Lines,<br>Where Relevant Passages<br>Or Relevant Figures Appear |
|                          |                          | Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (if<br>known) |  |                                   |                                                    |                                                                                 |
|                          | BA**                     | CN-2735985-Y                                                                         |  | 10-26-2005                        | Shanghai Dahua Medical<br>Apparatus Co., Ltd       | √                                                                               |
|                          | BB**                     | EP-0128683-A2                                                                        |  | 12-19-1984                        | Baxter Travenol Laboratories,<br>Inc               |                                                                                 |
|                          | BC**                     | EP-0171749-A1                                                                        |  | 02-19-1986                        | Terumo Corp                                        |                                                                                 |
|                          | BD**                     | EP-0208061-A1                                                                        |  | 01-14-1987                        | Biotest Pharma GmbH                                |                                                                                 |
|                          | BE**                     | EP-257755-A1                                                                         |  | 03-02-1988                        | Haemonetics Corp                                   |                                                                                 |
|                          | BF**                     | EP-0578086-A1                                                                        |  | 01-12-1994                        | Terumo Corp                                        |                                                                                 |
|                          | BG**                     | EP-619145-A2                                                                         |  | 10-12-1994                        | Electromedics, Inc                                 |                                                                                 |
|                          | BH**                     | EP-0654277-A1                                                                        |  | 05-24-1995                        | Cobe Laboratories, Inc                             |                                                                                 |
|                          | BI**                     | EP-664159-A1                                                                         |  | 07-26-1995                        | Haemonetics Corp                                   |                                                                                 |
|                          | BJ**                     | EP-799645-A1                                                                         |  | 10-08-1997                        | Haemonetics Corp                                   |                                                                                 |
|                          | BK**                     | EP-0885619-A1                                                                        |  | 12-23-1998                        | Terumo Corp                                        |                                                                                 |
|                          | BL**                     | EP-1057534-A1                                                                        |  | 12-06-2000                        | Haemonetics Corp                                   |                                                                                 |
|                          | BM**                     | EP-1295619-A2                                                                        |  | 03-26-2003                        | Terumo Corp                                        |                                                                                 |
|                          | BN**                     | EP-1374927-A1                                                                        |  | 01-02-2004                        | Terumo Corp                                        |                                                                                 |
|                          | BO**                     | FR-2258898-A1                                                                        |  | 08-22-1975                        | Heraeus Christ GmbH,dt                             |                                                                                 |
|                          | BP**                     | GB-2047110-A                                                                         |  | 11-26-1980                        | Hogman, C F                                        |                                                                                 |
|                          | BQ**                     | JP-S59-006952                                                                        |  | 01-14-1984                        | Hitachi Koki KK                                    | √                                                                               |
|                          | BR**                     | JP-S59-069166                                                                        |  | 04-19-1984                        | Nikkiso Co Ltd.                                    | √                                                                               |
|                          | BS**                     | JP-H02-052665                                                                        |  | 02-22-1990                        | Nissho KK                                          | √                                                                               |
|                          | BT**                     | JP-H03-131268                                                                        |  | 06-04-1991                        | Fresenius AG                                       | √                                                                               |
|                          | BU**                     | JP-H07-075746                                                                        |  | 03-20-1995                        | Electromedics Inc.                                 | √                                                                               |
|                          | BV**                     | JP-H08-131539                                                                        |  | 05-28-1996                        | Terumo Corp.                                       | √                                                                               |
|                          | BW**                     | JP-H09-192215                                                                        |  | 07-29-1997                        | Nakane Takaharu                                    | √                                                                               |
|                          | BX**                     | JP-2002-291872-A                                                                     |  | 10-08-2002                        | Terumo Corp                                        | √                                                                               |
|                          | BY**                     | JP-2008-506424-A                                                                     |  | 03-06-2008                        |                                                    | √                                                                               |
|                          | BZ**                     | SU-660718-A1                                                                         |  | 05-05-1979                        | Sp K B Biofizicheskoy<br>Apparatu                  |                                                                                 |
|                          | BA1**                    | SU-762982-A1                                                                         |  | 09-15-1980                        | Sp K B Biofizicheskoy<br>Apparatu                  |                                                                                 |
|                          | BB1**                    | SU-1146098-A1                                                                        |  | 03-23-1985                        | Sp K B Biofiz App                                  |                                                                                 |
|                          | BC1**                    | WO-1985/02561-A1                                                                     |  | 06-20-1985                        | Baxter Travenol Laboratories,<br>Inc               |                                                                                 |
|                          | BD1**                    | WO-1990/00059-A1                                                                     |  | 01-11-1990                        | Sirchia, Girolamo                                  |                                                                                 |
|                          | BE1**                    | WO-1990/07383-A1                                                                     |  | 07-12-1990                        | Haemonetics Corp                                   |                                                                                 |
|                          | BF1**                    | WO-1994/06535-A1                                                                     |  | 03-31-1994                        | Fischel, Halbert                                   |                                                                                 |
|                          | BG1**                    | WO-1996/11747-A2                                                                     |  | 04-25-1996                        | Transfusion, Technologies<br>Corporation           |                                                                                 |
|                          | BH1**                    | WO-1996/33023-A1                                                                     |  | 10-24-1996                        | Cobe Laboratories, Inc                             |                                                                                 |
|                          | BI1**                    | WO-2002/05059-A2                                                                     |  | 01-17-2002                        | Baxter Int                                         |                                                                                 |

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| Examiner<br>Signature | /LESLIE R DEAK/ (05/02/2024) | Date<br>Considered |  |
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|                                                                                                                                              |   |    |   |                          |                       |
|----------------------------------------------------------------------------------------------------------------------------------------------|---|----|---|--------------------------|-----------------------|
| Substitute for form 1449/PTO<br><br><b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><br><i>(Use as many sheets as necessary)</i> |   |    |   | <b>Complete if Known</b> |                       |
|                                                                                                                                              |   |    |   | Application Number       | Not Yet Assigned      |
|                                                                                                                                              |   |    |   | Filing Date              | Concurrently Herewith |
|                                                                                                                                              |   |    |   | First Named Inventor     | Michael Ragusa        |
|                                                                                                                                              |   |    |   | Art Unit                 | 3781                  |
|                                                                                                                                              |   |    |   | Examiner Name            | Not Yet Assigned      |
| Sheet                                                                                                                                        | 6 | of | 6 | Attorney Docket Number   | 130670-80104          |

|       |                   |            |             |                          |
|-------|-------------------|------------|-------------|--------------------------|
| BJ1** | WO-2007/041716-A1 | 04-12-2007 | Gambro, Inc | <input type="checkbox"/> |
|-------|-------------------|------------|-------------|--------------------------|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. \* CITE NO.: Those application(s) which are marked with an single asterisk (\*) next to the Cite No. are not supplied (under 37 CFR 1.98(a)(2)(iii)) because that application was filed after June 30, 2003 or is available in the IFW. \*\* CITE NO.: Those document(s) which are marked with an double asterisk (\*\*) next to the Cite No. are not supplied because they were previously cited by or submitted to the Office in a prior application relied upon in this application for an earlier filing date under 35 U.S.C. 120. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

| NON PATENT LITERATURE DOCUMENTS |                       |                                                                                                                                                                                                                                                                 |                |
|---------------------------------|-----------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|
| Examiner Initials*              | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>2</sup> |
|                                 | CA**                  | Haemonetics Nomogram - Male, 2 pages, May 1990.                                                                                                                                                                                                                 |                |
|                                 | CB**                  | LEMMENS et al., Estimating blood volume in obese and morbidly obese patients. Obes Surg. 2006 Jun;16(6):773-6.                                                                                                                                                  |                |
|                                 | CC**                  | NADLER et al., Prediction of blood volume in normal human adults. Surgery. 1962 Feb;51(2):224-32.                                                                                                                                                               |                |
|                                 | CD**                  | WINTERS, Complications of donor apheresis. J Clin Apher. 2006 Jul;21(2):132-41.                                                                                                                                                                                 |                |
|                                 | CE**                  | International Search Report and Written Opinion for Application No. PCT/US2018/033826, dated August 3, 2018, 10 pages.                                                                                                                                          |                |
|                                 | CF**                  | International Search Report and Written Opinion for Application No. PCT/US2018/057528, dated January 7, 2019, 17 pages.                                                                                                                                         |                |

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

|                    |                              |                 |  |
|--------------------|------------------------------|-----------------|--|
| Examiner Signature | /LESLIE R DEAK/ {05/02/2024} | Date Considered |  |
|--------------------|------------------------------|-----------------|--|

ME1 36057896v.1

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D/

Terumo v. Haemonetics - PGR2025-00077  
 Petitioner Terumo Exhibit 1002-0114

PTO/SB/92 (07-16)  
Approved for use through 12/31/2020. OMB 0561-0031  
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

## Certificate of Mailing or Transmission under 37 CFR 1.8

I hereby certify that this correspondence is being:

1. ☐ Deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to:  
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P.O. Box 1450  
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Date

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3. ☒ EFS-Web transmitted to the USPTO.

\_\_\_\_\_  
/Jonathan C. Lovely, Reg. No. 60,821/  
Signature

\_\_\_\_\_  
March 22, 2021  
Date

\_\_\_\_\_  
Jonathan C. Lovely  
Typed or printed name

\_\_\_\_\_  
(617) 449-6556  
Telephone number

Note: Each paper must have its own certificate of mailing or transmission, or this certificate must identify each submitted paper:

IDS (Citation) by Applicant (230 References) (6 pages)

ME1 36057896V.1

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D/

Terumo v. Haemonetics - PGR2025-00077  
Petitioner Terumo Exhibit 1002-0115

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: December 8, 2022  
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Utility Application of:  
Michael Ragusa

Application No.: 17/205,400

Confirmation No.: 4686

Filed: March 18, 2021

Art Unit: N/A

For: SYSTEM AND METHOD FOR COLLECTING  
PLASMA

Examiner: Not Yet Assigned

**INFORMATION DISCLOSURE STATEMENT (IDS)**

MS Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR 1.97, Applicant hereby makes of record the following additional documents. A PTO Form SB/08 and a full copy of each of the documents required under 37 CFR 1.98(a)(2) accompany this statement.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 C.F.R. § 1.97(b)(3)).

In accordance with 37 C.F.R. § 1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patents and U.S. patent applications. Applicant submits herewith copies of foreign patents and non-patent literature in accordance with 37 C.F.R. § 1.98(a)(2).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D/

Terumo v. Haemonetics - PGR2025-00077  
Petitioner Terumo Exhibit 1002-0116



Application No.: 17/205,400

Docket No.: 130670-80104

The Examiner is advised that the following applications contain subject matter that may be related to the present application:

| U.S. Application | Filing Date        | Publication No. / Patent No. | Status    | Atty. Docket No. |
|------------------|--------------------|------------------------------|-----------|------------------|
| 15/608,183       | May 30, 2017       | 10,758,652                   | Issued    | 130670-08002     |
| 16/866,078       | May 4, 2020        | 10,980,926                   | Issued    | 130670-08005     |
| 17/205,374       | March 18, 2021     | 2021-0205509                 | Published | 130670-08006     |
| 17/943,410       | September 13, 2022 |                              | Pending   | 130670-08007     |
| 15/793,339       | October 25, 2017   | 10,792,416                   | Issued    | 130670-80102     |
| 16/931,333       | July 16, 2020      | 10,980,934                   | Issued    | 130670-80103     |

/LESLIE R DEAK/ (05/02/2024)

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed references.

Applicant believes no fee is due with this response.

Dated: December 8, 2022

Respectfully submitted,  
 Electronic signature: /Jonathan C. Lovely, Reg.  
 No. 60,821/  
 Jonathan C. Lovely  
 Registration No.: 60,821  
 MCCARTER & ENGLISH, LLP  
 265 Franklin Street  
 Boston, Massachusetts 02110  
 (617) 449-6556  
 (617) 607-9200 (Fax)  
 Attorney/Agent For Applicant

Doc code: IDS

Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)

Approved for use through 11/30/2020. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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|                                                                                                     |                        |                  |
|-----------------------------------------------------------------------------------------------------|------------------------|------------------|
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | 3799             |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

| U.S. PATENTS                                                                                               |         |                                      |                            |                        |                                                 |                                                                          | Remove                                                                   |                |
|------------------------------------------------------------------------------------------------------------|---------|--------------------------------------|----------------------------|------------------------|-------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|----------------|
| Examiner Initial*                                                                                          | Cite No | Patent Number                        | Kind Code <sup>1</sup>     | Issue Date             | Name of Patentee or Applicant of cited Document | Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear |                                                                          |                |
|                                                                                                            | 1       |                                      |                            |                        |                                                 |                                                                          |                                                                          |                |
| If you wish to add additional U.S. Patent citation information please click the Add button.                |         |                                      |                            |                        |                                                 |                                                                          | Add                                                                      |                |
| U.S. PATENT APPLICATION PUBLICATIONS                                                                       |         |                                      |                            |                        |                                                 |                                                                          | Remove                                                                   |                |
| Examiner Initial*                                                                                          | Cite No | Publication Number                   | Kind Code <sup>1</sup>     | Publication Date       | Name of Patentee or Applicant of cited Document | Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear |                                                                          |                |
|                                                                                                            | 1       | 20060226086                          | A1                         | 2006-10-12             | Robinson et al.                                 |                                                                          |                                                                          |                |
|                                                                                                            | 2       | 20210205509                          | A1                         | 2021-07-08             | Ragusa                                          |                                                                          |                                                                          |                |
| If you wish to add additional U.S. Published Application citation information please click the Add button. |         |                                      |                            |                        |                                                 |                                                                          | Add                                                                      |                |
| FOREIGN PATENT DOCUMENTS                                                                                   |         |                                      |                            |                        |                                                 |                                                                          | Remove                                                                   |                |
| Examiner Initial*                                                                                          | Cite No | Foreign Document Number <sup>3</sup> | Country Code <sup>2i</sup> | Kind Code <sup>4</sup> | Publication Date                                | Name of Patentee or Applicant of cited Document                          | Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear | T <sup>5</sup> |
|                                                                                                            | 1       | 1128887                              | EP                         | A1                     | 2001-09-05                                      | Baxter Int                                                               |                                                                          |                |
| If you wish to add additional Foreign Patent Document citation information please click the Add button.    |         |                                      |                            |                        |                                                 |                                                                          | Add                                                                      |                |
| NON-PATENT LITERATURE DOCUMENTS                                                                            |         |                                      |                            |                        |                                                 |                                                                          | Remove                                                                   |                |

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

|                        |                  |
|------------------------|------------------|
| Application Number     | 17205400         |
| Filing Date            | 2021-03-18       |
| First Named Inventor   | Michael Ragusa   |
| Art Unit               | 3799             |
| Examiner Name          | Not Yet Assigned |
| Attorney Docket Number | 130670-80104     |

| Examiner Initials* | Cite No | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>5</sup> |
|--------------------|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|
|                    | 1       |                                                                                                                                                                                                                                                                 |                |

If you wish to add additional non-patent literature document citation information please click the Add button

**EXAMINER SIGNATURE**

|                    |                              |                 |  |
|--------------------|------------------------------|-----------------|--|
| Examiner Signature | /LESLIE R DEAK/ {05/02/2024} | Date Considered |  |
|--------------------|------------------------------|-----------------|--|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> See Kind Codes of USPTO Patent Documents at [www.USPTO.GOV](http://www.USPTO.GOV) or MPEP 901.04. <sup>2</sup> Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>3</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>4</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>5</sup> Applicant is to place a check mark here if English language translation is attached.

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
( Not for submission under 37 CFR 1.99)

|                        |                  |
|------------------------|------------------|
| Application Number     | 17205400         |
| Filing Date            | 2021-03-18       |
| First Named Inventor   | Michael Ragusa   |
| Art Unit               | 3799             |
| Examiner Name          | Not Yet Assigned |
| Attorney Docket Number | 130670-80104     |

**CERTIFICATION STATEMENT**

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

**OR**

That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

**SIGNATURE**

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

|            |                                       |                     |            |
|------------|---------------------------------------|---------------------|------------|
| Signature  | /Jonathan C. Lovely, Reg. No. 60,821/ | Date (YYYY-MM-DD)   | 2021-07-14 |
| Name/Print | Jonathan C. Lovely                    | Registration Number | 60,821     |

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

## Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: July 14, 2021  
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Utility Application of:  
Michael Ragusa

Application No.: 17/205,400

Confirmation No.: 4686

Filed: March 18, 2021

Art Unit: 3799

For: SYSTEM AND METHOD FOR COLLECTING  
PLASMA

Examiner: Not Yet Assigned

**INFORMATION DISCLOSURE STATEMENT (IDS)**

MS Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR 1.97, Applicant hereby makes of record the following additional documents. A PTO Form SB/08 and a full copy of each of the documents required under 37 CFR 1.98(a)(2) accompany this statement.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 C.F.R. § 1.97(b)(3)).

In accordance with 37 C.F.R. § 1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patent applications. Applicant submits herewith a copy of the cited foreign patent in accordance with 37 C.F.R. § 1.98(a)(2).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D/

Terumo v. Haemonetics - PGR2025-00077  
Petitioner Terumo Exhibit 1002-0122

Application No.: 17/205,400

Docket No.: 130670-80104

The Examiner is advised that the following co-pending applications contain subject matter that may be related to the present application:

| U.S. Application | Filing Date      | Publication No. / Patent No. | Status    | Atty. Docket No. |
|------------------|------------------|------------------------------|-----------|------------------|
| 15/608,183       | May 30, 2017     | 10,758,652                   | Issued    | 130670-08002     |
| 16/866,078       | May 4, 2020      | 10,980,926                   | Issued    | 130670-08005     |
| 17/205,374       | March 18, 2021   | 2021-0205509                 | Published | 130670-08006     |
| 15/793,339       | October 25, 2017 | 10,792,416                   | Issued    | 130670-80102     |
| 16/931,333       | July 16, 2020    | 10,980,934                   | Issued    | 130670-80103     |

/LESLIE R DEAK/ {05/02/2024}

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed references.

Applicant believes no fee is due with this response.

Dated: July 14, 2021

Respectfully submitted,  
 Electronic signature: /Jonathan C. Lovely, Reg.  
 No. 60,821/  
 Jonathan C. Lovely  
 Registration No.: 60,821  
 MCCARTER & ENGLISH, LLP  
 265 Franklin Street  
 Boston, Massachusetts 02110  
 (617) 449-6556  
 (617) 607-9200 (Fax)  
 Attorney/Agent For Applicant

**PE2E SEARCH - Search History (Prior Art)**

| Ref # | Hits | Search Query                                                                                                                                                              | DBs                               | Default Operator | Plurals | British Equivalents | Time Stamp          |
|-------|------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------|------------------|---------|---------------------|---------------------|
| L1    | 2    | ("20180344910").PN.                                                                                                                                                       | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 11:36 AM |
| L2    | 1    | ( (A61M1/029 and A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415 and A61M2230/207).CPC. )                                                                        | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 11:37 AM |
| L3    | 1    | ( (A61M1/029 and A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415).CPC. )                                                                                         | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 11:37 AM |
| L4    | 20   | ( (A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415).CPC. )                                                                                                       | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 11:37 AM |
| L5    | 3    | "20120175313"                                                                                                                                                             | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 12:01 PM |
| L6    | 2    | "20030125881"                                                                                                                                                             | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 12:16 PM |
| L7    | 27   | 2009/0215602                                                                                                                                                              | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 12:17 PM |
| L8    | 3    | "20090215602"                                                                                                                                                             | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 12:18 PM |
| L9    | 2    | L1 AND ( (A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC. ) | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 12:25 PM |
| L10   | 8637 | ( (A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC. )        | (US-PGPUB; USPAT; USOCR; DERWENT) | OR               | OFF     | OFF                 | 2019/10/28 12:25 PM |



|     |      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                             |    |     |     |                     |
|-----|------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------|----|-----|-----|---------------------|
| L11 | 1805 | L10 and hematocrit                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2019/10/28 12:26 PM |
| L12 | 1    | "I11" and (hematocrit with anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2019/10/28 12:26 PM |
| L13 | 1    | "I10" and (hematocrit with anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2019/10/28 12:30 PM |
| L14 | 2    | "I10" and (hematocrit same anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2019/10/28 12:30 PM |
| L15 | 44   | ((("RAGUSA") near3 ("Michael"))).INV.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | (US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT) | OR | OFF | OFF | 2019/10/28 12:31 PM |
| L16 | 2    | "I15" and (hematocrit same anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2019/10/28 12:31 PM |
| L17 | 183  | ("20010000185" "20020062100" "1025059" "1611725" "20010027156" "20020043492" "20020120227" "20030055375" "20030066807" "20030125881" "20030175150" "20040186409" "20050209522" "20050235733" "20060058167" "20060155236" "20070112289" "20080146993" "20120175313" "20140039373" "20140356851" "20180344921" "2087778" "2661150" "2750107" "2792172" "3096283" "3145713" "3239136" "3244362" "3244363" "3409213" "3456875" "3489145" "3565330" "3655058" "3737096" "3774840" "3987961" "4007871" "4010894" "4014497" "4040965" "4056224" "4082217" "4086924" "4140268" "4142670" "4151844" "4197847" "4285464" "4300717" "4303193" "4321921" "4387848" "4425114" "4430072" "4447221" "4457747" "4464167" "4466888" "4482342" "4490135" "4530691" "4534863" "4643714" "4647279" "4655742" "4680025" "4684361" "4692136" "4708712" "4713176" "4734089" "4740202" "4740313" "4755300" "4767396" "4795419" "4795448" "4806247" "4806252" "48 | (US-PGPUB; USPAT)                           | OR | OFF | OFF | 2019/10/28 12:37 PM |

|     |   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                      |    |     |     |                        |
|-----|---|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|----|-----|-----|------------------------|
|     |   | 08307" 4850995" 486<br>9812" 4871462" 4876<br>013" 4889524" 49118<br>33" 4934995" 494054<br>3" 4943273" 4968295"<br> 4983156" 4983158" <br>4985153" 4994188" 5<br>039401" 5045048" 50<br>98372" 5098373" 510<br>0372" 5100564" 5112<br>298" 5114396" 51356<br>67" 5141486" 514729<br>0" 5154716" 5174894"<br> 5194145" 5217426" <br>5217427" 5234403" 5<br>254248" 5273517" 52<br>77701" 5298016" 529<br>8171" 5300060" 5316<br>540" 5318511" 53185<br>12" 5348533" 536854<br>2" 5368555" 5386734"<br> 5387174" 5387187" <br>5403272" 5405308" 5<br>417650" 5431814" 54<br>37598" 5437624" 546<br>2667" 5470483" 5484<br>396" 5494592" 55056<br>85" 5514070" 554306<br>2" 5551941" 5585007"<br> 5607579" 5649903" <br>5651766" 5656163" 5<br>665061" 5712798" 57<br>28060" 5733253" 573<br>3446" 5733545" 5738<br>792" 5762791" 57796<br>60" 5783085" 579235<br>1" 5849203" 5882289"<br> 5906589" 5919125" <br>5964724" 5970432" 5<br>980760" 6007725" 60<br>59979" 6207063" 623<br>4989" 6296602" 6464<br>624" 6497676" 65583<br>07" 6623443" 674319<br>2" 7115205" 7186231"<br> 7270645" 7704454" <br>8628489" 8702637" 8<br>759094").PN. |                                      |    |     |     |                        |
| L18 | 2 | ("20180344910").PN.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2020/02/27<br>09:46 AM |
| L19 | 3 | "I15" and (hematocrit<br>same anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2020/05/05<br>01:39 PM |
| L20 | 1 | ("10758652").PN.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | (USPAT; USOCR)                       | OR | OFF | OFF | 2020/11/05<br>03:16 PM |
| L21 | 0 | ("20120175313").PN.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | (USPAT; USOCR)                       | OR | OFF | OFF | 2020/11/05<br>04:22 PM |

|     |     |                                                                                                                                                               |                                                                                                                                                                   |    |     |     |                        |
|-----|-----|---------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|-----|-----|------------------------|
| L22 | 1   | "20120175313"                                                                                                                                                 | (USPAT)                                                                                                                                                           | OR | OFF | OFF | 2020/11/05<br>04:22 PM |
| L23 | 10  | ("4713176"   "6348156"<br>  "6875191"   "7011761"<br>  "7087177"   "7297272"<br>  "7708710"  <br>"8075468").PN. OR<br>("8852140").URPN.                       | (US-PGPUB; USPAT;<br>USOCR)                                                                                                                                       | OR | OFF | OFF | 2020/11/05<br>04:22 PM |
| L24 | 8   | L23 and prim\$3                                                                                                                                               | (US-PGPUB; USPAT;<br>USOCR)                                                                                                                                       | OR | OFF | OFF | 2020/11/05<br>04:22 PM |
| L25 | 0   | (10/302682).APP.                                                                                                                                              | (USPAT; USOCR)                                                                                                                                                    | OR | OFF | OFF | 2020/11/05<br>04:26 PM |
| L26 | 1   | "20140100507"                                                                                                                                                 | (USPAT; USOCR)                                                                                                                                                    | OR | OFF | OFF | 2020/11/05<br>04:28 PM |
| L27 | 120 | A61M1/024.cpc.                                                                                                                                                | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                                              | OR | OFF | OFF | 2021/02/01<br>01:20 PM |
| L28 | 708 | G01n15/05.cpc.                                                                                                                                                | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                                              | OR | OFF | OFF | 2021/02/01<br>01:21 PM |
| L29 | 150 | G01n2015/055.cpc.                                                                                                                                             | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                                              | OR | OFF | OFF | 2021/02/01<br>01:21 PM |
| L30 | 3   | ((US-20030125881-<br>A1).did. AND<br>PGPB.dbnm.) OR ((US-<br>10758652-B2 OR US-<br>6348156-B1).did. AND<br>USPT.dbnm.)                                        | (US-PGPUB; USPAT;<br>USOCR; FIT (AU, AP,<br>AT, CA, CH, CN, DD,<br>DE, EA, EP, ES, FR,<br>GB, JP, KR, OA, RU,<br>SU, WO); FPRS; EPO;<br>JPO; DERWENT;<br>IBM_TDB) | OR | ON  | ON  | 2024/04/30<br>12:21 PM |
| L31 | 0   | L30 AND touchscreen                                                                                                                                           | (US-PGPUB; USPAT;<br>USOCR; FIT (AU, AP,<br>AT, CA, CH, CN, DD,<br>DE, EA, EP, ES, FR,<br>GB, JP, KR, OA, RU,<br>SU, WO); FPRS; EPO;<br>JPO; DERWENT;<br>IBM_TDB) | OR | ON  | ON  | 2024/04/30<br>12:21 PM |
| L32 | 0   | touchscreen WITH<br>plasmapheresis                                                                                                                            | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                                              | OR | OFF | OFF | 2024/04/30<br>12:22 PM |
| L33 | 4   | touchscreen SAME<br>plasmapheresis                                                                                                                            | (US-PGPUB; USPAT;<br>USOCR; DERWENT)                                                                                                                              | OR | OFF | OFF | 2024/04/30<br>12:22 PM |
| L34 | 16  | "10980926"                                                                                                                                                    | (US-PGPUB; USPAT;<br>USOCR; FIT (AU, AP,<br>AT, CA, CH, CN, DD,<br>DE, EA, EP, ES, FR,<br>GB, JP, KR, OA, RU,<br>SU, WO); EPO; JPO;<br>DERWENT)                   | OR | ON  | ON  | 2024/04/30<br>03:40 PM |
| L35 | 200 | ("1025059"   "1611725"<br>  "2087778"   "2661150"<br>  "2750107"   "2792172"<br>  "3096283"   "3145713"<br>  "3239136"   "3244362"<br>  "3244363"   "3409213" | (US-PGPUB; USPAT;<br>USOCR)                                                                                                                                       | OR | ON  | ON  | 2024/04/30<br>04:01 PM |

|  |  |                       |  |  |  |  |  |
|--|--|-----------------------|--|--|--|--|--|
|  |  | "3456875"   "3489145" |  |  |  |  |  |
|  |  | "3565330"   "3655058" |  |  |  |  |  |
|  |  | "3737096"   "3774840" |  |  |  |  |  |
|  |  | "3987961"   "4007871" |  |  |  |  |  |
|  |  | "4010894"   "4014497" |  |  |  |  |  |
|  |  | "4040965"   "4056224" |  |  |  |  |  |
|  |  | "4082217"   "4086924" |  |  |  |  |  |
|  |  | "4140268"   "4142670" |  |  |  |  |  |
|  |  | "4151844"   "4197847" |  |  |  |  |  |
|  |  | "4285464"   "4300717" |  |  |  |  |  |
|  |  | "4303193"   "4321921" |  |  |  |  |  |
|  |  | "4387848"   "4425114" |  |  |  |  |  |
|  |  | "4430072"   "4447221" |  |  |  |  |  |
|  |  | "4457747"   "4464167" |  |  |  |  |  |
|  |  | "4466888"   "4482342" |  |  |  |  |  |
|  |  | "4490135"   "4530691" |  |  |  |  |  |
|  |  | "4534863"   "4643714" |  |  |  |  |  |
|  |  | "4647279"   "4655742" |  |  |  |  |  |
|  |  | "4680025"   "4684361" |  |  |  |  |  |
|  |  | "4692136"   "4708712" |  |  |  |  |  |
|  |  | "4713176"   "4734089" |  |  |  |  |  |
|  |  | "4740202"   "4740313" |  |  |  |  |  |
|  |  | "4755300"   "4767396" |  |  |  |  |  |
|  |  | "4795419"   "4795448" |  |  |  |  |  |
|  |  | "4806247"   "4806252" |  |  |  |  |  |
|  |  | "4808307"   "4850995" |  |  |  |  |  |
|  |  | "4869812"   "4871462" |  |  |  |  |  |
|  |  | "4876013"   "4889524" |  |  |  |  |  |
|  |  | "4911833"   "4934995" |  |  |  |  |  |
|  |  | "4940543"   "4943273" |  |  |  |  |  |
|  |  | "4968295"   "4983156" |  |  |  |  |  |
|  |  | "4983158"   "4985153" |  |  |  |  |  |
|  |  | "4994188"   "5039401" |  |  |  |  |  |
|  |  | "5045048"   "5098372" |  |  |  |  |  |
|  |  | "5098373"   "5100372" |  |  |  |  |  |
|  |  | "5100564"   "5112298" |  |  |  |  |  |
|  |  | "5114396"   "5135667" |  |  |  |  |  |
|  |  | "5141486"   "5147290" |  |  |  |  |  |
|  |  | "5154716"   "5174894" |  |  |  |  |  |
|  |  | "5194145"   "5217426" |  |  |  |  |  |
|  |  | "5217427"   "5234403" |  |  |  |  |  |
|  |  | "5254248"   "5273517" |  |  |  |  |  |
|  |  | "5277701"   "5298016" |  |  |  |  |  |
|  |  | "5298171"   "5300060" |  |  |  |  |  |
|  |  | "5316540"   "5318511" |  |  |  |  |  |
|  |  | "5318512"   "5348533" |  |  |  |  |  |
|  |  | "5368542"   "5368555" |  |  |  |  |  |
|  |  | "5386734"   "5387174" |  |  |  |  |  |
|  |  | "5387187"   "5403272" |  |  |  |  |  |
|  |  | "5405308"   "5417650" |  |  |  |  |  |
|  |  | "5431814"   "5437598" |  |  |  |  |  |
|  |  | "5437624"   "5462667" |  |  |  |  |  |
|  |  | "5470483"   "5484396" |  |  |  |  |  |
|  |  | "5494592"   "5505685" |  |  |  |  |  |
|  |  | "5514070"   "5543062" |  |  |  |  |  |
|  |  | "5551941"   "5585007" |  |  |  |  |  |
|  |  | "5607579"   "5649903" |  |  |  |  |  |
|  |  | "5651766"   "5656163" |  |  |  |  |  |

|     |    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                      |    |     |     |                        |
|-----|----|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|----|-----|-----|------------------------|
|     |    | "5665061"   "5712798"<br>"5728060"   "5733253"<br>"5733446"   "5733545"<br>"5738792"   "5762791"<br>"5779660"   "5783085"<br>"5792351"   "5849203"<br>"5882289"   "5906589"<br>"5919125"   "5964724"<br>"5970432"   "5980760"<br>"6007725"   "6059979"<br>"6207063"   "6234989"<br>"6296602"   "6464624"<br>"6497676"   "6558307"<br>"6623443"   "6743192"<br>"7115205"   "7186231"<br>"7270645"   "7704454"<br>"8628489"   "8702637"<br>"8759094"   "9283316"<br>"10758652"  <br>"20010000185"  <br>"20010027156"  <br>"20020043492"  <br>"20020062100"  <br>"20020120227"  <br>"20030055375"  <br>"20030066807"  <br>"20030125881"  <br>"20030175150"  <br>"20040186409"  <br>"20050209522"  <br>"20050235733"  <br>"20060058167"  <br>"20060155236"  <br>"20070112289"  <br>"20080146993"  <br>"20120175313"  <br>"20140039373"  <br>"20140356851"  <br>"20180344910"  <br>"20180344921").pn.<br>AND (PGPB   USPT  <br>USOC).dbnm.<br>("20180344910").PN. |                                      |    |     |     |                        |
| L36 | 2  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L37 | 11 | ( (A61M1/029 and<br>A61M1/3672 and<br>A61M1/3693 and<br>A61M1/38 and<br>A61M2202/0415 and<br>A61M2230/207).CPC. )                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L38 | 11 | ( (A61M1/029 and<br>A61M1/3672 and<br>A61M1/3693 and<br>A61M1/38 and<br>A61M2202/0415).CPC.<br>)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/04/30<br>04:36 PM |

|     |       |                                                                                                                                                                           |                                             |    |     |     |                     |
|-----|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------|----|-----|-----|---------------------|
| L39 | 53    | ( ( A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415).CPC. )                                                                                                      | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L40 | 7     | "20120175313"                                                                                                                                                             | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L41 | 7     | "20030125881"                                                                                                                                                             | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L42 | 43    | 2009/0215602                                                                                                                                                              | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L43 | 13    | "20090215602"                                                                                                                                                             | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L44 | 2     | L1 AND ( (A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC. ) | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L45 | 12466 | ( (A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC. )        | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L46 | 2470  | L10 and hematocrit                                                                                                                                                        | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L47 | 7     | "I11" and (hematocrit with anticoagulant)                                                                                                                                 | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L48 | 6     | "I10" and (hematocrit with anticoagulant)                                                                                                                                 | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L49 | 16    | "I10" and (hematocrit same anticoagulant)                                                                                                                                 | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L50 | 59    | ((("RAGUSA") near3 ("Michael"))).INV.                                                                                                                                     | (US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT) | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L51 | 11    | "I15" and (hematocrit same anticoagulant)                                                                                                                                 | (US-PGPUB; USPAT; USOCR; DERWENT)           | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L52 | 183   | ("20010000185" "20020062100" "1025059" "1611725" "20010027156" "20020043492" "20020120227" "20030055375                                                                   | (US-PGPUB; USPAT)                           | OR | OFF | OFF | 2024/04/30 04:36 PM |

|  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  |  |  |  |
|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|
|  |  | " 20030066807" 2003<br>0125881" 2003017515<br>0" 20040186409" 200<br>50209522" 200502357<br>33" 20060058167" 20<br>060155236" 20070112<br>289" 20080146993" 2<br>0120175313" 2014003<br>9373" 20140356851" <br>20180344921" 208777<br>8" 2661150" 2750107"<br> 2792172" 3096283" <br>3145713" 3239136" 3<br>244362" 3244363" 34<br>09213" 3456875" 348<br>9145" 3565330" 3655<br>058" 3737096" 37748<br>40" 3987961" 400787<br>1" 4010894" 4014497"<br> 4040965" 4056224" <br>4082217" 4086924" 4<br>140268" 4142670" 41<br>51844" 4197847" 428<br>5464" 4300717" 4303<br>193" 4321921" 43878<br>48" 4425114" 443007<br>2" 4447221" 4457747"<br> 4464167" 4466888" <br>4482342" 4490135" 4<br>530691" 4534863" 46<br>43714" 4647279" 465<br>5742" 4680025" 4684<br>361" 4692136" 47087<br>12" 4713176" 473408<br>9" 4740202" 4740313"<br> 4755300" 4767396" <br>4795419" 4795448" 4<br>806247" 4806252" 48<br>08307" 4850995" 486<br>9812" 4871462" 4876<br>013" 4889524" 49118<br>33" 4934995" 494054<br>3" 4943273" 4968295"<br> 4983156" 4983158" <br>4985153" 4994188" 5<br>039401" 5045048" 50<br>98372" 5098373" 510<br>0372" 5100564" 5112<br>298" 5114396" 51356<br>67" 5141486" 514729<br>0" 5154716" 5174894"<br> 5194145" 5217426" <br>5217427" 5234403" 5<br>254248" 5273517" 52<br>77701" 5298016" 529<br>8171" 5300060" 5316<br>540" 5318511" 53185<br>12" 5348533" 536854 |  |  |  |  |
|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|

|     |     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                      |    |     |     |                        |
|-----|-----|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|----|-----|-----|------------------------|
|     |     | 2" 5368555" 5386734"<br> 5387174" 5387187" <br>5403272" 5405308" 5<br>417650" 5431814" 54<br>37598" 5437624" 546<br>2667" 5470483" 5484<br>396" 5494592" 55056<br>85" 5514070" 554306<br>2" 5551941" 5585007"<br> 5607579" 5649903" <br>5651766" 5656163" 5<br>665061" 5712798" 57<br>28060" 5733253" 573<br>3446" 5733545" 5738<br>792" 5762791" 57796<br>60" 5783085" 579235<br>1" 5849203" 5882289"<br> 5906589" 5919125" <br>5964724" 5970432" 5<br>980760" 6007725" 60<br>59979" 6207063" 623<br>4989" 6296602" 6464<br>624" 6497676" 65583<br>07" 6623443" 674319<br>2" 7115205" 7186231"<br> 7270645" 7704454" <br>8628489" 8702637" 8<br>759094").PN. |                                      |    |     |     |                        |
| L53 | 2   | ("20180344910").PN.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L54 | 11  | "I15" and (hematocrit<br>same anticoagulant)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L55 | 1   | ("10758652").PN.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | (USPAT; USOCR)                       | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L56 | 0   | ("20120175313").PN.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | (USPAT; USOCR)                       | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L57 | 5   | "20120175313"                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | (USPAT)                              | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L58 | 13  | ("4713176"   "6348156"<br>  "6875191"   "7011761"<br>  "7087177"   "7297272"<br>  "7708710"  <br>"8075468").PN. OR<br>("8852140").URPN.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | (US-PGPUB; USPAT;<br>USOCR)          | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L59 | 9   | L23 and prim\$3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | (US-PGPUB; USPAT;<br>USOCR)          | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L60 | 0   | (10/302682).APP.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | (USPAT; USOCR)                       | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L61 | 2   | "20140100507"                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | (USPAT; USOCR)                       | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L62 | 190 | A61M1/024.cpc.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/04/30<br>04:36 PM |
| L63 | 987 | G01n15/05.cpc.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | (US-PGPUB; USPAT;<br>USOCR; DERWENT) | OR | OFF | OFF | 2024/04/30<br>04:36 PM |



|     |     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                              |    |     |     |                     |
|-----|-----|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|----|-----|-----|---------------------|
| L64 | 220 | G01n2015/055.cpc.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | (US-PGPUB; USPAT; USOCR; DERWENT)                                                                                                            | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L65 | 3   | ((US-20030125881-A1).did. AND PGPB.dbnm.) OR ((US-10758652-B2 OR US-6348156-B1).did. AND USPT.dbnm.)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | (US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB) | OR | ON  | ON  | 2024/04/30 04:36 PM |
| L66 | 0   | L30 AND touchscreen                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | (US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB) | OR | ON  | ON  | 2024/04/30 04:36 PM |
| L67 | 0   | touchscreen WITH plasmapheresis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | (US-PGPUB; USPAT; USOCR; DERWENT)                                                                                                            | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L68 | 4   | touchscreen SAME plasmapheresis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | (US-PGPUB; USPAT; USOCR; DERWENT)                                                                                                            | OR | OFF | OFF | 2024/04/30 04:36 PM |
| L69 | 16  | "10980926"                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | (US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); EPO; JPO; DERWENT)                | OR | ON  | ON  | 2024/04/30 04:36 PM |
| L70 | 200 | ("1025059"   "1611725"   "2087778"   "2661150"   "2750107"   "2792172"   "3096283"   "3145713"   "3239136"   "3244362"   "3244363"   "3409213"   "3456875"   "3489145"   "3565330"   "3655058"   "3737096"   "3774840"   "3987961"   "4007871"   "4010894"   "4014497"   "4040965"   "4056224"   "4082217"   "4086924"   "4140268"   "4142670"   "4151844"   "4197847"   "4285464"   "4300717"   "4303193"   "4321921"   "4387848"   "4425114"   "4430072"   "4447221"   "4457747"   "4464167"   "4466888"   "4482342"   "4490135"   "4530691"   "4534863"   "4643714"   "4647279"   "4655742"   "4680025"   "4684361"   "4692136"   "4708712"   "4713176"   "4734089") | (US-PGPUB; USPAT; USOCR)                                                                                                                     | OR | ON  | ON  | 2024/04/30 04:36 PM |

|  |  |                       |  |  |  |  |  |
|--|--|-----------------------|--|--|--|--|--|
|  |  | "4740202"   "4740313" |  |  |  |  |  |
|  |  | "4755300"   "4767396" |  |  |  |  |  |
|  |  | "4795419"   "4795448" |  |  |  |  |  |
|  |  | "4806247"   "4806252" |  |  |  |  |  |
|  |  | "4808307"   "4850995" |  |  |  |  |  |
|  |  | "4869812"   "4871462" |  |  |  |  |  |
|  |  | "4876013"   "4889524" |  |  |  |  |  |
|  |  | "4911833"   "4934995" |  |  |  |  |  |
|  |  | "4940543"   "4943273" |  |  |  |  |  |
|  |  | "4968295"   "4983156" |  |  |  |  |  |
|  |  | "4983158"   "4985153" |  |  |  |  |  |
|  |  | "4994188"   "5039401" |  |  |  |  |  |
|  |  | "5045048"   "5098372" |  |  |  |  |  |
|  |  | "5098373"   "5100372" |  |  |  |  |  |
|  |  | "5100564"   "5112298" |  |  |  |  |  |
|  |  | "5114396"   "5135667" |  |  |  |  |  |
|  |  | "5141486"   "5147290" |  |  |  |  |  |
|  |  | "5154716"   "5174894" |  |  |  |  |  |
|  |  | "5194145"   "5217426" |  |  |  |  |  |
|  |  | "5217427"   "5234403" |  |  |  |  |  |
|  |  | "5254248"   "5273517" |  |  |  |  |  |
|  |  | "5277701"   "5298016" |  |  |  |  |  |
|  |  | "5298171"   "5300060" |  |  |  |  |  |
|  |  | "5316540"   "5318511" |  |  |  |  |  |
|  |  | "5318512"   "5348533" |  |  |  |  |  |
|  |  | "5368542"   "5368555" |  |  |  |  |  |
|  |  | "5386734"   "5387174" |  |  |  |  |  |
|  |  | "5387187"   "5403272" |  |  |  |  |  |
|  |  | "5405308"   "5417650" |  |  |  |  |  |
|  |  | "5431814"   "5437598" |  |  |  |  |  |
|  |  | "5437624"   "5462667" |  |  |  |  |  |
|  |  | "5470483"   "5484396" |  |  |  |  |  |
|  |  | "5494592"   "5505685" |  |  |  |  |  |
|  |  | "5514070"   "5543062" |  |  |  |  |  |
|  |  | "5551941"   "5585007" |  |  |  |  |  |
|  |  | "5607579"   "5649903" |  |  |  |  |  |
|  |  | "5651766"   "5656163" |  |  |  |  |  |
|  |  | "5665061"   "5712798" |  |  |  |  |  |
|  |  | "5728060"   "5733253" |  |  |  |  |  |
|  |  | "5733446"   "5733545" |  |  |  |  |  |
|  |  | "5738792"   "5762791" |  |  |  |  |  |
|  |  | "5779660"   "5783085" |  |  |  |  |  |
|  |  | "5792351"   "5849203" |  |  |  |  |  |
|  |  | "5882289"   "5906589" |  |  |  |  |  |
|  |  | "5919125"   "5964724" |  |  |  |  |  |
|  |  | "5970432"   "5980760" |  |  |  |  |  |
|  |  | "6007725"   "6059979" |  |  |  |  |  |
|  |  | "6207063"   "6234989" |  |  |  |  |  |
|  |  | "6296602"   "6464624" |  |  |  |  |  |
|  |  | "6497676"   "6558307" |  |  |  |  |  |
|  |  | "6623443"   "6743192" |  |  |  |  |  |
|  |  | "7115205"   "7186231" |  |  |  |  |  |
|  |  | "7270645"   "7704454" |  |  |  |  |  |
|  |  | "8628489"   "8702637" |  |  |  |  |  |
|  |  | "8759094"   "9283316" |  |  |  |  |  |
|  |  | "10758652"            |  |  |  |  |  |
|  |  | "20010000185"         |  |  |  |  |  |
|  |  | "20010027156"         |  |  |  |  |  |

|  |  |                                                                                                                                                                                                                                                                                                                                                                                                               |  |  |  |  |  |
|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|
|  |  | "20020043492"  <br>"20020062100"  <br>"20020120227"  <br>"20030055375"  <br>"20030066807"  <br>"20030125881"  <br>"20030175150"  <br>"20040186409"  <br>"20050209522"  <br>"20050235733"  <br>"20060058167"  <br>"20060155236"  <br>"20070112289"  <br>"20080146993"  <br>"20120175313"  <br>"20140039373"  <br>"20140356851"  <br>"20180344910"  <br>"20180344921").pn.<br>AND (PGPB   USPT  <br>USOC).dbnm. |  |  |  |  |  |
|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|

**PE2E SEARCH - Search History (Interference)**

There are no Interference searches to show.

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: March 22, 2021  
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Utility Application of:  
Michael Ragusa

Application No.: 17/205,400

Confirmation No.: N/A

Filed: March 18, 2021

Art Unit: 3781

For: SYSTEM AND METHOD FOR COLLECTING  
PLASMA

Examiner: Not Yet Assigned

**INFORMATION DISCLOSURE STATEMENT (IDS)**

MS Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 C.F.R. §§ 1.56, 1.97, and 1.98, the attention of the United States Patent and Trademark Office is hereby directed to the references listed on the attached PTO/SB/08. It is respectfully requested that the information be expressly considered during the prosecution of the above-identified application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

This Information Disclosure Statement is filed within three months of the U.S. filing date (37 C.F.R. § 1.97(b)(1)).

In accordance with 37 C.F.R. § 1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patents and U.S. patent applications.

In accordance with 37 C.F.R. § 1.98(d)(1) and as noted by a double-asterisk next to the Cite No. on the attached PTO/SB/08, the cited references are not supplied because they were previously

ME1 36057893v.1

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D/

Terumo v. Haemonetics - PGR2025-00077  
Petitioner Terumo Exhibit 1002-0136

Application No.: 17/205,400

Docket No.: 130670-80104

cited by or submitted to the Office in prior application numbers 16/931333 filed July 16, 2020, 15/793339 filed October 25, 2017, and 15/608183 filed May 30, 2017 and relied on in the above-identified application for an earlier effective filing date under 35 U.S.C. § 120.

The Examiner is advised that the following co-pending application contains subject matter that may be related to the present application:

| U.S. Application | Filing Date      | Publication No. / Patent No. | Status  | Atty. Docket No. |
|------------------|------------------|------------------------------|---------|------------------|
| 15/608,183       | May 30, 2017     | 10,758,652                   | Issued  | 130670-08002     |
| 16/866,078       | May 4, 2020      | 2020-0261630                 | Allowed | 130670-08005     |
| 17/205,374       | March 18, 2021   |                              | Pending | 130670-08006     |
| 15/793,339       | October 25, 2017 | 10,792,416                   | Issued  | 130670-80102     |
| 16/931,333       | July 16, 2020    | 2020-0345924                 | Allowed | 130670-80103     |

/LESLIE R DEAK/ (05/02/2024)

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed references.

Application No.: 17/205,400

Docket No.: 130670-80104

Applicant believes no fee is due with this response.

Dated: March 22, 2021

Respectfully submitted,  
Electronic signature: /Jonathan C. Lovely, Reg.  
No. 60,821/  
Jonathan C. Lovely  
Registration No.: 60,821  
MCCARTER & ENGLISH, LLP  
265 Franklin Street  
Boston, Massachusetts 02110  
(617) 449-6556  
(617) 607-9200 (Fax)  
Attorney/Agent For Applicant

Doc code: IDS

Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (01-22)

Approved for use through 05/31/2024. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

|                                                                                                     |                        |                  |
|-----------------------------------------------------------------------------------------------------|------------------------|------------------|
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | N/A              |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

| U.S. PATENTS                                                                                               |         |                                      |                            |                        |                                                 |                                                                          | Remove                                                                   |                |
|------------------------------------------------------------------------------------------------------------|---------|--------------------------------------|----------------------------|------------------------|-------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|----------------|
| Examiner Initial*                                                                                          | Cite No | Patent Number                        | Kind Code <sup>1</sup>     | Issue Date             | Name of Patentee or Applicant of cited Document | Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear |                                                                          |                |
|                                                                                                            | 1       | 8075468                              | B2                         | 2011-12-13             | Min et al.                                      |                                                                          |                                                                          |                |
| If you wish to add additional U.S. Patent citation information please click the Add button.                |         |                                      |                            |                        |                                                 |                                                                          | Add                                                                      |                |
| U.S. PATENT APPLICATION PUBLICATIONS                                                                       |         |                                      |                            |                        |                                                 |                                                                          | Remove                                                                   |                |
| Examiner Initial*                                                                                          | Cite No | Publication Number                   | Kind Code <sup>1</sup>     | Publication Date       | Name of Patentee or Applicant of cited Document | Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear |                                                                          |                |
|                                                                                                            | 1       | 20090215602                          | A1                         | 2009-08-27             | Min et al.                                      |                                                                          |                                                                          |                |
|                                                                                                            | 2       | 20230001059                          | A1                         | 2023-01-05             | Ragusa, Michael                                 |                                                                          |                                                                          |                |
| If you wish to add additional U.S. Published Application citation information please click the Add button. |         |                                      |                            |                        |                                                 |                                                                          | Add                                                                      |                |
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| Examiner Initial*                                                                                          | Cite No | Foreign Document Number <sup>3</sup> | Country Code <sup>2i</sup> | Kind Code <sup>4</sup> | Publication Date                                | Name of Patentee or Applicant of cited Document                          | Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear | T <sup>5</sup> |
|                                                                                                            | 1       |                                      |                            |                        |                                                 |                                                                          |                                                                          |                |
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|-----------------------------------------------------------------------------------------------------|------------------------|------------------|
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | N/A              |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

| Examiner Initials* | Cite No | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>5</sup> |
|--------------------|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|
|                    | 1       |                                                                                                                                                                                                                                                                 |                |

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|                    |  |                 |  |
|--------------------|--|-----------------|--|
| Examiner Signature |  | Date Considered |  |
|--------------------|--|-----------------|--|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> See Kind Codes of USPTO Patent Documents at [www.USPTO.GOV](http://www.USPTO.GOV) or MPEP 901.04. <sup>2</sup> Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>3</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>4</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>5</sup> Applicant is to place a check mark here if English language translation is attached.



|                                                                                                     |                        |                  |
|-----------------------------------------------------------------------------------------------------|------------------------|------------------|
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | N/A              |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

### CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

**OR**

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

### SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

|            |                                       |                     |            |
|------------|---------------------------------------|---------------------|------------|
| Signature  | /Jonathan C. Lovely, Reg. No. 60,821/ | Date (YYYY-MM-DD)   | 2023-01-17 |
| Name/Print | Jonathan C. Lovely                    | Registration Number | 60,821     |

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

## Privacy Act Statement

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The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
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I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: January 17, 2023  
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Utility Application of:  
Michael Ragusa

Application No.: 17/205,400

Confirmation No.: 4686

Filed: March 18, 2021

Art Unit: N/A

For: SYSTEM AND METHOD FOR COLLECTING  
PLASMA

Examiner: Not Yet Assigned

**INFORMATION DISCLOSURE STATEMENT (IDS)**

MS Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR 1.97, Applicant hereby makes of record the following additional documents. A PTO Form SB/08a and a full copy of each of the documents required under 37 CFR 1.98(a)(2) accompany this statement.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 C.F.R. § 1.97(b)(3)).

In accordance with 37 C.F.R. § 1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patents and U.S. patent applications.

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be

an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed references.

Applicant believes no fee is due with this response.

Dated: January 17, 2023

Respectfully submitted,  
Electronic signature: /Jonathan C. Lovely, Reg.  
No. 60,821/  
Jonathan C. Lovely  
Registration No.: 60,821  
MCCARTER & ENGLISH, LLP  
265 Franklin Street  
Boston, Massachusetts 02110  
(617) 449-6556  
(617) 607-9200 (Fax)  
Attorney/Agent For Applicant

| Electronic Acknowledgement Receipt   |                                         |
|--------------------------------------|-----------------------------------------|
| EFS ID:                              | 47377086                                |
| Application Number:                  | 17205400                                |
| International Application Number:    |                                         |
| Confirmation Number:                 | 4686                                    |
| Title of Invention:                  | SYSTEM AND METHOD FOR COLLECTING PLASMA |
| First Named Inventor/Applicant Name: | Michael Ragusa                          |
| Customer Number:                     | 86738                                   |
| Filer:                               | Jonathan Lovely                         |
| Filer Authorized By:                 |                                         |
| Attorney Docket Number:              | 130670-80104                            |
| Receipt Date:                        | 17-JAN-2023                             |
| Filing Date:                         | 18-MAR-2021                             |
| Time Stamp:                          | 11:58:41                                |
| Application Type:                    | Utility under 35 USC 111(a)             |

### Payment information:

|                        |    |
|------------------------|----|
| Submitted with Payment | no |
|------------------------|----|

### File Listing:

| Document Number | Document Description                               | File Name                                                        | File Size(Bytes)/<br>Message Digest                 | Multi Part /.zip | Pages (if appl.) |
|-----------------|----------------------------------------------------|------------------------------------------------------------------|-----------------------------------------------------|------------------|------------------|
| 1               | Information Disclosure Statement (IDS) Form (SB08) | 130670-80104_-_Information_Disclosure_Statement_Fillable_PDF.pdf | 1263200<br>aea70d91cbb87a642b34504556290d30e6b5f8b7 | no               | 4                |

### Warnings:

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                    |                                          |                                                       |    |   |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|------------------------------------------|-------------------------------------------------------|----|---|
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                    |                                          |                                                       |    |   |
| 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Transmittal Letter | Information_Disclosure_State<br>ment.pdf | 22280<br><br>4f17cd35fe971e424691bfd83301d2d1ac2d552b | no | 2 |
| <b>Warnings:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                    |                                          |                                                       |    |   |
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                    |                                          |                                                       |    |   |
| <b>Total Files Size (in bytes):</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                    |                                          | 1285480                                               |    |   |
| <p><b>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</b></p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b><br/> <b>If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</b></p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b><br/> <b>If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</b></p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b><br/> <b>If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</b></p> |                    |                                          |                                                       |    |   |

Doc code: IDS

Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (01-22)

Approved for use through 05/31/2024. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

|                                                                                                     |                        |                  |
|-----------------------------------------------------------------------------------------------------|------------------------|------------------|
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | N/A              |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

| U.S. PATENTS                                                                                               |         |                                      |                            |                        |                                                 |                                                                          | Remove                                                                   |                |
|------------------------------------------------------------------------------------------------------------|---------|--------------------------------------|----------------------------|------------------------|-------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|----------------|
| Examiner Initial*                                                                                          | Cite No | Patent Number                        | Kind Code <sup>1</sup>     | Issue Date             | Name of Patentee or Applicant of cited Document | Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear |                                                                          |                |
|                                                                                                            | 1       | 6200287                              | B1                         | 2001-03-13             | Keller et al.                                   |                                                                          |                                                                          |                |
| If you wish to add additional U.S. Patent citation information please click the Add button.                |         |                                      |                            |                        |                                                 |                                                                          | Add                                                                      |                |
| U.S. PATENT APPLICATION PUBLICATIONS                                                                       |         |                                      |                            |                        |                                                 |                                                                          | Remove                                                                   |                |
| Examiner Initial*                                                                                          | Cite No | Publication Number                   | Kind Code <sup>1</sup>     | Publication Date       | Name of Patentee or Applicant of cited Document | Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear |                                                                          |                |
|                                                                                                            | 1       | 20050131334                          | A1                         | 2005-06-16             | Langley et al.                                  |                                                                          |                                                                          |                |
|                                                                                                            | 2       | 20140100507                          | A1                         | 2014-04-10             | Flexman, Greg                                   |                                                                          |                                                                          |                |
| If you wish to add additional U.S. Published Application citation information please click the Add button. |         |                                      |                            |                        |                                                 |                                                                          | Add                                                                      |                |
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| Examiner Initial*                                                                                          | Cite No | Foreign Document Number <sup>3</sup> | Country Code <sup>2i</sup> | Kind Code <sup>4</sup> | Publication Date                                | Name of Patentee or Applicant of cited Document                          | Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear | T <sup>5</sup> |
|                                                                                                            | 1       | 103354755                            | CN                         | A                      | 2013-10-16                                      | Haemonetics Corp                                                         |                                                                          | ×              |
|                                                                                                            | 2       | 69434848                             | DE                         |                        | 2007-04-12                                      | Gambro Inc                                                               |                                                                          | ☒              |

|                                                                                                     |                        |                  |
|-----------------------------------------------------------------------------------------------------|------------------------|------------------|
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
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|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

|  |   |             |    |    |            |                            |                                     |
|--|---|-------------|----|----|------------|----------------------------|-------------------------------------|
|  | 3 | 2003-516175 | JP | A  | 2003-05-13 | Baxter International, Inc. | <input checked="" type="checkbox"/> |
|  | 4 | 2012/091720 | WO | A1 | 2012-07-05 | Haemonetics Corp           | <input type="checkbox"/>            |
|  | 5 | 2019/084278 | WO | A1 | 2019-05-02 | Haemonetics Corp           | <input type="checkbox"/>            |

If you wish to add additional Foreign Patent Document citation information please click the Add button

#### NON-PATENT LITERATURE DOCUMENTS

| Examiner Initials* | Cite No | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>5</sup> |
|--------------------|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|
|                    | 1       |                                                                                                                                                                                                                                                                 |                |

If you wish to add additional non-patent literature document citation information please click the Add button

#### EXAMINER SIGNATURE

|                    |  |                 |  |
|--------------------|--|-----------------|--|
| Examiner Signature |  | Date Considered |  |
|--------------------|--|-----------------|--|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> See Kind Codes of USPTO Patent Documents at [www.USPTO.GOV](http://www.USPTO.GOV) or MPEP 901.04. <sup>2</sup> Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>3</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>4</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>5</sup> Applicant is to place a check mark here if English language translation is attached.



|                                                                                                     |                        |                  |
|-----------------------------------------------------------------------------------------------------|------------------------|------------------|
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|            |                                       |                     |            |
|------------|---------------------------------------|---------------------|------------|
| Signature  | /Jonathan C. Lovely, Reg. No. 60,821/ | Date (YYYY-MM-DD)   | 2022-12-08 |
| Name/Print | Jonathan C. Lovely                    | Registration Number | 60,821     |

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I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: December 8, 2022  
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Utility Application of:  
Michael Ragusa

Application No.: 17/205,400

Confirmation No.: 4686

Filed: March 18, 2021

Art Unit: N/A

For: SYSTEM AND METHOD FOR COLLECTING  
PLASMA

Examiner: Not Yet Assigned

**INFORMATION DISCLOSURE STATEMENT (IDS)**

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Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

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Application No.: 17/205,400

Docket No.: 130670-80104

The Examiner is advised that the following applications contain subject matter that may be related to the present application:

| <b>U.S. Application</b> | <b>Filing Date</b> | <b>Publication No. / Patent No.</b> | <b>Status</b> | <b>Atty. Docket No.</b> |
|-------------------------|--------------------|-------------------------------------|---------------|-------------------------|
| 15/608,183              | May 30, 2017       | 10,758,652                          | Issued        | 130670-08002            |
| 16/866,078              | May 4, 2020        | 10,980,926                          | Issued        | 130670-08005            |
| 17/205,374              | March 18, 2021     | 2021-0205509                        | Published     | 130670-08006            |
| 17/943,410              | September 13, 2022 |                                     | Pending       | 130670-08007            |
| 15/793,339              | October 25, 2017   | 10,792,416                          | Issued        | 130670-80102            |
| 16/931,333              | July 16, 2020      | 10,980,934                          | Issued        | 130670-80103            |

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

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Applicant believes no fee is due with this response.

Dated: December 8, 2022

Respectfully submitted,  
Electronic signature: /Jonathan C. Lovely, Reg.  
No. 60,821/  
Jonathan C. Lovely  
Registration No.: 60,821  
MCCARTER & ENGLISH, LLP  
265 Franklin Street  
Boston, Massachusetts 02110  
(617) 449-6556  
(617) 607-9200 (Fax)  
Attorney/Agent For Applicant

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System and method for collecting platelets and anticipating plasma return

**Inventor(s):** PAGES ETIENNE ± (PAGES ETIENNE)**Applicant(s):** HAEMONETICS CORP ± (HAEMONETICS CORPORATION)

**Classification:** - international: A61M37/00  
 - cooperative: A61M1/0272 (EP); A61M1/3603 (EP); A61M1/3696 (EP); A61M1/38 (EP); A61M2202/0415 (EP); A61M2202/0427 (EP)

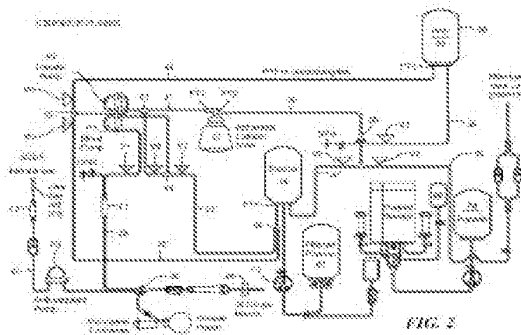
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Abstract of CN103354755 (A)

A blood processing system for collecting plasma reduced platelets and anticipating plasma return includes a venous access device, a blood component separation device, a first return line, a recirculation line, and a second return line. The venous access device draws whole blood from a subject and returns blood components to the subject using a first pump. The blood component separation device separates the drawn blood into a first blood component and a second blood component, and sends the first blood component to a first blood component bag. The first return line fluidly connects the venous-access device and the blood component separation device. The recirculation line connects the first blood component container and the separation device. The second return line fluidly connects the first blood component container and the first return line and is configured to return the first blood component within the first blood container to the subject.







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(71) 申请人 美国血液技术公司  
地址 美国马萨诸塞

(72) 发明人 E·帕热斯

(74) 专利代理机构 中国国际贸易促进委员会专  
利商标事务所 11038

代理人 焦丽雅

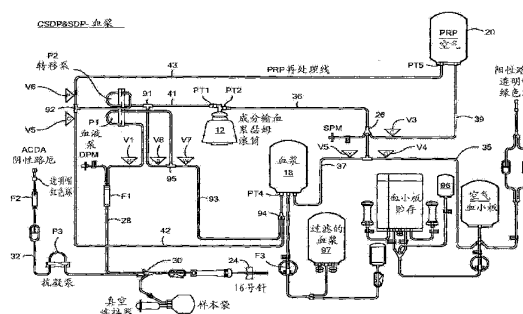
权利要求书4页 说明书9页 附图4页

### (54) 发明名称

用于收集血小板和预期血浆返回的系统和方法

### (57) 摘要

用于收集血浆减少的血小板并预期血浆返回的血液处理系统包括静脉接入装置、血液成分分离装置、第一返回线、再循环线和第二返回线。使用第一泵，静脉接入装置从受试者抽取全血并将血液成分返回至受试者。血液成分分离装置将抽取的血液分离成第一血液成分和第二血液成分，并且将第一血液成分传送至第一血液成分袋。第一返回线流体连接静脉接入装置和血液成分分离装置。再循环线连接第一血液成分容器和分离装置。第二返回线流体连接第一血液成分容器和第一返回线，并且构造成将第一血液容器内的第一血液成分返回至受试者。



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1. 一种用于收集血浆减少的血小板和预期血浆返回的方法,其包括:
  - a) 从供体抽取全血;
  - b) 将抗凝剂引入从供体抽取的全血中;
  - c) 将抗凝全血引入分离室中,分离室将抗凝全血分离成多种血液成分。
  - d) 将从抗凝全血分离出的血浆转移至血浆容器中;
  - e) 将来自血浆容器的第一体积的血浆返回至供体;
  - f) 重复步骤 a 至 d;
  - g) 从分离室中将富含血小板的血浆提取至富含血小板的血浆容器中;和
  - h) 将分离室内剩余的血液成分返回至供体。
2. 根据权利要求 1 的方法,进一步包括:
  - i) 重复步骤 a 至 c,以将分离装置部分填充抗凝全血;
  - j) 将来自富含血小板的血浆容器的富含血小板的血浆重新引入分离室中;
  - k) 将来自分离室的血浆转移至血浆容器中;和
  - l) 将重新引入的富含血小板的血浆再处理,以在分离装置内形成扩大的血小板层。
3. 根据权利要求 2 的方法,进一步包括:
  - m) 将来自血浆容器的血浆返回至供体,同时再处理富含血小板的血浆。
4. 根据权利要求 2 的方法,进一步包括:
  - m) 将来自血浆容器的血浆返回至供体,同时将富含血小板的血浆重新引入分离室中。
5. 根据权利要求 2 的方法,进一步包括:
  - m) 使用浪涌淘洗方法取出分离装置内的扩大的血小板层,使得将血小板转移至血小板容器中;和
  - n) 将分离室内剩余的血液成分返回至供体。
6. 根据权利要求 5 的方法,进一步包括在停歇时间过程中将来自血浆容器的血浆返回至供体。
7. 根据权利要求 1 的方法,进一步包括:

计算额外身体体积和血管内不足中的至少一个,并且步骤(e)过程中返回的血浆体积至少部分基于计算的额外身体体积或血管内不足。
8. 根据权利要求 1 的方法,其中从分离室提取富含血小板的血浆包括通过浪涌淘洗提取富含血小板的血浆。
9. 根据权利要求 8 的方法,其中通过浪涌淘洗从分离室提取富含血小板的血浆包括用血浆浪涌。
10. 一种用于收集血浆减少的血小板和预期血浆返回的系统,其包括:

使用第一泵从患者抽取第一体积的全血和将血液成分返回至患者的静脉接入装置;

用于将抽取的血液分离成第一血液成分和第二血液成分的血液成分分离装置,血液成分分离装置构造成将第一血液成分传送至第一血液成分袋和将第二血液成分传送至第二血液成分袋;

流体连接静脉接入装置和血液成分分离装置的第一返回线,用于将分离装置中剩余的血液成分返回至患者;

连接第一血液成分容器和分离装置的再循环线,其中通过再循环线和再循环泵将第一

血液成分容器内的第一血液成分重新引入分离室中 ;和

流体连接第一血液成分容器和第一返回线的第二返回线,并构造造成将第一血液容器内的第一血液成分返回至患者。

11. 根据权利要求 10 的系统,其中第一泵将第一血液成分容器内的第一血液成分返回至患者。

12. 根据权利要求 10 的系统,其中第一泵将分离装置中剩余的血液成分返回至患者。

13. 根据权利要求 10 的系统,其中分离装置是离心滚筒。

14. 根据权利要求 10 的系统,其中第一血液成分是血浆,而第二血液成分是血小板。

15. 根据权利要求 10 的系统,其中除了第一和第二血液成分外,分离装置将全血分离成第三种血液成分。

16. 根据权利要求 15 的系统,其中分离装置内剩余的血液成分包括第三种血液成分。

17. 根据权利要求 15 的系统,其中第三种血液成分是红细胞。

18. 根据权利要求 10 的系统,其中使用浪涌淘洗方法从分离装置中取出第二血液成分。

19. 根据权利要求 18 的系统,其中浪涌淘洗方法包括以递增的速率通过再循环线将第一血液成分重新引入血液成分分离装置中,直至从血液成分分离装置中取出第二血液成分。

20. 根据权利要求 10 的系统,进一步包括连接抗凝剂来源的抗凝剂线,抗凝剂线将抗凝剂引入抽取的血液中。

21. 根据权利要求 10 的系统,其中第二血液成分是血小板,并且在第二血液成分容器内收集预定量的血小板后,重新引入血液成分分离装置中,使得从分离装置提取血浆减少的血小板产品。

22. 根据权利要求 10 的系统,进一步包括流体连接第二血液成分袋和血液成分分离装置的重新引入线,其中从患者抽取第二体积的全血时,将第二血液成分袋内的第二血液成分重新引入血液成分分离装置中,由此在血液成分分离装置内形成扩大的第二血液成分层,使用浪涌淘洗方法从血液成分分离装置中取出扩大的第二血液成分层。

23. 根据权利要求 22 的系统,其中随着将第二血液成分重新引入血液成分分离装置中,将第一血液成分容器内的第一血液成分返回至患者。

24. 根据权利要求 10 的系统,其中在停歇时间过程中将第一血液成分容器内的第一血液成分返回至患者。

25. 根据权利要求 10 的系统,进一步包括控制器,控制器计算额外身体体积和血管内不足中的至少一个,至少部分基于计算的额外身体体积或血管内不足,系统通过第二返回线返回一定体积的第一血液成分。

26. 一种用于收集血浆减少的血小板和预期血浆返回的系统,其包括:

用于从患者抽取第一体积的全血并将血液成分返回至患者的装置,

用于将抽取的血液分离成第一血液成分和第二血液成分的血液成分分离装置,血液成分分离装置构造造成将第一血液成分传送至第一血液成分袋和将第二血液成分袋传送至第二血液成分袋;

流体连接用于抽取第一体积全血的装置和血液成分分离装置的第一返回装置,第一返

回装置构造成将分离装置内剩余的血液成分返回至患者，

连接第二血液成分容器和分离装置的再循环装置，其中再循环装置将第二血液成分容器内的第二血液成分重新引入分离装置中；和

流体连接第一血液成分容器和第一返回装置的第二返回装置，并且构造成将第一血液成分容器内的第一血液成分返回至患者。

27. 根据权利要求 26 的系统，其中用于抽取全血的装置包括第一泵，第一泵构造成将第一血液成分容器内的第一血液成分返回至受试者。

28. 根据权利要求 27 的系统，其中第一泵还构造成将分离装置中剩余的血液成分返回至受试者。

29. 根据权利要求 26 的系统，进一步包括用于控制流体通过系统的流动的控制器，控制器重复地将供体的全血抽取至分离装置中，从分离装置提取第一和第二血液成分，使用第二返回装置将第一血液成分容器内的第一血液成分返回至受试者，并且使用第一返回装置将分离装置内剩余的成分返回至受试者，其中在第二血液成分容器中获得预定体积的第二血液成分后，将来自第二血液成分容器的第二血液成分重新引入分离装置中。

30. 根据权利要求 29 的方法，其中控制器计算额外身体体积和血管内不足中的至少一个，使用第二返回装置返回的第一血液成分的量至少部分基于额外身体体积和血管内不足中的至少一个。

31. 根据权利要求 26 的系统，其中第一血液成分是血浆，而第二血液成分是血小板。

32. 根据权利要求 26 的系统，其中除了第一和第二血液成分外，分离装置将全血分离成第三种血液成分。

33. 根据权利要求 32 的系统，其中分离装置内剩余的血液成分包括第三种血液成分。

34. 根据权利要求 32 的系统，其中第三种血液成分是红细胞。

35. 根据权利要求 26 的系统，其中使用浪涌淘洗方法从分离装置中取出第二血液成分。

36. 根据权利要求 35 的系统，其中浪涌淘洗方法包括以递增的速率通过再循环装置将第一血液成分重新引入血液成分分离装置中，直至从血液成分分离装置中取出第二血液成分。

37. 根据权利要求 26 的系统，进一步包括用于将抗凝剂引入抽取的全血中的装置。

38. 根据权利要求 26 的系统，其中第二血液成分是血小板，并且在第二血液成分容器内收集预定量的血小板后，重新被引入血液成分分离装置中，使得从分离装置提取血浆减少的血小板产品。

39. 根据权利要求 26 的系统，进一步包括流体连接第二血液成分袋和血液成分分离装置的重新引入装置，其中从受试者抽取第二体积的全血时，将第二血液成分袋内的第二血液成分重新引入血液成分分离装置中，由此在血液成分分离装置内形成扩大的第二血液成分层，使用浪涌淘洗方法从血液成分分离装置中取出扩大的第二血液成分层。

40. 一种用于收集血浆减少的血小板和预期血浆返回的方法，其包括：

a) 从来源抽取全血；

b) 将抗凝剂引入从来源抽取的全血中；

c) 将抗凝全血引入分离室中，分离室将抗凝全血分离成多种血液成分。

- d) 将从抗凝全血分离出的血浆转移至血浆容器中；
- e) 将来自血浆容器的第一体积的血浆返回至来源；
- f) 重复步骤 a 至 d；
- g) 从分离室将富含血小板的血浆提取至富含血小板的血浆容器中；和
- h) 将分离室内剩余的血液成分返回至来源。

41. 根据权利要求 40 的方法,进一步包括：

- i) 重复步骤 a 至 c,以将分离装置部分填充抗凝全血；
- j) 将来自富含血小板的血浆容器的富含血小板的血浆重新引入分离室中；
- k) 将来自分离室的血浆转移至血浆容器中；和
- l) 将重新引入的富含血小板的血浆再处理,以在分离装置内形成扩大的血小板层。

42. 根据权利要求 41 的方法,进一步包括：

- m) 将来自血浆容器的血浆返回至来源,同时再处理富含血小板的血浆。

43. 根据权利要求 41 的方法,进一步包括：

- m) 将来自血浆容器的血浆返回至来源,同时将富含血小板的血浆重新引入分离室中。

44. 根据权利要求 41 的方法,进一步包括：

- m) 使用浪涌淘洗方法取出分离装置内的扩大的血小板层,使得将血小板转移至血小板容器中；和

- n) 将分离室内剩余的血液成分返回至来源。

45. 根据权利要求 44 的方法,进一步包括在停歇时间过程中将来自血浆容器的血浆返回至来源。

46. 根据权利要求 40 的方法,进一步包括：

计算额外身体体积和血管内不足中的至少一个,并且步骤(e)过程中返回的血浆体积至少部分基于计算的额外身体体积或血管内不足。

47. 根据权利要求 40 的方法,其中从分离室提取富含血小板的血浆包括通过浪涌淘洗提取富含血小板的血浆。

48. 根据权利要求 47 的方法,其中通过浪涌淘洗从分离室提取富含血小板的血浆包括用血浆浪涌。

49. 一种用于收集血浆减少的血小板的方法,其包括：

- a) 从来源抽取全血；
- b) 将抗凝剂引入从来源抽取的全血中；
- c) 将抗凝全血引入分离室中,分离室将抗凝全血分离成多种血液成分。
- d) 将从抗凝全血分离出的血浆转移至血浆容器中；
- e) 将来自血浆容器的第一体积的血浆返回至来源；
- f) 重复步骤 a 至 d；
- g) 从分离室将富含血小板的血浆提取至富含血小板的血浆容器中；和
- h) 取出分离室内剩余的血液成分。

## 用于收集血小板和预期血浆返回的系统和方法

### 技术领域

[0001] 本发明涉及用于血液处理和血液成分收集的系统和方法,并且特别涉及用于收集血小板和预期血浆返回的系统和方法。

### 背景技术

[0002] 成分输血是其中自临时从患者中取出的全血中分离和收集单独的血液成分的程序。通常,通过插入患者手臂静脉的针取出全血并放入细胞分离器中,如离心滚筒。一旦将全血分成其各种成分,可以从离心滚筒中取出一种或多种成分。将剩余的成分与任选的用来补足取出成分体积的代偿流体一起返回患者。取出和返回的过程持续至收集到一定量的所需成分,在这一点停止该过程。成分输血系统的重要特征是将处理过的但不需要的成分返回至供体。分离的血液成分可以包括,例如,高密度成分,如红细胞,中密度成分,如血小板或白细胞,和较低密度的成分,如血浆。

[0003] 在通过成分输血可观察到的各种血液成分产物中,对血浆减少的血小板的需求正快速增长。这特别是因为,随着癌症治疗的提高,需要将越来越多的血小板给药于造血功能降低的患者,但所述患者可能不需要输入用于悬浮血小板的血浆。血小板是位于骨髓中的称为巨核细胞的大细胞的碎片,并且主要通过执行凝集功能来促进止血。血小板在组织愈合中也起着作用。成人体的正常血小板计数为 150,000-400,000 个/mm<sup>3</sup>。低于 20,000 个/mm<sup>3</sup> 的血小板计数会引起各种问题,如自发性出血。

[0004] 血小板具有 4-6 天的短半衰期,并且供体的数量有限。因此,在生产血浆减少的血小板(plasma reduced platelet)产物中,重要的是以最大产量和所需的含量从供体提供的全血中收集血小板。此外,已知血浆减少的血小板产物受到白细胞的污染可能导致严重的中间并发症,如 GVH 反应。因此,将白细胞污染的水平保持尽可能的低,同时有效收集血小板也是非常重要的。为此,已经研发了各种技术。例如,使用“浪涌(surge)”技术,在收集全血并在离心机内离心分离成较高密度、中密度和较低密度成分并收集血浆(称为“抽取”步骤)后,通过离心以浪涌流速(例如,随着时间增加的流速)来提供血浆。通过进行浪涌,可以优先从中密度成分(其作为主要包含血小板和白细胞的混合物的血沉棕黄层存在)中转移出血小板,并以提高的产量生产血浆减少的血小板产物。

[0005] 替代使用浪涌技术,也可以通过层“推动(push)”从离心机提取出血小板层,其中将抗凝的全血引入滚筒中直至推出血小板层,或通过使用浪涌和推动方法的组合。收集所需的一种或多种成分后,将主要包含红细胞和柠檬酸盐化血浆的残余血液成分返回至供体(称为“返回”步骤)。

[0006] 如上所述,在许多血液成分输血程序和应用中,将不需要的成分(例如,未收集的成分)返回至供体。除了污染问题(例如,待返回至供体的污染、微粒等),必须考虑患者的舒适性。例如,将柠檬酸盐化血浆返回患者太快或一次返回太多柠檬酸盐化血浆给患者可能引起患者明显的不舒适性。此外,必须注意限制体外的流体体积(例如,额外身体体积)和/或体内流体的减少(例如,血管内不足)。

[0007] 发明概述

[0008] 根据本发明一个实施方案,提供了一种用于收集血浆减少的血小板和预期血浆返回的方法。首先从供体抽取全血,抗凝,并引入分离室中。分离室将抗凝的全血分离成各种血液成分。该方法然后将从抗凝全血分离的血浆转移至血浆容器中,并且将来自血浆容器的第一体积的血浆返回至供体。该方法然后重复抽取、抗凝、引入和转移步骤,以将分离装置填充其他抗凝全血。

[0009] 一旦将抗凝全血引入分离室中(例如,填充该室),该方法从分离室提取富含血小板的血浆(“PRP”)(例如,使用浪涌淘洗方法和/或用血浆浪涌)并放入 PRP 室中。该方法然后将分离室内剩余的血液成分返回至供体,并重复抽取、抗凝和引入步骤,直至分离室再次部分填充抗凝全血。一旦分离室部分填充,该方法然后将来自 PRP 容器的 PRP 再次引入分离室中,将来自分离室的血浆转移至血浆容器中,并且将重新引入的 PRP 再处理,以在分离装置内形成扩大的血小板层。

[0010] 根据一些实施方案,该方法可以预期血浆返回,并且将血浆容器内的血浆返回至供体,同时将 PRP 重新引入分离室和/或再处理 PRP。该方法然后再一次重复抽取、抗凝和引入步骤,以填充分离室,使用浪涌淘洗方法取出分离室内扩大的血小板层,使得将血小板转移至血小板容器中。该方法然后将分离室内剩余的血液成分返回至供体。

[0011] 根据相关的实施方案,该方法还可以在停歇时间(dead time)(目前的成分输血程序既没有抽取也没有将血液或血液成分返回至供体过程中的时间)过程中将血浆容器的血浆返回至供体。此外,该方法可以计算额外身体体积和/或血管内不足,并且返回至供体的血浆的第一体积可以基于,或至少部分基于计算的额外身体体积或血管内不足。

[0012] 根据本发明的另一个实施方案,用于收集血浆减少的血小板和预期血浆返回的系统包括静脉接入装置、血液成分分离装置、第一返回线、再循环线和第二返回线。静脉接入装置构造成使用第一泵从患者抽取第一体积的全血并将血液成分返回至患者。血液成分分离装置(例如,离心滚筒)将抽取的血液分离成第一血液成分(例如,血浆)和第二血液成分(例如,血小板),并且构造成将第一血液成分传送至第一血液成分袋以及将第二血液成分传送至第二血液成分袋。

[0013] 第一返回线流体连接静脉接入装置和血液成分分离装置,并且构造成将分离装置中剩余的血液成分返回至患者。再循环线连接第一血液成分容器和分离装置。第二返回线流体连接第一血液成分容器和第一返回线,并且构造成将第一血液容器内的第一血液成分返回至患者。还可以将第一血液成分容器内的第一血液成分通过再循环线和再循环泵重新引入分离室内。

[0014] 第一泵可以用于将第一血液成分容器内的第一血液成分和分离装置内剩余的血液成分返回至患者。除了第一和第二血液成分外,分离装置还可以将全血分离成第三种血液成分(例如,红细胞),并且分离装置中剩余的血液成分可以包括第三种血液成分。

[0015] 在一些实施方案中,可以使用浪涌淘洗方法从分离装置中取出第二血液成分。浪涌淘洗方法包括通过再循环线将第一血液成分以递增的速率重新引入血液成分分离装置中,直至第二血液成分从血液成分分离装置中取出。第二血液成分可以是血小板并且可以在第二血液成分容器内收集了预定量的血小板后重新引入血液成分分离装置中,使得从分离装置提取血浆减少的血小板产物。



[0016] 系统还可以包括抗凝剂线和重新引入线。抗凝剂线可以连接抗凝剂来源,并且可以将抗凝剂引入吸出的血液中。重新引入线可以流体连接第二血液成分袋和血液成分分离装置。当从患者抽出第二体积的全血在血液成分分离装置内形成扩大的第二血液成分层时,可以将第二血液成分袋内的第二血液成分重新引入血液成分分离装置中。

[0017] 随着将第二血液成分重新引入血液成分分离装置中和/或在停歇时间过程中,系统可以将第一血液成分返回至患者。系统还可以包括计算额外身体体积和血管内不足中的至少一种的控制器。系统然后可以通过第二返回线返回一定体积的第一血液成分,所述体积至少部分基于计算的额外身体体积或血管内不足。

[0018] 根据本发明再进一步的实施方案,用于收集血浆减少的血小板的系统可以包括(1)用于从患者抽取第一体积的全血并将血液成分返回至患者的装置,(2)用于将抽取的血液分离成第一血液成分和第二血液成分的血液成分分离装置,(3)流体连接用于抽取第一体积全血的装置和血液成分分离装置并用于将分离装置内剩余的血液成分返回至患者的第一返回装置,(4)连接第二血液成分容器和分离装置的再循环装置,和(5)流体连接第一血液成分容器和第一返回装置的第二返回装置。血液成分分离装置可以构造成将第一血液成分传送至第一血液成分袋以及将第二血液成分传送至第二血液成分袋。再循环装置可以将第二血液成分容器内的第二血液成分重新引入分离装置中。第二返回装置可以构造成将第一血液容器内的第一血液成分返回至患者。

[0019] 用于抽取全血的装置可以包括构造成将第一血液成分容器内的第一血液成分返回至患者的第一泵。第一泵还可以将分离装置中剩余的血液成分返回至患者。

[0020] 根据其他实施方案,系统还可以包括用于控制流体通过系统流动的控制器。控制器可以重复地将来自供体的全血抽取至分离装置中,从分离装置提取第一和第二血液成分,使用第二返回装置将第一血液成分返回至患者,并使用第一返回装置将分离装置中的剩余成分返回至患者。此外,在第二血液成分容器中获得预定体积的第二血液成分后,可以将来自第二血液成分容器的第二血液成分重新引入分离装置中。控制器还可以计算额外身体体积和/或血管内不足,并且使用第二返回装置返回的血浆含量可以(至少部分)基于额外身体体积和/或血管内不足。

[0021] 此外,系统还可以包括用于将抗凝剂引入抽取的全血中的装置,和流体连接第二血液成分袋和血液成分分离装置的再循环装置。当从患者抽出第二体积的全血以在血液成分分离装置内形成扩大的第二血液成分层时,可以将第二血液成分袋内的第二血液成分重新引入血液成分分离装置中。可以使用浪涌淘洗方法从血液成分分离装置中取出扩大的第二血液成分层。另外地或替换地,第二血液成分可以是血小板,并且在第二血液成分容器内收集预定量的血小板后,可以重新引入血液成分分离装置中,使得从分离装置提取血浆减少的血小板产物。

[0022] 根据其他实施方案,提供了用于收集血浆减少的血小板和预期血浆返回的方法。首先从来源抽取全血,抗凝,并引入分离室中。分离室将抗凝的全血分离成多种血液成分。然后该方法将从抗凝全血分离的血浆转移至血浆容器中,并且将第一体积的来自血浆容器的血浆返回至来源。该方法然后重复抽取、抗凝、引入和转移步骤,以将分离装置填充其他抗凝全血。

[0023] 一旦将抗凝全血引入分离室中(例如,填充该室),该方法从分离室提取富含血小

板的血浆(“PRP”) (例如,使用浪涌淘洗方法和 / 或用血浆浪涌) 并放入 PRP 室中。该方法然后将分离室内剩余的血液成分返回至来源,并重复抽取、抗凝和引入步骤,直至分离室再次部分填充抗凝全血。一旦分离室部分填充,该方法然后将来自 PRP 容器的 PRP 再次引入分离室中,将来自分离室的血浆转移至血浆容器中,并且将重新引入的 PRP 再处理,以在分离装置内形成扩大的血小板层。

[0024] 根据一些实施方案,该方法可以预期血浆返回,并且将血浆容器内的血浆返回至来源,同时将 PRP 重新引入分离室和 / 或再处理 PRP。该方法然后再一次重复抽取、抗凝和引入步骤,以充充分离室,使用浪涌淘洗方法取出分离装置内扩大的血小板层,使得将血小板转移至血小板容器中。该方法然后将分离室内剩余的血液成分返回至来源。

[0025] 根据相关的实施方案,该方法还可以在停歇时间过程中将血浆容器内的血浆返回至来源。此外,该方法可以计算额外身体体积和 / 或血管内不足,并且返回至来源的血浆的第一体积可以至少部分基于计算的额外身体体积或血管内不足。

[0026] 在再进一步的实施方案中,用于收集血浆减少的血小板的方法包括从来源抽取全血,并将抗凝剂引入从来源抽取的全血中,并且将抗凝的全血引入分离室中。分离室又可以将抗凝的全血分离成多种血液成分。该方法然后将从抗凝全血分离出的血浆转移至血浆容器中,将来自血浆容器的第一体积的血浆返回至来源,并且重复以上步骤。另外,该方法还可以从分离室提取富含血小板的血浆,并放入富含血小板的血浆容器中,并且从分离室取出剩余的血液成分。

[0027] 附图简述

[0028] 通过参考以下详述以及参考附图将更容易地理解本发明之前的特征,其中:

[0029] 图 1 是根据本发明一个实施方案的成分输血仪的示意图。

[0030] 图 2 是根据本发明一个实施方案,可以与图 1 的仪器一起使用的一次性系统的示意图。

[0031] 图 3 是根据本发明一个实施方案,可以与图 1 的仪器一起使用的离心滚筒的侧视图。

[0032] 图 4 是根据本发明一个实施方案,描绘了用于从供体收集血浆减少的血小板并预期血浆返回的方法的流程图。

[0033] 特定实施方案的详述

[0034] 参考图 1 和 2,成分输血设备 10 使用血液成分分离装置,如用于将抗凝的全血分离成其组成成分的标准 Latham 型离心机 11,如 US 专利 No. 3, 145, 713 中所述的,按引用并入并文中。可以使用其他类型的分离室和装置,如,但不限于,整体吹塑离心滚筒,如 U. S. 专利 No. 4, 983, 156 和 4, 943, 273 中所述的,按引用并入本文中。离心机 11 包括转筒 12 以及通常通过旋转封口 74 紧密结合滚筒内部的固定输入和输出口 PT1 和 PT2 (参见图 3)。当阀 11 打开时,离心机 11 的输入口 PT1 通过血液微聚集滤器 F1、管 28 和 Y- 接头 30 与静脉接入装置 24 (例如,放血针) 流体连通。在首先集合然后供应全血的情况中,静脉接入装置 24 可以由全血袋(未显示)替代。管 28 与血液具有相容性,设备 10 中的所有管道也是这样。离心机 11 的出口 PT2 通过管 36、阀 V2 和管 37 与悬挂在台秤 33 上的标记为血浆的第一容器 18 选择性地连接。标记为血小板的第二容器 20 通过管 36、阀 V3 和管 39 与出口 PT2 选择性地连接。此外,标记为血小板存储的第三个容器 22 通过管 36、阀 V4 和管 35 与

出口 PT2 选择性地连接。第二容器 20 和第三个容器 22 也可以分别通过台秤 67 和 77 来悬挂。如以下更详细的讨论,一些实施方案还可以包括管 93,一端与血浆容器 18 流体连接(通过接头 94),而另一端与管 41 流体连接(例如,通过接头 95)。管 93 可以用于将血浆容器 18 内的柠檬酸盐化血浆在停歇时间过程中返回至供体和 / 或同时处理离心机 11 内的全血。

[0035] 用于存储抗凝剂的袋或容器 16 通过细菌滤器 F2、管 32 和 Y- 接头 30 与静脉接入装置 / 放血针 24 流体连通。细菌滤器 F2 防止抗凝剂(ACD) 容器 16 中的任何细菌进入系统中。容器 16、18、20 和 22 优选是由血液相容材料制得的塑料袋。蠕动泵 P1、P2 和 P3,与阀 V1、V2、V3 和 V4 一起,响应由线路传感器 14、供体压力监控器(DPM) M1、系统压力监控器(SPM) M2 和空气检测器 D1、D2 和 D3 产生的信号而控制通过设备 10 流动的方向和持续时间。空气检测器 D1、D2 和 D3 检测流体的不存在或存在。压力监控器 M1 和 M2 监控设备 10 内的压力水平。线路传感器 14 是光学传感器并且检测从出口 PT2 通过线路传感器 14 的血液成分的存在。

[0036] 在最初的运行中,给泵 P1 和 P3 通电,给设备 10 的管 28 灌注来自容器 16 的抗凝剂。在到达空气检测器 D1 前,抗凝剂通过滤器 F2 和 Y- 接头 30。空气检测器 D1 感受到在 D1 存在抗凝剂并终止抗凝剂灌注运行。在灌注运行过程中,阀 V2 打开并且抗凝剂置换的滚筒中的无菌空气进入血浆容器 18 的顶部开口 PT3。然后将静脉接入装置 24 插入供体中并且准备开始进行抽取步骤。

[0037] 图 4 是根据本发明一个实施方案,描绘了用于从患者收集血液成分(例如,血小板)并预期将柠檬酸盐化血浆返回至患者的方法的流程图。在抽取步骤 401 过程中,从患者抽取全血,通常是以约 80ml/min 的速率,并且使用泵 P1 和 P3 与抗凝剂混合(步骤 402)(往回参考图 1-2)。泵 P3 将来自容器 16 的抗凝剂与从患者或集合袋抽取的全血混合。阀 V1 打开,在通过进口 PT1 泵入分离装置 12 中之前,使抗凝的全血通过管 28 和血液滤器 F1。

[0038] 将全血通过进料管(未显示)引入分离装置 12 的底部,图 4 的步骤 403。抗凝剂与全血的比例通常为约 1:10。可以在控制器(未显示)(其可以是,例如,微处理器)的控制下,根据所需的实验方案来进行成分输血设备 10 中的每个泵和阀的运行。

[0039] 参考图 3,离心机 11 具有固定的进口 PT1 和固定的出口 PT2。旋转封口 74 将固定的进口 PT1 流体连接滚筒 12 较低的内部部分,将出口 PT2 流体连接滚筒内部的较上部分,用于收集分离的级分。核心 72 占据与滚筒 12 内部同轴的体积并且在核心 72 的壁和外滚筒壁 70 之间提供分离区。

[0040] 随着滚筒 12 旋转,离心力将滚筒底部容纳的抗凝全血分离成红细胞(RBC)、白细胞(WBC)、血小板和血浆。滚筒 12 的转速可以选择,例如,在 4,000 至 6,000rpm 范围内,并且通常是 4,800rpm。根据成分密度,将血液分成不同的级分。将较高密度成分,即 RBC60,推动至滚筒 12 的外壁 70,而较低密度的血浆 66 位于核心 72 附近。在血浆 66 和 RBC60 之间形成血沉棕黄层 61。血沉棕黄层 61 由血小板内层 64、血小板和 WBC 的过渡层 68 和 WBC 外层 62 构成。血浆 66 是从分离区离出口最近的成分,并且随着其他抗凝全血通过进口 PT1 进入滚筒 12,血浆 66 是通过出口 PT2 从滚筒 12 转移出的第一流体成分。随着血浆 66 从滚筒 12 中转移出来,将其通过线 36 和 37 转移至血浆容器 18 (图 4 的步骤 404)。

[0041] 返回至图 1,转移出的血浆通过线传感器 14、管 36、3- 通 T- 接头 26 和阀 V2(在打开状态),并进入第一容器 18。通过泵 P2 将进入第一容器 18 中的血浆经由管 42、阀 V5(打

开状态)、Y- 接头 92 和管 40 自较低的开口 PT4 从容器 18 中抽取,并且经由 Y- 接头 91 和线 41 通过进口 PT1 再循环至滚筒 12 中。再循环的血浆稀释了进入滚筒 12 中的抗凝全血并且使血液成分更快分离。将光学传感器 21 应用于滚筒 12 的肩部,用于监控从滚筒 12 的外壁 70 逐渐且同轴地朝向核心 72 前进时的每层血液成分。光学传感器可以安置在能够检测到血沉棕黄层到达特定半径的位置,并且响应检测可以终止从供体 401 抽取全血并将全血引入滚筒 402 的步骤。

[0042] 如 1999 年 9 月 9 日提交的共同未决的发明名称为“用于生产血液制品的成分输血装置和方法”的 U. S. 专利申请 09/392,880 中所述的,可以响应至少一个与全血相关的特征,如全血的血细胞比容值、血小板数量、血液总量等,来改变滚筒 12 处理的全血量,按引用将该篇文献并入本文中。如之前所述的,这种变量控制可以在微计算机的控制下进行。或者,可以人工执行每一步。

[0043] 如上所述,本发明的一些实施方案将血浆容器内的血浆(例如,柠檬酸盐化血浆)在成分输血过程中以不同间隔返回,以预期血浆返回和避免在成分输血过程结束时返回大的体积(例如,为了提高患者舒适性)。为此,系统 10 可以暂停抽取步骤(步骤 401),并将血浆容器内含有的一些或全部血浆返回至供体。特别地,一旦暂停抽取步骤(步骤 401),成分输血系统 10 可以逆转抽取 / 返回泵 P1 的方向,打开阀 V6,通过出口 PT4 从血浆容器 18 抽取血浆,并通过线 93 和 28 将血浆返回至患者 / 供体。

[0044] 在该步骤过程中返回至患者 / 供体的血浆的体积可以取决于多个因素,包括,但不限于,额外身体体积(“ECV”)和 / 或血管内不足(“IVD”)。例如,控制器可以基于来自之前循环(例如,给定的成分输血程序中之前的循环或来自现有技术程序的循环)的数据计算 ECV 或 IVD,并且确定 ECV/IVD 是否超过了估算的总血液体积(“TBV”) (例如,从供体特征估算的,如性别、大小和重量)的预定百分比。如果系统 10 (例如,控制器 / 微处理器)确定 ECV/IVD 超出了 TBV 的预定百分比,那么系统 10 可以如上所述暂停抽取(例如,步骤 401)并且返回血浆。另外地或替换地,如果从目前的循环分离出的血浆体积等于为完成滚筒填充仍然要抽取的全血的体积,系统 10 可以启动血浆返回(步骤 405)。为了保持和 / 或提高血浆返回步骤(步骤 405)过程中的血液分离,离心机 11 可以继续旋转,并且通过滚筒 12 将血浆循环(例如,使用泵 P2 和线 42)。

[0045] 通过暂停抽取步骤(步骤 401)和启动预期的血浆返回步骤(步骤 405),系统 10 能够在很大程度上降低 ECV 和 IVD。此外,预期的血浆返回过程可以确保在多个步骤中以明显的时间间隔(例如,几分钟)来进行柠檬酸盐化血浆返回至患者 / 供体。如以上所讨论的,这有助于提高患者舒适性和降低将柠檬酸盐化血浆返回至患者 / 供体相关的风险。

[0046] 一旦完成血浆返回步骤,系统可以继续从患者 / 供体抽取全血(例如,为了完成滚筒填充)(步骤 406)并且从分离室 11/ 滚筒 12 提取血小板。从滚筒 12 提取血小板至容器中,图 4 的步骤 407。从滚筒 12 提取血小板时,可以使用各种方法,包括,但不限于,静止(dwelling)、浪涌和 / 或推动方法。为了说明的目的,现在将详细描述基于静止和浪涌技术的小血小板提取。

[0047] 将全血引入离心机 11 中后,图 4 的步骤 406,将阀 V1 关闭,并且将泵 P1 停止,使得不再从供体抽取血液,并且开始静止。在静止过程中,泵 P2 将血浆 66 以适当的速率(例如,约 100ml/min,在图 4 中)通过滚筒 12 再循环约 20 至 30 秒钟。在该流速下,通过血浆稀释

血沉棕黄层 61 并扩展,但血小板没有离开滚筒 12。血沉棕黄层的稀释使较重的白细胞沉淀至血沉棕黄层的外侧,导致较轻的血小板层 64 和较重的白细胞层 62 之间更好的分离。结果,减少了过渡层 68。静止阶段还可以稳定滚筒 12 中的流动模式,并且使得微泡有更多时间离开滚筒 12 并且被清除。

[0048] 静止后,开始浪涌步骤。在浪涌中,以 5-10ml/min 的增量提高泵 P2 的速度,以再循环血浆直至达到约 200-250ml/min 的血小板浪涌速度。血小板浪涌速度是血小板可以离开滚筒 12 但红细胞或白细胞没有离开的速度。离开滚筒的血浆变成含有血小板的浑浊物,并且线传感器 14 检测到这种浑浊。线传感器 14 由 LED 和光检测器组成,LED 发射通过正离开滚筒 12 的血液成分的光,而光检测器接受通过成分后的光。光检测器接受的光量与通过线的流体密度相关。

[0049] 当血小板首先开始离开滚筒 12 时,线传感器输出开始降低。打开阀 V3,并关闭阀 V2,将血小板收集在容器 20 中。一旦从滚筒中取出大部分的血小板,离开滚筒的流体变得不太浑浊。线传感器 14 检测到这种浑浊的降低,于是关闭阀 V3。

[0050] 重要的是注意到在任何“停歇”时间过程中(例如,没有从患者/供体抽取全血过程中的时间,离心机 11 停止过程中的任何时间等),系统 10 可以将血浆袋 18 内所含的血浆返回至患者/供体。例如,当系统 10 从离心滚筒 12 中取出/提取出血小板时和/或在上述的静止过程中,系统 10 也可以以上述的相似方式将容器 18 内所含的血浆返回至患者/供体(例如,通过逆转泵 P1 并通过线 93 抽取血浆)。

[0051] 如果在浪涌过程中发生了血浆返回(例如,血浆通过滚筒 12 的再循环),抽取/返回泵 P1 和再循环泵 P2 都可以从血浆容器 18 抽取血浆,并且阀 V5 和 V7 都打开。抽取/返回泵 P1 可以通过管 93 抽取血浆,而再循环泵 P2 可以通过管 42 抽取血浆。为了防止分开的血浆流混合以及彼此干扰,位于接头 91 和 95 之间的阀 V8 (图 2) 可以关闭。

[0052] 收集血小板后,启动返回步骤 409 (参见图 4)。在返回步骤 409 过程中,停止滚筒 12 的旋转,并且通过逆转泵 P1 的旋转,阀 V1 打开,经由静脉接入装置 24 将滚筒 12 中的剩余血液成分返回至供体。还将阀 V2 打开,使空气在返回过程中进入离心滚筒中。来自容器 18 的血浆稀释了滚筒 12 中剩余的血液成分。即,随着阀 V2 打开,泵 P2 将血浆与滚筒 12 中剩余的成分混合,用血浆稀释正返回的红细胞成分加快了返回时间。当滚筒中剩余的血液成分返回至供体时,停止返回步骤 409。

[0053] 参照图 4,重复从供体抽取全血(步骤 401)、将抗凝剂引入全血(步骤 402)、将全血引入分离室(步骤 403)、将血浆转移至血浆容器 18(步骤 404)、将血浆返回患者/供体(步骤 405)、继续全血抽取(步骤 406)、从分离室提取血小板(步骤 407)、返回血浆(步骤 408)和将剩余成分返回供体(步骤 409)的步骤,直至在容器 20 中获得所需体积的血小板,步骤 410。通常,将步骤 401-409 重复两次至四次,每个循环处理约 450-500ml 全血。所获得的血小板浓度通常为约  $1.5 \times 10^6 / \mu\text{L}$ 。

[0054] 然后通过将容器 20 中的血小板(富含血小板的血浆)重新引入滚筒 12 中,图 4 的步骤 412,系统可以再处理容器 20 中的血小板。重新引入血小板形成了比只处理一个循环的抗凝全血获得的大几倍的血小板层。例如,在一些实施方案中,血小板层体积大致等于乘以循环加一获得的血小板数的一个循环的平均体积。通过泵 P2,经由管 43、阀 V6 (打开位置)、Y-接头 92 和管 40 从容器 20 的开口 PT5 抽取血小板,并通过进口 PT1 经由 Y-接头

91 和线 41 输入滚筒 12 中。为了最小化血小板和滚筒 12 之间的接触,在重新引入血小板之前,滚筒 12 可以部分地填充从通体 401 抽取的抗凝全血,图 4 的步骤 411。全血在滚筒 12 外围形成细胞床,作为滚筒外围与血小板之间的缓冲剂,降低血小板凝集。另外地或替换地,可以在血小板重新引入过程中将抗凝全血加入分离室中,使得血小板层朝向淘洗半径,或在血小板重新引入后,用于完成血小板分离和标准化启动血小板提取的条件。

[0055] 值得注意的是,如果重新引入滚筒 12 中并且再处理的血小板是富含血小板的血浆(“PRP”)形式(血小板悬浮于血浆内),那么滚筒 12 内的离心力将导致 PRP 丢弃悬浮的血小板,由此除去血浆。这种游离的血浆将从滚筒 12 排出,并传送至血浆容器 18,作为附加的流体(例如,附加的 PRP、血浆、抗凝全血等)进入滚筒 12。

[0056] 随着血小板再处理形成血浆减少的血小板产品(以下将更详细讨论),系统 10 可以再一次地将容器 18 内的血浆返回至患者/供体(步骤 413)。例如,随着将容器 20 的血小板重新引入滚筒 12 中,系统 10 可以打开阀 V7,并使用抽取/返回泵 P1,通过线 93 从容器 18 的开口 PT4 抽取血浆,并通过线 28 和静脉接入装置 24 将血浆返回至患者/供体。系统 10 然后可以从患者/供体抽取全血,并将滚筒 12 填充抗凝全血,步骤 414。

[0057] 例如,使用浪涌或推动方法,然后从目前停留在滚筒 12 中的血小板层提取出血浆减少的血小板浓缩物,图 4 的步骤 415。通过线传感器 14、管 36、3-通 Y-接头 26 和阀 V4 (打开状态),将血浆减少的血小板产品传送至容器 22 中。血小板产品浓度通常为  $2.6 \times 10^6/\mu\text{L}$  至  $5.2 \times 10^6/\mu\text{L}$ ,其是只进行一个抗凝全血循环时获得的血小板的 2-3 倍。一旦从滚筒 12 中提取出血浆减少的血小板浓缩物并收集在容器 22 中,系统 10 然后可以返回滚筒 12 内剩余的任何血液成分和血浆容器 18 内的任何仍然剩余的血浆,参见图 4 的步骤 416。

[0058] 应当注意浪涌淘洗技术可以使用血浆以外的各种流体,从分离室提取血小板和/或减少血浆的血小板产品(例如,可以使用盐溶液)。此外,重新引入分离室的血小板可以重新抗凝来防止血小板凝固和/或凝集。例如,血小板收集袋 20 或减少血浆的血小板产品袋 22 可以预先装载一定量的抗凝剂,使得从分离室抽取出来时,血小板和/或减少血浆的血小板产品与抗凝剂混合。另外地或替换地,可以在从患者抽取全血时,加入足量的抗凝剂,使得在再处理之前,血小板中仍然存在足够的抗凝剂。在任一种情况中,必须相对于患者的安全性来称重全血和/或提取的血小板中添加的抗凝剂含量。特别地,应当限制抗凝剂的含量,以防止大量抗凝剂返回至患者。

[0059] 还应当注意一旦收集到血小板或减少血浆的血小板产品,可以加入血小板防腐剂溶液来帮助防腐和存储血小板,用于之后的使用。可以在收集后(例如,从分离袋或存储容器 96)将防腐剂溶液加入血小板和血小板产品中,或血小板收集袋 20 和减少血浆的血小板产品袋 22 可以预先装载添加剂溶液。

[0060] 通过预期将返回至供体的血浆总量以及在多个步骤中返回血浆,本发明的各个实施方案能够提供优于现有技术的多个优点。例如,通过不是在程序结束时返回全部血浆,本发明的各个实施方案能够很大程度上降低与返回大体积的柠檬酸盐化血浆相关的患者的不适性和风险。此外,通过在“停歇”时间过程中返回血浆,本发明的一些实施方案能够减少总的程序时间,以及程序过程中任何给定时间的 ECV/IVD。此外,因为可以在处理过程中返回血浆并且显著降低了 EVC/IVD,本发明的各个实施方案不需要将盐水(或其他代偿流体)返回至患者来降低 ECV。

[0061] 尽管上述的实施方案讨论了将血浆返回至患者 / 供体,但不需要返回全部血浆。例如,本发明的一些实施方案可以保留一部分收集的血浆。在这样的实施方案中,可以使用 F3 过滤血浆并存储在滤过的血浆容器 97 内。

[0062] 如果需要另外的减少血浆的血小板产品,现在可以重复上述的每一个步骤,直至收集到所需量的血浆减少的血小板产品。在各个实施方案中,可以将血浆加入血浆减少的血小板产品中,以将血浆减少的产品调节至预定的体积或浓度。

[0063] 尽管按照从患者 / 供体抽取全血并将不需要的成分返回至供体来描述了以上的实施方案,但本发明的其他实施方案可以用于无供体处理。例如,如上所述,在其中首先集合全血然后提供给分离装置 11 的情况中,静脉接入装置 24 可以由全血袋(未显示)替代。在这样的实施方案中,来自血浆容器 18 的血浆和分离装置 11 中剩余的血液成分可以返回至一个或多个存储袋 / 容器(例如,全部返回至一个容器中或返回至分开的容器中)或返回至全血袋中。这样的实施方案将仍然具有优于现有技术系统的优点,因为很大程度上减少了处理时间(例如,因为在停歇时间过程中将血浆传送至容器,等)。

[0064] 所述的本发明的实施方案仅仅是示例性的并且各种改变和变化将是本领域技术人员显而易见的。确定所有这样的改变和变化在本发明的范围内。

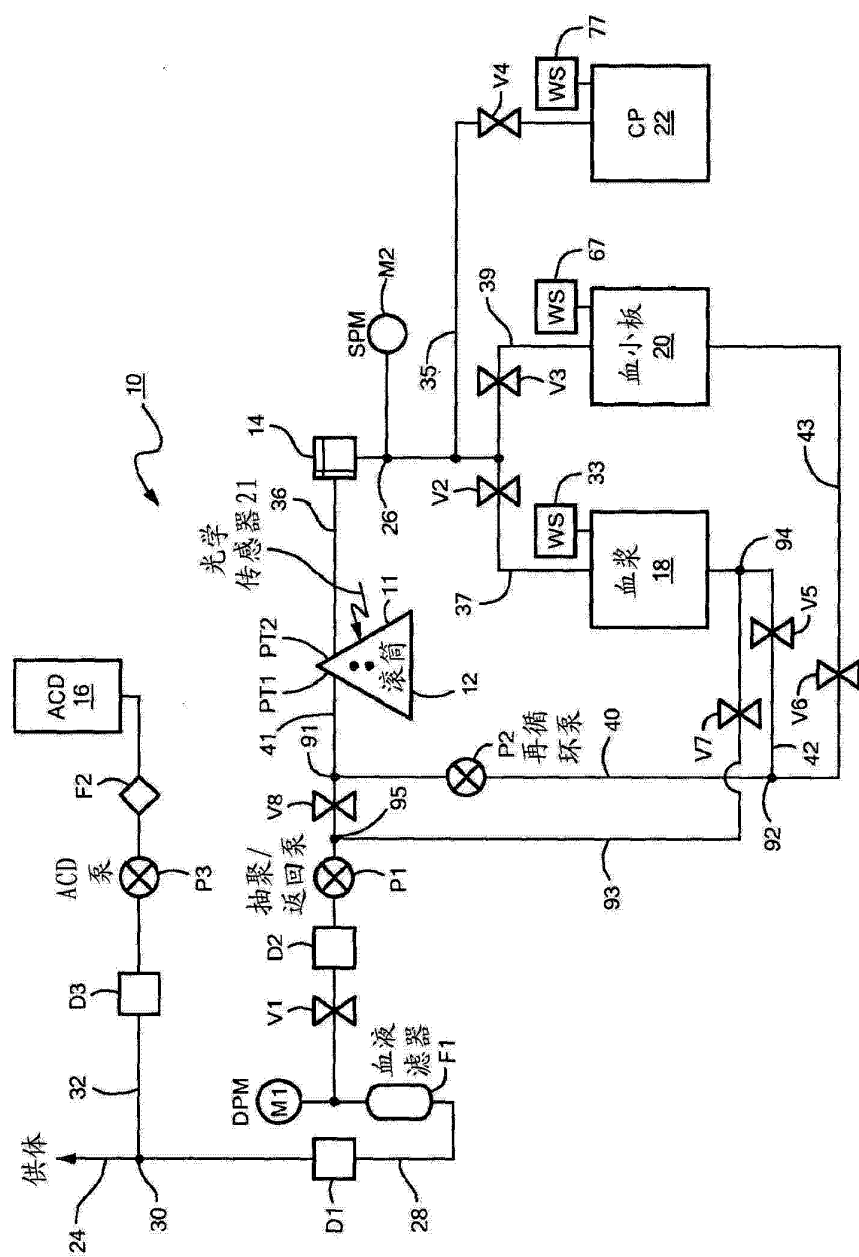


图 1



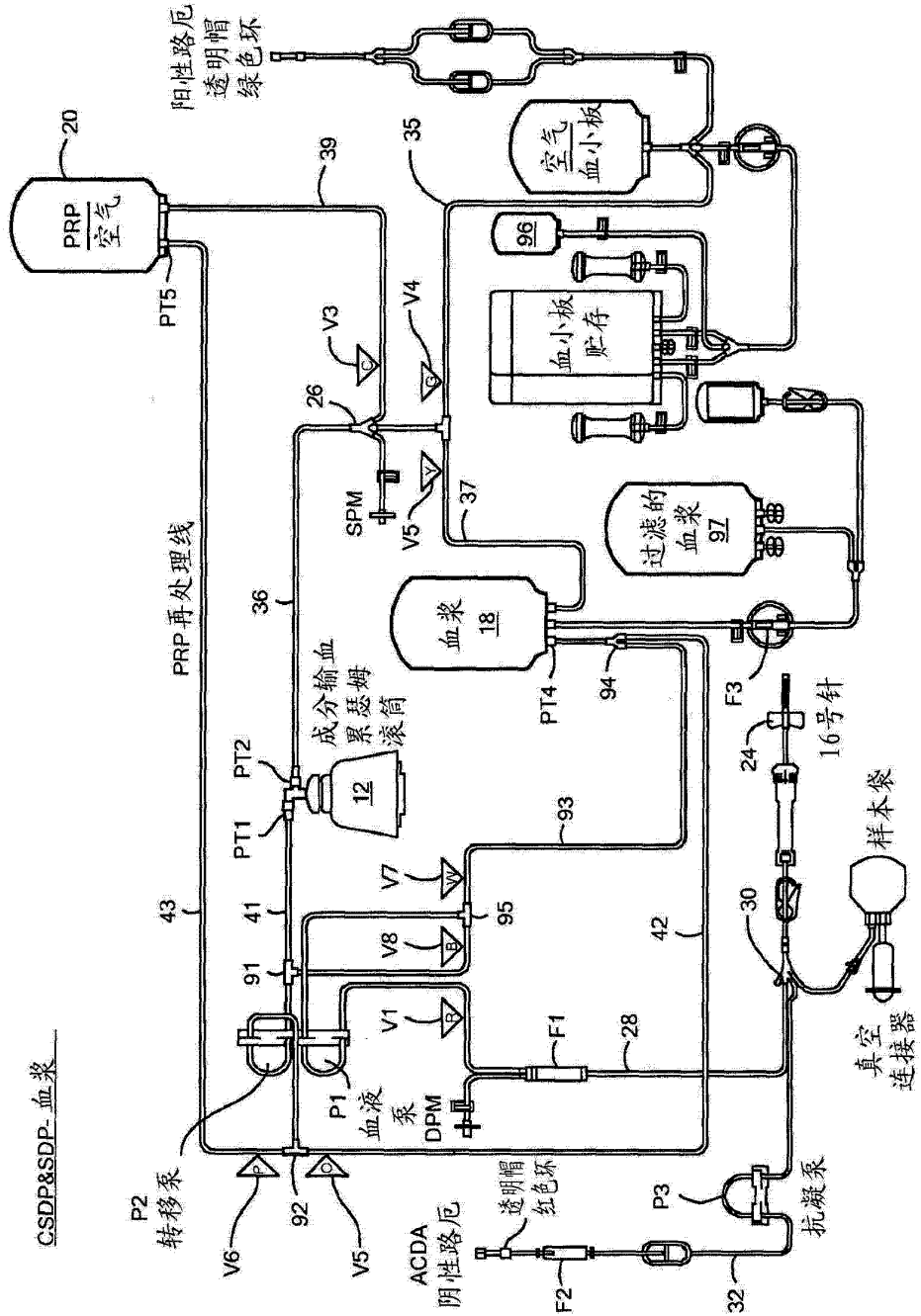


图 2

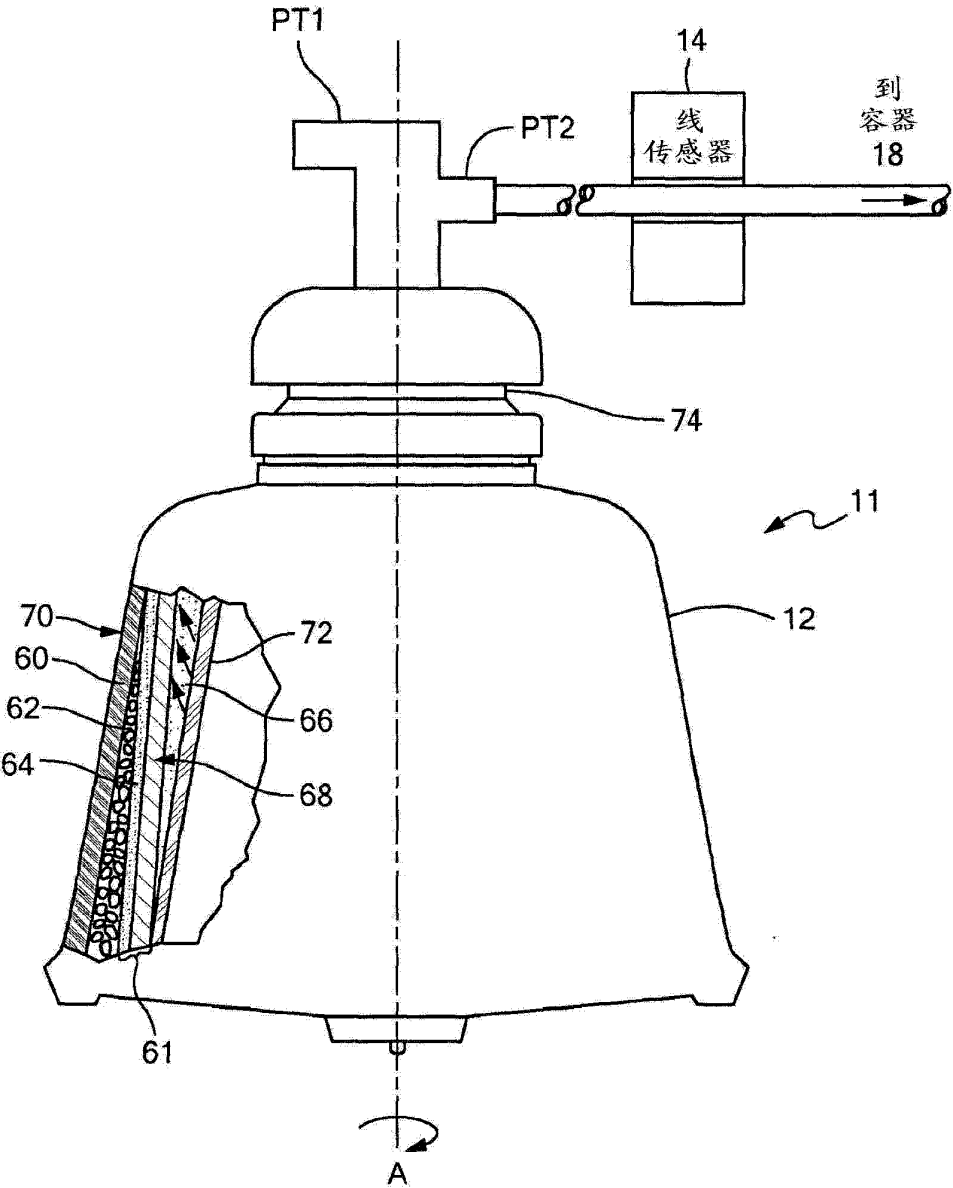


图 3

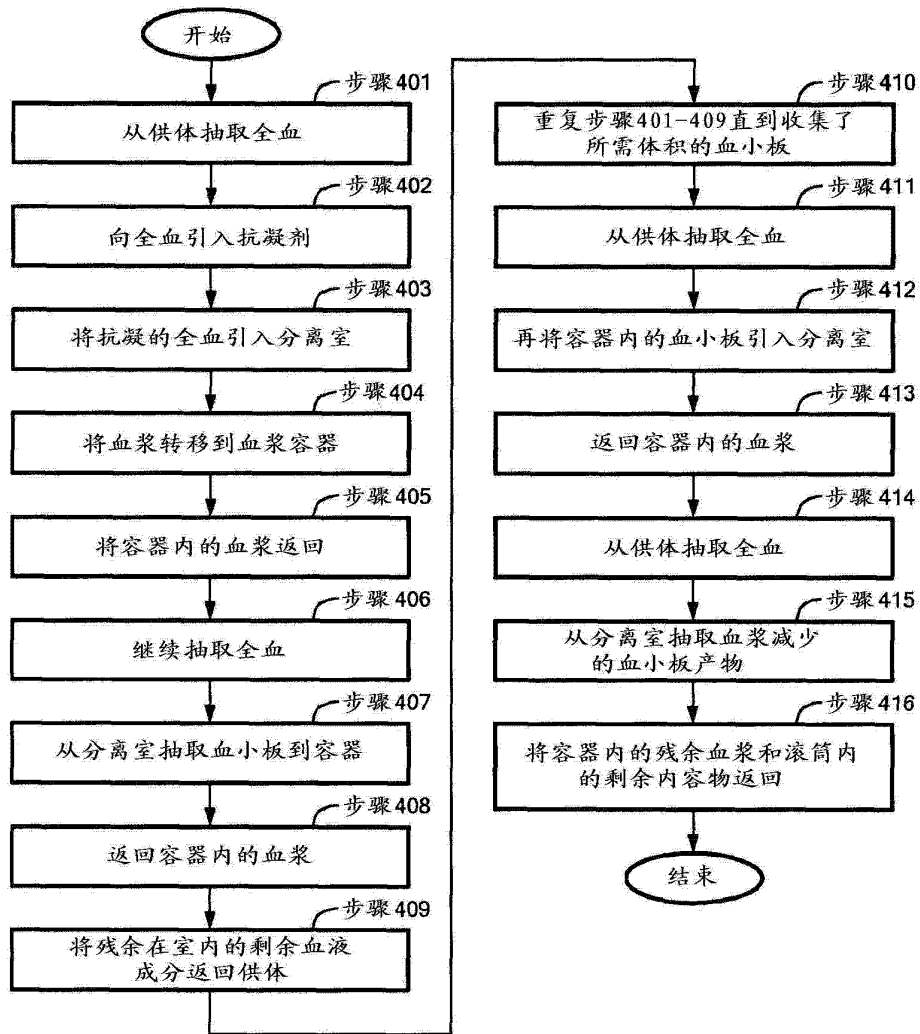


图 4



Espacenet

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## Optimized blood component collection system

**Inventor(s):** LANGLEY ROBERT W [US]; KELLER JOHN J [US]; URDAHL STEVEN GAGE [US] ± (LANGLEY, ROBERT W, ; KELLER, JOHN J, ; URDAHL, STEVEN GAGE)

**Applicant(s):** GAMBRO INC [US] ± (GAMBRO INC)

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**Application number:** DE1994634848T 19941021

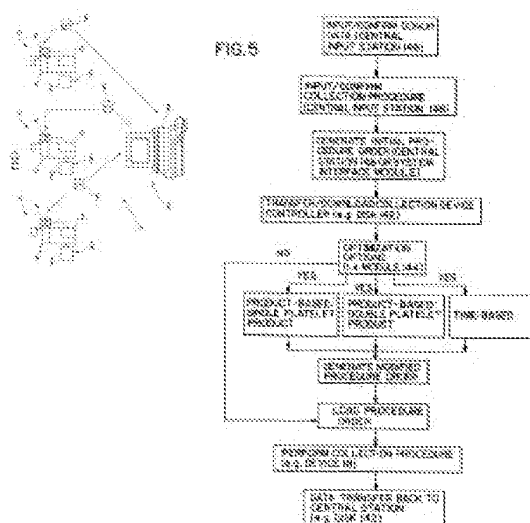
**Priority number(s):** US19930140254 19931021

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Abstract not available for DE69434848 (T2)

Abstract of corresponding document: EP0654277 (A1)

A blood component collection system with optimization capabilities. In one embodiment, process parameters are derived from an input/configured predetermined blood component yield and which is based upon the maximization of at least one process parameter. Thereafter, the blood component collection procedure is performed with these derived process control parameters. In another embodiment, process parameters are derived from an input total procedure time from a maximized value for at least one of the other process control parameters so as to maximize blood component yield in this fixed time. Thereafter, the blood component collection procedure is performed with these derived parameters.





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(73) Patentinhaber:

**Gambro Inc., Lakewood, Col., US**

(72) Erfinder:

**Langley, Robert W., Westminster, Colorado 80030, US; Keller, John J., Northglenn Colorado 80241, US; Urdahl, Steven Gage, Golden, Colorado 80401, US**

(74) Vertreter:

**Schwabe, Sandmair, Marx, 81677 München**

(54) Bezeichnung: **Optimiertes System zur Sammlung von Blutkomponenten mit Optimierer**

Anmerkung: Innerhalb von neun Monaten nach der Bekanntmachung des Hinweises auf die Erteilung des europäischen Patents kann jedermann beim Europäischen Patentamt gegen das erteilte europäische Patent Einspruch einlegen. Der Einspruch ist schriftlich einzureichen und zu begründen. Er gilt erst als eingelegt, wenn die Einspruchsgebühr entrichtet worden ist (Art. 99 (1) Europäisches Patentübereinkommen).

Die Übersetzung ist gemäß Artikel II § 3 Abs. 1 IntPatÜG 1991 vom Patentinhaber eingereicht worden. Sie wurde vom Deutschen Patent- und Markenamt inhaltlich nicht geprüft.

## Beschreibung

### Gebiet der Erfindung

**[0001]** Die vorliegende Erfindung betrifft allgemein das Gebiet der Blutkomponenten-Sammelsysteme und insbesondere das Bereitstellen von Organisationsmöglichkeiten durch das Aufnehmen von Optimierungsprinzipien in derartige Systeme.

### Hintergrund der Erfindung

**[0002]** Die Verwendung von Blut, das Spendern abgenommen und Empfängern infundiert wird, ist für den Zweck der Behandlung von medizinischen Notfällen und unter anderen Umständen wohlbekannt. In letzter Zeit wurden ausgewählte Blutkomponenten für die spätere Infusion bei Empfängern, die eine Blutkomponententherapie benötigen, aus Blut getrennt und gesammelt. Die primären Blutkomponenten enthalten Blutplättchen, rote Blutkörperchen, weiße Blutkörperchen und Plasma.

**[0003]** Um Blutkomponenten zu sammeln, wird einem Spender durch eine Nadelbaueinheit oder durch eine andere Blutzugangsvorrichtung Blut abgenommen, das anschließend unter Verwendung von Zentrifugieren oder anderen geeigneten Trennungstechniken verarbeitet wird, um die gewünschten Komponenten zu isolieren und zu sammeln. Diese Prozedur wird am wirkungsvollsten in einem Online-Prozess ausgeführt, bei dem einem Spender Blut abgenommen, über einen extrakorporalen Einwegkreis verarbeitet, um die gewünschten Komponenten zu erhalten, und anschließend an den Spender zurückgegeben wird. Ein Blutkomponenten-Sammelsystem, das für diesen Typ der Blutkomponenten-Sammelprozedur vorgesehen ist, ist COBE Spectra™, das von dem Anmelder der vorliegenden Anmeldung kommerziell zur Verfügung steht.

**[0004]** Der Ausstoß einer bestimmten Sammlung von Blutkomponenten ist ein wesentlicher Faktor. In den Vereinigten Staaten muss z. B. gegenwärtig ein Ausstoß einer Sammlung von Blutkomponenten zugeordnet sein, damit es sich um ein nutzbares Blutkomponenten-Produkt handelt. Wie in EP-A-0 580 299 offenbart ist, erfüllt COBE Spectra™ gegenwärtig diese Forderung, indem bestimmte biologische Daten des Spenders, wie etwa Größe, Gewicht, Geschlecht und Hämatokritwert, im Voraus konfigurierte, von der Bedienperson eingegebene Daten, wie etwa die Gesamtprozedurdauer, und systembezogene Daten, wie etwa der Typ der Sammelprozedur (z. B. Einnadel- oder Zweinadelprozedur) und die Sammeleffizienz, verarbeitet werden, um bestimmte Prozessparameter, wie etwa die Einlassströmung in das COBE Spectra™ (eine kombinierte Strömung des Vollbluts vom Spender, üblicherweise zuzüglich einer Strömung von Antikoagulans) sowie einen vorhergesagten Blutkomponenten Ausstoß, zu erzeugen.

**[0005]** Eine zusätzliche Betrachtung, die den Blutkomponenten-Ausstoß in den Vereinigten Staaten gegenwärtig betrifft, ist, dass er die Produktklassifizierung bestimmt. In Bezug auf Blutplättchen wird gegenwärtig ein Einfach-Blutplättchen-Produkt als eine Sammlung von  $3 \cdot 10^{11}$  Blutplättchen betrachtet und ein Doppel-Blutplättchen-Produkt als eine Sammlung von  $6 \cdot 10^{11}$  Blutplättchen betrachtet. Wenn die Sammlung im Bereich zwischen  $3 \cdot 10^{11}$  und  $6 \cdot 10^{11}$  Blutplättchen liegt, wird sie trotzdem als ein Einfach-Blutplättchen-Produkt betrachtet. Diese Klassifizierung als ein Einfach- oder Doppel-Blutplättchen-Produkt ist für Blutkomponenten-Sammeleinrichtungen (z. B. Blutbanken/Blutzentren) relevant, da ein Doppel-Blutplättchen-Produkt einen höheren Verkaufspreis hat als ein Einfach-Blutplättchen-Produkt und außerdem üblicherweise einer größeren Anzahl von Patienten nützt. Der Ausstoß einer bestimmten Sammlung von Blutkomponenten kann außerdem eine relevante Betrachtung für bestimmte therapeutische Behandlungen sein.

**[0006]** Weitere wichtige Betrachtungen in Bezug auf Blutkomponenten-Sammelsysteme betreffen den Spender. Blutkomponenten-Sammeleinrichtungen erfahren z. B. nicht nur einen Anstieg der Gesamtforderung nach Blutkomponenten, sondern die Forderung schwankt nun üblicherweise ebenso zwischen den Blutkomponententypen. Darüber hinaus ist nicht nur der Zustrom von Spendern in vielen Fällen leider unzureichend, sondern Spender-Zeitbeschränkungen werden immer vorherrschender. Ferner kann der von einem Spender erreichbare Ausstoß zwischen den Blutkomponenten variieren (d. h. ein Spender kann eine bessere Quelle für Blutplättchen als eine Quelle für rote Blutkörperchen sein).

**[0007]** Auf der Grundlage des Vorhergehenden wird die Organisation der verschiedenen Aspekte von Blutkomponenten-Sammelsystemen immer wichtiger.

## Zusammenfassung der Erfindung

**[0008]** Die vorliegende Erfindung ist in den unabhängigen Ansprüchen definiert und betrifft in einer Anwendung ein Blutkomponenten-Sammelsystem, das Organisationsmöglichkeiten bereitstellt, indem Optimierungsprinzipien aufgenommen werden.

**[0009]** Im Allgemeinen und in diesem Fall verwendet die vorliegende Erfindung Prinzipien zur Optimierung in Bezug auf den Spender, das Blutkomponenten-Sammelsystem und/oder das gewünschte Blutkomponentenprodukt. Die vorliegende Erfindung kann z. B. so angepasst werden, dass sie für die Sammlung einer vorgegebenen Menge wenigstens einer vorgegebenen Blutkomponente (oder typischer für die Sammlung derartiger Blutkomponenten in einem bestimmten Bereich) in einer "minimalen" Zeitdauer und/oder für die Sammlung einer "maximalen" Menge wenigstens einer vorgegebenen Blutkomponente in einer festen Zeitdauer jeweils auf der Grundlage bestimmter Prozessbedingungen dient. Die vorliegende Erfindung kann darüber hinaus in der Weise angepasst werden, dass sie der Blutkomponenten-Bestandssteuerung dient, indem sie anhand der Blutkomponentenforderung und/oder anhand des vorhandenen Bestandes auf der Spenderauswahl und/oder auf der Sammlungsprozedurauswahl in Bezug auf den zu sammelnden Blutkomponententyp basiert. Außerdem kann die vorliegende Erfindung in der Weise angepasst werden, dass sie eine weitere Spenderorganisation schafft, indem der Blutkomponententyp bzw. die Blutkomponententypen von dem Spender gesammelt werden, der einen maximalen Ausstoß erzielt.

**[0010]** Die vorliegende Erfindung kann in einem Aspekt als ein Blutkomponenten-Sammelsystem charakterisiert werden, das optimierungsartige Möglichkeiten auf der Grundlage von Blutkomponentenprodukten besitzt. Eine Ausführungsform umfasst ein Verfahren zum Sammeln von wenigstens einer vorgegebenen Blutkomponente (z. B. zur Sammlung von Blutplättchen, roten Blutkörperchen) aus einer Quelle des Vollbluts unter Verwendung eines Blutkomponenten-Sammelsystems, das eine Blutkomponenten-Sammelvorrichtung enthält und eine Sammelprozedur verwendet. Im Einzelnen wird ein gewünschter Ausstoß der vorgegebenen Blutkomponente bzw. der vorgegebenen Blutkomponenten festgelegt (wobei ein derartiger Ausstoß einen einzelnen Ausstoß oder einen Bereich von Ausstößen enthält), wobei für das Blutkomponenten-Sammelsystem biologische Daten bezüglich der Quelle bereitgestellt werden. Darüber hinaus wird jedem der verschiedenen Prozessparameter, die in der Sammelprozedur verwendet werden, ein Wert oder eine Größe zugeordnet. Die Größe von wenigstens einem dieser Prozessparameter wird aus den biologischen Daten und aus dem gewünschten Ausstoß abgeleitet. Diese Größen, die alle Größen von Prozessparametern enthalten, die aus dem gewünschten Ausstoß abgeleitet sind, werden in das Blutkomponenten-Sammelsystem eingegeben. Anschließend wird die Sammelprozedur mit der Blutkomponenten-Sammelvorrichtung und mit den eingegebenen Prozessparametern ausgeführt, um den gewünschten Ausstoß der wenigstens einen vorgegebenen Blutkomponente bzw. Blutkomponenten aus der Vollblutquelle zu sammeln.

**[0011]** Die vorliegende Erfindung kann in einem weiteren Aspekt als ein Blutkomponenten-Sammelsystem mit zeitbasierten optimierungsähnlichen Möglichkeiten charakterisiert werden. Eine Ausführungsform davon ist ein Verfahren zum Sammeln von wenigstens einer vorgegebenen Blutkomponente von einer Quelle des Vollbluts unter Verwendung eines Blutkomponenten-Sammelsystems, das eine Blutkomponenten-Sammelvorrichtung enthält und eine Sammelprozedur verwendet. Eine Strömung des Vollbluts von der Quelle sowie eine Strömung von Antikoagulans werden an das Blutkomponenten-Sammelsystem geliefert und bilden gemeinsam eine Einlassströmung. In dem Verfahren wird (z. B. anhand der zeitlichen Verfügbarkeit des Spenders) eine Gesamtprozedurdauer für die Sammelprozedur festgelegt. Von dieser festgelegten Gesamtprozedurdauer wird wenigstens eine mögliche Einlassströmung für das System abgeleitet. Es wird eine weitere mögliche Einlassströmung für das System abgeleitet, die eine "optimale" Sammeleffizienz schafft und effektiv der Spitzenwert einer glockenförmigen Ausstoß-/Einlassströmungskurve (d. h. die Einlassströmung, die den maximalen Blutkomponentenausstoß erzeugt) ist. Demzufolge wird dann, wenn die Einlassströmung auf der Grundlage der Gesamtprozedurzeit größer als die Einlassströmung auf der Grundlage des maximalen Ausstoßes ist und somit eine Einlassströmung auf dem Abschnitt der Ausstoß-/Einlassströmungskurve mit abfallenden Anstieg ist, die Einlassströmungsgröße auf der Grundlage des maximalen Ausstoßes bei dem Verhalten der Sammelprozedur verwendet. Wenn dagegen die Einlassströmung auf der Grundlage der Gesamtprozedurzeit kleiner als die Einlassströmung auf der Grundlage des maximalen Ausstoßes ist und somit eine Einlassströmung auf dem Abschnitt der Ausstoß-/Einlassströmungskurve mit ansteigendem Anstieg ist, wird die Einlassströmung auf der Grundlage der Gesamtprozedurzeit bei dem Verhalten der Sammelprozedur verwendet.

**[0012]** Die vorliegende Erfindung schafft eine größere Effizienz bei der Blutkomponentensammlung und -organisation. Die vorliegende Erfindung kann z. B. verwendet werden, um Komponentenbestände von Blutbanken/Blutzentren mit geplanten Bedarfsangaben zu vergleichen und die Sammelprozeduren so einzustellen,



dass sie diese Bedarfsangaben erfüllen. Die vorliegende Erfindung schafft des Weiteren Vorteile für Spender. Im Einzelnen können bestimmte Informationen bezüglich der physischen und medizinischen Charakteristiken des Spenders in dem System gespeichert werden und bei späteren Besuchen durch den Spender verwendet werden, um Größen für die verschiedenen Prozesssteuerungsparameter abzuleiten. Für einen Spender mit einer Antikoagulans-Unverträglichkeit kann z. B. die Größe der Antikoagulans-Infusionsrate in der Weise eingestellt werden, dass sie die Verträglichkeitsgrenze des Spenders nicht übersteigt.

#### Kurzbeschreibung der Zeichnung

**[0013]** Fig. 1 ist eine schematische Darstellung eines Blutkomponenten-Sammelsystems gemäß den Prinzipien der vorliegenden Erfindung;

**[0014]** Fig. 2 ist eine schematische Darstellung einer Ausführungsform einer Blutkomponenten-Trennbauereinheit, die eine Zweinadelkonfiguration verwendet und in dem Blutkomponenten-Sammelsystems von Fig. 1 enthalten sein kann;

**[0015]** Fig. 3 ist eine schematische Darstellung einer Ausführungsform einer Blutkomponenten-Trennbauereinheit, die eine Einnadelkonfiguration verwendet und in dem Blutkomponenten-Sammelsystems von Fig. 1 enthalten sein kann;

**[0016]** Fig. 4a und 4b sind eine perspektivische Ansicht bzw. eine Draufsicht eines Typs eines Einwegverarbeitungskanals, der in der Blutkomponenten-Sammelvorrichtung der Fig. 2 und Fig. 3 verwendet wird;

**[0017]** Fig. 5 ist ein Ablaufplan einer Blutkomponenten-Sammelprozedur, bei der Prinzipien der vorliegenden Erfindung genutzt werden;

**[0018]** Fig. 6 ist ein Ablaufplan eines Optimierungsmodells zum Ableiten von wenigstens einem optimalen Prozessparameter aus einem gewünschten Blutkomponentenausstoß oder aus einer Gesamtprozedurdauer gemäß den Prinzipien der vorliegenden Erfindung;

**[0019]** Fig. 7 ist ein Ablaufplan eines Optimierungsmodells zum Ableiten von wenigstens einem optimalen Prozessparameter aus einem gewünschten Blutkomponentenausstoß oder aus einer Gesamtprozedurdauer gemäß den Prinzipien der vorliegenden Erfindung; und

**[0020]** Fig. 8 ist eine Ausstoß-/Einlassströmungskurve.

#### Ausführliche Beschreibung

**[0021]** Die vorliegende Erfindung wird unter Bezugnahme auf die beigelegte Zeichnung beschrieben, die bei der Veranschaulichung ihrer vorhandenen Merkmale unterstützt. Eine Anwendung der vorliegenden Erfindung ist in einem Blutkomponenten-Sammelsystem realisiert, das wenigstens einen Blutkomponententyp (z. B. Blutplättchen, rote Blutkörperchen, weiße Blutkörperchen, Plasma) aus einer Quelle des Vollbluts (z. B. von einem Spender) unter Nutzung einer Sammelprozedur, die aus einer üblicherweise in der Einrichtung konfigurierten/von der Bedienperson eingegebenen Aufgabe (Aufgaben) und der "Maximierung" wenigstens eines Prozesssteuerungsparameters abgeleitet wird, trennt, entfernt und sammelt. Dieser Typ der Ableitung wird in dieser Beschreibung als ein "Optimierungsprozess" bezeichnet und die abgeleiteten Prozesssteuerungsparameter werden in dieser Beschreibung als "optimale Werte" bezeichnet.

**[0022]** In Fig. 1 ist die vorliegende Erfindung in dem Blutkomponenten-Sammelsystem **2** ausgeführt, das üblicherweise in einer Blutbank/einem Blutzentrum (nicht gezeigt) realisiert ist. Das System **2** enthält eine Optimierungsbauereinheit **140** (z. B. einen/mehrere geeignete Mikroprozessoren, wie etwa einen IBM-kompatiblen PC und Software) und wenigstens eine Blutkomponenten-Sammelbauereinheit **10** (wobei drei gezeigt sind), die jeweils eine Blutkomponenten-Sammelvorrichtung **18** als einen integralen Bestandteil hiervon enthält. Wie im Folgenden erläutert wird, sind die Optimierungsbauereinheit **140** (oder wenigstens ein Abschnitt hiervon) und zugeordnete Blutkomponenten-Sammelbauereinheiten **10** vorzugsweise in geeigneter Weise miteinander verbunden, können jedoch ebenso vollständig getrennt sein. Das heißt, die Optimierungsprozeduren gemäß den Prinzipien der vorliegenden Erfindung sind nicht darauf beschränkt, dass sie an einer bestimmten Stelle ausgeführt werden.

**[0023]** Die Optimierungsbauereinheit **140** enthält im Allgemeinen eine zentrale Eingabestation **148** (z. B. einen

geeigneten Mikroprozessor, wie etwa einen IBM-kompatiblen PC und zugeordnete Software) zum Eingeben und Halten von spenderbezogenen Daten und üblicherweise außerdem zum Vorbereiten eines Anfangsprozedurauftrags (der Prozesssteuerungsparameter, die aus den spenderbezogenen Daten und anderen Betrachtungen abgeleitet werden) für einen bestimmten Spender. Diese Prozeduren können außerdem in dem geeigneten Bedienperson-Schnittstellenmodul **16** ausgeführt werden, so dass keine zentrale Eingabestation **148** erforderlich ist. Wenn jedoch eine zentrale Eingabestation **148** verwendet wird, werden diese spenderbezogenen Daten und/oder der Anfangsprozedurauftrag an eines der Bedienperson-Schnittstellenmodule **16** übertragen (z. B. an einen geeigneten Mikroprozessor, wie etwa an einen IBM-kompatiblen Mikroprozessor, der über eine RS232- oder über eine andere spezielle Laborschnittstelle mit der Vorrichtung **18** verbunden ist, einschließlich einer Vorrichtung PCP **30** der Digital Equipment Corp., die auch als der DEC-PC 325SL bekannt ist und einen 386-er Prozessor verwendet), die sich bei jeder Blutkomponenten-Sammelvorrichtung **18** befinden und die vorzugsweise, wie angegeben wurde, mit einem Optimierungsmodul **144** (einem Teil der Optimierungsbauereinheit **140**) verbunden sind, um die Bedienperson mit einer oder mehreren Optimierungsmöglichkeiten zu versorgen. Diese Optimierungsmöglichkeiten liefern anhand einer oder mehrerer festgelegter Bedingungen/Aufgaben (z. B. des eingegebenen Blutkomponentenausstoßes, der eingegebenen Prozedurdauer) und einer bestimmten Abweichung für die Prozesssteuerungsparameter eine andere Gruppe von Prozesssteuerungsparametern als der Anfangsprozedurauftrag. Wenn eine Optimierungsmöglichkeit ausgewählt wird, wird der Prozedurauftrag in der Weise modifiziert, dass er die Ergebnisse der Optimierung widerspiegelt, wird die Sammelprozedur mit den Ergebnissen der Optimierung initialisiert/neu initialisiert (d. h. wird die Sammelprozedur im Fall einer Optimierung, die ausgeführt wird, nachdem die Sammelprozedur initialisiert wurde, neu initialisiert, weshalb sie als eine nachgeschaltete Optimierung bezeichnet wird) und wird anschließend die Sammelprozedur mit der Blutkomponenten-Sammelvorrichtung **18** ausgeführt.

**[0024]** Verschiedene Ausführungsformen der Blutkomponenten-Sammelbaueinheiten können die Prinzipien der vorliegenden Erfindung enthalten. Wie oben erwähnt wurde, ist jedoch festgestellt worden, dass Online-Techniken verhältnismäßig wirkungsvoll sind, so dass die vorliegende Erfindung unter Bezugnahme auf derartige Techniken beschrieben wird. Eine Ausführungsform einer Online-Technik und der zugeordneten Vorrichtungen, die in dem Blutkomponenten-Sammelsystem **2** von Fig. 1 enthalten sein können, ist in Fig. 2 dargestellt. Die Blutkomponenten-Sammelbaueinheit **10'** verwendet eine Online-Technik dahingehend, dass ein Spender **14** (z. B. die Vollblutquelle) durch eine Fluidverbindung mit der Blutkomponenten-Sammelvorrichtung **18** direkt in das System **10'** eingebunden ist. Diese spezielle Online-Technik wird genauer als eine Zweinadelkonfiguration bezeichnet, da zwei Fluidverbindungen zwischen dem Spender **14** und der Blutkomponenten-Sammelvorrichtung **18** vorhanden sind.

**[0025]** Der Spender **14** steht mit der Blutkomponenten-Sammelvorrichtung **18** durch eine Einlassleitung **22** und eine (nicht gezeigte) geeignete Nadelbaueinheit in einer Fluidverbindung. Somit wird der Blutkomponenten-Sammelvorrichtung **18** unter Verwendung einer Einlasspumpe **26** (z. B. einer Peristaltikpumpe), um diese Strömung auf Wunsch/bei Bedarf aufrechtzuerhalten, über die Einlassleitung **22** ununterbrochen Vollblut von dem Spender **14** für eine Trennung der gewünschten Blutkomponenten) hiervon zugeführt. Bevor das Blut des Spenders **14** in die Blutkomponenten-Sammelvorrichtung **18** eintritt, kann dem Vollblut unter Verwendung einer AC-Pumpe **32** (z. B. einer Peristaltikpumpe) ein Antikoagulans aus einem Antikoagulans-Behälter ("AC") hinzugefügt werden, um diese spezielle Strömung auf Wunsch/bei Bedarf aufrechtzuerhalten. Demzufolge enthält die Einlassströmung in die Blutkomponenten-Sammelvorrichtung **18** üblicherweise sowohl eine Strömung des Vollbluts vom Spender **14** als auch eine Strömung des Antikoagulans von dem AC-Behälter **30**.

**[0026]** Die Blutkomponenten-Sammelvorrichtung **18** trennt das Vollblut, das online durch den Spender **14** geliefert wird, in drei Hauptbestandteile, und zwar Blutplättchen, eine Kombination aus roten und weißen Blutkörperchen ("RBC/WBC") und Plasma. Die von der Blutkomponenten-Vorrichtung **18** gesammelten Blutplättchen werden über eine bzw. mehrere Blutplättchen-Sammelleitungen **34** über eine Sammelpumpe **36** zu einem oder mehreren Blutplättchen-Sammelbeuteln **38** geleitet. Das Plasma und die RBC/WBC werden über eine Plasmaleitung **42** bzw. eine RBC/WBC-Leitung **46**, die beide mit einer (nicht gezeigten) zweiten Nadelbaueinheit an dem Spender **14** verbunden sind, über eine Spenderrückleitung **50** wieder an den Spender **14** zurückgegeben. Die Plasmaleitung **42** enthält eine Plasmapumpe **40** (z. B. eine Peristaltikpumpe), um die Strömung des Plasmas auf Wunsch/bei Bedarf aufrechtzuerhalten. Obgleich das Plasma in der oben beschriebenen Weise wieder an den Spender **14** zurückgegeben werden kann, kann es in einigen Fällen erwünscht sein, das getrennte Plasma zu sammeln. Dabei kann ein Plasmasammelbeutel **54** vorgesehen und mit der Plasmaleitung **42** verbunden sein (wobei die Verbindung in Strichlinien gezeigt ist). In diesem Fall kann ein geeignetes Ventil **56** in der Plasmaleitung **42** vorhanden sein.

**[0027]** Die Blutkomponenten-Trennbaueinheit **10''** von Fig. 3 ist abgesehen davon, dass eine (nicht gezeigte)

Einnadelbaueinheit den Spender **14** in die Blutkomponenten-Trennbaueinheit **10** einbindet, ähnlich der Zweinadelkonfiguration von Fig. 2. Demzufolge sind ähnliche Komponenten soweit geeignet in ähnlicher Weise bezeichnet. Bei der Einnadelkonfiguration von Fig. 3 fließt das Vollblut des Spenders **14** anfangs durch eine Spenderzugangsleitung **62** und in eine Einlassleitung **66**, die mit der Blutkomponenten-Sammelvorrichtung **18** in Fluidverbindung steht, so dass die Blutplättchen in der oben beschriebenen Weise getrennt und gesammelt werden. Das Plasma und RBC aus der Blutkomponenten-Sammelvorrichtung **18** fließen durch die Plasma- bzw. RBC/WBC-Leitungen **42**, **46**, die beide mit einer Rückfluss-Steuereinheit **74** in Fluidverbindung stehen. Wie oben angegeben kann das Plasma jedoch alternativ zu einem Plasmasammelbeutel **54** geleitet werden. Wenn das Plasma nicht gesammelt wird, werden RBC/WBC und Plasma durch die Rückfluss-Steuereinheit **74** über eine Spenderrückleitung **70**, die mit der Spenderzugangsleitung **62** verbunden ist, an den Spender **14** zurückgegeben. Da, wie erkannt wird, lediglich eine einzige Leitung, und zwar die Spenderzugangsleitung **62**, mit dem Spender **14** direkt verbunden ist, wird Blut entweder vom Spender **14** entnommen oder an diesen zurückgegeben, so dass die Prozedur in Bezug auf den Spender **14** gegenüber einer kontinuierlichen eine zwei-stufige Prozedur ist.

**[0028]** Die Blutkomponenten-Sammelvorrichtung **18**, die in der Blutkomponenten-Sammelbaueinheit **10** verwendet wird, ist in den Fig. 4A-B genauer dargestellt. Diese Vorrichtung **18** ist Gegenstand des US-Patents Nr. 4.387.848 an Kellogg u. a. mit dem Titel "CENTRIFUGE ASSEMBLY", das am 14. Juni 1983 erteilt wurde und dessen Offenbarung in ihrer Gesamtheit in dieser Beschreibung durch Literaturhinweis eingeschlossen ist. Diese Vorrichtung **18** steht außerdem vom Anmelder der vorliegenden Anmeldung kommerziell zur Verfügung und ist somit im System COBE Spectra™ enthalten.

**[0029]** In den Fig. 4A-B verwendet die Blutkomponenten-Sammelvorrichtung **18** einen Verarbeitungskanal **80**, um den gewünschten extrakorporalen Einwegkreis zu schaffen. Der Kanal **80** ist in einer Nut angeordnet, die direkt oder indirekt in einem (nicht gezeigten) Zentrifugenrotor ausgebildet ist (z. B. kann eine getrennte Fülleinrichtung den Kanal **80** aufnehmen und an dem Zentrifugenrotor befestigt sein) und ist in der Form dargestellt, die er während der Verarbeitung annimmt (z. B. während Blut durch ihn hindurchfließt). Alle folgenden Bezugnahmen in dieser Beschreibung auf die strukturellen und funktionellen Charakteristiken der Blutkomponenten-Sammelvorrichtung **18** beziehen sich auf den Verarbeitungskanal **80** in dem dargestellten Zustand.

**[0030]** Der Verarbeitungskanal **80** enthält im Allgemeinen eine erste Stufe **84**, um rote Blutkörperchen ("RBC") und weiße Blutkörperchen ("WBC") aus an Blutplättchen reichem Plasma gemeinsam zu trennen, eine zweite Stufe **92**, um anschließend Blutplättchen aus dem an Blutplättchen reichen Plasma zu trennen, einen Übergangsabschnitt **88**, der eine Trennung zwischen der ersten Stufe **84** und der zweiten Stufe **92** definiert, und eine Kontrollkammer **124**, um eine geeignete Grenzfläche zwischen der ersten Stufe **84** und der zweiten Stufe **92**, und zwar die Position der Grenzfläche zwischen RBC/WBC und an Blutplättchen reichem Plasma in dem Übergangsabschnitt **88**, aufrechtzuerhalten.

**[0031]** Die erste Stufe **84** erstreckt sich von einem Ende der Kontrollkammer **124** längs eines bogenförmigen Wegs im Allgemeinen einwärts zu der Achse **132**, um die sich der Verarbeitungskanal **80** über den Zentrifugenrotor dreht, bis sie am Übergangsabschnitt **88** endet. Das Ende der ersten Stufe **84**, das an die Kontrollkammer **124** angrenzt, ist im Einzelnen in einem größeren radialen Abstand von der Achse **132** positioniert als das Ende der ersten Stufe **84**, das an den Übergangsabschnitt **88** angrenzt. Ein Einlassrohr **96** steht mit der ersten Stufe **84** zwischen deren beiden Enden in Fluidverbindung, um Vollblut in den Verarbeitungskanal **80** einzuleiten, und ein RBC/WBC-Rohr **100** ist in der Kontrollkammer **124** vorgesehen, um die getrennten RBC/WBC aus dem Kanal **80** zu entnehmen. Sowohl das Einlassrohr **96** als auch das RBC/WBC-Rohr **100** verlaufen außerhalb der drehbaren Vorrichtung **18** für eine Verbindung mit dem Spender **14** und/oder mit den Sammelbeuteln **38**, **54**.

**[0032]** Wenn sich während der Drehung des Zentrifugenrotors RBC/WBC an der Außenwand in der ersten Stufe **84** absetzen, werden sie infolge der erhöhten Zentrifugalkräfte an dem RBC/WBC-Rohr **100** im Vergleich zu dem Übergangsabschnitt **88** geleitet und bilden eine Gegenströmung zu dem RBC/WBC-Rohr **100** zur Entnahme aus dem Kanal **80**. Das heißt, da sich die erste Stufe **84** ausgehend von dem Übergangsabschnitt **88** längs eines bogenförmigen Wegs im Allgemeinen auswärts weg von der Achse **132** zu der Kontrollkammer **124** erstreckt, bildet der Zentrifugalkraftunterschied längs der ersten Stufe **84** die beschriebene Gegenströmung der getrennten RBC/WBC. Darüber hinaus unterstützt der Übergangsabschnitt **88** ebenfalls die Bildung dieser Gegenströmung, da er sich ausgehend von der ersten Stufe **84** zu der zweiten Stufe **92** längs eines bogenförmigen Wegs im Allgemeinen einwärts zu der Achse **132** erstreckt.

**[0033]** Das an Blutplättchen reiche Plasma, das eine niedrigere Dichte als die RBC und WBC aufweist, strömt

zur Weiterverarbeitung über den Übergangsabschnitt **88** von der ersten Stufe **84** hinaus in die zweite Stufe **92**, während die RBC/WBC in der oben beschriebenen Weise zurück zum RBC/WBC-Rohr **100** geleitet werden. Die zweite Stufe **92** beginnt am radial innersten Teil des Übergangsabschnitts **88** und erstreckt sich längs eines bogenförmigen Wegs im Allgemeinen auswärts von der Achse **132** weg zu einer Blutplättchen-Sammelkammer **104**. Die Blutplättchen werden an der Blutplättchen-Sammelkammer **104** durch ein Blutplättchenrohr **108**, das bei der Blutplättchen-Sammelkammer **104** mit einer Außenwand des Verarbeitungskanals **80** verbindet, aus dem Verarbeitungskanal **80** entnommen. Anschließend erstreckt sich die zweite Stufe **92** längs eines bogenförmigen Wegs im Allgemeinen einwärts zu der Achse **132**, bis sie an dem Plasmarohr **112** endet. Sowohl das Blutplättchenrohr **108** als auch das Plasmarohr **112** verlaufen außerhalb der drehbaren Vorrichtung **18** zur Verbindung mit dem Blutplättchen-Sammelbeutel bzw. mit den Blutplättchen-Sammelbeuteln **38** bzw. mit dem Spender **14**/dem Plasmasammelbeutel bzw. den Plasmasammelbeuteln **54**.

**[0034]** Blutplättchen, die sich in dem Anfangsabschnitt der zweiten Stufe **92** zwischen dem Übergangsabschnitt **88** und der Blutplättchen-Sammelkammer **104** nicht von dem Plasma trennen, werden in dem Abschnitt der zweiten Stufe **92** zwischen der Blutplättchen-Sammelkammer **104** und dem Plasmarohr **112** getrennt. Diese Blutplättchen strömen infolge der Konfiguration dieses Abschnitts der zweiten Stufe **92** in der entgegengesetzten Richtung der Strömung des an Blutplättchen reichen Plasmas/des an Blutplättchen armen Plasmas durch die zweite Stufe **92** zurück zu der Blutplättchen-Sammelkammer **104**. Das heißt, die Blutplättchen-Sammelkammer **104** nimmt die radial äußerste Position in der zweiten Stufe **92** ein, so dass alle Blutplättchen, unabhängig davon, wo die Trennung in der zweiten Stufe **92** erfolgt, zur Entnahme aus dem Kanal **80** zu der Blutplättchen-Sammelkammer **104** strömen.

**[0035]** An Blutplättchen armes Plasma tritt aus der zweiten Stufe **92** aus und strömt durch das Plasmarohr **112**, das mit der Innenwand des Verarbeitungskanals **80** verbindet, aus und/oder weiter durch den restlichen Abschnitt des Verarbeitungskanals **80** zu der Kontrollkammer **124**. Plasma, das zu der Kontrollkammer **124** strömt, tritt aus dem Kanal durch das Kontrollrohr **114** aus, das mit dem RBC/WBC-Rohr **100** in ein einziges Auslassrohr **120** mündet. Die Positionierungen und die Durchmesser des RBC/WBC-Rohrs **100** und des Kontrollrohrs **114** und deren Verbindung in dem gemeinsamen Auslassrohr **120** regulieren unter Verwendung von Massenerhaltungsprinzipien die Position der Grenzfläche von RBC/WBC und an Blutplättchen reichem Plasma in dem Übergangsabschnitt **88**.

**[0036]** Die Blutkomponenten-Sammelvorrichtung **18** enthält ein Vorhersagemodell **20** (das wie oben angemerkt, wie in Fig. 1 gezeigt ist, vorteilhaft mit dem Bedienperson-Eingabemodul **16** verbunden ist und verwendet werden kann, um das Vorhersagemodell **20** zu konfigurieren und/oder eine Bedienpersoneingabe von verschiedenen Parametern zulässt, die durch das Vorhersagemodell **20** zu verwenden sind) zum Vorhersagen eines Blutplättchenausstoßes unter Verwendung einer Zusammenstellung von Algorithmen, bevor eine Sammelprozedur begonnen wird. Das Vorhersagemodell **20** kann von der Optimierungsbaueinheit **140** verwendet werden, die den Prinzipien der vorliegenden Erfindung zugeordnet ist und somit an dieser Stelle kurz beschrieben wird. Trotz der folgenden Erläuterung der Spezifiken des Vorhersagemodells **20** wird ein Fachmann erkennen, dass das Vorhersagemodell **20** den funktionellen und Betriebscharakteristiken der hier beschriebenen Blutkomponenten-Sammelvorrichtung **18** zugeordnet ist. Daher können und werden wahrscheinlich die in dem Vorhersagemodell **20** verwendeten Algorithmen bei anderen Blutkomponenten-Sammelvorrichtungen, die von der vorliegenden Erfindung verwendet werden können, variieren. Darüber hinaus können natürlich sogar für das Vorhersagemodell **20** unterschiedliche Algorithmen verwendet werden. Die Algorithmen sind ferner speziell für die Blutplättchensammlung geeignet und können sich und werden sich wahrscheinlich somit ändern, wenn sie in Verbindung mit anderen Blutkomponententypen, wie etwa mit roten Blutkörperchen, verwendet werden.

**[0037]** Das Vorhersagemodell **20** wird üblicherweise durch die Einrichtung (z. B. Blutbank/Blutzentrum) für eine bestimmte (z. B. Einnadel- oder Zweinadel-)Blutkomponenten-Sammelprozedur, die von der Einrichtung verwendet wird, konfiguriert und ist in Fig. 2 in Bezug auf die Zweinadelprozedur und eine Blutplättchen-Sammelprozedur dargestellt. Dabei müssen eine AC-Infusionsrate (d. h. die Rate, mit der ein Antikoagulans pro Blutvolumen des Spenders **14** an den Spender **14** abgegeben wird) und das AC-Verhältnis (d. h. die gemeinsame Strömung von AC und Blut durch die Einlassleitung **22** in Bezug auf die Strömung von AC durch die Leitung **22**) (durch Konfiguration oder modifizierte Eingabe, wie im Folgenden erläutert wird) festgelegt werden. Darüber hinaus muss dann, wenn in der Sammelprozedur Plasma in dem Plasmasammelbeutel **54** gesammelt werden soll, außerdem unter Berücksichtigung der medizinischen und physischen Charakteristiken des Spenders **14** die maximale Menge des Plasmas festgelegt werden, die gesammelt werden soll.

**[0038]** Es gibt zwei alternative Möglichkeiten zur Festlegung der Plasma-Volumengrenze. Die erste Alterna-

tive in Bezug auf die Plasma-Volumengrenze besteht darin, eine Gewichtsgrenze bereitzustellen (z. B. 0-500 Pfund), die mit dem Gewicht des Spenders **14** zusammenhängt und in der im Folgenden beschriebenen Weise eingegeben wird. Dabei kann eine Plasmavolumen-Obergrenze (z. B. 10-1500 ml) für ein Gewicht eines Spenders **14** festgelegt werden, das diese Grenze überschreitet, und eine Plasmavolumen-Untergrenze (z. B. 10-1500 ml) für ein Gewicht eines Spenders **14** festgelegt werden, das kleiner als diese Grenze ist. Wenn die Gewichtsgrenze z. B. 175 Pfund beträgt, kann die Plasmavolumen-Obergrenze für ein Gewicht des Spenders **14**, das größer oder gleich 175 Pfund ist, bei 600 ml liegen und kann die Plasmavolumen-Untergrenze für ein Gewicht des Spenders **14**, das kleiner als 175 Pfund ist, bei 500 ml liegen.

**[0039]** Die zweite Alternative für eine Plasmavolumengrenze besteht darin, das Vorhersagemodell **20** in der Weise zu konfigurieren, dass die Plasmavolumengrenze als ein Anteil des totalen Blutvolumens des Spenders **14** ausgedrückt wird, das gemäß der unten stehenden Gleichung 10 berechnet wird. Die Plasmavolumengrenze kann z. B. als 1–15 % des totalen Blutvolumens des Spenders **14** festgelegt werden und wird vorzugsweise als etwa 12 % dieses Volumens festgelegt.

**[0040]** Bevor das Vorhersagemodell **20** seine Ausstoßvorhersagefunktion ausführt, benötigt es weitere Informationen. Zum Beispiel wird üblicherweise die Gesamtdauer der Prozedur von der Bedienperson eingegeben oder vom Benutzer (z. B. von der Blutbank/dem Blutzentrum) im Voraus konfiguriert. Wenn sie konfiguriert wird, beträgt die Prozedurdauer üblicherweise 100 Minuten. Darüber hinaus wird die Gesamtdauer der Prozedur dadurch beeinflusst, ob für die Blutkomponenten-Sammelvorrichtung **18** eine Untersetzungswahlmöglichkeit verwendet wird, um die Trennung der verschiedenen Blutkomponenten zu verbessern. Wenn diese Untersetzungswahlmöglichkeit ausgewählt wird, wird die Winkelgeschwindigkeit der Blutkomponenten-Sammelvorrichtung **18** während der Blutplättchen-Sammelprozedur schrittweise verringert. Die Untersetzungswahlmöglichkeit könnte z. B. Winkelgeschwindigkeiten für die Vorrichtung **18** von 2400, 2200 und 2000 minbereinstellen, die jeweils für eine festgelegte Dauer gelten.

**[0041]** Auf der Grundlage des Vorhergehenden standardisiert die Konfiguration des Vorhersagemodells **20** in Bezug auf die Blutkomponenten-Trennbaueinheit **10'** und das zugeordnete Protokoll das Einrichtungsprotokoll für den "normalen" Betrieb. Für einen bestimmten Spender **14** kann es jedoch erwünscht sein, die "Konfiguration" für einen Verarbeitungsdurchlauf zu ändern. Demzufolge verwendet das Vorhersagemodell **20** eine Prozedur, bei der bestimmte Parameter, die in den folgenden Gleichungen verwendet werden, einmalig verändert werden können. Diese werden als modifizierte Eingabedaten bezeichnet und die zugeordneten Parameter sind die Prozedurdauer (z. B. 10-999 Minuten), die Eingangsdurchflussmenge in die Vorrichtung **18** (z. B. 0-150 ml/min für die Baueinheit von Fig. 2 und 0 bis 50 ml/min für die Baueinheit von Fig. 2), die wie oben diskutierte AC-Verhältnis-Wahlmöglichkeit (3–50), das Soll-Blutplättchen-Sammelvolumen (z. B. 10-9999 ml), die Soll-Blutplättchen-Sammelkonzentration (z. B.  $100-8000 \cdot 10^6 \text{ ml}^{-1}$ ) und das Soll-Plasmavolumen der Quelle, das gesammelt werden soll (z. B. 0–9999 ml). Darüber hinaus können weitere Parameter, wie etwa die AC-Infusionsrate (0,8–1,1), die Untersetzungswahlmöglichkeit (ja oder nein), die Nadel-Wahlmöglichkeit (eine oder zwei) und die Wahlmöglichkeit der starken Strömung (ja oder nein) außerdem als modifizierte Eingabedaten durch eine Bedienperson eingegeben werden.

**[0042]** Nachdem das Vorhersagemodell **20** in der oben beschriebenen Weise konfiguriert wurde, werden die folgenden Zusatzinformationen bereitgestellt und in den verschiedenen Berechnungen der Gleichungen 1–22, die im Folgenden dargestellt sind, verwendet: (1) Nadel-Wahlmöglichkeit, und zwar, ob die Prozedur eine Zweinadelprozedur (Fig. 2) oder eine Einnadelprozedur (Fig. 3) ist; (2) Durchlauf-Kennzahl zur Zuordnung der Daten/Ausgabe, die durch die verschiedenen Gleichungen bei einem bestimmten Spender **14** und einem Verarbeitungsdurchlauf erzeugt werden; (3) das Geschlecht des Spenders **14**; (4) die Größe des Spenders **14**; (5) das Gewicht des Spenders **14**; (6) das Vollblutvolumen, das durch die folgende Gleichung 10 berechnet wird; (7) der Hämatokrit-Wert des Spenders **14**, entweder anhand einer Anfangsschätzung und einer anschließenden Aktualisierung auf der Grundlage der Analyse der Blutprobe des Spenders **14** (z. B. durch einen Zellenzähler) oder direkt von einer derartigen Analyse eingegeben; (8) die vorläufige Blutplättchen-Anzahl, entweder anhand einer Anfangsschätzung und einer anschließenden Aktualisierung auf der Grundlage der Analyse der Blutprobe des Spenders **14** (z. B. durch einen Zellenzähler) oder direkt von einer derartigen Analyse eingegeben; und (9) ob in Verbindung mit der Blutplättchensammlung eine Plasmasammlung erwünscht ist.

**[0043]** Anhand der oben genannten Anfangskonfiguration und der anschließenden Dateneingabe (mit Ausnahme bei Eingabe als modifizierte Eingabedaten) werden durch das Vorhersagemodell **20** die folgenden Ausgaben erzeugt: (1) Blutplättchenausstoß; (2) Eingangsdurchflussmenge; (3) AG-Verhältnis; (4) Prozedurdauer; (5) Blutplättchen-Sammelvolumen; (6) Blutplättchen-Sammelkonzentration; (7) Plasmavolumen der Quelle; (8) AC in den Blutplättchen- und in den Plasmasammelbeuteln **38**, **54**; (9) endgültige Blutplättchen-Anzahl; (10)

AC-Infusionsrate; und (11) Ausgabefreigabe. Diese Informationen werden zumindest teilweise in den folgenden Gleichungen verwendet, um u. a. den Wert des vorhergesagten Blutplättchenausstoßes der gesammelten Blutplättchen für die Zweinadelprozedur von Fig. 2 und ebenfalls für die Einnadelprozedur von Fig. 3 zu erzeugen. Die Unterschiede zwischen diesen Prozeduren in Bezug auf das Vorhersagemodell **20** werden in dieser Beschreibung gekennzeichnet. Es wird erkannt, dass einige der Gleichungen bei der Berechnung des vorhergesagten Blutplättchenausstoßes verwendet werden, wohingegen andere Gleichungen verwendet werden, um Zusatzinformationen zur Ausgabe und zu Informationszwecken zu erzeugen. Die Variablen oder Parameter und die damit verbundenen Einheiten der Gleichungen sind nach den Gleichungen im Variablenindex angegeben.

Blutplättchenausstoß:

$$Y = 1 \cdot 10^6 C_{PR} V_B F_Y [1 - \exp[-E_C (f_{BP} - 0,12)]] \quad (1)$$

wobei:

$$f_{BP} = (Q_{IN} t_E + 50)(1 - 1/R) V_B \quad (2)$$

und wobei:

$$Q_{IN} = R Q_{AC} = 0,001 \mid V_B PR \leq 150 \quad (3)$$

ist.

**[0044]** Der Blutplättchenausstoß kann alternativ ausgedrückt werden als:

$$Y = 1 \cdot 10^6 C_{PR} V_B F_Y [1 - \exp[-E_C (0,001 \mid (R - 1) P t_E \cdot 50 (1 - 1/R) / V_B - 0,12)]] \geq 0 \quad (4)$$

Blutplättchensammeleffizienz:

$$E_C = C_1 - C_2 \exp[9,91(1 - 1/R)H] Q_{INA} \geq 0 \quad (5)$$

wobei die Konstante  $C_1$  wie folgt definiert ist:

$C_1 = 0,803$  – Zweinadelprozedur, ohne Untersetzung

$C_1 = 0,840$  – Zweinadelprozedur, mit Untersetzung

wobei die Konstante  $C_2$  wie folgt definiert ist:

$C_2 = 4,08 \cdot 10^{-5}$  – Zweinadelprozedur, ohne Untersetzung

– Zweinadelprozedur, mit Untersetzung

und wobei:

$$Q_{INA} = Q_{IN} (t_E / t_P) \quad (6)$$

ist.

**[0045]** In Gleichung 6 kann  $t_P$  als Konfigurationsdaten oder wie oben als modifizierte Daten bereitgestellt werden oder alternativ aus der Auflösung der Gleichung 4 nach  $t_E$  abgeleitet werden.

Effektive Prozedurdauer:

$$\begin{aligned} t_E &= t_F, Q_{IN} \leq 45 \\ &= t_P - 500(1/45 - 1/Q_{IN}), Q_{IN} > 45 \end{aligned} \quad (7)$$

**[0046]** Für  $Q_{IN} > 45$  wird nur das Protokoll für starke Strömung verwendet.

Konstante der AC-Infusionsrate:

$$I = 1000 Q_{IN} / (PR V_B) \quad (8)$$

**[0047]** Alternativ zur Verwendung von Gleichung 8 für die Ableitung der Konstante  $I$  der AC-Infusionsrate kann diese als Konfigurationsdaten oder modifizierte Eingabedaten gemäß dem oben Stehenden bereitgestellt

werden.

#### AC-Verhältnis

**[0048]** Anfangs kann das AC-Verhältnis als Konfigurationsdaten oder modifizierte Eingabedaten gemäß dem oben Stehenden bereitgestellt werden. Bei der Konfiguration ist es wie folgt definiert:

$$\begin{aligned} R &= 1 + 2,51/H && \text{klein} \\ &= 1,33 (1 + 2,51/H) && \text{mittelgroß} \\ &= 1,67 (1 + 2,51/H) && \text{groß} \end{aligned} \quad (9)$$

Totales Blutvolumen:

$$\begin{aligned} V_B &= 604 + 0,006012 L^3 + 14,6 W \text{ ml (männlich)} \\ &= 183 + 0,005835 L^3 + 15,0 W \text{ ml (weiblich)} \end{aligned} \quad (10)$$

Plasmasammelfaktor:

**[0049]** Die Steuerung der AC-Infusionsrate hält die AC-Strömung zum Spender auf dem folgenden Wert:

$$Q_{ACD} = 0,001 I V_B \quad (11)$$

wobei die ihm zugeordnete Einlassströmung:

$$Q_{INO} = R Q_{ACD} = 0,001 I R V_B \quad (12)$$

ist.

**[0050]** Wie durch Gleichung 3 angegeben ist, die das AC enthält, das zu dem Blutplättchen-Sammelbeutel **38** und zu dem Plasmasammelbeutel **54** fließt, ist  $Q_{IN}$  zu der Gesamt-AC-Strömung proportional.  $P$  (Gleichung 13) ist der Faktor, um den  $Q_{IN}$  in Bezug auf den Fall, wenn AC nicht gesammelt wird, durch die Sammlung von AC vergrößert wird. Das heißt

$$P = Q_{IN}/Q_{INO} = (\text{Mittelwert } Q_{AC})/Q_{ACD} \quad (13)$$

wobei:

$$P = 1 + (f_{ACP}/Q_{ACD})[V_C/(t_P - 150/Q_{IN}) + V_{SP}/(t_P - 500/Q_{IN})] \quad (14)$$

und wobei:

$$f_{ACP} = [(R - 1)(1 - H)]^{-1} \quad (15)$$

ist.

Blutplättchen-Sammelvolumen:

$$V_C = 1 \cdot 10^{-6} Y/[C_B (1 + f_{ACP})] \quad (16)$$

Plasmavolumen der Quelle:

**[0051]** Es werden folgende vier Auswahlmöglichkeiten bereitgestellt:

$$\left. \begin{aligned}
 &= 0 \\
 V_{SP} &= V_{CON} - V_C \\
 &= f_{SP} V_B - V_C \\
 &= \text{als modifizierte Eingabe festgelegt}
 \end{aligned} \right\} \geq 0 \quad (17)$$

wobei:

$$\begin{aligned}
 V_{CON} &= V_{CONL}, W < WC \\
 V_{CONR}, W &\geq WC
 \end{aligned} \quad (18)$$

und wobei:

$$0,01 \leq f_{SP} \leq 0,15 \quad (19)$$

ist.

Endgültiger Zählwert des Spenders:

$$C_{PO} = C_{PR} \exp[-E_C(0,001 \ln(R-1)Pt_E + 50(1 - 1/R)/V_B - 0,12)] \leq C_{PR} \quad (20)$$

Es erfolgt eine Warnung, falls  $C_{PO} < 100$  ist.

Sammelvolumen:

$$V_{BC} = V_C (1 + f_{ACP}) \quad (21)$$

$$V_{SPB} = V_{SP} (1 + f_{ACP}) \quad (22)$$

**[0052]** Die Hauptgleichung, die für die Ausstoßvorhersage durch das Vorhersagemodell 20 zu lösen ist, ist Gleichung 4. Demzufolge sind die Gleichungen 1–3 und 5–22 Hilfsgleichungen für Gleichung 4, obgleich sie verwendet werden können, um andere Ausgabedaten und/oder Informationen, die von Gleichung 4 benötigt werden, zu berechnen. Im Hinblick auf die Art, in der die Gleichungen 1–22 gelöst werden, basieren alle Iterationsschleifen auf der Technik der schrittweisen Näherung, bei der jede Iteration eine Wiederholung der vorhergehenden, jedoch unter Verwendung aktualisierter Parameterwerte, die in der vorhergehenden Iteration berechnet wurden, ist. Dieser Prozess wird fortgesetzt, bis alle Konvergenzkriterien erfüllt sind. Die Konvergenzkriterien bestehen darin, dass die Variablendifferenz bei aufeinanderfolgenden Iterationen  $\leq 1$  für  $V_C$ ,  $\leq 0,2$  für  $t_E$  und  $\leq 10$  für  $C_B$  ist.

**[0053]** Wie oben angemerkt wurde, basiert das Vorhergehende auf einer Zweinadelkonfiguration, wie sie in [Fig. 2](#) dargestellt ist. Wenn die Einnadelkonfiguration, wie etwa jene, die in [Fig. 3](#) dargestellt ist, verwendet wird, wird anstelle von Gleichung 7 die folgende Gleichung 7' verwendet, wobei die Konstanten  $C_1$  und  $C_2$  für Gleichung 5 wie folgt lauten:

$$C_1 = 0,803$$

$$C_2 = 8,54 \cdot 10^{-5}$$

$$\begin{aligned}
 t_E &= t_P, Q_{IN} \leq 20 \\
 &= t_P - 215 (1/20 - 1/Q_{IN}) + Q_{IN} > 20
 \end{aligned} \quad (7')$$



## Variablenindex

Symbole für Gleichungen:

|            |                                                                                                          |
|------------|----------------------------------------------------------------------------------------------------------|
| $C_1, C_2$ | = Konstanten in den Gleichungen der Blutplättchensammeleffizienz                                         |
| $C_B$      | = Blutplättchenkonzentration im Sammelbeutel, ausgedrückt als $10^3$ Blutplättchen/Mikroliter            |
| $C_{PO}$   | = endgültiger Spenderzählwert, ausgedrückt als $10^3$ Blutplättchen/Mikroliter                           |
| $C_{PR}$   | = vorläufiger Spenderzählwert, ausgedrückt als $10^3$ Blutplättchen/Mikroliter                           |
| $E_c$      | = Blutplättchensammeleffizienz                                                                           |
| $f_{ACP}$  | = AC, Ausgedrückt als Anteil des Blutplasmavolumens                                                      |
| $f_{BP}$   | = Anteil von $V_B$ , der in der Blutplättchensammelprozedur verarbeitet wird                             |
| $f_{SP}$   | = $V_{CON}$ , ausgedrückt als ein Anteil von $V_B$                                                       |
| $F_Y$      | = benutzerspezifischer (z. B. für die Blutbank/das Blutzentrum spezifischer) Ausstoß-Kalibrierungsfaktor |
| H          | = Hämatokrit-Wert des Spenders oder Patienten                                                            |
| I          | = Konstante der AC-Infusionsrate                                                                         |
| L          | = Größe des Spenders oder Patienten in Zoll                                                              |
| P          | = Plasmasammelfaktor                                                                                     |
| $Q_{AC}$   | = AC-Strömung in ml/min                                                                                  |
| $Q_{ACD}$  | = AC-Strömung, die in den Spender für Blutplättchensammelprozeduren infundiert wird, in ml/min           |
| $Q_{IN}$   | = Einlassströmung in ml/min                                                                              |
| $Q_{INA}$  | = gemittelte Einlassströmung für Blutplättchenprozeduren in ml/min                                       |
| $Q_{INO}$  | = $RQ_{ACD}$ = Einlassströmung, die $Q_{ACD}$ zugeordnet ist, in ml/min                                  |
| R          | = AC-Verhältnis                                                                                          |
| $t_E$      | = äquivalente Prozedurdauer in min                                                                       |
| $t_P$      | = Prozedurdauer in min                                                                                   |
| $V_B$      | = totales Blutvolumen des Spenders oder Patienten in ml                                                  |
| $V_C$      | = Volumen des reinen Plasmas in dem Plasmasammelbeutel in ml                                             |
| $V_{CB}$   | = Gesamtvolumen im Blutplättchensammelbeutel in ml                                                       |
| $V_{CON}$  | = Volumenbeschränkung für das gesamte gesammelte reine Plasma in ml                                      |
| $V_{CONH}$ | = höherer Wert von $V_{CON}$ in ml                                                                       |
| $V_{CONL}$ | = niedrigerer Wert von $V_{CON}$ in ml                                                                   |
| $V_{SP}$   | = Volumen des reinen Plasmas in dem Plasmabeutel der Quelle in ml                                        |
| $V_{SPB}$  | = Gesamtvolumen in dem Quellen-Plasmabeutel in ml                                                        |
| W          | = Gewicht des Spenders oder Patienten in Pfund                                                           |
| $W_C$      | = Gewichtsbeschränkung, die $V_{CON}$ zugeordnet ist, in Pfund                                           |
| Y          | = Blutplättchenausstoß, Anzahl der Blutplättchen.                                                        |

**[0054]** Wie oben angemerkt wurde, verbindet die Optimierungsbaueinheit **140** gemäß den Prinzipien der vorliegenden Erfindung mit einer oder mehreren Blutkomponenten-Sammelbaueinheiten **10** oder stellt zumindest Informationen für diese bereit, um ein Blutplättchen-Sammelsystem **2** zu schaffen. Das heißt, obgleich definitiv Vorteile des Vorhandenseins einer Schnittstelle zwischen der Optimierungsbaueinheit **140**, insbesondere zwischen dem Optimierungsmodul **144**, und der Blutkomponenten-Sammelvorrichtung **18** vorhanden sind, kann die Optimierungsprozedur an irgendeiner Stelle ausgeführt werden und eine Eingabe in die Blutkomponenten-Sammelvorrichtung **18** auf beliebige Weise erfolgen. Da die allgemeinen Prinzipien der Blutkomponenten-Sammelbaueinheit **10** in Bezug auf die Sammelbaueinheiten **10**, **10''** beschrieben wurden, die die Blutkomponenten-Sammelvorrichtung **18** und ihre verschiedenen Merkmale enthalten, wird die Optimierungsbaueinheit **140** in Bezug auf diese Baueinheiten **10'**, **10''** beschrieben. Es wird jedoch anerkannt, dass die grundlegenden Optimierungsprinzipien der vorliegenden Erfindung nicht auf diese Sammelprozeduren und/oder Vorrichtungen beschränkt sind.

**[0055]** Wie angemerkt wurde (Fig. 1), enthält die Optimierungsbaueinheit **140** im Allgemeinen für jede Blutkomponenten-Sammelvorrichtung **18** eine zentrale Eingabestation **148** sowie ein Optimierungsmodul **144**. Anfangs sollte angemerkt werden, dass das Optimierungsmodul **144** von der internen Steuerung der Blutkomponenten-Sammelvorrichtung **18**, auf die durch das Bedienperson-Schnittstellenmodul **16** zugegriffen werden kann, getrennt sein kann. Allerdings ist das Optimierungsmodul **144** üblicherweise gemeinsam mit dem oben beschriebenen Vorhersagemodul **20** mit dieser internen Steuerung integriert.

**[0056]** In Fig. 5 wird die Optimierungsbaueinheit **140** in Bezug auf eine Standardprozedur beschrieben. Die zentrale Eingabestation **148** wird üblicherweise durch Blutbanken/Blutzentren als Haupteinrichtung für die Ein-

gabe und Organisation von Spenderdaten verwendet. Bei der zentralen Eingabestation **148** werden Informationen bezüglich eines Spenders, wie etwa Geschlecht, Größe, Gewicht und demographische Angaben, eingegeben. Darüber hinaus können Informationen bezüglich des Hämatokrit-Wertes des Spenders und einer vorläufigen Anzahl der Blutkomponenten, die beide von einer Blutprobe des Spenders erhalten und durch bekannte Techniken, wie etwa durch Zellenzähleinrichtungen, bestimmt werden können, ebenfalls bei der zentralen Station **148** eingegeben werden. Außer spenderbezogenen Daten können bei der zentralen Eingabestation **148** der bestimmte Typ der Sammelprozedur, der für den Spender zu verwenden ist (z. B. Einnadel- oder Zweinadel-), eingegeben/bestätigt werden. Anhand dieser Informationen und bestimmter für die Einrichtung standardisierter Bedingungen (z. B. Gesamtdauer der Prozedur, Sammeleffizienz, AC-Infusionsrate) wird daraufhin ein Anfangsprozedurauftrag erzeugt, der die verschiedenen Prozesssteuerungsparameter festlegt, die der ausgewählten Sammelprozedur zugeordnet sind.

**[0057]** Der Anfangsprozedurauftrag kann dann bei Bedarf/auf Wunsch unter Verwendung des Bedienperson-Schnittstellenmoduls **16** durch eine Computerspeicherplatte **142** (Fig. 1) oder, wenn ein (nicht gezeigtes) Netzwerksystem realisiert ist, elektronisch in die interne Steuerung einer Blutkomponenten-Sammelvorrichtung **18** übertragen/heruntergeladen werden. Wenn dieses Bedienperson-Schnittstellenmodul **16** vorhanden ist, kann es natürlich für die Anfangseingabe von Spenderdaten und/oder für die Erzeugung des Anfangsprozedurauftrags verwendet werden, wodurch die Notwendigkeit für eine zentrale Eingabestation **148** vermieden wird. Es kann jedoch effizienter sein, die zentrale Eingabestation zu verwenden. Obgleich dieser Anfangsprozedurauftrag in dem Sammelvorgang verwendet werden kann, kann er in Übereinstimmung mit den Prinzipien der vorliegenden Erfindung optimiert werden, um einen oder mehrere optimale Werte für Prozesssteuerungsparameter zu erhalten. Wie angemerkt wurde, kann dieser Optimierungsprozess verwendet werden, bevor die Sammelprozedur tatsächlich begonnen wird, während er jedoch auch während einer gegebenen Sammelprozedur begonnen werden und daher als nachgeschaltete Optimierung bezeichnet werden kann.

**[0058]** In Bezug auf die verschiedenen Optimierungswahlmöglichkeiten können Prozesssteuerungsparameter für eine produktbasierte Optimierung abgeleitet werden. Im Einzelnen leitet die Optimierungsbauereinheit **140** und insbesondere das Optimierungsmodul **144**, wie im Folgenden in Bezug auf die Optimierungsmodelle **152** (Fig. 6), **172** (Fig. 7) erläutert wird, Prozesssteuerungsparameter zum Erreichen eines vorgegebenen Ausstoßes von Blutkomponenten durch eine Maximierung wenigstens eines Prozessparameters ab. Wie oben angemerkt wurde, enthält in den Vereinigten Staaten ein Einfach-Blutplättchen-Produkt (SPP)  $3 \cdot 10^{11}$  Blutplättchen und ein Doppel-Blutplättchen-Produkt (DPP)  $6 \cdot 10^{11}$  Blutplättchen. Demzufolge kann das Optimierungsmodul **144** in der Weise konfiguriert sein, dass es mehrere produktbasierte Optimierungen, wie etwa SPP und DPP, bereitstellt. Obgleich die genauen Werte für aktuelle US-SPP und -DPP in das Optimierungsmodul **144** konfiguriert werden können, um die Wahrscheinlichkeit zu erhöhen, dass der tatsächliche Ausstoß die Ausstoßforderungen für aktuelle US-SPP und -DPP erreicht oder übersteigt, kann die Einrichtung ein SPP auf  $3,5 \cdot 10^{11}$  Blutplättchen und ein DPP auf  $7,0 \cdot 10^{11}$  Blutplättchen konfigurieren (um z. B. effektiv einen Vertrauensgrad sicherzustellen, dass der festgelegte Ausstoß tatsächlich erreicht wird).

**[0059]** Außerdem kann das Optimierungsmodul **144** so konfiguriert sein, dass es eine zeitbasierte Optimierung schafft. Das heißt, für eine vorgegebene Zeitdauer, in der ein Spender zur Verfügung steht, leitet das Optimierungsmodul **144** diejenigen Prozessparameter ab, die in Bezug auf eine Maximierung wenigstens eines der Prozesssteuerungsparameter die Sammlung einer "maximalen" Menge von Blutplättchen in dieser Zeitperiode zulassen.

**[0060]** Nachdem die Optimierung abgeschlossen ist, werden die Werte für die hierdurch erzeugten verschiedenen Prozesssteuerungsparameter sowie alle Hilfwerte/vorher festgelegten Werte in die interne Steuerung der Blutsammelvorrichtung **18** heruntergeladen, so dass die Sammelprozedur begonnen oder, wie es gemäß diesen Werten der Fall sein kann, neu begonnen (nachgeschaltete Optimierung) werden kann. Nachdem die Prozedur abgeschlossen ist, können bestimmte Daten (über die Speicherplatte **142** oder elektronisch, wie angemerkt wurde) zur Weiterverwendung in Bezug auf den bestimmten Spender wieder zur zentralen Eingabestation **148** übertragen werden. Außerdem können diese Informationen sowie die Anfangseingabe verwendet werden, um verschiedene Typen von Berichten (z. B. einzelne Durchläufe, Spender/Patient, zusammenfassende Berichte) zu erzeugen, die bei der Organisation der Blutbank/des Blutzentrums weiter unterstützen können. Das heißt, diese Informationen können bei der Ableitung von nachfolgenden Prozeduraufträgen für den bestimmten Spender verwendet werden. Wenn z. B. in der Sammelprozedur eine bestimmte AC-Infusionsrate verwendet wurde, die bestimmte Auswirkungen auf den Spender hatte, kann diese in der zentralen Eingabestation **148** aufgezeichnet werden, so dass für spätere Spenden durch den Spender eine niedrigere AC-Infusionsrate vorgeschlagen/gefordert wird.

**[0061]** Ein Modell, das in dem Optimierungsmodul **144** enthalten sein kann, ist in Fig. 6 gezeigt und wird in Bezug auf Blutplättchen-Sammlungen gemäß der Zweinadelkonfiguration von Fig. 2 beschrieben, obgleich das Modul **144** bei einer Vielzahl weiterer Sammelprozeduren verwendet werden kann und die Einnadelkonfiguration von Fig. 3 enthält sowie bei verschiedenen anderen Blutkomponenten verwendet werden kann. Anfangs sollte angemerkt werden, dass in Fig. 6 alle Bezugnahmen auf "Ableitungen" tatsächlich in dem oben erläuterten Vorhersagemodell **20** erfolgen, so dass entweder eine geeignete Schnittstelle zwischen dem Vorhersagemodell **20** und dem Optimierungsmodul **144** vorhanden ist oder das Optimierungsmodul **144** tatsächlich das Vorhersagemodell **20** enthält. Wie darüber hinaus angemerkt wurde, ist das Vorhersagemodell **20** speziell für die Blutkomponenten-Sammelvorrichtung **18** und für Blutplättchensammlungen. Wie angemerkt wurde, würde sich daher dann, wenn andere Vorrichtungen verwendet werden, das zugeordnete Vorhersagemodell ebenfalls ändern. Darüber hinaus kann sich das zugeordnete Vorhersagemodell auch in dem Fall ändern, wenn andere Blutkomponenten, wie etwa rote Blutkörperchen, gesammelt werden sollen.

**[0062]** Das Optimierungsmodell **152** von Fig. 6 kann sowohl für produktbasierte Optimierungen als auch für zeitbasierte Optimierungen verwendet werden. Anfangs wird das Optimierungsmodell **152** in Bezug auf eine produktbasierte Optimierung beschrieben. Das heißt, die Grundaufgabe der Optimierung besteht darin, einen vorgegebenen Ausstoß (oder einen Ausstoß in einem Ausstoßbereich) von Blutplättchen (oder eines anderen Blutkomponententyps), vorzugsweise innerhalb der minimalen Zeitdauer, zu erreichen.

**[0063]** Das Optimierungsmodell **152** von Fig. 6 enthält vier Iterationsschleifen. Die erste Schleife **156** ist im Allgemeinen eine Ableitung einer Einlassströmung ( $Q_{IN}$ ), die einer festgelegten AC-Infusionsrate ( $I_{SPEC}$ ) zugeordnet ist, die für die vorliegende Erfindung üblicherweise auf einen Maximalwert eingestellt und bei der Eingabestation **154** eingegeben wird. Diese Ableitung wird daraufhin durch die Verarbeitungsstation **158** ausgeführt und enthält die Auflösung der Gleichungen **4**, **8**, **14** und **16** und/oder deren Hilfsgleichungen durch das Vorhersagemodell **20**, wie oben erläutert wurde.

**[0064]** Natürlich gibt es ein unterschiedliches Konvergenzkriterium/verschiedene Konvergenzkriterien, die in der ersten Schleife **156** enthalten sein können. Die Konvergenz kann z. B. in der ersten Schleife **156** unter Verwendung einer binären Suchtechnik auf der Ist-Einlassströmung ( $Q_{IN-C}$ ) basieren. In diesem Fall bleiben bei der Lösung der angegebenen Gleichungen in der Verarbeitungsstation **158** bestimmte Parameter bei der iterativen Ableitung der Einlassströmung ( $Q_{IN}$ ) feststehend, wodurch die festgelegte AC-Infusionsrate ( $I_{SPEC}$ ) erreicht wird, wobei diese Parameter ebenfalls bei der Eingabestation **154** festgelegt werden. Diese enthalten das totale Blutvolumen ( $V_B$ ), das unter Verwendung von Gleichung 10 berechnet werden kann, da die Größe, das Gewicht und das Geschlecht des Spenders bei der zentralen Eingabestation **148** eingegeben werden, und das AC-Verhältnis ( $R$ ), das unter Verwendung von Gleichung 9 berechnet werden kann, da der Hämatokrit-Wert ( $H$ ) des Spenders bestimmt worden ist oder auf einen bestimmten Wert festgelegt werden kann. Darüber hinaus bleibt die Gesamtprozedurdauer ( $t_p$ ) bei jeder iterativen Ableitung der Einlassströmung ( $Q_{IN}$ ), die der festgelegten AC-Infusionsrate ( $I_{SPEC}$ ) in der ersten Schleife **156** zugeordnet ist, feststehend. Da jedoch die Gesamtprozedurdauer ( $t_p$ ) bei einer produktbasierten Optimierung nicht bekannt ist und daher bei der Eingabestation **154** nicht festgelegt werden kann, wird anfangs eine Ist-Gesamtprozedurdauer ( $t_{p-C}$ ) angenommen (diese Annahme ist z. B. in dem Optimierungsmodell **152** konfiguriert, und da in dem Vorhersagemodell **20**, wie oben angemerkt wurde, ein Bereich von Gesamtprozedurdauern bereitgestellt wird, wird in diesem Abschnitt des Optimierungsmodells **152** üblicherweise die mittlere Gesamtprozedurdauer ( $t_p$ ) als die Ist-Anfangsgesamtprozedurdauer ( $t_{p-C}$ ) konfiguriert). Die Bezeichnung "Ist" wird in diesem Fall für die Gesamtprozedurdauer verwendet, da das Optimierungsmodell **152** für eine Einstellung der Gesamtprozedurdauer nach jeder iterativen Bestimmung der Einlassströmung ( $Q_{IN}$ ) dient, die in der zweiten Schleife **160** die festgelegte AC-Infusionsrate ( $I_{SPEC}$ ) bereitstellt, um, wie im Folgenden genauer erläutert wird, bei einer produktbasierten Optimierung bei Bedarf den Soll-Ausstoß ( $Y$ ) zu erreichen.

**[0065]** Die Konvergenz bei der binären Suchtechnik auf der Grundlage der Einlassströmung kann im Allgemeinen durch Annehmen eines Istwertes für die Einlassströmung ( $Q_{IN-C}$ ), Berechnen eines Ist-Plasmasammelfaktors ( $P_C$ ) unter Verwendung der Ist-Gesamtprozedurdauer ( $t_{p-C}$ ), Berechnen einer Ist-AC-Infusionsrate ( $I_C$ ) unter Verwendung der Ist-Einlassströmung ( $Q_{IN-C}$ ) und des Ist-Plasmasammelfaktors ( $P_C$ ) und Einstellen der Ist-Einlassströmung ( $Q_{IN-C}$ ) (bei der Parameter-Aktualisierung in der ersten Schleife **156**) in Übereinstimmung mit der ausgewählten binären Suchtechnik, bis eine vorgegebene Konvergenz zwischen den zwei letzten Werten für die Ist-Einlassströmung ( $Q_{IN-C}$ ) vorhanden ist (d. h. bis die Differenz zwischen den beiden letzten Werten von  $Q_{IN-C}$  kleiner als ein vorgegebener Betrag ist, d. h., bis das Konvergenzkriterium erfüllt ist), sichergestellt werden. Bei einer binären Suchtechnik gibt es immer Konvergenz (d. h. das Konvergenzkriterium wird immer erfüllt), so dass das Optimierungsmodell **152** die erste Schleife **156** immer verlässt und in die zweite Schleife **160** eintritt.

**[0066]** Als eine Alternative zu dem angegebenen Konvergenzkriterium/zu den angegebenen Konvergenzkriterien auf der Grundlage der Einlassströmung und der angegebenen binären Suchtechnik besteht eine andere Möglichkeit darin, die Konvergenz auf die festgelegte AC-Infusionsrate ( $I_{SPEC}$ ) zu beziehen und eine iterative Ableitung zu verwenden, um die Soll-Einlassströmung ( $Q_{IN}$ ) zu bestimmen. In diesem Fall wird die erste Schleife **156** ebenfalls verwendet, um die Einlassströmung ( $Q_{IN}$ ), die die festgelegte AC-Infusionsrate ( $I_{SPEC}$ ) bei der Verarbeitungsstation **158** bereitstellt, aus bestimmten festgelegten Parametern iterativ noch einmal abzuleiten. Das heißt, die erste Schleife **156** dient weiterhin der Maximierung der Einlassströmung ( $Q_{IN}$ ) anhand der festgelegten AC-Infusionsrate ( $I_{SPEC}$ ), die dem Spender **14** zugeordnet werden sollte. Dies erfolgt wiederum hauptsächlich durch die Lösung der Gleichungen 4, 8, 14 und 16 und/oder deren Hilfsgleichungen durch das oben erläuterte Vorhersagemodell **20**.

**[0067]** Für die Lösung der oben angegebenen Gleichungen in Bezug auf das Konvergenzkriterium auf der Grundlage der Infusionsrate bleiben bestimmte Parameter bei der iterativen Ableitung der Einlassströmung ( $Q_{IN}$ ) feststehend, wodurch in der ersten Schleife **156** die festgelegte AC-Infusionsrate ( $I_{SPEC}$ ) erreicht wird und diese Parameter außerdem bei der Eingabestation **154** festgelegt werden. Diese enthalten die festgelegte AC-Infusionsrate ( $I_{SPEC}$ ), die bekannt ist und üblicherweise ein Maximalwert für den Spender **14** ist, das totale Blutvolumen ( $V_B$ ), das unter Verwendung von Gleichung 10 berechnet werden kann, da Größe, Gewicht und Geschlecht des Spenders **14** in die zentrale Eingabestation **148** eingegeben werden, und das AC-Verhältnis ( $R$ ), das unter Verwendung von Gleichung 9 berechnet werden kann, da der Hämatokrit-Wert ( $H$ ) des Spenders **14** in Übereinstimmung mit dem oben Stehenden (z. B. über eine Direktanalyse mit einem Zellenzähler) bestimmt und anschließend in die zentrale Eingabestation **148** eingegeben worden ist oder als modifizierte Eingabedaten eingegeben werden kann. Darüber hinaus bleibt ( $t_p$ ) bei jeder iterativen Ableitung der Einlassströmung ( $Q_{IN}$ ), die der festgelegten AC-Infusionsrate ( $I_{SPEC}$ ) zugeordnet ist, feststehend. Allerdings ist die Gesamtprozedurdauer ( $t_p$ ) im Fall einer produktbasierten Optimierung wieder nicht bekannt und kann daher nicht bei der Eingabestation **154** festgelegt werden. Daher wird anfangs eine Ist-Gesamtprozedurdauer ( $t_{p,c}$ ) angenommen (wobei diese Annahme z. B. in dem Optimierungsmodell **152** konfiguriert wird und in die erste Schleife **156** des Optimierungsmodells üblicherweise die mittlere Gesamtprozedurdauer ( $t_p$ ) **152** konfiguriert wird, da in dem Vorhersagemodell **20**, wie oben angegeben wurde, ein Bereich der Gesamtprozedurdauern bereitgestellt wird). Die Bezeichnung "Ist-" für die Gesamtprozedurdauer wird aus den oben angegebenen Gründen in Bezug auf die Einstellung der Gesamtprozedurdauer in der zweiten Schleife **160** verwendet, falls diese den Soll-Ausstoß ( $Y$ ) erreichen muss.

**[0068]** Die Lösung der Gleichungen 4, 8, 14 und 16 erfordert außerdem, dass bestimmte Werte für einige der restlichen Parameter angenommen werden, während nochmals weitere Parameter aus dieser Annahme abgeleitet werden. In diesem Fall wird eine iterative Prozedur verwendet, wobei in den nächsten iterativen Berechnungen aktualisierte Werte/Ist-Werte verwendet werden. Alle Parameter, die sich bei jeder Iteration der ersten Schleife **156** ändern, sind hier mit einem Index "c" bezeichnet, um anzugeben, dass der neueste Ist-Wert zu verwenden ist. Obgleich die Ableitung dieser Einlassströmung ( $Q_{IN}$ ), die die festgelegte AC-Infusionsrate ( $I_{SPEC}$ ) erzeugt, über die Gleichungen 4, 8, 14 und 16 auf eine Vielzahl von Arten ausgeführt werden kann, besteht eine Möglichkeit darin, einen Ist-Wert für den Plasmasammelfaktor ( $P_c$ ) anzunehmen, anschließend unter Verwendung der festgelegten AC-Infusionsrate ( $I_{SPEC}$ ) die Ist-Einlassströmung ( $Q_{IN,c}$ ) zu berechnen, dann den Ist-Ausstoß ( $Y_c$ ) zu berechnen, daraufhin unter Verwendung des Ist-Ausstoßes ( $Y_c$ ) den Ist-Plasmasammelfaktor ( $P_c$ ) zu berechnen und diese Prozedur mit den Ist-Werten zu wiederholen, bis eine annehmbare Konvergenz bei der Ist-Einlassströmung ( $Q_{IN,c}$ ) in Bezug auf die festgelegte AC-Infusionsrate ( $I_{SPEC}$ ) vorhanden ist (z. B. dann, wenn das besondere Konvergenzkriterium/die besonderen Konvergenzkriterien erfüllt/eingehalten werden). Wenn auf der Grundlage der Infusionsrate eine annehmbare Konvergenz vorhanden ist, verlässt das Optimierungsmodell **152** die erste Schleife **156** und tritt in die zweite Schleife **160** ein. Als Schutz für Fälle, in denen es keine Konvergenz gibt, kann eine maximale Anzahl von Iterationen für die erste Schleife **156** festgelegt sein (nicht gezeigt).

**[0069]** Die zweite Schleife **160** des Optimierungsmodells **152** ist eine Iteration der Gesamtprozedurdauer ( $t_p$ ). Das heißt, die zweite Schleife **160** ist eine iterative Einstellung der Ist-Gesamtprozedurdauer ( $t_{p,c}$ ). In der zweiten Schleife **160** und bei einer produktbasierten Optimierung wird das Modell **152** ursprünglich niemals bei dem ersten Komparator **162** aussteigen, da die Gesamtprozedurdauer ( $t_p$ ) bei der Eingabestation **154** nicht festgelegt worden ist. Demzufolge geht das Optimierungsmodell **152** zum zweiten Komparator **166** über, wo die Konvergenzkriterien (d. h. mehr als eine Prüfung) aufgestellt werden. Ein Konvergenzkriterium, das bei dem zweiten Komparator **166** geprüft wird, besteht darin, ob der Ist-Ausstoß ( $Y_c$ ) größer oder gleich dem Soll- und festgelegten Ausstoß ( $Y$ ) ist. In diesem Fall kann der Ist-Ausstoß ( $Y_c$ ) für den Vergleich mit dem Soll- und festgelegten Ausstoß ( $Y$ ) anhand der bei der Eingabestation **154** festgelegten Werte, der bei der Verarbeitungsstation **158** abgeleiteten Werte und der Ist-Gesamtprozedurdauer ( $t_{p,c}$ ) berechnet werden (in einigen Fällen kann die-

se Berechnung des Ist-Ausstoßes ( $Y_c$ ) in der ersten Schleife **156** ausgeführt worden sein und braucht in der zweiten Schleife **160** nicht wiederholt zu werden). Wie im Folgenden erläutert wird, verlässt das Modell **152** die zweite Schleife **160** und verlässt tatsächlich den gesamten Durchlauf zum Ausstieg **151**, wenn das Ausstoß-Konvergenzkriterium erfüllt ist. In diesem Fall sind die festgelegten/abgeleiteten Werte "optimal" und die Sammelprozedur könnte in der Vorrichtung **18** unter Verwendung der festgestellten Werte für die verschiedenen Steuerungsparameter ausgeführt werden.

**[0070]** Wenn das Kriterium auf der Grundlage des Ausstoßes bei dem zweiten Komparator **166** nicht erfüllt ist, sucht der zweite Komparator **166** nach einem Konvergenzkriterium auf der Grundlage der Gesamtprozedurdauer, das dem oben in Bezug auf das Kriterium auf der Grundlage der Einlassströmung erläuterten ähnlich sein kann (z. B. unter Verwendung einer binären Suchtechnik, wobei das Konvergenzkriterium dann eine vorgegebene Differenz zwischen den beiden neuesten Ist-Werten der Gesamtprozedurdauer ( $t_{p,c}$ ) ist). Nachdem nach dem ersten Durchlauf der zweiten Schleife **160** das angegebene Kriterium auf der Grundlage des Ausstoßes nicht erfüllt ist und das Konvergenzkriterium der Gesamtprozedurdauer nicht erfüllt ist, wird die Ist-Gesamtprozedurdauer ( $t_{p,c}$ ) eingestellt und das Modell **152** kehrt zur ersten Schleife **156** zurück. Das heißt, jedes Mal, wenn die Ist-Gesamtprozedurdauer ( $t_{p,c}$ ) in der zweiten Schleife **160** eingestellt wird, wird die vollständige erste Schleife **152** wiederholt (d. h. unter Verwendung der Ist-Gesamtprozedurdauer ( $t_{p,c}$ ), die durch die Einstellung in der zweiten Schleife **160** bereitgestellt wird, eine neue Einlassströmung ( $Q_{in}$ ), die der festgelegten AC-Infusionsrate ( $I_{SPEC}$ ) zugeordnet ist, abgeleitet). In der zweiten Schleife **160** könnte ein anderes Konvergenzkriterium/könnten andere Konvergenzkriterien verwendet werden, wie etwa das Festlegen einer maximalen Anzahl von Iterationen, die von der zweiten Schleife **160** ausgeführt werden sollen.

**[0071]** Wenn das Kriterium auf der Grundlage des Ausstoßes in der zweiten Schleife **160** nicht erfüllt ist und das Konvergenzkriterium auf der Grundlage der Gesamtprozedurdauer bei dem zweiten Komparator **166** in der zweiten Schleife **160** erfüllt ist, verlässt das Optimierungsmodell **152** die zweite Schleife **160** und tritt in die dritte Schleife **164** ein. Die dritte Schleife **164** ist eine iterative Einstellung des AG-Verhältnisses ( $R$ ). Allerdings greift das Modell **152** anfangs auf den dritten Komparator **169** zu, wenn Konvergenzkriterien (d. h. mehr als ein Kriterium) geprüft werden. Ein Konvergenzkriterium ist wieder das oben angegebene Kriterium auf der Grundlage des Ausstoßes. Wenn dieses Kriterium auf der Grundlage des Ausstoßes wiederum nicht erfüllt ist, wird im dritten Komparator **169** ein Konvergenzkriterium auf der Grundlage des AC-Verhältnisses geprüft. Dieses kann dem oben erläuterten Kriterium auf der Grundlage der Einlassströmung ähnlich sein (z. B. unter Verwendung einer binären Suchtechnik, wobei sich das Konvergenzkriterium auf die beiden neuesten Ist-Werte des AC-Verhältnisses bezieht). Nachdem beim ersten Durchlauf der dritten Schleife **164** das Kriterium auf der Grundlage des Ausstoßes nicht erfüllt ist und das Konvergenzkriterium auf der Grundlage des AC-Verhältnisses nicht erfüllt ist, wird das AC-Verhältnis eingestellt und kehrt das Optimierungsmodell **152** zur ersten Schleife **152** zurück. Das heißt, jedes Mal, wenn das AC-Verhältnis ( $R$ ) in der dritten Schleife **164** eingestellt wird, werden die erste und die zweite Schleife **156**, **160** jeweils vollständig wiederholt. In der dritten Schleife **164** könnten ein anderes Konvergenzkriterium/andere Konvergenzkriterien wie etwa die Festlegung einer maximalen Anzahl von Iterationen der dritten Schleife **164** verwendet werden.

**[0072]** Falls das Konvergenzkriterium auf der Grundlage des Ausstoßes in der zweiten bzw. in der dritten Schleife **160**, **164** und in dem zweiten bzw. in dem dritten Komparator **166**, **169** nicht erfüllt ist und das Konvergenzkriterium auf der Grundlage des AC-Verhältnisses bei dem dritten Komparator **169** in der dritten Schleife **164** erfüllt ist, verlässt das Optimierungsmodell **152** die dritte Schleife **164** und tritt in die vierte Schleife **168** ein. Die vierte Schleife **168** ist eine iterative Einstellung der festgelegten AC-Infusionsrate ( $I_{SPEC}$ ). Allerdings tritt das Optimierungsmodell **152** anfangs in den vierten Komparator **170** ein, wo die Konvergenzkriterien (d. h. mehr als ein Konvergenzkriterium) geprüft werden. Ein Konvergenzkriterium ist das erwähnte Konvergenzkriterium auf der Grundlage des Ausstoßes. Falls das erwähnte Konvergenzkriterium auf der Grundlage des Ausstoßes bei dem vierten Komparator **170** nicht erfüllt ist, wird bei dem vierten Komparator **170** ein Kriterium auf der Grundlage der AC-Infusionsrate geprüft. Dies kann ähnlich dem oben diskutierten Kriterium auf der Grundlage der Einlassströmung (z. B. unter Verwendung einer binären Suchtechnik, wobei das Konvergenzkriterium die zwei neuesten Ist-Werte der AC-Infusionsrate sind) sein. Nachdem nach dem ersten Durchlauf der vierten Schleife **168** das Kriterium auf der Grundlage des Ausstoßes nicht erfüllt war und das Konvergenzkriterium auf der Grundlage der AC-Infusionsrate nicht erfüllt war, wird die AC-Infusionsrate eingestellt und kehrt das Modell **152** zu der ersten Schleife **152** zurück. Das heißt, jedes Mal, wenn die festgelegte AC-Infusionsrate ( $I_{SPEC}$ ) eingestellt wird, wird die Gesamtheit der ersten, zweiten und dritten Schleife **156**, **160**, **164** in dieser Reihenfolge wiederholt (wobei das AC-Verhältnis bei jeder Iteration der vierten Schleife **168** auf seinen Anfangswert zurückgesetzt wird, wie er in die Eingabestation **154** eingegeben worden ist). In der vierten Schleife **168** kann ein anderes Konvergenzkriterium/können andere Konvergenzkriterien wie etwa die Festlegung einer Maximalzahl von Iterationen der vierten Schleife **168** verwendet werden. In Fällen, in denen die festgelegte AC-Infusions-

rate ( $I_{SPEC}$ ) tatsächlich die maximale AC-Infusionsrate ist, wird die vierte Schleife **168** üblicherweise nur ein einziges Mal mit einer einmaligen Erhöhung der AC-Infusionsrate von z. B. 20 % (kann z. B. durch die Einrichtung konfiguriert werden) ausgeführt.

**[0073]** Wenn in den vorstehenden Schleifen die Konvergenzkriterien auf der Grundlage des Ausstoßes erfüllt sind, verlässt sie das Optimierungsmodell **152**, wenn die Kriterien erfüllt sind, zum Ausstieg **151**, wobei die festgelegten/abgeleiteten Werte (d. h. Ist-Werte) für die verschiedenen Prozesssteuerungsparameter zur Ausführung der Sammelprozedur für die Vorrichtung **18** bereitgestellt werden können. Allerdings kann es wie etwa dann, wenn sie das Optimierungsmodell **152** anhand dessen, dass das Konvergenzkriterium auf der Grundlage der AC-Infusionsrate erfüllt ist, zum Austritt **151** verlässt, Fälle geben, wo keine Optimierung stattfindet.

**[0074]** Das Optimierungsmodell **152** kann ebenfalls für eine Zeitoptimierung verwendet werden. Das heißt, das Optimierungsmodell leitet durch Maximierung wenigstens eines der Prozessparameter optimale Prozessparameter für eine vorgegebene Gesamtprozedurdauer ( $t_p$ ) ab, um die Blutplättchensammlung (oder für andere Blutkomponententypen) zu maximieren. In diesem Fall führt das Optimierungsmodell **152** nur die erste Schleife **156** aus, um unter Verwendung der Eingabegesamtprozedurdauer ( $t_p$ ) in dieser iterativen Ableitung anstelle der oben erwähnten angenommenen Gesamtprozedurdauer ( $t_p$ ) die Einlassströmung ( $Q_{IN}$ ) abzuleiten, die einer festgelegten AC-Infusionsrate ( $I_{SPEC}$ ) (üblicherweise ein Maximalwert) zugeordnet ist. Wenn es wie oben in der produktbasierten Optimierung definiert eine akzeptable Konvergenz gibt, so dass das Modell **152** die erste Schleife **156** verlässt, kann in der ersten Schleife **156** der Ist-Ausstoß ( $Y_c$ ) berechnet werden (wobei er aber bereits wieder in der ersten Schleife **156** bei der Verarbeitungsstation **158** berechnet worden sein kann, so dass keine weitere Berechnung erforderlich ist), wobei das Konvergenzkriterium bei dem ersten Komparator **162** erfüllt ist, wenn in die zweite Schleife **160** eingetreten wird (d. h., wenn in einer zeitbasierten Optimierung bei der Eingabestation **154** eine Gesamtprozedurdauer festgelegt wird, tritt das Modell **152**, wenn es in die zweite Schleife **158** eintritt, aus). Im Ergebnis sind die Einlassströmung ( $Q_{IN}$ ) und die AC-Infusionsrate ( $I$ ) optimal, wobei die Sammelprozedur mit diesen Werten ausgeführt werden kann.

**[0075]** In Fig. 7 ist ein weiteres Optimierungsmodell dargestellt, das sowohl für produktbasierte als auch für zeitbasierte Optimierungen verwendet werden kann. Wie im Fall des Optimierungsmodells **152** kann das Optimierungsmodell **172** mit dem Vorhersagemodell **20** verbunden sein oder das Vorhersagemodell **20** tatsächlich integral enthalten, so dass im Folgenden auf die Gleichungen 1–22 Bezug genommen wird. Im Allgemeinen beruht das Optimierungsmodell **172** auf dem Prinzip, dass eine Optimierung stattfindet, wenn in der Ableitung verschiedener Prozesssteuerungsparameter eine optimale Einlassströmung ( $Q_L$ ) verwendet wird, die einer optimalen Systemsammlung effizient zugeordnet ist. Anhand von Fig. 8 ist eine repräsentative Einlassströmungs-( $Q_{IN}$ )/Ausstoß-( $Y$ )-Kurve dargestellt, die die optimale Einlassströmung ( $Q_L$ ) zeigt, die dem maximalen Ausstoß ( $Y_{MAX}$ ) zugeordnet ist. Diese optimale Einlassströmung ( $Q_L$ ) ist mathematisch durch die unten dargestellte Gleichung 23 ausgedrückt, die sich aus Differenzieren von Gleichung 4 des Vorhersagemodells **20** nach der Einlassströmung ( $Q_{IN}$ ) ergibt. Wie gewürdigt werden sollte, kann die optimale Einlassströmung mathematisch auf folgende Weise ausgedrückt werden, wo in dem zugeordneten Vorhersagemodell verschiedene Algorithmen (ob auf der Grundlage der Sammlung von anderen Blutkomponenten als Blutplättchen, verschiedener Sammelvorrichtungen oder alternativer Ableitungen der verschiedenen Parameter mit derselben Sammelprozedur und -vorrichtung) verwendet werden.

$$Q_L = \left( \frac{C_1}{2C_2} \right) e^{-9,91(1-1/R)H} - C_3 \quad (23)$$

$$C_3 = \frac{1}{2(t_p / K_7 - 1/K_9)}, \quad \begin{array}{l} Q_0 \geq 45 \text{ für zwei Nadeln ("DN")} \\ \geq 20 \text{ für eine Nadel ("SN")} \end{array} \quad (24)$$

$$= 0, \quad \begin{array}{l} Q_0 < 45 \text{ für DN} \\ < 20 \text{ für SN} \end{array} \quad (25)$$

$$\begin{array}{ll} K_7 = 500 \text{ (DN)} & K_9 = 45 \text{ (DN)} \\ = 215 \text{ (SN)} & = 20 \text{ (SN)} \end{array} \quad (26)$$

$$\begin{array}{l} C_1 = 0,803 \text{ (SN, DN ohne Untersetzung)} \\ = 0,840 \text{ (DN mit Untersetzung)} \end{array} \quad (27)$$

$$C_2 = 4,08 \cdot 10^{-5} (\text{DN})$$

$$= 8,54 \cdot 10^{-5} (\text{SN})$$

(28)

**[0076]** Anhand des Vorstehenden ist die optimale Einlassströmung ( $Q_L$ ) hinsichtlich der Sammelvorrichtung tatsächlich "optimal".

**[0077]** Wieder anhand von Fig. 7 wird das Optimierungsmodell **172** anfangs hinsichtlich einer produktbasierten Optimierung beschrieben, bei der bei der Eingabestation **184** der Soll Ausstoß ( $Y$ ) festgelegt wird. Im Allgemeinen wird die Einlassströmung ( $Q_{IN}$ ), die einer festgelegten AC-Infusionsrate ( $I_{SPEC}$ ) (üblicherweise die maximale AC-Infusionsrate und ebenfalls bei der Eingabestation **184** festgelegt) zugeordnet ist, aus bestimmten anderen festgelegten Parametern iterativ abgeleitet. Insbesondere dann, wenn die maximale AC-Infusionsrate ( $I_{MAX}$ ) und das maximale AC-Verhältnis ( $R_{MAX}$ ) festgelegt werden, ist die Einlassströmung ( $Q_{IN}$ ) in dieser Einlassströmungsberechnung anhand der physiologischen Betrachtungen des Spenders **14** optimal. Dies erfolgt hauptsächlich durch die Lösung der Gleichungen 4, 8, 14 und 16 und/oder deren Hilfsgleichungen durch das oben diskutierte Vorhersagemodell **20**. Zur Lösung dieser Gleichungen bleiben bestimmte Parameter in der iterativen Ableitung der Einlassströmung ( $Q_{IN}$ ) feststehend, was die festgelegte AC-Infusionsrate ( $I_{SPEC}$ ) erzielt, wobei diese Parameter ebenfalls bei der Eingabestation **184** festgelegt werden. Diese enthalten das totale Blutvolumen ( $V_B$ ), das unter Verwendung von Gleichung 10 berechnet werden kann, da die Größe, das Gewicht und das Geschlecht des Spenders in die zentrale Eingabestation **148** eingegeben werden, und das AC-Verhältnis ( $R$ ), das unter Verwendung von Gleichung 9 berechnet werden kann, da der Hämatokrit-Wert ( $H$ ) des Spenders bestimmt worden ist oder auf einen Maximalwert festgelegt werden kann. Darüber hinaus bleibt die Gesamtprozedurdauer ( $t_p$ ) in jeder iterativen Ableitung der Einlassströmung ( $Q_{IN}$ ), die der festgelegten AC-Infusionsrate ( $I_{SPEC}$ ) zugeordnet ist, feststehend. Da die Gesamtprozedurdauer ( $t_p$ ) im Fall einer produktbasierten Optimierung nicht bekannt ist und somit nicht bei der Eingabestation **184** festgelegt werden kann, wird aber anfangs eine Ist-Gesamtprozedurdauer ( $t_{p,c}$ ) angenommen (wobei diese Annahme z. B. in das Optimierungsmodell **172** konfiguriert wird und in diesem Abschnitt des Optimierungsmodells **172** üblicherweise die mittlere Gesamtprozedurdauer ( $t_p$ ) als die Anfangs-Ist-Gesamtprozedurdauer ( $t_{p,c}$ ) konfiguriert wird, da in dem Vorhersagemodell **20** wie oben angemerkt ein Bereich von Gesamtprozedurdauern vorgesehen ist). Die Bezeichnung "Ist" wird in diesem Fall für die Gesamtprozedurdauer verwendet, da das Optimierungsmodell **172** für eine Einstellung der Gesamtprozedurdauer nach jeder iterativen Bestimmung der Einlassströmung ( $Q_{IN}$ ) dient, die die festgelegte AC-Infusionsrate ( $I_{SPEC}$ ) bereitstellt, um, wie im Folgenden genauer erläutert wird, bei einer produktbasierten Optimierung bei Bedarf den Soll-Ausstoß ( $Y$ ) zu erreichen.

**[0078]** Die Lösung der Gleichungen 4, 8, 14 und 16 erfordert außerdem, dass für bestimmte verbleibende Parameter anfangs bestimmte Werte angenommen werden. In diesem Fall wird bei der Lösung der Ausstoßgleichung (Gleichung 4) (und einschließlich deren Hilfsgleichungen wie oben angemerkt) eine iterative Prozedur verwendet, wobei in der nächsten iterativen Berechnung bzw. in den nächsten iterativen Berechnungen bei der Verarbeitungsstation **188** aktualisierte Werte verwendet werden. Obgleich die Ableitung dieser Einlassströmung ( $Q_{IN}$ ), die die festgelegte (üblicherweise maximale) AC-Infusionsrate ( $I_{SPEC}$ ) erzeugt, über die Gleichungen 4, 8, 14 und 16 auf eine Vielzahl von Arten ausgeführt werden kann, besteht eine Möglichkeit darin, einen Ist-Wert für den Plasmasammelfaktor ( $P$ ) anzunehmen, anschließend unter Verwendung der festgelegten AC-Infusionsrate ( $I_{SPEC}$ ) die Ist-Einlassströmung ( $Q_{IN,c}$ ) zu berechnen, daraufhin den Ist-Ausstoß ( $Y_c$ ) zu berechnen, daraufhin unter Verwendung des Ist-Ausstoßes ( $Y_c$ ) den Ist-Plasmasammelfaktor ( $P_c$ ) zu berechnen und diese Prozedur mit den aktualisierten Parametern zu wiederholen, alles innerhalb der Bearbeitungsstation **188**, bis bei der Ist-Einlassströmung ( $Q_{IN,c}$ ) in Bezug auf die festgelegte AC-Infusionsrate ( $I_{SPEC}$ ) eine annehmbare Konvergenz vorhanden ist.

**[0079]** Außer der Berechnung der Ist-Einlassströmung ( $Q_{IN,c}$ ), die der festgelegten AC-Infusionsrate ( $I_{SPEC}$ ) zugeordnet ist, wird bei der Verarbeitungsstation **192** die oben diskutierte optimale Einlassströmung ( $Q_L$ ) berechnet. Folglich kann bei dem ersten Komparator **176** ein Vergleich zwischen der Ist-Einlassströmung ( $Q_{IN,c}$ ), die in der oben beschriebenen Weise abgeleitet wurde, und der optimalen Einlassströmung ( $Q_L$ ) vorgenommen werden. Wenn die Ist-Einlassströmung ( $Q_{IN,c}$ ) bei dem ersten Komparator **176** kleiner als die optimale Einlassströmung ( $Q_L$ ) ist, sind die festgelegten Werte für die verschiedenen Parameter, die der Einlassströmung ( $Q_{IN}$ ) zugeordnet sind, "optimal", d. h. das AC-Verhältnis ( $R$ ) und die AC-Infusionsrate ( $I$ ), die bei der Eingabestation **184** festgelegt worden sind. Anschließend wird der Ist-Ausstoß ( $Y_c$ ) (der bei der Verarbeitungsstation **188** bei der Ableitung der Ist-Einlassströmung ( $Q_{IN,c}$ ) berechnet wurde, die der festgelegten AC-Infusionsrate ( $I_{SPEC}$ ) zugeordnet ist) bei dem zweiten Komparator **180** mit dem Einlassausstoß ( $Y$ ) verglichen. Falls es zwischen diesen Ausstoßwerten eine akzeptable Konvergenz gegeben hat, ist die Ist-Gesamtprozedurdauer ( $t_{p,c}$ ) ebenfalls "optimal". Dagegen wird dann, wenn es zwischen diesen Ausstoßwerten keine akzeptable Konvergenz gegeben hat, die Ist-Gesamtprozedurdauer ( $t_{p,c}$ ) bei der Einstellstation **196** eingestellt und die vorstehende iterative

Ableitung der Ist-Einlassströmung ( $Q_{IN-C}$ ), die der festgelegten AC-Infusionsrate ( $I_{SPEC}$ ) zugeordnet ist, wiederholt (d. h. unter Verwendung der anfangs festgelegten AC-Infusionsrate ( $I_{SPEC}$ ) und der neu eingestellten Ist-Gesamtprozedurdauer ( $t_{p-C}$ ) iterativ in der oben beschriebenen Weise eine neue Ist-Einlassströmung ( $Q_{IN-C}$ ) abgeleitet), bis diese Konvergenz erreicht ist.

**[0080]** Falls wieder anhand des ersten Komparators **176** die Ist-Einlassströmung ( $Q_{IN-C}$ ), die der festgelegten AC-Infusionsrate ( $I_{SPEC}$ ) zugeordnet ist, die bei der Verarbeitungsstation **188** abgeleitet wird, größer als die optimale Einlassströmung ( $Q_L$ ) ist, wird bei der Verarbeitungsstation **188** allgemein in der oben beschriebenen Weise (d. h., die anfangs festgelegte AC-Infusionsrate ( $I_{SPEC}$ ) wird in dieser Ableitung ignoriert und iterativ eine Ist-AC-Infusionsrate ( $I_C$ ) abgeleitet, die mit der Einlassströmung ( $Q_L$ ) übereinstimmt) iterativ eine Ist-AC-Infusionsrate ( $I_C$ ) abgeleitet, die dieser besonderen Einlassströmung ( $Q_L$ ) zugeordnet ist. In diesem Fall ist die Ist-Einlassströmung ( $Q_{IN-C}$ ) immer gleich der optimalen Einlassströmung ( $Q_L$ ) bei dem ersten Komparator **176**, wobei dieses Optimierungsmodell **172** anschließend für den Ausstoßvergleich gemäß der oben beschriebenen Prozedur zu dem zweiten Komparator **180** übergeht.

**[0081]** Das Optimierungsmodell **172** kann ebenfalls für eine zeitbasierte Optimierung verwendet werden. In diesem Fall wird bei der Eingabestation **184** die Gesamtprozedurdauer ( $t_p$ ) als eine festgelegte Gesamtprozedurdauer ( $t_{p-SPEC}$ ) festgelegt und somit nicht als eine produktbasierte Optimierung angenommen. Daraufhin geht das Optimierungsmodell **172** mit Ausnahme bei dem zweiten Komparator **180** in der gleichen Weise wie oben hinsichtlich der produktbasierten Optimierung diskutiert vor. Da kein Ausstoß eingegeben wurde, wird bei dem zweiten Komparator **180** kein Ausstoßvergleich vorgenommen. Stattdessen wird bei dem zweiten Komparator **180** ein Gesamtprozedurdauervergleich vorgenommen. Da die Ist-Gesamtprozedurdauer ( $t_{p-C}$ ) in dieser zeitbasierten Optimierung gleich der festgelegten Gesamtprozedurdauer ( $t_{p-SPEC}$ ) eingestellt wurde, bevor das Modell **172** zu der Verarbeitungsstation **188** übergang, steigt das Modell **172** für eine zeitbasierte Optimierung jedes Mal bei dem zweiten Komparator aus.

**[0082]** Außer auf die oben beschriebene produktbasierte und zeitbasierte Optimierung können die Prinzipien der vorliegenden Erfindung auf andere Anwendungen erweitert werden, die sich auf die Verbesserung der Blutkomponentensystemorganisation beziehen. Zum Beispiel kann eine Optimierung in Übereinstimmung mit Prinzipien der vorliegenden Erfindung so erweitert werden, dass sie Spenderorganisationsfragen umfasst. In einem solchen Fall wäre eine weitere "Optimierung", die dem Blutkomponenten-Sammelprozess zugeordnet ist, das Sammeln von Blutkomponenten, wie es durch den vorhandenen Bestand vorgeschrieben wird (d. h. die Verwendung einer Optimierung, wie sie durch den vorhandenen Bestand vorgeschrieben wird (d. h. die Verwendung einer Optimierung als Bestandssteuerung)). Das heißt, Informationen, die sich auf den Bestand der verschiedenen Typen von Blutkomponenten in der Blutbank/in dem Blutzentrum und/oder auf den Bedarf an einer oder an mehreren Blutkomponententypen beziehen, könnten so unterhalten werden, dass spezifische Sammelprozeduren ausgewählt werden können, um an eine niedrige Versorgung mit einem gegebenen Blutkomponententyp und/oder an einen hohen Bedarf an einem solchen Blutkomponententyp anzupassen. Genaue können dann, wenn die Versorgung mit roten Blutkörperchen niedrig und/oder der Bedarf an roten Blutkörperchen hoch ist oder angenommen wird, dass er dies in naher Zukunft sein wird, an die Bedienpersonen Aufforderungen ausgegeben werden, dass während einer gegebenen Zeitdauer nach Möglichkeit von Spendern rote Blutkörperchen zur Sammlung ausgewählt werden sollen. Verwandt damit sind die Optimierungsprinzipien der vorliegenden Erfindung auf die Unterhaltung von Daten über Blutkomponentensammlungen von einem gegebenen Spender anwendbar, so dass eine Bestimmung vorgenommen werden kann, welcher Typ oder welche Typen von Blutkomponenten von einem bestimmten Spender in der Sammelprozedur den maximalen Ausstoß lieferten. Das heißt, von früheren Blutkomponentenspenden können Informationen gesammelt und unterhalten werden, so dass für einen bestimmten Spender eine Bestimmung vorgenommen werden kann, bei welchem Typ oder bei welchen Typen von Blutkomponenten der Spender die Neigung hat, maximale Ausstöße dafür zu erzeugen.

**[0083]** Abgesehen von der vorstehenden Beschreibung der vorliegenden Erfindung in Bezug auf einen Online-Blutkomponenten-Sammelprozess schätzt der Fachmann auf dem Gebiet, dass die Quelle von Blut der Blutkomponenten-Sammelvorrichtung gegenüber deren Empfang direkt von dem Spender von einem (nicht gezeigten) geeigneten Blutbehälter geliefert werden kann, der mit der Blutkomponenten-Sammelvorrichtung **18** verbunden ist. Darüber hinaus kann das Blut natürlich von alternativen Quellen wie etwa von Tieren geliefert werden. Wie in Fig. 3 veranschaulicht ist, kann die beschriebene Blutplättchen-Ernteprozedur darüber hinaus unter Verwendung einer Einnadelkonfiguration ausgeführt werden. Außerdem ist die vorliegende Erfindung auf die Sammlung anderer Typen von Blutkomponenten wie etwa roten Blutkörperchen, weißen Blutkörperchen und/oder Plasma anwendbar und ist weiter auf die gleichzeitige Sammlung mehr als eines Blutkomponententyps anwendbar. Im Fall der Sammlung roter Blutkörperchen und der Optimierung gemäß den Prin-



zipien der vorliegenden Erfindung sollte die Blutgruppe des Spenders bekannt sein und in verschiedenen Algorithmen verwendet werden. Darüber hinaus ist die vorliegende Erfindung nicht darauf beschränkt, dass die Quelle Vollblut ist. Das heißt, die Prinzipien der vorliegenden Erfindung können auf die Entfernung einer Komponente aus irgendeiner Flüssigkeit anwendbar sein.

**[0084]** Die vorstehende Beschreibung der vorliegenden Erfindung ist für Veranschaulichungs- und Beschreibungszwecke dargestellt worden. Darüber hinaus soll die Beschreibung die Erfindung nicht auf die hier offenbarte Form beschränken. Dementsprechend liegen Änderungen und Abwandlungen, die den obigen Lehren und der Sachkenntnis und dem Wissenstand des relevanten Gebiets entsprechen, im Umfang der vorliegenden Erfindung. Ferner sollen die hier beschriebenen Ausführungsformen die besten bekannten Ausführungsarten der Verwirklichung der Erfindung erläutern und ermöglichen, dass ein anderer Fachmann auf dem Gebiet die Erfindung und diese weiteren Ausführungsformen auch mit verschiedenen, durch die besonderen Anwendungen oder Verwendungen der vorliegenden Erfindung erforderlichen, Abwandlungen nutzen kann. Die beigefügten Ansprüche sollen so verstanden werden, dass sie alternative Ausführungsformen in dem durch den Stand der Technik möglichen Umfang enthalten.

### Patentansprüche

1. Verfahren zum Programmieren eines Blutkomponenten-Sammelsystems (2), das anschließend eine Blutkomponente von einem Spender unter Verwendung einer Blutkomponenten-Sammelprozedur sammelt, wobei die Sammelprozedur mehrere Steuerparameter umfasst, **dadurch gekennzeichnet**, dass das Verfahren die folgenden Schritte umfasst:

Bereitstellen biologischer Daten, die sich auf den Spender beziehen; Zuordnen einer Größe zu jedem Steuerparameter wenigstens anhand des Bereitstellungsschrittes;

Optimieren der Größe wenigstens eines der Steuerparameter in Bezug sowohl auf Spenderbeschränkungen als auch auf Systembeschränkungen, wobei der Optimierungsschritt zulässt, eine erste und/oder eine zweite Bedingung zu erfüllen, wobei die erste Bedingung das Sammeln einer vorgegebenen Menge der Blutkomponenten innerhalb einer minimalen Zeitdauer ist und die zweite Bedingung das Sammeln einer maximalen Menge der Blutkomponenten innerhalb einer vorgegebenen Zeitdauer ist;

Eingeben der Größen der Steuerparameter in die Blutkomponenten-Sammelvorrichtung nach dem Optimierungsschritt.

2. Verfahren nach Anspruch 1, das ferner den folgenden Schritt umfasst:

Auswählen eines vorgegebenen Blutkomponententyps anhand eines Bestandes des vorgegebenen Blutkomponententyps und/oder einer Anforderung für den vorgegebenen Blutkomponententyp.

3. Verfahren nach Anspruch 1 oder 2, das ferner den folgenden Schritt umfasst:

Auswählen eines Blutkomponententyps, der von dem Spender gesammelt wird, anhand von Daten, die über den Spender für mehrere Sammelprozeduren, die früher an dem Spender ausgeführt wurden, gehalten werden.

4. Verfahren nach Anspruch 3, bei dem:

die Daten eine Angabe darüber bereitstellen, dass der Spender die Neigung hat, für einen Blutkomponententyp aus dem Auswahlschritt einen höheren Ausstoß als für andere Blutkomponententypen zu erzeugen.

5. Verfahren nach einem der vorhergehenden Ansprüche, das ferner den folgenden Schritt umfasst:

Erhalten von Daten bezüglich der Sammelprozedur für die Verwendung in nachfolgenden Sammelprozeduren, die unter Verwendung des Spenders ausgeführt werden.

6. Blutkomponenten-Sammelsystem (2), das umfasst:

eine Zentrifugen-Blutkomponenten-Sammelvorrichtung (18), um eine Sammelprozedur auszuführen, die mehrere Steuerparameter umfasst;

Mittel, um biologische Daten bezüglich eines Spenders zu empfangen;

Mittel (144), um jedem der Steuerparameter wenigstens anhand der Bereitstellungsmittel eine Größe zuzuordnen;

Mittel (144), um die Größe wenigstens eines der Steuerparameter in Bezug sowohl auf Spenderbeschränkungen als auch auf Systembeschränkungen zu optimieren, wobei die Optimierungsmittel ermöglichen, eine erste und/oder eine zweite Bedingung zu erfüllen, wobei die erste Bedingung das Sammeln einer vorgegebenen Menge der Blutkomponenten innerhalb einer minimalen Zeitdauer ist und die zweite Bedingung das Sammeln einer maximalen Menge der Blutkomponenten innerhalb einer vorgegebenen Zeitdauer ist;

Mittel (148), um die optimierten Größen der Parameter in die Blutkomponenten-Sammelvorrichtung einzugeben; und

Mittel, um die Sammelprozedur an der Blutkomponenten-Sammelvorrichtung unter Verwendung der Parameter auszuführen, um die Blutkomponenten von dem Spender zu sammeln, um die erste und/oder die zweite Bedingung zu erfüllen.

7. System nach Anspruch 6, das ferner umfasst:

Mittel (148), um einen vorgegebenen Blutkomponententyp anhand eines Bestandes des vorgegebenen Blutkomponententyps und/oder einer Anforderung für den vorgegebenen Blutkomponententyp auszuwählen.

8. System nach Anspruch 6 oder 7, das ferner umfasst:

Mittel (148), um einen von dem Spender zu sammelnden Blutkomponententyp anhand von Daten auszuwählen, die über den Spender für mehrere Sammelprozeduren, die früher unter Verwendung des Spenders ausgeführt wurden, zu halten.

9. System nach Anspruch 8, bei dem:

die Daten eine Angabe darüber bereitstellen, dass der Spender die Neigung hat, für einen Blutkomponententyp von dem Auswahlschritt einen höheren Ausstoß als für andere Blutkomponententypen zu erzeugen.

10. System nach einem der Ansprüche 6 bis 9, das ferner umfasst:

Mittel, um Daten über die Sammelprozedur für die Verwendung in späteren Sammelprozeduren, die unter Verwendung des Spenders ausgeführt werden, zu halten.

Es folgen 8 Blatt Zeichnungen

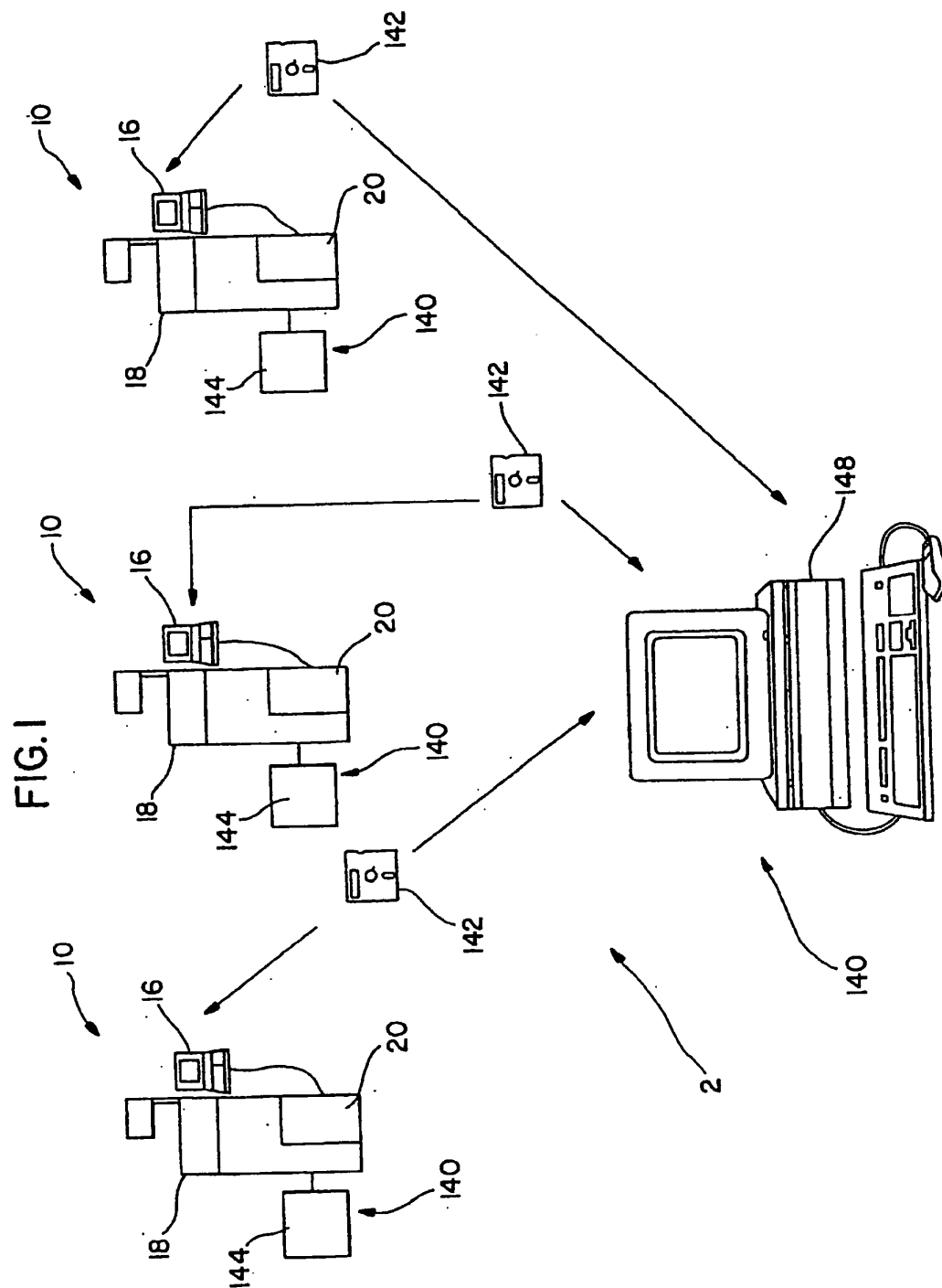


FIG.2

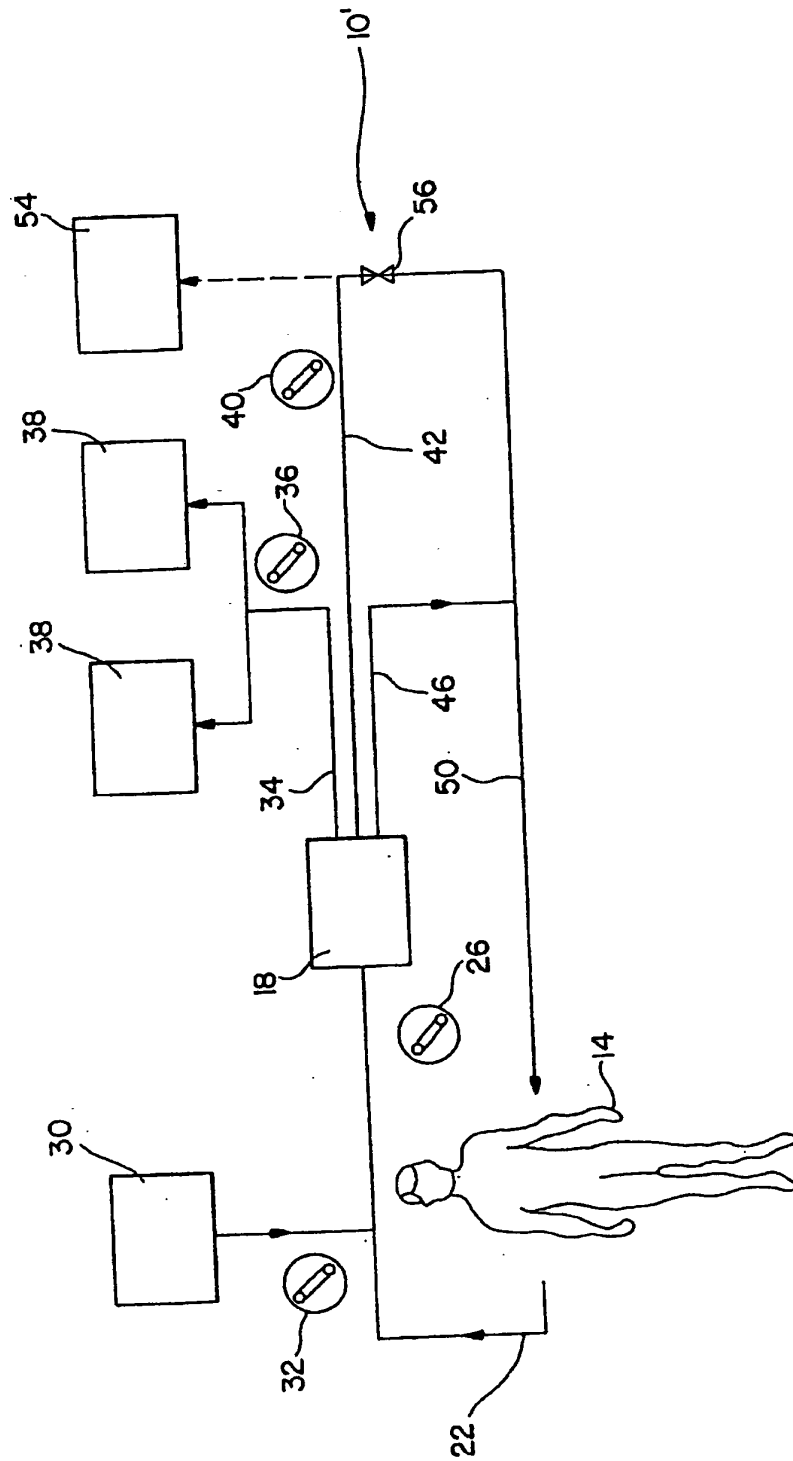


FIG. 3

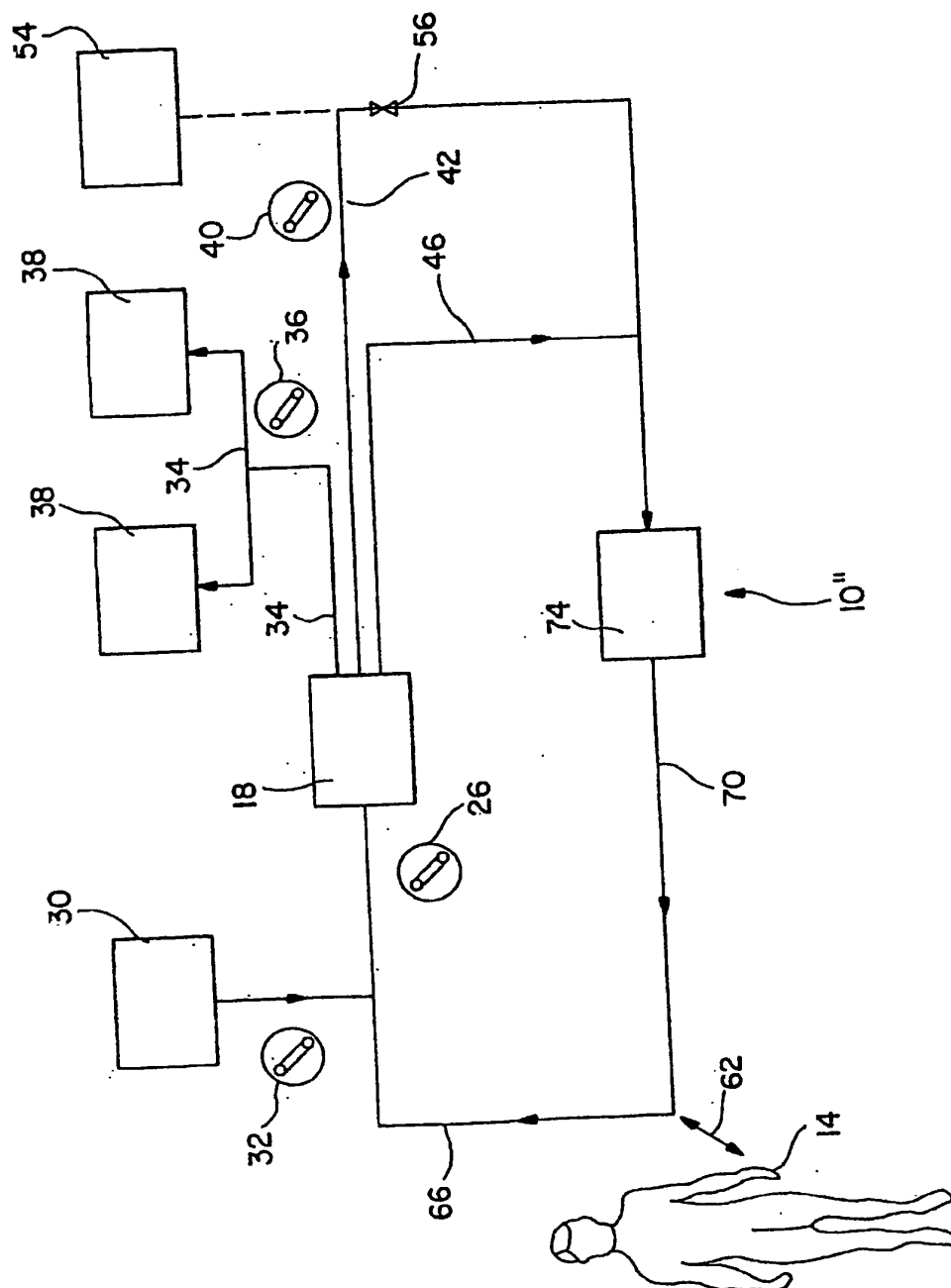


FIG. 4A

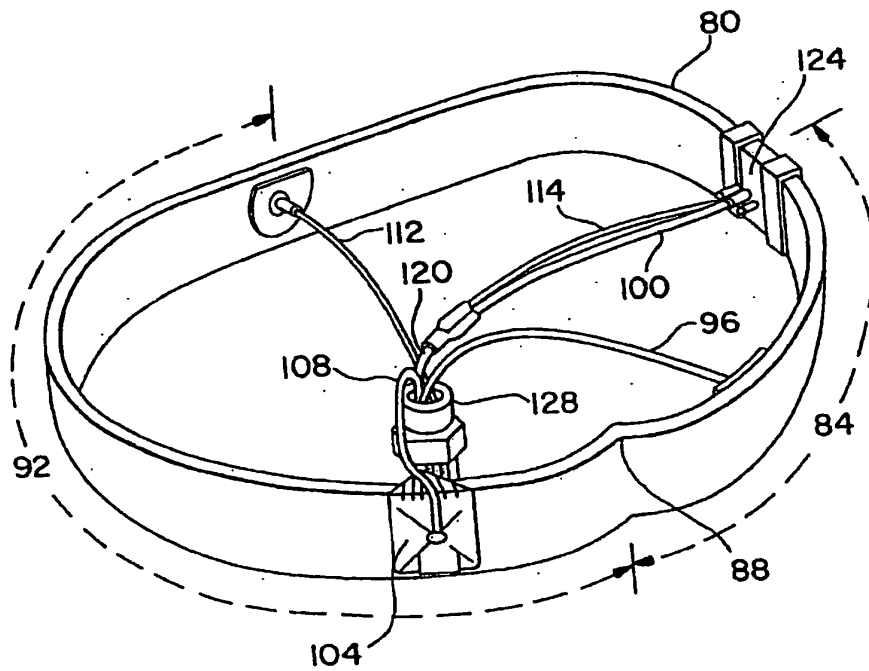


Fig. 5

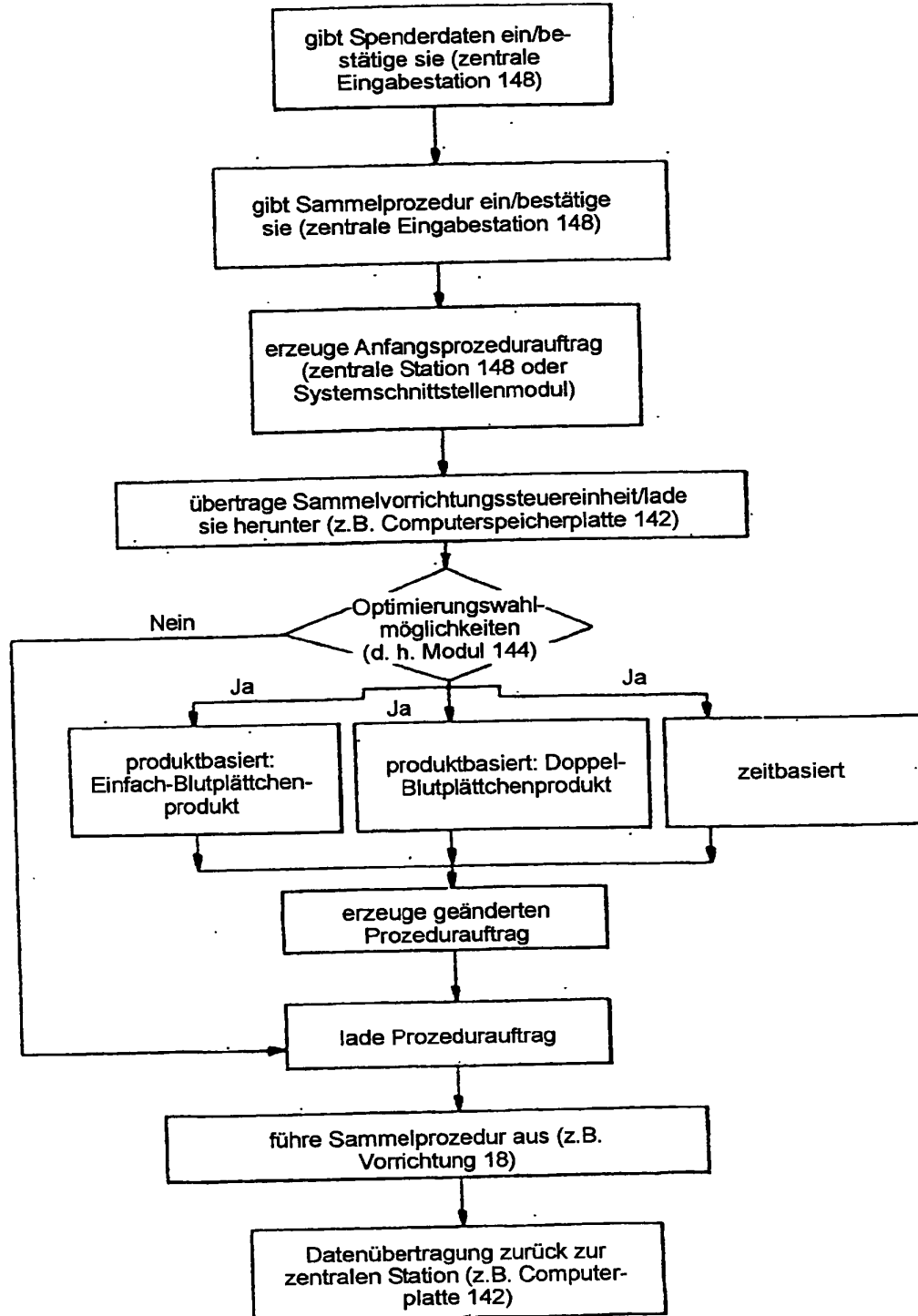


Fig. 6

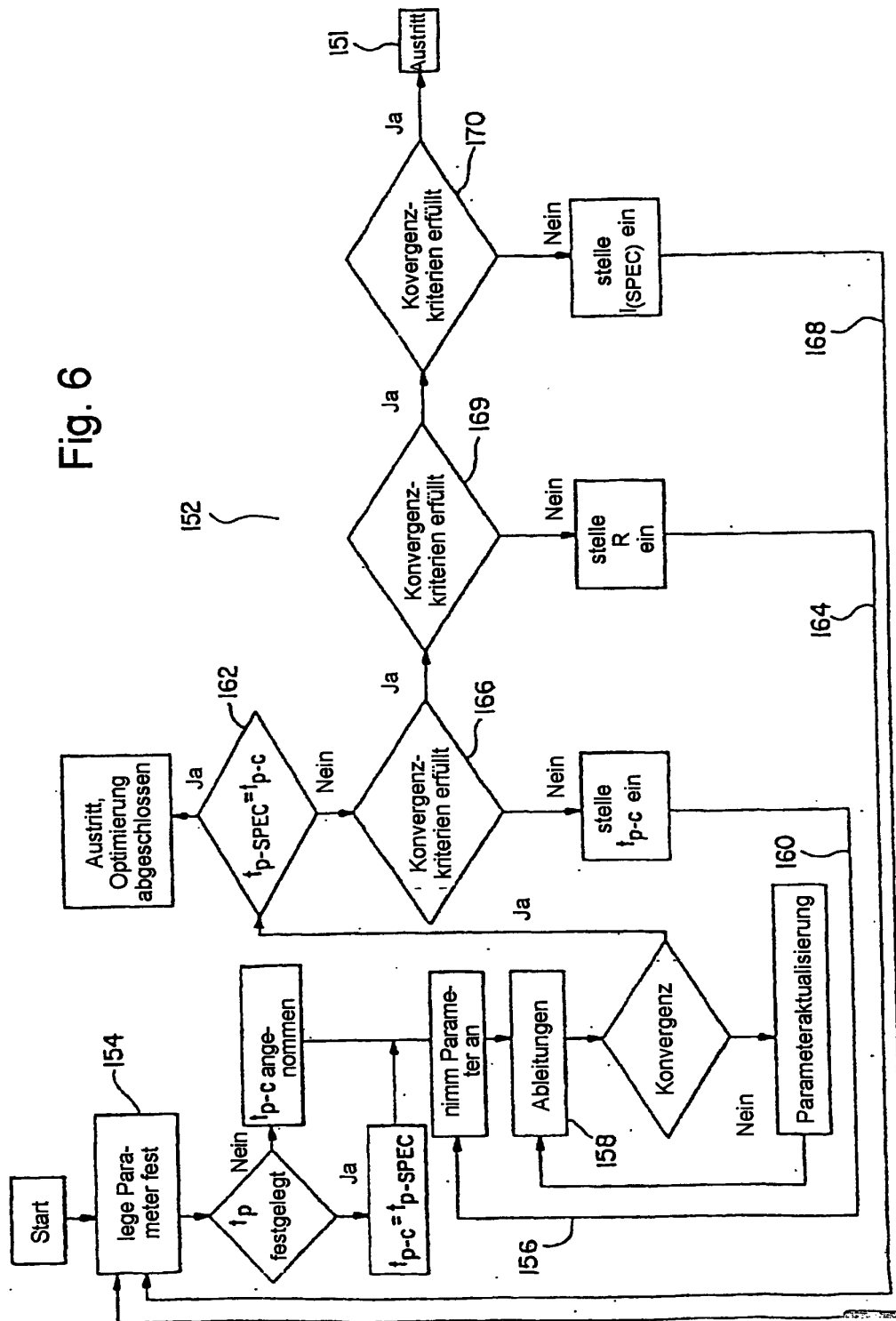




Fig. 7

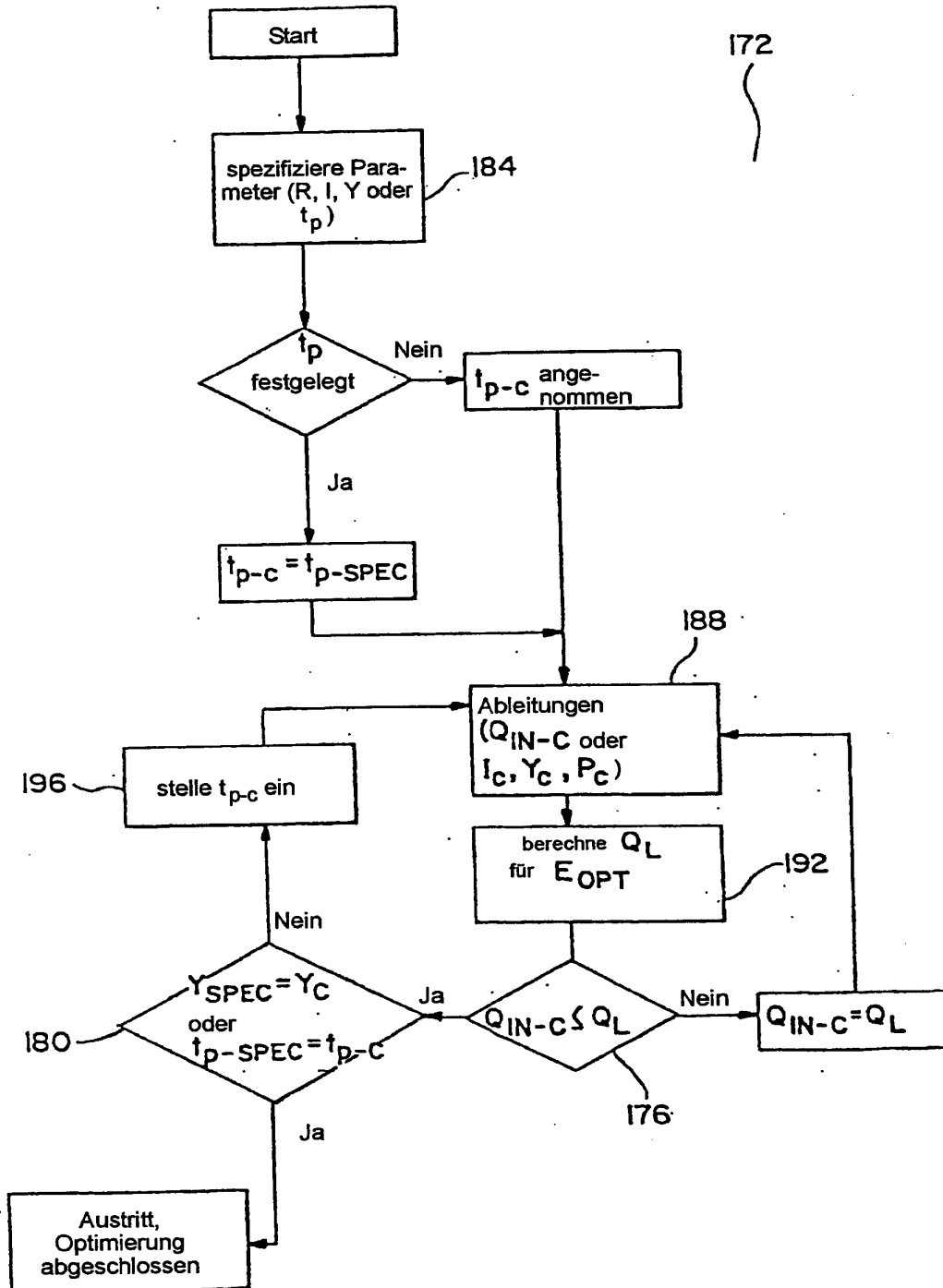
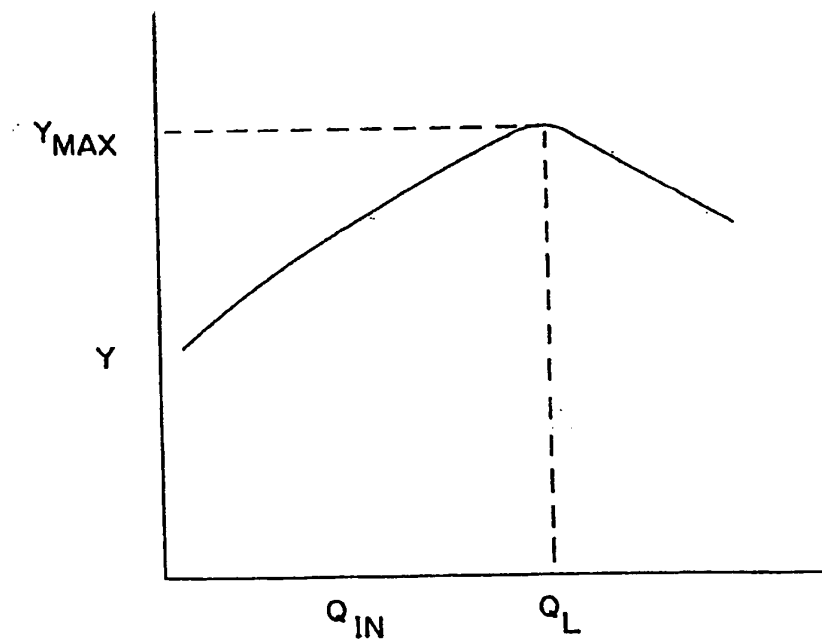


FIG. 8





Espacenet

## Bibliographic data: JP2003516175 (A) — 2003-05-13

**AUTOMATED COLLECTION SYSTEMS AND METHODS FOR OBTAINING RED BLOOD CELLS, PLATELETS, AND PLASMA FROM WHOLE BLOOD**

**Inventor(s):**

**Applicant(s):**

**Classification:** - **international:** A61M1/02; A61M1/36; G01N33/48; A61M1/30; (IPC1-7): A61M1/02; G01N33/48  
 - **cooperative:** A61M1/0222 (EP, US); A61M1/0231 (EP, US); A61M1/30 (EP); A61M1/302 (EP, US); A61M1/303 (EP, US); A61M1/308 (EP, US); A61M1/3603 (EP, US); A61M1/3633 (EP); A61M1/3693 (EP, US); A61M1/3696 (EP, US); A61M2202/0427 (EP); A61M2202/0429 (EP); A61M2205/3393 (EP); A61M2205/60 (EP); A61M2230/207 (EP) [more](#)

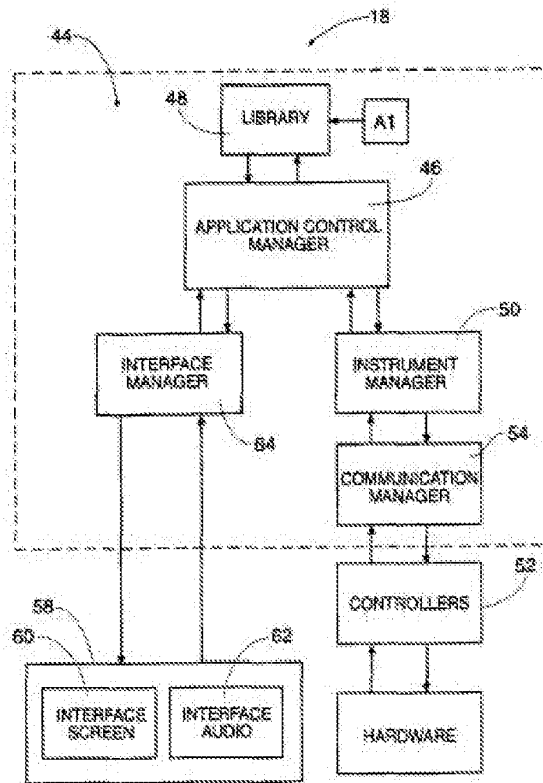
**Application number:** JP20010531449 20001012

**Priority number(s):** US19990419742 19991016 ; WO2000US28206 20001012

**Also published as:** AU1198401 (A) BR0014802 (A) CA2386040 (A1) CN100478038 (C) CN1407907 (A) [more](#)

Abstract not available for JP2003516175 (A)  
 Abstract of corresponding document: WO0128621 (A1)

Blood processing systems and methods separate blood drawn from a donor into red blood cells and platelets. The systems and methods operate in a first mode to collect platelets while returning red blood cells to the donor. The systems and methods operate in a second mode to concurrently collect both platelets and red blood cells without returning platelets or red blood cells to the donor.



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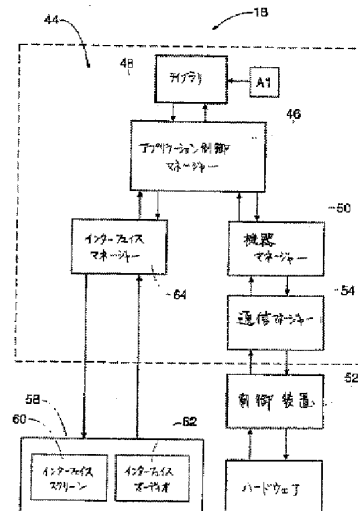
(71) 出願人 バクスター・インターナショナル・インコーポレイテッド  
BAXTER INTERNATIONAL INCORPORATED  
アメリカ合衆国 60015 イリノイ州、  
ディアフィールド、ワン・バクスター・パークウェイ (番地なし)  
(72) 発明者 ピース, ジェニファー エイ.  
アメリカ合衆国 イリノイ 60004, アーリントン ハイ츠, ウッズ ドライブ  
ナンバー 1715 1606  
(74) 代理人 弁理士 山本 秀策 (外2名)

最終頁に続く

(54) 【発明の名称】 全血から赤血球、血小板および血漿を得るための自動収集システムおよび方法

(57) 【要約】

血液処理システムおよび方法は、ドナーから引き出した血液を赤血球と血小板に分離する。これらのシステムおよび方法は、第一モードでは、赤血球をドナーに戻しつつ、血小板を収集するように作動する。これらのシステムおよび方法は、第二モードでは、血小板または赤血球をドナーに戻すことなく、血小板および赤血球の両方を同時に収集するように作動する。1つの実施形態において、本発明は、血液処理システムであって、該システムは、分離チャンバおよび制御装置を含み、該分離チャンバは、ドナーから引き出した血液を赤血球と血小板に分離するように作動し、そして該制御装置は、第一モードにおいて、赤血球を該ドナーに戻しつつ、血小板を収集するように作動し、そして第二モードにおいて、血小板も赤血球も該ドナーに戻すことなく、血小板および赤血球を収集するように作動する、システムである。



**【特許請求の範囲】**

**【請求項1】** 血液処理システムであって、該システムは、分離チャンバおよび制御装置を含み、

該分離チャンバは、ドナーから引き出した血液を赤血球と血小板に分離するように作動し、そして

該制御装置は、第一モードにおいて、赤血球を該ドナーに戻しつつ、血小板を収集するように作動し、そして第二モードにおいて、血小板も赤血球も該ドナーに戻すことなく、血小板および赤血球を収集するように作動する、システム。

**【請求項2】** 請求項1に記載の血液処理システムであって、

ここで、前記分離チャンバが、前記血液から、血小板を実質的に含まない血漿を分離するように作動し、そして

ここで、前記第一モードにおいて、血小板を実質的に含まない該血漿の少なくとも一部が、前記ドナーに戻され、そして前記第二モードにおいて、血小板を実質的に含まない該血漿の全部が、収集されそして該ドナーに戻されない、システム。

**【請求項3】** 血液を引き出してそして該血液を前記ドナーに戻すための単一の針をさらに備える、請求項1に記載の血液処理システム。

**【請求項4】** 血小板から白血球を除去するための要素をさらに備える、請求項1に記載の血液処理システム。

**【請求項5】** 赤血球から白血球を除去するための要素をさらに備える、請求項1に記載の血液処理システム。

**【請求項6】** 赤血球と混合するための血液添加剤溶液の供給源をさらに備える、請求項1に記載の血液処理システム。

**【請求項7】** 前記第一モードおよび第二モードについて血小板の所望の収量を設定するためのインプットをさらに備える、請求項1に記載の血液処理システム。

**【請求項8】** 前記第二モードについて赤血球の所望の収量を設定するためのインプットをさらに備える、請求項1に記載の血液処理システム。

【請求項9】 前記制御装置が、前記第二モード中に収集した前記赤血球の一部を前記ドナーに戻して赤血球の所望の収量を達成する、第三モードで作動可能である、請求項1に記載の血液処理システム。

【請求項10】 血液処理方法であって、該方法は、以下の工程：

ドナーから引き出した血液を赤血球と血小板に分離する工程；および

第一モードにおいて、赤血球を該ドナーに戻しつつ、血小板を収集するように作動する工程；および

第二モードにおいて、血小板濃縮物も赤血球も該ドナーに戻すことなく、血小板および赤血球の両方を同時に収集するように作動する工程、  
を包含する、方法。

【請求項11】 請求項10に記載の血液処理方法であって、該方法は、前記血液から、血小板を実質的に含まない血漿を分離する工程をさらに包含し、

ここで、前記第一モードにおいて、血小板を実質的に含まない該血漿の少なくとも一部が、前記ドナーに戻され、そして前記第二モードにおいて、血小板を実質的に含まない該血漿の全部が、収集されそして該ドナーに戻される、  
血液処理方法。

【請求項12】 前記第一モードおよび第二モード中に収集した前記血小板を、収集した血小板を実質的に含まない前記血漿の少なくとも一部で再懸濁する工程をさらに包含する、請求項11に記載の血液処理方法。

【請求項13】 単一の針を使用して血液を引き出してそして該血液を前記ドナーに戻す工程をさらに包含する、請求項10に記載の血液処理方法。

【請求項14】 前記第一モードおよび第二モード中に収集した血小板から白血球を除去する工程をさらに包含する、請求項10に記載の血液処理方法。

【請求項15】 前記第二モード中に収集した赤血球から白血球を除去する工程をさらに包含する、請求項10に記載の血液処理方法。

【請求項16】 前記第二モード中に収集した赤血球と、血液添加剤溶液とを混合する工程をさらに包含する、請求項10に記載の血液処理方法。

【請求項17】 前記第一モードおよび第二モードについて血小板の所望の収量を設定する工程をさらに包含する、請求項10に記載の血液処理方法。

【請求項18】 前記第二モードについて赤血球の所望の収量を設定する工程をさらに包含する、請求項10に記載の血液処理方法。

【請求項19】 前記第二モード中に収集した前記赤血球の一部を前記ドナーに戻して赤血球の所望の収量を達成する、第三モードで作動する工程をさらに包含する、請求項10に記載の血液処理方法。

【請求項20】 血液処理アセンブリであって、該アセンブリは、以下：

血液源に装着されている、主要経路；

該主要経路に連結された第一分枝経路であって、血液添加剤溶液を保持する収集容器を備える、第一分枝経路；

該第一分枝経路の下流で該主要経路に連結された第二分枝経路であって、第二の収集容器を備える、第二分枝経路；および

該第二の分枝経路中にある、白血球除去フィルター、  
を備える、アセンブリ。

【請求項21】 通気経路をさらに含み、該通気経路が、前記第二の収集容器および前記主要経路に連結されて、前記白血球除去フィルターをバイパスする経路において該第二の収集容器から空気を逃すためにある、請求項20に記載の血液処理アセンブリ。



**【発明の詳細な説明】****【0001】****(発明の分野)**

本発明は、遠心血液処理システムおよび装置に関する。

**【0002】****(発明の背景)**

特定の治療法では、大量の血液成分を輸血する。例えば、化学療法を受けている患者には、日常的に、多数の血小板を輸血する必要がある人もいる。手動血液バッグシステムは、単に、個々のドナーからこれらの多数の血小板を収集する効率的な方法ではない。

**【0003】**

今日では、この要求を満たすために、多数の血小板を収集するのに、オンライン血液分離システムが使用されている。オンラインシステムは、ドナーと共に、連続プロセスで、全血から血小板濃縮物を分離するのに必要な分離工程を実行する。オンラインシステムは、ドナーからの全血の流れを確立し、この流れから所望の血小板を分離し、そして残留している赤血球および血漿をドナーに戻し、全ては、連続的な流れループで行われる。

**【0004】**

オンラインシステムを使用すると、大量の全血（例えば、2.0リットル）が処理できる。その大きな処理容量に起因して、高い収量の濃縮血小板（例えば、流体200mlに懸濁した $4 \times 10^{11}$ 個の血小板）が収集できる。それにもかかわらず、依然として、高い容量のオンライン血液収集環境（血小板および赤血球のような、必要性が大きい細胞血液成分の高い収量が実現できる）での使用に適する様式で、血液成分から赤血球のような細胞リッチな濃縮物を収集するシステムおよび方法をさらに改良する必要がある。

**【0005】****(発明の要旨)**

本発明は、ドナーから引き出した血液を赤血球と血小板に分離する血液処理システムおよび方法を提供する。該システムおよび方法は、第一および第二モード

で作動する。

【0006】

第一作動モードでは、該システムおよび方法は、全血を処理して、そして血小板を収集する。第一モードでは、赤血球は、同時には収集されずに、該ドナーに戻される。

【0007】

第二作動モードでは、該システムおよび方法は、全血を処理し、そして対応するさらなる容量の血小板と共に赤血球を同時に収集する。第二モード中にて、血液成分は、該ドナーに戻されない。

【0008】

1実施態様では、該システムおよび方法はまた、第三モードで作動する。第三作動モードでは、該システムおよび方法は、最終血液容量トリミング (trimming) 機能を実行する。該容量トリミング機能中にて、収集した赤血球容量の一部は、該ドナーに戻ることができる。該容量トリミング機能は、実際に収集した成分容量が目標収集容量を超えないことを保証する。

【0009】

本発明は、その精神または本質的な特徴から逸脱することなく、いくつかの形態で具体化され得る。本発明の範囲は、後述の詳細な説明ではなく、添付の請求の範囲で規定される。これらの請求の範囲と等価の意味および範囲内に入る全ての実施態様は、従って、請求の範囲に包含されると解釈される。本発明は、以下の詳細な説明で述べたかまたは図面で示した部分の構成および配置の詳細には限定されない。本発明は、他の実施態様および種々の他の様式で、実施できる。これらの専門用語および語句は、説明に使用されており、限定と見なすべきではない。

【0010】

(好ましい実施態様の説明)

図1は、概略形態で、自動血液収集手順を実行するためのオンライン血液処理システム10を示す。

【0011】

図示しているように、システム10は、単一針血液収集ネットワークを備えるが、二重針ネットワークもまた、使用できる。

#### 【0012】

##### I. システムの概要

システム10は、耐久性ハードウェア要素の配置を備え、その作動は、処理制御装置18で管理されている。これらのハードウェア要素は、遠心機12を備え、ここで、ドナーからの全血(WB)は、血小板、血漿および赤血球に分離される。使用できる代表的な遠心機は、Brownらの米国特許第5,690,602号で示されており、その内容は、本明細書中で参考として援用されている。

#### 【0013】

これらのハードウェア要素はまた、種々のポンプ（これらは、典型的には、蠕動性である）（P1～P7と命名する）ならびに種々のインラインクランプおよびバルブ（V1～V7と命名する）を備える。もちろん、他の型のハードウェア要素（ソレノイド、圧力モニターなどのようなもの）は、典型的には存在し得るが、図1では図示していない。

#### 【0014】

システム10はまた、典型的には、ある形態のディスポーサブル流体処理アセンブリ14を備え、これは、これらのハードウェア要素と共同で使用される。図示した実施態様では、アセンブリ14は、処理チャンバ16を備え、これらは、2個のステージ24および32を有する。使用中、遠心機12は、処理チャンバ16を回転して、血液成分を遠心分離する。

#### 【0015】

この二段階処理チャンバ16の構成は、変更し得る。例えば、それは、Cullinsらの米国特許第4,146,172号（その内容は、本明細書中で参考として援用されている）で示されそして記載された処理チャンバのような、二重バッグの形態をとることができる。あるいは、この処理チャンバ16は、Brownの米国特許第5,632,893号（その内容は、本明細書中で参考として援用されている）で示され記載したような、細長い二段階一体型バッグの形態をとることができる。

## 【0016】

図示した血液処理システム10では、処理アセンブリ14はまた、流体回路を形成する可撓性チューブのアレイを備える。この流体回路は、処理チャンバ16からおよび処理チャンバ16に流体を運搬する。ポンプP1～P7およびバルブV1～V7は、このチュービングと係合して、この流体の流れを所定様式で管理する。この流体回路は、さらに、処理中に液体を分配しそして受容する多数の容器（C1～C5と命名されている）を備える。

## 【0017】

制御装置18は、アセンブリ14を使用する1つまたはそれ以上の処理作業を実行するために、種々のハードウェア要素の操作を管理する。制御装置18はまた、血液成分の分離および収集を最大化においてオペレーターを補助する、処理条件および出力情報のリアルタイム評価を実行する。

## 【0018】

システム10は、多様な種類の血液分離プロセスを達成するように、構成され得る。図1は、単一のドナーから、以下の(i)、(ii)および(iii)を収集するために、単一針22を使用して自動手順を実行するように構成されたシステム10を示す：(i)（例えば、2治療単位より多い）血漿（PC）に懸濁した所望の収量の濃縮された血小板（これは、（所望の場合に）白血球を実質的に含まないように提供され得る）；(ii)（例えば、約100%の血球容量で約200mlまたは約85%の血球容量で約230mlより多くの）所望の容量の濃縮された赤血球（RBC）（これもまた、（所望の場合）白血球を実質的に含まないように提供され得る）；および(iii)（所望の場合）所望の容量の低血小板（platelet-poor）血漿（PPP）。

## 【0019】

システム10は、許容可能な血液容量に対する適用可能な調節により管理されるので、種々の容量のPC、PPPおよびRBC産物を収集できる。例えば、米国では、システム10が現在提供し得る成分容量反復は、例えば、以下を含む：(i) 各々1治療単位のPC、PPPおよびRBC；または(ii) 各々1治療単位のPCおよびRBC；または(iii) 2治療単位のPCおよび1単位のR

B C。

【0020】

これらの血液処理目的を達成するためのシステム10の操作のさらなる詳細は、以下で記述する。

【0021】

I I. システム制御装置

制御装置18は、先に記載したようなシステム10の全体的なプロセス制御およびモニタリング機能を実行する。

【0022】

図示した好ましい実施態様（図2を参照）では、この制御装置は、主要処理ユニット（MPU）44を含む。好ましい実施態様では、MPU44は、Motorola Corporation製の68030型マイクロプロセッサを含むが、他の型の通常のマイクロプロセッサが、使用できる。

【0023】

好ましい実施態様では、MPU44は、従来のリアルタイムなマルチタスキング（multi-tasking）を使用して、MPUサイクルを処理タスクに割り付ける。周期的なタイマーインターラプト（例えば、5ミリ秒毎）は、実行中のタスクを強制排除（preempt）し、実行準備完了状態にある他のタスクをスケジュールする。もし、再スケジュールが要求されるなら、この準備完了状態において、最も優先順位が高いタスクがスケジュールされる。さもないければ、準備完了状態にあるリスト上の次のタスクが、スケジュールされる。

【0024】

（A. ハードウェア制御）

MPU44は、アプリケーション制御マネージャー46を備える。アプリケーション制御マネージャー46は、制御アプリケーションのライブラリ48の起動を管理する。各制御アプリケーションは、所定の様式でこのシステムハードウェア（例えば、遠心機12、ポンプP1～P7およびバルブV1～V7）を使用して、所定の機能的タスクを実行する手順を命令する。図示した好ましい実施態様では、これらのアプリケーションは、MPU44において、EPROMで、処理

ソフトウェアとして常駐している。

【0025】

機器マネージャー50もまた、MPU44において、EPROMで、処理ソフトウェアとして常駐している。機器マネージャー50は、アプリケーション制御マネージャー46と通信している。機器マネージャー50はまた、このシステムのポンプ、ソレノイド、バルブおよび他の機能的ハードウェア用の、ローレベル周辺制御装置52と通信している。

【0026】

図2で示すように、アプリケーション制御マネージャー46は、起動したアプリケーションでコールアップとき、機器マネージャー50に特定の機能コマンドを送る。機器マネージャー50は、この機能を実行するための周辺制御装置（単数または複数）52を識別し、そしてハードウェア仕様コマンドをコンパイルする。周辺制御装置52は、このハードウェアと直接通信して、このハードウェア仕様コマンドを実行し、これが、このハードウェアを特定の様式で作動させる。通信マネージャー54は、ローレベルプロトコルを管理し、そして機器マネージャー50と周辺制御装置52との間を通信する。

【0027】

また、図2で示すように、機器マネージャー50はまた、この処理手順の操作条件および機能条件についての状態データを、アプリケーション制御マネージャー46に戻し伝える。この状態データは、例えば、流体の流速、感知した圧力、および測定された流体容量によって表わされる。

【0028】

アプリケーション制御マネージャー46は、ディスプレイ用の選択した状態データをオペレータに伝達する。アプリケーション制御マネージャー46は、操作条件および機能条件を、手順アプリケーションA1および性能モニタリングアプリケーションA2に伝達する。

【0029】

(B. オペレータインターフェイス)

図示した実施形態では、MPU44はまた、対話式ユーザーインターフェイス

58を含む。インターフェイス58により、オペレータは、システム10の操作に関する情報を見て理解できるようになる。インターフェイス58により、また、オペレータは、アプリケーション制御マネージャー46に備わっているアプリケーションを選択するだけでなく、システム10の一定の機能および性能規準を変えることができるようになる。

#### 【0030】

インターフェイス58は、インターフェイススクリーン60、および好ましくは、オーディオ装置62を含む。インターフェイススクリーン60は、アルファベット-数字のフォーマットで、かつ、図式画像として、オペレータが見るための情報を表示する。オーディオ装置62は、オペレータの注意を引くためにか、またはオペレータの行為を認知するためかのいずれかのために、音響プロンプトを供給する。

#### 【0031】

図示した好ましい実施形態では、インターフェイススクリーン60はまた、入力装置として役立つ。それは、通常のタッチ起動により、オペレータからの入力を受信する。あるいは、またはタッチ起動と組み合わせて、入力装置とし、マウスまたはキーボードが使用され得る。

#### 【0032】

インターフェイスマネージャー64は、インターフェイススクリーン60およびオーディオ装置62と連絡している。インターフェイスマネージャー64は、順に、アプリケーション制御マネージャー46と連絡している。インターフェイスマネージャー64は、MPU44において、EPROMで、処理ソフトウェアとして備わっている。

#### 【0033】

MPU44およびインターフェイス58のさらなる詳細は、Lyleらの米国特許第5,581,687号で開示されており、その内容は、本明細書中で参考として援用されている。

#### 【0034】

(C. システム制御機能)

(図2で示すように) 図示した実施形態では、ライブラリ48は、少なくとも1個のシステム制御アプリケーションA1を含む。システム制御アプリケーションA1は、いくつかの特定の(しかし、相関した)ユーティリティー機能を含む。もちろん、ユーティリティー機能の数および種類は、変えることができる。

#### 【0035】

図示した実施形態では、ユーティリティー機能F1は、システム10の血小板収量(Y1d)を誘導する。ユーティリティー機能F1は、その分離効率によるシステム10の瞬間的な物理的状态と収集に利用できる循環血小板数によるドナーの瞬間的な生理学的状態の両方を確認する。これらにより、ユーティリティー機能F1は、処理期間にわたって、連続的に、血小板の瞬間的な収量を誘導する。

#### 【0036】

別のユーティリティー機能F2は、選択した情報ステータス値およびパラメータを生じさせるために、計算した血小板少量(Y1d)および他の処理状態に依存している。これらの値およびパラメータは、インターフェイス58に表示されて、オペレータが最適な性能条件を確立し維持するのを助ける。ユーティリティー機能F2により誘導されたステータス値およびパラメータは、変えることができる。例えば、図示した実施形態では、ユーティリティー機能F2は、処理されるべき残留容量、残りの処理時間、および成分収集容量および速度を報告する。

#### 【0037】

他のユーティリティー機能は、最適な処理状態を確立し維持するために、アプリケーション制御マネージャー46により使用する進行中の処理状態に基づいて、制御変数を生じる。例えば、1ユーティリティー機能F3は、第一ステージ24で、血小板分離条件を最適化するために、制御変数を生じさせる。別のユーティリティー機能F4は、クエン酸塩抗凝血剤がPPPと共にドナーに戻って潜在的なクエン酸毒性反応を回避する速度を制御するために、制御変数を生じる。

#### 【0038】

これらのユーティリティー機能および他のユーティリティー機能のさらなる詳細は、Brownの米国特許第5,676,841号で見出され、その内容は、



本明細書中で参考として援用されている。依存している種々のユーティリティー機能の要旨は、本明細書の最後に見られる。

#### 【0039】

(III. システム操作)

図示した実施形態では、システム10は、少なくとも3つの処理目的を達成するように調整される。第一目的は、所望収量の濃縮血小板(PC)を収集することにある。第二目的は、収集したPCの保存媒体として供するために、所望容量のPPPを収集することにある。第三目的は、所望容量の赤血球(RBC)を収集することにある。他の目的は、例えば、保存用の追加容量のPPPを収集するために、確立され得る。

#### 【0040】

これらの目的を達成するために、ユーティリティー機能F1は、システム10を調整して、少なくとも3つの異なる作動モードで、血液を収集し処理する。

#### 【0041】

第一作動モードでは、システム10は、全血を処理し、そしてPCおよびPPPを収集するように調整される。第一モードでは、RBCは、同時には収集されず、ドナーに戻される。所望容量よりも過剰のPPPもまた、ドナーに戻され得る。

#### 【0042】

第二作動モードでは、システム10は、全血を処理し、そして付随した追加容量のPCおよびPPPと共にRBCを同時に収集するように調整される。第二モード中にて、血液成分は、ドナーには戻されない。

#### 【0043】

第三作動モードでは、システム10は、最終血液容量トリミング機能を実行するように調整される。この容量トリミング機能中にて、収集したRBC容量の一部、または収集したPPP容量の一部または全部、またはそれらの両方は、ドナーに戻ることができる。この容量トリミング機能は、実際に収集された成分容量が収集用の目標容量を超えないことを保証する。

#### 【0044】

この処理手順の着手時点で、オペレータは、インターフェイス58を使用して、収集する所望のPC収量 ( $Y_{ldGoal}$ )、収集する所望のRBC容量 ( $RBC_{Goal}$ ) および収集する所望のPPP容量 ( $PPP_{Goal}$ ) を入力する。

制御装置18は、システム10を調整して、第一作動モードで、血液処理を続行する。制御装置18は、第一作動モードから第二作動モードへの変化および第二作動モードから第三作動モードへの変化を命令する際の2つの処理変数を考慮している。第一処理変数は、所望の血小板収量を得るのに必要な残留全血容量（すなわち、 $V_{brem}$  (ml)）である。第二処理変数は、所望容量の赤血球 ( $RBC_{Goal}$ )（すなわち、 $V_{bRBC}$ ）を得るために処理する必要がある全血の容量である。

#### 【0045】

$V_{brem} = V_{bRBC}$  のとき、制御装置18は、第一作動モードから第二作動モードへと切り替わる。 $V_{brem}$  がゼロになるとき、この制御装置は、第二作動モードから第三作動モードへと切り替わる。

#### 【0046】

(i)  $V_{brem}$  の計算

ユーティリティ機能F2は、 $Y_{ldGoal}$  を得るために処理する必要がある全血容量を誘導する第一ユーティリティ機能F1による $Y_{ld}$ の計算に依存している。血液処理中にて、ユーティリティ機能F2は、現在の作動効率 $\eta_{Plt}$ を反映するように補正しつつ、この手順の残りにわたって、収集する残留収量を予想平均血小板数で割ることにより、所望血小板収量 $V_{brem}$  (ml) を得るのに必要な追加処理容量を連続的に誘導する。

#### 【0047】

図示した実施形態では、ユーティリティ機能F2は、以下の式を使用して、この値を誘導する：

#### 【0048】

【数1】

$$Vb_{rem} = \frac{200,000 \times (Yld_{Goal} - Yld_{Current})}{\eta_{Plt} \times ACDil \times (Plt_{Current} + Plt_{Post})}$$

ここで：

$Yld_{Goal}$ は、所望血小板収量 ( $k/\mu l$ ) である；

$Vb_{rem}$ は、 $Yld_{Goal}$ を得るのに必要な追加処理容量 ( $ml$ ) である。

【0049】

$Yld_{Current}$ は、(以下の「要旨」で述べる) 現在処理値に基づいてユーティリティー機能F1により計算した現在血小板収量 ( $k/\mu l$ ) である。

【0050】

$\eta_{Plt}$ は、現在の(瞬間的な)血小板収集効率であり、これは、(以下の「要旨」で述べる) 現在処理値に基づいて、計算できる。

【0051】

$ACDil$ は、(以下の「要旨」で述べる) 抗凝血剤希釈因子である。

【0052】

$Plt_{Current}$ は、現在の(瞬間的な)循環ドナー血小板数であり、これは、(以下の「要旨」で述べる) 現在処理値に基づいて、計算される。

【0053】

$Plt_{Post}$ は、処理後の予想ドナー血小板数であり、これもまた、(以下の「要旨」で述べる) 全処理値に基づいて、計算される。

【0054】

(ii)  $V_{RBC}$ の計算

ユーティリティー機能F2は、 $RBC_{Goal}$ に基づいて、そして、ドナーの全血ヘマトクリット容量 ( $Hct$ ) を考慮することにより、 $V_{RBC}$ を誘導する。ドナーの全血ヘマトクリット容量  $Hct$  は、この手順の着手時に測定した値、または手順の過程でオンライン感知した値を含み得る。

【0055】

図示した実施形態では、 $Hct$ は、直接的には測定または感知されない。その

代わりに、制御装置18は、この分離チャンバに入る全血の見かけ血球容量値 $H_b$ に依存している。 $H_b$ は、感知された流動状態および理論的な要件に基づいて、制御装置18により誘導される。 $H_b$ の誘導は、以下の「要旨」で、さらに詳細に説明する。

【0056】

$H_b$ に基づいて、ユーティリティー機能F2は、以下の式を使って、 $V_{bRBC}$ を誘導できる：

【0057】

【数2】

$$V_{bRBC} = \frac{RBC_{Goal} + Buf}{H_b}$$

ここで：

$Buf$ は、所定緩衝液容量（例えば、20ml）である。

【0058】

図示した実施形態では、ユーティリティー機能F2は、 $V_{bRBC}$ の計算容量を、例えば、10で割り切れる次に最も高い整数に切り上げることにより、さらなる容量緩衝液を供給する。

【0059】

図示した実施形態では、ユーティリティー機能F2はまた、 $V_{bRBC}$ の計算値と所定最大容量（例えば、600mL）とを比較する。もし、 $V_{bRBC}$ が所定最大値に等しいかそれを超えるなら、ユーティリティー機能F2は、その値を、規定より少ない容量（例えば、595mL）まで切り下げる。

【0060】

(iii) 第一作動モード

第一または非同時作動モードでは、システム10は、全血を処理し、そして保存用のPCおよびPPPを収集する。第一モード中にて、RBCおよび未収集容量のPPPは、ドナーに戻される。

## 【0061】

図1で示したシステム10は、単一の管腔静脈切開針22を使用する。この非同時モード中にて、制御装置18は、一連のドローサイクルおよびリターンサイクルで、システム10を作動する。ドローサイクル（図3）中にて、制御装置18は、針22を通して、ドナーのWBを処理用チャンバ16に供給する。リターンサイクル（図4）中にて、制御装置18は、同じ針22を通して、RBCおよびPPP血液成分をドナーに戻す。

## 【0062】

図示した実施形態では、システム10は、一連のドローサイクルおよびリターンサイクル中にて、中断することなく、チャンバ16で分離を起こすことができるように設計されている。さらに特定すると、システム10は、ドローレザバ66を含む。ドローサイクル（図3）中にて、一定量のドナーのWBは、レザバ66にプールされ、その容量の過剰量は、処理用チャンバ16に送られる。システム10はまた、リターンレザバ68を含む。リターンサイクル（図4を参照）中にてドナーに定期的に戻すために、ドローサイクル中にて、リターンレザバ68では、一定量のRBCが集まる。このリターンサイクル中では、WBは、ドローレザバ66からチャンバ16へと運搬されて、分離を中断せずに行う。

## 【0063】

非同時モード（図3）のドローサイクルでは、全血ポンプP1は、WBを、針22から、第一配管分枝20を通して、ドローレザバ66に入れる。その間、補助配管分枝26は、容器C2から抗凝血剤ポンプP3を通してWB流れに入る抗凝血剤を計量する。抗凝血剤の種類は、変えることができるものの、図示した実施形態は、ACDAを使用し、これは、フェレーシスで一般的に使用される抗凝血剤である。

## 【0064】

容器C2は、生理食塩水溶液を収容している。別の補助配管分枝28は、この生理食塩水を、処理を開始する前にアセンブリ14から空気感作し一掃する際に使用するために、インラインバルブV1を経由して、第一配管分枝20へと運搬する。生理食塩水溶液はまた、再度、処理後に導入されて、ドナーに戻すため

に、アセンブリ14からの残留成分をフラッシュする。

【0065】

処理制御装置18は、重量スケール70から、処理情報を受信する。重量スケール70は、ドローレザバ66で収集したWBの容量をモニターする。一旦、重量スケール70が、所望容量のWBがドローレザバ66内に存在していることを指示すると、制御装置18は、全血処理ポンプP2に対して、ドローレザバ66から入口分枝36を通して処置チャンバ16の第一ステージ24へとWBを連続的に運搬するように作動する命令を出す。制御装置18は、全血処理ポンプP2（これは、（例えば、50ml／分で）連続的に作動して、一定量の抗凝血血液をレザバ66に収集する）よりも高い流速（例えば、100ml／分）で、全血ポンプP1を作動する。重量スケール70を使用して重量をモニターすることにより、この制御装置は、断続的に、全血入口ポンプP1を作動して、ドローレザバ66において、所望容量のWBを維持する。

【0066】

抗凝血WBは、処理チャンバ16の第一ステージ24に入ってそれを満たす。そこで、遠心機12の回転中に発生した遠心力により、WBは、赤血球（RBC）と血小板リッチな（platelet-rich）血漿（PRP）に分離される。

【0067】

PRPポンプP4は、処理チャンバ16の第一ステージ24から、処理チャンバ16の第二ステージ32へと輸送するための第二配管分枝30へと、PRPを引き出すように作動する。そこで、PRPは、血小板濃縮物（PC）と低血小板血漿（PPP）に分離される。

【0068】

制御装置18は、処理チャンバ16の第一ステージ24内のRBCとPRPの間のインターフェイスの位置を光学的にモニターする。制御装置18は、PRPポンプP4を作動して、このインターフェイスを、処理チャンバ24の第一ステージ24内の所望位置で保持する。これにより、このインターフェイスを占めている白血球の相当部分がPRP流れに入ることを回避する。

## 【0069】

必要に応じて、このPRPはまた、白血球を除去するために、第二ステージ32での分離前に、フィルターFを通して運搬され得る。フィルターFは、Nishimuraらの米国特許第4,936,998号（その内容は、本明細書中で参考として援用されている）で開示された種類の繊維を含む濾過材を使用できる。これらの繊維を含む濾過材は、SEPACELLの商品名のフィルターで、Asahi Medical Companyから市販されている。

## 【0070】

システム10は、再循環配管分枝34および付属再循環ポンプP5を含む。処理制御装置18は、ポンプP5を作動して、処理チャンバ16の第一ステージ24に入るWBと再混合するために、処理チャンバ16の第一ステージ24を出ていくPRPの一部を反らす。PRPの再循環により、第一ステージ24の入口領域において、RBCおよびPRPの最大分離を生じる所望の状態が確立される。

## 【0071】

RBC分枝38は、このRBCを、処理チャンバ16の第一ステージ24から、リターンレザバ68（これは、バルブV3で制御される）へと運搬する。重量スケール72は、容器C4に収集されたPPPの容量をモニターする。

## 【0072】

PPP分枝40は、PPPポンプP7を作動することにより、処理チャンバ16の第二ステージ32からPPPを運搬する。バルブV5を開くことにより、このPPPの全部または一部は、ポンプP7の流速に依存して、収集容器C4に向けることができる。重量スケール74は、容器C4で収集されたPPPの容量をモニターする。収集されなかったPPPは、リターンレザバ68へと流入し、この場所で、それは、このRBCと混ざる。

## 【0073】

第二作動モード（これは、後に説明する）中にて、比較的に多量のPPP（すなわち、約50%～75%のPPPgoal）は、典型的には、ドナーに戻ることなく、収集される。このことを見込んで、制御装置16は、第一モード中にPPPが収集される速度を制限する。これにより、この手順の最後において、余剰容量

のPPPが収集されることが避けられる。第一作動モード中にPPPが収集される速度を制限することにより、制御装置18は、引き続いた血液容量トリミング機能の時間を短くし、それにより、全体的な処置時間を短くする。少量の余剰PPPにより、また、この血液容量トリミング機能中にドナーに戻る抗凝血剤（これは、PPPで運ばれる）の量が少なくなるので、血液容量トリミング機能中において、より高いリターン流速を使用することが可能となる。

#### 【0074】

制御装置18は、重量スケール72から処理情報を受信し、リターンレザバ68内のRBCおよびPPPの容量をモニターする。予め設定した容量があるとき、制御装置18は、システム10の作動を、ドローサイクルからリターンサイクルへとシフトする。

#### 【0075】

リターンサイクル（図4）では、制御装置18は、全血入口ポンプP1および抗凝血剤ポンプP3を停止し、そして血液リターンポンプP6を始動する。リターン分枝42は、針22を通して、リターンレザバ68にあるRBCおよびPPPをドナーへと運搬する。

#### 【0076】

一方では、制御装置18は、このリターンサイクルにある間、WB処理ポンプP2、PRPポンプP4および再循環ポンプP5を作動状態に保って、チャンバ16の第一ステージ24および第二ステージ32を通してドローレザバ66にプールされたWBを連続的に処理する。

#### 【0077】

重量スケール72が、リターンレザバ68の内容物がドナーに運搬されたことを表示したとき、制御装置18は、システム10の操作を別のドローサイクルへとシフトする。

#### 【0078】

制御装置18は、 $V_{brem} = V_{bRbc}$ となるまで、連続ドローサイクルとリターンドロースサイクルとの間で切り換える。 $V_{brem} = V_{bRbc}$ のとき、制御装置18は、リターンレザバ68の内容物をドナーに戻す最終リターンサイクルを命令す



る。リターンレザバ68の内容物を戻すとすぐに、制御装置18は、第一作動モードから第二作動モードへと切り換える。

#### 【0079】

##### (iv) 同時収集モード

第二または同時収集モード(図5)では、制御装置18は、システム10を調整して、持続ドローサイクルで作動して、全血を処理し、そして付随した追加容量のPCおよびPPPと共に、目標容量のRBCを同時に収集する。この同時収集モード中にて、制御装置18は、システム10の操作をリターンサイクルには切り換えない。この同時収集モード中にて、ただ1つの持続ドローサイクルだけが存在し、そして成分はドナーへは戻されない。

#### 【0080】

同時収集モードの持続ドローサイクルの間、制御装置18は、ドローレザバ6にある全血の大余剰容量が収集されることを避ける。図示した実施形態では、制御装置18は、非同時収集モードのドローサイクル中に維持される差と比較して、全血入口ポンプP1と全血処理ポンプP2との間で低い流速差を維持することにより、この目的を達成する。例えば、図示した実施形態では、全血入口ポンプP1は、全血処理ポンプP2の上方で、例えば、僅か1mL/分の最小差で、作動される。

#### 【0081】

僅かな緩衝容量の全血のみが、同時収集モードの持続ドローサイクルの間、ドローレザバ66内で、維持されることをさらに保証するために、重量スケール70は、ドローレザバ66内で感知された容量の血液が特定の最低緩衝容量(例えば、5g)を超えるときはいつでも、全血入口ポンプP1および抗凝血剤ポンプP3をオフに切り換える。

#### 【0082】

同時収集モードの持続ドローサイクルの間、赤血球は、バルブV4(これは、この目的のために開いており、バルブV3は閉じていて、それにより、リターンレザバ68では、RBCは集まらない)を経由して、収集容器C4へと向けられる。重量スケール108は、収集容器C4の重量をモニターする。

## 【0083】

チャンバ16の第二ステージ32では、付随容量のPCが集まり、その間、（PPPポンプP7およびバルブV5（これは、開いている）を作動することにより）、収集容器C3では、付随容量のPPPが集まる。バルブV3は、閉じられ、そのようにして、リターンレザバ68には、PPPが集まらない。

## 【0084】

制御装置18は、同時収集モードの持続ドロースサイクルの間、V<sub>brem</sub>を誘導する。V<sub>brem</sub>がゼロになるとき、制御装置18は、この同時収集モードを終了する。

## 【0085】

（（iv）血液容量トリミング機能）

図示した実施形態（図6を参照）では、この同時収集モードの最後に、制御装置18は、重量スケール108および74を使用して、それぞれ、収集したRBCおよびPPPの容量を評価する。

## 【0086】

収集したRBCの容量がRBC<sub>goal</sub>を超える場合、制御装置18は、インラインリターンポンプP6を作動することにより、収集容器C4から、分枝経路43（バルブV6は開いている）を通して、リターン経路42（バルブV2は開いている）へと、過剰なRBC容量をドナーに戻すリターンサイクルに入るように、システム10に命令を出す。

## 【0087】

同様に、もし、収集したPPPの容量がPPP<sub>goal</sub>を超えるなら、制御装置18は、インラインリターンポンプP6を作動することにより、収集容器C3から、分枝経路45（バルブV7は開いており、バルブV5は閉じている）を通して、リターン経路42へと、過剰なPPP容量をドナーに戻すリターンサイクルに入るように、システム10に命令を出す。

## 【0088】

この血液容量トリミング機能の最後に、制御装置18は、所定流体交換容量と共に、システム10にある残留血液をドナーに戻すように、生理食塩水再注入操

作の命令を出す。

【0089】

((v) 収集後処理)

((1) PPP)

PPPの保持は、この成分分離プロセス中およびその後において、複数の目的に役立ち得る。

【0090】

PPPの保持は、処理の間、治療目的に役立つ。PPPは、この成分分離プロセスの間、WBに計量して供給された抗凝血剤の殆どを含有する。PPPの全部をドナーに戻す代わりに、その一部を保持することにより、処理中にドナーが受容する抗凝血剤の全体容量は、少なくなる。この減少は、大量の血液を処理する場合、特に重要である。処理中におけるPPPの保持はまた、処理中において、ドナーの循環血小板数を高くかつ均一に保つ。

【0091】

システム10はまた、保持したPPPから処理利益を誘導できる。例えば、システム10は、代替再循環モードにおいて、第一隔室24に入ってくるWBと混合するために、PRPの代わりに、保持したPPPの一部を再循環できる。さもないと、処理の間、WBの流れが一時的に停止するなら、システム10は、流体ラインを開いた状態で保つために、抗凝血「キープオープン (keep open)」流体として、保持容量のPPPを利用できる。それに加えて、この分離プロセスの最後に、システム10は、リターン経路42を通してRBCをドナーに戻すために第一ステージ隔室24から再懸濁し一掃するように、「リンスバック (rinse back)」流体として、保持容量のPPPを利用できる。

【0092】

((2) PC)

この分離プロセス後、システム10はまた、再懸濁モードでは、収集容器C5において、移動および保存用の第二ステージ24で、PCを再懸濁するために、保持したPPPの一部を利用するように作動する。PCの再懸濁および収集容器C5への移動は、手動でまたはオンラインで、達成できる。

## 【0093】

好ましくは、PCを保存する容器C5は、DEHP可塑化ポリ塩化ビニル材料と比較した場合、血小板の保存に有利な高い気体透過性を有する材料から製造される。例えば、(Gajewskiらの米国特許第4,140,162号で開示されているような)ポリオレフィン材料、またはトリメリト酸トリ-2-エチルヘキシル(TEHTM)が使用できる。

## 【0094】

((2) RBC)

図示した実施形態(図7を参照)では、保存用に収集したRBC容量を処理するために、使い捨て収集セット76が提供される。

## 【0095】

セット76は、移動経路78を含む。移動経路78は、密封自由端80を有し、これは、無菌様式で、RBC収集容器C4(図7を参照)上の密封チューブセグメント82に連結されるように設計される。Spencerの米国特許第4,412,835号で示されたもののような公知の無菌連結機構(図示せず)は、移動経路78をチューブセグメント82に連結するのに使用できる。これらの機構は、配管末端間において、溶融シールを形成し、これは、一旦、冷却すると、無菌溶接を形成する。

## 【0096】

第一バッグ84は、一定長の試料配管86を通して、移動経路78と連絡している。第一バッグ84は、赤血球添加剤溶液S、例えば、SAG-MまたはADSOLID(登録商標)Solution(Baxter Healthcare Corporation)を含有する。収集セット76をRBC収集容器C4に連結することによって、試料配管86にある通常のインライン脆弱カニューレ106が開かれ、赤血球添加剤溶液Sは、収集したRBC容量と混合するために、第一バッグ84から収集容器C4へと移動される。添加剤溶液とRBCとの混合物は、次いで、第一バッグ84に戻って移動できる。

## 【0097】

第一バッグ84内の残留空気はインライン通気チャンバ88に排出でき、これ

は、移動経路78と連絡している。同時に、第一バッグ84内に存在している収集したRBC容量のアリコートは、試料配管86に急送できる。

【0098】

配管86は、好ましくは、識別コード90を有し、これは、第一バッグ84上に印刷または塗布されたコード90と同じである。配管86は、次いで、通常のスナップアパート (snap-apart) シールで閉じられ、第一バッグ84は、このRBC容量を保存するために、収集セット76から引き離される。配管86は、さらに、通常のチューブシーラーを使用してセグメントで密封されて、分析および交差試験用に、このRBCの複数の試料を単離できる。

【0099】

セット76はまた、第二バッグ92を含み、これは、分枝経路94を通して、第一バッグ84の下流にある移動経路78と連絡している。分枝経路94は、インラインフィルター96を含む。インラインフィルター96は、赤血球から白血球を選択的に除去する濾過材98を運ぶ。このフィルターは、例えば、R-3000 Red Blood Cell Filter (Asahi Medical) から構成できる。

【0100】

赤血球および添加剤溶液の混合物は、第一バッグ84をバイパスして、収集バッグC4から、インラインフィルター96を通して、第二バッグ92へと移動できる。このようにして、セット76は、白血球を事実上含まない赤血球（これは、長期間の保存に適当である）を供給する。

【0101】

通気経路100は、インラインフィルター96をバイパスして、第二バッグ92から移動経路78へと伸長している。経路100で通常の剥離カニューレ106を開くことにより、第二バッグ92内の残留空気は、経路100を通して、インライン通気チャンバ88へと排出できる。経路100内の逆止め弁104により、経路100内の空気および液体の流れは、バッグ92から離れることができるが、逆方向には行かない。

【0102】

同時に、第二バッグ92内に存在している収集したRBCのアリコートは、通気経路100内へと急送できる。通気経路100は、識別コード102を有し、これは、第二バッグ92上に印刷または塗布されたコード102と同じである。通気経路100および分枝経路94は、通常のスナップアパートシールで閉じられ、第二バッグ92は、移動経路78から引き離すことができる。経路100もまた、セグメントで密封され、分析および交差試験用に、このRBCの複数の試料を密封できる。

### 【0103】

収集セット76は、長期間の保存に適当な赤血球産物（これは、保存前には、白血球を含まないか白血球が少ないかいずれかである）を供給するために、可撓性を与える。

### 【0104】

（IV. 種々の処理ユーティリティ機能の要約）

（A. 誘導血小板の収量）

ユーティリティ機能F1は、システム10の血小板分離効率（ $\eta_{Plt}$ ）の連続的な計算を行う。ユーティリティ機能F1は、全血中で利用できる全血漿容量に対して、ドナーの全血から分離した血漿容量の割合と同じであるように、血小板分離効率 $\eta_{Plt}$ を処理する。ユーティリティ機能F1は、それにより、ドナーの全血から分離した血漿容量中の各血小板が収獲されたと仮定している。

### 【0105】

ドナーの血球容量は、処理中に抗凝血剤希釈および血漿枯渇効果が原因で変化し、そのようにして、分離効率 $\eta_{Plt}$ は、一定値には留まらず、この手順全体を通して変化する。ユーティリティ機能F1は、収量を漸進的にモニターすることにより、これらのプロセス依存的な変化と競争する。これらの収量は、増分精算容量（incremental cleared volumes）（ $\Delta Clr Vol$ ）と呼ばれているが、以下のようにして、現在の分離効率 $\eta_{Plt}$ を、ドナー全血（これは、抗凝血剤で希釈し処理した）の現在の増分容量と掛けることにより、計算される：

式（1）

【0106】

【数3】

$$\Delta ClrVol = ACDil \times \eta_{Plt} \times \Delta VOL_{Proc}$$

ここで、

$\Delta Vol_{proc}$ は、処理される増分全血容量であり、そして

$ACDil$ は、この増分全血容量に対する抗凝血剤希釈因子であり、以下のよう  
にして計算される：

式（2）

【0107】

【数4】

$$ACDil = \frac{AC}{AC+1}$$

ここで：

$AC$ は、全血容量と抗凝血剤容量との選択比（例えば、10：1または「10」）である。 $AC$ は、この処理期間中の一定値を含み得る。あるいは、 $AC$ は、この処理期間中において、所定の規準に従って、段階様式で変わり得る。

【0108】

例えば、 $AC$ は、初期設定時間の間、処理の着手時では、より小さい比で設定でき、次いで、引き続いた期間の後、段階的に上昇できる；例えば、 $AC$ は、処理の最初の1分間では、6：1に設定でき、次いで、次の2.5～3分間では、8：1に上昇でき、最後に、10：1の処理レベルまで上昇できる。

【0109】

抗凝血剤の導入はまた、第二処理ステージ32に入るPRPの入口圧力をモニターすることにより、行い得る。例えば、 $AC$ は、その初期圧力（例えば、50

0 mmHg) が設定閾値レベル (例えば、200 mmHg ~ 300 mmHg) まで落ちるまで、6 : 1 に設定できる。AC は、次いで、10 : 1 の処理レベルまで段階的に上昇できるのに対して、その圧力をモニタリングすることで、それが所望のレベルのままになることを保証する。

### 【0110】

ユーティリティ機能 F1 もまた、ドナーの現在の循環血小板数 ( $Plt_{circ}$ ) (これは、1 マイクロリットル ( $\mu l$ ) の血漿容量 (または  $k/\mu l$ ) あたり、1000 個の血小板によって、表わされる) の連続的な概算を行う。 $\eta_{Plt}$  と同様に、 $Plt_{circ}$  は、その希釈効果および枯渇効果のために、処理の間、変化する。ユーティリティ機能 F1 はまた、各増分精算血漿容量 ( $\Delta ClrVol$ ) (これは、 $\eta_{Plt}$  の瞬間的な計算に基づいている) を循環血小板数  $Plt_{circ}$  と掛けることにより、少しずつ漸進的に、この血小板収量をモニターする。その積は、増分血小板収量 ( $\Delta yld$ ) であり、これは、典型的には、 $e^n$  として表わされ、ここで、 $e^n = 0.5 \times 10^n$  個の血小板 ( $e^{11} = 0.5 \times 10^{11}$  個の血小板) である。

### 【0111】

任意の一定時間では、増分血小板収量  $\Delta Yld$  の合計は、現在の血小板収量  $Yld_{current}$  を構成し、これはまた、以下のようにして表わすことができる：式 (3)

### 【0112】

【数5】

$$Yld_{current} = Yld_{old} + \frac{\Delta ClrVol \times Plt_{cur}}{100,000}$$

ここで：

$Yld_{old}$  は、最後に計算した  $Yld_{current}$  であり、そして  
式 (4)

### 【0113】



【数6】

$$\Delta Yld = \frac{\Delta ClrVol \times Plt_{Current}}{100,000}$$

であり、ここで：

$Plt_{Current}$  は、ドナーの循環血小板数の現在の（瞬間的な）概算値である。

【0114】

$\Delta Yld$  は、ユニットを均衡させるために、式（4）において、100,000で割っている。

【0115】

以下は、ユーティリティー機能F1による上記処理変数の誘導でのさらに詳細な説明を提供する。

【0116】

（i）全体的な分離効率  $\eta_{Plt}$  の誘導

全体的なシステム効率  $\eta_{Plt}$  は、以下で表わすように、このシステムの部品の個々の効率の積である：

式（5）

【0117】

【数7】

$$\eta_{Plt} = \eta_{1stSep} \times \eta_{2ndSep} \times \eta_{Anc}$$

ここで：

$\eta_{1stSep}$  は、第一分離段階においてWBからPRPを分離する効率である。

【0118】

$\eta_{2ndSep}$  は、第二分離段階においてPRPからPCを分離する効率である。

## 【0119】

$\eta_{Anc}$  は、このシステムの他の補助処理段階の効率の積である。

## 【0120】

(1. 第一段階分離効率  $\eta_{1stSep}$ )

ユーティリティー機能 F 1 は、以下の式を使用して、測定および実験処理値に基づいて、処理の過程で、 $\eta_{1stSep}$  を連続的に誘導する。

式 (6)

## 【0121】

【数8】

$$\eta_{sep} = \frac{Q_p}{(1-H_b) Q_b}$$

ここで：

$Q_b$  は、測定した全血流速 (ml / 分) である。

## 【0122】

$Q_p$  は、測定した P R P 流速 (ml / 分) である。

## 【0123】

$H_b$  は、第一段階分離隔室に入る抗凝血全血の見かけ血球容量である。 $H_b$  は、感知した流動要件および理論要件に基づいて、このユーティリティーにより誘導した値である。ユーティリティー機能 F 1 には、従って、実際の W B 血球容量を測定するためのオンライン血球容量センサを必要としない。

## 【0124】

ユーティリティー機能 F 1 は、以下の関係に基づいて、 $H_b$  を誘導する：

式 (7)

## 【0125】

【数9】

$$H_b = \frac{H_{rbc}(Q_b - Q_p)}{Q_b}$$

ここで：

$H_{rbc}$ は、第一段階分離チャンバの感知した作動条件および物理的寸法に基づいて、第一段階分離チャンバ内でのRBC床の見かけ血球容量である。 $H_b$ と同様に、ユーティリティー機能F1には、以下の式に従ってユーティリティー機能により誘導した $H_{rbc}$ を決定する物理的センサを必要としない：

式(8)

【0126】

【数10】

$$H_{rbc} = 1 - \left( \frac{\beta}{gA\kappa S_v} (q_b - q_p) \right)^{\frac{1}{k+1}}$$

ここで：

$q_b$ は、入口血流速度 ( $\text{cm}^3/\text{秒}$ ) であり、これは、既知量であり、 $\text{ml}/\text{分}$ に変換したとき、式(6)にて、 $Q_b$ に一致している。

【0127】

$q_p$ は、測定したPRP流速 ( $\text{cm}^3/\text{秒}$ ) であり、これは、既知量であり、 $\text{ml}/\text{分}$ に変換したとき、式(6)にて、 $Q_p$ に一致している。

【0128】

$\beta$ は、剪断速度依存項であり、そして $S_r$ は、赤血球沈降係数 (秒) である。実験データに基づいて、式(8)は、 $\beta/S_r = 15.8 \times 10^6 \text{秒}^{-1}$ と仮定する。

【0129】

Aは、既知寸法の分離チャンバの面積 ( $\text{cm}^2$ ) である。

【0130】

gは、遠心加速度（cm／秒<sup>3</sup>）であり、これは、第一分離チャンバの半径（既知量）を回転速度の二乗 $\Omega^2$ （rad／秒<sup>2</sup>）（他の既知量）と掛けた値である。

【0131】

kは、粘性定数＝0.625であり、 $\kappa$ は、kおよび他の粘性定数 $\alpha = 4.5$ に基づいた粘性定数であり、ここで：

式（9）

【0132】

【数11】

$$\kappa = \frac{k+2}{\alpha} \left[ \frac{k+2}{k+1} \right]^{k+1} = 1.272$$

式（8）は、以下の式（10）で表わされる関係から誘導される：

式（10）

【0133】

【数12】

$$H_{rbc} (1 - H_{rbc})^{(k+1)} = \frac{\beta H_b q_b}{g A k S_v}$$

これは、BrownのThe Physics of Continuous Flow Centrifugal Cell Separation, 「Artificial Organs」 1989; 13 (1) : 4~20))で示されている。式（8）は、 $H_{rbc}$ について、式（10）を解く。

【0134】

（2. 第二ステージ分離効率 $\eta_{2ndSep}$ ）

ユーティリティー機能F1はまた、アルゴリズムに基づいて、処置の過程にわたって、 $\eta_{2ndSep}$ を連続的に誘導し、これは、コンピューターモデル化により誘

導され、それらのサイズ（平均血小板容量、またはMPV）、流速（ $Q_p$ ）、分離ステージ32の面積（A）、および遠心加速度（g、これは、第二ステージのスピ半径を回転速度の二乗 $\Omega^2$ と掛けた値である）の関数として、常用対数（log-normal ly）分布した血小板のどの部分が第二分離ステージ32で収集されたかを計算する。

### 【0135】

このアルゴリズムは、ある関数によって表わすことができ、これは、単一無次元パラメータ  $g A S_p / Q_p$  によって、 $\eta_{2ndsep}$ を表したが、

ここで：

$$S_p = 1.8 \times 10^{-9} MPV^{2/3} \text{ (秒)} \text{ であり、そして}$$

MPVは、平均血小板容量（フェムトリットル、fl、または立方ミクロン）であり、これは、処理前に収集されたドナーの血液試料から、通常の方法により、測定できる。異なるカウンタを使用することが原因で、MPVは変動し得る。このユーティリティー機能は、従って、使用するカウンタの種類に従って、その関数で使用するためのMPVを標準化する探索表を含み得る。あるいは、MPVは、臨床血小板プレカウント  $Plt_{PRE}$  の統計的な評価から誘導した関数に基づいて概算でき、これは、このユーティリティー機能を使用できる。本発明者は、このような臨床データの評価に基づいて、このMPV関数を以下のようにして表わすことができると考えている：

$$MPV (fl) = 11.5 - 0.009 Plt_{PRE} (k/\mu l)$$

### 【0136】

#### 【数13】

$$MPV (fl) \approx 11.5 - 0.009 Plt_{PRE} (k/\mu l)$$

### （3. 補助分離効率 $\eta_{Anc}$ ）

$\eta_{Anc}$ は、この処理システムの他の部分の効率（血小板損失による）を考慮に入れている。 $\eta_{Anc}$ は、第一ステージチャンバから第二ステージチャンバへと血

血小板（PRP中）を輸送する効率；この白血球除去フィルターによって血小板（これもまた、PRP中）を輸送する効率；処理後、第二ステージチャンバから血小板（PC中）を再懸濁し輸送する効率；および単一針または二重針のいずれかの構成で先に処理した血液を再処理する効率を考慮に入れている。

### 【0137】

これらの補助プロセス工程の効率は、臨床データに基づいて評価できるか、またはコンピューターモデル化に基づいて概算できる。これらの要件に基づいて、 $\eta_{Anc}$ について予測した値を割り当てることができ、等式（5）は、これを、所定の手順の過程にわたって、定数として処理する。

### 【0138】

（B. ドナー血小板数（ $Plt_{circ}$ ）の誘導）

ユーティリティー機能F1は、処理中のドナーの現在の循環血小板数 $Plt_{circ}$ を予測する動力学的モデルに依存している。このモデルは、ドナーの血液容量を概算し、次いで、以下の関係に従って、処理中の希釈効果および枯渇効果を概算して、 $Plt_{circ}$ を誘導する：

等式（11）

### 【0139】

### 【数14】

$$Plt_{circ} = [(Dilution) \times Plt_{pre}] - (Depletion)$$

ここで：

$Plt_{pre}$ は、処理が始まる前のドナーの循環血小板数（ $k/\mu l$ ）であり、これは、処理前にドナーから取り出した全血の試料から、通常の方法により、測定できる。異なるカウンタを使用することが原因で、 $Plt_{pre}$ には、変動があり得る。（例えば、Peoplesら、「A Multi-Site Study of Variables Affecting Platelet Counting for Blood Component Quality C

ontrol」 Transfusion (Special Abstract Supplement, 47th Annual Meeting), 34巻、105号、1994年10月 補遺を参照)。このユーティリティー機能は、従って、使用するカウンタの種類に従って、その関数で使用するための全ての血小板数（例えば、Plt<sub>pre</sub>およびPlt<sub>post</sub>（下記））を標準化する探索表を含み得る。

#### 【0140】

Dilutionは、ドナーの見かけ循環血液容量の上昇（これは、このシステムの感作容量および抗凝血剤の送達により、引き起こされる）が原因で、ドナーの処理前循環血小板数Plt<sub>pre</sub>を低下させる因子である。Dilutionはまた、この手順の間、腎臓による血管空間からの流体の連続除去を考慮に入れる。

#### 【0141】

Depletionは、処理によるドナーの利用できる循環血小板プールの枯渇を考慮に入れる因子である。Depletionはまた、処理中にて、この循環血液容量へと血小板を戻す際の脾臓のカウンタ流動化を考慮に入れている。

#### 【0142】

(1. 希釈の概算)

ユーティリティー機能F1は、以下の式に基づいて、この希釈因子を概算する：

等式(12)

#### 【0143】

【数15】

$$Dilution = 1 - \frac{Prime + \frac{2ACD}{3} - PPP}{DonVol}$$

ここで：

Primeは、このシステムの感作容量（ml）である。

## 【0144】

A C Dは、使用する抗凝血剤の容量（この誘導が行われる時間に依存して、現在または終点）（m l）である。

## 【0145】

P P Pは、収集されるP P Pの容量（現在または目標）（m l）である。

## 【0146】

D o n V o l（m l）は、ドナーの身長、体重および性別を考慮に入れたモデルに基づいたドナーの血液容量である。これらのモデルは、回帰によって線形化したドナーの体重に対する血液容量をプロットする実験データを使用して、以下のさらに簡素化した式へとさらに簡単にされる：

等式（13）

## 【0147】

【数16】

$$DonVol=1024+51Wgt(r^2=0.87)$$

ここで：

W g tは、ドナーの体重（k g）である。

## 【0148】

（2．枯渇の概算）

血小板の連続収集は、利用できる循環血小板プールを枯渇させる。一次モデルは、ドナーの血小板数がドナーの循環血液容量（D o n V o l）で割った血小板収量（Y l d）（現在または目標）だけ少なくなることを予測しており、これは、以下のようにして表わされる：

等式（14）

## 【0149】

【数17】



$$Dep1 = \frac{100,000Y1d}{DonVol}$$

ここで：

Y1dは、現在の瞬間的な血小板収量または目標血小板収量（ $k/\mu l$ ）である。等式（14）では、Y1dは、単位を均衡させるために、100,000を掛けられている。

#### 【0150】

等式（14）は、代替血小板の脾臓流動化（これは、脾臓流動化因子（またはSpleen）と呼ばれている）を考慮していない。Spleenは、少ない血小板数のドナーが、それにもかかわらず、脾臓で、多くの血小板蓄積を有する。処理中にて、循環血小板をドナーの血液から引き出すにつれて、脾臓は、それが蓄積している血小板を血液中に放出し、それにより、循環血小板の低下を部分的に相殺する。本発明者は、血小板プレカウントがドナー間で広範囲に変わるものの、利用できる全血小板容量は、ドナー間で極めて一定に保たれることを発見した。平均の見かけドナー容量は、血液1リットルあたり、 $3.10 \pm 0.25 ml$ の血小板である。その変動計数は、8.1%であり、これは、正常なドナーで見られる血球容量の変動係数よりも僅かに高いにすぎない。

#### 【0151】

この流動化因子Spleenは、実際に測定した枯渇とDep1（等式（14））とを比較することから誘導され、これは、PltPreの関数として、プロットされ線形化される。Spleen（これは、1の下限に制限される）は、以下のようにして示される：

等式（15）

#### 【0152】

#### 【数18】

$$Spleen = [2.25 - 0.004 Plt_{Pre}] \geq 1$$

等式(14)および(15)に基づいて、このユーティリティー機能は、以下のようにして、Depletionを誘導する：

等式(16)

【0153】

【数19】

$$Depletion = \frac{100,000 Yld}{Spleen \times DonVol}$$

(C. リアルタイム手順の改良)

オペレータは、この手順の開始時にて、どのドナーについても、常に現在の血小板プレカウント  $Plt_{Pre}$  を知っている訳ではない。ユーティリティー機能 F1 は、初期設定パラメータ下にて、このシステムを起動させるか、または先の手順から評価する。ユーティリティー機能 F1 は、この手順中にて、後に、オペレータにより、実際の血小板プレカウント  $Plt_{Pre}$  を入力させる。ユーティリティー機能 F1 は、新たに入力した値を反映するように、1 セットの条件下にて決定した血小板収量を再計算する。ユーティリティー機能 F1 は、有効クリアード容量を計算するために現在の収量を使用し、次いで、その容量を使用して新たな現在の収量を計算して、脾臓流動化の血小板プレカウント依存特性を維持する。

【0154】

ユーティリティー機能 F1 は、現在の収量を使用して、以下のようにして、有効クリアード容量を計算する：

等式(17)

【0155】

【数20】

$$ClrVol = \frac{100,000 \times DonVol \times Yld_{Current}}{\left[ DonVol - Prime - \frac{ACD}{3} + \frac{PPP}{2} \right] \times Pre_{old} - \frac{50,000 \times Yld_{current}}{Spleen_{old}}}$$

ここで：

Cl r V o l は、クリアード血漿容量である。

【0156】

Don V o l は、等式（13）に従って計算したドナーの循環血液容量である。

【0157】

Y l d<sub>current</sub> は、現在の処理条件に基づいて等式（3）に従って計算した現在の血小板収量である。

【0158】

P r i m e は、血液側感作容量（ml）である。

【0159】

A C D は、使用した抗凝血剤の容量（ml）である。

【0160】

P P P は、収集した低血小板血漿の容量（ml）である。

【0161】

P r e<sub>old</sub> は、処理開始前に入力した処理前ドナー血小板数（k／μl）である。

【0162】

S p l e e n<sub>old</sub> は、P r e<sub>old</sub> に基づいて等式（16）を使って計算した脾臓流動化因子である。

【0163】

ユーティリティー機能 F 1 は、以下のようにして、新たな現在の収量を計算するために、等式（17）を使って計算した Cl r V o l を使用する。

【0164】

等式（18）

【0165】

【数21】

$$Yld_{New} = \left[ \frac{DonVol - Prime - \frac{ACD}{3} + \frac{PPP}{2}}{DonVol + \frac{ClrVol}{2 \times Spleen_{New}}} \right] \times \left[ \frac{ClrVol \times Pre_{New}}{100,000} \right]$$

ここで：

$Pre_{New}$ は、処理中に入力した修正ドナー血小板プレカウント（ $k/\mu l$ ）である。

【0166】

$Yld_{New}$ は、修正ドナー血小板プレカウント  $Pre_{New}$ を考慮に入れた新たな血小板収量である。

【0167】

$ClrVol$ は、等式（17）に従って計算したクリアード血漿容量である。

【0168】

$DonVol$ は、等式（13）に従って計算したドナーの循環血液容量であり、等式（17）のものと同じである。

【0169】

$Prime$ は、血液側感作容量（ $ml$ ）であり、等式（17）のものと同じである。

【0170】

$ACD$ は、使用した抗凝血剤の容量（ $ml$ ）であり、等式（17）のものと同じである。

【0171】

$PPP$ は、収集した低血小板血漿の容量（ $ml$ ）であり、等式（17）のものと同じである。

【0172】

$Spleen_{New}$ は、 $Pre_{New}$ に基づいて等式（15）を使って計算した脾臓

流動化因子である。

【0173】

(D. 残りの手順の時間)

ユーティリティー機能F2はまた、以下のようにして、残りの収集時間 ( $t_{rem}$ ) (分) を計算できる：

等式 (19)

【0174】

【数22】

$$t_{rem} = \frac{Vb_{rem}}{Q_b}$$

ここで：

$Vb_{rem}$ は、処理すべき残留容量であり、これは、現在の処理条件に基づいて、等式 (19) を使って計算される。

【0175】

$Q_b$ は、全血の流速であり、これは、ユーザーにより設定されるか、またはそうでなければ制御装置18により誘導されるかのいずれかである。

【0176】

(E. 血漿の収集)

ユーティリティー機能F2は、以下のようにして、血漿収集容量 ( $PPPG_{goal}$ , ml) を誘導するための種々の血漿収集要件を加える：

等式 (20)

【0177】

【数23】

$$PPP_{Goal} = PPP_{PC} + PPP_{Source} + PPP_{Reinfuse} + PPP_{Waste} + PPP_{CollCham}$$

ここで：

$PPP_{PC}$ は、PC産物から選択される低血小板血漿の容量であり、これは、250mlの典型的な初期設定値を有することができるか、またはそうでなければ、現在の処理条件に基づいて、制御装置18により計算できる。

【0178】

$PPP_{Source}$ は、血漿源として収集用を選択される低血小板血漿の容量である。

【0179】

$PPP_{Waste}$ は、種々の処理目的のために蓄積するように選択された低血小板血漿の容量（初期設定値＝30ml）である。

【0180】

$PPP_{CollCham}$ は、血漿収集チャンバの容量（初期設定値＝40ml）である。

【0181】

$PPP_{Reinfuse}$ は、処理中に再注入する低血小板血漿の容量である。

【0182】

（F．血漿収集速度）

ユーティリティー機能F2は、以下のようにして、血漿収集速度（ $Q_{PPP}$ ）（ml／分）を計算する：

等式（21）

【0183】

【数24】

$$Q_{PPP} = \frac{PPP_{Goal} - PPP_{Current}}{t_{rem}}$$

ここで：

$PPP_{Goal}$ は、所望の低血小板血漿の収集容量（ml）である。

【0184】

$PPP_{Current}$ は、収集した低血小板血漿の現在の容量（ml）である。

【0185】

$t_{rem}$ は、現在の処理条件に基づいて等式（19）を使って計算した収集残留時間である。

【0186】

（G. 見込み全AC用途）

ユーティリティー機能F2はまた、以下のようにして、処理中に使用することが予想される抗凝血剤の全容量（ $ACD_{End}$ ）を計算できる：

等式（22）

【0187】

【数25】

$$ACD_{End} = ACD_{Current} + \frac{Q_b \times t_{rem}}{1 + AC}$$

ここで：

$ACD_{Current}$ は、使用した抗凝血剤の現在の容量（ml）である。

【0188】

ACは、選択した抗凝血剤の割合である。

【0189】

$Q_b$ は、全血の流速であり、これは、現在の処理条件に基づいて、ユーザーにより設定されるか、またはそうでなければ制御装置18により計算されるかのい

ずれかである。

【0190】

$t_{rem}$ は、現在の処理条件に基づいて等式(19)を使って計算した収集残留時間である。

【0191】

本発明の種々の特徴は、上記の特許請求の範囲で述べている。

【0192】

【図面の簡単な説明】

【図1】

図1は、オンライン血液処理システムの概略図である。

【図2】

図2は、図1で示した血液処理システムの操作を管理する制御装置の概略図である。

【図3】

図3は、図1で示した血液処理システムの概略図であり、このシステムは、非同時収集モード中にドローサイクルを実行するように、この制御装置で調整される。

【図4】

図4は、図1で示した血液処理システムの概略図であり、このシステムは、非同時収集モード中にリターンサイクルを実行するように、この制御装置で調整される。

【図5】

図5は、図1で示した血液処理システムの概略図であり、このシステムは、非同時収集モードを実行するように、この制御装置で調整される。

【図6】

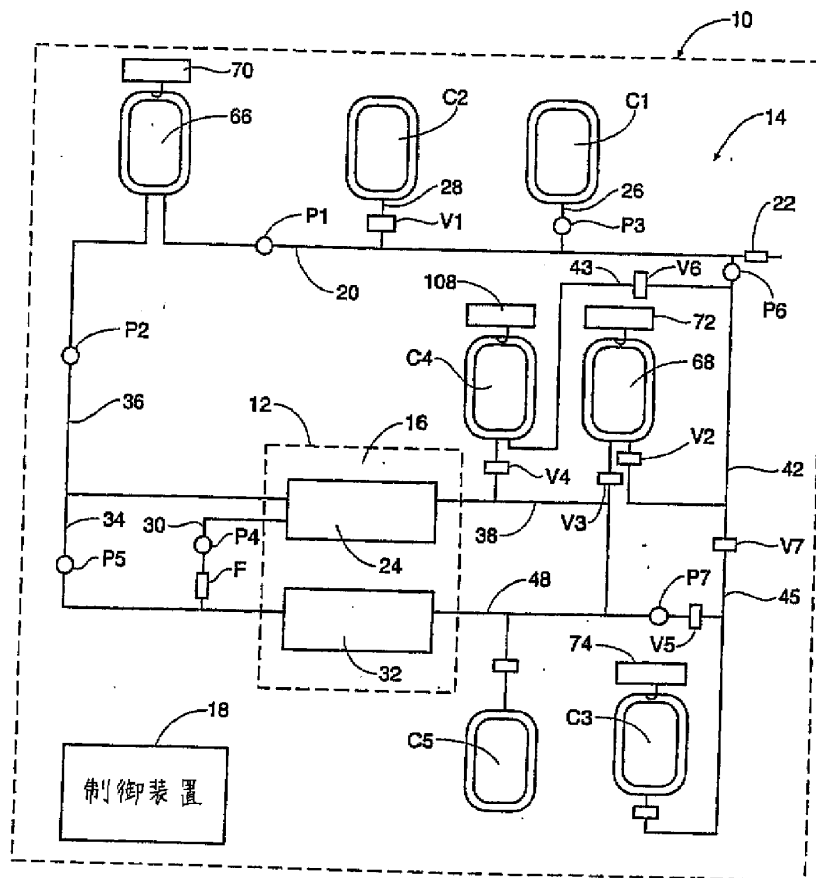
図6は、図1で示した血液処理システムの概略図であり、このシステムは、血液容量トリミング機能を実行するように、制御装置で調整される。

【図7】

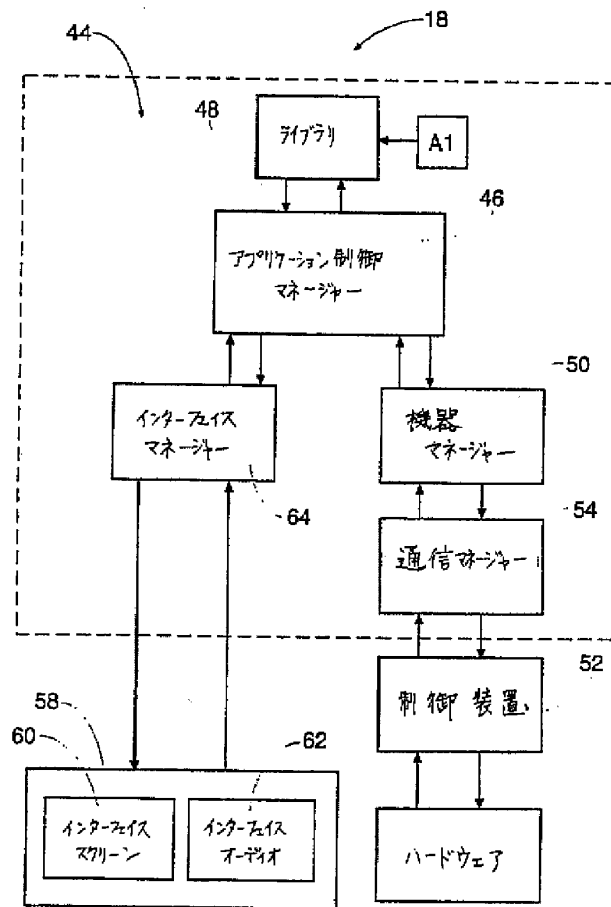


図7は、血液収集セットの正面図であり、これは、使用中にて、図1で示したシステムで収集した後の赤血球を、保存前にさらに処理するために受容する。

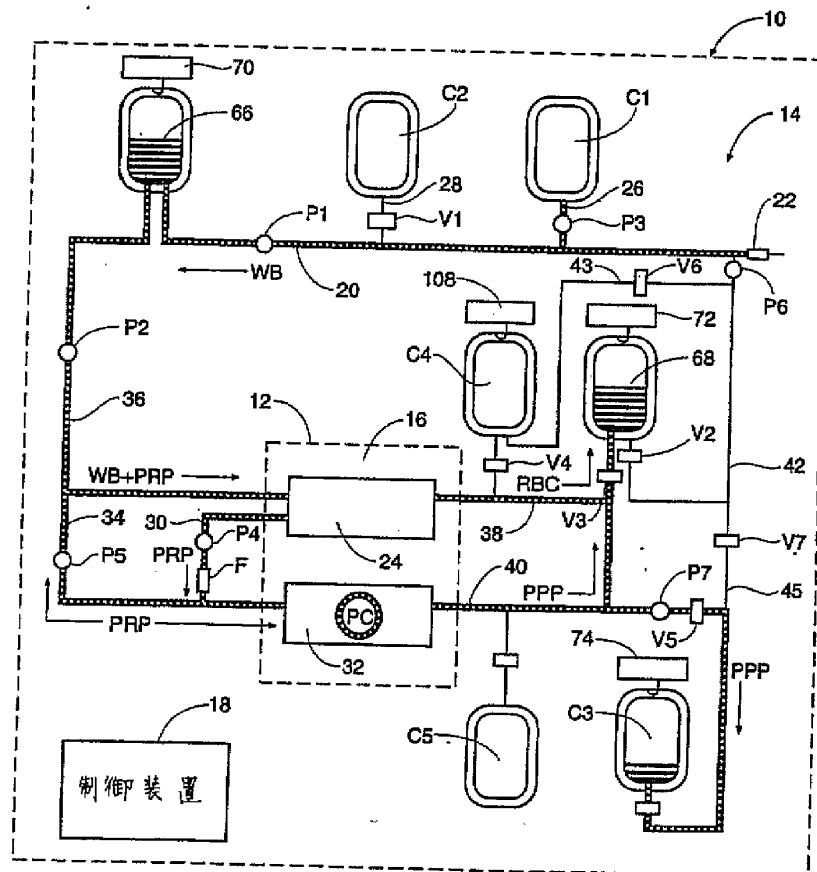
【図1】



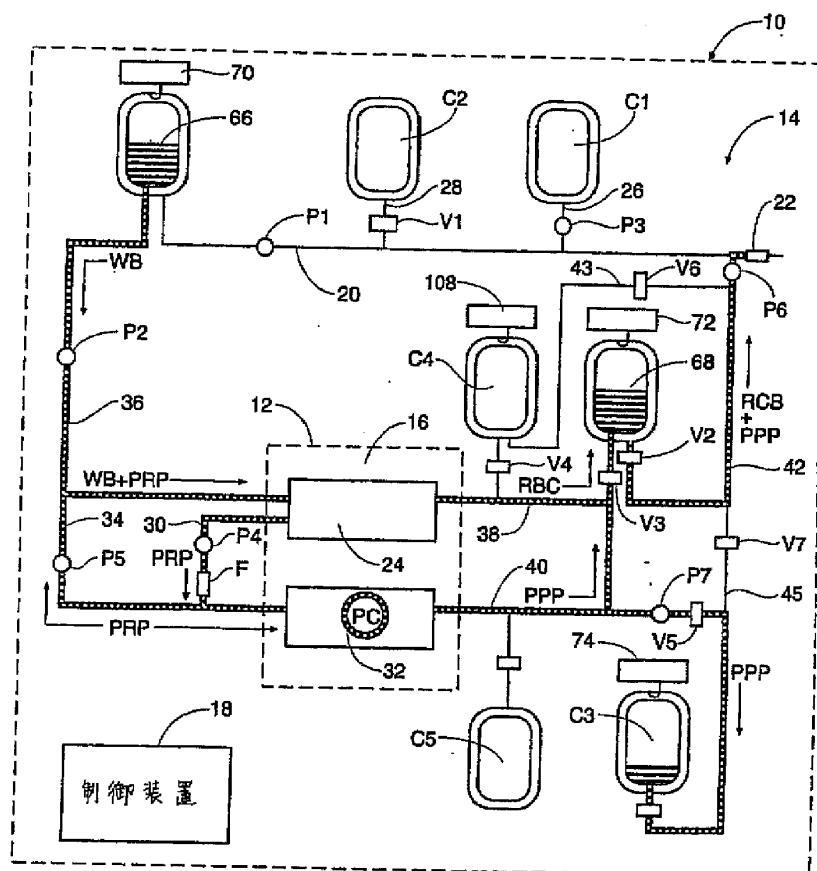
【図2】



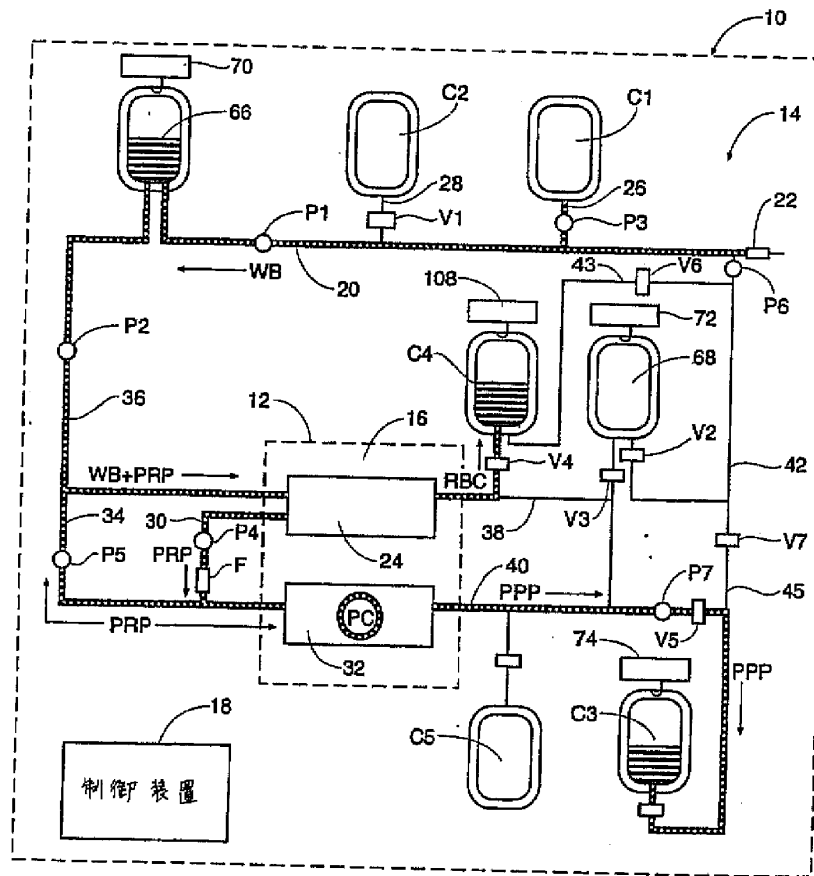
【図3】



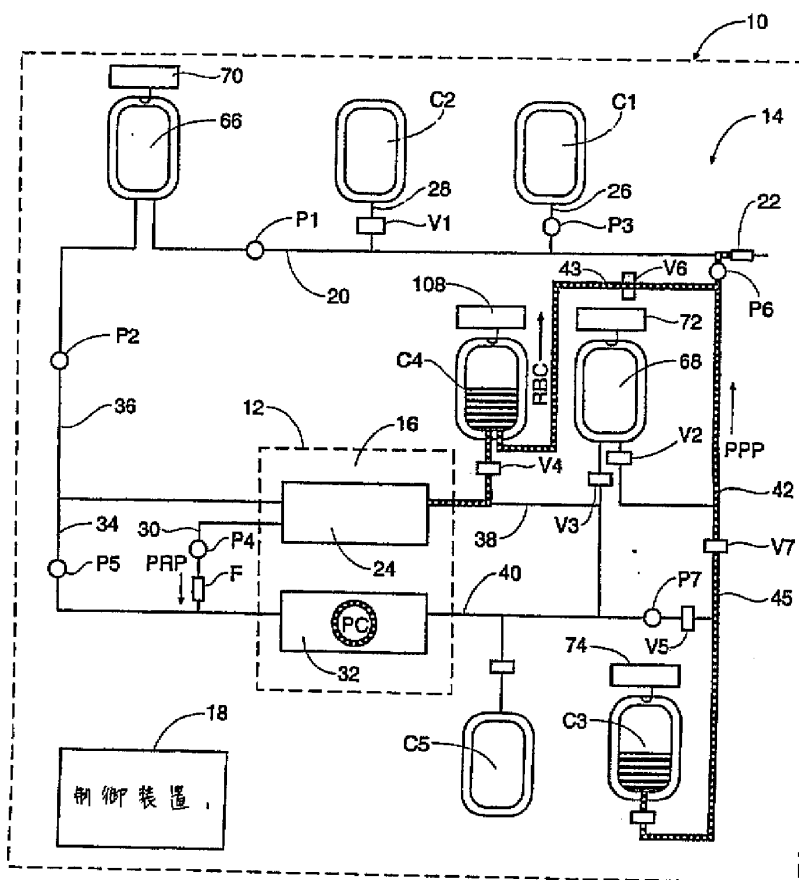
【図4】



【図5】



【図6】



【図7】

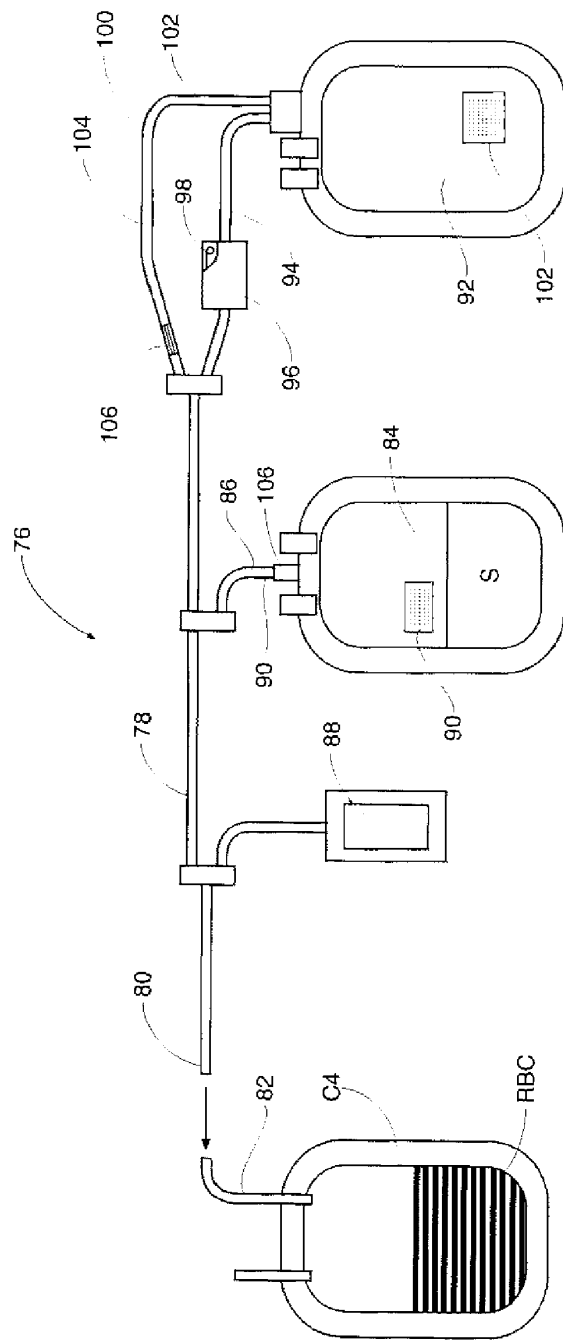


Fig. 7

## 【国際調査報告】

| INTERNATIONAL SEARCH REPORT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                  | International application No.<br>PCT/US00/25206                   |                                                                                                          |                                                                                                                                                                                                    |                                                                                       |                                                                                                                                                                              |                                                                                                                                                                      |                                                                                                                                                                                                                                                  |                                                                              |                                               |                                                                                                        |   |  |            |   |                                                                              |      |     |                                                                      |      |     |                                                                   |      |     |                                                                          |      |
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| <b>A. CLASSIFICATION OF SUBJECT MATTER</b><br>IPC(7) : A61M 37/00; B01D 33/15; C02F 1/58<br>US CL : 604/4.01, 6.09, 6.02; 210/767, 782<br>According to International Patent Classification (IPC) or to both national classification and IPC                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                  |                                                                   |                                                                                                          |                                                                                                                                                                                                    |                                                                                       |                                                                                                                                                                              |                                                                                                                                                                      |                                                                                                                                                                                                                                                  |                                                                              |                                               |                                                                                                        |   |  |            |   |                                                                              |      |     |                                                                      |      |     |                                                                   |      |     |                                                                          |      |
| <b>B. FIELDS SEARCHED</b><br>Minimum documentation searched (classification system followed by classification symbols)<br>U.S. : 604/4.01, 5.01-5.04, 6.01-6.05, 6.07, 6.09, 6.15, 6.16; 210/767, 782, 651, 85, 88, 109, 739, 745<br>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched<br>Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                  |                                                                   |                                                                                                          |                                                                                                                                                                                                    |                                                                                       |                                                                                                                                                                              |                                                                                                                                                                      |                                                                                                                                                                                                                                                  |                                                                              |                                               |                                                                                                        |   |  |            |   |                                                                              |      |     |                                                                      |      |     |                                                                   |      |     |                                                                          |      |
| <b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b> <table border="1"> <thead> <tr> <th>Category *</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X</td> <td>US 5,730,883 A (Brown) 24 May 1998 (24.05.1998) entire document.</td> <td>1-6, 10-16</td> </tr> <tr> <td>---</td> <td></td> <td></td> </tr> <tr> <td>Y</td> <td></td> <td>7-9, 17-21</td> </tr> <tr> <td>Y</td> <td>US 5,849,203 A (Brown et al.) 15 December 1998 (15.12.1998) entire document.</td> <td>1-23</td> </tr> <tr> <td>A,P</td> <td>US 5,051,147 A (Bischof) 18 April 2000 (18.04.2000) entire document.</td> <td>1-23</td> </tr> <tr> <td>A,P</td> <td>US 5,071,421 A (Brown) 06 June 2000 (06.06.2000) entire document.</td> <td>1-23</td> </tr> <tr> <td>X,P</td> <td>US 5,071,413 A (Brown et al.) 06 June 2000 (06.06.2000) entire document.</td> <td>1-23</td> </tr> </tbody> </table>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                  |                                                                   | Category *                                                                                               | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                 | Relevant to claim No.                                                                 | X                                                                                                                                                                            | US 5,730,883 A (Brown) 24 May 1998 (24.05.1998) entire document.                                                                                                     | 1-6, 10-16                                                                                                                                                                                                                                       | ---                                                                          |                                               |                                                                                                        | Y |  | 7-9, 17-21 | Y | US 5,849,203 A (Brown et al.) 15 December 1998 (15.12.1998) entire document. | 1-23 | A,P | US 5,051,147 A (Bischof) 18 April 2000 (18.04.2000) entire document. | 1-23 | A,P | US 5,071,421 A (Brown) 06 June 2000 (06.06.2000) entire document. | 1-23 | X,P | US 5,071,413 A (Brown et al.) 06 June 2000 (06.06.2000) entire document. | 1-23 |
| Category *                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                               | Relevant to claim No.                                             |                                                                                                          |                                                                                                                                                                                                    |                                                                                       |                                                                                                                                                                              |                                                                                                                                                                      |                                                                                                                                                                                                                                                  |                                                                              |                                               |                                                                                                        |   |  |            |   |                                                                              |      |     |                                                                      |      |     |                                                                   |      |     |                                                                          |      |
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| A,P                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | US 5,051,147 A (Bischof) 18 April 2000 (18.04.2000) entire document.                                                                                                                                                                             | 1-23                                                              |                                                                                                          |                                                                                                                                                                                                    |                                                                                       |                                                                                                                                                                              |                                                                                                                                                                      |                                                                                                                                                                                                                                                  |                                                                              |                                               |                                                                                                        |   |  |            |   |                                                                              |      |     |                                                                      |      |     |                                                                   |      |     |                                                                          |      |
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| <input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                  |                                                                   |                                                                                                          |                                                                                                                                                                                                    |                                                                                       |                                                                                                                                                                              |                                                                                                                                                                      |                                                                                                                                                                                                                                                  |                                                                              |                                               |                                                                                                        |   |  |            |   |                                                                              |      |     |                                                                      |      |     |                                                                   |      |     |                                                                          |      |
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| "P" document published prior to the international filing date but later than the priority date claimed                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                  |                                                                   |                                                                                                          |                                                                                                                                                                                                    |                                                                                       |                                                                                                                                                                              |                                                                                                                                                                      |                                                                                                                                                                                                                                                  |                                                                              |                                               |                                                                                                        |   |  |            |   |                                                                              |      |     |                                                                      |      |     |                                                                   |      |     |                                                                          |      |
| Date of the actual completion of the international search<br>29 January 2001 (29.01.2001)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                  | Date of mailing of the international search report<br>22 MAR 2001 |                                                                                                          |                                                                                                                                                                                                    |                                                                                       |                                                                                                                                                                              |                                                                                                                                                                      |                                                                                                                                                                                                                                                  |                                                                              |                                               |                                                                                                        |   |  |            |   |                                                                              |      |     |                                                                      |      |     |                                                                   |      |     |                                                                          |      |
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フロントページの続き

- (72)発明者 パットノ, ティモシー ジェイ.  
アメリカ合衆国 イリノイ 60202, エ  
バンストーン, ミシガン ナンバー 2  
542
- (72)発明者 スティナフ, ラッセル ディー.  
アメリカ合衆国 イリノイ 60004, ア  
ーリントン ハイツ, プレイサイド ド  
ライブ 615
- (72)発明者 ナヤク, アビナシュ  
アメリカ合衆国 イリノイ 60030, グ  
レイスレイク, ネビル ドライブ ナン  
バー 5 365
- (72)発明者 フォリー, ジョン ティー.  
アメリカ合衆国 イリノイ 60090, ウ  
ィーリング, ストーン プレイス 455
- (72)発明者 ウェバー, マーク  
アメリカ合衆国 イリノイ 60102, ア  
ルゴンクム, バーチ 800
- (72)発明者 ダンカン, タミー  
アメリカ合衆国 イリノイ 60081, ス  
プリング グローブ, バーウィン スト  
リート 1412
- (72)発明者 ブリックハン, プライアン ジェイ.  
アメリカ合衆国 イリノイ 60099, シ  
オン, ハーバー リッジ ドライブ  
3309

F ターム(参考) 2G045 BB10 CA24  
4C077 AA12 BB02 BB04 EE01 EE06  
HH03 JJ03 JJ22 JJ24 KK25  
KK30 NN02 NN03



Espacenet

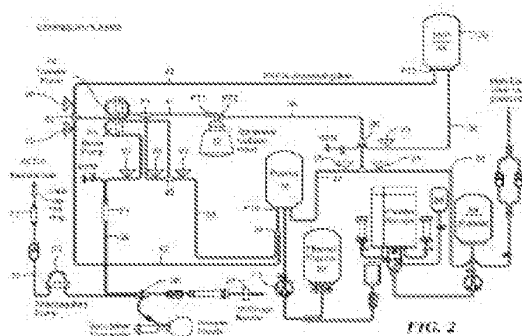
Bibliographic data: WO2012091720 (A1) — 2012-07-05

## SYSTEM AND METHOD FOR COLLECTING PLATELETS AND ANTICIPATING PLASMA RETURN

**Inventor(s):** PAGES ETIENNE [FR] ± (PAGES, ETIENNE)**Applicant(s):** HAEMONETICS CORP [US]; PAGES ETIENNE [FR] ±  
(HAEMONETICS CORPORATION, ; PAGES, ETIENNE)**Classification:** - **international:** A61M37/00  
- **cooperative:** A61M1/0272 (EP); A61M1/3603 (EP); A61M1/3696 (EP); A61M1/38 (EP); A61M2202/0415 (EP); A61M2202/0427 (EP)**Application number:** WO2010US62540 20101230 Global Dossier**Priority number (s):** WO2010US62540 20101230**Also published as:** CN103354755 (A) CN103354755 (B) EP2658596 (A1) EP2658596 (A4) EP2658596 (B1) more

## Abstract of WO2012091720 (A1)

A blood processing system for collecting plasma reduced platelets and anticipating plasma return includes a venous access device, a blood component separation device, a first return line, a recirculation line, and a second return line. The venous access device draws whole blood from a subject and returns blood components to the subject using a first pump. The blood component separation device separates the drawn blood into a first blood component and a second blood component, and sends the first blood component to a first blood component bag. The first return line fluidly connects the venous-access device and the blood component separation device. The recirculation line connects the first blood component container and the separation device. The second return line fluidly connects the first blood component container and the first return line and is



configured to return the first blood component within the first blood container to the subject.



(51) International Patent Classification:  
*A61M 37/00* (2006.01)

(21) International Application Number:  
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(22) International Filing Date:  
30 December 2010 (30.12.2010)

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(71) Applicant (for all designated States except US): **HAE-MONETICS CORPORATION** [US/US]; 400 Wood Road, Braintree, MA 02184 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **PAGES, Etienne** [FR/FR]; 25 Impasse de La Prairie, F-01170 Cessy (FR).

(74) Agents: **SUNSTEIN, Bruce, D.** et al.; Sunstein Kann Murphy & Timbers LLP, 125 Summer Street, Boston, MA 02110-1618 (US).

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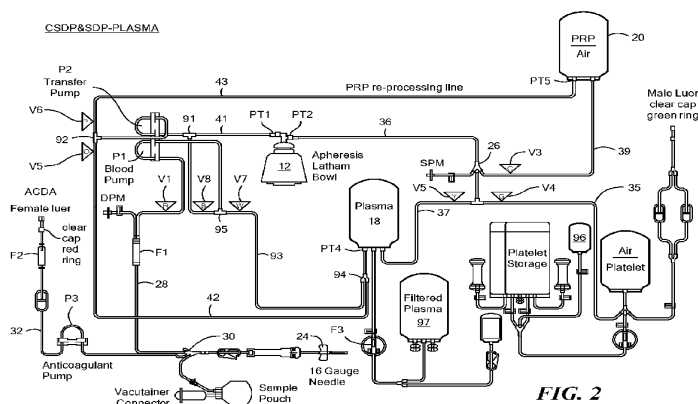
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(54) Title: SYSTEM AND METHOD FOR COLLECTING PLATELETS AND ANTICIPATING PLASMA RETURN



(57) Abstract: A blood processing system for collecting plasma reduced platelets and anticipating plasma return includes a venous access device, a blood component separation device, a first return line, a recirculation line, and a second return line. The venous access device draws whole blood from a subject and returns blood components to the subject using a first pump. The blood component separation device separates the drawn blood into a first blood component and a second blood component, and sends the first blood component to a first blood component bag. The first return line fluidly connects the venous-access device and the blood component separation device. The recirculation line connects the first blood component container and the separation device. The second return line fluidly connects the first blood component container and the first return line and is configured to return the first blood component within the first blood container to the subject.

## System and Method for Collecting Platelets and Anticipating Plasma Return

5

### Technical Field

The present invention relates to systems and methods for blood processing and blood component collection, and particularly to systems and methods for collecting platelets and anticipating plasma return.

### Background Art

10       Apheresis is a procedure in which individual blood components can be separated and collected from whole blood temporarily withdrawn from a subject. Typically, whole blood is withdrawn through a needle inserted into a vein of the subject's arm and into a cell separator, such as a centrifugal bowl. Once the whole blood is separated into its various components, one or more of the components can be removed from the centrifugal  
15       bowl. The remaining components can be returned to the subject along with optional compensation fluid to make up for the volume of the removed component. The process of drawing and returning continues until the quantity of the desired component has been collected, at which point the process is stopped. A central feature of apheresis systems is that the processed but unwanted components are returned to the donor. Blood  
20       components separated may include, for example, a high density component such as red blood cells, an intermediate density component such as platelets or white blood cells, and a lower density component such as plasma.

      Among various blood component products obtainable through apheresis, the demand for plasma reduced platelet products is rapidly growing. This is particularly  
25       because, with the improvement in cancer therapy, there is a need to administer more and more platelets to patients with lowered hemopoietic function, but the same patients may not need to be transfused with the plasma used to suspend platelets. Platelets are fragments of a large cell located in the marrow called a megakaryocyte and primarily contribute to hemostasis by performing aggregation function. Platelets also have a role in

tissue healing. Normal platelet counts in adults are 150,000-400,000/mm<sup>3</sup>. Platelet counts under 20,000/mm<sup>3</sup> can cause various troubles such as spontaneous bleeding.

Platelets have a short half-life of 4-6 days and the number of donors is limited. Therefore, in producing plasma reduced platelet products, it is important to harvest  
5 platelets from the whole blood supplied by a donor at a maximum yield and in a required amount. Further, it is known that the contamination of plasma reduced platelet product by white blood cells can lead to serious medial complications, such as GVH reactions. Therefore, it is also very important to keep the level of contamination by white blood  
10 cells as low as possible, while efficiently collecting platelets. To this end, various techniques have been developed. For example, using “surge” technology, after whole blood is collected and concentrically separated within a centrifuge into higher density, intermediate density and lower density components and plasma is harvested (so-called “draw” step), plasma is supplied through the centrifuge at a surge flow rate (e.g., a flow  
15 rate that increases with time). By performing the surge, platelets can be preferentially displaced from the intermediate density components (which exist as a buffy coat mainly comprising a mixture of platelets and white blood cells), and plasma reduced platelet products can be produced at an increased yield.

Instead of using surge technology, the platelet layer can also be extracted from the centrifuge by means of a layer “push” in which anticoagulated whole blood is introduced  
20 into the bowl until the platelet layer is pushed out, or by using a combination of surge and push methodologies. After harvesting a desired component or components, the residual blood components mostly comprising red blood cells and citrated plasma are returned to the donor (so-called “return” step).

As mentioned above, in many blood apheresis procedures and applications,  
25 unwanted components (e.g., the components that are not collected) are returned to the donor. In addition to contamination concerns (e.g., contamination, particulates, etc. being returned to the donor), the comfort of the subject must be taken into consideration. For example, returning citrated plasma to the subject too quickly or returning too much citrated plasma to the subject at one time can cause significant discomfort to the patient.  
30 Additionally, care must be taken to limit the volume of fluid outside of the body (e.g.,

extra-corporeal volume) and/or the reduction of fluid in the body (e.g., intra-vascular deficit).

### **Summary of the Invention**

In accordance with one embodiment of the invention, a method for collecting  
5 plasma reduced platelets and anticipating plasma return is presented. Whole blood is first drawn from the donor, anticoagulated, and introduced into a separation chamber. The separation chamber separates the anticoagulated whole blood into a number of blood components. The method then transfers plasma separated from the anticoagulated whole blood to a plasma container, and returns a first volume of the plasma from the plasma  
10 container back to the donor. The method then repeats the drawing, anticoagulating, introducing, and transferring steps to fill the separation device with additional anticoagulated whole blood.

Once the anticoagulated whole blood is introduced into the separation chamber (e.g., to fill the chamber), the method extracts platelet rich plasma ("PRP") from the  
15 separation chamber (e.g., using a surge elutriation method and/or surging with plasma) and into a PRP container. The method may then return the blood components remaining within the separation chamber to the donor and repeat the drawing, anticoagulating, and introducing steps to, once again, partially fill the separation device with anticoagulated whole blood. Once the separation device is partially filled, the method may then  
20 reintroduce PRP from the PRP container into the separation chamber, transfer plasma from the separation chamber to the plasma container, and reprocess the reintroduced PRP to create an enlarged layer of platelets within the separation device.

In accordance with some embodiments, the method may anticipate plasma return and return plasma within the plasma container to the donor while reintroducing the PRP  
25 into the separation chamber and/or reprocessing the PRP. The method may then, once again repeat the drawing, anticoagulating, and introducing steps to fill the separation chamber, remove the enlarged layer of platelets within the separation device using a surge elutriation method such that the platelets are transferred to a platelets container. The method may then return the blood components remaining within the separation  
30 chamber to the donor.

In accordance with related embodiments, the method may also return plasma from the plasma container to the donor during dead times (times during which current apheresis procedures neither draw nor return blood or blood components to the donor). Additionally, the method may calculate an extra-corporeal volume and/or an intra-vascular deficit, and the first volume of plasma returned to the donor may be based, at least in part, upon the calculated extra-corporeal volume or intra-vascular deficit.

In accordance with another embodiment of the present invention, a system for collecting plasma reduced platelets and anticipating plasma return includes a venous access device, a blood component separation device, a first return line, a recirculation line, and a second return line. The venous access device is configured to draw a first volume of whole blood from a subject and return blood components to the subject using a first pump. The blood component separation device (e.g., a centrifuge bowl) separates the drawn blood into a first blood component (e.g., plasma) and a second blood component (e.g., platelets), and is configured to send the first blood component to a first blood component bag and the second blood component to a second blood component bag.

The first return line fluidly connects the venous-access device and the blood component separation device and is configured to return blood components remaining in the separation device to the subject. The recirculation line connects the first blood component container and the separation device. The second return line fluidly connects the first blood component container and the first return line, and is configured to return the first blood component within the first blood container to the subject. The first blood component within the first blood component container may also be reintroduced into the separation chamber through the recirculation line and a recirculation pump.

The first pump may be used to return the first blood component within the first blood component container, and the blood components remaining in the separation device to the subject. The separation device may also separate the whole blood into a third blood component (e.g., red blood cells) in addition to the first and second blood components, and the blood components remaining in the separation device may include the third blood component.

In some embodiments, the second blood component may be removed from the separation device using a surge elutriation method. The surge elutriation method includes



reintroducing the first blood component into the blood component separation device through the recirculation line at an increasing rate until the second blood component is removed from the blood component separation device. The second blood component may be platelets and may be reintroduced into the blood component separation device after a predetermined amount of platelets is collected within the second blood component container so as to extract a plasma reduced platelet product from the separation device.

The system may also include an anticoagulant line and a reintroduction line. The anticoagulant line may be connected to an anticoagulant source, and may introduce anticoagulant into the drawn blood. The reintroduction line may fluidly connect the second blood component bag and the blood component separation device. The second blood component within the second blood component bag may be reintroduced into the blood component separation device when a second volume of whole blood is withdrawn from the subject to create an enlarged layer of the second blood component within the blood component separation device. The enlarged layer of second blood component may be removed from the blood component separation device using a surge elutriation method.

The system may return the first blood component to the subject as the second blood component is reintroduced into the blood component separation device and/or during dead times. The system may also include a controller that calculates at least one of an extra-corporeal volume and an intra-vascular deficit. The system may then return a volume of first blood component via the second return line based, at least in part, upon the calculated extra-corporeal volume or intra-vascular deficit.

In accordance with still further embodiments of the present invention, a system for collecting plasma reduced platelets may include (1) means for drawing a first volume of whole blood from a subject and returning blood components to the subject, (2) a blood component separation means for separating the drawn blood into a first blood component and a second blood component, (3) a first return means fluidly connecting the means for drawing a first volume of whole blood and the blood component separation means and for returning blood components remaining in the separation means to the subject, (4) a recirculation means connecting the second blood component container and the separation means, and (5) a second return means fluidly connecting the first blood component

container and the first return means. The blood component separation means may be configured to send the first blood component to a first blood component bag and the second blood component to a second blood component bag. The recirculation means may reintroduce the second blood component within the second blood component container  
5 into the separation means. The second return means may be configured to return the first blood component within the first blood container to the subject.

The means for drawing whole blood may include a first pump that is configured to return the first blood component within the first blood component container to the subject. The first pump may also return the blood components remaining in the separation  
10 means to the subject.

In accordance with additional embodiments, the system may also include a controller for controlling the flow of fluids through the system. The controller may repeatedly draw whole blood from the donor into the separation means, extract first and second blood components from the separation means, return first blood components to  
15 the subject using the second return means, and return remaining components in the separation means back to the subject using the first return means. Additionally, after a predetermined volume of second blood component has been sequestered in the second blood component container, the second blood component from the second blood component container may be reintroduced into the separation means. The controller may  
20 also calculate an extra-corporeal volume and/or an intra-vascular deficit, and the amount of plasma returned using the second return means may be based (at least in part) on the extra-corporeal volume and/or an intra-vascular deficit.

Moreover, the system may also include means for introducing anticoagulant into the drawn whole blood, and a reintroduction means fluidly connecting the second blood  
25 component bag and the blood component separation means. The second blood component within the second blood component bag may be reintroduced into the blood component separation means when a second volume of whole blood is withdrawn from the subject to create an enlarged layer of the second blood component within the blood component separation means. The enlarged layer of second blood component may be removed from  
30 the blood component separation means using a surge elutriation method. Additionally or alternatively, the second blood component may be platelets and may be reintroduced into

the blood component separation means after a predetermined amount of platelets is collected within the second blood component container so as to extract a plasma reduced platelet product from the separation means.

In accordance with additional embodiments, a method for collecting plasma  
5 reduced platelets and anticipating plasma return is presented. Whole blood is first drawn from a source, anticoagulated, and introduced into a separation chamber. The separation chamber separates the anticoagulated whole blood into a number of blood components. The method then transfers plasma separated from the anticoagulated whole blood to a plasma container, and returns a first volume of the plasma from the plasma container to  
10 the source. The method then repeats the drawing, anticoagulating, introducing, and transferring steps to fill the separation device with additional anticoagulated whole blood.

Once the anticoagulated whole blood is introduced into the separation chamber (e.g., to fill the chamber), the method extracts platelet rich plasma ("PRP") from the separation chamber (e.g., using a surge elutriation method and/or surging with plasma)  
15 and into a PRP container. The method may then return the blood components remaining within the separation chamber to the source, and repeat the drawing, anticoagulating, and introducing steps to, once again, partially fill the separation device with anticoagulated whole blood. Once the separation device is partially filled, the method may then reintroduce PRP from the PRP container into the separation chamber, transfer plasma  
20 from the separation chamber to the plasma container, and reprocess the reintroduced PRP to create an enlarged layer of platelets within the separation device.

In accordance with some embodiments, the method may anticipate plasma return and return plasma within the plasma container to the source while reintroducing the PRP into the separation chamber and/or reprocessing the PRP. The method may then, once  
25 again repeat the drawing, anticoagulating, and introducing steps to fill the separation chamber, remove the enlarged layer of platelets within the separation device using a surge elutriation method such that the platelets are transferred to a platelets container. The method may then return the blood components remaining within the separation chamber to the source.

30 In accordance with related embodiments, the method may also return plasma from the plasma container to the source during dead times. Additionally, the method may

calculate an extra-corporeal volume and/or an intra-vascular deficit, and the first volume of plasma returned to the source may be based, at least in part, upon the calculated extra-corporeal volume or intra-vascular deficit.

In still further embodiments, a method for collecting plasma reduced platelets may include drawing whole blood from a source, introducing anticoagulant into the whole blood drawn from the source, and introducing the anticoagulated whole blood into a separation chamber. The separation chamber, in turn, may separate the anticoagulated whole blood into a number of blood components. The method may then transfer plasma separated from the anticoagulated whole blood to a plasma container, return a first volume of the plasma from the plasma container back to the source, and repeat the above steps. Additionally, the method may also extract platelet rich plasma from the separation chamber into a platelet rich plasma container, and remove the remaining blood components from the separation chamber.

#### **Brief Description of the Drawings**

The foregoing features of the invention will be more readily understood by reference to the following detailed description, taken with reference to the accompanying drawings, in which:

Fig. 1 is a schematic diagram of an apheresis machine, in accordance with one embodiment of the invention;

Fig. 2 is a schematic diagram of a disposable system for use with the machine of Fig. 1, in accordance with one embodiment of the invention;

Fig. 3 is a side view of a centrifuge bowl for use with the machine of Fig. 1, in accordance with one embodiment of the invention; and

Fig. 4 is a flow chart depicting a method for collecting plasma reduced platelets from a donor and anticipating plasma return, in accordance with one embodiment of the invention.

#### **Detailed Description of Specific Embodiments**

Referring to Figs. 1 and 2, an apheresis apparatus 10 uses a blood component separation device, such as a standard Latham type centrifuge 11 for separating

anticoagulated whole blood into its constituent components, as described in US Patent No. 3,145,713, which is hereby incorporated by reference. Other types of separation chambers and devices may be used, such as, without limitation, an integral blow-molded centrifuge bowl, as described in U.S. Pat. Nos. 4,983,156 and 4,943,273, which are hereby incorporated by reference. The centrifuge 11 includes a rotating bowl 12 and stationary input and output ports PT1 and PT2 that are typically closely coupled to the bowl interior by a rotary seal 74 (see Fig. 3). The input port PT1 of the centrifuge 11 is in fluid communication with a venous access device 24 (e.g., a phlebotomy needle) via a blood micro-aggregate filter F1, a tube 28 and a Y-connector 30 when a valve V1 is open. The venous access device 24 may be replaced with a whole blood bag (not shown) in case the whole blood is to be first pooled and then supplied. The tube 28 has compatibility with blood, as is all the tubing in the apparatus 10. The outlet port PT2 of the centrifuge 11 is selectively coupled by a tube 36, a valve V2 and a tube 37 with a first container 18 labeled plasma suspended from a weight scale 33. A second container 20 labeled platelets is selectively coupled via the tube 36, a valve V3 and a tube 39 to the outlet port PT2. Additionally, a third container 22 labeled platelet storage is selectively coupled via the tube 36, a valve V4 and a tube 35 to the outlet port PT2. Both second container 20 and third container 22 may also be suspended by weight scales 67 and 77, respectively. As discussed in greater detail below, some embodiments may also include a tube 93 fluidly connected to the plasma container 18 at one end (via connector 94) and tube 41 at the other end (e.g. via connector 95). The tube 93 may be used to return citrated plasma within the plasma container 18 to the donor during dead times and/or while processing the whole blood within the centrifuge 11.

A bag or container 16 for storing an anticoagulant is in fluid communication with the venous access device/phlebotomy needle 24 via a bacteria filter F2, a tube 32 and the Y-connector 30. The bacteria filter F2 prevents any bacteria in the anticoagulant (ACD) container 16 from entering the system. Containers 16, 18, 20, and 22 are preferably plastic bags made of a blood compatible material. Peristaltic pumps P1, P2 and P3, together with the valves V1, V2, V3, and V4 control the direction and duration of flow through the apparatus 10 in response to signals generated by a line sensor 14, a donor pressure monitor (DPM) M1, a system pressure monitor (SPM) M2 and air detectors D1,

D2 and D3. The air detectors D1, D2 and D3 detect the absence or presence of fluid. The pressure monitors M1 and M2 monitor pressure levels within the apparatus 10. The line sensor 14 is an optical sensor and detects the presence of blood components passing through the line sensor 14 from the output port PT2.

5 In initial operation, the pumps P1 and P3 are energized to prime the tube 28 of the apparatus 10 with the anticoagulant from the container 16. The anticoagulant passes through the filter F2 and Y-connector 30 before reaching the air detector D1. The air detector D1 senses the presence of the anticoagulant at D1 and terminates the anticoagulant priming operation. During the priming operation, the valve V2 is open and  
10 sterile air displaced from bowl 12 by the anticoagulant enters the top port PT3 of the plasma container 18. The venous access device 24 is then inserted into the donor and the draw step is ready to be commenced.

Fig. 4 is a flowchart depicting a method for collecting blood components (e.g., platelets) from a subject and anticipating return of citrated plasma to the subject, in  
15 accordance with one embodiment of the invention. During draw step 401, whole blood is drawn from the subject, typically at a rate of about 80 ml/min. and mixed with the anticoagulant using the pumps P1 and P3 (Step 402) (referring back to Figs. 1-2). The pump P3 mixes the anticoagulant from the container 16 with the whole blood drawn from the subject or a bag in which it is pooled. The valve V1 is open, allowing the  
20 anticoagulated whole blood to pass through the tube 28 and blood filter F1 before being pumped into the separation device 12 through the inlet port PT1.

The whole blood is introduced into the bottom of the separation device 12 through a feed tube (not shown), step 403 of Fig. 4. The ratio of the anticoagulant to whole blood is typically about 1:10. The operation of each of the pumps and valves in the apheresis  
25 apparatus 10 can be performed in accordance with desired protocols under the control of a controller (not shown), which may be, for example, a microprocessor.

Referring to FIG. 3, the centrifuge 11 has the fixed inlet port PT1 and the fixed outlet port PT2. The rotary seal 74 fluidly couples the stationary inlet port PT1 to the lower interior portion of the bowl 12, and the outlet port PT2 to an upper portion of the  
30 bowl interior for collecting separated fractions. A core 72 occupies a volume coaxial

with the interior of bowl 12 and provides a separation region between the wall of the core 72 and the outer bowl wall 70.

As the bowl 12 is rotated, centrifugal forces separate the anticoagulated whole blood admitted into the bottom of the bowl into red blood cells (RBC), white blood cells (WBC), platelets and plasma. The number of rotations of the bowl 12 can be selected, for example, within a range of 4,000 to 6,000 rpm, and is typically 4,800 rpm. The blood is separated into different fractions in accordance with the component densities. The higher density component, i.e., RBC 60, is forced to the outer wall 70 of the bowl 12 while the lower density plasma 66 lies nearer the core 72. A buffy coat 61 is formed between the plasma 66 and the RBC 60. The buffy coat 61 is made up of an inner layer of platelets 64, a transitional layer 68 of platelets and WBC, and an outer layer of WBC 62. The plasma 66 is the component closest to the outlet port from the separation region and is the first fluid component displaced from the bowl 12 via the outlet port PT2 as additional anticoagulated whole blood enters the bowl 12 through the inlet port PT1. As the plasma 66 is displaced from the bowl 12, it is transferred to the plasma container 18 through lines 36 and 37 (Step 404 of Fig. 4).

Returning to Fig. 1, the displaced plasma passes through the line sensor 14, the tube 36, a 3-way T-connector 26, and the valve V2 (in the open position) and enters the first container 18. The plasma entering the first container 18 is drawn from the container 18 by the pump P2 via tube 42, valve V5 (in the open position), Y-connector 92 and tube 40 from the lower port PT4 and is recirculated into the bowl 12 through the inlet port PT1 via Y-connector 91 and line 41. The recirculated plasma dilutes the anticoagulated whole blood entering the bowl 12 and allows the blood components to separate more readily. An optical sensor 21 is applied to a shoulder portion of the bowl 12 for monitoring each layer of the blood components as they gradually and coaxially advance toward the core 72 from the outer wall 70 of the bowl 12. The optical sensor 21 may be mounted in a position at which it can detect the buffy coat reaching a particular radius, and the steps of drawing the whole blood from the donor 401 and introducing the whole blood into the bowl 402 may be terminated in response to the detection.

The amount of whole blood processed by the bowl 12 may be varied in response to at least one characteristic associated with the whole blood, such as the hematocrit

value, the number of platelets, the total amount of blood or the like of the whole blood, as described in copending U.S. patent application 09/392,880, filed September 9, 1999, entitled Apheresis Apparatus and Method for Producing Blood Products, which is hereby incorporated by reference. This variable control can be implemented under the control of a microcomputer, as aforementioned. Alternatively, each of them can be implemented manually.

As mentioned above, some embodiments of the present invention return plasma within the plasma container (e.g., citrated plasma) at various intervals during the apheresis process in order to anticipate plasma return and avoid returning a large volume at the end of the apheresis process (e.g., to improve patient comfort). To that end, the system 10 may pause the draw step (Step 401), and return some or all of the plasma contained within plasma container 18 to the donor. In particular, once the draw step (Step 401) is paused, the apheresis system 10 may reverse the direction of the draw/return pump P1, open valve V6, draw plasma from the plasma container 18 through outlet port PT4, and return the plasma to the patient/donor via lines 93 and 28.

The volume of plasma returned to the patient/donor during this step may depend upon a number of factors including, but not limited to the extra-corporeal volume ("ECV") and/or intra-vascular deficit ("IVD"). For example, the controller may calculate the ECV or IVD based upon data from previous cycles (e.g., previous cycles in a given apheresis procedure or cycles from a prior procedure), and determine if the ECV/IVD exceeds a predetermined percentage of estimated total blood volume ("TBV") (e.g., as estimated from donor characteristics such as gender, size, and weight). If the system 10 (e.g., the controller/microprocessor) determines that the ECV/IVD exceeds the predetermined percentage of TBV, then the system 10 may pause the draw (e.g., Step 401) and return plasma as discussed above. Additionally or alternatively, the system 10 may initiate the plasma return (Step 405) if the volume of plasma separated from the current cycle is equal to the volume of whole blood still to be drawn to complete the bowl filling. In order to preserve and/or improve blood separation during the plasma return step (Step 405), the centrifuge 11 may continue to spin and plasma may be circulated through the bowl 12 (e.g., using pump P2 and line 42).



By pausing the draw step (Step 401) and initiating the anticipated plasma return step (Step 405), the system 10 is able to greatly reduce the ECV and IVD. Additionally, the anticipated plasma return process also ensures that the return of citrated plasma to the patient/donor occurs over multiple steps with a significant time interval (e.g., several  
5 minutes) between. As discussed above, this helps improve patient comfort and reduces the risks associated with returning citrated plasma to the patient/donor.

Once the plasma return step is complete, the system may continue to draw whole blood from the patient/donor (e.g., in order to complete bowl filling) (Step 406) and extract platelets from the separation chamber 11/bowl 12. The platelets are extracted  
10 from the bowl 12 into a container, step 407 of Fig. 4. When extracting the platelets from the bowl 12, various methodologies may be employed, including, without limitation, dwell, surge, and/or push methodologies. For illustrative purposes, platelet extraction based on a dwell and surge technique will now be described in detail.

After the whole blood has been introduced into the centrifuge 11, step 406 of  
15 Fig.4, the valve V1 is closed and the pump P1 is stopped so that blood is no longer drawn from the donor, and dwell is commenced. During the dwell, the pump P2 recirculates plasma 66 through the bowl 12 at a moderate rate (for example, about 100 ml/min. in Fig. 4) for about 20 to 30 seconds. At this flow rate, the buffy coat 61 is diluted by the plasma and widens but the platelets do not leave the bowl 12. The dilution of the buffy coat  
20 allows the heavier white blood cells to sediment to the outer side of the buffy coat, resulting in a better separation between the lighter platelets layer 64 and the heavier white blood cells layer 62. As a result, the transitional layer 68 is reduced. The dwell period also allows the flow patterns in the bowl 12 to stabilize and allows more time for microbubbles to leave the bowl 12 and be purged.

25 After dwell, the surge step is commenced. In the surge, the speed of the pump P2 is increased in 5-10 ml/min. increments to recirculate plasma until reaching a platelet surge velocity of about 200-250 ml/min. The platelet surge velocity is the velocity at which platelets can leave the bowl 12 but not red blood cells or white blood cells. The plasma exiting the bowl becomes cloudy with platelets and this cloudiness is detected by  
30 the line sensor 14. The line sensor 14 consists of an LED which emits light through blood components leaving the bowl 12 and a photo detector which receives the light after

it passes through the components. The amount of light received by the photo detector is correlated to the density of the fluid passing through the line.

When platelets first start leaving the bowl 12, the line sensor output starts to decrease. The valve V3 is opened and the valve V2 is closed and the platelets are collected in container 20. Once the majority of the platelets are removed from the bowl 12, the fluid exiting the bowl becomes less cloudy. This lessening of cloudiness is detected by the line sensor 14, whereupon valve V3 is closed.

It is important to note that during any “dead” times (e.g., time during which whole blood is not being drawn from the patient/donor, any time during which the centrifuge 11 is stopped, etc), the system 10 may return plasma contained within the plasma bag 18 to the patient/donor. For example, while the system 10 removes/extracts the platelets from the centrifuge bowl 12 and/or during the dwell step described above, the system 10 may also return plasma contained within the container 18 to the patient/donor in a manner similar to that described above (e.g., by reversing the pump P1 and drawing the plasma through line 93.

If the plasma return occurs during the surge process (e.g., the recirculation of plasma through the bowl 12), both the draw/return pump P1 and the recirculation pump P2 may draw plasma from the plasma container 18 and both valves V5 and V7 may be open. The draw/return pump P1 may draw the plasma through tube 93 and the recirculation pump P2 may draw plasma through tube 42. To prevent the separate plasma flows from mixing and interfering with one another, valve V8 (Fig. 2), located between connectors 91 and 95 may be closed.

After the platelets have been collected, return step 409 (see Fig. 4) is initiated. During return step 409, the rotation of the bowl 12 is stopped and the remaining blood components in the bowl 12 are returned to the donor by reversal of rotation of the pump P1 via the venous access device 24 with the valve V1 open. The valve V2 is also opened to allow air to enter the centrifuge bowl during the return. The plasma from the container 18 dilutes the remaining blood components in the bowl 12. Namely, the pump P2 mixes the plasma with the returning components in the bowl 12 with the valve V2 open, diluting the returning red blood cells component with plasma to speed up the return time. When

the remaining blood components in the bowl have been returned to the donor, the return step 409 is terminated.

Referring to Fig. 4, the steps of drawing whole blood from the donor (Step 401), introducing anticoagulant into the whole blood (Step 402), introducing the whole blood into a separation chamber (Step 403), transferring plasma to the plasma container 18 (Step 404), returning plasma to the patient/donor (Step 405), continuing whole blood draw (Step 406), extracting platelets from the separation chamber (Step 407), returning plasma (Step 408), and returning the remaining components back to the donor (Step 409), are repeated until a desired volume of platelets is sequestered in the container 20, step 410. Typically, steps 401-409 are repeated two to four times, with about 450-500 ml of whole blood processed per cycle. The sequestered platelet concentration is typically about  $1.5 \times 10^6/\mu\text{L}$ .

The system may then re-process the platelets within container 20 by re-introducing the platelets (platelet rich plasma) in container 20 into the bowl 12, step 412 of Fig. 4. Reintroducing the platelets forms a layer of platelets that is several times larger than that obtained by processing only one cycle of whole anticoagulated blood. For example, in some embodiments, the platelet layer volume is approximately equal to the average volume of one cycle multiplied by the number of platelet sequestering cycles plus one. The platelets are drawn from port PT5 of container 20 by pump P2 via tube 43, valve V6 (in the open position), Y-connector 92, and tube 40, and input into bowl 12 through the inlet port PT1 via Y-connector 91 and line 41. To minimize contact between the platelets and bowl 12, the bowl 12 may be partly filled with anticoagulated whole blood drawn from the donor 401 prior to re-introduction of the platelets, step 411 of Fig. 4. The whole blood forms a cell bed at the periphery of the bowl 12 that serves as a buffer between the periphery of the bowl and the platelets, reducing platelet clumping. Additionally or alternatively, whole anticoagulated blood may be added to the separation chamber during platelet reintroduction so as to bring platelet layer towards the elutriation radius, or after platelet reintroduction for perfecting platelet separation and standardizing conditions of initiating platelet extraction.

It is worth noting that, if the platelets being reintroduced into the bowl 12 and reprocessed are in the form of platelet rich plasma ("PRP")(platelets suspended within

plasma), the centrifugal forces within the bowl 12 will cause the PRP to abandon the suspended platelets, thereby freeing the plasma. This freed plasma will be displaced from the bowl 12 and sent to the plasma container 18 as additional fluid (e.g., additional PRP, plasma, anticoagulated whole blood, etc.) enters the bowl 12.

5           As the platelets are reprocessed to form the plasma reduced platelet product (discussed in greater detail below), the system 10 may, once again, return plasma within the container 18 to the patient/donor (Step 413). For example, as the platelets from container 20 are being reintroduced into the bowl 12, the system 10 may open valve V7 and use the draw/return pump P1 to draw plasma from port PT4 of container 18 through  
10 line 93, and return the plasma to the patient/donor through line 28 and the venous access device 24. The system 10 may then draw whole blood from the patient/donor and fill the bowl 12 with anticoagulated whole blood, step 414.

          Using, for example, surge or push methodologies, the plasma reduced platelet concentrate is then extracted from the layer of platelets that now reside in bowl 12, step  
15 415 of Fig. 4. The plasma reduced platelet product is sequestered in container 22 via line sensor 14, tube 36, 3-way T-connector 26 and valve V4 (in the open position). Platelet product concentration is typically in the range of  $2.6 \times 10^6/\mu\text{L}$  to  $5.2 \times 10^6/\mu\text{L}$ , which is 2-3 times that of platelets sequestered when processing only one cycle of whole anticoagulated blood. Once the plasma reduced platelet concentrate is extracted from the  
20 bowl 12 and collected within container 22, the system 10 may then return any blood components remaining within the bowl 12 and any plasma still remaining within the plasma container 18, step 416 of Fig. 4.

          It should be noted that the surge elutriation technique may use a variety of fluids other than plasma to extract the platelets and/or the reduced plasma platelet product from  
25 the separation chamber (e.g., saline solution may be used). Additionally, the platelets that are reintroduced into the separation chamber may be re-anticoagulated to prevent the platelets from coagulating and/or clumping. For example, the platelet collection bag 20 or the reduced plasma platelet product bag 22 may be pre-loaded with a quantity of anticoagulant so that the platelets and/or reduced plasma platelet product mix with the  
30 anticoagulant as they are drawn from the separation chamber. Additionally or alternatively, sufficient anticoagulant may be added as the whole blood is withdrawn

from the subject such that enough anticoagulant is still present in the platelets prior to re-processing. In either scenario, the amount of anticoagulant added the whole blood and/or extracted platelets must be weighed against the safety of the subject. In particular, the amount of anticoagulant should be limited so as to prevent a large quantity of  
5 anticoagulant being returned to the subject.

It should also be noted that once the platelets and the reduced plasma platelet product are collected, a platelet preservative solution may be added to help preserve and store the platelets for later use. The preservative solution can be added to the platelets and platelet product after collection (e.g., from a separate bag or storage container 96), or the  
10 platelet collection bag 20 and the reduced plasma platelet product bag 22 may be pre-loaded with the additive solution.

By anticipating the total amount of plasma that will be returned to the donor and returning the plasma in multiple steps, various embodiments of the present invention are able to provide numerous advantages over the prior art. For example, by not returning all  
15 of the plasma at the end of the procedure, various embodiments of the present invention are able to greatly reduce patient discomfort and the risks associated with returning large volumes of citrated plasma. Additionally, by returning plasma during “dead” times, some embodiments of the present invention are able to reduce the overall procedure time, and the ECV/IVD at any given time during the procedure. Furthermore, because plasma may  
20 be returned during processing and the EVC/IVD is significantly reduced, various embodiments of the present invention do not need to return saline (or other compensation fluid) to the patient to reduce the ECV.

Although the embodiments described above discuss returning the plasma to the patient/donor, not all of the plasma needs to be returned. For example, some  
25 embodiments of the present invention may save a portion of the collected plasma. In such embodiments, the plasma may be filtered using F3 and stored within filtered plasma container 97.

If additional reduced plasma platelet product is required, each of the steps described above may now be repeated until a desired quantity of plasma reduced platelet  
30 product is collected. In various embodiments, plasma may be added to the plasma

reduced platelet product so as to adjust the plasma reduced product to a predetermined volume or concentration.

Although the above embodiments are described as withdrawing whole blood from a patient/donor and returning unwanted components back to the donor, other  
5    embodiments of the present invention may be used for donor-free processing. For example, as discussed above, the venous access device 24 may be replaced with a whole blood bag (not shown) in cases in which the whole blood is to be first pooled and then supplied to the separation device 11. In such embodiments, the plasma from the plasma  
10    container 18 and the blood components remaining in the separation device 11 may be returned to one or more storage bags/containers (e.g., all into one container or into separate containers) or returned to the whole blood bag. Such embodiments would still have advantages over the prior art systems because of the greatly reduced processing time (e.g., because plasma is sent to the containers during dead times, etc.)

The described embodiments of the invention are intended to be merely exemplary  
15    and numerous variations and modifications will be apparent to those skilled in the art. All such variations and modifications are intended to be within the scope of the present invention.

We claim:

1. A method for collecting plasma reduced platelets and anticipating plasma return comprising:

- a) drawing whole blood from a donor;
- 5       b) introducing anticoagulant into the whole blood drawn from the donor;
- c) introducing the anticoagulated whole blood into a separation chamber, the separation chamber separating the anticoagulated whole blood into a number of blood components;
- d) transferring plasma separated from the anticoagulated whole blood to a plasma  
10    container;
- e) returning a first volume of the plasma from the plasma container back to the donor;
- f) repeating steps a through d;
- g) extracting platelet rich plasma from the separation chamber into a platelet rich  
15    plasma container; and
- h) returning the remaining blood components within the separation chamber to the donor.

2. A method according to claim 1 further comprising:

- 20       i) repeating steps a through c to partially fill the separation device with anticoagulated whole blood;
- j) reintroducing platelet rich plasma from the platelet rich plasma container into the separation chamber;
- k) transferring plasma from the separation chamber to the plasma container; and
- 25       l) reprocessing the reintroduced platelet rich plasma to create an enlarged layer of platelets within the separation device.

3. A method according to claim 2, further comprising

- 30       m) returning plasma from the plasma container to the donor while reprocessing the platelet rich plasma.

4. A method according to claim 2, further comprising

m) returning plasma from the plasma container to the donor while reintroducing the platelet rich plasma into the separation chamber.

5 5. A method according to claim 2 further comprising:

m) removing the enlarged layer of platelets within the separation device using a surge elutriation method such that the platelets are transferred to a platelets container; and

n) returning the blood components remaining within the separation chamber to the donor.

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6. A method according to claim 5, further comprising returning plasma from the plasma container to the donor during dead times.

7. A method according to claim 1, further comprising:

15 calculating at least one of an extra-corporeal volume and an intra-vascular deficit, the volume of plasma returned during step (e) being based, at least in part, upon the calculated extra-corporeal volume or intra-vascular deficit.

8. A method according to claim 1, wherein extracting platelet rich plasma from the separation chamber includes extracting the platelet rich plasma by surge elutriation.

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9. A method according to claim 8, wherein extracting the platelet rich plasma from the separation chamber by surge elutriation includes surging with plasma.

25 10. A system for collecting plasma reduced platelets and anticipating plasma return comprising:

a venous access device for drawing a first volume of whole blood from a subject and returning blood components to the subject using a first pump;

30 a blood component separation device for separating the drawn blood into a first blood component and a second blood component, the blood component separation device



configured to send the first blood component to a first blood component bag and the second blood component to a second blood component bag;

a first return line fluidly connecting the venous-access device and the blood component separation device for returning blood components remaining in the separation device to the subject;

a recirculation line connecting the first blood component container and the separation device, wherein the first blood component within the first blood component container is reintroduced into the separation chamber through the recirculation line and a recirculation pump; and

a second return line fluidly connecting the first blood component container and the first return line and configured to return the first blood component within the first blood container to the subject.

11. A system according to claim 10, wherein the first pump returns the first blood component within the first blood component container to the subject.

12. A system according to claim 10, wherein the first pump returns the blood components remaining in the separation device to the subject.

13. A system according to claim 10, wherein the separation device is a centrifuge bowl.

14. A system according to claim 10, wherein the first blood component is plasma and the second blood component is platelets.

15. A system according to claim 10, wherein the separation device separates the whole blood into a third blood component in addition to the first and second blood components.

16. A system according to claim 15, wherein blood components remaining in the separation device includes the third blood component.

17. A system according to claim 15, wherein the third blood component is red blood cells.

18. A system according to claim 10, wherein the second blood component is removed  
5 from the separation device using a surge elutriation method.

19. A system according to claim 18, wherein the surge elutriation method includes reintroducing the first blood component into the blood component separation device through the recirculation line at an increasing rate until the second blood component is  
10 removed from the blood component separation device.

20. A system according to claim 10, further comprising an anticoagulant line connected to an anticoagulant source, the anticoagulant line introducing anticoagulant into the  
15 drawn blood.

21. A system according to claim 10, wherein the second blood component is platelets and is reintroduced into the blood component separation device after a predetermined amount of platelets is collected within the second blood component container so as to extract a plasma reduced platelet product from the separation device.  
20

22. A system according to claim 10, further comprising a reintroduction line fluidly connecting the second blood component bag and the blood component separation device, wherein the second blood component within the second blood component bag is reintroduced into the blood component separation device when a second volume of whole  
25 blood is withdrawn from the subject, thereby creating an enlarged layer of the second blood component within the blood component separation device, the enlarged layer of second blood component being removed from the blood component separation device using a surge elutriation method.

23. A system according to claim 22, wherein the first blood component within the first blood component container is returned to the subject as the second blood component is reintroduced into the into the blood component separation device.

5 24. A system according to claim 10, wherein the first blood component within the first blood component container is returned to the subject during dead times.

25. A system according to claim 10, further comprising a controller, the controller calculating at least one of an extra-corporeal volume and an intra-vascular deficit, the  
10 system returning a volume of first blood component via the second return line based, at least in part, upon the calculated extra-corporeal volume or intra-vascular deficit.

26. A system for collecting plasma reduced platelets and anticipating plasma return comprising:

15 means for drawing a first volume of whole blood from a subject and returning blood components to the subject;

a blood component separation means for separating the drawn blood into a first blood component and a second blood component, the blood component separation means configured to send the first blood component to a first blood component bag and the

20 second blood component to a second blood component bag;

a first return means fluidly connecting the means for drawing a first volume of whole blood and the blood component separation means, the first return means configured to return blood components remaining in the separation means to the subject;

a recirculation means connecting the second blood component container and the  
25 separation means, wherein the recirculation means reintroduces the second blood component within the second blood component container into the separation means; and

a second return means fluidly connecting the first blood component container and the first return means and configured to return the first blood component within the first blood container to the subject.

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27. A system according to claim 26, wherein the means for drawing whole blood includes a first pump, the first pump configured to return the first blood component within the first blood component container to the subject.

5 28. A system according to claim 27, wherein the first pump is also configured to return the blood components remaining in the separation means to the subject.

29. A system according to claim 26, further comprising a controller for controlling the flow of fluids through the system, the controller repeatedly drawing whole blood from the  
10 donor into the separation means, extracting first and second blood components from the separation means, returning first blood components within the first blood component container to the subject using the second return means, and returning remaining components in the separation means back to the subject using the first return means, wherein after a predetermined volume of second blood component has been sequestered  
15 in the second blood component container, the second blood component from the second blood component container is reintroduced into the separation means.

30. A system according to claim 29, wherein the controller calculates at least one of an extra-corporeal volume and an intra-vascular deficit, the amount of first blood component  
20 returned using the second return means being based at least in part on the at least one of an extra-corporeal volume and an intra-vascular deficit.

31. A system according to claim 26, wherein the first blood component is plasma and the second blood component is platelets.  
25

32. A system according to claim 26, wherein the separation means separates the whole blood into a third blood component in addition to the first and second blood components.

33. A system according to claim 32, wherein blood components remaining in the  
30 separation means includes the third blood component.

34. A system according to claim 32, wherein the third blood component is red blood cells.

35. A system according to claim 26, wherein the second blood component is removed  
5 from the separation device using a surge elutriation method.

36. A system according to claim 35, wherein the surge elutriation method includes reintroducing the first blood component into the blood component separation means through the recirculation means at an increasing rate until the second blood component is  
10 removed from the blood component separation means.

37. A system according to claim 26, further comprising means for introducing anticoagulant into the drawn whole blood.

15 38. A system according to claim 26, wherein the second blood component is platelets and is reintroduced into the blood component separation means after a predetermined amount of platelets is collected within the second blood component container so as to extract a plasma reduced platelet product from the separation means.

20 39. A system according to claim 26, further comprising a reintroduction means fluidly connecting the second blood component bag and the blood component separation means, wherein the second blood component within the second blood component bag is reintroduced into the blood component separation means when a second volume of whole blood is withdrawn from the subject, thereby creating an enlarged layer of the second  
25 blood component within the blood component separation means, the enlarged layer of second blood component being removed from the blood component separation means using a surge elutriation method.

40. A method for collecting plasma reduced platelets and anticipating plasma return  
30 comprising:

a) drawing whole blood from a source;

- b) introducing anticoagulant into the whole blood drawn from the source;
- c) introducing the anticoagulated whole blood into a separation chamber, the separation chamber separating the anticoagulated whole blood into a number of blood components;
- 5 d) transferring plasma separated from the anticoagulated whole blood to a plasma container;
- e) returning a first volume of the plasma from the plasma container to the source;
- f) repeating steps a through d;
- g) extracting platelet rich plasma from the separation chamber into a platelet rich
- 10 plasma container; and
- h) returning the remaining blood components within the separation chamber to the source.

41. A method according to claim 40 further comprising:

- 15 i) repeating steps a through c to partially fill the separation device with anticoagulated whole blood;
- j) reintroducing platelet rich plasma from the platelet rich plasma container into the separation chamber;
- k) transferring plasma from the separation chamber to the plasma container; and
- 20 l) reprocessing the reintroduced platelet rich plasma to create an enlarged layer of platelets within the separation device.

42. A method according to claim 41, further comprising

- 25 m) returning plasma from the plasma container to the source while reprocessing the platelet rich plasma.

43. A method according to claim 41, further comprising

- 30 n) returning plasma from the plasma container to the source while reintroducing the platelet rich plasma into the separation chamber.

44. A method according to claim 41 further comprising:

m) removing the enlarged layer of platelets within the separation device using a surge elutriation method such that the platelets are transferred to a platelets container; and  
n) returning the blood components remaining within the separation chamber to the source.

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45. A method according to claim 44, further comprising returning plasma from the plasma container to the source during dead times.

46. A method according to claim 40, further comprising:

10 calculating at least one of an extra-corporeal volume and an intra-vascular deficit, the volume of plasma returned during step (e) being based, at least in part, upon the calculated extra-corporeal volume or intra-vascular deficit.

47. A method according to claim 40, wherein extracting platelet rich plasma from the separation chamber includes extracting the platelet rich plasma by surge elutriation.

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48. A method according to claim 47, wherein extracting the platelet rich plasma from the separation chamber by surge elutriation includes surging with plasma.

49. A method for collecting plasma reduced platelets comprising:

20

a) drawing whole blood from a source;

b) introducing anticoagulant into the whole blood drawn from the source;

c) introducing the anticoagulated whole blood into a separation chamber, the separation chamber separating the anticoagulated whole blood into a number of blood

25

components;

d) transferring plasma separated from the anticoagulated whole blood to a plasma container;

e) returning a first volume of the plasma from the plasma container back to the source;

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f) repeating steps a through d;

g) extracting platelet rich plasma from the separation chamber into a platelet rich plasma container; and

h) removing the remaining blood components from the separation chamber.

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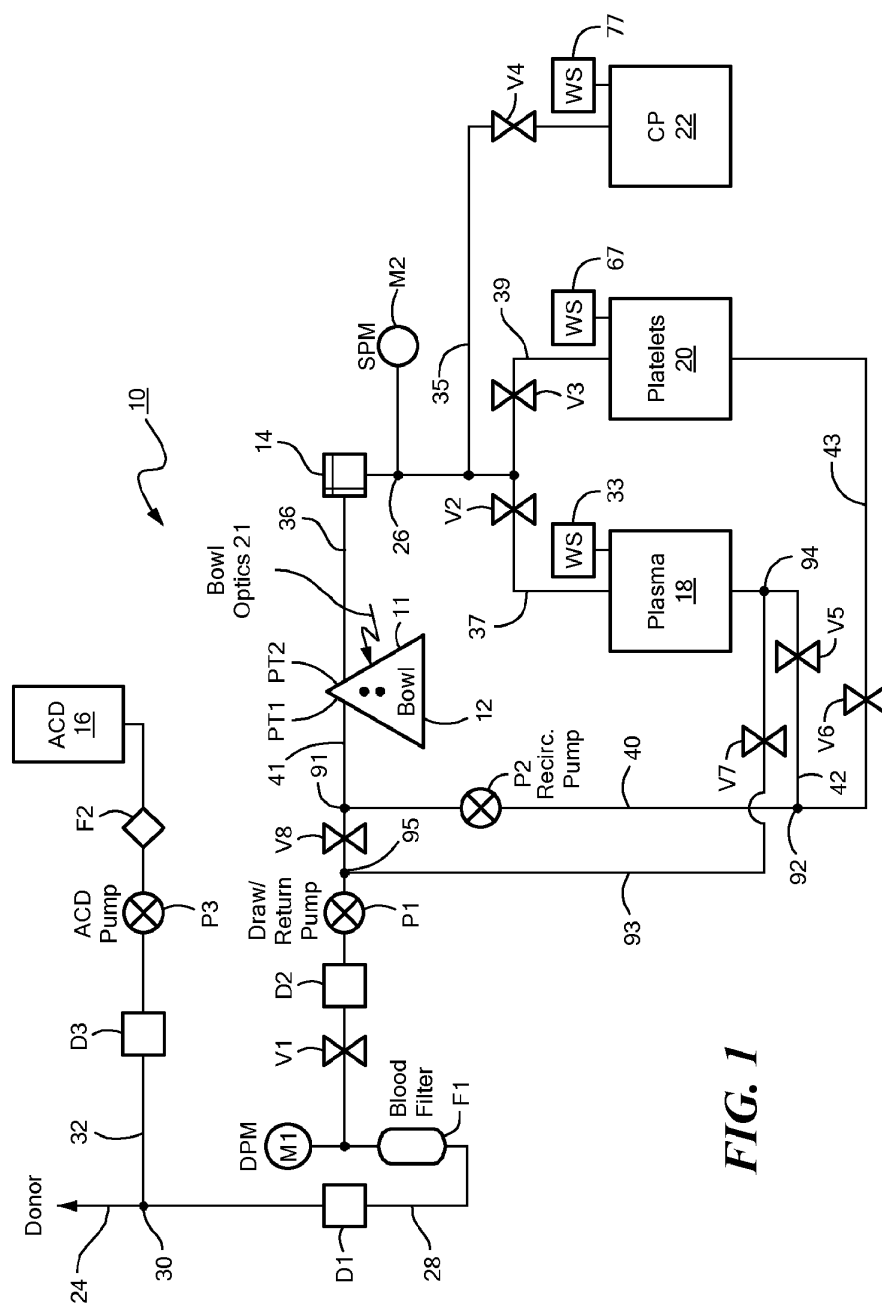


**FIG. 1**

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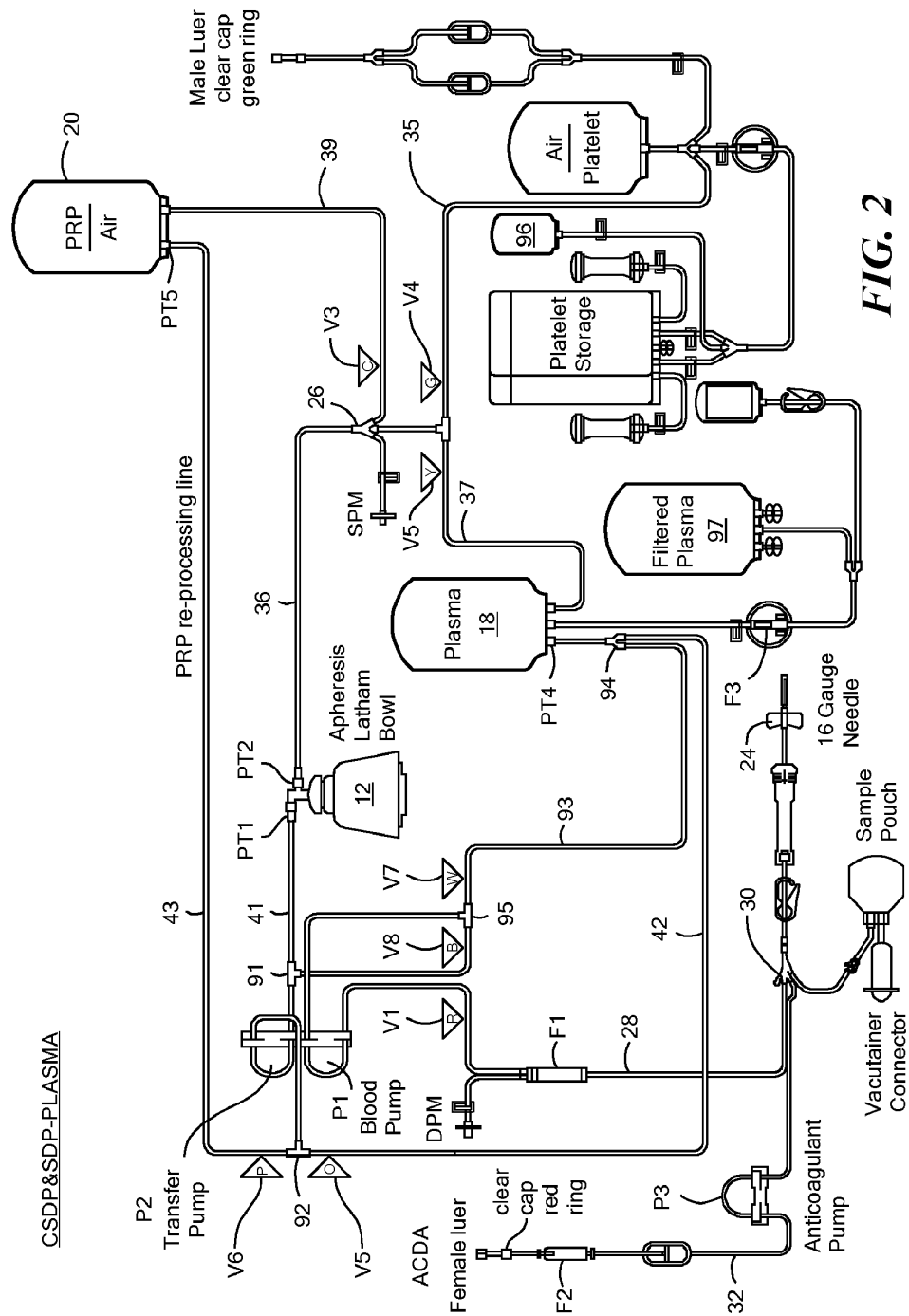


FIG. 2

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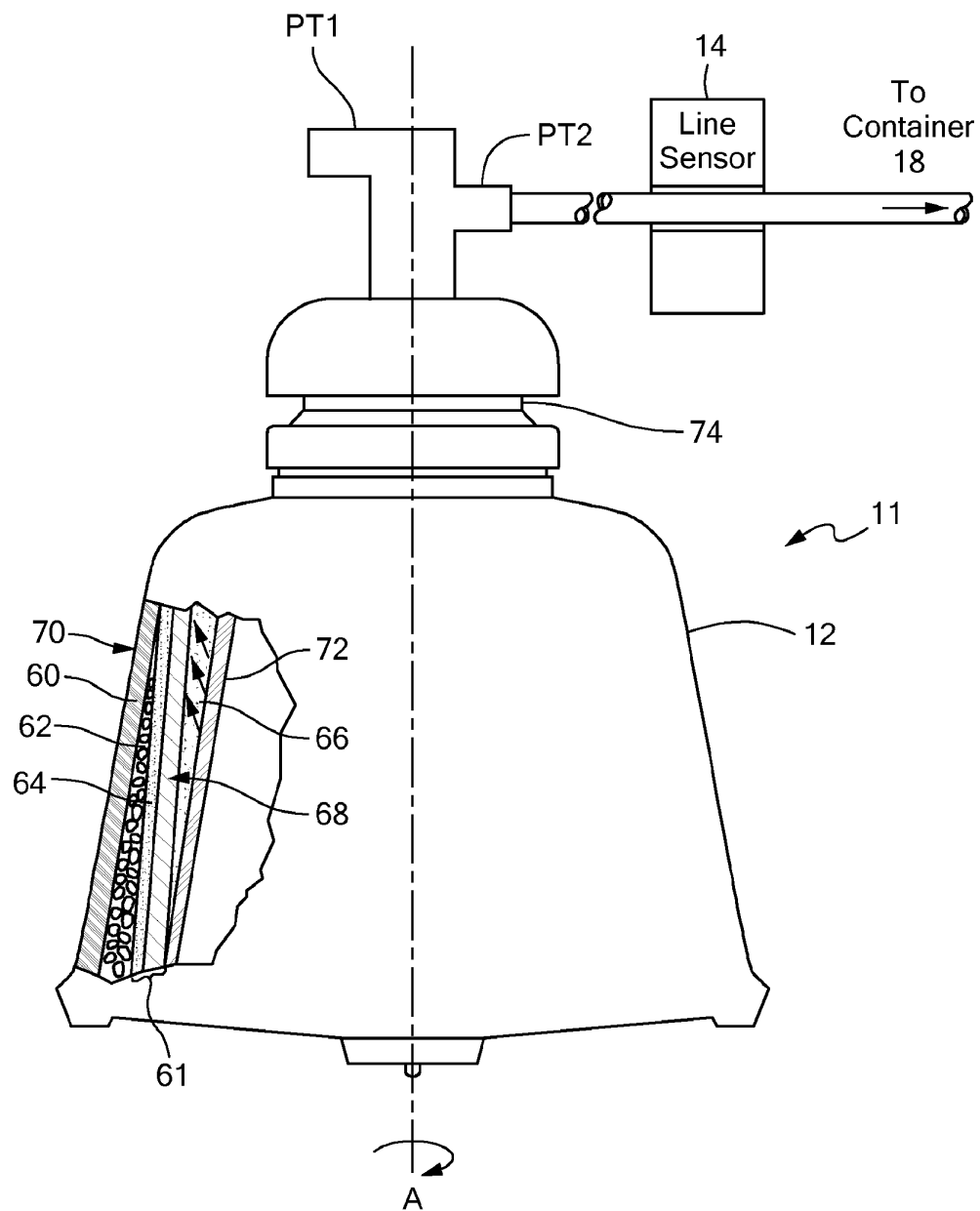
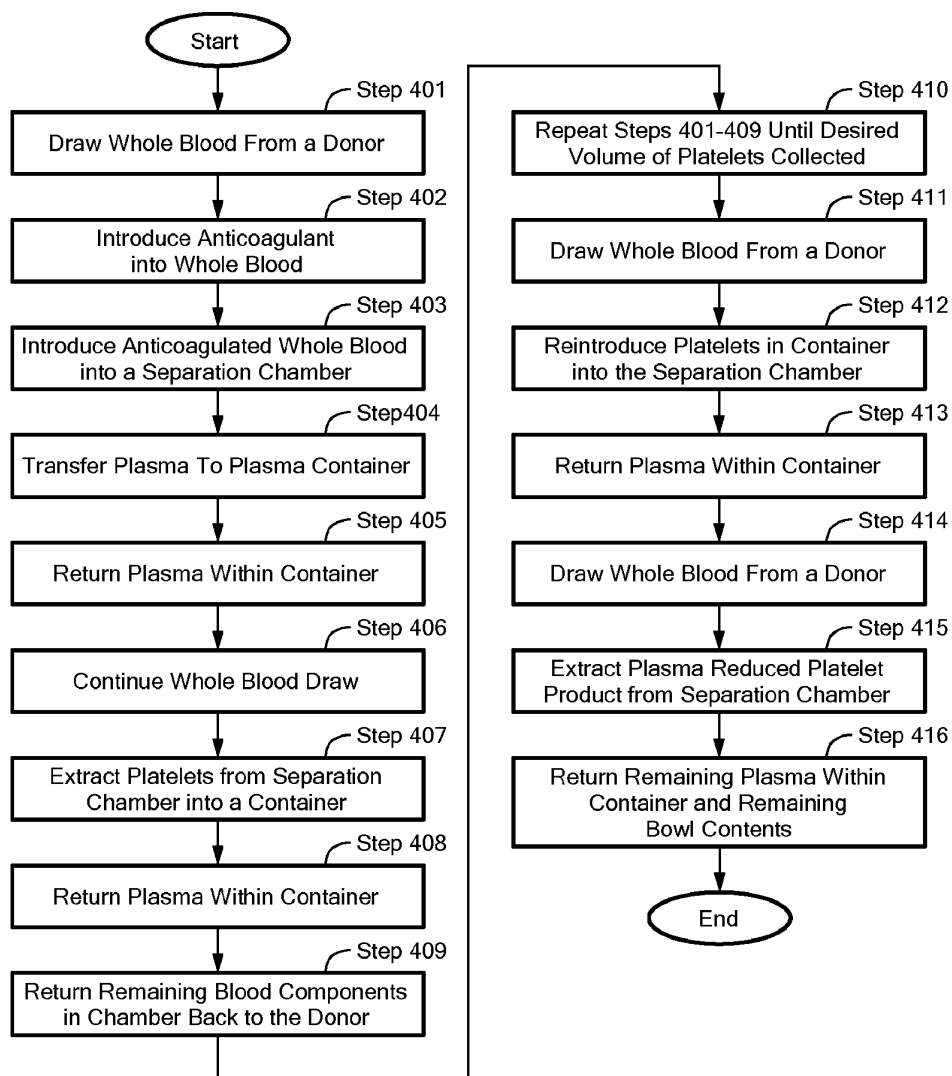


**FIG. 3**

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**FIG. 4**

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 10/62540

| <b>A. CLASSIFICATION OF SUBJECT MATTER</b><br>IPC(8) - A61M 37/00 (2011.01)<br>USPC - 604/6.04<br>According to International Patent Classification (IPC) or to both national classification and IPC                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                              |                                                                                            |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| <b>B. FIELDS SEARCHED</b><br>Minimum documentation searched (classification system followed by classification symbols)<br>IPC(8): A61M 37/00 (2011.01)<br>USPC: 604/6.04<br>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched<br>IPC(8): A61M 37/00 (2011.01)<br>USPC: 604/6.04; 210/634, 644-646; 604/4.01, 5.01, 6.01, 6.04, 6.07, 6.11, 6.15<br>Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)<br>USPTO PubWEST (USPT, PGPUB, EPAB, JPAB); collect\$, 'plasma reduced platelets', 'plasma return', 'whole blood', anticoagulant, separat\$, chamber, container, 'platelet rich plasma', blood, plasma, calculat\$, 'extra-corporeal volume', 'extracorporeal volume' Google Scholar; 'collecting platelet reduced plasma anticipating plasma return'                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                              |                                                                                            |
| <b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                              |                                                                                            |
| Category*                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                           | Relevant to claim No.                                                                      |
| X<br>---<br>Y                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | US 2010/0234788 A1 (PAGES, et al.) 16 September 2010 (16.09.2010), [Abstract], para[0005],[0010]-[0014], [0016], [0017], [0019], [0020], [0023], [0027], [0028], [0031], [0033], [0034], [0036]-[0038], [0040]-[0044], [0056]-[0060]; Fig. 1 | 1-6, 8-24, 26-29, 31-45, 47-49<br>-----<br>7, 25, 30, 46                                   |
| Y                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | US 2009/0217202 A1 (FOLEY, et al.) 27 August 2009 (27.08.2009), para[0056], [0069]-[0071]                                                                                                                                                    | 7, 25, 30, 46                                                                              |
| <input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                              |                                                                                            |
| * Special categories of cited documents:<br>"A" document defining the general state of the art which is not considered to be of particular relevance<br>"E" earlier application or patent but published on or after the international filing date<br>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)<br>"O" document referring to an oral disclosure, use, exhibition or other means<br>"P" document published prior to the international filing date but later than the priority date claimed<br>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention<br>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone<br>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art<br>"&" document member of the same patent family |                                                                                                                                                                                                                                              |                                                                                            |
| Date of the actual completion of the international search<br>21 February 2011 (21.02.2011)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                              | Date of mailing of the international search report<br><b>03 MAR 2011</b>                   |
| Name and mailing address of the ISA/US<br>Mail Stop PCT, Attn: ISA/US, Commissioner for Patents<br>P.O. Box 1450, Alexandria, Virginia 22313-1450<br>Facsimile No. 571-273-3201                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                              | Authorized officer:<br>Lee W. Young<br>PCT Helpdesk: 571-272-4300<br>PCT OSP: 571-272-7774 |

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## SYSTEM AND METHOD FOR COLLECTING PLASMA

**Inventor(s):** RAGUSA MICHAEL [US] ± (RAGUSA, Michael)**Applicant(s):** HAEMONETICS CORP [US] ± (HAEMONETICS CORPORATION)

**Classification:** - international: A61M1/36  
 - cooperative: A61M1/3496 (EP, KR); A61M1/36 (KR);  
A61M1/3672 (EP, KR); A61M1/3693 (EP, KR);  
A61M1/385 (EP, KR); A61M2202/0415 (EP, KR);  
A61M2205/3306 (EP, KR); A61M2205/3393 (EP,  
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**Application number:** WO2018US57528 20181025 Global Dossier**Priority number(s):** US201715793339 20171025

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EP3700606 (A1) EP3700606 (A4) more

## Abstract of WO2019084278 (A1)

A method for collecting plasma includes determining the weight, height, and hematocrit of a donor, and calculating a donor plasma volume and a target plasma collection volume. The target plasma collection volume is based on the donor plasma volume and a target percentage of plasma. The method then withdraws blood from the donor through a line connected to a blood component separation device, and introduces anticoagulant into the withdrawn blood. The blood component separation device separates the blood into a plasma component and a second blood component, and the plasma component is collected from the blood component separation device and into a plasma collection container. The method may then calculate the volume of pure plasma collected within the plasma collection container, and continue processing/collecting until the calculated volume of pure plasma equals the target plasma collection volume.



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- (71) **Applicant:** **HAEMONETICS CORPORATION**  
[US/US]; 400 Wood Road, Braintree, MA 02184 (US).
- (72) **Inventor:** **RAGUSA, Michael**; 4 Willow Circle, Hingham, MA 02043 (US).
- (74) **Agent:** **LOVELY, Jonathan, C.** et al.; McCarter & English, LLP, 265 Franklin Street, Boston, MA 02110 (US).
- (81) **Designated States** (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(54) **Title:** SYSTEM AND METHOD FOR COLLECTING PLASMA

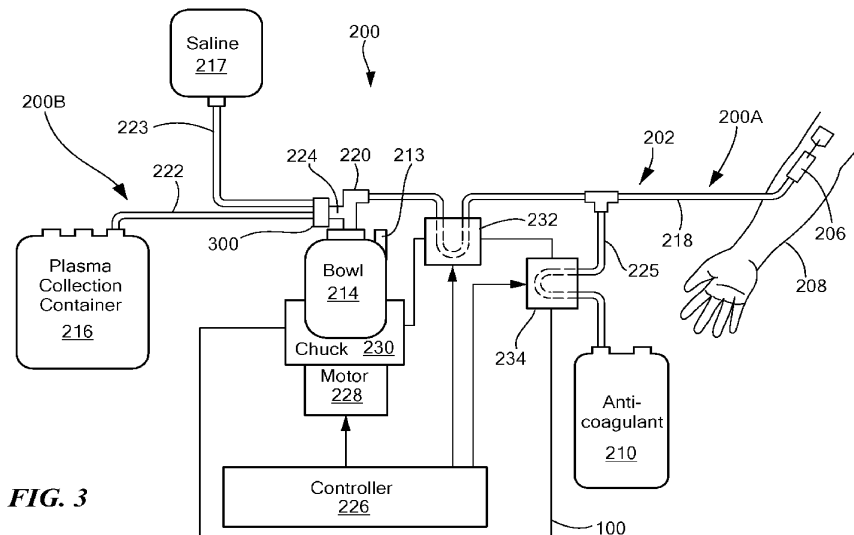


**FIG. 3**

(57) **Abstract:** A method for collecting plasma includes determining the weight, height, and hematocrit of a donor, and calculating a donor plasma volume and a target plasma collection volume. The target plasma collection volume is based on the donor plasma volume and a target percentage of plasma. The method then withdraws blood from the donor through a line connected to a blood component separation device, and introduces anticoagulant into the withdrawn blood. The blood component separation device separates the blood into a plasma component and a second blood component, and the plasma component is collected from the blood component separation device and into a plasma collection container. The method may then calculate the volume of pure plasma collected within the plasma collection container, and continue processing/collecting until the calculated volume of pure plasma equals the target plasma collection volume.

[Continued on next page]

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**Declarations under Rule 4.17:**

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

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## **System and Method for Collecting Plasma**

### **Priority**

**[0001]** This patent application claims priority from United States Patent Application No. 15/793,339, entitled “System and Method for Collecting Plasma,” filed October 25, 2017, attorney docket number 130670-08003 (formerly 1611/C86), and naming Michael Ragusa as inventor, the disclosure of which is incorporated herein, in its entirety, by reference.

**[0002]** United States Application No. 15/793,339, in turn, is a continuation-in-part of and claims priority from all priority dates of U.S. Patent Application No. 15/608,183, entitled “System and Method for Collecting Plasma,” filed May 30, 2017, attorney docket number 130670-08002 (formerly 1611/C80), and naming Michael Ragusa as inventor, the disclosure of which is incorporated herein, in its entirety, by reference.

### **Technical Field**

**[0003]** The present invention relates to systems and methods for blood apheresis, and more particularly system and methods for collecting a plasma product.

### **Background Art**

**[0004]** Apheresis is a procedure in which individual blood components can be separated and collected from whole blood temporarily withdrawn from a subject. Typically, whole blood is withdrawn through a needle inserted into a vein of the subjects arm and into a cell separator, such as a centrifugal bowl. Once the whole blood is separated into its various components, one or more of the components (e.g., plasma) can be removed from the centrifugal bowl. The remaining components can be returned to the subject along with optional compensation fluid to make up for the volume of the removed component. The process of drawing and returning continues until the quantity of the desired component has been collected, at which point the process is stopped. A central feature of apheresis systems is that the processed but unwanted components are returned to the donor. Separated blood components may include, for example, a high density

component such as red blood cells, an intermediate density component such as platelets or white blood cells, and a lower density component such as plasma.

**[0005]** Many jurisdictions have regulations regarding the amount of whole blood and/or blood components that can be removed from a donor. For example, the U.S. Food and Drug Administration (“the FDA”) sets both an upper limit on the volume of plasma that may be collected (e.g., 800 ml for an adult weighing more than 175 pounds) as well as an upper limit on the total collection volume (e.g., 880 ml for an adult weighing more than 175 pounds). Prior art plasma collection systems are unable to determine the total volume of plasma that has been collected (e.g., because the product collected is a mixture of plasma and anticoagulant) and, therefore collect based on the total collection volume, even if the total volume of plasma that has been collected is below the limit prescribed by the FDA. Additionally, prior art collection systems do not tailor the amount of plasma collected to the individual (e.g., other than what weight group they fall into) and, therefore, the percentage of the patient’s plasma that is collected varies widely from patient to patient (e.g., only 23% percent of the plasma is collected for some patients and 29% - or greater – of the plasma is collected for others).

### **Summary of the Invention**

**[0006]** In accordance with some embodiments of the present invention, a method for collecting plasma includes determining the weight and hematocrit of a donor, and inserting a venous-access device into the donor. Once the venous access device is inserted, the method may withdraw whole blood from the donor through the venous-access device and a draw line that is connected to a blood component separation device. The method may then introduce anticoagulant into the withdrawn whole blood through an anticoagulant line and separate, using the blood component separation device, the withdrawn whole blood into a plasma component and at least a second blood component. Once separated, the plasma component may be collected from the blood component separation device and into a plasma collection container. During processing, the method may calculate (1) a percentage of anticoagulant in the collected plasma component, and (2) a volume of pure plasma collected within the plasma collection container. The volume of pure plasma may be based, at least in part, on the calculated percentage of anticoagulant in the collected plasma component. The method may continue the process (e.g., withdrawing whole blood, introducing anticoagulant into the whole blood, separating the blood, collecting the plasma, and calculating the percentage of

anticoagulant and volume of pure plasma) until a target volume of pure plasma is collected within the plasma collection container.

**[0007]** In some embodiments, the method may determine a change in volume within an anticoagulant container, and the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the change in volume within the anticoagulant container. Additionally or alternatively, the method may determine a volume of anticoagulant introduced into the whole blood based on a number of rotations of an anticoagulant pump. In such embodiments, the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the number of rotations of the anticoagulant pump. The method may also determine a volume of anticoagulant within the blood component separation device, and the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the volume of anticoagulant within the blood component separation device.

**[0008]** In further embodiments, the method may monitor the volume and/or weight of the plasma component collected within the plasma collection container (e.g., using a weight sensor), and the calculated volume of pure plasma collected within the plasma collection device may be based, at least in part, on the monitored volume and/or weight of the collected plasma component. Additionally or alternatively, determining the hematocrit of the donor may include monitoring a volume of red blood cells collection within the blood separation device. In such embodiments, the determined hematocrit of the donor may be based, at least in part, on the monitored volume of red blood cells collected within the blood separation device and the volume of whole blood withdrawn from the donor.

**[0009]** The target volume of pure plasma may be based, at least in part, on the weight of the donor. The percentage of anticoagulant in the collected plasma component may include at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant that is added to the system during a priming step. After collecting at least a portion of the target volume of pure plasma, the method may return the second blood component to the donor through a return line.

**[0010]** In accordance with additional embodiments, a system for collecting plasma includes a venous-access device for drawing whole blood from a subject and returning blood components to the subject, and a blood component separation device for separating the drawn blood into a plasma component and a second blood component. The blood component separation device has an outlet and is configured to send the plasma

component to a plasma container. The system may also include a blood draw line fluidly connected to the venous-access device and an anticoagulant line connected to an anticoagulant source. The blood draw line transports drawn whole blood to the blood component separation device, and the flow through the blood draw line may be controlled by a blood draw pump. The anticoagulant line may introduce anticoagulant into the drawn whole blood.

**[0011]** Additionally, the system may include a controller that controls the operation of the centrifuge bowl. The controller may also calculate (1) a percentage of anticoagulant in the collected plasma component, and (2) a volume of pure plasma collected within the plasma container. The volume of pure plasma may be based, at least in part, upon the percentage of anticoagulant in the collected plasma component. The controller may stop the blood draw pump when a target volume of pure plasma (e.g., based, at least in part, on the weight of the donor) is collected within the plasma container. In some embodiments, the percentage of anticoagulant in the collected plasma component may be based, at least in part, on the volume of anticoagulant added to the drawn whole blood and the subject's hematocrit.

**[0012]** The system may also include an anticoagulant source weight sensor that measures the weight of the anticoagulant source. The controller may monitor the change in volume within the anticoagulant container based on the measured weight of the anticoagulant source, and the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the change in volume within the anticoagulant source. Additionally or alternatively, the controller may monitor the number of rotations of an anticoagulant pump to determine a volume of anticoagulant introduced into the whole blood. In such embodiments, the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the number of rotations of the anticoagulant pump.

**[0013]** In some embodiments, the system may include an optical sensor located on the blood component separation device. The optical sensor may 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 percentage of anticoagulant in the collected plasma may be based, at least in part, on the volume of anticoagulant within the blood component separation device.

**[0014]** In additional embodiments, the system may also include a plasma container weight sensor that monitors a volume and/or weight of the plasma component collected within the plasma collection container. The calculated volume of pure plasma collected within the plasma collection container may be based, at least in part, on the monitored volume and/or weight of collected plasma component. The system may also have an optical sensor located on the blood component separation device. The optical sensor may monitor the volume of red blood cells collected within the blood separation device. The controller may then determine the subject's hematocrit based, at least in part, upon on the monitored volume of red blood cells collected within the blood separation device and the volume of whole blood withdrawn from the donor. The percentage of anticoagulant in the collected plasma component may include at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant added to the system during a priming step.

**[0015]** In accordance with additional embodiments, a method for collecting plasma determines the weight, height, and hematocrit of a donor, and calculates a donor plasma volume based, at least in part, on the weight, height and hematocrit of the donor. The method then calculates a target plasma collection volume based, at least in part, on the calculated donor plasma volume and a target percentage of plasma (e.g., between 26.5 and 29.5 percent of the donor's plasma volume), and withdraws whole blood from the donor through the venous-access device and a first line that is connected to a blood component separation device. As the whole blood is withdrawn, the method may introduce anticoagulant into the withdrawn whole blood through an anticoagulant line.

**[0016]** The blood component separation device separates the withdrawn whole blood into a plasma component and at least a second blood component, and the method may collect the plasma component from the blood component separation device and into a plasma collection container. During processing, the method may calculate a volume of pure plasma collected within the plasma collection container. The method continues the withdrawing, introduction of anticoagulant, separating, collecting, and calculating steps until the volume of pure plasma collected within the plasma collection container equals the target plasma collection volume.

**[0017]** In some embodiments, after collecting at least a portion of the target plasma collection volume, the method may return the contents of the blood component separation device to the donor through the first line. Additionally or alternatively, the method may calculate an intravascular deficit based, at least in part on, the volume of

pure plasma collected and the volume of the contents of the blood component separation device that are returned to the donor. The method may also return a volume of saline to the donor to obtain a target intravascular deficit. The target intravascular deficit may be between -250 and 500 milliliters (e.g., it may be 0 milliliters or 250 milliliters). The donor plasma volume may be calculated based, at least in part, on the donor's body mass index that, in turn, is calculated based on the donor's weight and height.

**[0018]** In further embodiments, the method may include calculating a percentage of anticoagulant in the collected plasma component. In such embodiments, the volume of pure plasma may be based, at least in part, on the calculated percentage of anticoagulant in the collected plasma component. The calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on a change in volume within the anticoagulant container, the number of rotations of the anticoagulant pump, and/or the volume of anticoagulant within the blood component separation device. The method may determine the change in volume within the anticoagulant container, the volume of anticoagulant introduced into the whole blood, and/or the volume of anticoagulant within the blood component separation device. The percentage of anticoagulant in the collected plasma component may include at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant added during a priming step.

**[0019]** In some embodiments, the method may include monitoring a volume or and/or weight of the plasma component collected within the plasma collection container. In such embodiments, the calculated volume of pure plasma collected within the plasma collection device may be based, at least in part, on the monitored volume and/or weight of collected plasma component. To determine the donor's hematocrit, the method may monitor the volume of red blood cells collected within the blood separation device. The hematocrit of the donor may be based, at least in part, on the monitored volume of red blood cells collected within the blood separation device and the volume of whole blood withdrawn from the donor.

**[0020]** In accordance with still further embodiments, a system for collecting plasma includes a venous-access device for drawing whole blood from a subject and returning blood components to the subject, and a blood component separation device for separating the drawn blood into a plasma component and a second blood component. The blood component separation device may have an outlet and may send the plasma component to a plasma container. The system may also have a first line and an

anticoagulant line. The first line may be fluidly connected to the venous-access device and may (1) transport drawn whole blood to the blood component separation device and (2) return fluid within the blood component separation device to the subject. The flow through the first line may be controlled by a first pump. The anticoagulant line may be connected to an anticoagulant source and may introduce anticoagulant into the drawn whole blood.

**[0021]** The system may also include a controller that controls the operation of the centrifuge bowl and the first pump. The controller may calculate (1) a donor plasma volume, (2) a target plasma collection volume, and (3) a volume of pure plasma collected within the plasma container. The donor plasma volume may be based, at least in part, on a weight and height of the donor and a hematocrit of the donor. The target plasma collection volume may be based, at least in part, on the calculated donor plasma volume and a target percentage of plasma. The volume of pure plasma collected within the plasma container may be based, at least in part, upon a percentage of anticoagulant in the collected plasma component. The controller may stop the first pump when the calculated volume of pure plasma collected within the plasma collection container equals the target plasma collection volume.

**[0022]** In further embodiments, the controller may return, after collecting at least a portion of the target plasma collection volume, fluid remaining within the blood component separation device via the first line. Additionally or alternatively, the controller may calculate an intravascular deficit based, at least in part on, the volume of pure plasma collected and the volume of the contents of the blood component separation device returned to the donor. The system may also include a saline line that fluidly connects to a saline source and the blood component separation device. The controller may return a volume of saline to the donor to obtain a target intravascular deficit (e.g., between -250 and 500 milliliters).

**[0023]** The controller may calculate the donor's body mass index based, at least in part, on the weight and height of the donor. The donor plasma volume may, in turn, be calculated based, at least in part, on the donor's body mass index. The target percentage of plasma may be between 26.5 and 29.5 percent (e.g., 28.5 percent) of the donor's plasma volume.

**[0024]** In additional embodiments, the controller may calculate the percentage of anticoagulant in the collected plasma component, for example, based on the volume of anticoagulant added to the drawn whole blood, and the subject's hematocrit. The system

may also include an anticoagulant source weight sensor that measures the weight of the anticoagulant source. The controller may then monitor a change in volume within the anticoagulant container based on the measured weight of the anticoagulant source. The calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the change in volume within the anticoagulant source. Additionally or alternatively the controller may monitor a number of rotations of the anticoagulant pump to determine the volume of anticoagulant introduced into the whole blood. In such embodiments, the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the number of rotations of the anticoagulant pump.

[0025] The system may also include an optical sensor and/or a plasma container weight sensor. The optical sensor may be located on the blood component separation device and may monitor the contents of the blood component separation device to determine if a volume of anticoagulant remains within the blood component separation device. The calculated percentage of anticoagulant in the collected plasma may then be based, at least in part, on the volume of anticoagulant within the blood component separation device. The plasma container weight sensor may monitor a volume and/or weight of the plasma component collected within the plasma container. The calculated volume of pure plasma collected within the plasma collection device may then be based, at least in part, on the monitored volume and/or weight of collected plasma component. The optical sensor may also monitor the volume of red blood cells collected within the blood separation device, and the controller may determine the subject's hematocrit based, at least in part, upon on the monitored volume of red blood cells collected within the blood separation device and the volume of whole blood withdrawn from the donor. The percentage of anticoagulant in the collected plasma component may include at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant added during a priming step.

#### **Brief Description of the Drawings**

[0026] The foregoing features of the invention will be more readily understood by reference to the following detailed description, taken with reference to the accompanying drawings, in which:

[0027] Fig. 1 schematically shows a perspective view of a blood processing system in accordance with some embodiments of the present invention.

[0028] Fig. 2 schematically shows a top view of the blood processing system of Figure 1, in accordance with some embodiments of the present invention;



[0029] Fig. 3 schematically shows a disposable set installed within the blood processing system of Figure 1, in accordance with some embodiments of the present invention.

[0030] Fig. 4 is a flowchart depicting a method of collecting plasma, in accordance with embodiments of the present invention.

[0031] Fig. 5 is a flowchart depicting an alternative method of collecting plasma, in accordance with further embodiments of the present invention.

### **Detailed Description of Specific Embodiments**

[0032] Illustrative embodiments of the present invention provide blood processing systems and methods for collecting a target volume of pure plasma. The system and method calculate a percentage of anticoagulant collected within a plasma collection container (e.g., in addition to the plasma that is collected within the container) based on the amount of anticoagulant added to the system and the hematocrit of the donor. The system/method may then calculate the volume of pure plasma (e.g., plasma without anticoagulant) that has been collected within the container. Further embodiments may tailor the volume of plasma collected based on the donor's plasma volume and a target percentage of plasma to collect. Details of the illustrative embodiments are discussed below.

[0033] As shown in Figures 1 and 2, the blood processing system 100 includes a cabinet 110 that houses the main components of the system 100 (e.g., the non-disposable components). Within the cabinet 110, the system 100 may include a first/blood pump 232 that draws whole blood from a subject, and a second/anticoagulant pump 234 that pumps anticoagulant through the system 100 and into the drawn whole blood. Additionally, the system 100 may include a number of valves that may be opened and/or closed to control the fluid flow through the system 100. For example, the system 100 may include a donor valve 120 that may open and close to selectively prevent and allow fluid flow through a donor line 218 (e.g., an inlet line; Fig. 3), and a plasma valve 130 that selectively prevents and allows fluid flow through an outlet/plasma line 222 (Fig. 3). Some embodiments may also include a saline valve 135 that selectively prevents and allows saline to flow through a saline line 223.

[0034] To facilitate the connection and installation of a disposable set and to support the corresponding fluid containers, the system 100 may include an anticoagulant pole 150 on which the anticoagulant solution container 210 (Fig. 3) may be hung, and a

saline pole 160 on which a saline solution container 217 (Fig. 3) may be hung (e.g., if the procedure being performed requires the use of saline). Additionally, in some applications, it may be necessary and/or desirable to filter the whole blood drawn from the subject for processing. To that end, the system 100 may include blood filter holder 170 in which the blood filter (located on the disposable set) may be placed.

**[0035]** As discussed in greater detail below, apheresis systems 100 in accordance with embodiments of the present invention withdraw whole blood from a subject through a venous access device 206 (Fig. 3) using the blood pump 232. As the system 100 withdraws the whole blood from the subject, the whole blood enters a blood component separation device 214, such as a Latham type centrifuge (other type of separation chambers and devices may be used, such as, without limitation, an integral blow-molded centrifuge bowl, as described in U.S. Patent Nos. 4,983,158 and 4,943,273, which are hereby incorporated by reference). The blood component separation device 214 separates the whole blood into its constituent components (e.g., red blood cells, white blood cell, plasma, and platelets). Accordingly, to facilitate operation of the separation device 214, the system 100 may also include a well 180 in which the separation device 214 may be placed and in which the separation device 214 rotates (e.g., to generate the centrifugal forces required to separate the whole blood).

**[0036]** To allow the user/technician to monitor the system operation and control/set the various parameters of the procedure, the system 100 may include a user interface 190 (e.g., a touch screen device) that displays the operation parameters, any alarm messages, and buttons which the user/technician may depress to control the various parameters. Additional components of the blood processing system 100 are discussed in greater detail below (e.g., in relation to the system operation).

**[0037]** FIG. 3 is a schematic block diagram of the blood processing system 100 and a disposable collection set 200 (with an inlet disposable set 200A and an outlet disposable set 200B) that may be loaded onto/into the blood processing system 100, in accordance with the present invention. The collection set 200 includes a venous access device 206 (e.g., a phlebotomy needle) for withdrawing blood from a donor's arm 208, a container of anti-coagulant 210, a centrifugation bowl 214 (e.g., a blood component separation device), a saline container 217, and a final plasma collection bag 216. The blood/inlet line 218 couples the venous access device 206 to an inlet port 220 of the bowl 214, the plasma/outlet line 222 couples an outlet port 224 of the bowl 214 to the plasma collection bag 216, and a saline line 223 connects the outlet port 224 of the bowl 214 to

the saline container 217. An anticoagulant line 225 connects the anti-coagulant container 210 to the inlet line 218. In addition to the components mentioned above and as shown in Figure 3, the blood processing system 100 includes a controller 226, a motor 228, and a centrifuge chuck 230. The controller 226 is operably coupled to the two pumps 232 and 234, and to the motor 228, which, in turn, drives the chuck 230. The controller 226 may be operably coupled to and in communication with the user interface 190.

**[0038]** In operation, the disposable collection set 200 (e.g., the inlet disposable set 200A and the outlet disposable set 200B) may be loaded onto/into the blood processing system 100 prior to blood processing. In particular, the blood/inlet line 218 is routed through the blood/first pump 232 and the anticoagulant line 225 from the anti-coagulant container 210 is routed through the anticoagulant/second pump 234. The centrifugation bowl 214 may then be securely loaded into the chuck 230. Once the bowl 214 is secured in place, the technician may install the outlet disposable set 200B. For example the technician may connect a bowl connector 300 to the outlet 224 of the bowl 214, install the plasma container 216 into the weight sensor 195, run the saline line 223 through valve 135, and run the plasma/outlet line 222 through valve 130 and the line sensor 185. Once the disposable set 200 is installed and the anticoagulant and saline containers 210/217 are connected, the system 100 is ready to begin blood processing.

**[0039]** Figure 4 is a flowchart depicting an exemplary method of collecting plasma in accordance with various embodiments of the present invention. Prior to connecting the donor to the blood processing device 100, it is beneficial (and perhaps necessary in some instances) to obtain/determine some information regarding the donor, namely, the donor's weight (Step 410) and hematocrit (Step 415). Not only does this information help determine if the individual is a viable donor and the volumes of blood components that may be withdrawn/collected (e.g., per the FDA guidelines), the hematocrit may be used during processing to help collect a target volume of plasma. The technician may obtain/determine the donor's weight by weighing the donor (e.g., on a scale). To obtain/determine the donor's hematocrit, the technician may draw a blood sample from the donor and test the sample of blood. Additionally or alternatively, as discussed in greater detail below, the system may determine the hematocrit during blood processing. For example, the blood processing device 100 may include a hematocrit sensor (not shown) that determines the hematocrit of the blood flowing into the blood processing device 100 and/or the system 100 may determine the hematocrit based on a volume of red blood cells collected within the bowl 214.

**[0040]** Once the lines 222/223 are in place and the technician has determined the donor's weight and/or hematocrit (if needed), the user/technician may insert the venous access device 206 into the donor's arm 208 (Step 420). Next, the controller 226 activates the two pumps 232, 234 and the motor 228. Operation of the two pumps 232, 234 causes whole blood to be drawn from the donor (step 425), anticoagulant from container 210 to be introduced into the drawn whole blood (step 430), and the now anticoagulated whole blood to be delivered to the inlet port 220 of the bowl 214.

**[0041]** It should be noted that the anticoagulant line 225 may also include a bacteria filter (not shown) that prevents any bacteria in the anticoagulant source 210, the anticoagulant, or the anticoagulant line 225 from entering the system 100 and/or the subject. Additionally, the anticoagulant line 225 may include an air detector 140 that detects the presence of air within the anticoagulant. The presence of air bubbles within any of the system 100 lines can be problematic for the operation the system 100 and may also be harmful to the subject if the air bubbles enter the blood stream. Therefore, the air detector may be connected to an interlock that stops the flow within the anticoagulant line 225 in the event that an air bubble is detected (e.g., by stopping the anticoagulant pump 234), thereby preventing the air bubbles from entering the subject.

**[0042]** As the anti-coagulated whole blood is withdrawn from the subject and contained within the blood component separation device 214, the blood component separation device 214 separates the whole blood into several blood components (Step 435). For example, the blood component separation device 214 may separate the whole blood into a first, second, third, and, perhaps, fourth blood component. More specifically, the blood component separation device 214 (and the centrifugal forces created by rotation of the separation device 214) can separate the whole blood into plasma, platelets, red blood cells ("RBC"), and, perhaps, white blood cells ("WBC"). The higher density component, i.e., RBC, is forced to the outer wall of the bowl 214 while the lower density plasma lies nearer the core. A buffy coat is formed between the plasma and the RBC. The buffy coat is made up of an inner layer of platelets, a transitional layer of platelets and WBC and an outer layer of WBC. The plasma is the component closest to the outlet port and is the first fluid component displaced from the bowl 214 via the outlet port 224 as additional anticoagulated whole blood enters the bowl 214 through the inlet port 220.

**[0043]** As shown in Figure 3, the system 100 may also include an optical sensor 213 that may be applied to a shoulder portion of the bowl 214. The optical sensor monitors each layer of the blood components as they gradually and coaxially advance

toward the core from the outer wall of the bowl 214. The optical sensor 213 may be mounted in a position (e.g., within the well 180) at which it can detect the buffy coat and/or the red blood cells reaching a particular radius, and the steps of drawing the whole blood from the subject/donor and introducing the whole blood into the bowl 12 may be altered and/or terminated in response to the detection.

**[0044]** Additionally, in some embodiments, the optical sensor 213 may be used to determine the hematocrit of the donor during processing. For example, as the bowl 214 fills with red blood cells and the optical sensor 213 detects the layer of red blood cells, the system 100 (e.g., the controller) can determine the volume of red blood cells within bowl 214 based on the location of the red blood cell layer and the fixed/known bowl volume. The system 100 may then calculate the donor hematocrit based on the volume of red blood cells within the bowl and the volume of whole blood that has been processed to that point.

**[0045]** Once the blood component separation device 214 has separated the blood into the various components, one or more of the components can be removed from the blood component separation device 214. For instance, the plasma may be removed to a plasma container 216 (e.g., a plasma bottle) through line 222 (Step 440). As noted above, some embodiments of the system 100 may include a weight sensor 195 (Fig. 1) that measures the amount of plasma collected. The plasma collection process may continue until a target volume of pure plasma (discussed in greater detail below) is collected within the plasma collection container 216. Although not shown, if the blood processing system 100 and/or the disposable set 200 include platelet, red blood cell, and/or white blood cell bags, each of the bags/containers may include similar weight sensors (e.g., load cells).

**[0046]** In some embodiments, the system 100 may also include a line sensor 185 (mentioned above) that can determine the type of fluid (e.g., plasma, platelets, red blood cells etc.) exiting the blood component separation device 214. In particular, the line sensor 185 consists of an LED which emits light through the blood components leaving the bowl 214 and a photo detector which receives the light after it passes through the components. The amount of light received by the photo detector is correlated to the density of the fluid passing through the line. For example, if plasma is exiting the bowl 214, the line sensor 185 will be able to detect when the plasma exiting the bowl 214 becomes cloudy with platelets (e.g., the fluid exiting the bowl 214 is changing from plasma to platelets). The system 100 may then use this information to either stop the

removal of blood components from the bowl 214, stop drawing whole blood from the subject, or redirect the flow by, for example, closing one valve and opening another.

**[0047]** It is important to note that during processing, the osmolarity of the red blood cells prevents the anticoagulant introduced into the whole blood from entering/remaining with the red blood cells (e.g., within the bowl 214). Rather, the anticoagulant mixes with the plasma component. Therefore, the anticoagulant exits the bowl 214 with the plasma and is collected within collection container 216 along with the plasma. In other words, the weight of the product measured by the weight sensor 195 is the weight of the plasma, as well as any anticoagulant that is mixed with the plasma – the weight provided by the weight sensor 195 is not the weight of pure plasma.

**[0048]** Additionally, whole blood contains a variable amount of plasma, as determined by the donor's hematocrit. The hematocrit for typical donors can vary from 38% to 54%, which means that for 100 ml of whole blood, the volume of plasma can vary from 36 to 62 ml. Furthermore, the amount of anticoagulant added to the withdrawn whole blood is fixed (e.g., it does not depend on the hematocrit of the donor), meaning that the percentage of anticoagulant in the collected plasma may vary from 9.7% to 12.7% for donor hematocrits between 38% to 54%, respectively. Therefore, not only does the volume measured by the weight sensor 195 include the volume of anticoagulant, that volume of anticoagulant may vary from donor to donor based on the hematocrit.

**[0049]** As mentioned above, some embodiments of the present invention continue the blood processing/separation procedure until a target volume of pure plasma (e.g., plasma only – without the volume of any anticoagulant mixed with the plasma included in the target volume) is collected within the plasma collection container 216. To that end, some embodiments of the present invention may calculate the volume of pure plasma within the plasma collection container 216. For example, the technician or the system 100 (e.g., the controller) may calculate the percentage of anticoagulant within the collected plasma (Step 455) (e.g., the plasma contained within the plasma collection container 216) based on the amount of anticoagulant added/metered into the whole blood and the hematocrit of the donor. The technician and/or system can calculate the percentage of anticoagulant according to the following equation, where AC is the amount of anticoagulant added to the system 100. As noted above, 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.

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

**[0050]** The amount of anticoagulant that is added to the system 100 can be determined in a number of ways. For example, the system 100 can base the amount of anticoagulant (e.g., the value of “AC” in the above equation) on the predetermined ratio of anticoagulant per unit of anticoagulated whole blood. In some embodiments, the value of “AC” may be the inverse of the predetermined ratio (e.g., “AC” would be 16 if the ratio of anticoagulant to anticoagulated whole blood was 1:16). Additionally or alternatively, the technician/system 100 can monitor the volume of anticoagulant added to the system. In such embodiments, the technician/system can monitor the volume of anticoagulant added to the system 100 based on the number of rotations of the anticoagulant pump (e.g., each rotation of the anticoagulant pump introduces a set volume of anticoagulant into the system 100) and/or based on the change in weight of the anticoagulant container 210 as measured by a weight sensor (discussed in greater detail below).

**[0051]** Once the technician/system 100 has calculated the percentage of anticoagulant within the plasma collection container 216, the technician/system 100 may then use this information to calculate the volume of pure plasma within the plasma collection container 216 (Step 465). For example, the technician/system 100 may determine the volume of anticoagulant within the container (based on the percentage of anticoagulant within the container 216) and subtract this volume from the total volume of fluid within the container 216 as measured by the weight sensor 195. The system 100 may continue to monitor the volume of pure plasma collected within the container 216 and continue processing whole blood (e.g., continue performing Steps 425, 430, 435, 440, 455, 460 and 465) until a target volume of pure plasma is collected within the plasma collection container 216 (Step 470) (e.g., 800 mL for an adult donor weighing more than 175 pounds or other limit prescribed by the FDA or similar governing body).

**[0052]** Once the system 100 has collected the target volume of pure plasma within the plasma collection container 216, the system 100 can return the remaining components (e.g., the components remaining within the bowl 214) to the subject (Step 475). For example, when all the plasma has been removed and the bowl 214 is full of RBCs (and any other blood component not collected), the controller 226 stops the draw of whole blood from the subject and reverses the direction of the blood/first pump 232 to draw the

RBCs (and other components) from the bowl 214 directly back to the subject.

Alternatively, if the system 100 is so equipped, the system may return the components to the subject via a dedicated return line.

**[0053]** In addition to the non-collected blood components (e.g., the components remaining in the bowl 214), the system 100 may also return saline to the patient/subject. The saline may be used as a compensation fluid to make up for the volume of the blood component (e.g., plasma) that was removed and collected, and is not being returned to the patient. To that end, during the return step (e.g., Step 475), the saline valve 135 may be opened to allow saline from the saline container 217 to flow through the saline line 223 and into the bowl 214 (via outlet 224), where it can be returned to the patient/donor with or after the remaining blood components.

**[0054]** It should be noted that some embodiments may perform some additional and optional steps to help determine the volume of pure plasma within the plasma collection container 216. For example, as mentioned above, some embodiments may monitor the change in weight of the anticoagulant container 210 (e.g., as measured by a weight sensor/load cell on the anticoagulant container 210) (step 445). This measurement provides an indication of the volume of anticoagulant that has been added to the system 100, and may be used help determine the percentage of anticoagulant within the plasma collection container 216. Additionally or alternatively, some embodiments may similarly, monitor the change in weight and/or volume of the plasma and anticoagulant collected within the plasma collection container 216 (e.g., via weight sensor 195) (step 450). This measurement may be used to calculate of the total volume of pure plasma collected within the plasma collection container 216 (e.g., to obtain the total weight from which to subtract the calculated volume of anticoagulant).

**[0055]** Some embodiments may also (optionally) monitor the volume of anticoagulant remaining in the bowl 214 (step 460) (e.g., anticoagulant that did not mix with the plasma and/or otherwise remained in the bowl). For example, the system 100 may utilize the optical sensor on the bowl 214 to determine whether any anticoagulant remains within the bowl 214. If it does, the method 400/system 100 may modify the calculation of the amount of pure plasma collected within the plasma collection container (e.g., either increase the calculated amount or decreased the calculated amount), based on the volume of anticoagulant remaining within the bowl 214.



**[0056]** The various embodiment of the present invention described above provide numerous benefits over prior art plasma collection systems. In particular, as noted above, prior art plasmapheresis devices end plasma collection based on a total volume of anticoagulated plasma (e.g., pure plasma plus the added anticoagulant). Although this is the easiest method because it requires only that the product collection container be weighed, the amount of true product – the pure plasma – is dependent on the donor's hematocrit. In other words, prior art systems will collect more plasma from low hematocrit donors than from high hematocrit donors because of the variation of the percentage of anticoagulant in the product. Various embodiments of the present invention address the issues of prior art systems by collecting a standard volume (e.g., a target volume) of pure plasma from each donor. As noted above, embodiments of the present invention accomplish this by using knowledge of the donor's hematocrit and the amount of anticoagulant collected within the plasma collection container 216 (e.g., by counting pump rotations and/or using scale/weight sensors, etc.) to determine the percentage of anticoagulant in the product. Additionally, by stopping the plasma collection process based on a volume of pure plasma collected, embodiments of the present invention are able to collect a greater volume of plasma as compared to prior art systems that stop based on a plasma/anticoagulant mixture.

**[0057]** Figure 5 shows an alternative method for collecting plasma, using the system (or similar system) shown within Figures 1-3, that bases the total volume of plasma to collect on the individual donor (e.g., based on their height, weight, hematocrit, blood volume and/or plasma volume). In a manner similar to that described above for the method shown in Figure 4, prior to connecting the donor to the blood processing device 100, the system/method may obtain/determine some information regarding the donor, namely, the donor's weight and height (Step 505) and hematocrit (Step 510). For example, the technician may obtain/determine the donor's weight by weighing the donor (e.g., on a scale) and the donor's height by measuring the donor. To obtain/determine the donor's hematocrit (e.g., in a manner similar to that described above), the technician may test a blood sample or the system may determine the hematocrit during blood processing using a hematocrit sensor and/or based on the volume of red blood cells collected within the bowl 214.

**[0058]** Using the donor height and weight, and the hematocrit, the system 100/method 500 may calculate the donor's plasma volume (e.g., the volume of plasma within the donor's blood) (Step 515). For example, the system 100/method 500 may

calculate the donor/subject's body mass index ("BMI") using the donor's height and weight (e.g.,  $BMI = \text{weight}/\text{height}^2$ ), and then the total blood volume within the donor/subject using the calculated BMI (e.g., see Lemmens et al., *Estimating Blood Volume in Obese and Morbidly Obese Patients*, Obesity Surgery, 2006:16, 773-776, the subject matter incorporated herein by reference). The total blood volume may be calculated using the following equation:

$$[0059] \text{InBV} = \frac{70}{\sqrt{BMI_p/22}}$$

[0060] In the above equation, InBV is the indexed blood volume (e.g., the donor's total blood volume), BMI<sub>p</sub> is the patient's BMI (e.g., kg/m<sup>2</sup>), 22 is the BMI value (e.g., also in kg/m<sup>2</sup>) for an ideal body weight (IBW), and 70 is the total blood volume (in mL/kg) for a donor at their ideal weight ( $BMI = 22 \text{ kg/m}^2$ ). Once the system 100 has calculated the total blood volume within the donor/subject, the system 100 (e.g., the controller) may then determine/calculate the volume of plasma within the donor's blood (Step 515) based, for example, on the donor's hematocrit.

[0061] As mentioned above, the embodiment shown in Figure 5 bases the volume of plasma to collect on the individual donor. To that end, once the system 100/method 500 has determined the donor's plasma volume, the system 100/method 500 may then calculate the target volume of plasma to collect (Step 520). For example, the system 100/method 500 may multiply the total plasma volume within the patient by a target percentage of plasma to collect to obtain the target plasma volume to collect (e.g., if the total plasma volume is 2700 ml and the target percentage to collect is 28.5%, then the target plasma volume to collect is 769.5 ml). The target percentage of plasma to collect may depend on the application and/or the donor, and may be input directly into the system 100 (e.g., using the user interface 190) or may be preset from the factory. In some embodiments, the target percentage may be between 26.5 and 30%, and preferably may be 28.5%. However, in other embodiments, the target percentage may be below 26.5% or above 30%.

[0062] Once the lines 222/223 are in place and the system 100/method 500 has calculated the target plasma volume, the user/technician may insert the venous access device 206 into the donor's arm 208 (Step 525). Next, in a manner similar to that described above for the method shown in Figure 4, the controller 226 activates the two pumps 232, 234 and the motor 228. Operation of the two pumps 232, 234 causes whole

blood to be drawn from the donor (step 530), anticoagulant from container 210 to be introduced into the drawn whole blood (step 535), and the now anticoagulated whole blood to be delivered to the inlet port 220 of the bowl 214.

**[0063]** As the anti-coagulated whole blood is withdrawn from the subject and introduced into the blood component separation device 214, the blood component separation device 214 separates the whole blood into the respective blood components (e.g., into plasma, platelets, RBC, and, perhaps, WBC) (Step 540). As discussed above, the higher density component, i.e., RBC, is forced to the outer wall of the bowl 214 and the plasma is the component closest to the outlet port and, therefore, is the first fluid component displaced from the bowl 214 via the outlet port 224 as additional anticoagulated whole blood enters the bowl 214 through the inlet port 220. During separation and processing, the optical sensor 213 monitors each layer of the blood components as they gradually and coaxially advance toward the core from the outer wall of the bowl 214, and the steps of drawing the whole blood from the subject/donor and introducing the whole blood into the bowl 12 may be altered and/or terminated in response to the detection. Additionally, as discussed above, the optical sensor 213 may be used to determine the hematocrit of the donor during processing (e.g., if it is not known and/or determined prior to the start of processing).

**[0064]** Once the blood component separation device 214 has separated the blood into the various components, the plasma may be removed to a plasma container 216 (e.g., a plasma bottle) through line 222 (Step 545). As noted above, some embodiments of the system 100 may include a weight sensor 195 (Fig. 1) that measures the amount of plasma collected. The plasma collection process may continue until the target plasma collection volume (discussed in greater detail below) is collected within the plasma collection container 216. If equipped with the line sensor 185, the system 100 may then use the information from the sensor 185 to either stop the removal of blood components from the bowl 214, stop drawing whole blood from the subject, or redirect the flow by, for example, closing one valve and opening another.

**[0065]** As mentioned above, some embodiments of the present invention continue the blood processing/separation procedure until a target plasma collection volume is collected. In order to ensure that this volume does not include the volume of any anticoagulant collected within the container 216, the target plasma collection volume should only include the volume of pure plasma (e.g., plasma only – without the volume of any anticoagulant mixed with the plasma included in the target volume). To that end and

in a manner similar to that described above, some embodiments of the present invention may calculate the volume of pure plasma within the plasma collection container 216. To determine the volume of pure plasma, the technician or the system 100 (e.g., the controller) may calculate the percentage of anticoagulant within the collected plasma (Step 560) (e.g., the plasma contained within the plasma collection container 216) based on the amount of anticoagulant added/metered into the whole blood and the hematocrit of the donor (see equation provided above). The amount of anticoagulant that is added to the system 100 can be determined in any of the ways mentioned above (e.g., based on the predetermined ratio of anticoagulant per unit of anticoagulated whole blood, by monitoring the volume of anticoagulant added to the system, etc.).

**[0066]** Once the technician/system 100 has calculated the percentage of anticoagulant within the plasma collection container 216, the technician/system 100 may then use this information to calculate the volume of pure plasma within the plasma collection container 216 (Step 570). For example, as discussed above, the technician/system 100 may determine the volume of anticoagulant within the container (based on the percentage of anticoagulant within the container 216) and subtract this volume from the total volume of fluid within the container 216 as measured by the weight sensor 195. The system 100 may continue to monitor the volume of pure plasma collected within the container 216 and continue processing whole blood (e.g., continue performing Steps 530, 535, 540, 545, 560, 570 and, possibly, steps 550, 555 and 565) until the volume of pure plasma collected within the plasma collection container 216 reaches the target plasma volume (Step 575) (e.g., as calculated based on the individual plasma volume of the donor and the target percentage of plasma to collect).

**[0067]** Once the system 100 has collected the target plasma volume within the plasma collection container 216, the system 100 can return the remaining components (e.g., the components remaining within the bowl 214) to the subject (Step 580) by stopping the draw of whole blood from the subject and reversing the direction of the blood/first pump 232 to draw the RBCs (and other components) from the bowl 214 and back to the subject (e.g., directly via the blood/inlet line 218 or, if so equipped, via a dedicated return line).

**[0068]** It is important to note that, because the system 100/method 500 collect and do not return some of the blood components (e.g., the plasma), the volume of fluid that is returned to the donor/subject is less than the volume that was removed. This, in turn, creates an intravascular deficit that is equal to the amount of plasma collected (e.g., the

volume of whole blood removed from the donor minus the volume of plasma collected/not returned). In instances in which the intravascular deficit is too large, the donor is at risk of fainting when the procedure is complete and they get up to leave the facility. To reduce the intravascular deficit (and the risk of donor injury), as noted above, some embodiments of the present invention return saline to the patient/subject (Step 585). The saline may be used as a compensation fluid to make up for the volume of the blood component (e.g., plasma) removed. To that end, during the return step (e.g., Step 580), the controller 226 (or the technician) may open the saline valve to allow saline from the saline container 217 to flow through the saline line 223 and into the bowl 214 (via outlet 224), where it can be returned to the patient/donor with or after the remaining blood components.

**[0069]** As mentioned above, the volume of plasma that is collected from the donor varies from donor to donor (e.g., because it is based on the donor's height, weight, hematocrit, and blood volume). Therefore, the volume of saline that is returned to the donor to reduce the intravascular deficit may similarly be dependent on the donor. To that end, when returning the contents of the separation device and the saline (Steps 580 and 585) to the donor, the system 100/method 500 may calculate the intravascular deficit (Step 590) based on the total volume of whole blood removed from the donor and the volume of blood components and saline that has been returned (or based on the volume of plasma collected and the volume of blood components and saline that have been returned). The system 100/method 500 may continue returning saline until the donor's intravascular deficit reaches a target intravascular deficit (Step 595).

**[0070]** The target intravascular deficit may be any intravascular deficit that reduces the donor's risk for fainting and may be the same for each donor. For example, the target intravascular deficit may be set to 0 mL or 250 mL for each donor. Alternatively, like the target plasma volume to collect, the target intravascular deficit may be different for each donor. In other words, the target intravascular deficit may be set to 0 mL for some donors and 250 mL for others. It should be noted that 0 and 250 mL are provided as examples only and other embodiments may have target intravascular deficits between 0 and 250, or greater than 250 mL. Additionally, in some instances, it may be beneficial to return more fluid to the donor than was removed/collected. In such instances, the target intravascular deficit may be set less than zero (e.g., -1 to -250 mL) so that the donor has more fluid/volume after the procedure than they did before the procedure.

**[0071]** Like the method 400 shown in Figure 4, the method 500 may similarly perform some additional and optional steps to help determine the volume of pure plasma within the plasma collection container 216. For example, some embodiments may monitor the change in weight of the anticoagulant container 210 (e.g., as measured by a weight sensor/load cell on the anticoagulant container 210) (step 550). This measurement provides an indication of the volume of anticoagulant that has been added to the system 100, and may be used help determine the percentage of anticoagulant within the plasma collection container 216. Additionally or alternatively, some embodiments may similarly, monitor the change in weight and/or volume of the plasma and anticoagulant collected within the plasma collection container 216 (e.g., via weight sensor 195) (step 555). This measurement may be used to calculate of the total volume of pure plasma collected within the plasma collection container 216 (e.g., to obtain the total weight from which to subtract the calculated volume of anticoagulant). Also, some embodiments may also monitor the volume of anticoagulant remaining in the bowl 214 (step 565) (e.g., anticoagulant that did not mix with the plasma and/or otherwise remained in the bowl) using the optical sensor on the bowl 214 to determine whether any anticoagulant remains within the bowl 214 and modify the calculation of the amount of pure plasma collected within the plasma collection container (e.g., either increase the calculated amount or decreased the calculated amount), based on the volume of anticoagulant remaining within the bowl 214.

**[0072]** As noted above, prior art systems that follow the current FDA nomogram for plasma collection collect a volume of plasma product (e.g., anticoagulant and plasma mixed together) based solely on the weight of the donor – the same volume is collected from every donor at the same weight. However, the total blood volume and plasma volume for two donors may vary greatly. For example, when comparing two donors in the same weight grouping according to the FDA nomogram – one obese and one not obese – the obese donor will effectively have a lower blood volume that the non-obese donor. Furthermore, with respect to the total plasma volume, donors with high hematocrit will have lower plasma volumes. In other words, because the total blood volume and total plasma volume vary from donor to donor (even among donors that weight the same), the percentage of the donor's plasma that is ultimately collected may vary widely from donor to donor. By tailoring the plasma collection to the donor (e.g., based on the donor's height, weight, BMI, hematocrit, total blood volume, and/or total plasma volume) and collecting a predetermined percent of plasma from each donor, embodiments of the preset

invention are able to collect a greater volume of plasma (e.g., pure plasma) from some donors but less plasma from more vulnerable donors (e.g., smaller donors with high hematocrit, donors with lower plasma volume, etc.), as compared to systems that do not base the collection volume on the individual donor.

**[0073]** Similarly, current systems do not tailor the saline return volume to the patient (e.g., each donor at a given level receives the same volume of saline, for example, if the target plasma product volume is 800 mL, the donor will receive 500 mL of saline). However, because prior art systems collect based on the volume of the plasma product (which includes both plasma and anticoagulant) and the volume of pure plasma that is actually collected (and therefore, the volume removed from the donor) varies based on the donor hematocrit, the intravascular deficit for each donor will vary. In other words, the volume of saline returned to the donor may be sufficient for some, but insufficient for others. By tailoring the saline return to the individual donor, embodiments of the present invention are able to ensure that each donor has the same intravascular deficit (if any) once the procedure is complete. This, in turn, allows embodiments of the present invention to achieve isovolemia for each donor and greatly reduce any adverse reactions that the donor may experience (e.g., falling, fainting, light-headedness, vasovagal reactions, etc.).

**[0074]** It is also important to note that, although the various embodiments discussed above are in relation to a blood processing system that collects plasma, the features discussed herein may be applied to any type of blood processing system. For example, the features described herein may be implemented on blood processing systems that collect and/or process red blood cells, platelets and/or white blood cells.

**[0075]** The embodiments of the invention described above are intended to be merely exemplary; numerous variations and modifications will be apparent to those skilled in the art. All such variations and modifications are intended to be within the scope of the present invention as defined in any appended claims.

What is claimed is:

1. A method for collecting plasma comprising:
  - (a) determining a weight and height of a donor;
  - (b) determining a hematocrit of the donor;
  - (c) calculating a donor plasma volume based, at least in part, on the weight and height of the donor and the hematocrit of the donor;
  - (d) calculating a target plasma collection volume based, at least in part, on the calculated donor plasma volume and a target percentage of plasma;
  - (e) withdrawing whole blood from the donor through the venous-access device and a first line, the first line connected to a blood component separation device;
  - (f) introducing anticoagulant into the withdrawn whole blood through an anticoagulant line;
  - (g) separating the withdrawn whole blood into a plasma component and at least a second blood component using the blood component separation device;
  - (h) collecting the plasma component from the blood component separation device and into a plasma collection container;
  - (i) calculating a volume of pure plasma collected within the plasma collection container; and
  - (j) continuing steps (e) through (i) until the calculated volume of pure plasma collected within the plasma collection container equals the target plasma collection volume.
2. A method according to claim 1, further comprising:

returning, after collecting at least a portion of the target plasma collection volume, the contents of the blood component separation device to the donor through the first line.
3. A method according to claim 2, further comprising:

calculating an intravascular deficit based, at least in part on, the volume of pure plasma collected and a volume of the contents of the blood component separation device returned to the donor.
4. A method according to claim 3, further comprising:

returning a volume of saline to the donor to obtain a target intravascular deficit.



5. A method according to claim 4, wherein the target intravascular deficit is 0 milliliters.
6. A method according to claim 4, wherein the target intravascular deficit is between -250 and 500 milliliters.
7. A method according to claim 1, further comprising:
  - calculating the donor's body mass index based, at least in part on the weight and height of the donor, the donor plasma volume calculated based, at least in part, on the donor's body mass index.
8. A method according to claim 1, wherein the target percentage of plasma is between 26.5 and 29.5 percent of the donor's plasma volume.
9. A method according to claim 1, further comprising:
  - inserting a venous-access device into the donor prior to step (e).
10. A method according to claim 1, further comprising:
  - calculating a percentage of anticoagulant in the collected plasma component, the volume of pure plasma based, at least in part, on the calculated percentage of anticoagulant in the collected plasma component.
11. A method according to claim 10, further comprising:
  - determining a change in volume within an anticoagulant container, the calculated percentage of anticoagulant in the collected plasma being based, at least in part, on the change in volume within the anticoagulant container.
12. A method according claim 10, further comprising:
  - determining a volume of anticoagulant introduced into the whole blood based on a number of rotations of an anticoagulant pump, the calculated percentage of anticoagulant in the collected plasma being based, at least in part, on the number of rotations of the anticoagulant pump.

13. A method according to claim 10, further comprising:

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

14. A method according to claim 10, wherein the percentage of anticoagulant in the collected plasma component includes at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant added during a priming step.

15. A method according to claim 1, further comprising:

monitoring a volume of plasma component collected within the plasma collection container, the calculated volume of pure plasma collected within the plasma collection device based, at least in part, on the monitored volume of collected plasma component.

16. 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 device based, at least in part, on the monitored weight of collected plasma component.

17. A method according to claim 1, wherein step (b) includes monitoring a volume of red blood cells collected within the blood separation device, the determined hematocrit of the donor based, at least in part, on the monitored volume of red blood cells collected within the blood separation device and a volume of whole blood withdrawn from the donor.

18. A system for collecting plasma comprising:

a venous-access device for drawing whole blood from a subject and returning blood components to the subject;

a blood component separation device for separating the drawn blood into a plasma component and a second blood component, the blood component separation device having an outlet and being configured to send the plasma component to a plasma container;

a first line fluidly connected to the venous-access device and configured to transport drawn whole blood to the blood component separation device and return fluid within the

blood component separation device to the subject, the flow through the first line being controlled by a first pump;

an anticoagulant line connected to an anticoagulant source, the anticoagulant line configured to introduce anticoagulant into the drawn whole blood; and

a controller configured to control the operation of the centrifuge bowl and the first pump, the controller configured to calculate (1) a donor plasma volume based, at least in part, on a weight and height of the donor and a hematocrit of the donor, (2) a target plasma collection volume based, at least in part, on the calculated donor plasma volume and a target percentage of plasma, and (3) a volume of pure plasma collected within the plasma container based, at least in part, upon a percentage of anticoagulant in the collected plasma component, the controller configured to stop the first pump when the calculated volume of pure plasma collected within the plasma collection container equals the target plasma collection volume.

19. A system according to claim 18, wherein the controller is further configured to:

return, after collecting at least a portion of the target plasma collection volume, fluid remaining within the blood component separation device via the first line.

20. A system according to claim 19, wherein the controller is further configured to:

calculate an intravascular deficit based, at least in part on, the volume of pure plasma collected and a volume of the contents of the blood component separation device returned to the donor.

21. A system according to claim 20, further comprising:

a saline line configured to fluidly connect to a saline source and the blood component separation device, the controller configured to return a volume of saline to the donor to obtain a target intravascular deficit.

22. A system according to claim 21, wherein the target intravascular deficit is between -250 and 500 milliliters.

23. A system according to claim 18, wherein the controller is further configured to:
- calculate the donor's body mass index based, at least in part, on the weight and height of the donor, the donor plasma volume calculated based, at least in part, on the donor's body mass index.
24. A system according to claim 18, wherein the target percentage of plasma is between 26.5 and 29.5 percent of the donor's plasma volume.
25. A system according to claim 18, wherein the controller is further configured to:
- calculate the percentage of anticoagulant in the collected plasma component.
26. A system according to claim 25, wherein the percentage of anticoagulant in the collected plasma component is based, at least in part, on a volume of anticoagulant added to the drawn whole blood and the subject's hematocrit.
27. A system according to claim 25, further comprising:
- an anticoagulant source weight sensor configured to measure the weight of the anticoagulant source, the controller further configured to monitor a change in volume within the anticoagulant container based on the measured weight of the anticoagulant source, the calculated percentage of anticoagulant in the collected plasma being based, at least in part, on the change in volume within the anticoagulant source.
28. A system according to claim 25, wherein the controller is configured to monitor a number of rotations of an anticoagulant pump to determine a volume of anticoagulant introduced into the whole blood, the calculated percentage of anticoagulant in the collected plasma being based, at least in part, on the number of rotations of the anticoagulant pump.
29. A system according to claim 25, further comprising:
- 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 percentage of anticoagulant in the collected plasma being based, at least in part, on the volume of anticoagulant within the blood component separation device.

30. A system according to claim 18, further comprising:

a plasma container weight sensor configured to monitor a volume of plasma component collected within the plasma container, the calculated volume of pure plasma collected within the plasma collection device based, at least in part, on the monitored volume of collected plasma component.

31. A system according to claim 18, further comprising:

a plasma container weight sensor configured to monitor a weight of plasma component collected within the plasma container, the calculated volume of pure plasma collected within the plasma collection device based, at least in part, on the monitored weight of collected plasma component.

32. A system according to claim 18, further comprising:

an optical sensor located on the blood component separation device and configured to monitor a volume of red blood cells collected within the blood 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 separation device and a volume of whole blood withdrawn from the donor.

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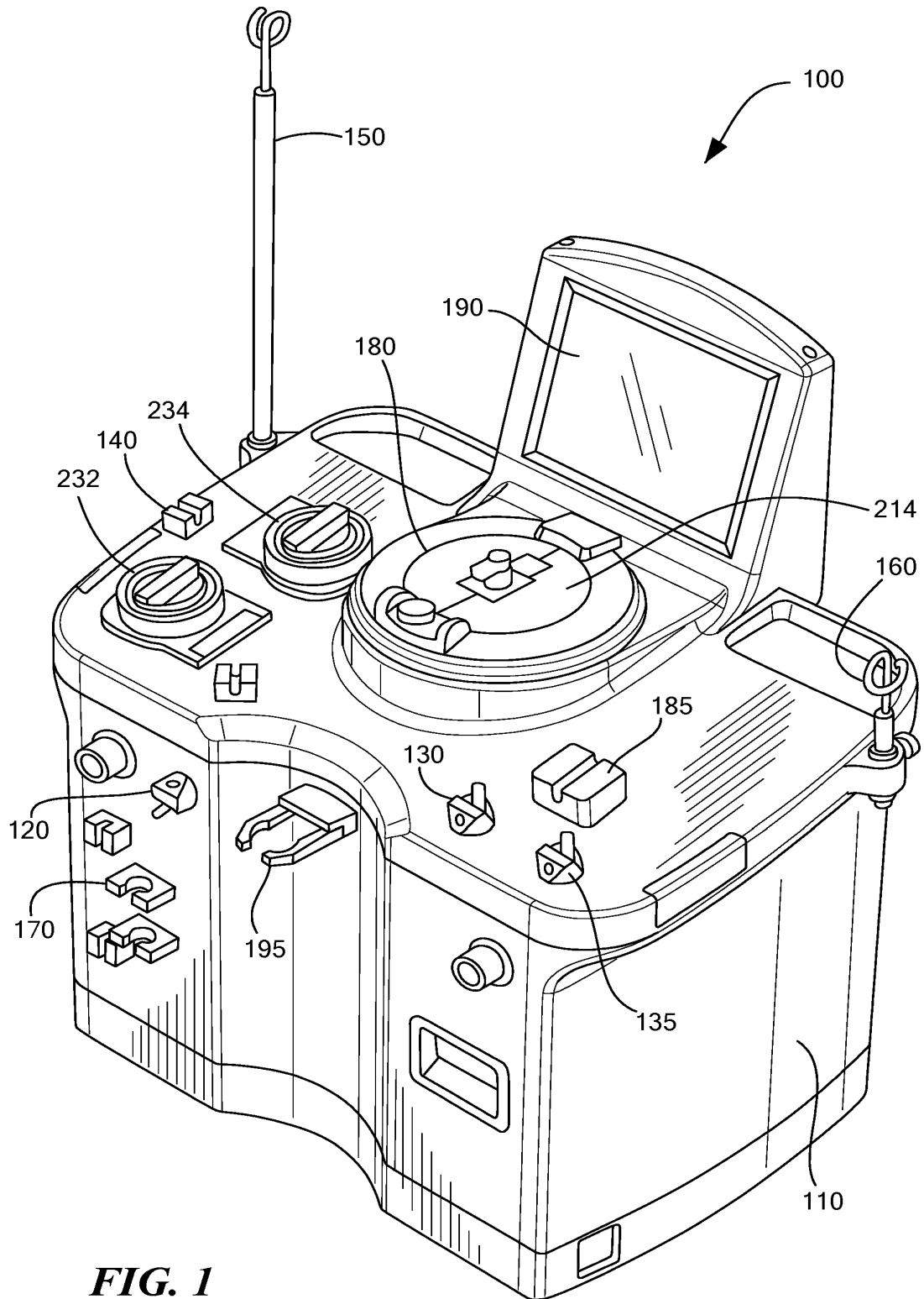


**FIG. 1**

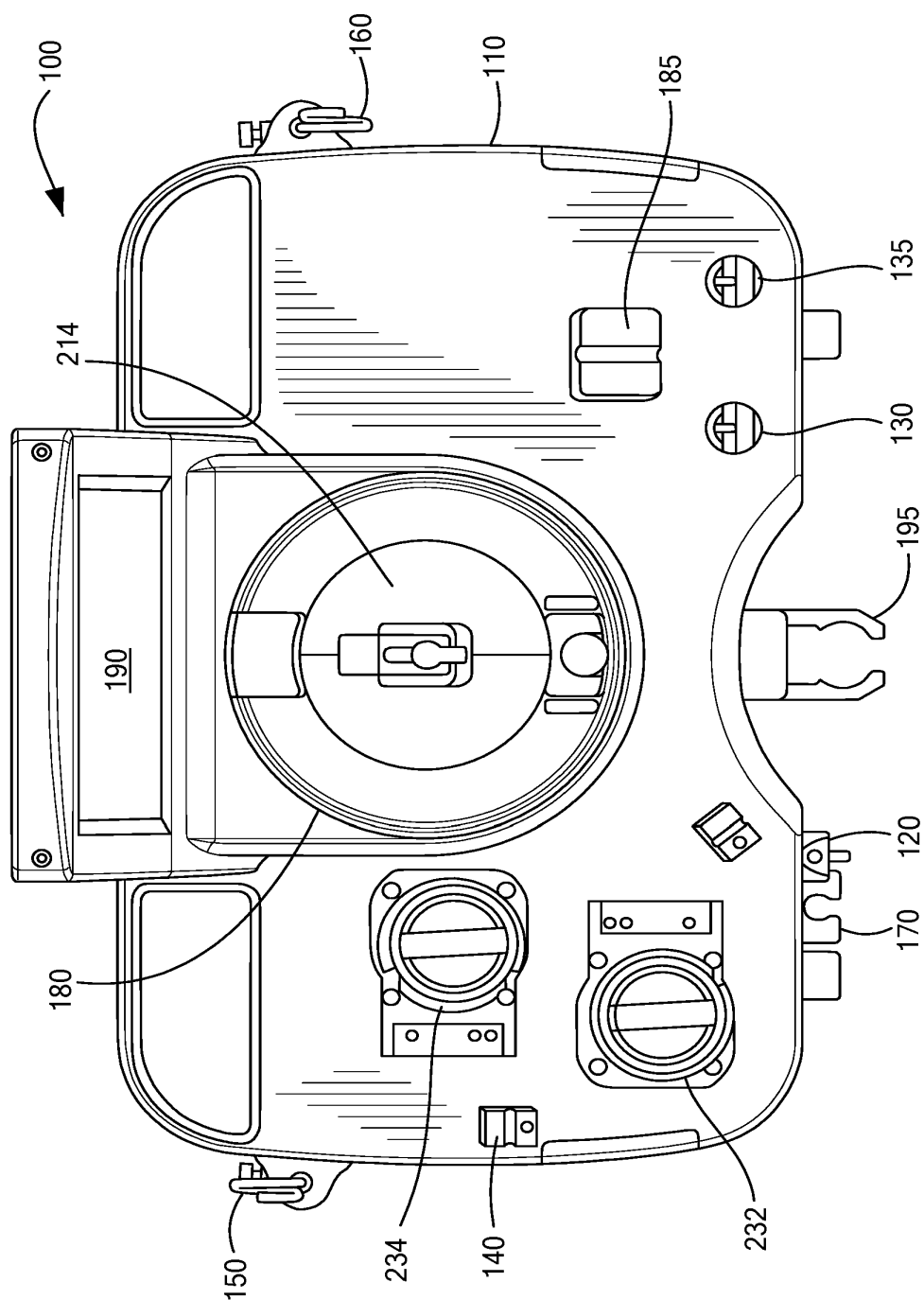


**FIG. 2**

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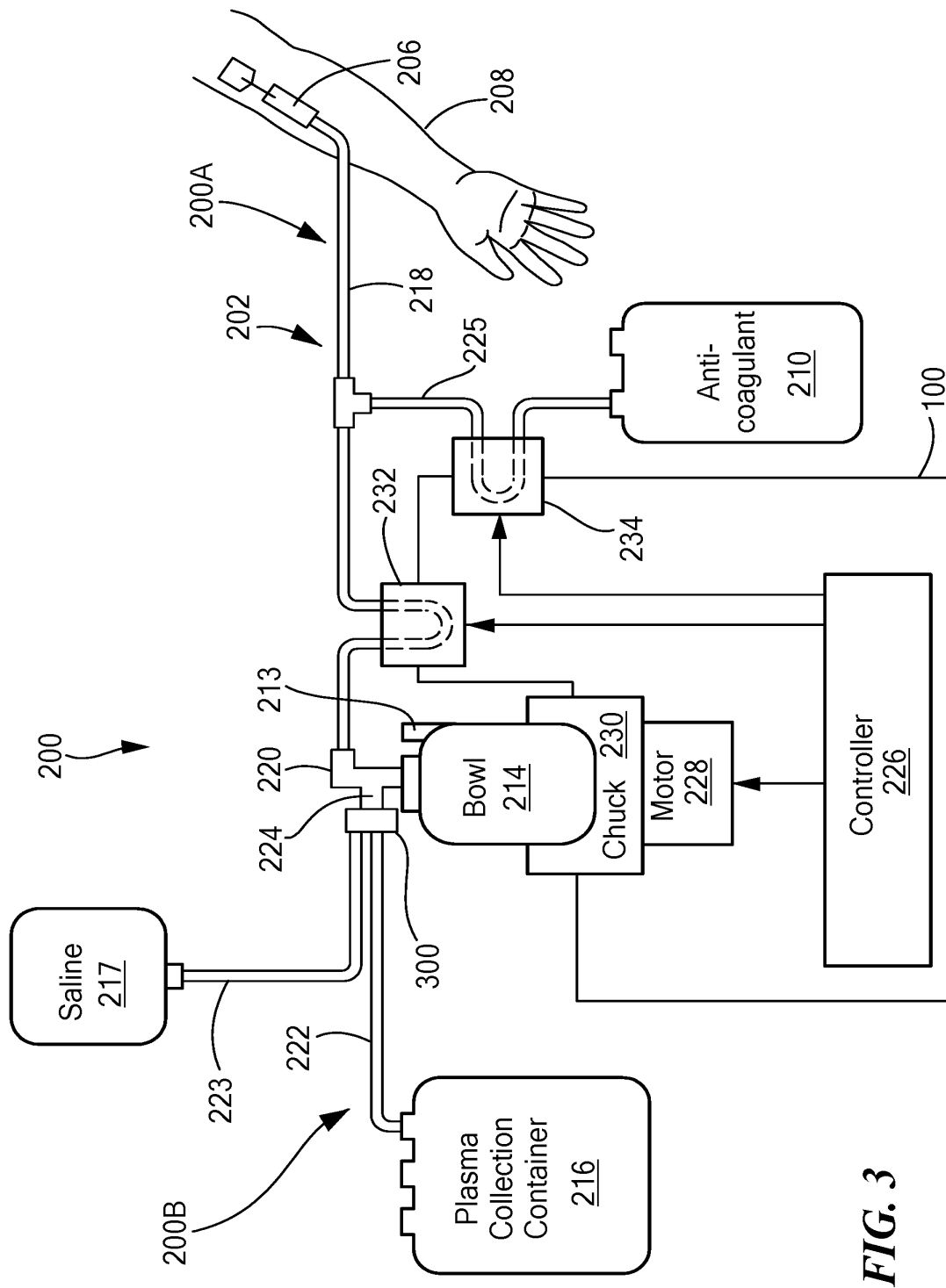
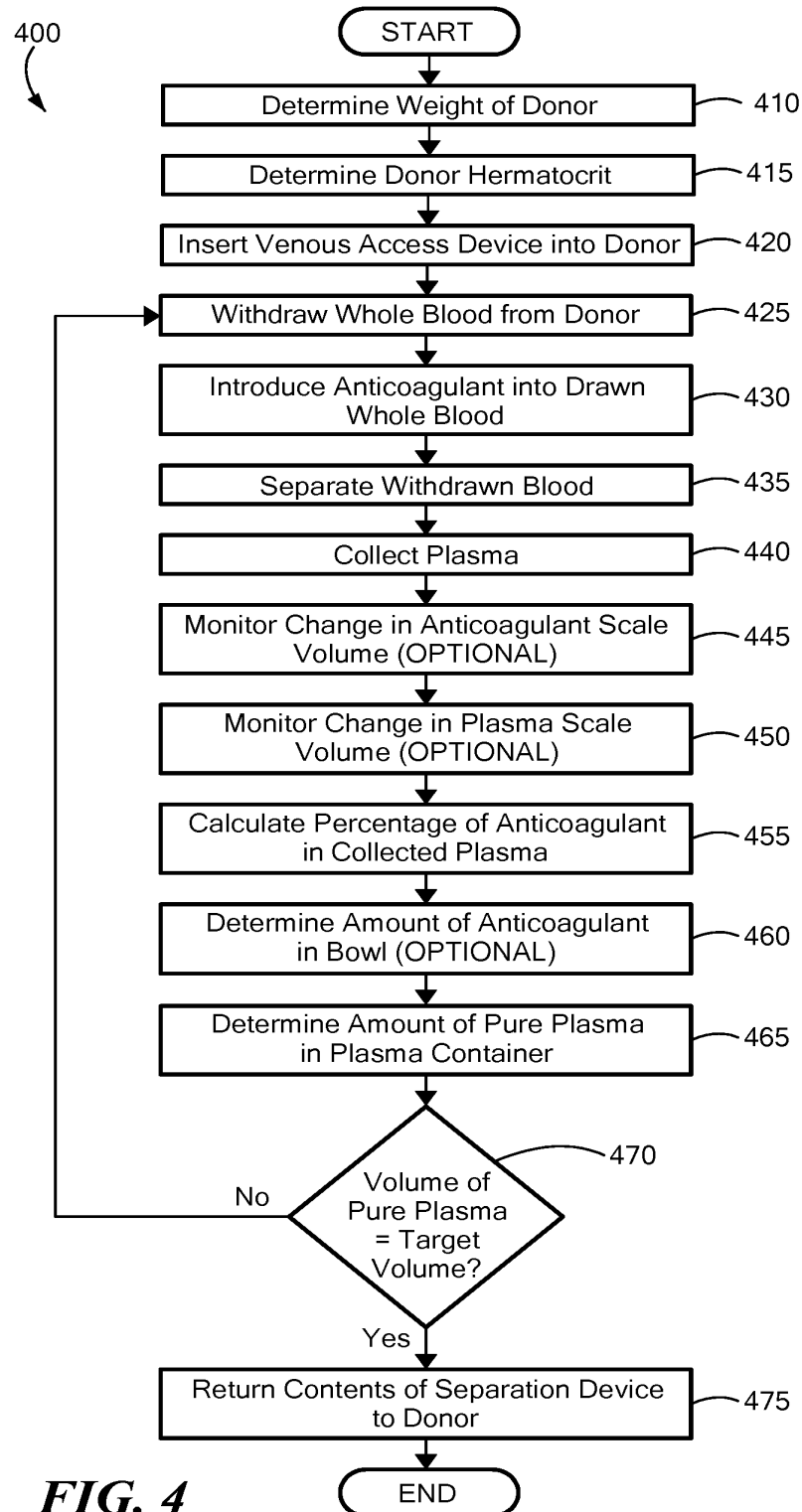


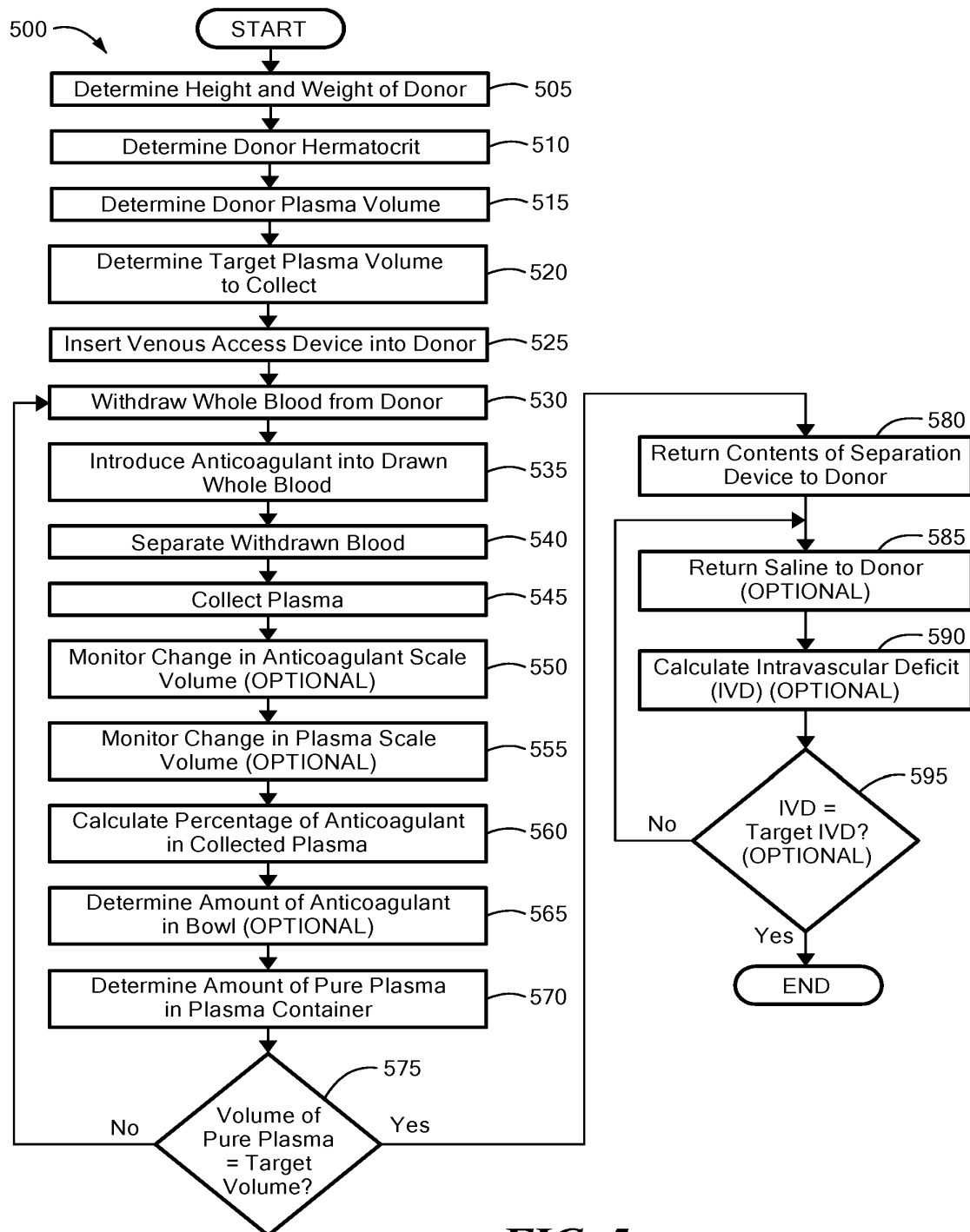
**FIG. 3**



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**FIG. 4**

5/5

**FIG. 5**

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 18/57528

A. CLASSIFICATION OF SUBJECT MATTER  
IPC(8) - A61M 1/36 (2018.01)  
CPC - A61M 1/3496

According to International Patent Classification (IPC) or to both national classification and IPC

## R FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

See Search History Document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

See Search History Document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History Document

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category*               | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                      | Relevant to claim No.                                                                           |
|-------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
| X<br>--<br>Y<br>--<br>A | US 2001/000185 A1 (KELLER et al.); 5 April 2001 (05.04.2001); entire document, especially Abstract, para. [0115]-[0116], [0264], [0269], [0272], [0275], [0280], [0316]-[0319], [0329]. | 1-2, 9, 15, 17<br>-----<br>3-6, 8, 10, 11-14, 16, 18-22, 24-28, 30-31<br>-----<br>7, 23, 29, 32 |
| Y<br>--<br>A            | US 2003/0125881 A1 (RYAN); 3 July 2003 (03.07.2003); entire document, especially Abstract, para. [0011]-[0012], [0014], [0019], [0021], [0026]-[0027], [0044].                          | 1, 8, 10-14, 16, 18-22, 24-28, 30-31<br>-----<br>7, 23, 29, 32                                  |
| Y                       | US 2002/0062100 A1 (PIERCE et al.); 23 May 2002 (23.05.2002); entire document, especially Abstract, para. [0111], [0137].                                                               | 3-6, 20-22                                                                                      |
| Y                       | US 2012/0175313 A1 (BARRY et al.); 12 July 2012 (12.07.2012); entire document, especially Abstract, para. [0057].                                                                       | 11, 13                                                                                          |
| Y                       | US 2014/0356851 A1 (HAEMONETICS CORPORATION); 4 December 2014 (04.12.2014); entire document, especially Abstract, para. [0030]-[0031].                                                  | 14                                                                                              |

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

18 December 2018

Date of mailing of the international search report

07 JAN 2019

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents  
P.O. Box 1450, Alexandria, Virginia 22313-1450  
Facsimile No. 571-273-8300

Authorized officer:

Lee W. Young

PCT Helpdesk: 571-272-4300  
PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)

Doc code: IDS

Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (01-22)

Approved for use through 05/31/2024. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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|                                                                                                     |                        |                  |
|-----------------------------------------------------------------------------------------------------|------------------------|------------------|
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | N/A              |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

| U.S. PATENTS                                                                                               |         |                                                                                                                                                                                                                                                                 |                            |                        |                                                 |                                                                          | Remove                                                                   |                |
|------------------------------------------------------------------------------------------------------------|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|------------------------|-------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|----------------|
| Examiner Initial*                                                                                          | Cite No | Patent Number                                                                                                                                                                                                                                                   | Kind Code <sup>1</sup>     | Issue Date             | Name of Patentee or Applicant of cited Document | Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear |                                                                          |                |
|                                                                                                            | 1       |                                                                                                                                                                                                                                                                 |                            |                        |                                                 |                                                                          |                                                                          |                |
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| Examiner Initial*                                                                                          | Cite No | Publication Number                                                                                                                                                                                                                                              | Kind Code <sup>1</sup>     | Publication Date       | Name of Patentee or Applicant of cited Document | Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear |                                                                          |                |
|                                                                                                            | 1       |                                                                                                                                                                                                                                                                 |                            |                        |                                                 |                                                                          |                                                                          |                |
| If you wish to add additional U.S. Published Application citation information please click the Add button. |         |                                                                                                                                                                                                                                                                 |                            |                        |                                                 |                                                                          | Add                                                                      |                |
| FOREIGN PATENT DOCUMENTS                                                                                   |         |                                                                                                                                                                                                                                                                 |                            |                        |                                                 |                                                                          | Remove                                                                   |                |
| Examiner Initial*                                                                                          | Cite No | Foreign Document Number <sup>3</sup>                                                                                                                                                                                                                            | Country Code <sup>2i</sup> | Kind Code <sup>4</sup> | Publication Date                                | Name of Patentee or Applicant of cited Document                          | Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear | T <sup>5</sup> |
|                                                                                                            | 1       | 2002-282352                                                                                                                                                                                                                                                     | JP                         | A                      | 2002-10-02                                      | Terumo Corp                                                              |                                                                          | ×              |
| If you wish to add additional Foreign Patent Document citation information please click the Add button.    |         |                                                                                                                                                                                                                                                                 |                            |                        |                                                 |                                                                          | Add                                                                      |                |
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| Examiner Initials*                                                                                         | Cite No | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published. |                            |                        |                                                 |                                                                          |                                                                          | T <sup>5</sup> |

|                                                                                                     |                        |                  |
|-----------------------------------------------------------------------------------------------------|------------------------|------------------|
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | N/A              |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |  |                 |  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|-----------------|--|
| 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  |                 |  |
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| <b>EXAMINER SIGNATURE</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |  |                 |  |
| Examiner Signature                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |  | Date Considered |  |
| *EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.                                                                                                                                                                                                                                                                                                                                                                                                |  |                 |  |
| <small> <sup>1</sup> See Kind Codes of USPTO Patent Documents at <a href="http://www.USPTO.GOV">www.USPTO.GOV</a> or MPEP 901.04. <sup>2</sup> Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>3</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>4</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>5</sup> Applicant is to place a check mark here if English language translation is attached.       </small> |  |                 |  |

|                                                                                                     |                        |                  |
|-----------------------------------------------------------------------------------------------------|------------------------|------------------|
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | N/A              |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

### CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

**OR**

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

### SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

|            |                                       |                     |            |
|------------|---------------------------------------|---------------------|------------|
| Signature  | /Jonathan C. Lovely, Reg. No. 60,821/ | Date (YYYY-MM-DD)   | 2022-04-04 |
| Name/Print | Jonathan C. Lovely                    | Registration Number | 60,821     |

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

## Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: April 4, 2022  
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Utility Application of:  
Michael Ragusa

Application No.: 17/205,400

Confirmation No.: 4686

Filed: March 18, 2021

Art Unit: N/A

For: SYSTEM AND METHOD FOR COLLECTING  
PLASMA

Examiner: Not Yet Assigned

**INFORMATION DISCLOSURE STATEMENT (IDS)**

MS Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR 1.97, Applicant hereby makes of record the following additional document. A PTO Form SB/08 and a full copy of the document required under 37 CFR 1.98(a)(2) accompany this statement.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 C.F.R. § 1.97(b)(3)).

Applicant submits herewith a copy of the cited foreign patent in accordance with 37 C.F.R. § 1.98(a)(2).



The Examiner is advised that the following applications contain subject matter that may be related to the present application:

| <b>U.S. Application</b> | <b>Filing Date</b> | <b>Publication No. / Patent No.</b> | <b>Status</b> | <b>Atty. Docket No.</b> |
|-------------------------|--------------------|-------------------------------------|---------------|-------------------------|
| 15/608,183              | May 30, 2017       | 10,758,652                          | Issued        | 130670-08002            |
| 16/866,078              | May 4, 2020        | 10,980,926                          | Issued        | 130670-08005            |
| 17/205,374              | March 18, 2021     | 2021-0205509                        | Published     | 130670-08006            |
| 15/793,339              | October 25, 2017   | 10,792,416                          | Issued        | 130670-80102            |
| 16/931,333              | July 16, 2020      | 10,980,934                          | Issued        | 130670-80103            |

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed reference.

Applicant believes no fee is due with this response.

Dated: April 4, 2022

Respectfully submitted,  
Electronic signature: /Jonathan C. Lovely, Reg.  
No. 60,821/  
Jonathan C. Lovely  
Registration No.: 60,821  
MCCARTER & ENGLISH, LLP  
265 Franklin Street  
Boston, Massachusetts 02110  
(617) 449-6556  
(617) 607-9200 (Fax)  
Attorney/Agent For Applicant

| Electronic Acknowledgement Receipt   |                                         |
|--------------------------------------|-----------------------------------------|
| EFS ID:                              | 45379223                                |
| Application Number:                  | 17205400                                |
| International Application Number:    |                                         |
| Confirmation Number:                 | 4686                                    |
| Title of Invention:                  | SYSTEM AND METHOD FOR COLLECTING PLASMA |
| First Named Inventor/Applicant Name: | Michael Ragusa                          |
| Customer Number:                     | 86738                                   |
| Filer:                               | Jonathan Lovely                         |
| Filer Authorized By:                 |                                         |
| Attorney Docket Number:              | 130670-80104                            |
| Receipt Date:                        | 04-APR-2022                             |
| Filing Date:                         | 18-MAR-2021                             |
| Time Stamp:                          | 07:24:33                                |
| Application Type:                    | Utility under 35 USC 111(a)             |

### Payment information:

| Submitted with Payment | no                   |                                      |                                          |                  |                  |
|------------------------|----------------------|--------------------------------------|------------------------------------------|------------------|------------------|
| <b>File Listing:</b>   |                      |                                      |                                          |                  |                  |
| Document Number        | Document Description | File Name                            | File Size(Bytes)/<br>Message Digest      | Multi Part /.zip | Pages (if appl.) |
| 1                      | Foreign Reference    | 130670-08006_-<br>_JP2002282352A.pdf | 767249                                   | no               | 14               |
|                        |                      |                                      | f6c8cd708d8e9564bfa68fe940aa69f5e55ac7ac |                  |                  |
| <b>Warnings:</b>       |                      |                                      |                                          |                  |                  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                    |                                                                          |                                                         |    |   |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|--------------------------------------------------------------------------|---------------------------------------------------------|----|---|
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                    |                                                                          |                                                         |    |   |
| 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Information Disclosure Statement (IDS) Form (SB08) | 130670-80104 -<br>_Information_Disclosure_State<br>ment_Fillable_PDF.pdf | 1263150<br><br>9a7e6a6ef7f4fb8fa219f580a9c5c9399e5d13bd | no | 4 |
| <b>Warnings:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                    |                                                                          |                                                         |    |   |
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                    |                                                                          |                                                         |    |   |
| A U.S. Patent Number Citation or a U.S. Publication Number Citation is required in the Information Disclosure Statement (IDS) form for autoloading of data into USPTO systems. You may remove the form to add the required data in order to correct the Informational Message if you are citing U.S. References. If you chose not to include U.S. References, the image of the form will be processed and be made available within the Image File Wrapper (IFW) system. However, no data will be extracted from this form. Any additional data such as Foreign Patent Documents or Non Patent Literature will be manually reviewed and keyed into USPTO systems.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                    |                                                                          |                                                         |    |   |
| 3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Transmittal Letter                                 | Information_Disclosure_State<br>ment.pdf                                 | 25198<br><br>3c73fb2d710f2c94677cd369f97368f032005195   | no | 2 |
| <b>Warnings:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                    |                                                                          |                                                         |    |   |
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                    |                                                                          |                                                         |    |   |
| <b>Total Files Size (in bytes):</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                    |                                                                          | 2055597                                                 |    |   |
| <p><b>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</b></p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b><br/> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b><br/> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b><br/> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p> |                                                    |                                                                          |                                                         |    |   |



Espacenet

**Bibliographic data: JP2002282352 (A) — 2002-10-02****BLOOD COMPONENT COLLECTING DEVICE**

**Inventor(s):** TAKAGI YOSHIMI ± (TAKAGI YOSHIMI)  
**Applicant(s):** TERUMO CORP ± (TERUMO CORP)  
**Classification:** - **international:** **A61M1/02**; (IPC1-7): A61M1/02  
- **cooperative:**  
**Application number:** JP20010087773 20010326  
**Priority number(s):** JP20010087773 20010326

**Abstract of JP2002282352 (A)**

**PROBLEM TO BE SOLVED:** To provide a blood component collecting device that can perform an appropriate collection of blood component according to a donor.  
**SOLUTION:** The blood component collecting device 1 shown in a figure 1 is the device that collects mainly plasma as a specific blood component and comprising a needle for collecting blood (means for collecting device) 29 that collects blood from a donor, an anticoagulant providing means that adds anticoagulant into the blood (23 in the third line and liquid feeding pump 12 in the second), a centrifuge 20 that centrifuges the blood that is collected by the needle 29 and to which anticoagulant is added by the anticoagulant providing means into multiple blood components, a plasma collecting bag (a blood component collecting bag) 25 that collects plasma to which the anticoagulant is contaminated, an input means 3 to which information on the donor is inputted, and a control unit (a control means) that controls the movement of the blood component collecting device 1, and a specific condition of the blood component collecting device 1 is set according to information on the donor. The above setting condition is preferably to be an aimed collecting volume for plasma itself not including anticoagulant.

(19) 日本国特許庁 (J P)

(12) 公開特許公報 (A)

(11) 特許出願公開番号  
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(71) 出願人 000109543

テルモ株式会社  
東京都渋谷区幡ヶ谷2丁目44番1号

(72) 発明者 高木 愛己

静岡県富士宮市三園平818番地 テルモ株  
式会社内

(74) 代理人 100091292

弁理士 増田 達哉

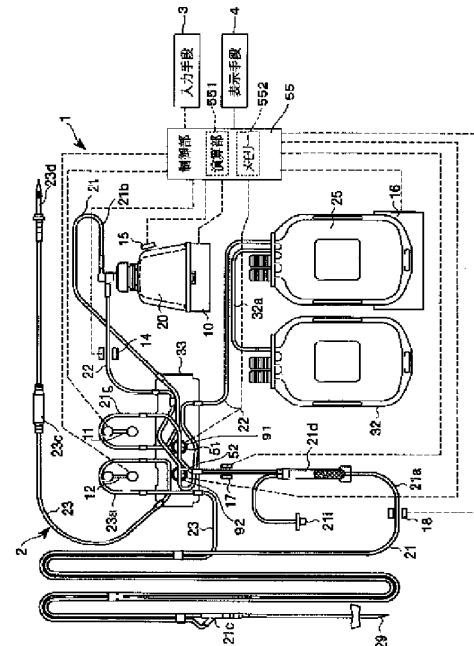
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(54) 【発明の名称】 血液成分採取装置

(57) 【要約】

【課題】 供血者に応じた適正な血液成分採取操作を行なうことができる血液成分採取装置を提供すること。

【解決手段】 図1に示す血液成分採取装置1は、所定の血液成分として、主に血漿を採取する装置であり、ドナー（供血者）から血液を採取する採血針（採血手段）29と、血液中に抗凝固剤を添加する抗凝固剤供給手段（第3のライン23および第2の送液ポンプ12）と、採血針29により採血され、抗凝固剤供給手段により抗凝固剤が添加された血液を複数の血液成分に遠心分離する遠心分離器20と、抗凝固剤が混入した血漿を採取する血漿採取バッグ（血液成分採取バッグ）25と、ドナーに関する情報を入力する入力手段3と、血液成分採取装置1の作動を制御する制御部（制御手段）とを有し、ドナーに関する情報に基づき、血液成分採取装置1の所定の条件を設定する。また、前記所定の条件は、抗凝固剤を除く血漿自体の目標とする採取量とするのが好ましい。



【特許請求の範囲】

【請求項1】 供血者から採取した血液を複数の血液成分に分離するとともに分離された血液成分を採取する血液成分採取装置であって、  
供血者から血液を採取する採血手段と、  
前記血液中に抗凝固剤を添加する抗凝固剤供給手段と、  
内部に貯血空間を有するローターと、該ローターの回転により前記採血手段により採取された血液を前記貯血空間内で複数の血液成分に遠心分離する遠心分離器と、  
前記貯血空間に連通し、所定の血液成分を採取する血液成分採取バッグと、  
前記所定の血液成分の採取量を検出する検出手段と、  
前記供血者に関する情報を入力する入力手段と、  
前記血液成分採取装置の作動を制御する制御手段とを有し、  
前記供血者に関する情報に基づき、前記血液成分採取装置の所定の条件を設定することを特徴とする血液成分採取装置。

【請求項2】 前記所定の条件は、前記所定の血液成分の目標とする採取量である請求項1に記載の血液成分採取装置。

【請求項3】 前記供血者から採取された血液を遠心分離し、前記所定の血液成分を、前記血液成分採取バッグ内に移送する血液成分採取工程と、  
残りの血液成分を前記供血者に返還する血液成分返還工程とを有する血液成分採取操作を複数サイクル行なうよう作動し、  
前記所定の血液成分の目標とする採取量に基づき、前記血液成分採取操作のサイクル数を決定する請求項2に記載の血液成分採取装置。

【請求項4】 前記血液成分採取バッグ内に採取された前記所定の血液成分の現在の採取量が、前記所定の血液成分の目標とする採取量の70～100％に到達した場合、あるいは、前記血液成分採取操作を前記サイクル数行なった場合には、前記血液成分採取操作を終了する請求項3に記載の血液成分採取装置。

【請求項5】 前記所定の血液成分の採取量には、抗凝固剤の混入量が含まれていない請求項2ないし4のいずれかに記載の血液成分採取装置。

【請求項6】 前記所定の血液成分は、主に血漿である請求項1ないし5のいずれかに記載の血液成分採取装置。

【発明の詳細な説明】

【0001】

【発明の属する技術分野】本発明は、血液から所定の血液成分を採取する血液成分採取装置に関する。

【0002】

【従来の技術】採血を行う場合、現在では、血液の有効利用および供血者の負担軽減などの理由から、採血血液を遠心分離などにより各血液成分に分離し、輸血者に必

要な成分だけを採取し、その他の成分は供血者に返還する成分採血が行われている。

【0003】このような成分採血では、例えば、血漿製剤を得る場合、供血者から採取した血液を血液成分採取回路に導入し、該血液成分採取回路に設置された遠心ボウルと呼ばれる遠心分離器により、血漿、バフィーコートおよび赤血球に分離し、その内の血漿は容器に回収されて血漿製剤とし、残りのバフィーコート（白血球、血小板）および赤血球は、供血者に返血（返還）することが行われる。

【0004】ところで、従来、成分採血を行なう場合、供血者に関する情報（例えば、身長、体重、性別等）を考慮せず、例えば、目標とする血漿の採取量（目標血漿採取量）を設定している。この場合、供血者に応じた適正な採取量を得るのが困難である。

【0005】また、通常、採取される血漿中には、抗凝固剤が混入しており、目標血漿採取量も、抗凝固剤の混入量を含んで設定されている。

【0006】このため、操作者は、血漿自体の採取量を把握することができず、供血者によっては、許容される量以上の血漿を採取してしまったり、あるいは、許容される量にはるかに満たない量で血漿採取を終了してしまったりすることがあり、好ましくない。

【0007】

【発明が解決しようとする課題】本発明の目的は、供血者に応じた適正な血液成分採取操作を行なうことができる血液成分採取装置を提供することにある。

【0008】

【課題を解決するための手段】このような目的は、下記（1）～（9）の本発明により達成される。

【0009】（1） 供血者から採取した血液を複数の血液成分に分離するとともに分離された血液成分を採取する血液成分採取装置であって、供血者から血液を採取する採血手段と、前記血液中に抗凝固剤を添加する抗凝固剤供給手段と、内部に貯血空間を有するローターと、該ローターの回転により前記採血手段により採取された血液を前記貯血空間内で複数の血液成分に遠心分離する遠心分離器と、前記貯血空間に連通し、所定の血液成分を採取する血液成分採取バッグと、前記所定の血液成分の採取量を検出する検出手段と、前記供血者に関する情報を入力する入力手段と、前記血液成分採取装置の作動を制御する制御手段とを有し、前記供血者に関する情報に基づき、前記血液成分採取装置の所定の条件を設定することを特徴とする血液成分採取装置。

【0010】（2） 前記所定の条件は、前記所定の血液成分の目標とする採取量である上記（1）に記載の血液成分採取装置。

【0011】（3） 前記供血者から採取された血液を遠心分離し、前記所定の血液成分を、前記血液成分採取バッグ内に移送する血液成分採取工程と、残りの血液成

分を前記供血者に返還する血液成分返還工程とを有する血液成分採取操作を複数サイクル行なうよう作動し、前記所定の血液成分の目標とする採取量に基づき、前記血液成分採取操作のサイクル数を決定する上記(2)に記載の血液成分採取装置。

【0012】(4) 前記血液成分採取バッグ内に採取された前記所定の血液成分の現在の採取量が、前記所定の血液成分の目標とする採取量の70～100%に到達した場合、あるいは、前記血液成分採取操作を前記サイクル数行なった場合には、前記血液成分採取操作を終了する上記(3)に記載の血液成分採取装置。

【0013】(5) 前記所定の血液成分の採取量には、抗凝固剤の混入量が含まれていない上記(2)ないし(4)のいずれかに記載の血液成分採取装置。

【0014】(6) 前記所定の条件を表示する表示手段を有する上記(1)ないし(5)のいずれかに記載の血液成分採取装置。

【0015】(7) 前記表示手段は、前記血液成分採取バッグ内に採取された前記所定の血液成分の現在の採取量を表示する上記(6)に記載の血液成分採取装置。

【0016】(8) 前記供血者に関する情報は、前記供血者の性別、体重および身長のうち少なくとも1つを含む上記(1)ないし(7)のいずれかに記載の血液成分採取装置。

【0017】(9) 前記所定の血液成分は、主に血漿である上記(1)ないし(8)のいずれかに記載の血液成分採取装置。

【0018】

【発明の実施の形態】以下、本発明の血液成分採取装置を添付図面に示す好適な実施形態に基づいて詳細に説明する。

【0019】図1は、本発明の血液成分採取装置の構成例を示す平面図であり、図2は、本発明の血液成分採取装置が備える遠心分離器に遠心分離器駆動装置が装着された状態の部分破断断面図であり、図3は、本発明の血液成分採取装置の作用を説明するためのフローチャートである。

【0020】以下、血液成分採取装置1を、所定の血液成分として、主に血漿を採取する血漿採取装置に適用した場合を一例として説明する。

【0021】図1に示す血液成分採取装置1は、ドナー(供血者)から血液を採取する採血針(採血手段)29と、内部に貯血空間146を有するローター142を備え、ローター142の回転により採血針29により採取された血液を貯血空間146内にて遠心分離する遠心分離器20と、遠心分離器20により分離された血漿を採取する血漿採取バッグ(血液成分採取バッグ)25とを備える血液成分採取回路(血漿採取回路)2を有し、ドナーから採取した血液を遠心分離し、血漿を採取した後、主に白血球、血小板および赤血球等の血漿以外の血

液成分(残りの血液成分)をドナーに返還する装置である。

【0022】血液成分採取装置1は、内部に貯血空間146を有するローター142と、貯血空間146に連通する流入口143および流出口144とを有し、ローター142の回転により流入口143より導入された血液を貯血空間146内で遠心分離する遠心分離器20と、採血手段である採血針29と遠心分離器20の流入口143とを接続するための第1のライン21と、遠心分離器20の流出口144に接続された第2のライン22と、第1のライン21に接続され、抗凝固剤注入のための第3のライン23と、第2のライン22と接続された血漿採取バッグ25と、血漿採取バッグ25とチューブ32aにより接続されたサブバッグ32とを備える血液成分採取回路2を有している。

【0023】また、血液成分採取装置1は、遠心分離器20のローター142を回転させるための遠心分離器駆動装置10と、第1のライン21のための第1の送液ポンプ11と、第3のライン23のための第2の送液ポンプ12と、血液成分採取回路2の流路の開閉を行うための第1の流路開閉手段51および第2の流路開閉手段52と、遠心分離器駆動装置10、第1の送液ポンプ11、第2の送液ポンプ12、第1の流路開閉手段51および第2の流路開閉手段52を制御するための制御部(制御手段)55と、濁度センサ14と、光学式センサ15と、重量センサ(検出手段)16と、第1の気泡センサ17と、第2の気泡センサ18と、入力手段3と、表示手段4とを備えている。

【0024】なお、本実施形態では、第3のライン23と第2の送液ポンプ12とで、ドナーから採取された血液中に抗凝固剤を添加する抗凝固剤供給手段が構成される。

【0025】以下、各部の構成について説明する。採血針29としては、例えば、金属針が使用される。

【0026】第1のライン21は、採血針29が接続された採血針側第1ライン21aと、遠心分離器20の流入口143とを接続された遠心分離器側第1ライン21bと、これらの間に配置された第1のポンプチューブ21gとを有している。

【0027】採血針側第1ライン21aは、気泡およびマイクロアグリゲート除去のためのチャンバー21dを備える。チャンバー21dには、通気性かつ菌不透過性のフィルター21iが接続されている。

【0028】第2のライン22は、一端が遠心分離器20の流出口144に接続され、他端が血漿採取バッグ25に接続されている。

【0029】第3のライン23は、一端が第1のライン21に設けられた接続用分岐コネクタ21cに接続されている。第3のライン23は、接続用分岐コネクタ21c側より、第2のポンプチューブ23a、気泡除去

用チャンバー23c、抗凝固剤容器接続用針23dを備えている。

【0030】上述した第1のライン21、第2のライン22および第3のライン23の形成に使用されるチューブ、各ポンプチューブ21g、23a、さらに、バッグに接続されているチューブ32aの構成材料としては、ポリ塩化ビニルが好ましい。

【0031】各チューブがポリ塩化ビニル製であれば、十分な可撓性、柔軟性が得られるので取り扱いがし易く、また、クレンメ等による閉塞にも適するからである。

【0032】なお、各ポンプチューブ21g、23aとしては、ローラーポンプにより押圧されても損傷を受けない程度の強度を備えるものが使用されている。

【0033】また、上述した分岐コネクター21cの構成材料についても、前記チューブの構成材料と同様のものを用いることができる。

【0034】血漿採取バッグ25は、血漿を採取するための容器であり、第2のライン22を介して、遠心分離器20に接続され、これにより、血漿採取バッグ25の内部は、ローター142の貯血空間146に連通している。

【0035】サブバッグ32は、血漿採取操作（血液成分採取操作）の終了後に、血漿採取バッグ25内から空気（エア）を排出し、これを貯留するための容器である。このサブバッグ32は、チューブ32aを介して血漿採取バッグ25に接続され、それらの内部同士が連通している。

【0036】これらの血漿採取バッグ25、サブバッグ32は、それぞれ、樹脂製の可撓性を有するシート材を重ね、その周縁部を融着（熱融着、高周波融着等）または接着して袋状にしたものが使用される。

【0037】血漿採取バッグ25、サブバッグ32に使用される材料としては、例えば、軟質ポリ塩化ビニルが好適に使用される。この軟質ポリ塩化ビニルにおける可塑剤としては、例えば、ジ（エチルヘキシル）フタレート（DEHP）、ジ（n-デシル）フタレート（DnDP）等が使用される。なお、このような可塑剤の含有量は、ポリ塩化ビニル100重量部に対し、30～70重量部程度とするのが好ましい。

【0038】そして、血液成分採取回路2の主要部分は、図1に示すように、カセット式となっている。血液成分採取回路2は、すべてのライン（第1のライン21、第2のライン22、第3のライン23）を部分的に収納しかつ部分的にそれらを保持し、言い換えれば、部分的にそれらが固定されたカセットハウジング33を備えている。

【0039】カセットハウジング33には、第1のポンプチューブ21gの両端部および第2のポンプチューブ23aの両端部が固定され、これらのポンプチューブ2

1g、23aは、それぞれ、カセットハウジング33より、後述する各送液ポンプ（例えば、ローラーポンプ等）11、12の形状に対応したループ状に突出している。このため、第1のポンプチューブ21gおよび第2のポンプチューブ23aは、各送液ポンプ11、12への装着が容易である。

【0040】さらに、カセットハウジング33は、カセットハウジング33内に位置する複数の開口部を備えている。具体的には、第1のポンプチューブ21gより採血針29側の第1のライン21を露出させかつ、第1の流路開閉手段51の侵入が可能な第1の開口部91、第2のライン22を露出させかつ第2の流路開閉手段52の侵入が可能な第2の開口部92を備えている。

【0041】血液成分採取装置1は、このカセットハウジング33を装着するカセットハウジング装着部（図示せず）を備えている。このため、カセットハウジング33を血液成分採取装置1のカセットハウジング装着部に装着することにより、カセットハウジング33の各開口部91、92より露出する部分の各ラインおよび各チューブが、自動的に対応する各流路開閉手段51、52に装着される。これにより血液成分採取回路2の装着が容易であるとともに、血漿採取（血液成分採取）の準備も迅速に行える。

【0042】また、血液成分採取装置1には、カセットハウジング装着部に近接して2つの送液ポンプ11、12が設けられている。このため、カセットハウジング33より露出する各ポンプチューブ21g、23aの各送液ポンプ11、12への装着も容易である。

【0043】血液成分採取回路2に設けられている遠心分離器20は、通常、遠心ボウルと呼ばれており、遠心力により血液を分離する。遠心分離器20としては、図2に示すものが使用される。

【0044】第1の流路開閉手段51は、ポンプチューブ21gより採血針側において第1のライン21の流路の途中を開閉するために設けられている。

【0045】第2の流路開閉手段52は、第2のライン22の流路の途中を開閉するために設けられている。

【0046】第1の流路開閉手段51および第2の流路開閉手段52は、ラインもしくはチューブの挿入部を備え、挿入部には、例えば、ソレノイド、電動モーター、シリンダ（油圧または空気圧）等の駆動源で作動するクランプを有する。具体的には、ソレノイドで作動する電磁クランプが好適である。

【0047】遠心分離器駆動装置10は、図2に示すように、遠心分離器20を収納するハウジング151と、脚部152と、駆動源であるモータ153と、遠心分離器20を保持する円盤状の固定台155とで構成されている。ハウジング151は、脚部152の上部に載置、固定されている。

【0048】また、ハウジング151の下面には、ボル



ト156によりスペーサー157を介してモータ153が固定されている。モータ153の回転軸154の先端部には、固定台155が回転軸154と同軸でかつ一体的に回転するように嵌入されており、固定台155の上部には、ローター142の底部が嵌合する凹部が形成されている。

【0049】また、遠心分離器20の上部145は、図示しない固定部材により、ハウジング151に固定されている。遠心分離器駆動装置10では、モータ153を駆動すると、固定台155およびそれに固定されたローター142が、あらかじめ設定された所定の遠心条件（例えば、回転数1000～6000rpm）で回転する。この遠心条件により、ローター142内の血液の分離パターン（例えば、分離する血液成分）を設定することができる。

【0050】なお、ローター142において、貯血空間146の容積は、例えば、100～350mL程度とされる。

【0051】また、ハウジング151の内壁には、遠心分離器20（貯血空間146）内で分離された血液成分の界面（例えば、血漿層131とバフィーコート層132との界面B、バフィーコート層132と赤血球層133との界面、血漿層と血球層の界面）の位置を光学的に検出する光学式センサ15が、取付部材158により設置、固定されている。

【0052】この光学式センサ15は、遠心分離器20の肩の部分に向けて光を照射する光源と、遠心ボウルから反射して戻ってくる光を受光する受光部で構成されている。つまり、LED（半導体レーザー等）のような発光素子と、フォトダイオードまたはCCDのような受光素子とが列状に配置され、発光素子から発せられた光の血液成分での反射光を受光素子により受光し、その受光量を光電変換するように構成されている。分離された血液成分（例えば、血漿層131とバフィーコート層132）により反射光の強度が異なるため、受光量が変化した受光素子に対応する位置が、界面Bの位置として検出される。

【0053】より具体的には、遠心分離器20の光が通過する位置が透明な液体（血漿や水）で充填されている時と、バフィーコート層132で充填されている時の、受光部での受光量の差から、バフィーコート層132が光通過部に到達したことが検知される。

【0054】バフィーコート層132を検出する位置は、光が遠心分離器（遠心ボウル）20内を通過する位置を変えることで調節され、通常は、光線通過位置を決めたら、そこで固定する。

【0055】重量センサ16は、血漿採取バッグ25内に採取された血漿の採取量を検出する検出手段を構成する。

【0056】濁度センサ14は、第2のライン22中を

流れる流体の濁度を検知するためのものであり、濁度に応じた電圧値を出力する。具体的には、濁度が高い時には低電圧値、濁度が低い時には高電圧値を出力する。

【0057】第1の気泡センサ17および第2の気泡センサ18は、それぞれ、第1のライン21内に空気が流れたことを検知するためのものである。

【0058】これらの濁度センサ14および各気泡センサ17、18としては、それぞれ、例えば、超音波センサ、光学式センサ、赤外線センサなどが使用できる。

【0059】第1のライン21の第1のポンプチューブ21gが装着される第1の送液ポンプ11ならびに第3のライン23の第2のポンプチューブ23aが装着される第2の送液ポンプ12としては、ローラーポンプなどの非血液接触型ポンプが好適である。

【0060】また、第1の送液ポンプ（血液ポンプ）11としては、いずれの方向にも血液を送ることができるものが使用される。具体的には、正回転と逆回転が可能なローラーポンプが用いられている。

【0061】制御部55は、例えば、マイクロコンピュータ等で構成されており、図1に示すように、遠心分離器駆動装置10、第1の送液ポンプ11、第2の送液ポンプ12、第1の流路開閉手段51、第2の流路開閉手段52、濁度センサ14、光学式センサ15、重量センサ16、第1の気泡センサ17および第2の気泡センサ18と、それぞれ、電気的に接続されている。

【0062】濁度センサ14、光学式センサ15、重量センサ16、第1の気泡センサ17および第2の気泡センサ18からの検出信号は、それぞれ、制御部55へ随時入力される。制御部55は、これらからの各検出信号に基づき、予め設定されたプログラムに従って、血液成分採取装置1の作動、すなわち、各送液ポンプ11、12の回転、停止、あるいは、回転方向（正転／逆転）を制御するとともに、必要に応じ、各流路開閉手段51、52の開閉および遠心分離器駆動装置10の作動を制御する。

【0063】また、この制御部55は、演算部551とメモリ552とを内蔵している。さらに、制御部55には、例えばキーボード等で構成された入力手段3と、例えば液晶ディスプレイ等で構成された表示手段4が、それぞれ電気的に接続されている。

【0064】このような制御部55は、ドナーから血液を採取し、その血液の成分（血液成分）のうち、血漿を採取するように血液成分採取装置1の作動を制御する。

【0065】具体的には、制御部55は、ドナーから採取された血液を遠心分離器20（貯血空間146）内に流入させ、遠心分離器20により分離された血漿を血漿採取バッグ25内に採取（移送）する血漿採取工程（血液成分採取工程）と、血液成分採取回路2内に残った血漿以外の血液成分（残りの血液成分）をドナーへ返還する血液成分返還工程とを有する血漿採取操作を行うよう

に、血液成分採取装置1の作動を制御する。

【0066】なお、本実施形態では、血漿採取工程において、血漿採取バッグ25内には、抗凝固剤が混入した血漿が採取され、重量センサ16では、この抗凝固剤が混入した血漿の重量が検出される。

【0067】以下の説明では、抗凝固剤が混入した血漿を「見かけの血漿」、その採取量を「見かけの血漿採取量」と言い、抗凝固剤を除いた血漿自体を「真の血漿」、その採取量を「真の血漿採取量」と言う。

【0068】また、制御部55は、必要に応じて、前記血漿採取操作を複数サイクル行なう。以下の説明では、各サイクルにおける血漿の採取量を「サイクル当たりの血漿採取量」と言う。

【0069】さらに、以下の説明では、目標とする血漿の採取量を、「目標血漿採取量」と言い、実際に採取さ

れた血漿の採取量を、「現在血漿採取量」と言う。

【0070】以下、血液成分採取装置1の使用法および作用について、図3を参照しつつ説明する。

【0071】なお、以下の説明では、血液成分採取装置1の所定の条件を、抗凝固剤を除いた血漿自体の目標とする採取量（真の目標血漿採取量）とする場合を一例として説明する。

【0072】まず、オペレーター（操作者）は、入力手段3を操作して、真の目標血漿採取量（表1参照）およびサイクル当たりの見かけの血漿採取量（表2参照）を入力する。これらのテーブルは、メモリー552に記憶される。なお、これらのテーブルは、予めメモリー552に記憶させておくこともできる。

【0073】

【表1】

表1

（真の目標血漿採取量D [mL]）

|         | 男性  | 女性  |
|---------|-----|-----|
| 40～44kg | —   | 300 |
| 45～49kg | 350 | 350 |
| 50～54kg | 400 | 400 |
| 55～59kg | 450 | 450 |
| 60～64kg | 500 | 500 |
| 65～69kg | 550 | 550 |
| 70kg～   | 600 | 600 |

【0074】

【表2】

表2

（サイクル当たりの見かけの血漿採取量A [mL]）

|         | 男性  | 女性  |
|---------|-----|-----|
| 40～44kg | —   | 120 |
| 45～49kg | 130 | 130 |
| 50～54kg | 140 | 140 |
| 55～59kg | 150 | 150 |
| 60～64kg | 160 | 160 |
| 65～69kg | 170 | 170 |
| 70kg～   | 180 | 180 |

【0075】また、オペレーターは、入力手段3を操作して、例えば、性別、体重、身長、年齢、ヘマトクリット値等のドナーに関する情報（以下、「ドナー情報」と言う。）、および、後述する抗凝固剤の採血血液に対する添加比率を入力する。

【0076】次に、オペレーターは、第3のライン23と採血針29とを抗凝固剤でプライミングし、その後、採血針29をドナーの血管に穿刺する。これにより、血漿の採取準備を完了する。

【0077】次に、オペレーターが図示しない採取開始スイッチをオンする。これにより、図3に示すプログラムが実行され、血漿の採取が行われる。

【0078】（1） まず、血液成分採取装置1は、条件設定工程を行なう。この条件設定工程では、制御部55は、真の目標血漿採取量D [mL]を採取するのに必要なサイクル数E [回]、および、見かけの目標血漿採取量G [mL]を求める（図3のステップS101）。

【0079】（11） まず、制御部55は、サイクル当たりの真の血漿採取量B [mL]を求める。

【0080】具体的には、制御部55の演算部551は、ドナー情報（性別および体重）に基づき、メモリー552に記憶されているテーブル（表2）から、サイクル当たりの見かけの血漿採取量A [mL]を得、次いで、このAを、メモリー552に予め記憶されている下

記式 (I-2) に代入して、A 中の抗凝固剤混入量 C [mL] を求め、さらに、これらの A および C を下記式 (I-1) に代入して、サイクル当たりの真の血漿採取量 B [mL] を求める。

$$B = A - C \quad \dots \dots \dots \text{式 (I-1)}$$

$$C [\text{第1サイクル}] = -0.0003A^2 + 0.3A + 0.4$$

$$[\text{第2サイクル以降}] = 0.2A \quad \dots \dots \dots \text{式 (I-2)}$$

【0083】また、サイクル当たりの見かけの血漿採取量 A [mL] は、ドナーのヘマトクリット値 (Hct) に基づき、下記式 (I-0) から求めることもできる。

【0084】なお、この式 (I-0) は、第1サイクル

$$A [\text{第1サイクル}] = 670 - 10 \times \text{Hct}$$

$$[\text{第2サイクル以降}] = 530 - 8 \times \text{Hct} \quad \dots \dots \dots \text{式 (I-0)}$$

【0086】(12) 次いで、制御部 55 は、真の目標血漿採取量 D [mL] を得るのに必要となるサイクル数 E [回] を求める。すなわち、制御部 55 は、真の目標血漿採取量 D [mL] に基づき、血漿採取操作 (血液成分採取操作) のサイクル数 E [回] を決定する。

【0087】具体的には、制御部 55 の演算部 551 は、ドナー情報 (性別および体重) に基づき、メモリー 552 に記憶されているテーブル (表 1) から、真の目

$$D \leq B [\text{第1サイクル}] + B [\text{第2サイクル}] + \dots$$

$$+ \dots + B [\text{第Eサイクル}] \quad \dots \dots \text{式 (II-1)}$$

【0089】なお、制御部 55 の演算部 551 は、真の目標血漿採取量 D [mL] を、ドナー情報 (性別、体重および身長) に基づき、メモリー 552 に予め記憶されている下記式 (II-0) から求めることもできる。な

$$D [\text{男性}] = (0.168 \text{Hi}^3 + 0.050 \text{Wt} + 0.444) \times 120$$

$$[\text{女性}] = (0.250 \text{Hi}^3 + 0.063 \text{Wt} + 0.662) \times 120$$

$$\dots \dots \dots \text{式 (II-0)}$$

Hi : 身長 [m]、Wt : 体重 [kg]

【0091】(13) 次いで、制御部 55 は、最終サイクルでのサイクル当たりの真の血漿採取量 F [mL] を求める。

【0092】具体的には、制御部 55 の演算部 551

$$F = D - \Sigma B \quad \dots \dots \dots \text{式 (III)}$$

$\Sigma B$  : B [第1サイクル] から B [第 (E-1) サイクル] までの和

【0094】(14) 次いで、制御部 55 は、見かけの目標血漿採取量 G [mL] を求める。

【0095】具体的には、制御部 55 の演算部 551 は、サイクル当たりの真の血漿採取量 B [mL]、A 中

$$G = \Sigma (B + C) + (F + C [\text{第Eサイクル}]) \quad \dots \dots \text{式 (IV)}$$

$$\Sigma (B + C) : (B + C) [\text{第1サイクル}] \text{ から } (B + C) [\text{第 (E-1) サイクル}] \text{ までの和}$$

【0097】なお、この条件設定工程で得られた真の目標血漿採取量 D [mL] は、表示手段 4 に表示される。これにより、オペレーターが設定条件を視認することができ、便利である。

【0098】また、サイクル当たりの見かけの血漿採取

【0081】なお、この式 (I-2) は、第1サイクルと第2サイクル以降とは、適用する式が異なり、また、この式 (I-2) は、適宜変更することもできる。

【0082】

と第2サイクル以降とは、適用する式が異なり、また、この式 (I-0) は、適宜変更することもできる。

【0085】

目標血漿採取量 D [mL] を得、次いで、サイクル当たりの真の血漿採取量 B [mL] の合計が、真の目標血漿採取量 D [mL] に最も近づき、かつ、真の目標血漿採取量 D [mL] を超える最も少ないサイクル数 E [回] を求める。すなわち、下記式 (II-1) を満たすようなサイクル数 E [回] を求める。

【0088】

お、この式 (II-0) は、性別により適用する式が異なる。

【0090】

は、真の目標血漿採取量 D [mL] およびサイクル当たりの真の血漿採取量 B [mL] を、下記式 (III) に代入して、最終サイクル (第 E サイクル) でのサイクル当たりの真の血漿採取量 F [mL] を求める。

【0093】

の抗凝固剤混入量 C [mL] および最終サイクル (第 E サイクル) でのサイクル当たりの真の血漿採取量 F [mL] を、下記式 (IV) に代入して、見かけの目標血漿採取量 G [mL] を求める。

【0096】

量 A [mL]、サイクル当たりの真の血漿採取量 B [mL]、あるいは、見かけの目標血漿採取量 G [mL] を、必要に応じて、表示手段 4 に表示するようにしてもよい。

【0099】(2) 次に、血液成分採取装置 1 は、血

漿採取工程を行なう。この血漿採取工程では、ローター142の貯血空間146内に、採血針（採血手段）29によりドナーから採血され、抗凝固剤供給手段により抗凝固剤が混入された血液を導入し、かかる血液を遠心分離することにより分離された抗凝固剤が混入した血漿（見かけの血漿）を血漿採取バッグ25内に採取する。

【0100】（21） 制御部55は、ドナーから見かけの血漿の採取を行なう（図3のステップS102）。

【0101】具体的には、制御部55は、第1の流路開閉手段51および第2の流路開閉手段52を開放し、第1の送液ポンプ11を所定の回転速度（好ましくは250mL/min以下程度、より好ましくは40～150mL/min程度、例えば、60mL/min）で作動（正転）するよう制御する。

【0102】また、この採血と同時に、制御部55の制御により、第2の送液ポンプ12を作動して、第3のライン23を介して、例えばACD-A液のような抗凝固剤を供給し、この抗凝固剤を採血血液中に混入させる。

【0103】このとき、第2の送液ポンプ12の回転速度は、制御部55により、オペレーターにより入力された所定比率（添加比率）で抗凝固剤が添加されるように制御される。

【0104】なお、この所定比率としては、好ましくは1/20～1/6程度とされ、例えば1/12とされる。

【0105】これにより、血液（抗凝固剤加血液）は、第1のライン21を介して移送され、遠心分離器20の流入口143より管体141を経てローター142の貯血空間146内に導入される。

【0106】このとき、遠心分離器20内の空気（減菌空気）は、第2のライン22を介して血漿採取バッグ25内に送り込まれる。

【0107】また、前記採血と同時にまたはこれと前後して、制御部55は、遠心分離器駆動装置10を作動し、ローター142を所定の回転数で回転するよう制御する。

【0108】このローター142の回転により、貯血空間146内に導入された血液は、内側から血漿層（PP層）131、バフィーコート層（BC層）132、赤血球層（CRC層）133の3層に分離される。

【0109】なお、ローター142の回転数としては、好ましくは3000～6000rpm程度、より好ましくは4000～5700rpm程度とされる。

【0110】さらに、前記採血および前記抗凝固剤の供給を継続し、貯血空間146の容量を越える血液（約270mL）が貯血空間146内に導入されると、貯血空間146内は完全に血液により満たされ、遠心分離器20の流出口144から見かけの血漿がオーバーフローす

$$W = (U - V) / 1.03 \dots \dots \dots \text{式}(V-1)$$

【0123】2： 次いで、制御部55の演算部551

る。

【0111】これにより、第2のライン22を介して、見かけの血漿を血漿採取バッグ25内に導入、採取する。

【0112】なお、血漿採取バッグ25は、その重量が重量センサ16により計測されており、計測された重量信号は制御部55に入力される。

【0113】（22） 次いで、制御部55は、血漿採取バッグ25内にサイクル当たりの見かけの血漿採取量A[mL]が採取されたか否かを判断する（図3のステップS103）。

【0114】具体的には、制御部55は、重量センサ16からの情報（重量信号）に基づき、後述する手順に従って、そのサイクルが開始されてから採取された見かけの血漿採取量W[mL]を求め、かかるW[mL]がA[mL]に到達したか否かを判断する。

【0115】なお、このサイクル当たりの見かけの血漿採取量A[mL]は、前記条件設定工程で得られたものである。

【0116】このステップS103において、血漿採取バッグ25内にサイクル当たりの見かけの血漿採取量A[mL]が採取されていない場合には、制御部55は、ステップS102に戻り、再度、ステップS102以降を繰り返す。

【0117】また、ステップS103において、血漿採取バッグ25内にサイクル当たりの見かけの血漿採取量A[mL]が採取された場合には、制御部55は、血漿採取工程を終了する。

【0118】具体的には、制御部55は、ローター142の回転および第1の送液ポンプ11の作動を停止するよう制御し、この血液成分採取工程を終了する。

【0119】この血漿採取工程では、制御部55の演算部551は、そのサイクルが開始されてから採取された見かけの血漿採取量W[mL]、および、真の現在血漿採取量Z[mL]を、血漿採取バッグ25の重量が1g増加する毎に、次の手順に従って算出する。以下に、その手順を示す。

【0120】1： まず、制御部55の演算部551は、重量センサ16からの重量信号に基づいて、実際に採取された見かけの血漿の重量（見かけの現在血漿重量）U[g]を得、次いで、このU、前サイクルまでに採取された見かけの血漿の重量V[g]を、下記式（V-1）に代入して、そのサイクルが開始されてから採取された見かけの血漿採取量W[mL]を求める。

【0121】なお、この式（V-1）において、定数「1.03」は、見かけの血漿の比重[g/mL]を表す。

【0122】

は、そのサイクルが開始されてから採取された見かけの

血漿採取量 $W$  [mL] を、下記式 (V-2) に代入して、 $W$  中の抗凝固剤混入量 $X$  [mL] を求める。

【0124】なお、この式 (V-2) は、第1サイクル

$$X [\text{第1サイクル}] = -0.0003W^2 + 0.3W + 0.4$$

$$[\text{第2サイクル以降}] = 0.2W \quad \dots \dots \text{式 (V-2)}$$

【0126】3: 次いで、制御部55の演算部551は、前サイクルまでに採取された真の血漿採取量 $Y$  [mL] と、そのサイクルが開始されてから採取された見かけの血漿採取量 $W$  [mL] および $W$  中の抗凝固剤混入量

$$Z = Y + (W - X) \quad \dots \dots \text{式 (V-3)}$$

【0128】なお、この真の現在血漿採取量 $Z$  [mL] は、表示手段4に表示される。これにより、オペレーターが真の現在血漿採取量 $Z$  [mL] をリアルタイムで視認することができ、便利である。

【0129】また、表示手段4には、 $W$  中の抗凝固剤混入量 $X$  [mL] 等を表示するようにしてもよいし、さらに、制御部55の演算部551において、ドナーに返還される抗凝固剤の量を求め、かかる量を表示するようにしてもよい。

【0130】(3) 次に、血液成分採取装置1は、血漿採取操作を終了するか否かを判断する。

【0131】具体的には、制御部55は、①真の現在血漿採取量 $Z$  [mL] が真の目標血漿採取量 $D$  [mL] の $M$  [%] に到達したか否か、あるいは、②血漿採取操作をサイクル数 $E$  [回] 行なったか否かを判断する (図3のステップS104)。

【0132】なお、①における $M$ としては、好ましくは70~100%程度、より好ましくは80~100%とされる。

【0133】また、血漿採取操作の終了条件①または②は、オペレーターが適宜選択することができる。

【0134】このステップS104において、①または②の条件を満足すると判断した場合には、制御部55は、終了工程に移行する。なお、この終了工程については、後に説明する。

【0135】また、ステップS104において、①または②の条件を満足していないと判断した場合には、制御部55は、血液成分返還工程に移行する。

【0136】(4) 次に、血液成分採取装置1は、血液成分返還工程を行なう。この血液成分採取工程では、血液成分採取回路2 (主に、ローター142の貯血空間146) 内に残った血液成分 (残りの血液成分) をドナーへ返還する。

【0137】(4.1) まず、制御部55は、ドナーへ残りの血液成分の返還を行なう (図3のステップS105)。

【0138】具体的には、制御部55は、第1の流路開閉手段51および第2の流路開閉手段52を開放した状態を維持しつつ、第1の送液ポンプ11を所定の回転速度 (好ましくは、30~100 mL/min程度、例えば

と第2サイクル以降とでは、適用する式が異なり、また、この式 (V-2) は、適宜変更することもできる。

【0125】

$X$  [mL] を、下記式 (V-3) に代入して、真の現在血漿採取量 $Z$  [mL] を求める。

【0127】

45 mL/min) で作動 (逆転) するよう制御する。

【0139】これにより、ローター142の貯血空間146内の残りの血液成分は、遠心分離器側第1ライン21b、採血針側第1ライン21aおよび採血針29を介して、ドナーへ返還される。

【0140】(4.2) 次いで、制御部55は、第1の気泡センサ17が空気を検出したか否かを判断する (図3のステップS106)。

【0141】このステップS106において、第1の気泡センサ17が空気を検出していない場合には、制御部55は、ステップS105に戻り、再度、ステップS105以降を繰り返す。

【0142】また、ステップS106において、第1の気泡センサ17が空気を検出した場合には、制御部55は、次サイクルの血漿採取操作の血漿採取工程に移行する。

【0143】具体的には、制御部55は、第1の気泡センサ17が第2のライン22の流路内の空気 (気泡) の存在を検出すると、第1の送液ポンプ11を所定の回転速度に低下 (変更) するように制御する。

【0144】そして、制御部55は、第1の送液ポンプ11を前記所定の回転速度で所定の回数、回転させた後、第1の流路開閉手段51および第2の流路開閉手段52を閉塞させ、かつ、第1の送液ポンプ11を停止するよう制御する。

【0145】なお、この第1の送液ポンプ11の回転速度としては、好ましくは1~80 mL/min程度、より好ましくは20~50 mL/min程度とされる。

【0146】また、第1の送液ポンプ11を所定の回転速度で回転させる回数としては、好ましくは1~15回程度、より好ましくは5~12回程度とされる。

【0147】これにより、血液成分採取回路2内の残りの血液成分が、ほぼ全てドナーへ返還される。

【0148】(5) また、前記ステップS104において、①または②の条件を満足すると判断した場合には、制御部55は、終了工程を行なう。この終了工程では、血液成分採取回路2 (主に、ローター142の貯血空間146) 内に残った血液成分 (残りの血液成分) をドナーへ返還する。

【0149】すなわち、この終了工程 (図3のステップ

S107、108)では、前記血液成分返還工程(ステップS105、106)と同様の工程を行なう。

【0150】これにより、血液成分採取回路2内の残りの血液成分が、ほぼ全てドナーへ返還され、血漿採取操作を終了する。

【0151】このような血液成分採取装置1では、ドナーの性別、体重および身長の中の少なくとも1つを含むドナー情報に基づき、血液成分採取装置1の所定の条件を設定するので、ドナーに応じた適正な血漿採取操作を行なうことができる。

【0152】また、血液成分採取装置1では、この所定の条件として、目標血漿採取量を設定するように構成されているので、ドナーに応じた適正な量の血漿を採取することができる。

【0153】特に、本実施形態の血液成分採取装置1では、抗凝固剤を除いた血漿自体の目標血漿採取量(真の目標血漿採取量)を設定するように構成され、さらに、前述したような終了条件①または②に基づき、血漿採取操作を終了するように構成されているので、ドナーからの血漿採取量が許容血漿採取量(通常、体内血液量の12%以下)から逸脱してしまうのを好適に防止し、安全性の向上を図ることができ、また、ドナーからの採取が許容される量に近い量の血漿(真の血漿)を採取することができるので、経済面での向上も図ることができる。

【0154】以上、本発明の血液成分採取装置を図示の実施形態に基づいて説明したが、本発明は、これらに限定されるものではなく、各部の構成は、同様の機能を有する任意の構成のものに置換することができる。

【0155】また、供血者に関する情報としては、前述したもの他、例えば、年齢、人種、国籍、血液型、病歴等の情報を適宜、追加することもできる。

【0156】また、供血者に関する情報に基づき、設定される血液成分採取装置の条件としては、実施形態で示したものに限定されないことは、言うまでもない。

【0157】また、本発明では、血液成分採取装置は、血漿を採取する血漿採取装置に適用する場合に限らず、血小板や、血小板および血漿を採取する血液成分採取装置にも適応することができる。

【0158】

【発明の効果】以上説明したように、本発明の血液成分採取装置によれば、供血者に関する情報に基づき、血液成分採取装置の所定の条件を設定するので、供血者に応じた適正な血液成分採取操作を行なうことができる。

【0159】また、この所定の条件として、所定の血液成分の目標とする採取量を設定した場合には、供血者に応じた適性な量の所定の血液成分を採取することができる。

【0160】特に、所定の条件を、抗凝固剤を除いた所定の血液成分自体の目標とする採取量とすることにより、供血者の体外血液循環量が許容体外循環量から逸脱

してしまうのを好適に防止し、安全性の向上を図ることができ、また、供血者からの採取が許容される量に近い量の血液成分を採取することができるので、経済面での向上も図ることができる。

【図面の簡単な説明】

【図1】本発明の血液成分採取装置の構成例を示す平面図である。

【図2】本発明の血液成分採取装置に使用される遠心分離器駆動装置の断面を示す図である。

【図3】血液成分採取工程の際の制御部の制御動作を示すフローチャートである。

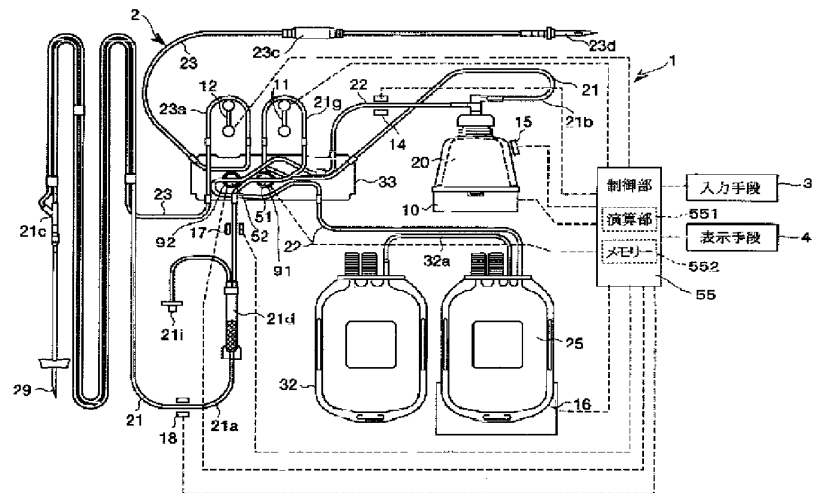
【符号の説明】

|     |           |
|-----|-----------|
| 1   | 血液成分採取装置  |
| 2   | 血液成分採取回路  |
| 10  | 遠心分離器駆動装置 |
| 11  | 第1の送液ポンプ  |
| 12  | 第2の送液ポンプ  |
| 14  | 濁度センサ     |
| 15  | 光学式センサ    |
| 16  | 重量センサ     |
| 17  | 第1の気泡センサ  |
| 18  | 第2の気泡センサ  |
| 20  | 遠心分離器     |
| 21  | 第1のライン    |
| 22  | 第2のライン    |
| 23  | 第3のライン    |
| 25  | 血漿採取バッグ   |
| 29  | 採血針       |
| 32  | サブバッグ     |
| 33  | カセットハウジング |
| 51  | 第1の流路開閉手段 |
| 52  | 第2の流路開閉手段 |
| 55  | 制御部       |
| 551 | 演算部       |
| 552 | メモリー      |
| 91  | 第1の開口部    |
| 92  | 第2の開口部    |
| 131 | 血漿層       |
| 132 | パフィーコート層  |
| 133 | 赤血球層      |
| 142 | ローター      |
| 143 | 流入口       |
| 144 | 流出口       |
| 145 | 上部        |
| 146 | 貯血空間      |
| 151 | ハウジング     |
| 152 | 脚部        |
| 153 | モータ       |
| 154 | 回転軸       |
| 155 | 固定台       |

( 1 ) 102-282352 ( P 2002-282352A )

|     |            |     |            |
|-----|------------|-----|------------|
| 156 | ボルト        | 21g | 第1のポンプチューブ |
| 157 | スペーサー      | 21i | フィルター      |
| 158 | 取付部材       | 23a | 第2のポンプチューブ |
| 21a | 採血針側第1ライン  | 23c | 気泡除去用チャンバー |
| 21b | 遠心分離器第1ライン | 23d | 抗凝固剤溶器接続用針 |
| 21c | 接続用分岐コネクタ  | 32a | チューブ       |
| 21d | チャンバー      |     |            |

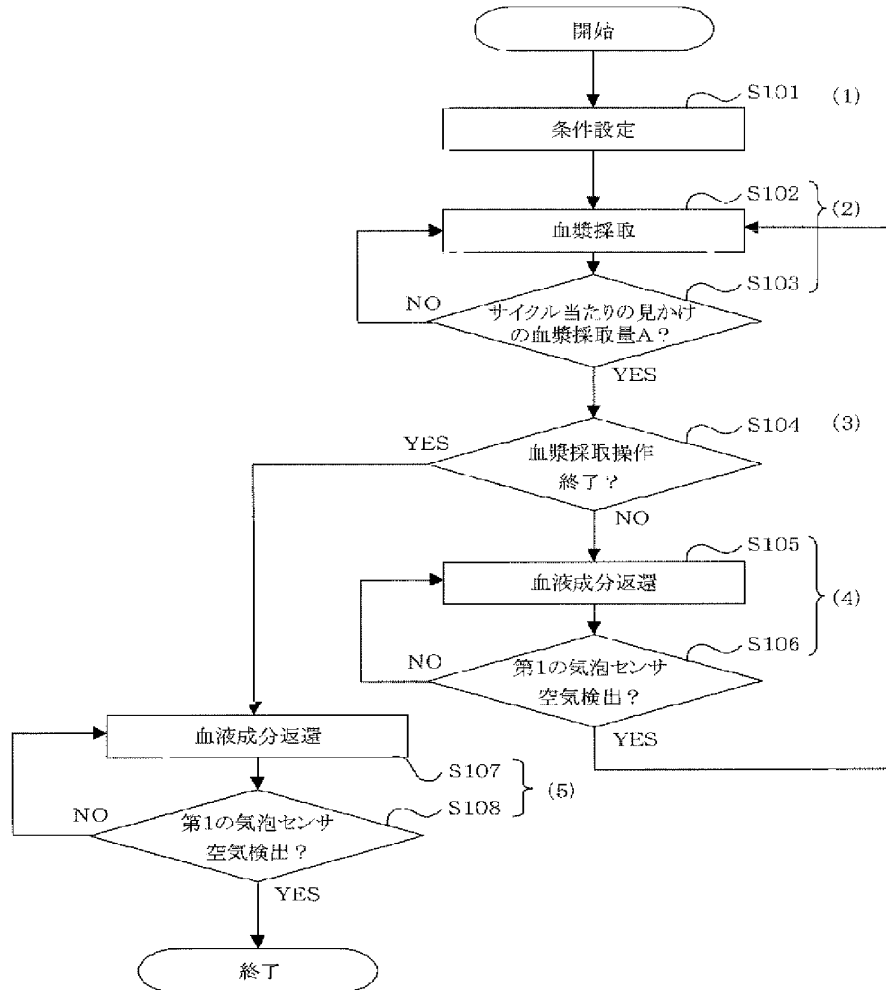
【図1】







【図3】



Doc code: IDS

Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)

Approved for use through 11/30/2020. OMB 0651-0031

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| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | N/A              |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

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|                                                                                                            | 1       | 5681273                              |                            | 1997-10-28             | Brown                                           |                                                                        |                                                                        |                |
|                                                                                                            | 2       | 8454548                              | B2                         | 2013-06-04             | Ohashi et al.                                   |                                                                        |                                                                        |                |
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|                                                                                                            | 1       | 2252788                              | RU                         | C1                     | 2005-05-27                                      | Mepotex                                                                |                                                                        | ×              |
|                                                                                                            | 2       | 2601449                              | RU                         | C2                     | 2016-11-10                                      | Fenval Ink                                                             |                                                                        | ☒              |

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|-----------------------------------------------------------------------------------------------------|------------------------|------------------|
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | N/A              |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

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| Examiner Signature                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |         | Date Considered                                                                                                                                                                                                                                                 |                |
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| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | N/A              |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

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Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

**OR**

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

### SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

|            |                                       |                     |            |
|------------|---------------------------------------|---------------------|------------|
| Signature  | /Jonathan C. Lovely, Reg. No. 60,821/ | Date (YYYY-MM-DD)   | 2021-11-18 |
| Name/Print | Jonathan C. Lovely                    | Registration Number | 60,821     |

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

## Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: November 18, 2021  
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104

Docket No.: 130670-80104  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Utility Application of:  
Michael Ragusa

Application No.: 17/205,400

Confirmation No.: 4686

Filed: March 18, 2021

Art Unit: N/A

For: SYSTEM AND METHOD FOR COLLECTING  
PLASMA

Examiner: Not Yet Assigned

**INFORMATION DISCLOSURE STATEMENT (IDS)**

MS Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR 1.97, Applicant hereby makes of record the following additional documents. A PTO Form SB/08 and a full copy of each of the documents required under 37 CFR 1.98(a)(2) accompany this statement.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 C.F.R. § 1.97(b)(3)).

In accordance with 37 C.F.R. § 1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patents. Applicant submits herewith copies of foreign patents in accordance with 37 C.F.R. § 1.98(a)(2).

The Examiner is advised that the following applications contain subject matter that may be related to the present application:

| <b>U.S. Application</b> | <b>Filing Date</b> | <b>Publication No. / Patent No.</b> | <b>Status</b> | <b>Atty. Docket No.</b> |
|-------------------------|--------------------|-------------------------------------|---------------|-------------------------|
| 15/608,183              | May 30, 2017       | 10,758,652                          | Issued        | 130670-08002            |
| 16/866,078              | May 4, 2020        | 10,980,926                          | Issued        | 130670-08005            |
| 17/205,374              | March 18, 2021     | 2021-0205509                        | Published     | 130670-08006            |
| 15/793,339              | October 25, 2017   | 10,792,416                          | Issued        | 130670-80102            |
| 16/931,333              | July 16, 2020      | 10,980,934                          | Issued        | 130670-80103            |

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed references.

Applicant believes no fee is due with this response.

Dated: November 18, 2021

Respectfully submitted,  
Electronic signature: /Jonathan C. Lovely, Reg.  
No. 60,821/  
Jonathan C. Lovely  
Registration No.: 60,821  
MCCARTER & ENGLISH, LLP  
265 Franklin Street  
Boston, Massachusetts 02110  
(617) 449-6556  
(617) 607-9200 (Fax)  
Attorney/Agent For Applicant

| Electronic Acknowledgement Receipt   |                                         |
|--------------------------------------|-----------------------------------------|
| EFS ID:                              | 44313564                                |
| Application Number:                  | 17205400                                |
| International Application Number:    |                                         |
| Confirmation Number:                 | 4686                                    |
| Title of Invention:                  | SYSTEM AND METHOD FOR COLLECTING PLASMA |
| First Named Inventor/Applicant Name: | Michael Ragusa                          |
| Customer Number:                     | 86738                                   |
| Filer:                               | Jonathan Lovely                         |
| Filer Authorized By:                 |                                         |
| Attorney Docket Number:              | 130670-80104                            |
| Receipt Date:                        | 18-NOV-2021                             |
| Filing Date:                         | 18-MAR-2021                             |
| Time Stamp:                          | 11:53:56                                |
| Application Type:                    | Utility under 35 USC 111(a)             |

**Payment information:**

|                        |    |
|------------------------|----|
| Submitted with Payment | no |
|------------------------|----|

**File Listing:**

| Document Number | Document Description | File Name                          | File Size(Bytes)/<br>Message Digest      | Multi Part /.zip | Pages (if appl.) |
|-----------------|----------------------|------------------------------------|------------------------------------------|------------------|------------------|
| 1               | Foreign Reference    | 130670-08006_-<br>_RU2252788C1.pdf | 422749                                   | no               | 8                |
|                 |                      |                                    | 3640de119a28c833667e0871c7c0ff792e2f799e |                  |                  |

**Warnings:**



|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                    |                                                                 |                                          |    |    |
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| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                    |                                                                 |                                          |    |    |
| 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Foreign Reference                                  | 135975-80102_-RU2601449C2.pdf                                   | 3861185                                  | no | 72 |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                    |                                                                 | bbc25aa687bdf8db3cf28ebb3f777b6c2a83dc97 |    |    |
| <b>Warnings:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                    |                                                                 |                                          |    |    |
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                    |                                                                 |                                          |    |    |
| 3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Information Disclosure Statement (IDS) Form (SB08) | 130670-80104_-Information_Disclosure_Statement_Fillable_PDF.pdf | 1034321                                  | no | 4  |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                    |                                                                 | 2901e85445d9f2a85cd32fac2eedecb43a1972b7 |    |    |
| <b>Warnings:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                    |                                                                 |                                          |    |    |
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                    |                                                                 |                                          |    |    |
| 4                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Transmittal Letter                                 | Information_Disclosure_Statement_IDS.pdf                        | 25166                                    | no | 2  |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                    |                                                                 | 2280d74d6e8226bd9d215e1c30030562e6e78d9c |    |    |
| <b>Warnings:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                    |                                                                 |                                          |    |    |
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                    |                                                                 |                                          |    |    |
| <b>Total Files Size (in bytes):</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                    |                                                                 | 5343421                                  |    |    |
| <p><b>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</b></p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b><br/> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b><br/> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b><br/> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p> |                                                    |                                                                 |                                          |    |    |



Espacenet

**Bibliographic data: RU2003131033 (A) — 2005-04-10****DEVICE FOR CARRYING OUT MEMBRANE-TYPE PLASMAPHERESIS IN SINGLE-NEEDLE MODE**

**Inventor(s):** Шишов Николай Михайлович (RU), ; Демина Надежда Алексеевна (RU), ; Зеленецкий Владимир Евгеньевич (RU), ; Крючкова Натали Александровна (RU), ; Федоров Федор Александрович (RU), ; Воинов Валерий Александрович (RU), ; Шишов Н.М. (RU), ; Демина Н.А. (RU), ; Зеленецкий В.Е. (RU), ; Крючкова Н.А. (RU), ; Федоров Ф.А. (RU), ; Воинов В.А. (RU)

**Applicant(s):** Общество с ограниченной ответственностью научно-технический центр "Мепотекс" (RU)

**Classification:** - international: **A61M1/16**; (IPC1-7): A61M1/16  
- cooperative:

**Application number:** RU20030131033 20031021

**Priority number(s):** RU20030131033 20031021

**Also published as:** RU2252788 (C1)

**Abstract of RU2252788 (C1)**

FIELD: medical engineering. ^ SUBSTANCE: device has line for taking blood and returning erythrocytic mass with air trap, line for supplying anticoagulant and hemodilution agent and forceps. Dosing member is mounted on anticoagulant line being chamber manufactured from plastic film-like material having an opening on one side for anticoagulant to be supplied and another opening for discharging it. Pump segment is set on line collecting blood as a flexible tube having an opening for supplying blood and another opening for delivering the blood to plasma filter connected to pressure control line having valve filter mounted thereon. Unit for supplying drug and discharging air is mounted on the air trap. It is manufactured as a tube with clamp. ^ EFFECT: enhanced effectiveness in applying continuous and safe plasmapheresis. ^ 1 dwg





ФЕДЕРАЛЬНАЯ СЛУЖБА  
 ПО ИНТЕЛЛЕКТУАЛЬНОЙ СОБСТВЕННОСТИ,  
 ПАТЕНТАМ И ТОВАРНЫМ ЗНАКАМ

(12) ОПИСАНИЕ ИЗОБРЕТЕНИЯ К ПАТЕНТУ

(21), (22) Заявка: 2003131033/14, 21.10.2003

(24) Дата начала действия патента: 21.10.2003

(45) Опубликовано: 27.05.2005 Бюл. № 15

(56) Список документов, цитированных в отчете о поиске: RU 2113863 C1, 27.06.1998. RU 2033188 C1, 20.04.1995. RU 2153389 C1, 27.07.2000. SU 685294 A, 15.09.1979. SU 487642 A, 15.10.1975.

Адрес для переписки:

140080, Московская обл., г. Лыткарино,  
 промзона Тураево, НИИП, АО "Интероко"

(72) Автор(ы):

Шишов Н.М. (RU),  
 Демина Н.А. (RU),  
 Зеленецкий В.Е. (RU),  
 Крючкова Н.А. (RU),  
 Федоров Ф.А. (RU),  
 Воинов В.А. (RU)

(73) Патентообладатель(ли):

Общество с ограниченной ответственностью  
 научно-технический центр "Мепотекс" (RU)

(54) УСТРОЙСТВО ДЛЯ ПРОВЕДЕНИЯ МЕМБРАННОГО ПЛАЗМАФЕРЕЗА ПО ОДНОИГОЛЬНОЙ СХЕМЕ

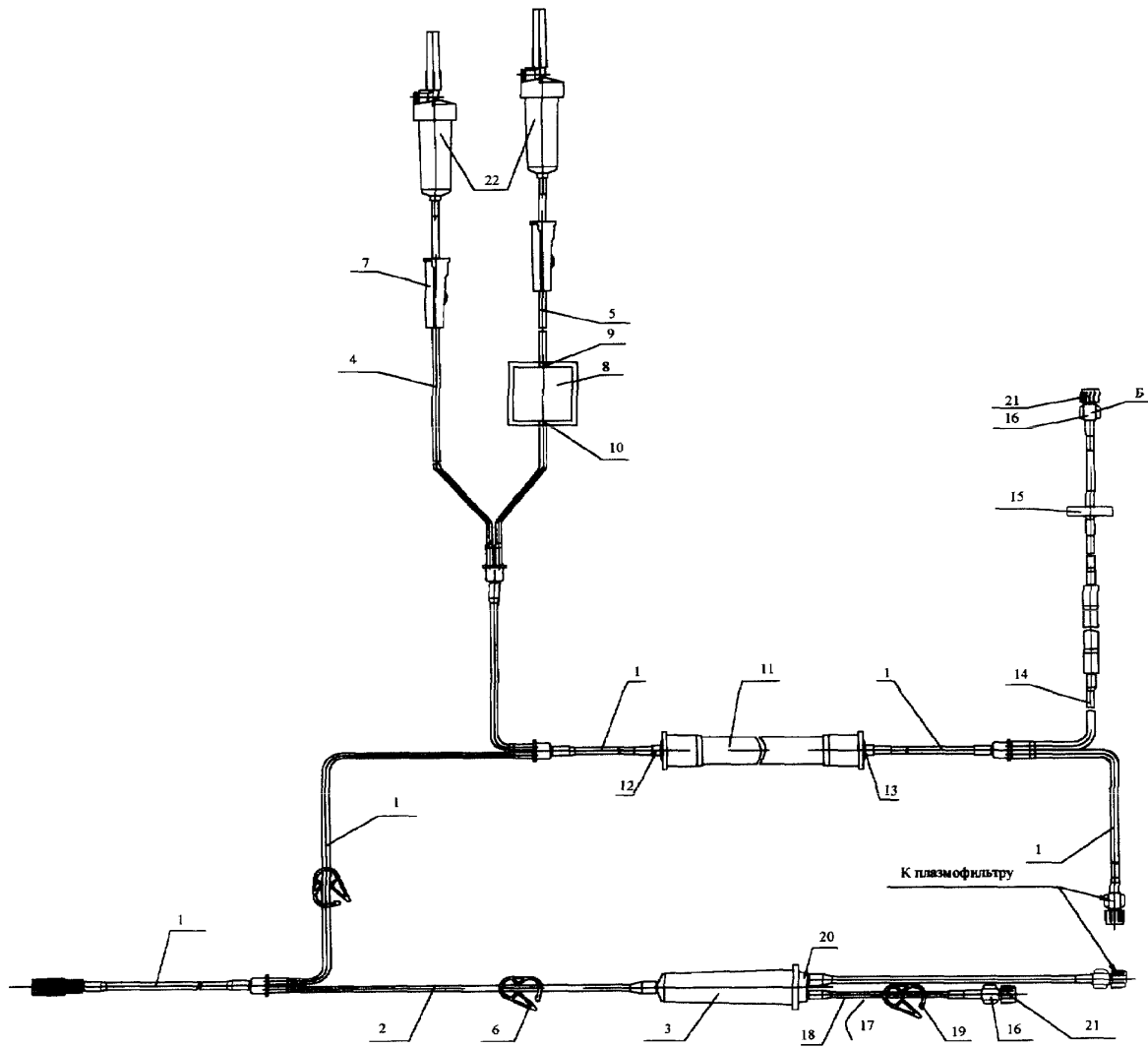
(57) Реферат:

Изобретение относится к медицинским изделиям и может быть использовано для лечебного и донорского плазмафереза, т.е. разделения крови на эрмассу и плазму, отвод плазмы, возврат эрмассы пациенту и введения плазмазамещающих растворов и антикоагулянта. Устройство включает магистраль забора крови и возврата эрмассы с ловушкой воздуха, магистрали для подачи гемодилютанта и антикоагулянта и зажимы. На магистрали для подачи антикоагулянта установлен дозирующий элемент в виде камеры, выполненной из пленочного пластичного

материала и имеющей с одной стороны отверстие для входа антикоагулянта, а с другой - отверстие для его выхода. На магистрали забора крови установлен насосный сегмент в виде трубки, выполненный из эластичного материала и имеющий отверстие для входа крови, отверстие для подачи крови к плазмафильтру, соединенное с магистралью контроля давления с расположенным на ней фильтром - клапаном. На ловушке воздуха установлен узел подачи лекарств и отвода воздуха, выполненный в виде трубки с зажимом. Изобретение позволит осуществить непрерывный и безопасный лечебный плазмаферез. 1 ил.

RU 2 252 788 C1

RU 2 252 788 C1



RUSSIAN FEDERATION



FEDERAL SERVICE  
FOR INTELLECTUAL PROPERTY,  
PATENTS AND TRADEMARKS

(19) **RU** (11) **2 252 788** (13) **C1**  
(51) Int. Cl.<sup>7</sup> **A 61 M 1/16**

(12) **ABSTRACT OF INVENTION**

(21), (22) Application: 2003131033/14, 21.10.2003

(24) Effective date for property rights: 21.10.2003

(45) Date of publication: 27.05.2005 Bull. 15

Mail address:

140080, Moskovskaja obl., g. Lytkarino,  
promzona Turaevo, NIIP, AO "Interoko"

(72) Inventor(s):

Shishov N.M. (RU),  
Demina N.A. (RU),  
Zelenetskij V.E. (RU),  
Krjuchkova N.A. (RU),  
Fedorov F.A. (RU),  
Voinov V.A. (RU)

(73) Proprietor(s):

Obshchestvo s ogranichennoj  
otvetstvennost'ju nauchno-tehnicheskij  
tsentr "Mepoteks" (RU)

(54) **DEVICE FOR CARRYING OUT MEMBRANE-TYPE PLASMAPHERESIS IN SINGLE-NEEDLE MODE**

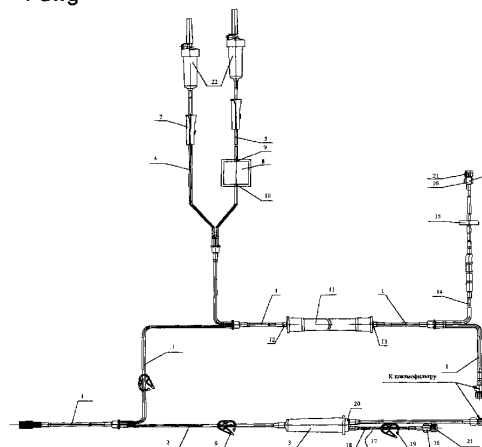
(57) Abstract:

FIELD: medical engineering.

SUBSTANCE: device has line for taking blood and returning erythrocytic mass with air trap, line for supplying anticoagulant and hemodilution agent and forceps. Dosing member is mounted on anticoagulant line being chamber manufactured from plastic film-like material having an opening on one side for anticoagulant to be supplied and another opening for discharging it. Pump segment is set on line collecting blood as a flexible tube having an opening for supplying blood and another opening for delivering the blood to plasma filter connected to pressure control line having valve filter mounted thereon. Unit for supplying drug and discharging air is mounted on the air trap. It is manufactured as a tube with clamp.

EFFECT: enhanced effectiveness in applying continuous and safe plasmapheresis.

1 dwg



Предлагаемое устройство для проведения мембранного плазмафереза по одноигольной схеме относится к медицинским изделиям и может быть использовано для лечебного и донорского мембранного плазмафереза, т.е. разделения крови на эрмассу и плазму, отвод плазмы, возврат эрмассы пациенту и введение плазмозамещающих растворов и  
 5 антикоагулянта. Плазмаферез признан наиболее эффективным методом, обеспечивающим радикальное удаление токсинов из организма вместе с плазмой.

Известно устройство для отделения плазмы под действием силы тяжести, включающее магистраль забора крови, мембранный плазмофильтр, накопительную емкость, соединенную с плазмофильтром второй магистралью, емкость для плазмы, соединенную с  
 10 плазмофильтром магистралью плазмы, емкость для гемодиллюанта с магистралью и средство ввода антикоагулянта, подсоединенное к магистрали забора крови. Емкость для гемодиллюанта подсоединена магистралью непосредственно к накопительной емкости [1].

Недостатком известного устройства является отсутствие возможности дозированной подачи антикоагулянта, что ведет к серьезным осложнениям при плазмаферезе, т.к. при  
 15 малом количестве антикоагулянта возможно тромбирование плазмофильтра, а при избыточном количестве - возможность противотока потоку отбираемой крови. Кроме того, использование этого устройства для лечебного плазмафереза затруднительно из-за осуществления возврата эрмассы пациенту только один раз. Конструкция устройства не обеспечивает устойчивого режима отбора крови, особенно при спадании вены.

20 Наиболее близким по технической сущности к предлагаемому устройству является устройство для осуществления мембранного плазмафереза по одноигольной схеме [2].

Известное устройство включает средство для отбора крови, мембранный плазмофильтр, накопительную емкость в виде шприца, емкости для гемодиллюанта и сбора плазмы, магистрали с зажимами и капельницами, средство ввода антикоагулянта и средство  
 25 контроля давления.

Недостатком этой конструкции устройства является отсутствие возможности непрерывной дозированной подачи антикоагулянта синхронно с забором крови при проведении донорского и лечебного плазмафереза, отсутствие защиты средства контроля давления от возможности заброса в него крови при увеличении давления в магистрали  
 30 забора крови. Кроме того, конструкция устройства не позволяет медперсоналу в процессе проведения плазмафереза регулировать высоту заполнения кровью ловушки воздуха и вводить дополнительно необходимые для пациента лекарства при возврате эрмассы, что создает неудобства в работе медперсонала и не обеспечивает безопасность пациента при проведении плазмафереза.

35 Цель изобретения - обеспечение непрерывной дозированной подачи антикоагулянта синхронно с забором крови при проведении донорского и лечебного плазмафереза, а также обеспечение безопасности пациента, надежности работы устройства и удобства в работе при проведении плазмафереза.

Для достижения поставленной цели предложено устройство для проведения  
 40 мембранного плазмафереза по одноигольной схеме, включающее магистраль забора крови и возврата эрмассы с ловушкой воздуха, магистрали для подачи гемодиллюанта и антикоагулянта и зажимы.

На магистрали для подачи антикоагулянта установлен дозирующий элемент в виде камеры, выполненной из пленочного эластичного материала и имеющей с одной стороны  
 45 отверстие для входа антикоагулянта, а с другой - отверстие для его выхода.

На магистрали забора крови установлен насосный сегмент в виде трубки, выполненной из эластичного материала, и имеющего отверстие для входа крови и отверстие для подачи крови к плазмофильтру, соединенное с магистралью контроля давления с расположенным на ней фильтром-клапаном.

50 На ловушке воздуха установлен узел подачи лекарств и отвода воздуха, выполненный в виде трубки с зажимом, один конец которой соединен с крышкой ловушки воздуха, а другой с коннектором типа "Луэр".

Для пояснения изобретения ниже приводится пример конкретного выполнения

устройства для проведения мембранного плазмафереза по одноигольной схеме со ссылками на чертеж, на котором изображен общий вид устройства.

Устройство содержит магистраль забора крови 1, магистраль возврата эрмассы 2 с ловушкой воздуха 3, магистраль подачи гемодилютанта 4, магистраль подачи  
5 антикоагулянта 5 и зажимы 6 и 7.

На магистрали подачи антикоагулянта установлен дозирующий элемент 8, выполненный в виде камеры из пленочного эластичного материала и имеющий с одной стороны отверстие 9 для входа антикоагулянта, а с другой - отверстие 10 для его выхода. Вместимость камеры составляет 2 мл антикоагулянта и рассчитана исходя из максимально  
10 возможной дозы антикоагулянта, вводимой за один цикл забора крови.

На магистрали забора крови 1 установлен насосный сегмент 11 в виде трубки из эластичного материала со специальными упруго-эластичными свойствами и имеющий отверстие 12 для входа крови и отверстие 13 для подачи крови к плазмодифильтру, соединенное с магистралью контроля давления 14, имеющей фильтр-клапан 15. Введение  
15 насосного сегмента в магистраль забора крови позволяет осуществлять непрерывный синхронный отбор крови из вены пациента и смешение ее с определенной дозой антикоагулянта перед насосным сегментом, что позволяет избежать осложнений, вызванных недостатком или избытком антикоагулянта, особенно при проведении донорского плазмафереза. Кроме того, непрерывная дозированная подача антикоагулянта в эксфузат ускоряет отбор плазмы из плазмодифильтра. Введение насосного сегмента  
20 позволяет осуществлять непрерывный возврат эрмассы после плазмодифильтра с одновременным введением пациенту гемодилютанта. Магистраль контроля давления 14 соединена при помощи коннектора типа "Луэр" 16 с прибором для измерения давления крови на входе в плазмодифильтр. Для исключения попадания крови в прибор для измерения  
25 давления на магистрали установлен фильтр-клапан 15, представляющий собой герметично соединенные крышку, корпус и расположенную внутри них мембрану, физические показатели которой позволяют беспрепятственно пропускать воздух, не создавая дополнительного сопротивления и в то же время удерживать столб жидкости, не давая ей попасть в прибор контроля давления, что обеспечивает надежность работы устройства и  
30 безопасность проведения процедуры плазмафереза.

Для создания удобства пользования устройством и обеспечения безопасности пациента при проведении плазмафереза на ловушке воздуха 3 установлен узел подачи лекарств и отвода воздуха 17, выполненный в виде трубки 18 с зажимом 19, один конец которой соединен с крышкой ловушки воздуха 20, а другой с коннектором типа "Луэр" 16 закрытый  
35 колпачком 21.

Такая конструкция устройства позволяет медперсоналу в процессе проведения плазмафереза, немного приоткрывая колпачок 21, регулировать высоту заполнения кровью ловушки воздуха за счет сбрасывания или подачи в нее воздуха и вводить дополнительно при помощи шприца, подсоединяя его к коннектору 16, необходимые для пациента  
40 лекарства.

Устройство для проведения мембранного плазмафереза по одноигольной схеме работает следующим образом.

Предварительно необходимо заполнить устройство, соединенное с плазмодифильтром и прибором контроля давления физраствором и вытеснить из устройства имеющийся воздух.  
45 Затем магистраль подачи антикоагулянта 5 подсоединяют при помощи капельницы 22 к емкости с антикоагулянтом, а магистраль подачи плазмозамещающего раствора 4 к емкости с раствором. Магистраль забора крови 1 соединяют с внутривенным катетером, который вводят в вену пациента. При помощи насосного сегмента 11 за один цикл производят забор дозы крови от пациента с одновременным забором дозы антикоагулянта  
50 (например, глюгицира) из дозирующего элемента 8 и подачей дозы антикоагулянта в магистраль забора крови 1 перед насосным сегментом. Кровь, смешанная с антикоагулянтом, подается насосным сегментом к плазмодифильтру. Давление крови в магистрали забора крови на выходе из насосного сегмента определяется прибором



контроля давления, к которому при помощи коннектора 16 подсоединяется магистраль  
 контроля давления, с расположенным на ней фильтр-клапаном 15, позволяющим избежать  
 попадание крови в прибор для измерения давления при резком повышении давления, что  
 обеспечивает надежность работы устройства. Эрмасса после плазмофильтра при помощи  
 5 насосного сегмента 11 возвращается пациенту по магистрали возврата эрмассы 2. В  
 зависимости от состояния пациента в процессе проведения плазмафереза медперсонал  
 может вводить необходимые лекарства, подсоединяясь шприцем к коннектору 16 узла  
 подачи лекарств 17. При значительном изменении уровня крови в ловушке воздуха,  
 опасном для пациента, медперсонал может регулировать уровень крови за счет  
 10 возможности отвода воздуха приоткрывая колпачок 21 коннектора 16. Осуществление  
 таких манипуляций обеспечивает безопасность пациента при проведении плазмафереза,  
 создает удобство в работе медперсонала.

Таким образом, предложенное устройство, используемое для проведения мембранного  
 плазмафереза по одноигольной схеме, позволит осуществлять донорский и лечебный  
 15 плазмаферез безопасно для пациента с возможностью точного дозирования и подачи  
 антикоагулянта с одновременным забором крови при помощи насосного сегмента,  
 обеспечит удобство в работе медперсонала.

Использованная литература

1. Япония, заявка №60-7852, А 61 М 1/04, 1985 г.
- 20 2. Россия, патент РФ №2113863, А 61 М 1/36, 1998 г.

#### Формула изобретения

Устройство для проведения мембранного плазмафереза по одноигольной схеме,  
 включающее магистраль забора крови и возврата эритроцитной массы с ловушкой воздуха,  
 25 магистраль для подачи гемодиллюанта и магистраль для подачи антикоагулянта,  
 отличающееся тем, что на магистрали для подачи антикоагулянта установлен дозирующий  
 элемент в виде емкости, выполненной из эластичного пленочного материала и имеющий с  
 одной стороны отверстие для входа антикоагулянта, с другой - отверстие для его  
 выхода, на магистрали забора крови установлен насосный сегмент в виде трубки из  
 30 эластичного материала, имеющий отверстие для входа крови и отверстие для подачи крови  
 к плазмофильтру, соединенное с магистралью контроля давления, имеющей фильтр-  
 клапан, при этом на ловушке воздуха установлен узел подачи лекарств и отвода воздуха,  
 выполненный в виде трубки с зажимом.

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Espacenet

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**DEVICE FOR MEMBRANE SEPARATION, SYSTEMS AND METHODS USING SAID DEVICES, AND DATA MANAGEMENT SYSTEMS AND METHODS**

**Inventor(s):** БОГГС Дэниел Р., ; БРАЙЕРТОН Марк Дж., ; КЮСТЕРС Бенджамин И., ; МИН Киунгиоон, ; ВЕГЕНЕР Кристофер Дж.

**Applicant(s):** Фенвал, Инк.

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**Abstract of RU2601449 (C2)**

FIELD: medicine. SUBSTANCE: invention relates to membrane separation devices for use in blood processing procedures. Filtration device comprises: cylindrical body; internal element installed inside the body; porous membrane, located at distance from the body wall or internal element surface to make annular clearance between them, wherein body and internal element can rotate in relation to each other; inlet for direction of whole blood in annular gap, first outlet to direct plasma passing through membrane to container for collection; and second outlet for direction of remaining blood

components from annular gap, wherein device also has a high perfusion area, covered with membrane, and static area and includes radial projection, which separates area of high perfusion from static area. EFFECT: technical result is increased degree and rate of blood separation. 9 cl, 2 tbl, 33 dwg

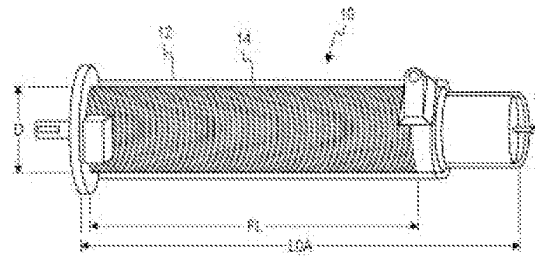


*Fig. 7*

РОССИЙСКАЯ ФЕДЕРАЦИЯ



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ФЕДЕРАЛЬНАЯ СЛУЖБА  
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Адрес для переписки:

129090, Москва, ул. Б. Спасская, 25, строение 3,  
ООО "Юридическая фирма Городисский и  
Партнеры"

(72) Автор(ы):

БОГГС Дэниел Р. (US),

БРАЙЕРТОН Марк Дж. (US),

КЮСТЕРС Бенджамин И. (US),

МИН Киунгиоон (US),

ВЕГЕНЕР Кристофер Дж. (US)

(73) Патентообладатель(и):

Фенвал, Инк. (US)

(54) УСТРОЙСТВА МЕМБРАННОГО РАЗДЕЛЕНИЯ, СИСТЕМЫ И СПОСОБЫ, ПРИМЕНЯЮЩИЕ  
УКАЗАННЫЕ УСТРОЙСТВА, И СИСТЕМЫ И СПОСОБЫ УПРАВЛЕНИЯ ДАННЫМИ

(57) Реферат:

Изобретение относится к мембранным устройствам разделения для применения в процедурах обработки крови. Устройство фильтрации крови содержит: цилиндрический корпус; внутренний элемент, установленный внутри корпуса; пористую мембрану, расположенную на расстоянии от стенки корпуса или поверхности внутреннего элемента с образованием кольцевого зазора между ними, при этом корпус и внутренний элемент могут

вращаться друг относительно друга; выпуск для направления цельной крови, в кольцевой зазор, первый выпуск для направления плазмы, проходящей через мембрану в контейнер для сбора; и второй выпуск для направления из кольцевого зазора оставшихся компонентов крови, причем устройство дополнительно содержит область высокой перфузии, покрытую мембраной, и непроточную область и содержит радиальный выступ, который отделяет область

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RU 2 601 449 C 2

высокой перфузии от непроточной области.  
Технический результат заключается в повышении

степени и скорости сепарации крови. 2 н. и 7 з.п.  
ф-лы, 2 табл., 33 ил.

RU 2601449 C2

RU 2601449 C2

RUSSIAN FEDERATION



FEDERAL SERVICE  
FOR INTELLECTUAL PROPERTY

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Mail address:

**129090, Moskva, ul. B. Spasskaja, 25, stroenie 3,  
OOO "Juridicheskaja firma Gorodisskij i Partnery"**

(72) Inventor(s):

**BOGGS Deniel R. (US),**

**BRAJERTON Mark Dzh. (US),**

**KJUSTERS Bendzhamin I. (US),**

**MIN Kiungioon (US),**

**VEGENER Kristofer Dzh. (US)**

(73) Proprietor(s):

**Fenval, Ink. (US)**

(54) **DEVICE FOR MEMBRANE SEPARATION, SYSTEMS AND METHODS USING SAID DEVICES, AND DATA MANAGEMENT SYSTEMS AND METHODS**

(57) Abstract:

FIELD: medicine.

SUBSTANCE: invention relates to membrane separation devices for use in blood processing procedures. Filtration device comprises: cylindrical body; internal element installed inside the body; porous membrane, located at distance from the body wall or internal element surface to make annular clearance between them, wherein body and internal element can rotate in relation to each other; inlet for direction of whole blood in annular gap, first outlet to direct plasma

passing through membrane to container for collection; and second outlet for direction of remaining blood components from annular gap, wherein device also has a high perfusion area, covered with membrane, and static area and includes radial projection, which separates area of high perfusion from static area.

EFFECT: technical result is increased degree and rate of blood separation.

9 cl, 2 tbl, 33 dwg

## ОБЛАСТЬ ТЕХНИКИ, К КОТОРОЙ ОТНОСИТСЯ ИЗОБРЕТЕНИЕ

Настоящая заявка относится, частично, к типу устройств разделения, использующих взаимно вращающиеся поверхности, по меньшей мере одна из которых содержит мембрану для фильтрации компонента от жидкости, проходящей между поверхностями; к контурам и системам потока жидкости, включающим в себя такой сепаратор; и к применению таких систем для отделения биологических клеток, таких как эритроциты, плазма или лейкоциты, от цельной крови, среды для хранения, среды взвеси, супернатанта и т.п.

## УРОВЕНЬ ТЕХНИКИ

Традиционное взятие крови продолжает опираться на ручное взятие цельной крови у здоровых доноров на станциях сдачи крови, при визитах доноров в центры крови или больницы и т.п. При типичном ручном взятии, цельная кровь берется путем ее простого протекания под воздействием силы тяжести и венозного давления из вены донора в контейнер для сбора. Объем забранной цельной крови обычно составляет "единицу", которая составляет около 450 мл.

Конкретнее, при таком взятии обычно применяется предварительно собранная конструкция трубок и контейнеров или пакетов, включая первичный контейнер из эластичного пластика или пакет для приема единицы цельной крови от донора и один или более вспомогательных контейнеров или пакетов. Кровь сначала

собирается в первичный контейнер, который также содержит противосвертывающее средство (обычно содержащее цитрат натрия, фосфат и декстрозу - часто называемое CPD). Консервант (часто называемый "раствор добавки" или AS, и обычно содержащий среду из физиологического раствора, аденина и глюкозы, которая называется SAG) может быть включен в качестве элемента большей по размеру конструкции пакетов и трубок, которые используются при обработке после сбора крови.

После сбора единицы цельной крови общепринятой практикой в банках крови является транспортировка единицы цельной крови, с помощью подсоединенных трубок и контейнеров, в лабораторию обработки компонентов крови, обычно называемую "вспомогательная лаборатория", для дальнейшей обработки. Дальнейшая обработка обычно включает в себя ручную загрузку первичного контейнера и связанных с ним трубок и вспомогательных контейнеров в центрифугу для разделения цельной крови на компоненты, такие как концентрированные эритроциты и обогащенная тромбоцитами плазма или обедненная тромбоцитами плазма. Данные компоненты затем вручную отжимаются из первичного контейнера в другие предварительно подсоединенные вспомогательные контейнеры, и могут опять центрифугироваться для выделения тромбоцитов из плазмы. После этого компоненты крови могут подвергаться лейкоредукции посредством фильтрации для дальнейшей обработки или хранения. Коротко говоря, данный процесс требует больших временных затрат, является трудоемким и подвержен возможным ошибкам, связанным с человеческим фактором.

Другой типовой задачей, выполняемой банками крови и центром переливания крови, является "промывание клеток". Оно может выполняться с целью удаления и/или замещения жидкой среды (или ее части), в которой суспендированы клетки, с целью концентрирования или дальнейшего концентрирования клеток в жидкой среде, и/или с целью очистки взвеси клеток путем удаления нежелательного клеточного или другого материала.

В предшествующих системах промывания клеток чаще всего применялось центрифугирование взвеси клеток, слив супернатанта, ресуспендирование концентрированных клеток в новых средах, а также возможное повторение данных

этапов до тех пор, пока клетки во взвеси не будут представлены в достаточно высокой или желательной по другим признакам концентрации. Центробежные сепараторы, используемые в обработке крови и компонентов крови, обычно использовались в таких способах промывания клеток.

5 Данные процессы также требуют достаточно больших временных затрат, поскольку требуют повторяющихся ручных манипуляций с кровью или компонентами крови и сборки или разборки различных устройств обработки жидкостей. Это, естественно, повышает не только стоимость, но и потенциал для связанной с человеческим фактором ошибки или погрешности. Соответственно, несмотря на десятилетия развития устройств  
10 и процессов разделения крови, продолжает существовать потребность в лучших и/или более эффективных устройствах, системах и способах разделения, применимых к базовым методикам взятия и обработки крови.

Хотя во многих предшествующих устройствах и процедурах разделения крови применялись принципы разделения центрифугированием, существует другой класс  
15 устройств, основанных на применении мембран, которые использовались для плазмафереза, то есть отделения плазмы от цельной крови. Конкретнее, устройства этого типа используют вращающиеся друг относительно друга поверхности, одна из которых содержит пористую мембрану. Обычно устройство имеет внешний неподвижный корпус и внутренний вращающийся ротор, покрытый пористой  
20 мембраной.

Одним из таких хорошо известных устройств для плазмафереза является сепаратор Autopheresis-C®, поставляемый Fenwal, Inc. из Lake Zurich, штат Иллинойс. Подробное описание сепаратора с вращающейся мембраной можно найти в патенте США No. 5194145, выданном Schoendorfer, который включен в настоящее описание посредством  
25 ссылки. В данном патенте описывается покрытый мембраной вращатель, имеющий внутреннюю систему сбора, размещенную в неподвижной оболочке. Кровь подается в кольцевое пространство или зазор между вращателем и оболочкой. Кровь перемещается вдоль продольной оси оболочки в направлении выходной области, при этом плазма проходит через мембрану за пределы оболочки в пакет для сбора.  
30 Оставшиеся компоненты крови, в основном, эритроциты, тромбоциты и лейкоциты, переходят в выходную область между вращателем и оболочкой, и затем обычно возвращаются донору.

Было обнаружено, что сепараторы с вращающейся мембраной обеспечивают отличную скорость фильтрации плазмы, в основном благодаря уникальным схемам  
35 потока (“вихри Тейлора”), возбуждаемым в зазоре между вращающейся мембраной и оболочкой. Вихри Тейлора помогают удерживать клетки крови от осаждения на мембрану и ее загрязнения или закупоривания.

Несмотря на то, что сепараторы с вращающейся мембраной широко использовались для сбора плазмы, они обычно не использовались для сбора других компонентов крови, в частности, эритроцитов. Сепараторы с вращающейся мембраной также обычно не  
40 использовались для промывания клеток. Один из примеров сепаратора с вращающейся мембраной, примененного для промывания клеток, таких как эритроциты, описан в патенте США No. 5053121, который также включен в настоящее описание посредством ссылки во всей своей полноте. Однако в системе, описанной в этом патенте, используется  
45 два отдельных вращателя, соединенных последовательно или параллельно, для промывания “выделенной” крови пациента. Другие описания применения сепараторов с вращающейся мембраной для разделения крови или компонентов крови, также можно найти в патентах США No. 5376263; 4776964; 4753729; 5135667 и 4755300.



Объект изобретения, изложенный в настоящей заявке, предоставляет дополнительные достижения в области мембранных сепараторов, потенциального снижения стоимости и различных других достижений и преимуществ по сравнению с предшествующим ручным сбором и обработкой крови.

## 5 СУЩНОСТЬ ИЗОБРЕТЕНИЯ

Настоящий объект изобретения имеет ряд аспектов, которые могут быть применены в различных комбинациях, и изложение одного или более конкретных вариантов осуществления приведено в целях изложения и описания, а не ограничения. В изложении сущности выделено только несколько аспектов данного объекта изобретения, и  
10 дополнительные аспекты изложены на чертежах и в приведенном ниже более подробном описании.

Посредством настоящего изложения, представлен мембранный сепаратор, который более эффективно разделяет цельную кровь на ее компоненты и может быть успешно применен в различных системах и процедурах обработки крови.

15 В частности, представлено устройство фильтрации крови, имеющее по существу цилиндрический корпус с внутренней стенкой и внутренним элементом, установленным внутри корпуса и имеющим внешнюю поверхность. Внутренняя стенка корпуса и/или внешняя поверхность внутреннего элемента включает в себя пористую мембрану, расположенную на расстоянии от передней стенки корпуса или поверхности внутреннего  
20 элемента, с образованием кольцевого зазора между ними, при этом корпус и внутренний элемент могут вращаться друг относительно друга. Впуск представлен для направления цельной крови, содержащей плазму и эритроциты, в кольцевой зазор, тогда как второй выпуск представлен для направления из кольцевого зазора оставшихся компонентов крови. Мембрана имеет площадь поверхности, достаточную для отделения плазмы с  
25 такой скоростью потока, что время нахождения эритроцитов в пределах кольцевого зазора является недостаточным для того, чтобы вызвать ненадлежащий гемолиз эритроцитов. В одном из вариантов осуществления, это достигается посредством предоставления внутреннего элемента, который имеет длину и/или диаметр, превышающий длину и диаметр внутренних элементов устройств предшествующего  
30 уровня техники. Конкретнее, внутренний элемент по настоящей заявке содержит ротор, который имеет длину, вплоть до 2,5 раз превышающую длину роторов предшествующих устройств с вращающейся мембраной, и диаметр, вплоть до 2,0 раз превышающий диаметр предшествующих устройств с вращающейся мембраной. Было обнаружено, что такие сепараторы обеспечивают улучшенную скорость отделения плазмы и также  
35 обеспечивают приемлемо низкие уровни гемолиза в сохраняемой крови. В одном конкретном варианте осуществления, длина внутреннего элемента составляет около 14 см и диаметр составляет около 3,8 см.

Также изложен способ создания мембранного устройства разделения. Способ включает в себя разработку модели, использующей входные данные, полученные  
40 полуэмпирически для существующего устройства фильтрации, имеющего пористую мембрану с заданными размерами, с целью получения заданных выходных данных. Модель применяется к гипотетическим устройствам фильтрации, имеющим мембраны с различными размерами, с тем чтобы получить спрогнозированные значения для заданных выходных данных. Спрогнозированные значения рассматриваются, и размеры  
45 мембраны выбираются на основании сравнения спрогнозированных значений заданных выходных данных. В одном из аспектов способ обеспечивает площадь поверхности мембраны, которая улучшает одну или более характеристик фильтрации. В конкретном примере, устройство фильтрации содержит внутренний элемент, имеющий

установленную на него мембрану, при этом внутренний элемент установлен с возможностью вращения относительно по существу цилиндрического корпуса, и внутренний элемент имеет диаметр и/или длину мембраны, позволяющие осуществлять фильтрацию без ненадлежащего лизиса эритроцитов в крови. В конкретном применении модели внутренний элемент имеет диаметр, вплоть до около 2,0 раз превышающий диаметр существующих устройств фильтрации и/или длину мембраны, вплоть до около 2,5 раз превышающую длину мембраны существующих устройств фильтрации.

В другом аспекте изложения представлен мембранный сепаратор в котором по меньшей мере две зоны или области созданы в зазоре между внутренним элементом и оболочкой таким образом, что это препятствует смешиванию жидкостей между двумя областями. Конкретнее, представлен мембранный сепаратор, в котором внутренняя стенка наружной структуры и/или внешняя поверхность внутренней структуры содержит радиальное ребро или выступ, который уменьшает зазор между двумя поверхностями, при этом задавая две области жидкостей, и выступ изолирует жидкости в двух областях с целью минимизации их смешивания.

#### КРАТКОЕ ОПИСАНИЕ ЧЕРТЕЖЕЙ

Указанные и другие характеристики объекта настоящего изобретения описаны в приведенном ниже подробном описании и показаны на прилагаемых фигурах, среди которых:

Фиг. 1 представляет собой вид в перспективе сепаратора с вращающейся мембраной, в парциальном сечении и с удалением частей для демонстрации деталей.

Фиг. 2 представляет собой продольный вид в поперечном сечении сепаратора с вращающейся мембраной с фиг. 1.

Фиг. 3 представляет собой контурное изображение выходных значений гематокрита и напряжения сдвига на стенке выпуска как функции относительной длины фильтрации и радиуса вращателя на основании теоретической проектной модели.

Фиг. 4 представляет собой контурное изображение выходных значений гематокрита и концентрации гемоглобина в плазме для выпуска как функции относительной длины фильтрации и радиуса вращателя на основании теоретической проектной модели, в которой тангенциальная скорость мембраны является постоянной.

Фиг. 5 представляет собой контурное изображение выходных значений гематокрита и числа Тейлора как функции относительной длины фильтрации и радиуса вращателя на основании теоретической проектной модели.

Фиг. 6 представляет собой трехмерный график концентрации гемоглобина в плазме как функции относительной длины фильтрации и радиуса вращателя на основании теоретической проектной модели.

Фиг. 7 представляет собой вид в перспективе устройства или сепаратора с вращающейся мембраной по настоящей заявке.

Фиг. 8 представляет собой схематический поперечный разрез сепаратора с вращающейся мембраной по настоящей заявке, при этом вращатель содержит радиально направленный выступ для задания отдельных областей жидкости.

Фиг. 9 представляет собой схематическое изображение автоматизированной системы разделения цельной крови для обработки ранее собранной цельной крови, содержащей одноразовый модуль контура циркуляции жидкости и долговременный контроллер или управляющий модуль, на который установлен модуль контура циркуляции жидкости.

Фиг. 10 представляет собой схему циркуляции, демонстрирующую один из вариантов осуществления потока жидкости через контур циркуляции жидкости, в соответствии с описанным в настоящем описании, для переработки единицы цельной крови в

концентрированный продукт эритроцитов и продукт плазмы.

Фиг. 11 аналогична фиг. 9, но демонстрирует несколько более подробное изображение компонентов одноразового контура, или модуля циркуляции жидкости, и долговременного модуля контроллера.

5 Фиг. 12 представляет собой схематическое изображение альтернативного варианта осуществления системы в соответствии с настоящим изложением, в котором система применяется для разделения ранее собранной цельной крови.

Фиг. 12A представляет собой схематическое изображение еще одного альтернативного варианта осуществления, аналогичного фиг. 12.

10 Фиг. 13 представляет собой вид в перспективе системы разделения крови с двумя насосами, такой как показана на фиг. 9, 11, 12 и 12A.

Фиг. 14 представляет собой схематическое изображение еще одной альтернативы, аналогичной фиг. 12, за исключением того, что она включает в себя три насоса, иллюстрирующей систему в фазе заполнения.

15 Фиг. 15 представляет собой схематическое изображение системы с фиг. 14, иллюстрирующее систему в фазе разделения.

Фиг. 15A представляет собой схематическое изображение еще одной альтернативной системы с тремя насосами, аналогичной фиг. 14 и 15.

Фиг. 16 представляет собой схематическое изображение автоматизированной системы сбора цельной крови в соответствии с настоящим изложением, демонстрирующее конфигурацию системы для автоматизированного кабинетного сбора и обработки 20 цельной крови донора в режиме заполнения.

Фиг. 17 представляет собой схематическое изображение системы с фиг. 16, демонстрирующее конфигурацию системы для сбора и разделения цельной крови на 25 эритроциты и плазму.

Фиг. 18 представляет собой схематическое изображение системы с фиг. 16, демонстрирующее конфигурацию системы для прополаскивания системы противосвертывающим средством после завершения взятия крови у донора.

Фиг. 19 представляет собой схематическое изображение системы с фиг. 16, 30 демонстрирующее конфигурацию системы в конце процедуры сбора крови.

Фиг. 20 представляет собой схематическое изображение системы с фиг. 16, демонстрирующее конфигурацию системы в необязательной конфигурации для фильтрации собранных эритроцитов через лейкоцитный фильтр.

Фиг. 21 представляет собой схематическое изображение альтернативного варианта осуществления автоматизированной системы сбора цельной крови относительно систем, 35 показанных на фиг. 16-20, в которой компонент контура циркуляции жидкости одноразового использования содержит встроенный фильтр лейкоредукции как часть линии извлечения устройства доступа к донору.

Фиг. 22 представляет собой схематическое изображение альтернативного варианта осуществления контура циркуляции жидкости одноразового использования с фиг. 21, 40 в котором фильтр лейкоредукции размещен в линии извлечения по ходу потока относительно входной точки, в которой противосвертывающее средство вводится в цельную кровь.

На фиг. 23 показан одноразовый набор, подходящий для промывания клеток в 45 соответствии со способом, изложенным в настоящем описании.

На фиг. 24 показан другой вариант осуществления одноразового набора, подходящего для промывания клеток в соответствии с альтернативным способом, изложенным в настоящем описании.

На фиг. 25 показан вариант осуществления панели управления устройства, подходящего для промывания клеток в соответствии со способом, изложенным в настоящем описании.

Фиг. 26-28 представляют собой блок-схемы этапов способа промывания клеток, изложенного в настоящем описании.

Фиг. 29 представляет собой блок-схему, иллюстрирующую способ управления данными в соответствии с настоящим изложением.

Фиг. 30 представляет собой схематическое изображение системы управления данными в соответствии с настоящим изложением в комбинации с контейнером для сбора и набором для обработки.

Фиг. 31 представляет собой блок-схему, иллюстрирующую различные этапы, которые включает в себя способ для управления данными в соответствии с настоящим изложением.

#### ПОДРОБНОЕ ОПИСАНИЕ

Более подробное описание сепаратора с вращающейся мембраной в соответствии с настоящим изложением и его применения в различных автоматизированных системах приведено ниже. Следует понимать, что приведенное ниже описание конкретных устройств и способов предлагается в качестве примера, и не является исчерпывающим описанием всех возможных вариаций или применений. Таким образом, не предполагается, что объем изложения является ограничивающим, и должен пониматься как включающий вариации или варианты осуществления, которые будут понятны специалистам.

Обратимся к фиг. 1 и 2, на которых показана система разделения или фракционирования крови с вращающейся мембраной, обозначенная в общем как 10. Такая система 10 обычно применяется для извлечения плазмы из цельной крови, полученной у отдельного донора-человека. В целях облегчения понимания, показано только устройство выделения плазмы и связанный с ним блок привода, хотя следует понимать, что такой сепаратор образует часть одноразовой системы, содержащей пакеты для сбора, пакеты с добавками, такими как физиологический раствор или ACD, возвратные пакеты, трубки, и т.д., и что также имеются ассоциированные системы управления и система контрольно-измерительных средств для функционирования устройства.

Система 10 содержит по существу цилиндрический корпус 12, установленный концентрически вокруг продольной вертикальной центральной оси. Внутренний элемент 14 установлен концентрически с центральной осью. Корпус и внутренний элемент имеют возможность вращения друг относительно друга. В предпочтительном варианте осуществления, в соответствии с проиллюстрированным, корпус является неподвижным, и внутренний элемент является вращающимся, при этом он вращается концентрически в пределах цилиндрического корпуса 12. Границы маршрута тока крови в общем случае определены зазором 16 между внутренней поверхностью корпуса 12 и внешней поверхностью ротационного вращателя 14. Пространство между корпусом и вращателем иногда называется зазором сдвига. Типовой зазор сдвига может составлять приблизительно 0,025-0,050 дюйма (0,067-0,127 см) и может иметь равномерный размер вдоль оси, например, когда ось вращателя и корпуса совпадают. Зазор сдвига также может изменяться, например, по окружности, когда оси корпуса и вращателя смещены друг относительно друга.

Зазор сдвига также может изменяться вдоль направления оси, например, предпочтительно, ширина зазора может увеличиваться в направлении потока с целью

ограничения гемолиза. Такая ширина зазора может изменяться в диапазоне от 0,025 до около 0,075 дюйма (0,06-0,19 см). Например, оси корпуса и ротора могут совпадать, и диаметр ротора может уменьшаться в направлении оси (направлении потока), тогда как диаметр внутренней поверхности корпуса остается постоянным, или диаметр

5 корпуса увеличивается, и диаметр ротора остается постоянным, или диаметр обеих поверхностей изменяется. Например, ширина зазора может составлять около 0,035 дюйма (0,088 см) в конце зазора со стороны начала потока, или у конца зазора около

10 впуска, и около 0,059 дюйма (0,15 см) в конце зазора со стороны конца потока. Ширина зазора может изменяться путем изменения внешнего диаметра ротора и/или внутреннего диаметра передней поверхности корпуса. Ширина зазора может изменяться линейно или пошагово, или некоторым другим желаемым образом. В любом случае, размер

ширины зазора предпочтительно выбирается таким образом, чтобы при желаемой относительной скорости вращения поток Тейлора-Куэтта, такой как вихри Тейлора, создавался в зазоре, и при этом ограничивался гемолиз.

15 Цельная кровь подается из впускной трубки 20 через впускное отверстие 22, которое направляет кровь во входную область тока крови по маршруту, касательному к окружности вокруг верхнего конца вращателя 14. В нижнем конце цилиндрического корпуса 12 внутренняя стенка корпуса имеет выпускное отверстие 34.

Цилиндрический корпус 12 заканчивается крышкой 40 верхнего конца, имеющей

20 концевую втулку 42, стенки которой являются немагнитными, и нижний конец 44 корпуса заканчивается выпускным отверстием 46 плазмы, концентрическим с центральной осью.

Вращатель 14 установлен с возможностью вращения между крышкой 40 верхнего конца и нижним концом 44 корпуса. Вращатель 14 содержит формованный центральный

25 сердечник или ротор 50, внешняя поверхность которого отформована для задания ряда разнесенных в пространстве кольцевых каналов или выступов 52, разделенных кольцевыми перемычками 54. Поверхностные каналы, задаваемые кольцевыми каналами 52, соединены друг с другом посредством продольных каналов 56. На каждом конце сердечника 50 эти каналы 56 связаны с центральным отверстием или трубой 58.

30 В проиллюстрированном варианте осуществления поверхность ротационного вращателя 14, по меньшей мере, частично, и, предпочтительно, по существу или полностью покрыта цилиндрической пористой мембраной 62. Мембрана 62 обычно имеет номинальный размер поры 0,6 мкм, но альтернативно могут использоваться другие размеры пор. Мембраны, подходящие для способов промывания, описанных в

35 настоящем описании, могут представлять собой волокнистые сетчатые мембраны, литые мембраны, трековые мембраны или мембраны других типов, которые будут известны квалифицированным специалистам в данной области техники. Например, в одном из вариантов осуществления, мембрана может содержать полиэфирную сетку (подложку) с частицами нейлона, отвержденными на ней, посредством чего создается

40 извилистый путь, через который пройдут только компоненты определенного размера. В другом варианте осуществления мембрана может быть сделана из тонкого (толщиной приблизительно 15 мкм) листа, например, поликарбоната. В данном варианте осуществления, поры (отверстия) могут быть больше, чем описанные выше. Например, поры могут составлять приблизительно 3-5 мкм. Размер пор может быть таким, чтобы

45 допускать прохождение небольших сформированных компонентов (например, тромбоцитов, микрочастиц, и т.д.), и чтобы при этом собирались нужные клетки (например, лейкоциты).

Ротационный вращатель устанавливается в крышку верхнего конца для вращения

вокруг стержня 64, который запрессован в крышку 40 конца с одной стороны и размещен внутри цилиндрической несущей поверхности 65 в концевом цилиндре 66, образующем часть ротационного вращателя 14. Внутренний вращатель или внешний корпус может вращаться посредством любого устройства или системы привода вращения. В соответствии с проиллюстрированным, концевой цилиндр 66 частично охвачен кольцом 68 из магнитного материала, используемым в косвенном управлении вращателем 14. Приводной двигатель 70, внешний по отношению к корпусу 12, подсоединен с целью поворота элемента 72 кольцевого магнитного привода, который содержит, по меньшей мере, пару внутренних постоянных магнитов 74. При вращении элемента 72 кольцевого магнитного привода магнитное притяжение между кольцом 68, расположенным внутри корпуса 12, и магнитами 74, расположенными вне корпуса, присоединяет вращатель 14 к внешнему приводу, вызывающему вращение вращателя 14.

На нижнем конце ротационного вращателя 14 центральное выпускное отверстие 58 связано с центральным каналом 76 в концевом подшипнике 78, который является концентрическим с центральной осью. Место установки концевого подшипника определяется внутренним фланцем 80, который формирует нижний край центрального отверстия 82. Центральное отверстие 82 соединено с выпускным отверстием 46 плазмы. Если поверхность внутренней стороны корпуса полностью или частично покрыта мембраной, пакет сбора жидкости или труба может размещаться под мембраной для сбора плазмы и направлять ее через впуск корпуса (не показано).

#### I. Конструкция мембранного сепаратора

В соответствии с одним из аспектов заявки, представлен сепаратор с вращающейся мембраной, который обеспечивает улучшенные скорости потока плазмы с приемлемо низким уровнем гемолиза в сохраняемой крови. Известны различные факторы, влияющие на скорость потока фильтрации через сепараторы с вращающейся мембраной, включающие в себя скорость вращения, размер зазора между вращающейся мембраной и оболочкой, эффективную площадь мембраны, концентрацию эритроцитов (или гематокрит) и вязкость крови. Предшествующие практики проектирования устройств с вращающейся мембраной были в значительной степени эмпирическими, и им до некоторой степени способствовали неясные феноменологические описания влияния различных параметров проектирования на производительность и гемолиз. Это оказалось неэффективным относительно времени разработки и затрат технических ресурсов.

Напротив, параметры сепаратора с вращающейся мембраной по настоящей заявке были определены на основании количественных дифференциальных моделей, которые принимают во внимание локальную скорость плазмы при прохождении через мембрану и локальную концентрацию гемоглобина. Данные дифференциальные модели интегрировались по длине устройства с целью получения суммарной скорости потока плазмы и концентрации гемоглобина в плазме на выходе устройства.

Способ включает операционные входные данные на основании геометрических параметров и условий функционирования существующего сепаратора Plasmacell-C, включая гематокрит донора, скорость входного потока крови, скорость вращения и эффективную площадь мембраны. Также учитывались геометрические входные данные для радиуса ротора, ширины кольцевого зазора и длины, по которой выполняется интегрирование. См. таблицу 1 ниже.

Для получения спрогнозированных значений для гипотетических сепараторов, радиус ротора и длина фильтрации изменялись от около 1,0 до около 2,0 раз по сравнению с текущими значениями Plasmacell-C с шагом 0,05, в результате чего была получена сетка пространства параметров проектирования размером 21×21 для каждой представляющей

интерес выходной переменной. Для всех устройств срез корпуса и зазор в выпуске сохранялись постоянными, и зазор во впуске и скорость вращения изменялись соответственно. Также разрабатывались модели, которые связывали вязкость и плотность крови с гематокритом, температурой и концентрацией противосвертывающего средства.

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| Таблица 1<br>Входные данные для расчета моделей      |          |
|------------------------------------------------------|----------|
| Параметр, единицы измерения                          | Значение |
| Скорость входного потока крови, мл/мин               | 106      |
| Входной гематокрит, %                                | 42       |
| Температура, °C                                      | 35       |
| Концентрация цитрата, %                              | 5,66     |
| Длина фильтрации, см                                 | 7,600    |
| Радиус ротора с мембраной, см                        | 1,3551   |
| Входной зазор, см                                    | 0,0673   |
| Выходной зазор, см                                   | 0,0584   |
| Эффективная доля мембраны                            | 0,50     |
| Ширина контактного участка мембраны, см              | 0,46     |
| Скорость вращения, об/мин                            | 3600     |
| Гематокрит для стенок, %                             | 0,90     |
| Радиус эритроцитов, мкм                              | 2,75     |
| Концентрация гемоглобина в эритроцитах, мг/дл        | 335,60   |
| Плотность плазмы, г/см <sup>3</sup>                  | 1,024    |
| Плотность упакованных эритроцитов, г/см <sup>3</sup> | 1,096    |
| Вязкость цитратной плазмы, сП                        | 1,39     |

В одной из реализаций способа, выходные данные для скорости потока плазмы и концентрации гемоглобина были получены для различных значений радиуса ротора, скорости вращения и длины интегрирования. Результаты моделирования показаны в наложенных контурных изображениях выходного гематокрита и выходного напряжения сдвига на стенке (фиг. 3), выходного гематокрита и выходной концентрации гемоглобина в плазме (фиг. 4), и выходного гематокрита и числа Тейлора (фиг. 5), во всех случаях - как функция относительной длины фильтрации и радиуса вращателя. При использовании в настоящем документе, "длина фильтрации" понимается как осевая длина центрального сердечника ротора 50 от начала до конца каналов или выступов 52. В общем смысле, она представляет собой длину мембраны, доступную для фильтрации. "Радиус вращателя" или "диаметр вращателя" понимается как радиус или диаметр ротора с прикрепленной мембраной. На фиг. 6 показаны результаты как функция длины фильтрации и радиуса вращателя на трехмерном графике, демонстрирующем увеличение гемоглобина с увеличением размеров устройств. Данные результаты затем оценивались с целью обеспечения наилучшего баланса высокой скорости потока плазмы с приемлемо низкими уровнями гемолиза.

Модели показали, что эффективная площадь мембраны имеет наиболее сильное положительное влияние на производительность. Кроме того, хотя увеличение площади мембраны путем увеличения диаметра ротора более положительно влияет на скорости потоков, чем увеличение площади мембраны путем увеличения длины ротора, оно также увеличивает возможность гемолиза вследствие повышенной скорости мембраны, и, вследствие этого, повышения сдвигающих сил в зазоре.

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Соответственно, моделирование позволило спрогнозировать длины и диаметры ротора, которые приведут к повышению площади мембран, применение которых также позволит иметь приемлемо низкие уровни гемолиза. Сепараторы-прототипы (на

основании результатов моделирования) были сделаны и протестированы с целью проверки результатов, спрогнозированных посредством моделирования. Ниже в таблице 2 приведено сравнение имеющегося устройства для плазмафереза Plasmacell-C с двумя потенциальными альтернативами, основанными на моделях.

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| Параметр, единицы измерения                       | Устройство   |            |            |
|---------------------------------------------------|--------------|------------|------------|
|                                                   | Plasmacell-C | RL 140-162 | RL 140-185 |
| Относительная длина фильтрации                    | 1,00         | 1,62       | 1,85       |
| Относительный радиус вращателя                    | 1,00         | 1,40       | 1,40       |
| Относительная скорость вращателя                  | 1,00         | 0,70       | 0,75       |
| Длина фильтрации, см                              | 7,600        | 12,311     | 14,059     |
| Радиус вращателя, см                              | 1,3551       | 1,8971     | 1,8971     |
| Скорость вращателя, об/мин                        | 3600         | 2520       | 2700       |
| Входной зазор, см                                 | 0,0673       | 0,0729     | 0,0749     |
| Выходной зазор, см                                | 0,0584       | 0,0584     | 0,0584     |
| Скорость входного потока, мл/мин                  | 106          | 106        | 106        |
| Входной гематокрит, %                             | 42           | 42         | 42         |
| Концентрация цитрата, %                           | 5,66         | 5,66       | 5,66       |
| Скорость потока плазмы, мл/мин                    | 36,33        | 47,42      | 50,57      |
| Выходной гематокрит, %                            | 63,90        | 76,00      | 80,32      |
| Выходная концентрация гемоглобина в плазме, мг/дл | 5,04         | 14,36      | 27,84      |
| Время пребывания, с                               | 2,98         | 7,99       | 9,77       |
| Центростремительное давление, мм рт. ст.          | 100,22       | 96,25      | 110,50     |
| Крутящий момент, Н·см                             | 1,045        | 3,319      | 4,442      |
| Выходное число Тейлора                            | 89,07        | 51,00      | 46,96      |

Со ссылкой на таблицу 2 и фиг. 7, сепаратор с вращающейся мембраной 10 содержит ротационный вращатель 14, который имеет диаметр вращателя D, длину фильтрации FL и суммарную длину LOA. В типичном устройстве плазмафереза, таком как сепаратор Plasmacell-C, ротор имеет диаметр D, составляющий приблизительно 2,79 см, длину фильтрации FL, составляющую приблизительно 7,62 см, и суммарную длину LOA, составляющую приблизительно 12,7 см.

В соответствии с настоящей заявкой, было обнаружено, что диаметр мембраны может быть увеличен вплоть до около 2,0 раз относительно диаметра мембраны, имеющегося в типичном устройстве плазмафереза, тогда как длина может быть увеличена вплоть до около 2,5 раз относительно длины вращающейся мембраны в типичном устройстве плазмафереза. Увеличение размера ротора в пределах данных периметров достаточно увеличивает площадь мембраны фильтра для обеспечения высокого скорости потока плазмы, при этом обеспечивая приемлемо низкий уровень гемолиза. В конкретном примере сепаратор с вращающейся мембраной по настоящей заявке может, предпочтительно, иметь диаметр D, составляющий 4,19 см, длину фильтрации FL, составляющую 14,02 см, и суммарную длину LOA, составляющую 19,56 см.

Прототипы сепараторов с вращающейся мембраной тестировались с бычьей и человеческой кровью для проверки результатов, спрогнозированных по моделям. Скорости потоков крови, составляющие 100 мл/мин, были получены при скоростях вращателя, изменяющихся в диапазоне 1000-3500 об/мин. Выходные уровни гематокрита, составляющие 80% и выше, были получены до достижения высоких уровней загрязнения мембраны. Время сбора 880 мл плазмы изменялось в диапазоне приблизительно между 18 и 20 минутами.

Как отмечалось выше, время нахождения эритроцитов в зазоре сдвига напрямую связано с величиной гемолиза. В устройствах разделения с вращающейся мембраной



существуют области потока вдоль осевой длины ротора, где поток жидкости является относительно стоячим, что приводит к образованию очагов гемолиза. Качество собранных эритроцитов ухудшается в той степени, в которой эритроциты из области с высоким гемолизом перемешиваются с потоком в области с низким гемолизом.

5 Соответственно, согласно другому аспекту заявки, представлен способ для создания отдельных областей потока жидкости в зазоре сепаратора с вращающейся мембраной без использования затворов. Отдельные области потока снижают или минимизируют влияние смешивания жидкостей между двумя областями потока. Отдельные области потока получают посредством наличия приподнятого ребра или выступа в зазоре для  
10 снижения или минимизации зазора между вращателем и внешним цилиндром. Предпочтительно, выступ или ребро представлено на поверхности ротора за пределами места, в котором к нему прикреплена вращающаяся мембрана.

Выступ, предпочтительно, расположен таким образом, чтобы задать границу области потока высокой перфузии. Радиальный размер выступа обратно пропорционален  
15 степени смешивания, допускаемой между двумя областями, которые он задает, при этом больший радиальный размер выступ допускает меньшее смешивание. Осевой размер или протяженность выступа также обратно пропорциональна допускаемой степени смешивания, при этом больший осевой размер допускает меньшее смешивание. Осевой размер выступа, предпочтительно, имеет размер, по меньшей мере, равный  
20 размеру зазора по длине в целях минимизации образования смежных потоков Тейлора, вызывающих нежелательное смешивание.

Обратимся к фиг. 8, на которой показано схематическое представление в поперечном сечении устройства 10 разделения с вращающейся мембраной. Устройство содержит неподвижный внешний цилиндр 12 и вращающийся внутренний цилиндр 14, на котором  
25 находится фильтрующий элемент. В соответствии с настоящей заявкой, внутренний цилиндр представлен с радиальным выступом 90. Этот выступ служит для разделения зазора 16 между вращателем и внешним корпусом на две области потока. Первая область 92 жидкости имеет стоячую, непроточную область потока, обычно в части вращателя, которая выходит за пределы мембраны фильтра. Вторая область 94 потока,  
30 которая обычно контактирует с мембраной фильтра, имеет область потока с высокой перфузией.

Поскольку первая область 92 потока является непроточной, кровь, находящаяся в ней, подвержена повышенным напряжениям сдвига в течение более продолжительных периодов времени, чем кровь во второй области 94 потока. Таким образом, кровь в  
35 первой области 92 потока часто может стать гемолизированной и имеет высокие концентрации свободного гемоглобина (Hb). Выступ 90 препятствует потоку жидкости между двумя областями потока, таким образом, минимизируя степень смешивания Hb-загрязненной крови в первой области 92 с кровью с низкой Hb во второй области 94.

Хотя показано, что выступ 90 составляет единой целое с ротором, он также может  
40 быть сформирован на внутренней стороне внешнего цилиндра для достижения того же самого эффекта. Как было отмечено выше, осевой размер выступа должен иметь длину, составляющую по меньшей мере одну величину зазора. Типичное устройство разделения с вращающейся мембраной для выполнения плазмафереза обычно имеет зазор между вращателем и герметизирующей стенкой, составляющий от 0,058 см до  
45 0,0673 см, и выступ в соответствии с настоящей заявкой мог бы иметь осевой размер в пределах того же общего диапазона. Однако большие осевые размеры для выступа приведут к сниженному смешиванию и, в одном из примеров, было обнаружено, что ротор, имеющий радиально вытянутый выступ с осевым размером 0,234 см, является

эффективным.

## II. Системы и способы для обработки ранее собранной цельной крови

Устройство разделения с вращающейся мембраной в соответствии с описанным выше может быть выгодно использовано в различных системах и способах обработки 5 крови, для которых предшествующие устройства обычно не подходили, особенно, в системах и процессе для получения эритроцитов. В одном из типов системы и способа, вращатель может быть использован для обработки во “вспомогательной лаборатории” ранее собранной цельной крови, как показано на фиг. 9-15А.

Обратимся к фиг. 9, на которой схематически проиллюстрированы одноразовый 10 контур циркуляции жидкости, или модуль А, и многоразовый долговременный контроллер, или модуль В, сконфигурированный для взаимодействия с потоком через контур жидкости А и управления им. Одноразовый контур жидкости А, как проиллюстрировано на фиг. 9, содержит множество компонентов, соединенных между собой гибкими пластиковыми трубками, определяющими маршрут потока между 15 компонентами. Контур, предпочтительно, заранее полностью собран и предварительно стерилизован, за исключением блока с контейнером цельной крови и контейнером клеточного консерванта. Конкретнее, проиллюстрированный одноразовый контур на фиг. 9 содержит контейнер 101 цельной крови и контейнер 102 с раствором клеточного консерванта, сепаратор 108 компонентов крови, контейнер 112 для сбора плазмы, 20 необязательный фильтр 113 редукции лейкоцитов, и контейнер 115 для сбора эритроцитов. Хотя это и не проиллюстрировано на фиг. 9, многоразовый модуль В может иметь крепления и связанные с ними весы для поддержания любого или всех контейнеров 101, 102, 112 и 115. В различных других вариантах осуществления, обсуждаемых в настоящем описании, такие крепления/весы могут не быть 25 проиллюстрированы, но понимается, что они являются частью описываемых систем.

Контейнер 101 для сбора цельной крови может представлять собой любой подходящий контейнер, но обычно он представляет собой гибкий пластиковый мешок или пакет, в который ранее было собрано приблизительно 450 мл цельной крови. Контейнер 101 может являться частью отдельной системы в процессе сбора, и затем 30 может присоединяться к остальной части жидкостного контура А, или может фактически являться частью контура А во время сбора. Во время сбора, в соответствии с обычной процедурой, цельная кровь смешивается с противосвертывающим средством, размещенным в первичном контейнере, с целью предотвращения преждевременной коагуляции. Соответственно, “цельная кровь” при использовании в настоящем описании 35 включает кровь, смешанную с противосвертывающим средством.

Гибкие пластиковые трубки 105 соединены с контейнером для сбора цельной крови, например, посредством стерильного соединительного устройства или другого подходящего механизма прикрепления, и задают маршрут потока цельной крови между 40 контейнером 101 с цельной кровью и соединением с трубками 103 раствора клеточного консерванта, которые выступают из контейнера 102 с раствором клеточного консерванта в соединение маршрута потока. Соединение маршрута потока между маршрутом потока цельной крови и маршрутом потока всех консервантов располагается во входном фиксаторе 116. Из соединения маршрут потока проходит через трубки 107 к впускному отверстию сепаратора 108.

Как показано на фиг. 9 настоящего описания, корпус сепаратора имеет выпуск, 45 который соединен с зазором между корпусом и ротором и с трубками 110 потока концентрированных эритроцитов для извлечения концентрированных эритроцитов из зазора сепаратора. Кроме того, корпус содержит выпуск из ротора, который соединен

со стороны мембраны, направленной в другую сторону от зазора (например, внутренняя часть ротора) и соединен с трубками 111 маршрута потока плазмы.

В целях снижения числа лейкоцитов, которые могут присутствовать в эритроцитах, одноразовый контур циркуляции жидкости А, необязательно, содержит фильтр 113  
 5 редукации лейкоцитов, который может представлять собой любую хорошо известную конструкцию для удаления лейкоцитов из концентрированных эритроцитов без чрезмерного гемолиза эритроцитов или снижения числа эритроцитов в собранном продукте. Концентрированные эритроциты из фильтра 113 редукации эритроцитов  
 10 проходят через удлинение 114 по маршруту потока концентрированных эритроцитов в контейнер 15 для хранения, который может быть сделан из любого подходящего пластикового материала, совместимого с хранением эритроцитов.

Многоразовый или долговременный модуль В контроллера, который схематически показан на фиг. 9, предпочтительно, содержит датчик 104 гематокрита для определения гематокрита и цельной крови, вытекающей из контейнера 101 цельной крови. Детектор  
 15 гематокрита может иметь любую подходящую схему или конструкцию, предпочтительно, в соответствии с описанным в патенте США No. 6419822, который настоящим включен в данное описание посредством ссылки.

Долговременный контроллер многоразового использования, или модуль В управления, содержит входной фиксатор 116, которым можно управлять с целью  
 20 контроля жидкости из контейнера 101 цельной крови или контейнера 102 клеточного консерванта, или, необязательно, одновременно и пропорционально из обоих контейнеров 101 и 102. Для контролирования потока крови в сепаратор, модуль многоразового использования содержит впускной насос 106, который также может  
 25 иметь любую подходящую конструкцию и может, например, представлять собой насос перистальтического типа, который функционирует посредством постепенного сжатия или сдавливания трубок 107, образующих маршрут впускного потока в сепаратор, насос с гибкой диафрагмой или другой подходящий насос. Датчик 117 давления  
 30 взаимодействует с маршрутом впускного потока между насосом 106 и сепаратором 108 с целью определения впускного давления насоса. Датчик может выдавать данные в систему управления для обеспечения функции тревоги в случае превышения давления, недостаточного давления, или и того, и другого.

В целях контроля скорости потока концентрированных эритроцитов от сепаратора 108, многоразовый модуль также содержит выпускной насос 109, который связан с  
 35 маршрутом 110 выпускного потока и функционирует аналогичным описанному в отношении впускного насоса 106 образом. Он также может иметь любую подходящую конструкцию, такую как перистальтический насос, структуру с гибкой диафрагмой или другую подходящую структуру насоса. Маршрут 111 потока плазмы, выходящей из сепаратора, предпочтительно, не контролируется насосом, и объемная скорость потока  
 40 через трубки маршрута потока плазмы представляет собой разность между впускной объемной скоростью потока из насоса 106 и выпускной объемной скоростью потока из насоса 109. Модуль В многоразового использования может, однако, также содержать фиксатор 118 для управления потоком плазмы через трубки 111 маршрута потока плазмы.

Одноразовый модуль А также может содержать контейнер 112 для сбора плазмы, имеющий жидкостное соединение с маршрутом потока плазмы, для приема плазмы,  
 45 отделенной сепаратором 108. Поскольку плазма проходит через пористую мембрану в сепараторе 108, плазма, которая собирается в контейнере 112, является в значительной степени безклеточной плазмой, и может подходить для введения пациентам,

замораживания с целью хранения или последующей обработки.

На фиг. 10 показан общий вид маршрута(-ов) потока жидкости через систему, проиллюстрированную на фиг. 9. В частности, на ней показан поток цельной крови из контейнера 101 с одной единицей цельной крови через детектор 104 гематокрита цельной крови к соединению в маршруте потока, расположенном в бинарном фиксаторе 116. Раствор для консервирования клеток, такой как раствор для консервирования эритроцитов, вытекает из контейнера 102 эритроцитов также к соединению в бинарном фиксаторе 116. В зависимости от этапов обработки, бинарный фиксатор допускает поток цельной крови или клеточного консерванта в остальную часть системы. Не обязательно, фиксатор 116 может представлять собой пропорциональный фиксатор, допускающий выбранный одновременный пропорциональный поток цельной крови и консерванта эритроцитов.

Из бинарного фиксатора 116 цельная кровь или жидкость клеточного консерванта протекает через впускной насос 106 и в устройство 108 разделения. Как объяснялось ранее, устройство разделения использует вращающиеся друг относительно друга корпус и ротор, на одном из которых находится мембрана, через которую может проходить плазма.

В одном из вариантов осуществления, мембрана находится на поверхности ротора, и плазма проходит через мембрану и через внутренний лабиринт протоков в пределах ротора, выходя в итоге в контейнер 112 для сбора плазмы. В случае, когда мембрана установлена на роторе, устройство обычно называется сепаратором с вращающейся мембраной, как показано на фиг. 10. Однако следует понимать, что мембрана потенциально может быть установлена на внутренней поверхности корпуса в направлении зазора между внутренней поверхностью стенки корпуса и внешней поверхностью мембраны, или мембрана может находиться и на внешней поверхности ротора, и на внутренней поверхности корпуса, с тем чтобы плазма проходила через мембраны одновременно, что потенциально увеличивается скорость разделения или производительность сепаратора 108. Из сепаратора 108 концентрированные эритроциты протекают через выпуск корпуса, соединенный с зазором между ротором и корпусом, и через маршрут 110 потока эритроцитов и выпускной насос 109, который контролирует скорость объемного потока концентрированных эритроцитов.

Хотя гематокрит концентрированных эритроцитов, удаленных из сепаратора 108, может меняться, ожидается, что гематокрит концентрированных эритроцитов будет составлять приблизительно 80-85%. Выпускной насос 109 закачивает концентрированные эритроциты в контейнер 115 для сбора эритроцитов и, необязательно, через фильтр редукиции лейкоцитов, расположенный на маршруте потока эритроцитов между насосом 109 и контейнером 115 для сбора. Воздействие насоса, выталкивающего концентрированные эритроциты через фильтр редукиции лейкоцитов, помогает поддерживать время обработки в пределах целесообразного диапазона по сравнению, например, со временем, которое потребовалось бы для потока концентрированных эритроцитов через фильтр редукиции лейкоцитов в ручной установке под воздействием гравитации.

Плазма, отделенная сепаратором 108, как показано на фиг. 10, протекает через устройство разделения, например, из выпуска, связанного с лабиринтом протоков внутри ротора, через единичный контрольный фиксатор 118 и в контейнер 112 для сбора плазмы. Как отмечалось ранее, поскольку плазма проходит через мембрану, она является в значительной степени безклеточной и подходящей для последующего введения пациентам, замораживания и/или для обработки, например, путем фракционирования,

с целью получения компонентов плазмы, предназначенных для использования в терапевтических продуктах.

Система также может содержать фильтр, такой как фильтр редукции лейкоцитов, в линии 111 потока плазмы, если есть необходимость.

5 Фиг. 11 иллюстрирует одну из версий потенциальной системы, использующей и одноразовый модуль А жидкостного контура, и многоразовый или долговременный модуль В контроллера. Хотя они показаны собранными друг с другом, модуль А жидкостного контура и долговременный модуль В имеют отдельное и независимое  
10 назначение и могут также использоваться с другими системами. Как можно видеть на фиг. 11, одноразовый модуль А удобно установлен напротив многоразового модуля В, который имеет связанные с ним навесы или опоры, некоторые из которых могут быть связаны с весами, для поддержания различных контейнеров одноразовой системы. Одноразовый модуль предпочтительно является, как указывалось ранее, предварительно собранным и предварительно простерилизованным. Контейнер с раствором клеточного  
15 консерванта может быть предварительно присоединен как часть одноразовой системы или может быть добавлен позднее, например, с помощью стерильного соединительного устройства или другого подходящего приспособления. Контейнер цельной крови, который содержит единицу ранее собранной цельной крови, также может быть предварительно присоединен к предварительно собранному жидкостному контуру или  
20 может быть присоединен посредством стерильного соединительного устройства или другого подходящего приспособления для соединения.

Поверхность многоразового модуля В содержит, в данном варианте осуществления, отдельный фиксатор 116а раствора для управления потоком раствора для консервации клеток из контейнера 102 раствора, который свисает с поднятой поддерживающий  
25 штанги раствора. Контейнер 101 цельной крови подвешен к весам. Весы могут иметь обычную конструкцию и могут выдавать сигнал измерения веса, который может быть использован системой управления модуля В для измерения количества цельной крови, которое остается в контейнере, и/или количества цельной крови, которое было обработано системой. Одноразовая система содержит маршрут 105 потока эритроцитов, который проходит из контейнера цельной крови через детектор 104 гематокрита и через  
30 отдельный фиксатор 116b цельной крови для управления потоком цельной крови из контейнера в систему. Маршрут 103 потока раствора клеточного консерванта и маршрут 105 потока цельной крови объединяются в соединении, таком как v-участок или у-участок, выше по ходу потока от впускного насоса 106. Объединенный маршрут потока  
35 проходит через впускной насос на впуск устройства 108 разделения. Как видно на фиг. 11, многоразовый модуль В содержит блок привода, такой как магнитный блок привода, для выполнения вращения ротора в пределах корпуса сепаратора без необходимости физического прохождения элементов или компонентов привода через корпус. В данной схеме расположения ротор содержит магнитно подсоединенный элемент привода,  
40 который вращается посредством магнитного блока привода, соединенного с многоразовым модулем. Система подробнее описана в патенте США No. 5194145, выданном Schoendrofer, который включен в настоящее описание посредством ссылки.

Выпуск концентрированных эритроцитов из сепаратора 108 присоединен к маршруту 110 потока эритроцитов, который проходит через выпускной насос 109 к впуску  
45 необязательного фильтра 113 редукции лейкоцитов. Среда фильтра, расположенная между впуском и выпуском фильтра редукции лейкоцитов, по существу, удаляет лейкоциты из эритроцитов. Трубки 114 маршрута потока эритроцитов передают эритроциты с выпуска фильтра в контейнер 115 для сбора эритроцитов.

Плазма пропускается из выпуска плазмы сепаратора через фиксатор 118 контроля потока плазмы в контейнер 112 для сбора плазмы. Аналогично контейнеру цельной крови, контейнер 115 концентрированных эритроцитов и контейнер 112 плазмы подвешиваются к весам, которые могут находиться в электронном взаимодействии с системой управления долговременного или многоразового модуля В с целью предоставления информации относительно количества концентрированных эритроцитов и/или плазмы, собранных из цельной крови, или относительно скорости сбора.

Хотя данная система была проиллюстрирована с определенными основными компонентами и свойствами в соответствии с описанным выше, не предполагается, что данное описание исключает добавление, при необходимости, других компонентов, таких как датчики, насосы, фильтры и т.п. Например, необязательно, может быть желательным проведение фильтрации плазмы до ее входа в контейнер для сбора плазмы, или может быть желательным исключение фильтра лейкоредукции для эритроцитов. Хотя плазма, удаленная из сепаратора 108, является в значительной степени безклеточной плазмой, может быть необходимой фильтрация плазмы с целью последующего введения или обработки. Не предполагается, что настоящее описание исключает возможное добавление дополнительных компонентов или удаление одного или более компонентов, описанных выше.

Обратимся теперь к обработке цельной крови в проиллюстрированной системе; процесс разделения начинается с заливки системы. “Заливка” относится к способу, посредством которого мембрана подготавливается (то есть, смачивается) до начала использования. Смачивание жидкостью помогает вытеснить воздух, присутствующий в матрице мембраны, до проведения индуцированного давлением потока через мембрану. Обычно небиологическая жидкость низкой вязкости, такая как раствор клеточного консерванта (раствор эритроцитов, такой как раствор Adsol), используется для смачивания с целью осуществления наиболее эффективного вытеснения воздуха. Во время заливки жидкость удаляется из пакета 102 раствора клеточного консерванта посредством впускного насоса 106 до тех пор, пока линия 103 раствора, линия 105 цельной крови, впускная линия 107 и устройство 108 с вращающейся мембраной не будут полностью заполнены раствором. Для обеспечения надлежащей заливки, впускной насос 106 может перемещаться по часовой стрелке и против часовой стрелки во время заливки. Цель заливки раствором состоит в предотвращении формирования поверхности раздела воздух-кровь посредством создания поверхности раздела раствор-кровь, а также в смачивании мембраны в устройстве разделения. Каждая из предпринимаемых мер позволяет снизить гемолиз эритроцитов.

После того как система была успешно залита, маршрут 103 потока клеточного раствора будет закрыт посредством впускного фиксатора 116. Проиллюстрированный впускной фиксатор представляет собой бинарный фиксатор, который может закрывать маршрут 103 потока раствора клеточной консервации или маршрут 107 потока цельной крови. Цельная кровь будет затем прокачана через маршрут 105 потока цельной крови и маршрут 107 впускного потока в сепаратор 108 посредством впускного насоса 106. Скорость потока впускного насоса 106 может изменяться от около 10 мл/мин до 150 мл/мин в зависимости от желаемого выхода продукта для конкретной процедуры. После того как цельная кровь выходит из контейнера 101, она проходит через детектор 104 гематокрита цельной крови, который генерирует оценку гематокрита цельной крови путем измерений отражения IR LED. Подробности относительно детектора гематокрита объяснены в патенте США No. 6419822 (Название: Systems and methods for sensing red blood cell hematocrit), включенном посредством ссылки. Значение гематокрита цельной

крови требуется для исходного алгоритма управления проиллюстрированной системы, но может быть важным в других системах.

После того как цельная кровь заполнила сепаратор 108, система начинает перемещать плазму из сепаратора, который разделяет цельную кровь, входящую в устройство с  
 5 вращающейся мембраной, на концентрат эритроцитов и практически безклеточную плазму. Упакованные эритроциты с гематокритом, составляющим приблизительно 80-85%, будут выкачаны из сепаратора 108 через маршрут 110 потока эритроцитов в лейкофилтр 113 эритроцитов посредством выпускного насоса 109. Выпускной насос пропускает упакованные эритроциты через лейкофилтр 113 эритроцитов, и концентрат  
 10 эритроцитов, который выходит из лейкофилтра 113 эритроцитов через линию 114 эритроцитов в пакет 115 продукта эритроцитов, будет успешно обеднен лейкоцитами и также обеднен тромбоцитами. Также возможно выполнить автоматизированное разделение цельной крови без использования лейкофилтра 113 эритроцитов. В этом случае лейкофилтр 114 эритроцитов будет удален из системы, и продукт 115  
 15 эритроцитов не будет обеднен лейкоцитами или тромбоцитами.

В течение процедуры плазма проходит через маршрут 111 потока плазмы в пакет 112 плазмы со скоростью потока, равной разности между скоростью потока впускного насоса 106 и скоростью потока выпускного насоса 109, что в настоящее время  
 выполняется в других приложениях разделения с вращающейся мембраной, таких как  
 20 применяются в инструменте Autopheresis-C®, поставляемом компанией Fenwal, Inc. Давление на мембране, сгенерированное вследствие различия в скоростях потока, отслеживается датчиком 117 давления. Измерения давления используются для контроля скорости потока плазмы с применением алгоритма, описанного в заявке на патент США No. 13/095633, поданной 27 апреля 2011 (Название: SYSTEMS AND METHODS  
 25 OF CONTROLLING FOULING DURING A FILTRATION PROCEDURE), настоящим включенной посредством ссылки.

Система на фиг. 9-11 будет продолжать разделять упакованные эритроциты и плазму до тех пор, пока пакет 101 цельной крови не станет пустым, что будет определено по прохождению воздуха через детектор 104 гематокрита цельной крови. В этот момент  
 30 линия 105 цельной крови будет закрыта, и линия раствора клеточного консерванта будет открыта посредством впускного фиксатора 116 для запуска промывания раствором или спуска. Во время промывания раствором, раствор консерванта будет удален из пакета 102 раствора и будет закачан в сепаратор 108 посредством впускного насоса 106. Маршрут 111 потока плазмы закрывается посредством фиксатора 118  
 35 плазмы во время промывания раствором. Промывание раствором используется для спуска любой крови, остающейся в системе, в контейнер 115 продукта эритроцитов. Промывание раствором также повысит объем контейнера 115 продукта эритроцитов до уровня, необходимого для надлежащего хранения эритроцитов. После окончания промывания раствором разделение единицы цельной крови завершается.

Обратимся к фиг. 12, на которой показана еще одна альтернативная система с двумя насосами. Данный вариант осуществления отличается от показанного на фиг. 9 в основном тем, что жидкость из раствора консерванта для клеток крови добавляется  
 40 после того как эритроциты были отделены от цельной крови. Конкретнее, контейнер/пакет 101, содержащий ранее собранную цельную кровь (предпочтительно уже объединенную с противосвертывающим средством), соединяется с одноразовой системой А через сегмент трубок 107, который ведет к сепаратору 108 крови. Насос 106 взаимодействует с трубками 107 с целью закачивания цельной крови в сепаратор 108. Контейнер 102, содержащий раствор добавки для консервации эритроцитов, соединяется

с контейнером 115 для сбора отделенных эритроцитов через трубки 114, через которые отделенные эритроциты также направляются в контейнер 115 через фильтр 114 лейкоцитов.

5 Стерильное соединение контейнеров 101, 102 с одноразовой системой может быть достигнуто посредством ряда различных способов. Контейнер 102 для раствора добавки может быть представлен как часть одноразовой системы А, и может быть объединен с остальной одноразовой частью (после стерилизации посредством, например, обработки 10 гамма- или электронным пучком) во время итоговой упаковки, после того как оставшаяся часть одноразовых элементов была стерилизована (посредством, например, обработки паром). Альтернативно, контейнер 102 может быть сформирован как единое целое с одноразовыми элементами. В еще одной альтернативе, и контейнер 102, и контейнер 101 цельной крови могут быть отдельными от остальных одноразовых элементов и могут подсоединяться в момент использования через, например, стерильные стержневые соединения 170, показанные схематически на фиг. 10. Такие стержневые 15 соединения, предпочтительно, имеют фильтр 0,2 мкм для поддержания стерильности.

В другом аспекте данного варианта осуществления, трубки 103, соединяющие контейнер 102 с раствором добавки с фильтром 62 лейкоцитов, также могут быть совместно сцеплены посредством насоса 109. В частности, насос 109 может представлять собой насос с двойным напором, который производит поток раствора добавки и поток 20 эритроцитов, выходящих из сепаратора 108, с целью контроля скорости каждого на основании внутреннего диаметра трубок 103 и 110.

В варианте осуществления с фиг. 12 также используется дополнительный датчик 117b давления для отслеживания встречного давления из фильтра 113 лейкоцитов. Если встречное давление станет чрезмерным, как в случае закупорки фильтра, датчик будет 25 осуществлять управление скоростью потока с целью обеспечения того, чтобы одноразовые элементы не разрывались вследствие избыточного давления.

### III. Заливка мембраны

В соответствии с другим аспектом изложения, представлен способ для заливки мембранного фильтра, посредством которого повышается вероятность того, что будет 30 достигнуто смачивание максимальной величины площади поверхности мембранного фильтра, в результате чего максимизируется площадь мембраны, доступная для фильтрации/разделения. В частности, когда система фильтра с вращающейся мембраной заливается в соответствии с описанным выше, при этом вращающаяся мембрана ориентирована таким образом, что ось вращения является, по существу, вертикальной, 35 раствор для заливки входит в верхний впускной канал вращающегося сепаратора, и гравитация направляет жидкость к выпуску на дне сепаратора. В таких обстоятельствах поверхностное натяжение жидкости заливки будет формировать поверхность раздела воздух-жидкость, которая может передвигаться неравномерно по поверхности мембраны, создавая нарушения. В результате этого определенные области мембраны 40 фильтра не будут увлажняться во время заливки, что повышает потенциал захвата воздуха матрицей мембраны. Таким образом, неувлажненная область мембраны становится недоступной для разделения, что негативно сказывается на эффективности разделения мембраной, до тех пор пока не будет создано достаточное давление для вытеснения воздуха.

45 Соответственно, представлен способ для заливки мембранного сепаратора, который позволяет равномернее смочить поверхность мембраны посредством обеспечения более равномерной поверхности раздела воздух-жидкость во время заливки. С этой целью жидкость заливки вводится в сепаратор таким образом, что она работает против силы



тяжести при продвижении поверхности раздела жидкость-воздух в верхнем направлении через поверхность мембраны. Это помогает обеспечить более равномерное смачивание мембраны, поскольку воздух, вытесненный во время заливки, может перемещаться в одном направлении, не будучи захваченным, при продвижении поверхности раздела  
 5 воздух-жидкость через мембрану.

Таким образом, в соответствии с данным альтернативным способом для заливки, жидкость заливки вводится в сепаратор через канал на дне сепаратора. Раствор для заливки продвигается вверх в корпусе сепаратора против силы тяжести для смачивания поверхности мембраны, при этом воздух выталкивается из сепаратора через канал на  
 10 верху сепаратора. Хотя такая заливка “снизу вверх” описывается в контексте сепаратора с вращающейся мембраной, оно также применима к мембранному сепаратору любого типа, которому требуется заливка жидкостью до начала использования.

В соответствии с фиг. 9 и 12, сепаратор 108 ориентирован вертикально, при этом мембранный сепаратор и корпус могут вращаться друг относительно друга вокруг, в  
 15 общем смысле, вертикальной оси, при этом канал для приема цельной крови расположен на верху сепаратора и каналы, через которые выходят отделенные эритроциты и плазма, расположены внизу сепаратора. Таким образом, в соответствии с одним из путей выполнения данного альтернативного способа заливки, и в соответствии с фиг. 1 и 2, раствор для заливки может быть введен через выходное отверстие 34 или выпускное  
 20 отверстие 46 плазмы сепаратора с вращающейся мембраной 10, при этом воздух выталкивается через впускное отверстие 22. В соответствии с другим путем выполнения данного альтернативного способа заливки, сепаратор 10 может быть инвертирован или перевернут для заливки, с тем чтобы выходное отверстие 34 и выпускное отверстие 46 плазмы находились на верху сепаратора 10, и впускное отверстие 22 находилось  
 25 внизу сепаратора 10. Раствор для заливки может затем быть введен через впуск 22, при этом поверхность раздела жидкость-воздух продвигается вверх, и воздух выталкивается через выходное отверстие 34 или выпускное отверстие 46 плазмы, или через оба отверстия. После заливки, сепаратору 10 может быть возвращена его исходная ориентация, в которой впускное отверстие 22 находится наверху, и выходное отверстие  
 30 34 и выпускное отверстие 46 плазмы находятся внизу.

Еще одна альтернатива, в которой может быть использована заливка “снизу вверх” сепаратора 108 крови, описанная выше, показана на фиг. 12A. В отличие от фиг. 12, впускная линия 107 для цельной крови соединяется с более низким каналом сепаратора 108 (к которому была присоединена выпускная линия 110 в варианте осуществления с  
 35 фиг. 12), тогда как выпускная линия 110 соединена с каналом на верху сепаратора 108 (к которому была присоединена впускная линия 107 в варианте осуществления с фиг. 12). Для заливки системы с фиг. 12A, фиксатор 116B открывается и насос 106 активируется для создания потока цельной крови (предпочтительно, с добавленным противосвертывающим средством) через впускную линию 107 таким образом, чтобы он входил в сепаратор 108 через канал в более низком конце корпуса. При заполнении  
 40 цельной кровью корпуса сепаратора воздух выталкивается через верхний канал, с тем чтобы удалить, по существу, весь воздух из устройства и осуществить смачивание мембраны фильтра.

После завершения заливки, система продолжает функционировать, как показано на  
 45 фиг. 12A, для разделения цельной крови на плазму, принимаемую в контейнере 112, и эритроциты, принимаемые в контейнере 115. В конце процедуры разделения сепаратор может промываться раствором добавки из контейнера 102.

Обратимся к фиг. 14 и 15, на которых показана еще одна альтернативная система

разделения крови в соответствии с настоящим изложением. Система с фиг. 14 и 15 аналогична системам с фиг. 9, 11 и 12, за исключением того, что модуль В содержит третий насос 119 для избирательного закачивания раствора добавки в сепаратор 108 в течение фазы заливки (как показано на фиг. 14), или к отделенным эритроцитам во время фазы разделения (как показано на фиг. 15). Система с фиг. 14 и 15 также содержит дополнительный фиксатор 120 для избирательного разрешения или предотвращения потока жидкости (отделенных эритроцитов и раствора добавки) через лейкофильтр 113 и в контейнер 115 эритроцитов. До начала заливки фиксатор 20 может недолго оставаться открытым, и насос 109 может выкачивать остаточный воздух из контейнера 115 и фильтра 113, минимизируя объем воздуха, остающийся в контейнере 115 в конце данной процедуры. Как и на фиг. 12А, в системе с фиг. 14 и 15 используется заливка “снизу вверх” сепаратора 108, за исключением использования раствора добавки в качестве жидкости для заливки вместо цельной крови. В течение заливки системы, как показано на фиг. 14, воздух из одноразовой системы А выталкивается в контейнер 101 цельной крови.

В течение фазы разделения система функционирует как показано на фиг. 15.

При завершении фазы разделения раствор добавки закачивается в сепаратор 108 (как показано в фазе заливки, проиллюстрированной на фиг. 14) для промывания сепаратора.

Обратимся к фиг. 15А, на которой показана еще одна альтернативная система. Система с фиг. 15А аналогична системе с фиг. 14 и 15 в том, что многоразовый компонент В содержит три насоса 106, 109 и 119. Однако система с фиг. 15А аналогична системе с фиг. 12А в том, что впускная линия 107 для цельной крови соединена с каналом внизу сепаратора 108, тогда как выпускная линия для отделенных эритроцитов соединена с каналом на верху сепаратора. Таким образом, в системе с фиг. 15А цельная кровь используется для заливки системы аналогично системе с фиг. 12А.

#### IV. Системы и способы управления данными

Система, описанная в настоящем описании, также может включать в себя решения по управлению данными. Весы и добавление устройств печатания этикеток к системе позволило бы пользователям получать этикетки с весом продукта напрямую из системы разделения по завершении процедуры. Это устраняет ручное взвешивание и запись данных, используемые в текущих способах обработки. Модуль В может содержать подходящий пользовательский интерфейс, такой как сенсорный экран, кнопочную панель или клавиатуру, а также сканер, чтобы предоставить пользователям возможность ввода информации, такой как пользовательский номер идентификации донора, идентификатор банка крови, номера набора жидкостного контура, номера партии, и т.д., которая также может улучшить эффективность управления данными в центрах производства крови.

Конкретнее, и в соответствии с еще одним аспектом настоящего изложения, представлен способ для автоматизации передачи данных, ассоциированных с контейнером для сбора цельной крови, а также другой относящейся к делу информации, в устройство обработки данных, используемое для последующего разделения цельной крови и конечного хранения контейнера или контейнеров для такого отделенного компонента или компонентов крови. Данный способ схематически проиллюстрирован на блок-схеме с фиг. 29, где представлен исходный контейнер (этап 122), который обычно содержит единицу ранее собранной цельной крови, хотя исходный контейнер может содержать ранее обработанный продукт крови. Исходный контейнер обычно имеет ассоциированные с ним данные, относящиеся к идентификации донора и времени,

места сбора и т.д., при этом такие данные предпочтительно находятся в машиночитаемом формате, таком как штрихкод или метка RFID. Эти данные затем извлекаются и передаются (этап 124), и затем ассоциируются с устройством обработки данных и контейнерами конечного хранения (этап 126).

5 Обратимся к фиг. 30, на котором показана одна из возможных систем для применения в качестве системы управления данными в соответствии с настоящим изложением. Представлен контейнер 128 для сбора крови и отдельное устройство 130 обработки данных, имеющее три контейнера 132, 134 и 136 для конечного хранения. Во время  
10 взятия цельной крови, информация идентификации донора кодируется и ассоциируется с контейнером для собранной цельной крови. Это может быть выполнено путем ручного помещения этикетки со штрихкодом для идентификатора донора на этикетку контейнера, иглу контейнера или трубки. Также это можно сделать посредством применения записывающего устройства RFID в месте сбора, передающего  
15 идентификатор донора с весов сбора или портативного устройства на метку RFID, прикрепленную к контейнеру для сбора. Использование RFID позволяет управлять большим объемом информации, включая такие данные, как тип контейнера, дата истечения срока годности, время сбора, объем сбора, идентификатор медсестры, место сбора и т.п.

Автоматизированная передача данных между контейнером 128 для сбора и  
20 комплектом 130 обработки/контейнерами 132, 134, 136 для хранения может происходить в контексте стерильного соединения контейнера 128 для сбора с комплектом 130 обработки. Например, может быть использована электромеханическая система, которая выполняет стерильное соединение контейнера для сбора цельной крови с комплектом обработки. Такая система изложена в предварительных заявках на патент США No.  
25 61/578690 и 61/585467, поданных 21 декабря 2011 и 11 января 2012, соответственно, которые включены в настоящее описание посредством ссылки. Устройство стерильного соединения может являться отдельно стоящим, как показано в указанных выше предварительных заявках, или может быть интегрировано с многократным модулем В, описанным выше. Альтернативно, система управления данными может быть просто  
30 связана с многократным модулем В, без устройства стерильного соединения, ассоциированного с ними. В любом случае устройство стерильного соединения или многократный модуль содержит программируемый контроллер, сконфигурированный для автоматического выполнения, или запроса выполнения пользователем, различных этапов способа управления данными, в соответствии с подробнее описанным ниже.

35 Система управления данными 138 включает в себя блок обработки, экран 140 для предоставления информации пользователю (такой как запросы и подтверждения), сенсорную панель 142 для предоставления пользователю возможности ввода информации и сканер/считыватель 144 для извлечения и передачи информации между контейнером 128 для сбора и комплектом 130 обработки. Система 138 также  
40 обеспечивает печать этикеток со штрихкодом или передачу данных на одну или более меток RFID, ассоциированных с комплектом обработки. Обратимся теперь к фиг. 31, на которой показана блок-схема, иллюстрирующая в общих чертах способ управления данными. Способ включает в себя загрузку пакета для сбора и комплекта обработки на многократный модуль и/или в устройство стерильного соединения (этап 140).  
45 Извлекаются данные, ассоциированные с комплектом обработки и данные, ассоциированные с контейнером для сбора (этапы 142 и 144). Как можно понять, порядок, в котором выполняются данные этапы, не является критичным. Как отмечалось выше, эти данные могут принимать форму штрихкода, метки RFID или другую форму,

при этом комплект обработки и ассоциированные с ним контейнеры для сбора имеют соответствующие данные из контейнера для сбора, ассоциированного с ними. Это может принимать форму печати этикеток со штрихкодами или записи данных на метку RFID (этапы 146 и 148). Контейнер для сбора и комплект обработки соединены друг с другом, предпочтительно в процедуре стерильного соединения (этап 150), при этом такое соединение происходит в период времени в течение последовательности выполнения описанных выше этапов.

Затем кровь в контейнере для сбора обрабатывается (этап 152). Затем информация комплекта обработки/контейнера для хранения извлекается и проверяется с использованием данных контейнера для сбора (этапы 154 и 156). После такой проверки контейнеры для хранения могут быть отсоединены от контейнера для сбора (этап 158).

Система по настоящему изложению помогает пользователю в выполнении этапов, описанных выше, тем, что она выдает запросы и подтверждения для различных этапов. Например, если идентифицирующая информация имеет форму штрихкода, то система запрашивает у пользователя сканирование идентификатора штрихкода комплекта обработки и идентификатора донора контейнера для сбора. Система будет затем печатать копии этикеток штрихкодов на принтере, который является частью системы или присоединен к ней, при этом тип и количество этикеток определяется типом загруженного комплекта обработки. Система затем запрашивает у пользователя нанесение этикеток со штрихкодом на контейнеры конечного хранения. После того как система разделяет кровь на ее компоненты, система запрашивает у пользователя сканирование идентификаторов штрихкода контейнера с конечными компонентами, с тем чтобы система могла проверить правильность информации штрихкода до отсоединения контейнеров для хранения от контейнера для сбора и комплекта обработки.

Если идентифицирующая информация ассоциирована с меткой RFID, то система автоматически сканирует метку RFID на контейнере для сбора и затем автоматически считывает информацию на RFID, включенной в комплект обработки. Затем система автоматически копирует информацию контейнера для сбора на метку или метки RFID, ассоциированные с контейнерами для хранения комплекта обработки. После того как система разделит кровь на ее компоненты, в соответствии с типом комплекта обработки, определенным инструментом, система будет считывать метку RFID на контейнерах конечных компонентов для обеспечения возможности проверки идентифицирующей информации до отсоединения контейнеров для хранения крови от комплекта обработки и контейнера для сбора.

Предполагается, что система может использовать и штрихкод, и RFID в качестве избыточных систем, и может включать некоторые или все этапы, описанные выше, в зависимости от конкретного случая. Хотя сканер штрихкодов/считыватель RFID описан как ассоциированный с многоразовым модулем В, он может представлять собой выделенную станцию, физически отдельную от самой машины обработки, но соединенную через программное обеспечение управления данными.

Хотя данный способ управления данными был описан в связи со сбором цельной крови в контейнер, отдельный от комплекта обработки и контейнеров для хранения, он с таким же успехом может использоваться в связи с системой или комплектом, в котором контейнер для сбора составляет одно целое с комплектом обработки и его контейнерами для хранения. Кроме того, способ может быть использован в связи с обработкой цельной крови, полученной напрямую у донора, как описано ниже, при этом данные идентификации донора предоставляются донором, а не контейнером для

сбора, или в процедуре промывания клеток, при этом данные идентификации ассоциированы с исходным контейнером.

#### V. Системы и способы для обработки цельной крови донора

В соответствии с еще одним аспектом настоящего изложения, сепаратор с вращающейся мембраной, описанный выше, может быть выгодно использован в одном этапе или в “кабинетном” сборе и разделении цельной крови на компоненты крови. Как описано ниже, представлена автоматизированная система сбора цельной крови, которая разделяет цельную кровь на одну единицу эритроцитов и плазму одновременно при взятии цельной крови у донора. Предполагается, что система является системой сбора “за один проход”, без реинфузии компонентов крови обратно донору. Система, предпочтительно, содержит одноразовый контур потока жидкости и долговременный многократный контроллер, который взаимодействует с контуром и управляет потоком жидкости через него. Контур потока, предпочтительно, представляет собой одноразовый предварительно простерилизованный контур потока жидкости, который, предпочтительно, содержит контейнеры для сбора эритроцитов и плазмы, противосвертывающее средство и растворы добавки эритроцитов, сепаратор и фистулу для обеспечения прохождения цельной крови от донора в жидкостный контур. Долговременный контроллер, предпочтительно, содержит управляемое микропроцессором электромеханическое устройство с механизмами клапанов, насосов и датчиков, сконфигурированными для управления потоком через контур, а также содержит системы безопасности и сигнальные функции, подходящие для процедуры взятия цельной крови.

Способ взятия крови с применением системы включает в себя выполнение прокола вены донора и извлечение цельной крови из донора в одноразовый контур, в котором она обрабатывается аппаратурой и компонентами жидкостного контура, в результате чего цельная кровь разделяется на желаемые компоненты эритроцитов и плазмы. Донор остается подключенным к системе в течение процедуры, и все жидкости остаются в линии тока одноразового набора до завершения процедуры. В “однопроходной” системе цельная кровь, предпочтительно, проходит через жидкостный контур только один раз, и ни один из компонентов крови не возвращается донору.

Эритроциты, получаемые в результате сбора, не обязательно должны подвергаться процессу лейкоредукции. Однако лейкоредукция посредством фильтрации может быть осуществлена с помощью фильтра лейкоредукции, предпочтительно, встроенного в одноразовый контур, или посредством использования отдельного контура обработки, который стерильно соединен с контейнером для сбора эритроцитов.

Аппаратура, предпочтительно, содержит интерфейс оператора, такой как сенсорный экран, кнопочная панель, мышь, клавиатура и т.д., для ввода информации и/или отображения информации. Индикатор сообщения позволяет оператору контролировать процедуру, собирать информацию о ее статусе и устранять любые сбойные ситуации при их появлении.

Обратимся к чертежам; на фиг. 16-19 можно видеть схематическое представление системы автоматизированного сбора цельной крови под общим обозначением 210, в соответствии с настоящим изложением, на различных стадиях или фазах функционирования. Система, предпочтительно, содержит многократный компонент 212 аппаратного обеспечения, который, предпочтительно, содержит насосы, фиксаторы и датчики давления для управления потоком жидкости, а также одноразовый предварительно собранный стерильный компонент 214 жидкостного контура, который может быть установлен на компонент аппаратного обеспечения и содержит различные

контейнеры/мешки, устройство доступа к донору или фистулу, и камеру разделения крови, при этом все элементы соединены друг с другом через стерильный маршрут жидкости, такой как гибкие пластиковые трубки. Контейнеры/мешки обычно являются сгибаемыми и сделаны из подходящего пластикового материала, хорошо известного в технике. Материал контейнеров может различаться в зависимости от применения, и может содержать непластифицированные материалы, такие как не содержащие ДЕНР полимеры, в частности, но не только, для хранения эритроцитов.

Конкретнее, проиллюстрированный компонент или модуль 214 жидкостного контура содержит устройство 216 доступа к донору, которое содержит первый отрезок трубок 218 в качестве линии извлечения, через которую цельная кровь извлекается из донора и вводится в жидкостный контур 214. Устройство 216 доступа к донору, предпочтительно, содержит иглу, в частности, малокалиберную иглу (18-21 калибра) с целью повышения комфорта донора, с наличием предохранителя иглы, при необходимости, для предотвращения случайных проколов иглой. Трубки 218 взаимодействуют с устройством разделения крови под общим обозначением 220 и, как описано выше, используются для введения цельной крови в сепаратор.

Второй отрезок трубок 222 обеспечивает обмен жидкостями между сепаратором 220 и первым контейнером/мешком 224 для приема отделенных концентрированных эритроцитов, тогда как третий отрезок трубок 226 обеспечивает обмен жидкостями между сепаратором 220 и вторым контейнером/мешком 228 для приема плазмы.

Жидкостный контур 214 также содержит источник противосвертывающего средства (например, CPD), которое находится в третьем контейнере 230, который взаимодействует с первым отрезком трубок 218 посредством четвертого отрезка трубок 232, соединенного с трубками 218, например, посредством Y-соединителя. Жидкостный контур 214 также может содержать источник раствора консерванта для эритроцитов, которые должны быть доставлены в контейнер/мешок 224. Раствор консерванта может находиться в отдельном мешке, связанном с контейнером 224. Альтернативно, контейнер 224 может быть предварительно заполнен объемом раствора консерванта, соответствующим количеству эритроцитов, которые будут приняты им в течение процедуры сбора.

Жидкостный контур 214 также содержит встроенную систему 234 взятия проб для асептического взятия проб крови до и в течение процедуры сдачи крови. Система 234 взятия проб содержит мешок, который взаимодействует с первым отрезком трубок 218 устройства доступа к донору через пятый отрезок трубок 236, расположенный выше по ходу потока относительно соединения между трубками 218 и трубками 232, через которые вводится противосвертывающее средство. Трубки 236, предпочтительно, взаимодействуют с трубками 218 через Y-соединитель или аналогичное устройство.

Долговременный компонент 212 аппаратного обеспечения, предпочтительно, содержит первый насос 238, который взаимодействует с трубками 218 для закачивания цельной крови в устройство 220 разделения и второй насос 240, который взаимодействует с трубками 222 для транспортировки, по существу, концентрированных эритроцитов из камеры 220 разделения в первый контейнер 224 для сбора. Насосы 238, 240 являются, предпочтительно, перистальтическими, или роликовыми, насосами, которые включают в себя ротор с одним или более роликами для сжатия трубок с целью обеспечения движения жидкости через них, хотя также могут быть использованы другие подходящие конструкции насосов, такие как насосы с гибкой диафрагмой. Компонент аппаратного обеспечения также, предпочтительно, содержит третий насос 242, который взаимодействует с трубками 232 для транспортировки противосвертывающего средства к трубкам 218 линии извлечения, через которые цельная кровь транспортируется в

сепаратор 220. Третий насос 242 обеспечивает дозирование потока противосвертывающего средства, и также способствует смачиванию и промыванию системы, как будет описано ниже. Однако третий насос 242 является необязательным, и противосвертывающее средство может дозироваться в линии извлечения 218 цельной крови посредством гравитационного потока, при этом трубки 232 имеют размер, обеспечивающий необходимую скорость потока в течение процедуры сбора.

Компонент 212 аппаратного обеспечения также, предпочтительно, содержит фиксаторы 244, 246, 248 и 250 для избирательной закупорки и открытия сегментов трубок 218, 232, 222 и 226, соответственно. Термин “фиксаторы” используется в настоящем документе в широком смысле, и включает в себя любой механизм, который взаимодействует с маршрутами потока, например, сегментами трубок жидкостного контура, с целью избирательного разрешения или предотвращения потока жидкости через них. Компонент 212 аппаратного обеспечения также, предпочтительно, содержит датчики 252, 254 давления в трубках 218 линии извлечения вблизи или смежно с иглой (датчик 252 давления) и вблизи или смежно с впуском сепаратора 220 (датчик 254 давления) для контроля впускного давления, например, для обнаружения коллапса вены. Также, предпочтительно, представлены весы (не показаны) по меньшей мере для первого контейнера 224 с целью предоставления обратной связи относительно объема собранных эритроцитов.

В соответствии с другим аспектом изложения, многоходовый компонент аппаратного обеспечения, предпочтительно, содержит программируемый контроллер 256 для приведения в действие насосов и фиксаторов и контроля датчиков давления и весов, с тем чтобы процедура сбора цельной крови могла быть, по существу, автоматизирована. Контроллер 256 содержит программируемый микропроцессор и, предпочтительно, включает в себя интерфейс оператора, такой как сенсорный экран и индикатор сообщения для обеспечения оператору возможности входа и просмотра данных и управления процедурой, сбора информации по ее статусу и устранение любых сбойных ситуаций при их появлении.

Для выполнения автоматизированной процедуры сборки и разделения с помощью автоматизированной системы 210 сбора крови, изложенной выше, одноразовый жидкостный контур 214 загружается в рабочее положение на многоходовом компоненте 212 аппаратного обеспечения, как показано на фиг. 16 в прилагаемых чертежах. В фазе или стадии, показанной на фиг. 16, система заливается жидкостью для существенного удаления воздуха и смачивания мембраны фильтра. На начальной стадии первый фиксатор 244 закрыт, с тем чтобы предотвратить обмен жидкостями между устройством 216 доступа к донору и камерой 220 разделения крови, и противосвертывающее средство прокачивается насосами 240 и 242 через трубки 218, сепаратор 212 и трубки 222 с целью заливки системы. Затем выполняется прокол вены донора с помощью иглы устройства доступа к донору с целью принятия цельной крови в трубки 218. В этот момент могут быть взяты пробы цельной крови посредством пакета 234 сбора проб.

Обратимся к фиг. 17; после заливки первый фиксатор 244 открывается для пропускания цельной крови через трубки 218 в сепаратор 220 крови, с помощью насоса 238, для начала фазы сбора/разделения процедуры сбора. Противосвертывающее средство продолжает дозироваться в линии извлечения сегмента 218 трубки через сегмент 232 трубки посредством третьего насоса 242. Эритроциты выходят из сепаратора 220 через трубки 222. Четвертый фиксатор 250 открывается для того, чтобы позволить плазме выйти из сепаратора 220 и пройти через трубку 226 во второй контейнер 228 для сбора. Первый насос 238 выдает поток цельной крови в сепаратор 220, при этом

впускное давление контролируется датчиком 254, тогда как эритроциты закачиваются из камеры 220 для разделения посредством второго насоса 240. Перепад расхода между первым насосом 238 и вторым насосом 240 обеспечивает выход отделенной плазмы из сепаратора 220 во второй контейнер 228 для сбора.

5 Обратимся к фиг. 18; когда объем эритроцитов в первом контейнере 224 для сбора достигает предварительно определенного объема (измеренного через вес первого контейнера 224 для сбора, определенный посредством весов), весы выдают контроллеру 256 сигнал, который запрашивает у контроллера завершение процедуры сбора посредством закрытия первого фиксатора 244, вследствие чего происходит закупорка  
10 линии 218 извлечения. Устройство 216 доступа к донору может быть извлечено из донора в этот момент. Если система должна промываться, то четвертый фиксатор 250 закрывается с целью закупорки для плазмы линии 226 потока ко второму контейнеру 228 для сбора. Первый насос 238 деактивируется, тогда как третий насос 242 продолжает доставлять противосвертывающее средство в сепаратор 220, при этом  
15 противосвертывающее средство выпускается в первый контейнер 224 для сбора через сегмент 222 трубки.

Обратимся к фиг. 19; после завершения цикла промывания, второй фиксатор 246 и третий фиксатор 248 закрываются, и второй насос 240 и третий насос 242 деактивируются.

20 В этот момент первый контейнер 224 для сбора, содержащий, по существу, концентрированные эритроциты, может быть отсоединен от одноразового жидкостного контура 214 для хранения или для способствования лейкофильтрации. Это может быть выполнено путем простого подвешивания контейнера 224 для сбора и допущения гравитационной фильтрации эритроцитов через фильтр лейкоредукции в контейнер для  
25 конечного хранения. Однако, в соответствии с другим аспектом изложения, и как показано на фиг. 20, может быть представлен третий контейнер 258 для сбора, который находится в жидкостном взаимодействии со вторым контейнером 224 для сбора через сегмент 260 трубки, при этом сегмент 260 трубки находится в жидкостном взаимодействии с сегментом 220 трубки через Y-соединитель, расположенный на  
30 сегменте 222 трубки между выпуском сепаратора 220 и вторым насосом 240. Затем может быть открыт третий фиксатор 248 для разрешения выходного потока концентрированных эритроцитов из контейнера 224 для сбора, при этом второй насос 240 активируется и выполняет закачку в обратном направлении для обеспечения потока концентрированных эритроцитов через фильтр редукции лейкоцитов 262 и в контейнер  
35 для сбора 258. Давление, созданное насосом 240, значительно ускоряет процесс фильтрации по сравнению с вызываемой гравитацией лейкофильтрацией эритроцитов.

В качестве еще одной альтернативы, лейкоредукция может быть выполнена в отношении цельной крови в течение фазы извлечения в процессе эксплуатации. Обратимся к фиг. 21 и 22; линия извлечения трубки 218 может содержать фильтр 264  
40 редукции лейкоцитов, который находится в одной линии с трубкой 218. Фильтр 264 расположен против направления потока от первого насоса 238, с тем чтобы насос прилагал достаточную силу извлечения к крови для ее извлечения через фильтр 264 во время сбора. Лейкофильтр 264 может быть расположен в сегменте 218 трубки, против направления потока относительно места, где противосвертывающее средство вводится  
45 в систему (как показано на фиг. 21) или по направлению потока относительно места, где противосвертывающее средство вводится в линию 218 извлечения (как показано на фиг. 22). Размещение по направлению потока от места подсоединения противосвертывающего средства позволяет использовать противосвертывающее



средство для смывания любой остающейся цельной крови из фильтра 264 после завершения извлечения из донора. Кроме того, размещение фильтра лейкоредукции в трубках 218 линии извлечения устраняет необходимость отдельного этапа фильтрации лейкоредукцией внизу по направлению потока, таким образом, дополнительно оптимизируя процесс сбора крови.

Ожидается, что автоматизированные однопроводные система и способ сбора цельной крови, описанные в настоящем описании, улучшат эффективность центра сбора крови и снизят расходы по эксплуатации путем выполнения разделения цельной крови на компоненты эритроцитов и плазмы без необходимости последующих ручных операций.

Кроме того, использование малокалиберных игл в устройствах доступа к донору, используемых в системе, должно повысить комфорт донора, тогда как использование вытяжного насоса позволяет системе достичь времени взятия, аналогичного обычному сбору цельной крови. Кроме того, за счет управления сбором цельной крови посредством микропроцессора предоставляется больше возможностей для управления данными, которых обычно не имеется в текущих способах ручного сбора цельной крови, включая использование интегрированных считывателей штрихкодов и/или технологии RFID, в соответствии с описанным выше.

В соответствии с другим аспектом изложения, ниже описаны способы, системы и устройства, пригодные для промывания биологических клеток, таких как клетки крови или другие компоненты крови или биологические компоненты.

#### VI. Системы и способы для промывания клеток

Промывание биологических клеток может иметь несколько целей. Например, промывание клеток может использоваться для замены жидкой среды, в которой биологические клетки суспендированы. В этом случае вторая жидкая среда добавляется для замены и/или разбавления исходной жидкой среды. Части исходной жидкой среды и замещающей жидкой среды отделяются от клеток. Дополнительные замещающие жидкие среды могут добавляться до тех пор, пока концентрация исходной жидкой среды не станет ниже определенной процентной величины. В дальнейшем клетки могут быть суспендированы, например, в замещающей среде.

Промывание клеток также может быть использовано для концентрирования или дополнительного концентрирования клеток в жидкой среде. Клетки, суспендированные в жидкой среде, промываются, в результате чего часть жидкой среды отделяется и удаляется из клеток.

Кроме того, промывание клеток может быть использовано для удаления нежелательных твердых частиц, таких как крупные твердые частицы, или нежелательного клеточного материала из взвеси клеток конкретного размера, или для “очистки” желаемой взвеси клеток или другой жидкости.

Способ, системы и устройство, описанные ниже, могут быть применены для промывания клеток по любой из описанных выше причин. В частности, но без ограничения, способы, системы и устройство, описанные ниже, могут быть применены для промывания клеток крови, таких как эритроциты, или белые клетки крови (лейкоциты), или тромбоциты.

В одном конкретном варианте осуществления взвесь, содержащая белые клетки крови в жидкой культуральной среде, может промываться с целью замены культуральной среды на другую среду, такую как физиологический раствор, до начала использования или дополнительной обработки. Взвесь клеток, содержащая белые клетки крови в жидкой культуральной среде, может доставляться и вводиться в сепаратор, такой как сепаратор с вращающейся мембраной. Сепаратор с вращающейся

5 мембраной имеет мембранный фильтр с размером пор, меньшим, чем размер белых клеток крови. В одном из вариантов осуществления, жидкая среда для промывания, содержащая замещающую жидкую среду, такую как физиологический раствор, также добавляется в сепаратор для разбавления жидкой культуральной среды. Сепаратор функционирует таким образом, что жидкости проходят через поры мембраны и  
 10 извлекаются как отходы. В данном варианте осуществления, при извлечении жидкости добавляется среда для промывания, в результате чего полученная взвесь клеток содержит белые клетки крови, суспендированные в замещающей жидкой среде (например, физиологическом растворе).

10 В другом варианте осуществления, взвесь клеток может подвергаться концентрированию (посредством удаления супернатанта) и сбора взвеси концентрированных клеток в контейнер набора обработки. Замещающая жидкость может быть введена в сепаратор, объединена с концентрированными клетками в контейнере, и затем клетки могут быть ресуспендированы в замещающей жидкости.  
 15 При необходимости ресуспендированные клетки/замещающая жидкость могут быть введены в сепаратор для дальнейшего концентрирования клеток, удаления супернатанта и ресуспендирования концентрированных клеток в дополнительной замещающей жидкости. Данный цикл может быть повторен при необходимости.

Аналогичные процессы могут быть применены для промывания эритроцитов, суспендированных в жидкой среде хранения. Взвесь клеток, содержащая эритроциты, суспендированные в жидкой среде хранения, может промываться с целью замещения жидкой среды хранения на другую среду, такую как физиологический раствор, до начала использования или дополнительной обработки. Взвесь клеток доставляется и вводится в сепаратор, такой как сепаратор с вращающейся мембраной. Сепаратор с  
 25 вращающейся мембраной имеет мембранный фильтр с размером пор, меньшим, чем размер эритроцитов. В одном из вариантов осуществления, среда для промывания, то есть замещающая жидкая среда, такая как физиологический раствор, также может добавляться в сепаратор для разбавления жидкой среды хранения. Сепаратор функционирует таким образом, что жидкость проходит через поры мембраны и  
 30 извлекается как отход. При извлечении жидкости добавляется среда для промывания, в результате чего полученная взвесь клеток содержит эритроциты, суспендированные в замещающей жидкой среде (то есть, физиологическом растворе). Жидкость для промывания и/или замещающая жидкость также может являться средой для хранения, которая содержит питательные вещества и другие компоненты, которые позволяют  
 35 осуществлять долговременное хранение клеток. Альтернативно, в другом варианте осуществления, эритроциты могут сначала быть сконцентрированы и удалены в контейнер, как в общих чертах описано выше. Замещающая жидкость может затем быть объединена с эритроцитами в контейнере. Замещающая жидкость может быть введена в контейнер напрямую, или может быть введена в сепаратор и через сепаратор,  
 40 и затем в контейнер.

Системы, способы и устройство для промывания клеток, описанные в настоящем документе, используют одноразовый набор, который включает в себя сепаратор, такой как сепаратор с вращающейся мембраной. Одноразовый набор с сепаратором с вращающейся мембраной устанавливается на компонент аппаратного обеспечения  
 45 системы, то есть устройство разделения. Устройство разделения содержит фиксаторы, насосы, двигатели, датчики обнаружения воздуха, измерительные датчики давления, Нв-детекторы, весы, и управляющую логическую схему/микропроцессор, включенную в микропроцессор. Управляющая логическая схема/микропроцессор принимает входные

данные и сигналы от оператора и/или различных датчиков, и управляет функционированием фиксаторов, насосов и двигателей.

Взвесь клеток, которая будет промываться, то есть клетки, суспендированные в среде, могут быть представлены в стерильном одноразовом исходном контейнере, который соединен, стерильным образом, с одноразовым набором. Среда для промывания, такая как физиологический раствор, или другая подходящая среда, также соединяется стерильным образом или предварительно прикрепляется к одноразовому набору. Управляющая логическая схема устройства управляет фиксаторами и насосами для передачи взвеси клеток через трубки одноразового набора на сепаратор (с вращающейся мембраной). Устройство разделения, через свою систему управления, также направляет раствор для промывания через трубки одноразового набора на сепаратор с вращающейся мембраной. Взвесь клеток и раствор для промывания могут быть смешаны внутри сепаратора с вращающейся мембраной, могут быть смешаны до введения в сепаратор с вращающейся мембраной, или могут быть объединены в контейнере, после того как взвесь клеток была сконцентрирована. Внутри сепаратора с вращающейся мембраной среда суспендирования отделяется от клеток, суспендированных в ней. Среда суспендирования и оставшаяся среда для промывания (если среда суспендирования и среда для промывания были объединены) выходит через канал для отходов, тогда как клетки проходят через отдельный выходной канал.

Если необходимо дальнейшее промывание и разбавление, то промытые клетки могут быть повторно пропущены через сепаратор с дополнительным объемом раствора для промывания. В одном из вариантов осуществления, клетки, которые должны промываться повторно, могут передаваться в один или более рабочих контейнеров, как будет описано ниже. Управляющая логическая схема устройства управляет фиксаторами и насосами для передачи взвеси клеток из рабочего контейнера через трубки на впуск сепаратора с вращающейся мембраной или на впуск второго сепаратора с вращающейся мембраной. Добавляется дополнительная среда для промывания, и процесс повторяется до тех пор, пока не будет достигнут приемлемый объем или концентрация клеток. Конечная взвесь клеток, содержащая клетки, предпочтительно, собирается в контейнере конечного продукта.

В соответствии с настоящим изложением, на фиг. 23-25 показаны примеры систем, подходящих для промывания биологических клеток, таких как эритроциты и белые клетки крови, но не ограничиваясь указанным. Как отмечалось выше, предполагается, что изложенные конкретные варианты осуществления являются примерами и не являются ограничивающими. Таким образом, в одном из вариантов осуществления, система, описанная в настоящем описании, содержит одноразовый набор 300 (фиг. 23 или 24) и компонент аппаратного обеспечения или устройство 400 (фиг. 25). Следует понимать, что одноразовые наборы 300 обработки, показанные на обеих фиг. 23 и 24, идентичны во многих отношениях, и общие цифровые обозначения используются на обеих фиг. 23 и 24 для идентификации идентичных или аналогичных элементов одноразовых наборов обработки. В той степени, в которой одноразовые наборы обработки различаются в структуре или в их использовании, такие различия обсуждаются ниже. Одноразовый набор 300 устанавливается на устройство 400 (фиг. 25), которое подробнее описывается ниже.

Как показано на фиг. 23-24, сепаратор 301 является частью типового одноразового набора 300. Дополнительно, как будет подробнее описано ниже, одноразовый набор 300 содержит трубки, Y-соединители, рабочий(-е) пакет(-ы), мешок(-ки) с пробами, пакет(-ы) конечного продукта, пакет(-ы) с отходами и стерильный(-е) фильтр(-ы).

Взвесь клеток, которая будет промываться, обычно представлена в исходном контейнере 302, показанном на фиг. 23 и 24 отсоединенным от одноразового набора. Как отмечалось выше, исходный контейнер 302 может быть прикреплен (стерильным образом) во время использования. Исходный контейнер 302 имеет один или более  
 5 каналов 303, 305 приема, один из которых может быть приспособлен для приема гвоздевого соединителя 304 (фиг. 23) одноразового набора 300. Конкретнее, исходный контейнер 302 соединен с одноразовым набором 300 через гвоздевой соединитель 304, который может соединяться с каналом 303 доступа. Более предпочтительно, однако, чтобы исходные контейнеры (и жидкости в них) не имели гвоздевого соединителя (как  
 10 показано на фиг. 24), и чтобы доступ к ним осуществлялся стерильным образом посредством использования стерильных стыковочных устройств, таких как BioWelder, поставляемое компанией Sartorius AG, или SCD IIB Tubing Welder, поставляемое компанией Terumo Medical Corporation. Также может быть представлен второй канал 305 доступа для извлечения жидкости из исходного пакета 302.

Как также показано на фиг. 23-24, сегмент 306 трубки может, необязательно, содержать подблок взятия проб в ответвительном соединителе 308. Одна из ветвей ответвительного соединителя 308 может содержать маршрут потока 310, приводящий к мешку или месту 312 с пробами. Мешок или место 312 с пробами позволяет  
 20 осуществлять сбор проб из входящей исходной жидкости. Поток к мешку или месту 312 с пробами обычно контролируется фиксатором 314. Другая ветвь ответвительного соединителя 308 соединена с трубками 316. Трубки 316 соединены с еще одним расположенным по ходу потока ответвительным соединителем 318. Ответвительный соединитель 318 взаимодействует с трубками 316 и трубками 320, что обеспечивает маршрут потока жидкости из рабочего пакета 322, что подробнее описано ниже. Сегмент  
 25 трубки 324 выходит из одного из каналов ответвительного соединителя 318 и соединяется с каналом еще одного расположенного по ходу потока ответвительного соединителя 326. Отдельный маршрут потока, задаваемый трубками 328, также соединен с каналом ответвительного соединителя 326. Трубки 328 могут содержать встроенный стерильный барьерный фильтр 330 для фильтрации любых частиц из жидкости, до того как она  
 30 попадет в маршрут потока, приводящий ко второму ответвительному соединителю 326 и, в итоге, к сепаратору 301.

В соответствии с системой, изложенной в настоящем описании, раствор для промывания может быть прикреплен (или предварительно прикреплен) к набору 300. Как показано на фиг. 23 и 24, трубки 332 (определяющие маршрут потока),  
 35 предпочтительно, содержат гвоздевой соединитель 334 на своем конце. Гвоздевой соединитель 334 представлен для установления взаимодействия потоков с контейнером жидкости для промывания, таким как одноразовый пакет, содержащий физиологический раствор или другой раствор (не показан). Среда или жидкость для промывания вытекает из источника жидкости для промывания через второй гвоздевой соединитель 334, через  
 40 сегмент трубки 332, где она фильтруется посредством стерильного барьерного фильтра 330, описанного выше, и затем проходит через трубки 328 к выходу ответвительного соединителя 326, описанного выше.

Сегмент трубки 336 задает маршрут потока, соединенный с одного конца с каналом ответвительного соединителя 326 и с впускным каналом сепаратора 301.  
 45 Предпочтительно, в соответствии с настоящим изложением, сепаратор 301 представляет собой сепаратор с вращающейся мембраной описанного выше типа.

Как показано на фиг. 23, 24 и 25, сепаратор 301 с вращающейся мембраной имеет, по меньшей мере, два выпускных канала. Выпуск 646 сепаратора 301 принимает отходы

от промывания (то есть, разбавленную среду взвеси), и соединен с трубками 338, который задают маршрут потока к контейнеру 340 для отходов. Контейнер для отходов содержит еще один соединительный канал 341 для получения проб или извлечения отходов из контейнера продукта.

5 Сепаратор 301, предпочтительно, содержит второй выпуск 648, который соединен с сегментом трубки 342. Другой конец сегмента трубки 342 соединен с ответвительным соединителем 344, который разветвляется и задает маршрут потока к одному или более рабочим контейнерам 322 и маршрут потока к контейнеру 350 конечного продукта. Контейнер 350 конечного продукта также может содержать мешок 352 с пробами (см.  
10 фиг. 23) и канал доступа или люэровский соединитель 354. Мешок 352 с пробами, показанный предварительно прикрепленным к держателю 352 трубок на фиг. 23, позволяет выполнять сбор проб конечного продукта. Контроль потока к мешку 352 с пробами, предпочтительно, осуществляется фиксатором 356. Маршрут потока через канал 354 доступа контролируется фиксатором 358.

15 Обратимся теперь к способу промывания с использованием набора 300 с фиг. 23 и 24; одноразовый набор 300 сначала устанавливается на панель 401 устройства разделения (то есть, аппаратного обеспечения) 400, показанную на фиг. 25. Устройство 400 содержит перистальтические насосы, фиксаторы и датчики, которые контролируют поток через одноразовый набор. Конкретнее, управление насосами, фиксаторами и  
20 т.п. обеспечивается программно-управляемым микропроцессором/контроллером устройства 400. Сегменты трубки 362, 366 и 368 (показанные на фиг. 23) избирательно стыкуются с перистальтическими насосами 402, 404 или 406 (показанными на фиг. 25). (Сегмент 368 насоса линии отходов может быть перемещен к линии 343 выпуска сепаратора, при необходимости). После того как одноразовый набор 300  
25 устанавливается на панели 401 управления устройства 400, взвесь клеток в пакете 302 продукта прикрепляется, как было описано ранее, посредством гвоздевого соединителя 304 или посредством стерильного соединения. Среда для промывания, представленная в контейнере (не показана), прикрепляется аналогично. В соответствии с функционированием устройства 400, фиксатор 360 открывается и позволяет взвеси  
30 клеток протечь из контейнера 302 продукта.

Поток взвеси клеток продвигается посредством воздействия перистальтического насоса через трубки 324, определяемые сегментом насоса 362, в сепаратор 301 с вращающейся мембраной. Аналогично, среда для промывания продвигается посредством воздействия перистальтических насосов через длину трубки 328,  
35 определяемую сегментом насоса 366, с клапанами 362 и 364 в открытом положении. Среда для промывания протекает через трубки 332, стерильный барьерный фильтр 330, трубки 328, Y-соединитель 326 и в сепаратор 301 с вращающейся мембраной. Среда для промывания и взвесь клеток могут быть последовательно введены в сепаратор 301 с вращающейся мембраной, допуская возникновение смешивания взвеси и раствора  
40 для промывания в пределах камеры (зазора) сепаратора 301 или в рабочем контейнере 322, как описано ниже. Альтернативно, среда для промывания и взвесь клеток могут быть объединены до введения в сепаратор 301, (например), через второй ответвительный соединитель 326.

В еще одной альтернативе, взвесь клеток может быть сначала введена из исходного  
45 контейнера 302 в сепаратор 301, как в общих чертах описано выше. Взвесь клеток концентрируется внутри сепаратора 301, что позволяет супернатанту пройти через мембрану, через выпускной канал 382, в контейнер 340 для отходов. Концентрированные клетки выходят из сепаратора 301 через канал 384 и направляются в рабочий контейнер

322.

После того как отделение концентрированных клеток от супернатанта взвеси клеток завершается, замещающая жидкость вводится из контейнера с замещающей жидкостью (не показан) в сепаратор 301 (для смыывания всех оставшихся клеток) и аналогично  
 5 направляется через канал 384 в рабочий контейнер 322. Концентрированные клетки ресуспендируются в замещающей жидкости внутри рабочего контейнера 322, как показано на фиг. 23. Если желательно или требуется дополнительное промывание, то система может быть предварительно запрограммирована или направлена другим способом на (повторное) введение ресуспендированных клеток/замещающей жидкости  
 10 в сепаратор 301, в котором отделение концентрированных клеток от супернатанта повторяется. Конечный клеточный продукт собирается в контейнере 350 конечного продукта, где он может быть ресуспендирован с дополнительной замещающей жидкостью.

Независимо от последовательности введения взвеси клеток/раствора для промывания  
 15 или используемого одноразового набора, вращательное воздействие устройства приводит к отделению клеток от оставшейся части жидкости, в который они были суспендированы, и/или от раствора для промывания. Предпочтительно, супернатант и раствор для промывания проходят через мембрану, тогда как искомые клетки концентрируются внутри камеры сепаратора. Отходы, возникающие при разделении  
 20 и включающие среду для промывания и среду супернатанта, выходят из канала 382 и протекают через трубки 338 в контейнер 340 для отходов. Поток отходов управляется перистальтическим насосом через часть трубок 338, определяемую сегментом насоса 368, к пакету 340 с продуктами отходов.

Как описано выше, взвесь концентрированных и разделенных клеток выходит из  
 25 второго выпуска 384 сепаратора 301 с вращающейся мембраной. Если дальнейшее промывание не требуется, то система управления закрывает фиксатор 370 и открывает фиксатор 372. Закрытие фиксатора 370 предотвращает протекание взвеси промытых клеток через трубки 346 и направляет ее через трубки 348 в пакет 350 конечного продукта. Контейнер 350 конечного продукта имеет вход для приема взвеси отделенных  
 30 и промытых клеток. Контейнер 354 конечного продукта соединен с датчиком 374 веса. Устройство разделения измеряет вес 374 контейнера с целью определения того, находится ли объем собранных клеток в контейнере 350 конечного продукта в приемлемом диапазоне и, следовательно, закончен ли цикл промывания.

Если желательно или требуется дополнительное промывание взвеси разделенных  
 35 клеток, то система управления устройства разделения закрывает фиксатор 372 и фиксатор 376, и открывает фиксатор 370. Закрытие фиксатора 372 предотвращает протекание взвеси клеток через трубки 348 и направляет ее через трубки 346 в рабочий пакет 322. Рабочий пакет 322 имеет впуск для приема взвеси разделенных клеток. Рабочий пакет 322 соединен с датчиком 378 веса. Система управления устройства  
 40 разделения определяет вес, воспринимаемый датчиком веса, с целью определения того, достаточно ли взвеси разделенных клеток присутствует в рабочем пакете 322 для проведения еще одного цикла промывания. Если определено, что присутствует достаточно взвеси, и желательно дополнительное промывание, то система управления устройства разделения открывает фиксатор 376 с целью открытия и направления взвеси  
 45 разбавленных и разделенных клеток через выход рабочего пакета 322, через трубки 320 в ответственный соединитель 318, и через датчик 380 обнаружения воздуха. Датчик 380 обнаружения воздуха обнаруживает воздух во взвеси клеток, которая проходит через трубки 324. Устройство управления и эксплуатации измеряет показания датчика

380 обнаружения воздуха и определяет, какие процессы должны быть выполнены далее.

Взвесь разделенных клеток, которая содержит клетки, суспендированные в разбавленной среде суспендирования, затем повторно проходит через процесс промывания, как описано выше. Процесс промывания может быть повторен столько раз, сколько необходимо, и, предпочтительно, до тех пор, пока взвесь разбавленных и разделенных клеток не будет иметь приемлемую остаточную концентрацию среды суспендирования. Конечная взвесь разбавленных и разделенных клеток собирается в пакете 350 конечного продукта.

Альтернативно, в отличие от повторения обработки жидкости через один рабочий контейнер, можно следовать процедуре обработки “пакетного типа” путем использования двух или более рабочих контейнеров 322 (в комбинации с контейнером 350 конечного продукта).

Одноразовый набор 300 обработки с фиг. 24, в частности, хорошо подходит для такой обработки “пакетного типа”. В соответствии с процедурой промывания клеток с использованием одноразового набора 300 с фиг. 24, клетки, первоначально выделенные из исходной среды суспендирования, удаляются из сепаратора 301 и вводятся в один из рабочих контейнеров 322a. Замещающая жидкость вводится в контейнер 322a, и клетки ресуспендируются. Ресуспендированные клетки в контейнере 322a могут затем быть введены в сепаратор 301, в котором они отделяются от супернатанта.

Концентрированные клетки выходят через выпуск 648 в сепаратор 301 и вводятся в новый (второй) рабочий контейнер 322b. Дополнительная замещающая жидкость может быть введена в рабочий контейнер 322b, и процесс может быть повторен, при необходимости, с еще одним новым (третьим) рабочим контейнером (не показан). Конечный клеточный продукт затем собирается в контейнере 350 конечного продукта, как описано выше.

В соответствии с описанным выше способом промывания клеток “пакетного типа”, сегменты трубки 370a, 370b и 320a, 320b могут быть соединены с фиксаторами (не показаны) для управления потоком во множество рабочих контейнеров 322a и 322b и потоком из них. Таким образом, например, фиксатор на линии 370a будет открыт, тогда как фиксатор на линии 370b будет закрыт, с тем чтобы клетки, выходящие из сепаратора 301, направлялись в (первый) рабочий контейнер 322a.

С целью дополнительного промывания, клетки, ресуспендированные в свежей замещающей жидкости из контейнера 322a, вводятся в сепаратор 301, где клетки отделяются от супернатанта, как было описано ранее. Система управления устройства 400 закрывает фиксатор (не показан на фиг. 24) на сегменте трубки 370a и открывает фиксатор (не показан на фиг. 24) на сегменте трубки 370b, с тем чтобы обеспечить возможность потока клеток в новый (второй) рабочий контейнер 322b. После итогового промывания фиксаторы (не показаны) на сегментах 370a, 370b, и т.д. закрываются, и фиксатор 372 (как показано, например, на фиг. 23) открывается, обеспечивая возможность сбора конечного продукта в контейнере 350.

На фиг. 24 показана передняя панель 401 устройства 400 разделения; то есть аппаратное обеспечение, которое включает в себя перистальтические насосы 402, 404 и 406. Как описано выше, сегменты насоса 362, 364 и 368 из одноразового набора избирательно соединяются с перистальтическими насосами 402, 404 и 406.

Перистальтические насосы сочленяются с жидкостным набором с фиг. 23 в сегментах насоса 362, 364 и 368, и продвигают взвесь клеток внутри одноразового набора, как будет понятно специалистам в данной области техники. Устройство 400 управления и эксплуатации также содержит фиксаторы 410, 412, 414. Фиксаторы 410, 412, 414 и 416

используются для управления потоком взвеси клеток через различные сегменты одноразового набора, как описано выше.

Устройство 400 также содержит несколько датчиков для измерения различных условий. Выходные данные датчиков используются устройством 400 при выполнении  
 5 цикла промывания. Один или более измерительных датчиков 426 давления могут быть представлены на устройстве 400 и могут быть соединены с одноразовым набором 300 в определенных точках для отслеживания давления во время процедуры. Измерительный датчик 426 давления может быть встроен в место контроля давления внутри линии (например, в сегмент трубки 336) для отслеживания давления внутри сепаратора 301.  
 10 Датчик детектора 438 воздуха также может быть соединен с одноразовым набором 300, при необходимости. Детектор 438 воздуха является необязательным и может быть представлен для обнаружения положения поверхностей раздела жидкость/воздух.

Устройство 400 содержит весы 440, 442, 444 и 446, на которых могут быть рассчитаны и взвешены конечный пакет, рабочий пакет, пакет взвеси клеток и любой  
 15 дополнительный пакет, соответственно. Веса пакетов отслеживаются датчиками веса и записываются в течение процедуры промывания. По измерениям датчиков веса устройство определяет, является ли каждый из пакетов пустым, частично заполненным или полным, и управляет компонентами устройства управления и эксплуатации 200, такими как перистальтические насосы и фиксаторы 410, 412, 414, 416, 418, 420, 422 и  
 20 424.

Устройство 400 содержит по меньшей мере один блок привода, или “вращатель” 448, который осуществляет не прямое управление сепаратором с вращающейся мембраной 301. Вращатель 448 может состоять из приводного двигателя, соединенного с устройством 400 и управляемого им, и подсоединенного для поворачивания кольцевого  
 25 элемента магнитного привода, содержащего, по меньшей мере, пару постоянных магнитов. При вращении кольцевого элемента привода магнитное притяжение между соответствующими магнитами внутри корпуса сепаратора с вращающейся мембраной вызывает вращение вращателя внутри корпуса сепаратора с вращающейся мембраной.

На фиг. 26-28 в форме диаграмм излагается способ промывания клеток в соответствии  
 30 с изложенным в настоящем описании. Этапы, описанные ниже, выполняются посредством программно-управляемого микропроцессорного блока устройства 400, при этом определенные этапы выполняются оператором, как было отмечено выше. Обратимся сначала к фиг. 26; устройство включается на этапе 500. Устройство проводит проверки автоматической калибровки 502, включающие в себя проверку  
 35 перистальтических насосов, фиксаторов и датчиков. Затем устройство 400 запрашивает у пользователя ввод выбранных процедурных параметров (этап 504), таких как выполняемая процедура промывания, объем промываемой взвеси клеток, число промываний, которое должно быть выполнено, и т.д. Оператор может затем выбирать и вводить процедурные параметры для процедуры промывания (этап 506).

40 Устройство (через контроллер) подтверждает ввод параметров 506, и затем запрашивает у оператора загрузку (этап 510) одноразового набора. Оператор затем загружает одноразовый набор (этап 512) в панель устройства 400. После установки одноразового набора, устройство подтверждает установку, как показано (этап 514).

После того как одноразовый набор установлен, устройство автоматически проверяет  
 45 правильность установки одноразового набора (этап 516). После того как устройство определяет, что одноразовый набор был установлен правильно, контроллер запрашивает у оператора подсоединение взвеси клеток и среды для промывания (этап 518). Затем оператор подсоединяет среду для промывания (такую как физиологический



раствор, но не ограничиваясь им) (этап 520) к одноразовому набору через гвоздевой соединитель, как было описано ранее. Затем оператор подсоединяет взвесь клеток внутри пакета с продуктом (этап 522) к одноразовому набору через гвоздевой соединитель.

5 Как показано на фиг. 27, после того как взвесь клеток и среда для промывания были подсоединены к одноразовому набору, оператор подтверждает, что растворы были подсоединены (этап 524). Устройство запрашивает у оператора взятие образца взвеси клеток (этап 526). Затем оператор или устройство открывает фиксатор 528 мешка для сбора проб с целью введения жидкости в мешок для сбора проб (этап 546). После того  
10 как мешок для сбора проб был заполнен, он запечатывается и удаляется (542) из одноразового набора. Оператор подтверждает (этап 544), что образец был взят. После удаления мешка для сбора проб одноразовый набор заливается (этап 546) для процесса промывания.

Затем контроллер устройства разделения начинает процесс промывания. Взвесь  
15 клеток, предназначенная для промывания, передается из своего контейнера (например, 302 с фиг. 23) через одноразовый набор на сепаратор 301 с вращающейся мембраной. Аналогично, среда для промывания передается из своего источника через одноразовый набор на сепаратор 301 с вращающейся мембраной. В предпочтительном варианте осуществления, исходные клетки взвеси клеток концентрируются и/или собираются в  
20 рабочем пакете (для дальнейшей обработки) или собираются в пакете конечного продукта, который впоследствии удаляется из одноразового набора. Если необходимо (дополнительное) промывание или разбавление взвеси клеток, то взвесь клеток в рабочем пакете может промываться (второй раз) той же самой или другой средой для промывания в соответствии с процессом, кратко описанным выше. До завершения  
25 каждого цикла промывания, измеряется и записывается объем или вес взвеси клеток (этап 550). Когда концентрация клеток в среде для промывания достигает приемлемого уровня, заполняется пакет конечного продукта.

Как показано на фиг. 28, как только собран желаемый объем конечного продукта, устройство управления и эксплуатации запрашивает у оператора взятия пробы и  
30 запечатывания пакета конечного продукта (этап 552). Мешок для сбора проб прикрепляется к пакету конечного продукта. Оператор затем запечатывает и удаляет из одноразового набора взвесь промытых клеток в пакет с конечным продуктом (этап 552). Затем пакет с конечным продуктом взбалтывается (этап 556). Оператор открывает мешок для сбора образцов путем удаления фиксатора (этап 558). Допускается заполнение  
35 мешка для сбора образцов (этап 560). После того как пакет с образцами заполнен, фиксатор закрывается и мешок для сбора образцов запечатывается и удаляется (этап 562). Затем оператор запечатывает линии одноразового набора (этап 564) и подтверждает, что пакет продукта был запечатан и удален, мешок для взятия проб был заполнен и удален, и что линии одноразового набора были запечатаны (этап 566). Затем  
40 устройство управления и эксплуатации запрашивает у оператора удаление одноразового набора, как показано на этапе 568. Затем оператор удаляет и выбрасывает одноразовый набор, как показано на этапе 570.

Таким образом, изложен улучшенный сепаратор с вращающейся мембраной, а также способы и системы для применения такой вращающейся мембраны. Описание,  
45 представленное выше, приведено в целях иллюстрации, и не предполагается, что оно ограничивает объем изложения каким-либо конкретным способом, системой или установкой или устройством, описанными в настоящем описании.

Формула изобретения

1. Устройство фильтрации крови, содержащее:  
по существу, цилиндрический корпус, имеющий внутреннюю стенку;  
5     внутренний элемент, установленный внутри корпуса и имеющий внешнюю  
поверхность;  
одно из внутренней стенки корпуса и внешней поверхности внутреннего элемента,  
содержащей пористую мембрану, расположенную на расстоянии от указанной стенки  
корпуса или указанной поверхности внутреннего элемента с образованием кольцевого  
10    зазора между ними,  
при этом корпус и внутренний элемент могут вращаться друг относительно друга;  
впуск для направления цельной крови, содержащей плазму и эритроциты, в кольцевой  
зазор;  
первый выпуск для направления плазмы, проходящей через мембрану, в контейнер  
15    для сбора; и  
второй выпуск для направления из кольцевого зазора оставшихся компонентов  
крови,  
при этом мембрана имеет площадь поверхности, достаточную для отделения плазмы  
с такой скоростью потока, что время нахождения эритроцитов в пределах кольцевого  
20    зазора является недостаточным для того, чтобы вызвать ненадлежащий гемолиз  
эритроцитов,  
причем устройство дополнительно содержит область высокой перфузии, покрытую  
мембраной, и непроточную область, продолжающуюся за пределы мембраны, и  
содержит радиальный выступ, продолжающийся от одной из внутренней стенки корпуса  
25    и внешней поверхности внутреннего элемента, с тем чтобы уменьшить кольцевой зазор  
между ними, при этом радиальный выступ отделяет область высокой перфузии от  
непроточной области.
2. Устройство фильтрации крови по п. 1, в котором внутренний элемент имеет  
диаметр, превышающий 2,79 см (1,1 дюйм), и/или длину фильтрации, превышающую  
30    7,62 см (3,0 дюйма).
3. Устройство фильтрации крови по любому из предыдущих пунктов, в котором  
внутренний элемент имеет диаметр вплоть до 5,59 см (2,2 дюйма) и длину фильтрации  
вплоть до 19,05 см (7,5 дюйма).
4. Устройство фильтрации крови по п. 1, в котором ротационный вращатель имеет  
35    диаметр около 1,65 дюйма и длину фильтрации около 5,52 дюйма.
5. Устройство фильтрации крови по п. 1, в котором радиальный выступ имеет осевой  
размер, не меньший размера кольцевого зазора.
6. Устройство фильтрации крови по п. 1, в котором радиальный выступ обеспечен  
на внешней поверхности внутреннего элемента.
- 40    7. Устройство фильтрации крови, содержащее:  
по существу, цилиндрический корпус, имеющий внутреннюю стенку;  
внутренний элемент, установленный внутри корпуса и имеющий внешнюю  
поверхность;  
одно из внутренней стенки корпуса и внешней поверхности внутреннего элемента,  
45    содержащей мембрану фильтра, расположенную на расстоянии от передней стенки  
корпуса или поверхности внутреннего элемента с образованием кольцевого зазора  
между ними,  
причем внешняя поверхность внутреннего элемента содержит область высокой

перфузии, покрытую мембраной, и непроточную область, продолжающуюся за пределы мембраны,

при этом корпус и внутренний элемент могут вращаться друг относительно друга;

радиальный выступ, продолжающийся от внутренней стенки корпуса или внешней  
5 поверхности внутреннего элемента, с тем чтобы уменьшить кольцевой зазор между  
ними, при этом радиальный выступ отделяет область высокой перфузии от непроточной  
области.

8. Устройство фильтрации крови по п. 7, в котором радиальный выступ имеет осевой  
размер, не меньший размера кольцевого зазора.

10 9. Устройство фильтрации крови по п. 7, в котором радиальный выступ обеспечен  
на внешней поверхности внутреннего элемента.

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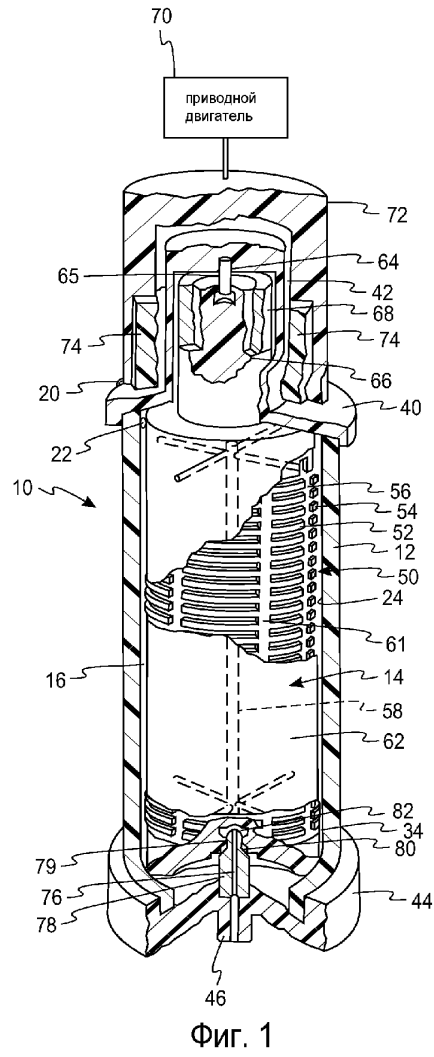
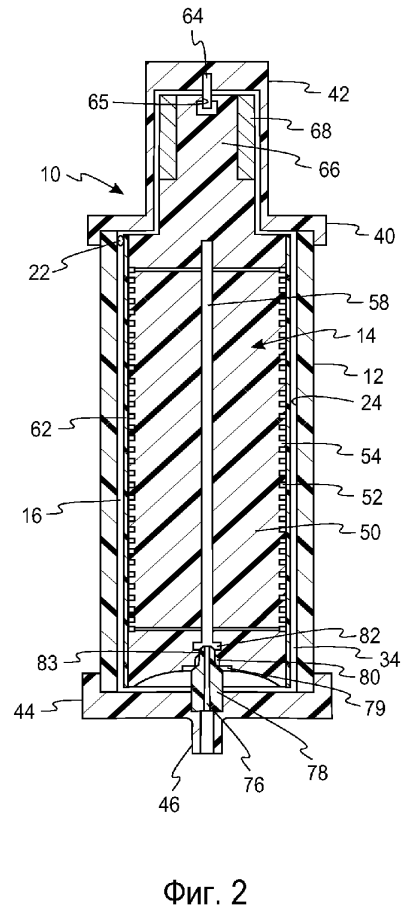
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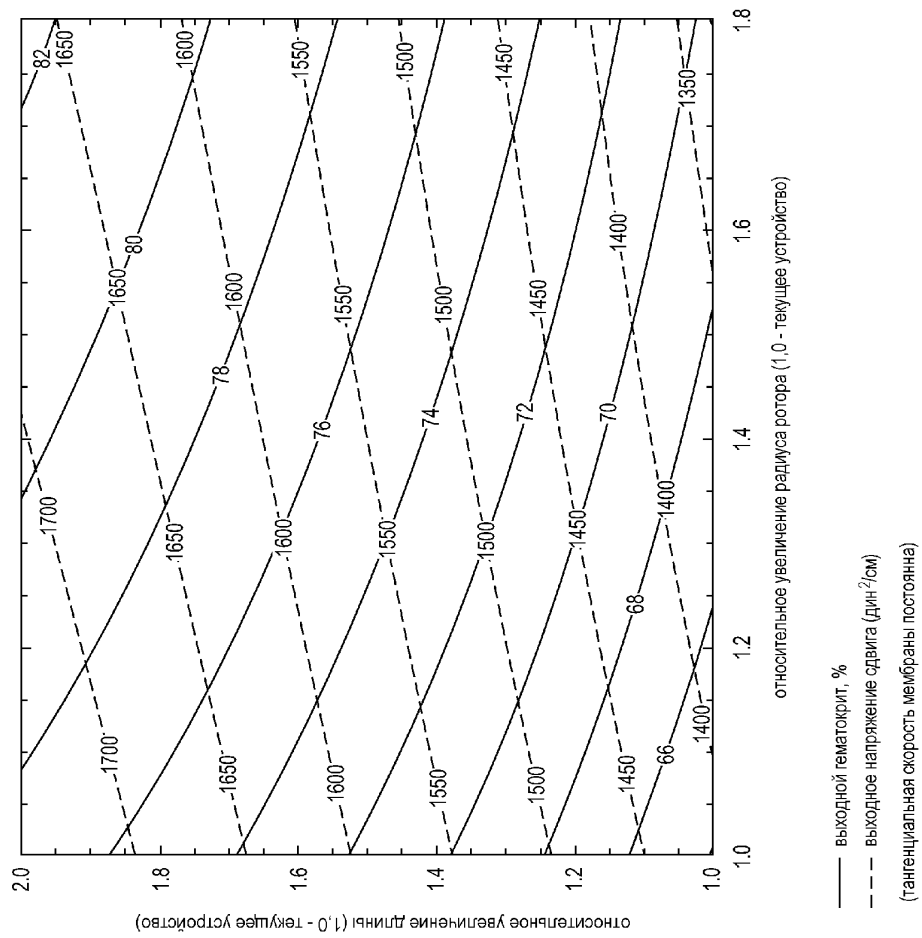
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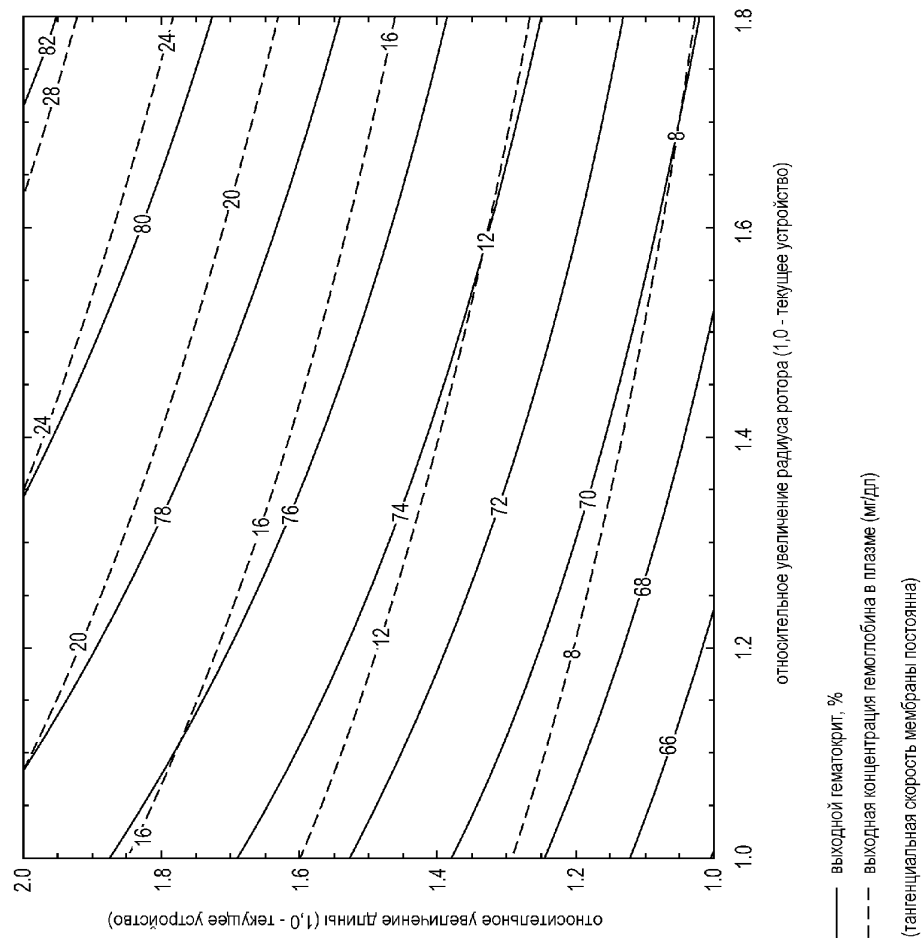
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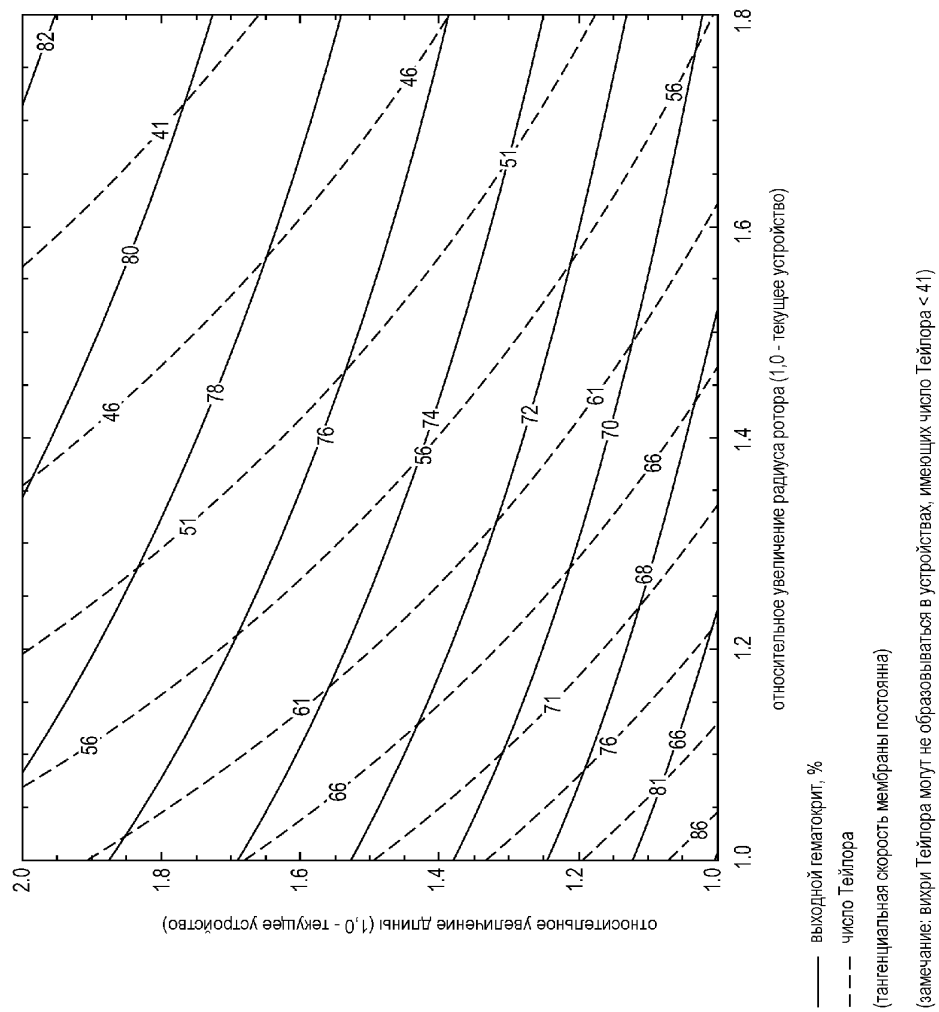
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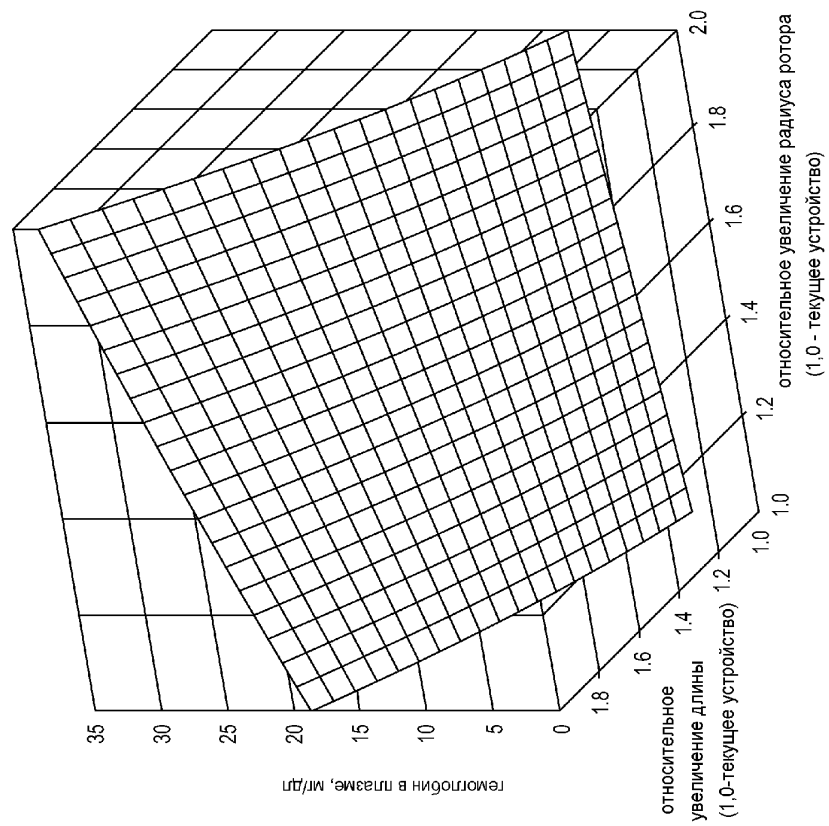
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Фиг. 5

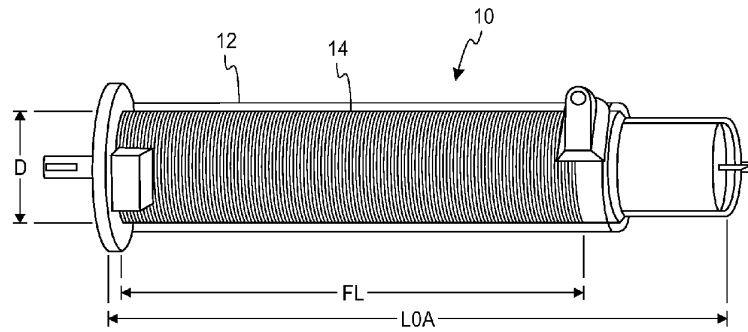


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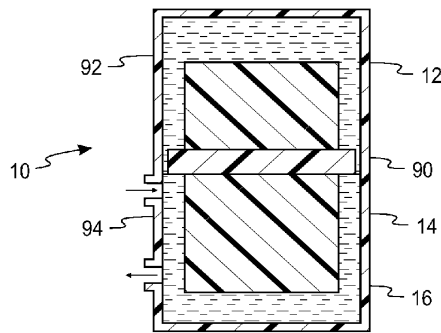




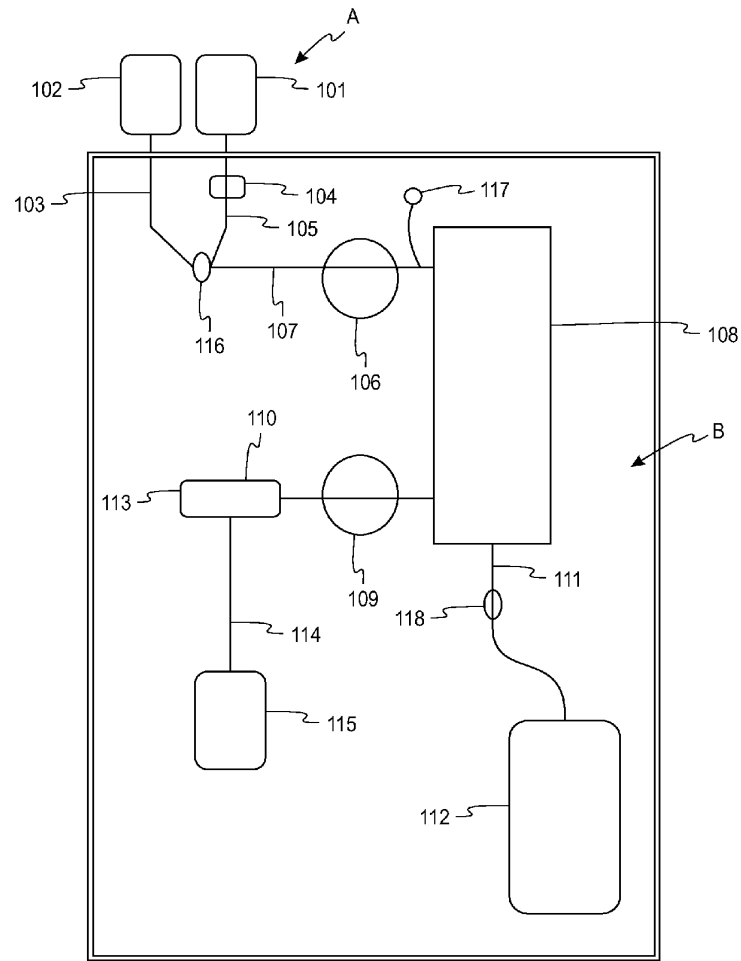
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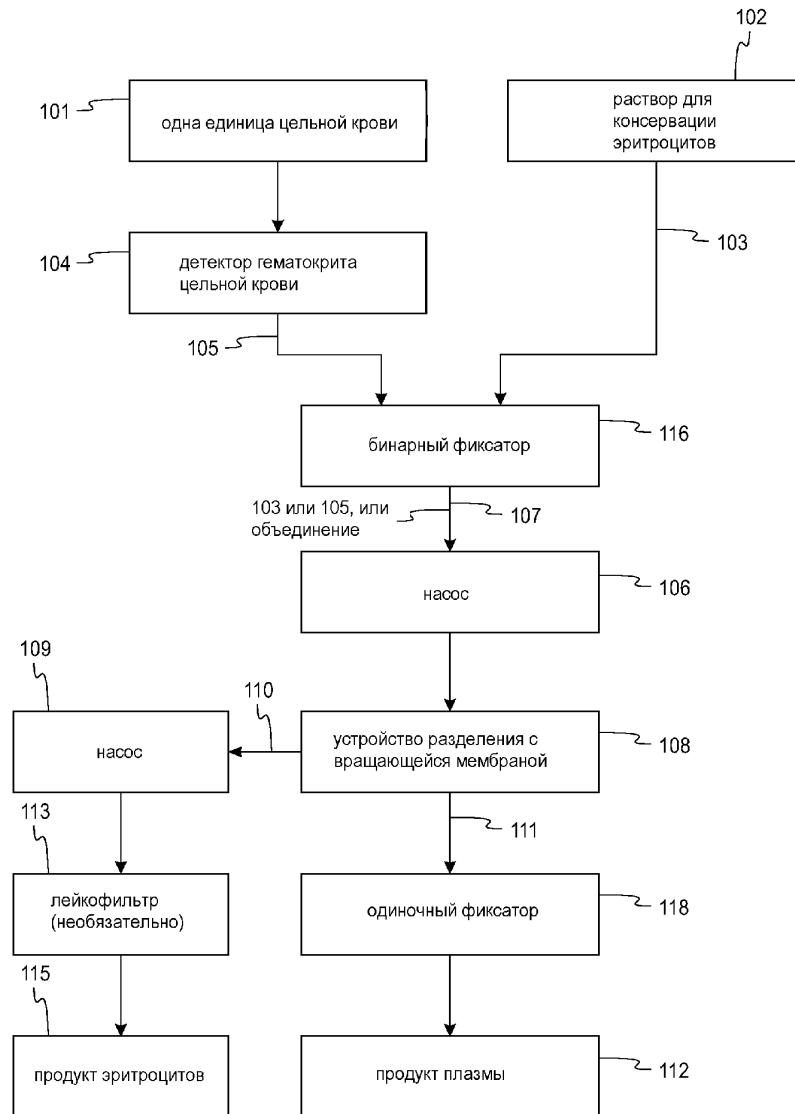
Фиг. 7



Фиг. 8

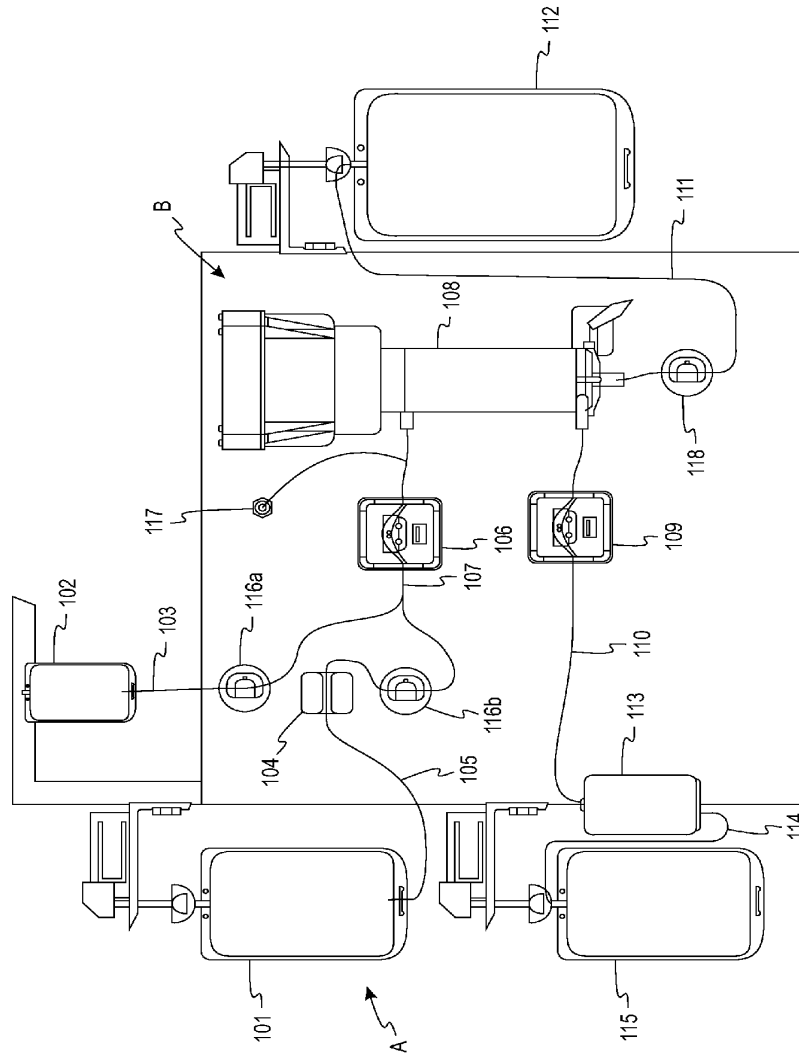


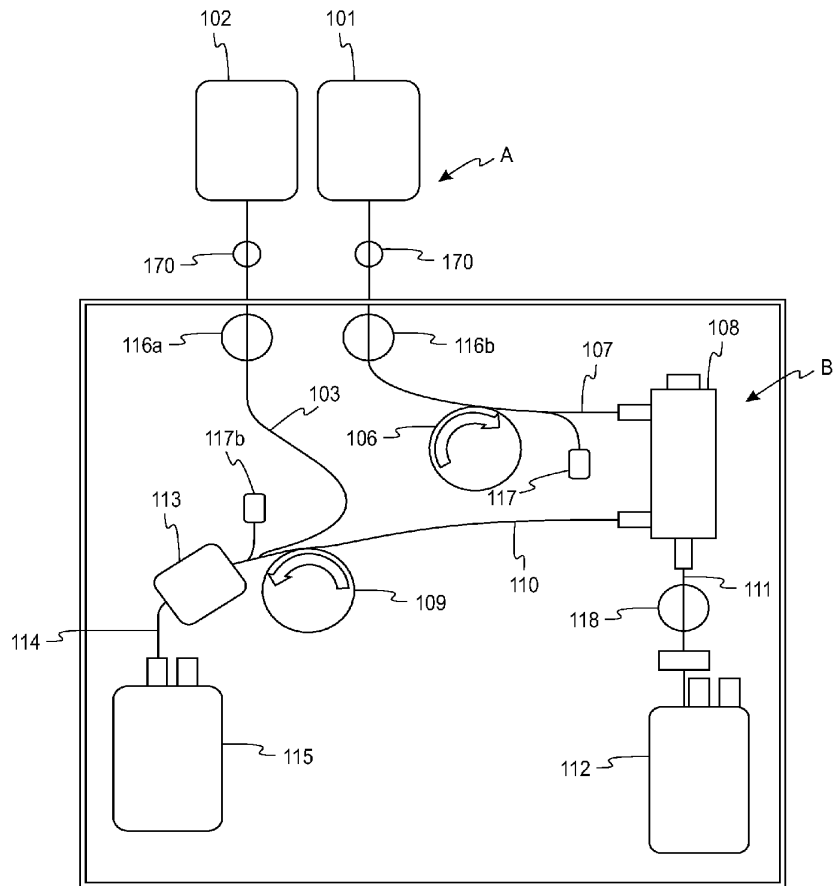
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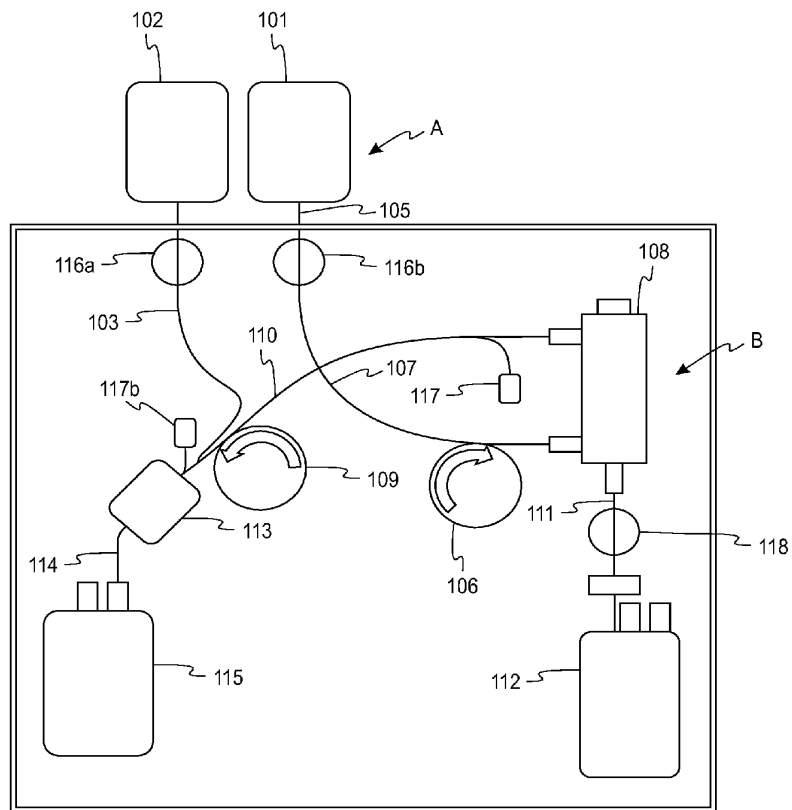
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Фиг. 11





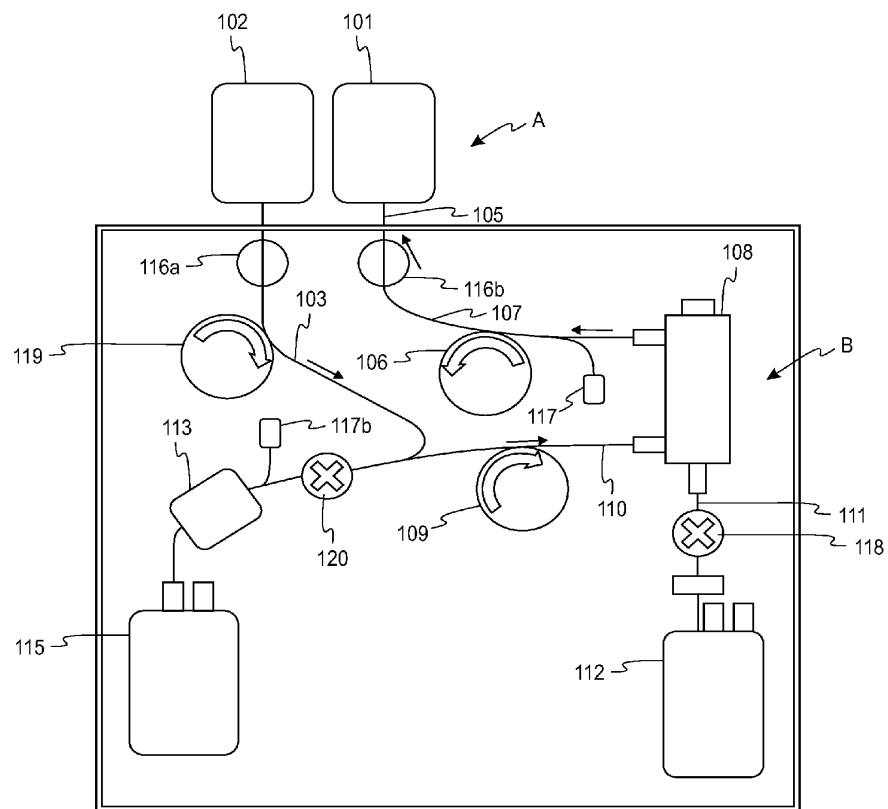
Фиг. 12



Фиг. 12а







направление  
работы насоса

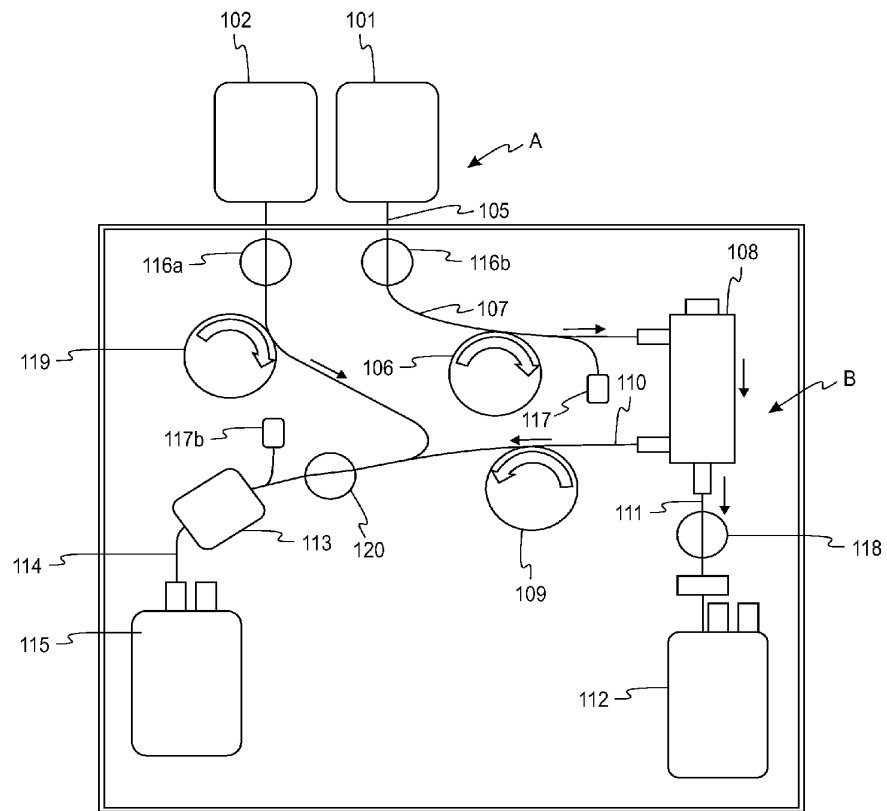
фиксатор

закрыт

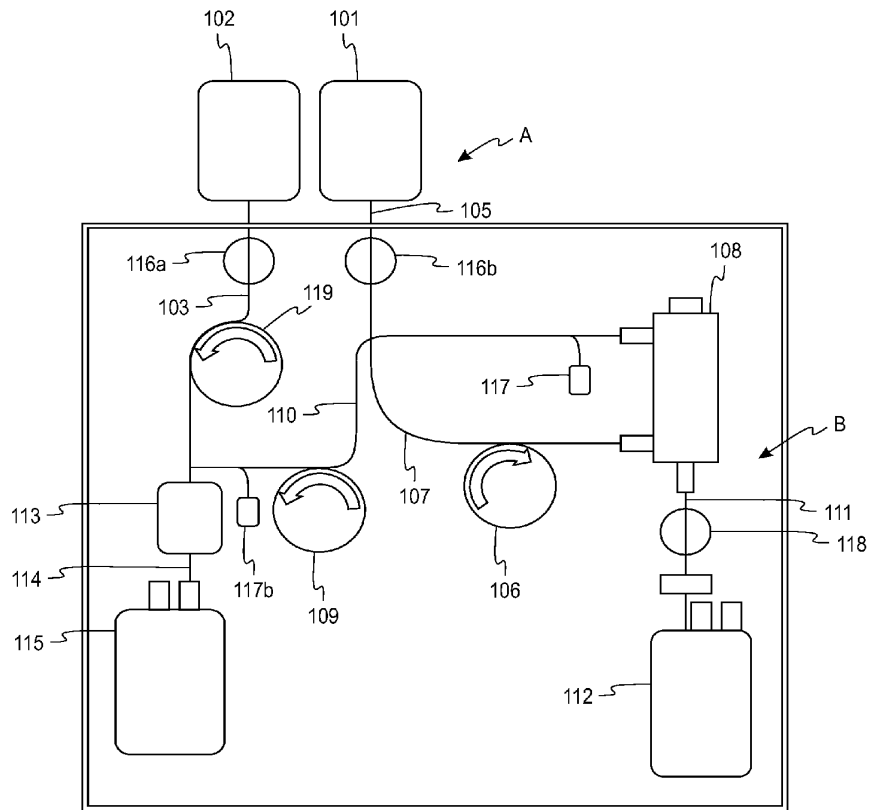
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Фиг. 14





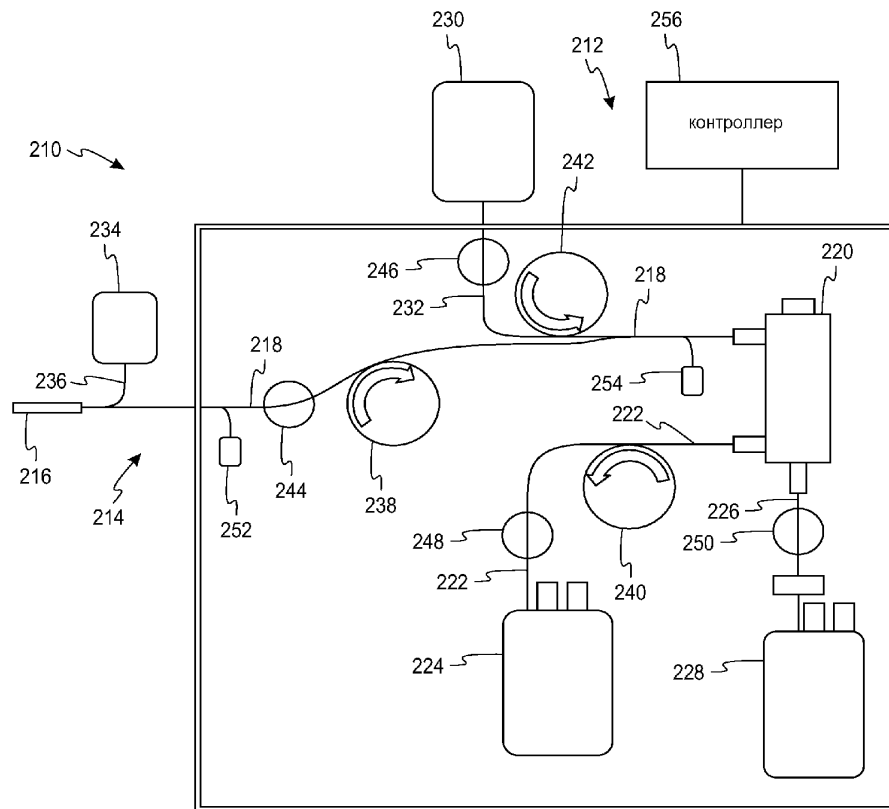
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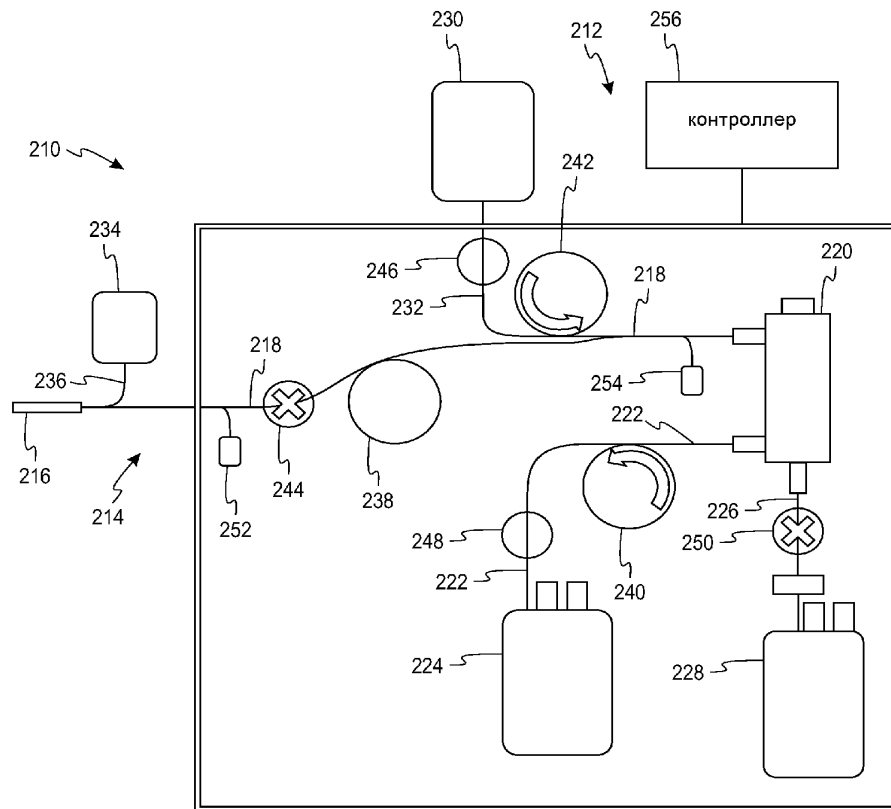
Фиг. 15а



Фиг. 16

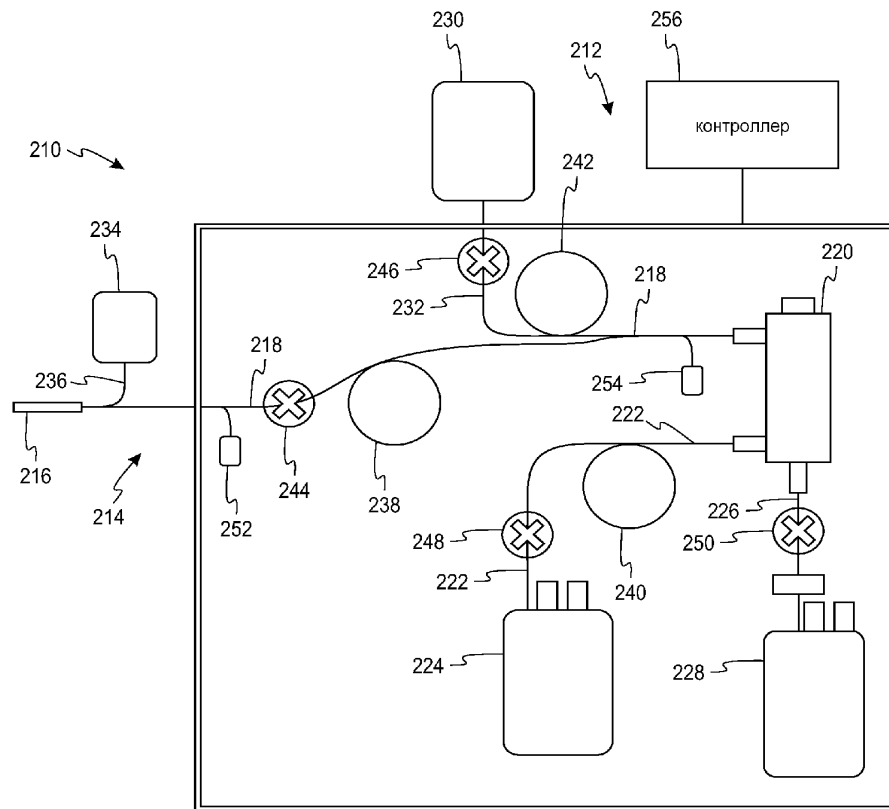


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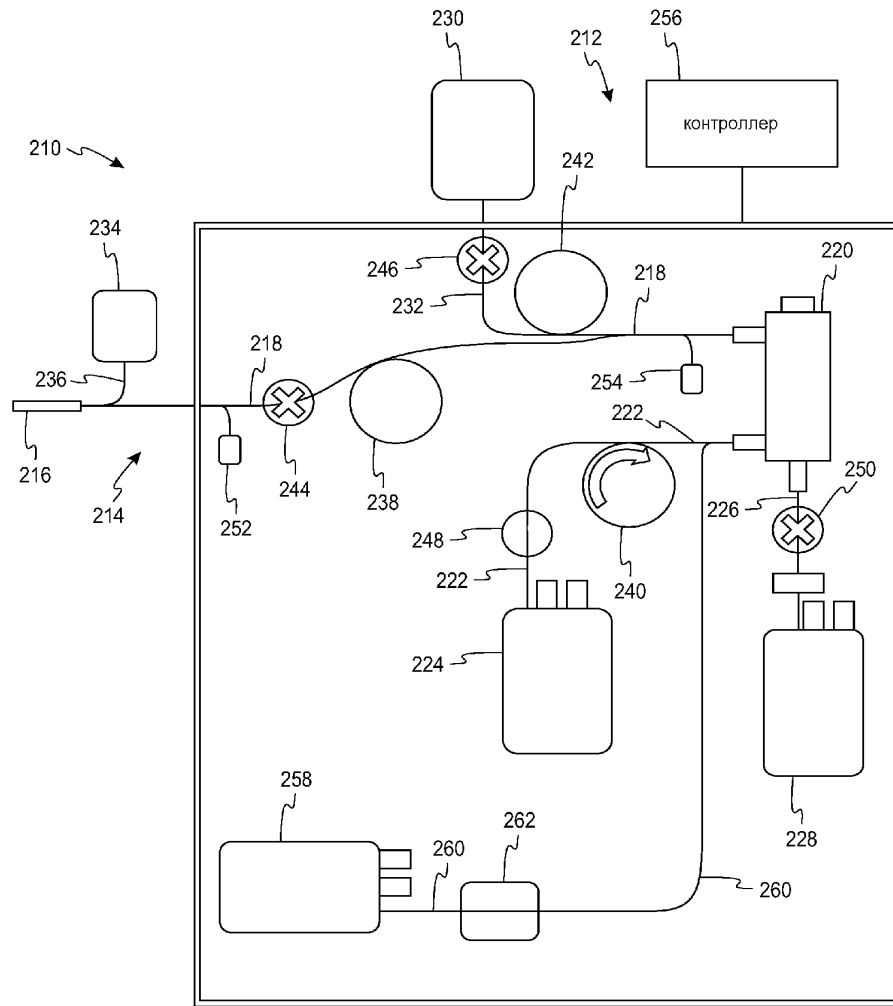
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|  |  открыт |

Фиг. 18

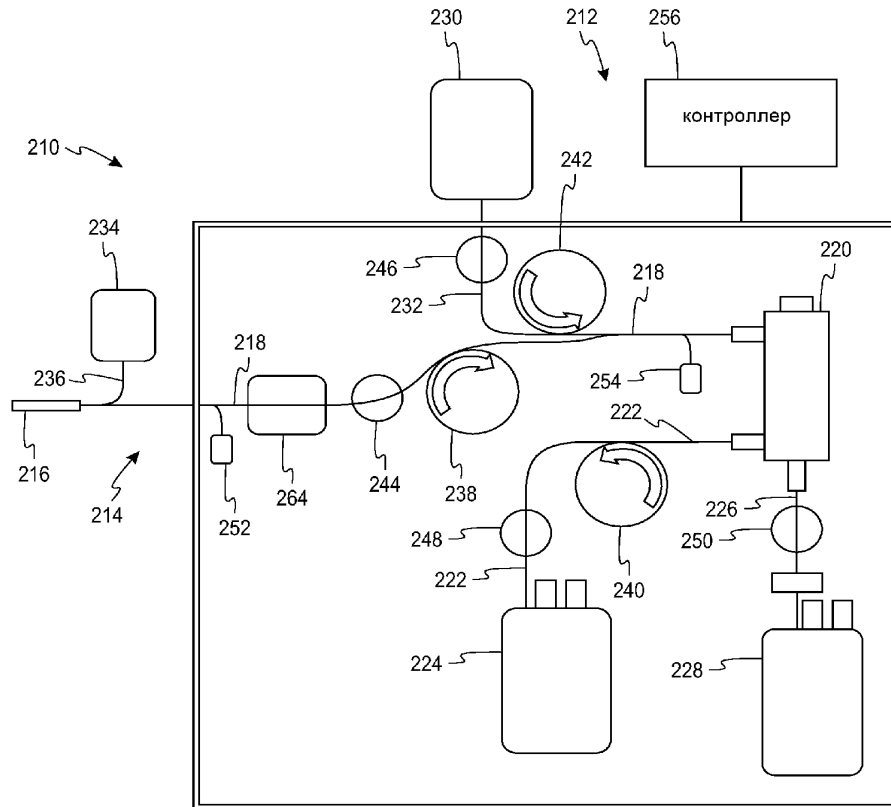


Фиг. 19

20/30



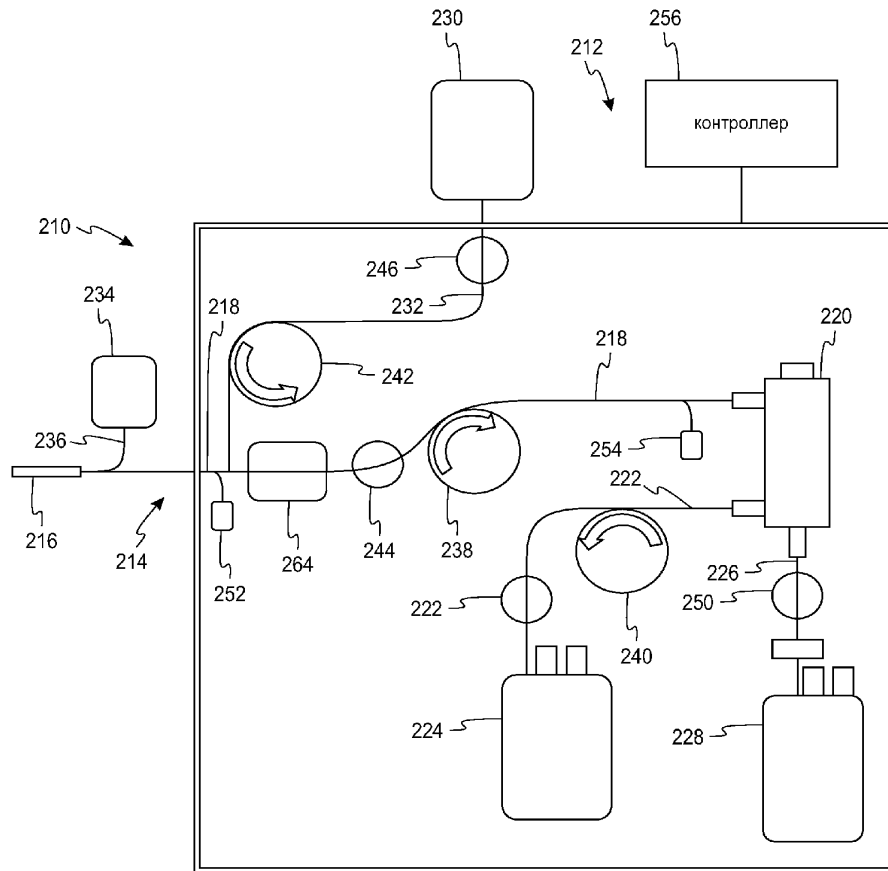
Фиг. 20



|                                                                                     |                                                                                            |
|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| направление<br>работы насоса                                                        | фиксатор                                                                                   |
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|  |  открыт |

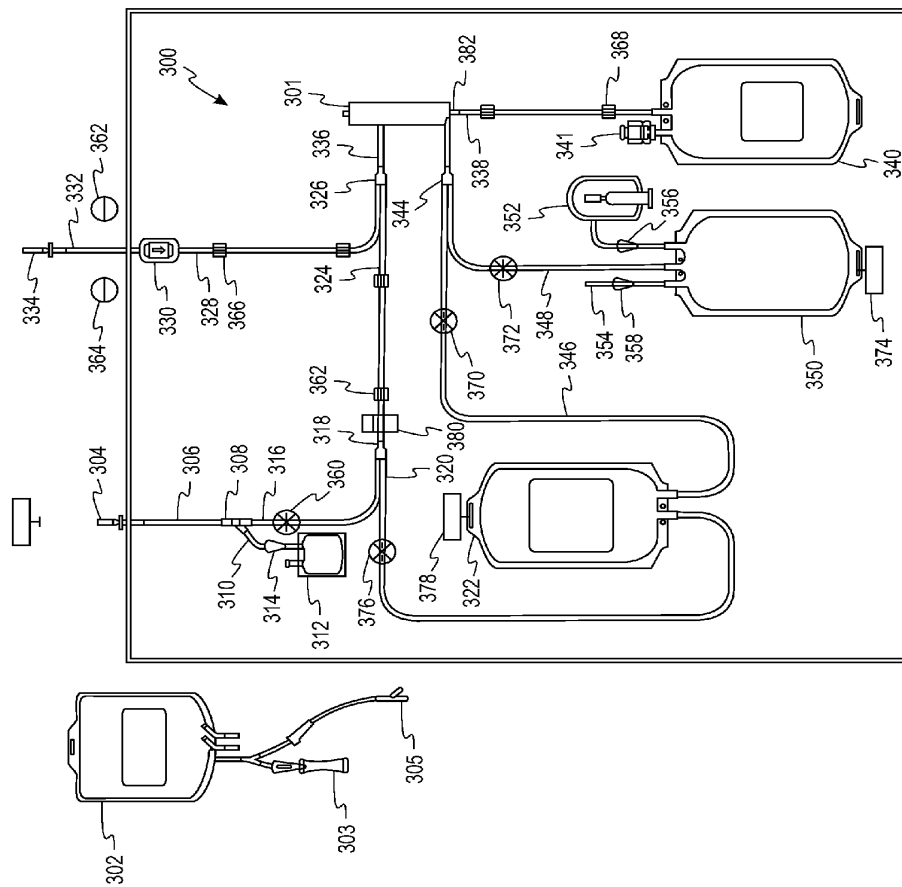
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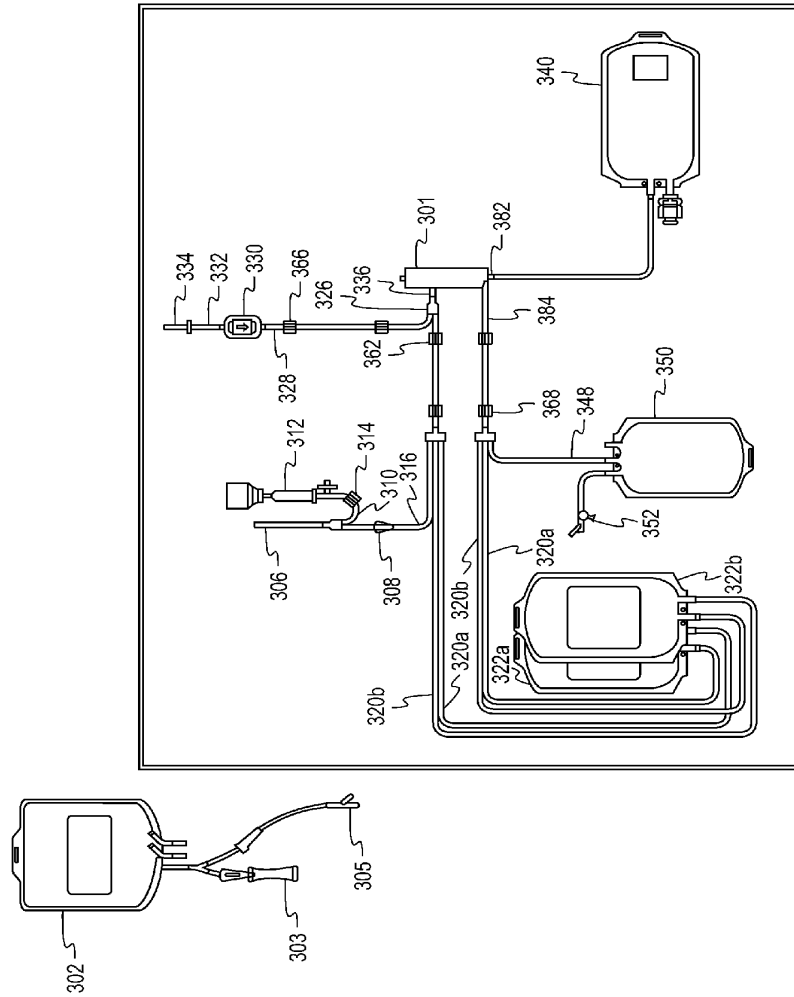


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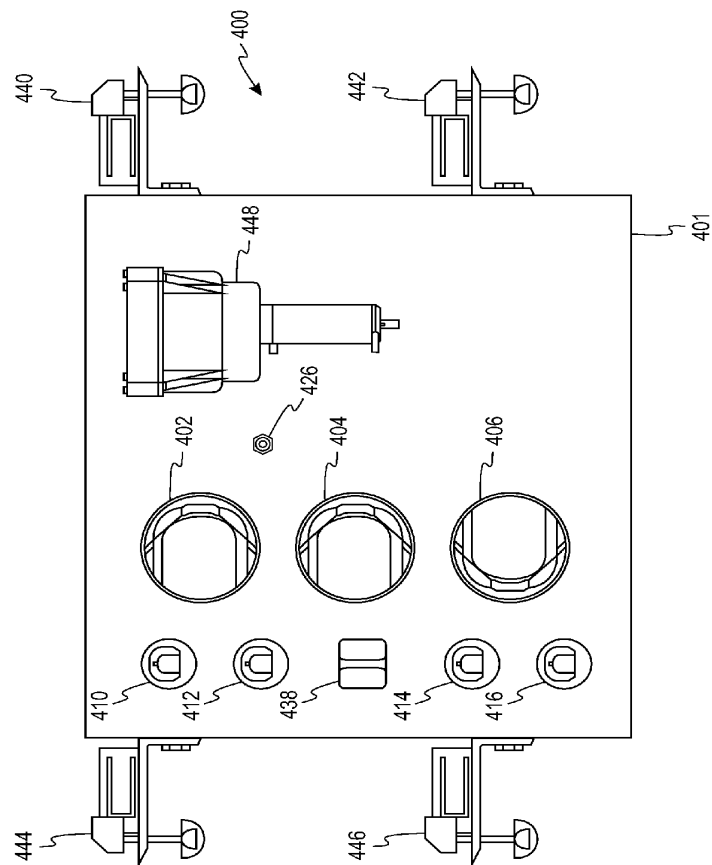
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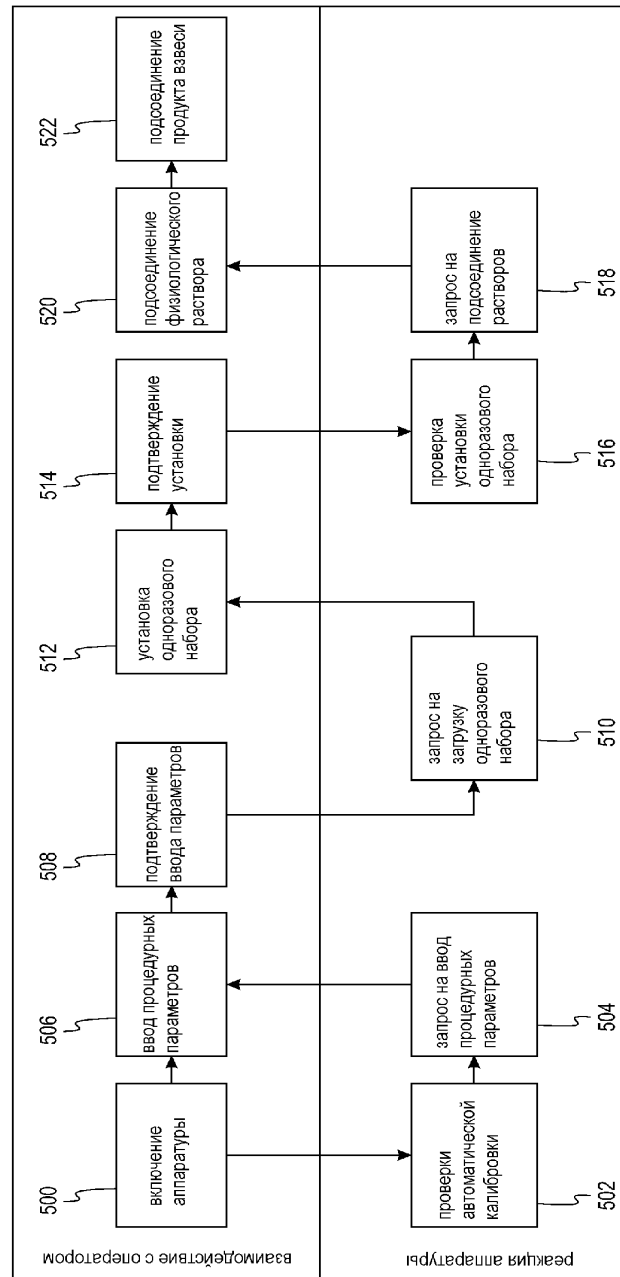


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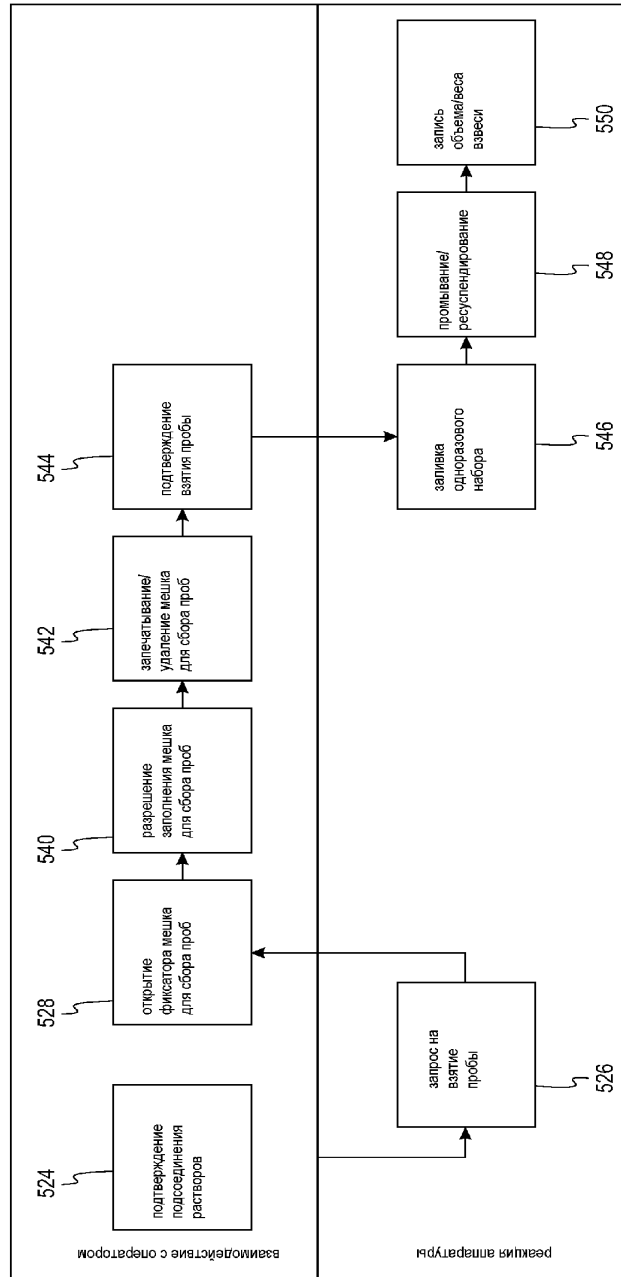


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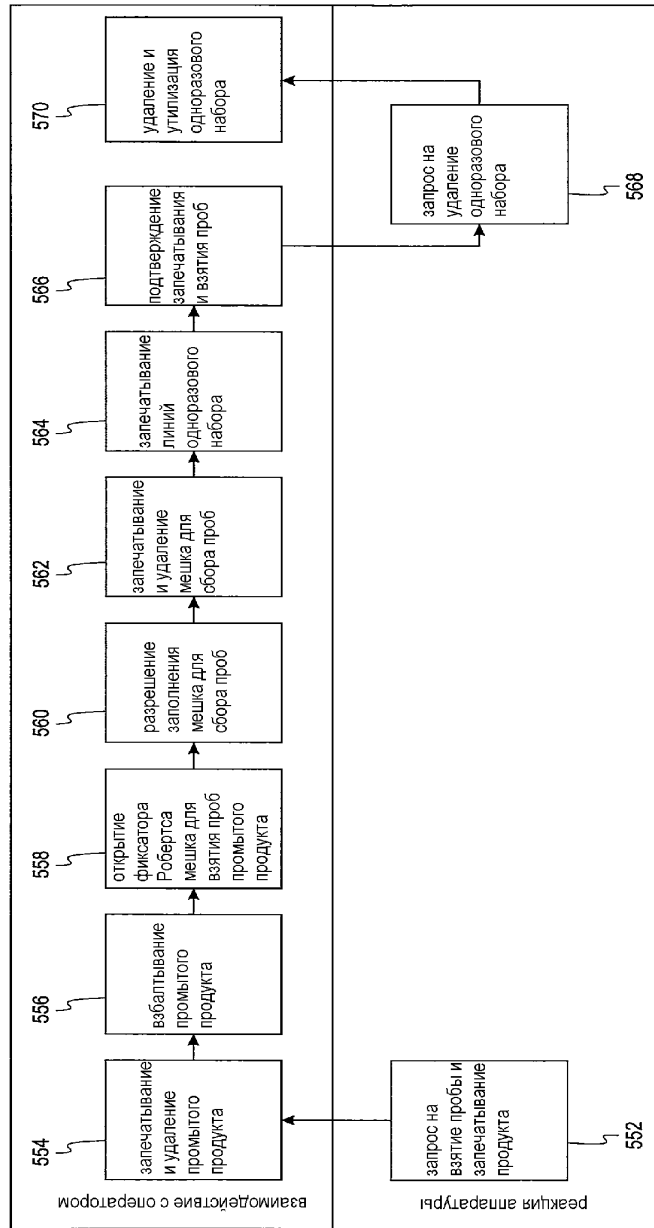


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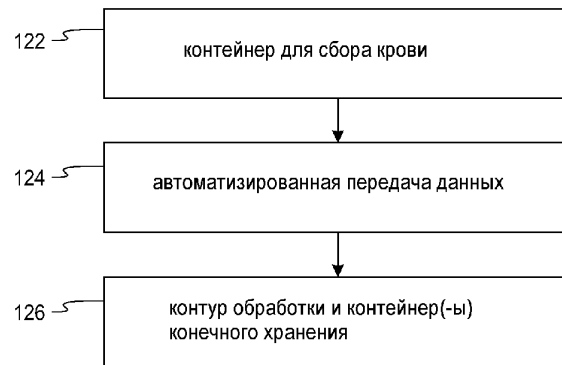


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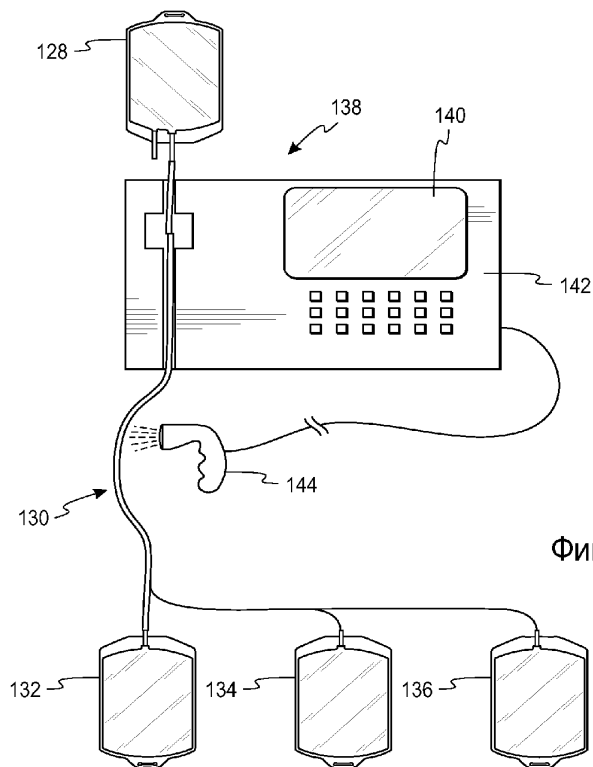
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29/30



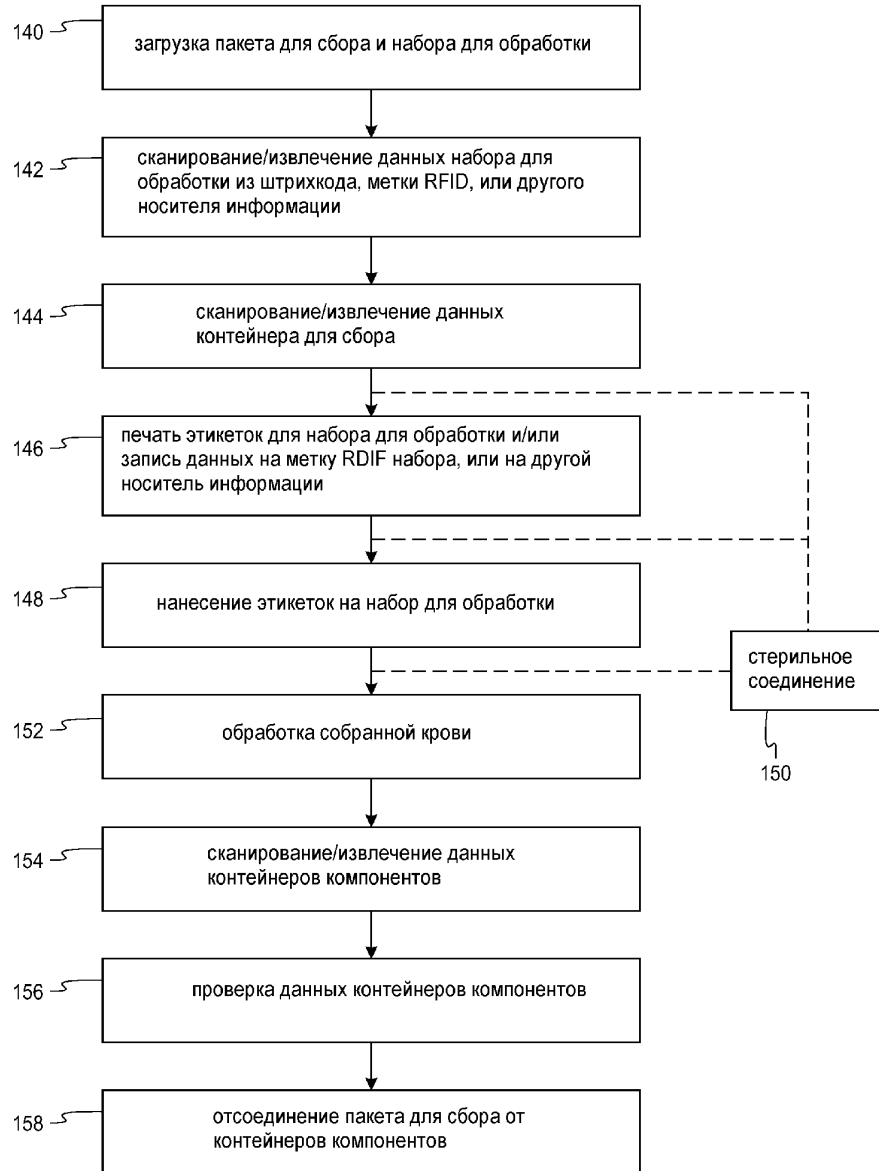
Фиг. 29



Фиг. 30



30/30



Фиг. 31

Doc code: IDS

Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)

Approved for use through 11/30/2020. OMB 0651-0031

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|-----------------------------------------------------------------------------------------------------|------------------------|------------------|
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | 3799             |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

| U.S. PATENTS                                                                                               |         |                                      |                            |                        |                                                 |                                                                          | Remove                                                                   |                |
|------------------------------------------------------------------------------------------------------------|---------|--------------------------------------|----------------------------|------------------------|-------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------------|----------------|
| Examiner Initial*                                                                                          | Cite No | Patent Number                        | Kind Code <sup>1</sup>     | Issue Date             | Name of Patentee or Applicant of cited Document | Pages, Columns, Lines where Relevant Passages or Relevant Figures Appear |                                                                          |                |
|                                                                                                            | 1       |                                      |                            |                        |                                                 |                                                                          |                                                                          |                |
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|                                                                                                            | 1       | 20060226086                          | A1                         | 2006-10-12             | Robinson et al.                                 |                                                                          |                                                                          |                |
|                                                                                                            | 2       | 20210205509                          | A1                         | 2021-07-08             | Ragusa                                          |                                                                          |                                                                          |                |
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|                                                                                                            | 1       | 1128887                              | EP                         | A1                     | 2001-09-05                                      | Baxter Int                                                               |                                                                          |                |
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| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | 3799             |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

| Examiner Initials* | Cite No | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>5</sup> |
|--------------------|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|
|                    | 1       |                                                                                                                                                                                                                                                                 |                |

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**EXAMINER SIGNATURE**

|                    |  |                 |  |
|--------------------|--|-----------------|--|
| Examiner Signature |  | Date Considered |  |
|--------------------|--|-----------------|--|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> See Kind Codes of USPTO Patent Documents at [www.USPTO.GOV](http://www.USPTO.GOV) or MPEP 901.04. <sup>2</sup> Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>3</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>4</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>5</sup> Applicant is to place a check mark here if English language translation is attached.

|                                                                                                     |                        |                  |
|-----------------------------------------------------------------------------------------------------|------------------------|------------------|
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>( Not for submission under 37 CFR 1.99) | Application Number     | 17205400         |
|                                                                                                     | Filing Date            | 2021-03-18       |
|                                                                                                     | First Named Inventor   | Michael Ragusa   |
|                                                                                                     | Art Unit               | 3799             |
|                                                                                                     | Examiner Name          | Not Yet Assigned |
|                                                                                                     | Attorney Docket Number | 130670-80104     |

### CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

**OR**

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

### SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

|            |                                       |                     |            |
|------------|---------------------------------------|---------------------|------------|
| Signature  | /Jonathan C. Lovely, Reg. No. 60,821/ | Date (YYYY-MM-DD)   | 2021-07-14 |
| Name/Print | Jonathan C. Lovely                    | Registration Number | 60,821     |

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

## Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: July 14, 2021  
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Utility Application of:  
Michael Ragusa

Application No.: 17/205,400

Confirmation No.: 4686

Filed: March 18, 2021

Art Unit: 3799

For: SYSTEM AND METHOD FOR COLLECTING  
PLASMA

Examiner: Not Yet Assigned

**INFORMATION DISCLOSURE STATEMENT (IDS)**

MS Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR 1.97, Applicant hereby makes of record the following additional documents. A PTO Form SB/08 and a full copy of each of the documents required under 37 CFR 1.98(a)(2) accompany this statement.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 C.F.R. § 1.97(b)(3)).

In accordance with 37 C.F.R. § 1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patent applications. Applicant submits herewith a copy of the cited foreign patent in accordance with 37 C.F.R. § 1.98(a)(2).

The Examiner is advised that the following co-pending applications contain subject matter that may be related to the present application:

| <b>U.S. Application</b> | <b>Filing Date</b> | <b>Publication No. / Patent No.</b> | <b>Status</b> | <b>Atty. Docket No.</b> |
|-------------------------|--------------------|-------------------------------------|---------------|-------------------------|
| 15/608,183              | May 30, 2017       | 10,758,652                          | Issued        | 130670-08002            |
| 16/866,078              | May 4, 2020        | 10,980,926                          | Issued        | 130670-08005            |
| 17/205,374              | March 18, 2021     | 2021-0205509                        | Published     | 130670-08006            |
| 15/793,339              | October 25, 2017   | 10,792,416                          | Issued        | 130670-80102            |
| 16/931,333              | July 16, 2020      | 10,980,934                          | Issued        | 130670-80103            |

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed references.

Applicant believes no fee is due with this response.

Dated: July 14, 2021

Respectfully submitted,  
 Electronic signature: /Jonathan C. Lovely, Reg.  
 No. 60,821/  
 Jonathan C. Lovely  
 Registration No.: 60,821  
 MCCARTER & ENGLISH, LLP  
 265 Franklin Street  
 Boston, Massachusetts 02110  
 (617) 449-6556  
 (617) 607-9200 (Fax)  
 Attorney/Agent For Applicant

| Electronic Acknowledgement Receipt   |                                         |
|--------------------------------------|-----------------------------------------|
| EFS ID:                              | 43247534                                |
| Application Number:                  | 17205400                                |
| International Application Number:    |                                         |
| Confirmation Number:                 | 4686                                    |
| Title of Invention:                  | SYSTEM AND METHOD FOR COLLECTING PLASMA |
| First Named Inventor/Applicant Name: | Michael Ragusa                          |
| Customer Number:                     | 86738                                   |
| Filer:                               | Jonathan Lovely                         |
| Filer Authorized By:                 |                                         |
| Attorney Docket Number:              | 130670-80104                            |
| Receipt Date:                        | 14-JUL-2021                             |
| Filing Date:                         | 18-MAR-2021                             |
| Time Stamp:                          | 15:08:19                                |
| Application Type:                    | Utility under 35 USC 111(a)             |

### Payment information:

|                        |    |
|------------------------|----|
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| Document Number | Document Description | File Name                          | File Size(Bytes)/<br>Message Digest      | Multi Part /.zip | Pages (if appl.) |
|-----------------|----------------------|------------------------------------|------------------------------------------|------------------|------------------|
| 1               | Foreign Reference    | 130670-80104_-<br>_EP1128887A1.pdf | 134969                                   | no               | 3                |
|                 |                      |                                    | 773b639750f77406c9770a79f45dbdce90c2da12 |                  |                  |

### Warnings:



|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                       |                                                                          |                                          |    |   |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|--------------------------------------------------------------------------|------------------------------------------|----|---|
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                       |                                                                          |                                          |    |   |
| 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Information Disclosure Statement (IDS)<br>Form (SB08) | 130670-80104_-<br>_Information_Disclosure_State<br>ment_Fillable_PDF.pdf | 1034219                                  | no | 4 |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                       |                                                                          | 3f4b7b0f20dcca2c14a4b88a84e6d09c4e02d079 |    |   |
| <b>Warnings:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                       |                                                                          |                                          |    |   |
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                       |                                                                          |                                          |    |   |
| 3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Transmittal Letter                                    | Information_Disclosure_State<br>ment.pdf                                 | 25174                                    | no | 2 |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                       |                                                                          | 4a6fe18aa25f7e7b6014e11b017c65cb4a69788c |    |   |
| <b>Warnings:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                       |                                                                          |                                          |    |   |
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                       |                                                                          |                                          |    |   |
| <b>Total Files Size (in bytes):</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                       |                                                                          | 1194362                                  |    |   |
| <p><b>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</b></p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b><br/> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b><br/> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b><br/> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p> |                                                       |                                                                          |                                          |    |   |



Espacenet

Bibliographic data: EP1128887 (A1) — 2001-09-05

## BLOOD PROCESSING SYSTEMS AND METHODS WITH SENSORS TO DETECT CONTAMINATION

**Inventor(s):** VISHNOI ROHIT [US]; WESTBERG TOM [US]; MULLER MATTHEW R [US]; SMITH KELLY B [US]; JOIE MICHEL L F [BE]; VANDLIK MARK R [US] ± (VISHNOI, ROHIT, ; WESTBERG, TOM, ; MULLER, MATTHEW, R, ; SMITH, KELLY, B, ; JOIE, MICHEL, L, F, ; VANDLIK, MARK, R)

**Applicant(s):** BAXTER INT [US] ± (BAXTER INTERNATIONAL INC)

**Classification:** - **international:** A61M1/02; A61M1/34; A61M1/36; B01D17/02; B01D21/24; B04B5/00; G01N21/27; G01N21/35; G01N33/48; G01N33/483; G01N33/49;  
(IPC1-7): A61M1/36; B04B5/04  
- **cooperative:** A61M1/0236 (EP); A61M1/3496 (EP); A61M1/3646 (EP); A61M1/3693 (EP); A61M1/3696 (EP); B01D17/0217 (EP); B01D21/2444 (EP); B01D21/245 (EP); B01D21/26 (EP); B01D21/262 (EP); B01D21/302 (EP); B01D21/34 (EP); A61M2202/0415 (EP); A61M2202/0429 (EP); A61M2205/125 (EP); A61M2205/128 (EP); A61M2205/331 (EP); A61M2205/3393 (EP); B01D2221/08 (EP); B01D2221/10 (EP)

**Application number:** EP20000961406 20000829 Global Dossier

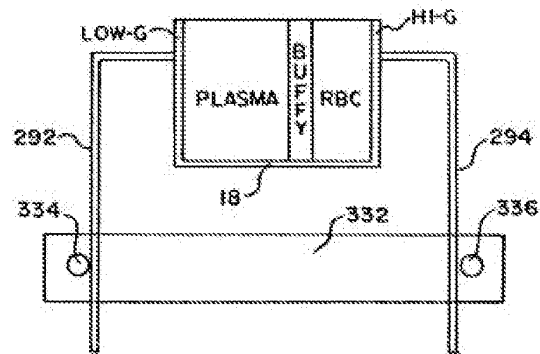
**Priority number(s):** WO2000US23697 20000829 ; US19990390492 19990903

**Also published as:** EP1128887 (A4) EP1128887 (B1) AT334708 (T) AT381359 (T) AU7336200 (A) more

Abstract not available for EP1128887 (A1)  
Abstract of corresponding document: WO0117652 (A1)

Blood processing systems and methods employ two sensors (334, 336), one (334) to detect a condition of plasma exiting a separation device (18) and another sensor (336) to detect a condition of a cellular component exiting the separation device (18). The first sensor (334) detects, e.g., contamination of the plasma due to the presence of

unwanted cellular components. The second sensor (336) detects, e.g., dilution of the cellular component due to presence of plasma. Blood processing parameters are carried out based, at least in part, by conditions detected by one or both of the sensors (334, 336).





Europäisches Patentamt

European Patent Office

Office européen des brevets

(11) Veröffentlichungsnummer:

(11) Publication number:

(11) Numéro de publication:

**EP 1 128 887 A0**

Internationale Anmeldung veröffentlicht durch die  
Weltorganisation für geistiges Eigentum unter der Nummer:

**WO 01/17652** (art. 158 des EPÜ).

International application published by the World  
Intellectual Property Organisation under number:

**WO 01/17652** (art. 158 of the EPC).

Demande internationale publiée par l'Organisation  
Mondiale de la Propriété sous le numéro:

**WO 01/17652** (art. 158 de la CBE).



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| APPLICATION NUMBER | FILING OR 371(C) DATE | FIRST NAMED APPLICANT | ATTY. DOCKET NO./TITLE |
|--------------------|-----------------------|-----------------------|------------------------|
| 17/205,400         | 03/18/2021            | Michael Ragusa        | 130670-80104           |

**CONFIRMATION NO. 4686**

86738  
MCCARTER & ENGLISH, LLP BOSTON  
265 Franklin Street  
Boston, MA 02110

**PUBLICATION NOTICE**



OC000000126826513

**Title:**SYSTEM AND METHOD FOR COLLECTING PLASMA

**Publication No.**US-2021-0205526-A1

**Publication Date:**07/08/2021

**NOTICE OF PUBLICATION OF APPLICATION**

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

The publication may be accessed through the USPTO's publically available Searchable Databases via the Internet at [www.uspto.gov](http://www.uspto.gov). The direct link to access the publication is currently <http://www.uspto.gov/patft/>.

The publication process established by the Office does not provide for mailing a copy of the publication to applicant. A copy of the publication may be obtained from the Office upon payment of the appropriate fee set forth in 37 CFR 1.19(a)(1). Orders for copies of patent application publications are handled by the USPTO's Public Records Division. The Public Records Division can be reached by telephone at (571) 272-3150 or (800) 972-6382, by facsimile at (571) 273-3250, by mail addressed to the United States Patent and Trademark Office, Public Records Division, Alexandria, VA 22313-1450 or via the Internet.

In addition, information on the status of the application, including the mailing date of Office actions and the dates of receipt of correspondence filed in the Office, may also be accessed via the Internet through the Patent Electronic Business Center at [www.uspto.gov](http://www.uspto.gov) using the public side of the Patent Application Information and Retrieval (PAIR) system. The direct link to access this status information is currently <https://portal.uspto.gov/pair/PublicPair>. Prior to publication, such status information is confidential and may only be obtained by applicant using the private side of PAIR.

Further assistance in electronically accessing the publication, or about PAIR, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

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| APPLICATION<br>NUMBER | FILING or<br>371(c) DATE | GRP ART<br>UNIT | FIL FEE REC'D | ATTY. DOCKET NO. | TOT CLAIMS | IND CLAIMS |
|-----------------------|--------------------------|-----------------|---------------|------------------|------------|------------|
| 17/205,400            | 03/18/2021               | 3781            | 3000          | 130670-80104     | 27         | 4          |

CONFIRMATION NO. 4686

86738

MCCARTER & ENGLISH, LLP BOSTON  
265 Franklin Street  
Boston, MA 02110

## FILING RECEIPT



0000000124437661

Date Mailed: 03/30/2021

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

**Please verify the accuracy of the data presented on this receipt.** If an error is noted on this Filing Receipt, please submit a written request for a corrected Filing Receipt, including a properly marked-up ADS showing the changes with strike-through for deletions and underlining for additions. If you received a "Notice to File Missing Parts" or other Notice requiring a response for this application, please submit any request for correction to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections provided that the request is grantable.

### Inventor(s)

Michael Ragusa, Hingham, MA;

### Applicant(s)

Haemonetics Corporation, Boston, MA;

**Power of Attorney:** The patent practitioners associated with Customer Number 86738

### Domestic Priority data as claimed by applicant

This application is a CON of 16/931,333 07/16/2020  
which is a CON of 15/793,339 10/25/2017 PAT 10792416  
which is a CIP of 15/608,183 05/30/2017 PAT 10758652

**Foreign Applications** for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see <http://www.uspto.gov> for more information.) - None.

*Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.*

**Permission to Access Application via Priority Document Exchange:** Yes

**Permission to Access Search Results:** Yes

Applicant may provide or rescind an authorization for access using Form PTO/SB/39 or Form PTO/SB/69 as appropriate.

**If Required, Foreign Filing License Granted:** 03/29/2021

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 17/205,400**

**Projected Publication Date:** 07/08/2021

**Non-Publication Request:** No

**Early Publication Request:** No  
**Title**

SYSTEM AND METHOD FOR COLLECTING PLASMA

**Preliminary Class**

604

**Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications:** No

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Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

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| <b>PATENT APPLICATION FEE DETERMINATION RECORD</b><br>Substitute for Form PTO-875                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                               |                                  |          |                                    |               | Application or Docket Number<br>17/205,400 |                    |                         |                    |                    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|----------|------------------------------------|---------------|--------------------------------------------|--------------------|-------------------------|--------------------|--------------------|
| <b>APPLICATION AS FILED - PART I</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                               |                                  |          |                                    |               |                                            |                    |                         |                    |                    |
| (Column 1)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                               | (Column 2)                       |          | SMALL ENTITY                       |               | OTHER THAN SMALL ENTITY                    |                    |                         |                    |                    |
| FOR                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | NUMBER FILED                                                                                                                                                                                                                  | NUMBER EXTRA                     | RATE(\$) | FEE(\$)                            |               | RATE(\$)                                   | FEE(\$)            |                         |                    |                    |
| BASIC FEE<br><small>(37 CFR 1.16(a), (b), or (c))</small>                                                                                                                                                                                                                                                                                                                                                                                                                                                           | N/A                                                                                                                                                                                                                           | N/A                              | N/A      |                                    |               | N/A                                        | 320                |                         |                    |                    |
| SEARCH FEE<br><small>(37 CFR 1.16(k), (j), or (m))</small>                                                                                                                                                                                                                                                                                                                                                                                                                                                          | N/A                                                                                                                                                                                                                           | N/A                              | N/A      |                                    |               | N/A                                        | 700                |                         |                    |                    |
| EXAMINATION FEE<br><small>(37 CFR 1.16(o), (p), or (q))</small>                                                                                                                                                                                                                                                                                                                                                                                                                                                     | N/A                                                                                                                                                                                                                           | N/A                              | N/A      |                                    |               | N/A                                        | 800                |                         |                    |                    |
| TOTAL CLAIMS<br><small>(37 CFR 1.16(i))</small>                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 27                                                                                                                                                                                                                            | minus 20 =<br>*                  | 7        |                                    |               | x 100 =                                    | 700                |                         |                    |                    |
| INDEPENDENT CLAIMS<br><small>(37 CFR 1.16(h))</small>                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 4                                                                                                                                                                                                                             | minus 3 =<br>*                   | 1        |                                    |               | x 480 =                                    | 480                |                         |                    |                    |
| APPLICATION SIZE FEE<br><small>(37 CFR 1.16(s))</small>                                                                                                                                                                                                                                                                                                                                                                                                                                                             | If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$310 (\$155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s). |                                  |          |                                    |               |                                            | 0.00               |                         |                    |                    |
| MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                               |                                  |          |                                    |               |                                            | 0.00               |                         |                    |                    |
| * If the difference in column 1 is less than zero, enter "0" in column 2.                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                               |                                  |          | TOTAL                              |               | TOTAL                                      | 3000               |                         |                    |                    |
| <b>APPLICATION AS AMENDED - PART II</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                               |                                  |          |                                    |               |                                            |                    |                         |                    |                    |
| (Column 1)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                               | (Column 2)                       |          | (Column 3)                         |               | SMALL ENTITY                               |                    | OTHER THAN SMALL ENTITY |                    |                    |
| AMENDMENT A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                               | CLAIMS REMAINING AFTER AMENDMENT |          | HIGHEST NUMBER PREVIOUSLY PAID FOR | PRESENT EXTRA | RATE(\$)                                   | ADDITIONAL FEE(\$) |                         | RATE(\$)           | ADDITIONAL FEE(\$) |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Total<br><small>(37 CFR 1.16(i))</small>                                                                                                                                                                                      | *                                | Minus    | **                                 | =             | x                                          | =                  |                         | x                  | =                  |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Independent<br><small>(37 CFR 1.16(h))</small>                                                                                                                                                                                | *                                | Minus    | ***                                | =             | x                                          | =                  |                         | x                  | =                  |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Application Size Fee (37 CFR 1.16(s))                                                                                                                                                                                         |                                  |          |                                    |               |                                            |                    |                         |                    |                    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))                                                                                                                                                               |                                  |          |                                    |               |                                            |                    |                         |                    |                    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                               |                                  |          |                                    |               | TOTAL<br>ADD'L FEE                         |                    |                         | TOTAL<br>ADD'L FEE |                    |
| AMENDMENT B                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                               | CLAIMS REMAINING AFTER AMENDMENT |          | HIGHEST NUMBER PREVIOUSLY PAID FOR | PRESENT EXTRA | RATE(\$)                                   | ADDITIONAL FEE(\$) |                         | RATE(\$)           | ADDITIONAL FEE(\$) |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Total<br><small>(37 CFR 1.16(i))</small>                                                                                                                                                                                      | *                                | Minus    | **                                 | =             | x                                          | =                  |                         | x                  | =                  |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Independent<br><small>(37 CFR 1.16(h))</small>                                                                                                                                                                                | *                                | Minus    | ***                                | =             | x                                          | =                  |                         | x                  | =                  |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Application Size Fee (37 CFR 1.16(s))                                                                                                                                                                                         |                                  |          |                                    |               |                                            |                    |                         |                    |                    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))                                                                                                                                                               |                                  |          |                                    |               |                                            |                    |                         |                    |                    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                               |                                  |          |                                    |               | TOTAL<br>ADD'L FEE                         |                    |                         | TOTAL<br>ADD'L FEE |                    |
| <div style="font-size: x-small;">             * If the entry in column 1 is less than the entry in column 2, write "0" in column 3.<br/>             ** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".<br/>             *** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".<br/>             The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.           </div> |                                                                                                                                                                                                                               |                                  |          |                                    |               |                                            |                    |                         |                    |                    |

|                                                                                                                                              |   |    |   |                          |                       |
|----------------------------------------------------------------------------------------------------------------------------------------------|---|----|---|--------------------------|-----------------------|
| Substitute for form 1449/PTO<br><br><b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><br><i>(Use as many sheets as necessary)</i> |   |    |   | <b>Complete if Known</b> |                       |
|                                                                                                                                              |   |    |   | Application Number       | Not Yet Assigned      |
|                                                                                                                                              |   |    |   | Filing Date              | Concurrently Herewith |
|                                                                                                                                              |   |    |   | First Named Inventor     | Michael Ragusa        |
|                                                                                                                                              |   |    |   | Art Unit                 | 3781                  |
|                                                                                                                                              |   |    |   | Examiner Name            | Not Yet Assigned      |
| Sheet                                                                                                                                        | 1 | of | 6 | Attorney Docket Number   | 130670-80104          |

| U.S. PATENT DOCUMENTS |                          |                                           |                                |                                                    |                                                                                 |
|-----------------------|--------------------------|-------------------------------------------|--------------------------------|----------------------------------------------------|---------------------------------------------------------------------------------|
| Examiner<br>Initials* | Cite<br>No. <sup>1</sup> | Document Number                           | Publication Date<br>MM-DD-YYYY | Name of Patentee or<br>Applicant of Cited Document | Pages, Columns, Lines, Where<br>Relevant Passages or Relevant<br>Figures Appear |
|                       |                          | Number-Kind Code <sup>2</sup> ( if known) |                                |                                                    |                                                                                 |
|                       | AA                       | US-1,025,059                              | 04-30-1912                     | Hatton et al.                                      |                                                                                 |
|                       | AB                       | US-1,611,725                              | 12-21-1926                     | Degerth et al.                                     |                                                                                 |
|                       | AC                       | US-2,087,778                              | 07-20-1937                     | Nelin                                              |                                                                                 |
|                       | AD                       | US-2,661,150                              | 12-01-1953                     | Abbott, Jr.                                        |                                                                                 |
|                       | AE                       | US-2,750,107                              | 06-12-1956                     | More                                               |                                                                                 |
|                       | AF                       | US-2,792,172                              | 05-14-1957                     | Tait                                               |                                                                                 |
|                       | AG                       | US-3,096,283                              | 07-02-1963                     | Hein                                               |                                                                                 |
|                       | AH                       | US-3,145,713                              | 08-25-1964                     | Latham, Jr.                                        |                                                                                 |
|                       | AI                       | US-3,239,136                              | 03-08-1966                     | Hein                                               |                                                                                 |
|                       | AJ                       | US-3,244,362                              | 04-05-1966                     | Hein                                               |                                                                                 |
|                       | AK                       | US-3,244,363                              | 04-05-1966                     | Hein                                               |                                                                                 |
|                       | AL                       | US-3,409,213                              | 11-05-1968                     | Latham, Jr.                                        |                                                                                 |
|                       | AM                       | US-3,456,875                              | 07-22-1969                     | Hein                                               |                                                                                 |
|                       | AN                       | US-3,489,145                              | 01-13-1970                     | Judson et al.                                      |                                                                                 |
|                       | AO                       | US-3,565,330                              | 02-23-1971                     | Latham, Jr.                                        |                                                                                 |
|                       | AP                       | US-3,655,058                              | 04-11-1972                     | Novak                                              |                                                                                 |
|                       | AQ                       | US-3,737,096                              | 06-05-1973                     | Jones et al.                                       |                                                                                 |
|                       | AR                       | US-3,774,840                              | 11-27-1973                     | Boatright                                          |                                                                                 |
|                       | AS                       | US-3,987,961                              | 10-26-1976                     | Sinn et al.                                        |                                                                                 |
|                       | AT                       | US-4,007,871                              | 02-15-1977                     | Jones et al.                                       |                                                                                 |
|                       | AU                       | US-4,010,894                              | 03-08-1977                     | Kellogg et al.                                     |                                                                                 |
|                       | AV                       | US-4,014,497                              | 03-29-1977                     | Spiewok et al.                                     |                                                                                 |
|                       | AW                       | US-4,040,965                              | 08-09-1977                     | Kohlheb                                            |                                                                                 |
|                       | AX                       | US-4,056,224                              | 11-01-1977                     | Lolachi                                            |                                                                                 |
|                       | AY                       | US-4,082,217                              | 04-04-1978                     | Westberg                                           |                                                                                 |
|                       | AZ                       | US-4,086,924                              | 05-02-1978                     | Latham, Jr.                                        |                                                                                 |
|                       | AA1                      | US-4,140,268                              | 02-20-1979                     | Lacour                                             |                                                                                 |
|                       | AB1                      | US-4,142,670                              | 03-06-1979                     | Ishimaru et al.                                    |                                                                                 |
|                       | AC1                      | US-4,151,844                              | 05-01-1979                     | Cullis et al.                                      |                                                                                 |
|                       | AD1                      | US-4,197,847                              | 04-15-1980                     | Djerassi                                           |                                                                                 |
|                       | AE1                      | US-4,285,464                              | 08-25-1981                     | Latham, Jr.                                        |                                                                                 |
|                       | AF1                      | US-4,300,717                              | 11-17-1981                     | Latham, Jr.                                        |                                                                                 |
|                       | AG1                      | US-4,303,193                              | 12-01-1981                     | Latham, Jr.                                        |                                                                                 |
|                       | AH1                      | US-4,321,921                              | 03-30-1982                     | Laszczower                                         |                                                                                 |
|                       | AI1                      | US-4,387,848                              | 06-14-1983                     | Kellogg et al.                                     |                                                                                 |
|                       | AJ1                      | US-4,425,114                              | 01-10-1984                     | Schoendorfer et al.                                |                                                                                 |
|                       | AK1                      | US-4,430,072                              | 02-07-1984                     | Kellogg et al.                                     |                                                                                 |
|                       | AL1                      | US-4,447,221                              | 05-08-1984                     | Mulzet                                             |                                                                                 |
|                       | AM1                      | US-4,457,747                              | 07-03-1984                     | Tu                                                 |                                                                                 |
|                       | AN1                      | US-4,464,167                              | 08-07-1984                     | Schoendorfer et al.                                |                                                                                 |
|                       | AO1                      | US-4,466,888                              | 08-21-1984                     | Verkaart                                           |                                                                                 |
|                       | AP1                      | US-4,482,342                              | 11-13-1984                     | Lueptow et al.                                     |                                                                                 |
|                       | AQ1                      | US-4,490,135                              | 12-25-1984                     | Troutner                                           |                                                                                 |
|                       | AR1                      | US-4,530,691                              | 07-23-1985                     | Brown                                              |                                                                                 |
|                       | AS1                      | US-4,534,863                              | 08-13-1985                     | Bacon et al.                                       |                                                                                 |

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|  | AU1 | US-4,647,279 | 03-03-1987 | Mulzet et al.       |  |
|  | AV1 | US-4,655,742 | 04-07-1987 | Vantard             |  |
|  | AW1 | US-4,680,025 | 07-14-1987 | Kruger et al.       |  |
|  | AX1 | US-4,684,361 | 08-04-1987 | Feldman et al.      |  |
|  | AY1 | US-4,692,136 | 09-08-1987 | Feldman et al.      |  |
|  | AZ1 | US-4,708,712 | 11-24-1987 | Mulzet              |  |
|  | AA2 | US-4,713,176 | 12-15-1987 | Schoendorfer et al. |  |
|  | AB2 | US-4,734,089 | 03-29-1988 | Cullis              |  |
|  | AC2 | US-4,740,202 | 04-26-1988 | Stacey et al.       |  |
|  | AD2 | US-4,740,313 | 04-26-1988 | Schoendorfer et al. |  |
|  | AE2 | US-4,755,300 | 07-05-1988 | Fischel et al.      |  |
|  | AF2 | US-4,767,396 | 08-30-1988 | Powers              |  |
|  | AG2 | US-4,795,419 | 01-03-1989 | Yawn et al.         |  |
|  | AH2 | US-4,795,448 | 01-03-1989 | Stacey et al.       |  |
|  | AI2 | US-4,806,247 | 02-21-1989 | Schoendorfer et al. |  |
|  | AJ2 | US-4,806,252 | 02-21-1989 | Brown et al.        |  |
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|  | AL2 | US-4,850,995 | 07-25-1989 | Tie et al.          |  |
|  | AM2 | US-4,869,812 | 09-26-1989 | Schoendorfer et al. |  |
|  | AN2 | US-4,871,462 | 10-03-1989 | Fischel et al.      |  |
|  | AO2 | US-4,876,013 | 10-24-1989 | Shmidt et al.       |  |
|  | AP2 | US-4,889,524 | 12-26-1989 | Fell et al.         |  |
|  | AQ2 | US-4,911,833 | 03-27-1990 | Schoendorfer et al. |  |
|  | AR2 | US-4,934,995 | 06-19-1990 | Cullis              |  |
|  | AS2 | US-4,940,543 | 07-10-1990 | Brown et al.        |  |
|  | AT2 | US-4,943,273 | 07-24-1990 | Pages               |  |
|  | AU2 | US-4,968,295 | 11-06-1990 | Neumann             |  |
|  | AV2 | US-4,983,156 | 01-08-1991 | Knelson             |  |
|  | AW2 | US-4,983,158 | 01-08-1991 | Headley             |  |
|  | AX2 | US-4,985,153 | 01-15-1991 | Kuroda et al.       |  |
|  | AY2 | US-4,994,188 | 02-19-1991 | Prince              |  |
|  | AZ2 | US-5,039,401 | 08-13-1991 | Columbus et al.     |  |
|  | AA3 | US-5,045,048 | 09-03-1991 | Kaleskas et al.     |  |
|  | AB3 | US-5,098,372 | 03-24-1992 | Jonsson             |  |
|  | AC3 | US-5,098,373 | 03-24-1992 | Polaschegg          |  |
|  | AD3 | US-5,100,372 | 03-31-1992 | Headley             |  |
|  | AE3 | US-5,100,564 | 03-31-1992 | Pall et al.         |  |
|  | AF3 | US-5,112,298 | 05-12-1992 | Prince et al.       |  |
|  | AG3 | US-5,114,396 | 05-19-1992 | Unger et al.        |  |
|  | AH3 | US-5,135,667 | 08-04-1992 | Schoendorfer        |  |
|  | AI3 | US-5,141,486 | 08-25-1992 | Antwiler            |  |
|  | AJ3 | US-5,147,290 | 09-15-1992 | Jonsson             |  |
|  | AK3 | US-5,154,716 | 10-13-1992 | Bauman et al.       |  |
|  | AL3 | US-5,174,894 | 12-29-1992 | Ohsawa et al.       |  |
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|  | AS3 | US-5,277,701 | 01-11-1994 | Christie et al.    |  |
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|  | AU3 | US-5,298,171 | 03-29-1994 | Biesel             |  |
|  | AV3 | US-5,300,060 | 04-05-1994 | Nelson             |  |
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|  | AY3 | US-5,318,512 | 06-07-1994 | Neumann            |  |
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|  | AA4 | US-5,368,542 | 11-29-1994 | McMannis et al.    |  |
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|  | AC4 | US-5,386,734 | 02-07-1995 | Pusinelli          |  |
|  | AD4 | US-5,387,174 | 02-07-1995 | Rochat             |  |
|  | AE4 | US-5,387,187 | 02-07-1995 | Fell et al.        |  |
|  | AF4 | US-5,403,272 | 04-04-1995 | Deniega et al.     |  |
|  | AG4 | US-5,405,308 | 04-11-1995 | Headley et al.     |  |
|  | AH4 | US-5,417,650 | 05-23-1995 | Gordon             |  |
|  | AI4 | US-5,431,814 | 07-11-1995 | Jorgensen          |  |
|  | AJ4 | US-5,437,598 | 08-01-1995 | Antwiler           |  |
|  | AK4 | US-5,437,624 | 08-01-1995 | Langley            |  |
|  | AL4 | US-5,462,667 | 10-31-1995 | Wollinsky et al.   |  |
|  | AM4 | US-5,470,483 | 11-28-1995 | Bene et al.        |  |
|  | AN4 | US-5,484,396 | 01-16-1996 | Naficy             |  |
|  | AO4 | US-5,494,592 | 02-27-1996 | Latham, Jr. et al. |  |
|  | AP4 | US-5,505,685 | 04-09-1996 | Antwiler           |  |
|  | AQ4 | US-5,514,070 | 05-07-1996 | Pages              |  |
|  | AR4 | US-5,543,062 | 08-06-1996 | Nishimura          |  |
|  | AS4 | US-5,551,941 | 09-03-1996 | Howell             |  |
|  | AT4 | US-5,585,007 | 12-17-1996 | Antanavich et al.  |  |
|  | AU4 | US-5,607,579 | 03-04-1997 | Latham, Jr. et al. |  |
|  | AV4 | US-5,649,903 | 07-22-1997 | Deniega et al.     |  |
|  | AW4 | US-5,651,766 | 07-29-1997 | Kingsley et al.    |  |
|  | AX4 | US-5,656,163 | 08-12-1997 | Brown              |  |
|  | AY4 | US-5,665,061 | 09-09-1997 | Antwiler           |  |
|  | AZ4 | US-5,712,798 | 01-27-1998 | Langley et al.     |  |
|  | AA5 | US-5,728,060 | 03-17-1998 | Kingsley et al.    |  |
|  | AB5 | US-5,733,253 | 03-31-1998 | Headley et al.     |  |
|  | AC5 | US-5,733,446 | 03-31-1998 | Holm               |  |
|  | AD5 | US-5,733,545 | 03-31-1998 | Hood, III          |  |
|  | AE5 | US-5,738,792 | 04-14-1998 | Schoendorfer       |  |
|  | AF5 | US-5,762,791 | 06-09-1998 | Deniega et al.     |  |
|  | AG5 | US-5,779,660 | 07-14-1998 | Kingsley et al.    |  |
|  | AH5 | US-5,783,085 | 07-21-1998 | Fischel            |  |
|  | AI5 | US-5,792,351 | 08-11-1998 | Wehrle et al.      |  |
|  | AJ5 | US-5,849,203 | 12-15-1998 | Brown et al.       |  |
|  | AK5 | US-5,882,289 | 03-16-1999 | Sakota et al.      |  |
|  | AL5 | US-5,906,589 | 05-25-1999 | Gordon et al.      |  |
|  | AM5 | US-5,919,125 | 07-06-1999 | Berch              |  |

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|                          | BA**                     | CN-2735985-Y                                                                         |  | 10-26-2005                        | Shanghai Dahua Medical<br>Apparatus Co., Ltd       | √                                                                               |
|                          | BB**                     | EP-0128683-A2                                                                        |  | 12-19-1984                        | Baxter Travenol Laboratories,<br>Inc               |                                                                                 |
|                          | BC**                     | EP-0171749-A1                                                                        |  | 02-19-1986                        | Terumo Corp                                        |                                                                                 |
|                          | BD**                     | EP-0208061-A1                                                                        |  | 01-14-1987                        | Biotest Pharma GmbH                                |                                                                                 |
|                          | BE**                     | EP-257755-A1                                                                         |  | 03-02-1988                        | Haemonetics Corp                                   |                                                                                 |
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|                          | BG**                     | EP-619145-A2                                                                         |  | 10-12-1994                        | Electromedics, Inc                                 |                                                                                 |
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|                          | BL**                     | EP-1057534-A1                                                                        |  | 12-06-2000                        | Haemonetics Corp                                   |                                                                                 |
|                          | BM**                     | EP-1295619-A2                                                                        |  | 03-26-2003                        | Terumo Corp                                        |                                                                                 |
|                          | BN**                     | EP-1374927-A1                                                                        |  | 01-02-2004                        | Terumo Corp                                        |                                                                                 |
|                          | BO**                     | FR-2258898-A1                                                                        |  | 08-22-1975                        | Heraeus Christ GmbH,dt                             |                                                                                 |
|                          | BP**                     | GB-2047110-A                                                                         |  | 11-26-1980                        | Hogman, C F                                        |                                                                                 |
|                          | BQ**                     | JP-S59-006952                                                                        |  | 01-14-1984                        | Hitachi Koki KK                                    | √                                                                               |
|                          | BR**                     | JP-S59-069166                                                                        |  | 04-19-1984                        | Nikkiso Co Ltd.                                    | √                                                                               |
|                          | BS**                     | JP-H02-052665                                                                        |  | 02-22-1990                        | Nissho KK                                          | √                                                                               |
|                          | BT**                     | JP-H03-131268                                                                        |  | 06-04-1991                        | Fresenius AG                                       | √                                                                               |
|                          | BU**                     | JP-H07-075746                                                                        |  | 03-20-1995                        | Electromedics Inc.                                 | √                                                                               |
|                          | BV**                     | JP-H08-131539                                                                        |  | 05-28-1996                        | Terumo Corp.                                       | √                                                                               |
|                          | BW**                     | JP-H09-192215                                                                        |  | 07-29-1997                        | Nakane Takaharu                                    | √                                                                               |
|                          | BX**                     | JP-2002-291872-A                                                                     |  | 10-08-2002                        | Terumo Corp                                        | √                                                                               |
|                          | BY**                     | JP-2008-506424-A                                                                     |  | 03-06-2008                        |                                                    | √                                                                               |
|                          | BZ**                     | SU-660718-A1                                                                         |  | 05-05-1979                        | Sp K B Biofizicheskoy<br>Apparatu                  |                                                                                 |
|                          | BA1**                    | SU-762982-A1                                                                         |  | 09-15-1980                        | Sp K B Biofizicheskoy<br>Apparatu                  |                                                                                 |
|                          | BB1**                    | SU-1146098-A1                                                                        |  | 03-23-1985                        | Sp K B Biofiz App                                  |                                                                                 |
|                          | BC1**                    | WO-1985/02561-A1                                                                     |  | 06-20-1985                        | Baxter Travenol Laboratories,<br>Inc               |                                                                                 |
|                          | BD1**                    | WO-1990/00059-A1                                                                     |  | 01-11-1990                        | Sirchia, Girolamo                                  |                                                                                 |
|                          | BE1**                    | WO-1990/07383-A1                                                                     |  | 07-12-1990                        | Haemonetics Corp                                   |                                                                                 |
|                          | BF1**                    | WO-1994/06535-A1                                                                     |  | 03-31-1994                        | Fischel, Halbert                                   |                                                                                 |
|                          | BG1**                    | WO-1996/11747-A2                                                                     |  | 04-25-1996                        | Transfusion, Technologies<br>Corporation           |                                                                                 |
|                          | BH1**                    | WO-1996/33023-A1                                                                     |  | 10-24-1996                        | Cobe Laboratories, Inc                             |                                                                                 |
|                          | BI1**                    | WO-2002/05059-A2                                                                     |  | 01-17-2002                        | Baxter Int                                         |                                                                                 |

|                       |  |                    |  |
|-----------------------|--|--------------------|--|
| Examiner<br>Signature |  | Date<br>Considered |  |
|-----------------------|--|--------------------|--|

|                                                                                                                                              |   |    |   |                          |                       |
|----------------------------------------------------------------------------------------------------------------------------------------------|---|----|---|--------------------------|-----------------------|
| Substitute for form 1449/PTO<br><br><b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><br><i>(Use as many sheets as necessary)</i> |   |    |   | <b>Complete if Known</b> |                       |
|                                                                                                                                              |   |    |   | Application Number       | Not Yet Assigned      |
|                                                                                                                                              |   |    |   | Filing Date              | Concurrently Herewith |
|                                                                                                                                              |   |    |   | First Named Inventor     | Michael Ragusa        |
|                                                                                                                                              |   |    |   | Art Unit                 | 3781                  |
|                                                                                                                                              |   |    |   | Examiner Name            | Not Yet Assigned      |
| Sheet                                                                                                                                        | 6 | of | 6 | Attorney Docket Number   | 130670-80104          |

|       |                   |            |             |                          |
|-------|-------------------|------------|-------------|--------------------------|
| BJ1** | WO-2007/041716-A1 | 04-12-2007 | Gambro, Inc | <input type="checkbox"/> |
|-------|-------------------|------------|-------------|--------------------------|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. \* CITE NO.: Those application(s) which are marked with an single asterisk (\*) next to the Cite No. are not supplied (under 37 CFR 1.98(a)(2)(iii)) because that application was filed after June 30, 2003 or is available in the IFW. \*\* CITE NO.: Those document(s) which are marked with an double asterisk (\*\*) next to the Cite No. are not supplied because they were previously cited by or submitted to the Office in a prior application relied upon in this application for an earlier filing date under 35 U.S.C. 120. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

| NON PATENT LITERATURE DOCUMENTS |                       |                                                                                                                                                                                                                                                                 |                |
|---------------------------------|-----------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|
| Examiner Initials*              | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>2</sup> |
|                                 | CA**                  | Haemonetics Nomogram - Male, 2 pages, May 1990.                                                                                                                                                                                                                 |                |
|                                 | CB**                  | LEMMENS et al., Estimating blood volume in obese and morbidly obese patients. Obes Surg. 2006 Jun;16(6):773-6.                                                                                                                                                  |                |
|                                 | CC**                  | NADLER et al., Prediction of blood volume in normal human adults. Surgery. 1962 Feb;51(2):224-32.                                                                                                                                                               |                |
|                                 | CD**                  | WINTERS, Complications of donor apheresis. J Clin Apher. 2006 Jul;21(2):132-41.                                                                                                                                                                                 |                |
|                                 | CE**                  | International Search Report and Written Opinion for Application No. PCT/US2018/033826, dated August 3, 2018, 10 pages.                                                                                                                                          |                |
|                                 | CF**                  | International Search Report and Written Opinion for Application No. PCT/US2018/057528, dated January 7, 2019, 17 pages.                                                                                                                                         |                |

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>Applicant is to place a check mark here if English language Translation is attached.

|                    |  |                 |  |
|--------------------|--|-----------------|--|
| Examiner Signature |  | Date Considered |  |
|--------------------|--|-----------------|--|

## Certificate of Mailing or Transmission under 37 CFR 1.8

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\_\_\_\_\_  
/Jonathan C. Lovely, Reg. No. 60,821/  
Signature

\_\_\_\_\_  
March 22, 2021  
Date

\_\_\_\_\_  
Jonathan C. Lovely  
Typed or printed name

\_\_\_\_\_  
(617) 449-6556  
Telephone number

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IDS (Citation) by Applicant (230 References) (6 pages)



| Electronic Acknowledgement Receipt   |                                         |
|--------------------------------------|-----------------------------------------|
| EFS ID:                              | 42238441                                |
| Application Number:                  | 17205400                                |
| International Application Number:    |                                         |
| Confirmation Number:                 | 4686                                    |
| Title of Invention:                  | SYSTEM AND METHOD FOR COLLECTING PLASMA |
| First Named Inventor/Applicant Name: | Michael Ragusa                          |
| Customer Number:                     | 86738                                   |
| Filer:                               | Jonathan Lovely                         |
| Filer Authorized By:                 |                                         |
| Attorney Docket Number:              | 130670-80104                            |
| Receipt Date:                        | 22-MAR-2021                             |
| Filing Date:                         |                                         |
| Time Stamp:                          | 13:33:14                                |
| Application Type:                    | Utility under 35 USC 111(a)             |

### Payment information:

| Submitted with Payment | no                   |                                         |                                                       |                  |                  |
|------------------------|----------------------|-----------------------------------------|-------------------------------------------------------|------------------|------------------|
| <b>File Listing:</b>   |                      |                                         |                                                       |                  |                  |
| Document Number        | Document Description | File Name                               | File Size(Bytes)/<br>Message Digest                   | Multi Part /.zip | Pages (if appl.) |
| 1                      | Transmittal Letter   | 130670-80104_IDS_Transmittal_Letter.PDF | 27092<br><br>b0ab9214737ab517b00c569c498105bc6e9c5b86 | no               | 3                |
| <b>Warnings:</b>       |                      |                                         |                                                       |                  |                  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                       |                           |                                          |    |   |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|---------------------------|------------------------------------------|----|---|
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                       |                           |                                          |    |   |
| 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Information Disclosure Statement (IDS)<br>Form (SB08) | 130670-80104_IDS_SB08.PDF | 93518                                    | no | 7 |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                       |                           | c06f59691db6661e97ce45abdd1308c414c5694f |    |   |
| <b>Warnings:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                       |                           |                                          |    |   |
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                       |                           |                                          |    |   |
| This is not an USPTO supplied IDS fillable form                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                       |                           |                                          |    |   |
| <b>Total Files Size (in bytes):</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                       |                           | 120610                                   |    |   |
| <p><b>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</b></p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b><br/> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b><br/> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b><br/> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p> |                                                       |                           |                                          |    |   |

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: March 22, 2021  
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Utility Application of:  
Michael Ragusa

Application No.: 17/205,400

Confirmation No.: N/A

Filed: March 18, 2021

Art Unit: 3781

For: SYSTEM AND METHOD FOR COLLECTING  
PLASMA

Examiner: Not Yet Assigned

**INFORMATION DISCLOSURE STATEMENT (IDS)**

MS Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 C.F.R. §§ 1.56, 1.97, and 1.98, the attention of the United States Patent and Trademark Office is hereby directed to the references listed on the attached PTO/SB/08. It is respectfully requested that the information be expressly considered during the prosecution of the above-identified application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

This Information Disclosure Statement is filed within three months of the U.S. filing date (37 C.F.R. § 1.97(b)(1)).

In accordance with 37 C.F.R. § 1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patents and U.S. patent applications.

In accordance with 37 C.F.R. § 1.98(d)(1) and as noted by a double-asterisk next to the Cite No. on the attached PTO/SB/08, the cited references are not supplied because they were previously

ME1 36057893v.1

cited by or submitted to the Office in prior application numbers 16/931333 filed July 16, 2020, 15/793339 filed October 25, 2017, and 15/608183 filed May 30, 2017 and relied on in the above-identified application for an earlier effective filing date under 35 U.S.C. § 120.

The Examiner is advised that the following co-pending application contains subject matter that may be related to the present application:

| <b>U.S. Application</b> | <b>Filing Date</b> | <b>Publication No. / Patent No.</b> | <b>Status</b> | <b>Atty. Docket No.</b> |
|-------------------------|--------------------|-------------------------------------|---------------|-------------------------|
| 15/608,183              | May 30, 2017       | 10,758,652                          | Issued        | 130670-08002            |
| 16/866,078              | May 4, 2020        | 2020-0261630                        | Allowed       | 130670-08005            |
| 17/205,374              | March 18, 2021     |                                     | Pending       | 130670-08006            |
| 15/793,339              | October 25, 2017   | 10,792,416                          | Issued        | 130670-80102            |
| 16/931,333              | July 16, 2020      | 2020-0345924                        | Allowed       | 130670-80103            |

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed references.

Application No.: 17/205,400

Docket No.: 130670-80104

Applicant believes no fee is due with this response.

Dated: March 22, 2021

Respectfully submitted,  
Electronic signature: /Jonathan C. Lovely, Reg.  
No. 60,821/  
Jonathan C. Lovely  
Registration No.: 60,821  
MCCARTER & ENGLISH, LLP  
265 Franklin Street  
Boston, Massachusetts 02110  
(617) 449-6556  
(617) 607-9200 (Fax)  
Attorney/Agent For Applicant

Doc Code: PA..  
Document Description: Power of Attorney

PTO/AIA/82A (07-13)  
Approved for use through 03/31/2021. OMB 0651-0035  
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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## TRANSMITTAL FOR POWER OF ATTORNEY TO ONE OR MORE REGISTERED PRACTITIONERS

NOTE: This form is to be submitted with the Power of Attorney by Applicant form (PTO/AIA/82B) to identify the application to which the Power of Attorney is directed, in accordance with 37 CFR 1.5, unless the application number and filing date are identified in the Power of Attorney by Applicant form. If neither form PTO/AIA/82A nor form PTO/AIA/82B identifies the application to which the Power of Attorney is directed, the Power of Attorney will not be recognized in the application.

|                                                                                                                                                                                        |                                         |                     |                |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|---------------------|----------------|
| Application Number                                                                                                                                                                     | Not Yet Assigned                        |                     |                |
| Filing Date                                                                                                                                                                            | Concurrently Herewith                   |                     |                |
| First Named Inventor                                                                                                                                                                   | Michael Ragusa                          |                     |                |
| Title                                                                                                                                                                                  | SYSTEM AND METHOD FOR COLLECTING PLASMA |                     |                |
| Art Unit                                                                                                                                                                               | N/A                                     |                     |                |
| Examiner Name                                                                                                                                                                          | Not Yet Assigned                        |                     |                |
| Attorney Docket Number                                                                                                                                                                 | 130670-80104                            |                     |                |
| <b>SIGNATURE of Applicant or Patent Practitioner</b>                                                                                                                                   |                                         |                     |                |
| Signature                                                                                                                                                                              | /Jonathan C. Lovely, Reg. No. 60,821/   | Date (Optional)     | March 18, 2021 |
| Name                                                                                                                                                                                   | Jonathan C. Lovely                      | Registration Number | 60,821         |
| Title (if Applicant is a juristic entity)                                                                                                                                              |                                         |                     |                |
| Applicant Name (if Applicant is a juristic entity)                                                                                                                                     |                                         |                     |                |
| <b>NOTE:</b> This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. If more than one applicant, use multiple forms. |                                         |                     |                |
| <input type="checkbox"/>                                                                                                                                                               | *Total of <u>1</u> forms are submitted. |                     |                |

## POWER OF ATTORNEY BY APPLICANT

I hereby revoke all previous powers of attorney given in the application identified in either the attached transmittal letter or the boxes below.

| Application Number | Filing Date |
|--------------------|-------------|
|                    |             |

(Note: The boxes above may be left blank if information is provided on form PTO/AIA/82A.)

- ☒ I hereby appoint the Patent Practitioner(s) associated with the following Customer Number as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above:
- OR
- ☐ I hereby appoint Practitioner(s) named in the attached list (form PTO/AIA/82C) as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the patent application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above. (Note: Complete form PTO/AIA/82C.)

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- ☒ The address associated with the above-mentioned Customer Number
- OR

☐ The address associated with Customer Number:

OR

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Address

City

State

Zip

Country

Telephone

Email

I am the Applicant (if the Applicant is a juristic entity, list the Applicant name in the box):

**Haemonetics Corporation**

- ☐ Inventor or Joint Inventor (title not required below)
- ☐ Legal Representative of a Deceased or Legally Incapacitated Inventor (title not required below)
- ☒ Assignee or Person to Whom the Inventor is Under an Obligation to Assign (provide signer's title if applicant is a juristic entity)
- ☐ Person Who Otherwise Shows Sufficient Proprietary Interest (e.g., a petition under 37 CFR 1.46(b)(2) was granted in the application or is concurrently being filed with this document) (provide signer's title if applicant is a juristic entity)

### SIGNATURE of Applicant for Patent

The undersigned (whose title is supplied below) is authorized to act on behalf of the applicant (e.g., where the applicant is a juristic entity).

Signature

Date (Optional)

Name

John F. Perullo

Title

Vice President, Associate General Counsel and Chief Intellectual Property Officer, Haemonetics Corporation

**NOTE:** Signature - This form must be signed by the applicant in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. If more than one applicant, use multiple forms.

☐ Total of forms are submitted.

This collection of information is required by 37 CFR 1.131, 1.32, and 1.33. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 3 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1480, Alexandria, VA 22313-1480.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

**DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN  
APPLICATION DATA SHEET (37 CFR 1.76)**

Title of  
Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA

As the below named inventor, I hereby declare that:

This declaration ☐ The attached application, or  
is directed to:

☒ United States application or PCT international application number 15/793,339  
filed on 10/25/2017

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby state that I have reviewed and understand the contents of the above identified specification,

I acknowledge the duty to disclose all information known to me that is material to patentability in accordance with Title 37, Code of Federal Regulations § 1.56.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

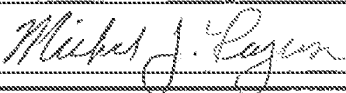
**WARNING:**

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

**LEGAL NAME OF INVENTOR**

Inventor: Michael Ragusa

Date (Optional): Oct 25, 2018

Signature: 

Note: An application data sheet (PTO/AIA/14 or equivalent), including naming the entire inventive entity, must accompany this form. Use an additional PTO/SB/AIA/01 form for each additional inventor.



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|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                         |                               |              |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|-------------------------------|--------------|
| <b>Application Data Sheet 37 CFR 1.76</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                         | <b>Attorney Docket Number</b> | 130670-80104 |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                         | <b>Application Number</b>     |              |
| <b>Title of Invention</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | SYSTEM AND METHOD FOR COLLECTING PLASMA |                               |              |
| <p>The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76. This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.</p> |                                         |                               |              |

**Secrecy Order 37 CFR 5.2:**

☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

**Inventor Information:**

|                                                                                                                                                                             |                                             |                       |                    |                                |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------|-----------------------|--------------------|--------------------------------|
| <b>Inventor</b>                                                                                                                                                             | 1 <span style="float: right;">Remove</span> |                       |                    |                                |
| <b>Legal Name</b>                                                                                                                                                           |                                             |                       |                    |                                |
| <b>Prefix</b>                                                                                                                                                               | <b>Given Name</b>                           | <b>Middle Name</b>    | <b>Family Name</b> | <b>Suffix</b>                  |
|                                                                                                                                                                             | Michael                                     |                       | Ragusa             |                                |
| <b>Residence Information (Select One)</b> • US Residency   Non US Residency   Active US Military Service                                                                    |                                             |                       |                    |                                |
| <b>City</b>                                                                                                                                                                 | Hingham                                     | <b>State/Province</b> | MA                 | <b>Country of Residence</b> US |
| <b>Mailing Address of Inventor:</b>                                                                                                                                         |                                             |                       |                    |                                |
| <b>Address 1</b>                                                                                                                                                            | 4 Willow Circle                             |                       |                    |                                |
| <b>Address 2</b>                                                                                                                                                            |                                             |                       |                    |                                |
| <b>City</b>                                                                                                                                                                 | Hingham                                     | <b>State/Province</b> | MA                 |                                |
| <b>Postal Code</b>                                                                                                                                                          | 02043                                       | <b>Country</b>        | US                 |                                |
| All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the Add button. <span style="float: right;">Add</span> |                                             |                       |                    |                                |

**Correspondence Information:**

|                                                                                                                                       |                     |                        |                           |
|---------------------------------------------------------------------------------------------------------------------------------------|---------------------|------------------------|---------------------------|
| Enter either Customer Number or complete the Correspondence Information section below.<br>For further information see 37 CFR 1.33(a). |                     |                        |                           |
| <input type="checkbox"/> An Address is being provided for the correspondence information of this application.                         |                     |                        |                           |
| <b>Customer Number</b>                                                                                                                | 86738               |                        |                           |
| <b>Email Address</b>                                                                                                                  | docket@mccarter.com | <span>Add Email</span> | <span>Remove Email</span> |

**Application Information:**

|                                                |                                         |                                                  |                          |
|------------------------------------------------|-----------------------------------------|--------------------------------------------------|--------------------------|
| <b>Title of the Invention</b>                  | SYSTEM AND METHOD FOR COLLECTING PLASMA |                                                  |                          |
| <b>Attorney Docket Number</b>                  | 130670-80104                            | <b>Small Entity Status Claimed</b>               | <input type="checkbox"/> |
| <b>Application Type</b>                        | Nonprovisional                          |                                                  |                          |
| <b>Subject Matter</b>                          | Utility                                 |                                                  |                          |
| <b>Total Number of Drawing Sheets (if any)</b> | 5                                       | <b>Suggested Figure for Publication (if any)</b> |                          |

|                                           |                                         |                        |              |
|-------------------------------------------|-----------------------------------------|------------------------|--------------|
| <b>Application Data Sheet 37 CFR 1.76</b> |                                         | Attorney Docket Number | 130670-80104 |
|                                           |                                         | Application Number     |              |
| Title of Invention                        | SYSTEM AND METHOD FOR COLLECTING PLASMA |                        |              |

**Filing By Reference:**

Only complete this section when filing an application by reference under 35 U.S.C. 111(c) and 37 CFR 1.57(a). Do not complete this section if application papers including a specification and any drawings are being filed. Any domestic benefit or foreign priority information must be provided in the appropriate section(s) below (i.e., "Domestic Benefit/National Stage Information" and "Foreign Priority Information").

For the purposes of a filing date under 37 CFR 1.53(b), the description and any drawings of the present application are replaced by this reference to the previously filed application, subject to conditions and requirements of 37 CFR 1.57(a).

|                                                        |                          |                                            |
|--------------------------------------------------------|--------------------------|--------------------------------------------|
| Application number of the previously filed application | Filing date (YYYY-MM-DD) | Intellectual Property Authority or Country |
|                                                        |                          |                                            |

**Publication Information:**

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)

☐ **Request Not to Publish.** I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application **has not and will not** be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

**Representative Information:**

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32). Either enter Customer Number or complete the Representative Name section below. If both sections are completed the customer Number will be used for the Representative Information during processing.

|                    |                                                  |                                              |                                                         |
|--------------------|--------------------------------------------------|----------------------------------------------|---------------------------------------------------------|
| Please Select One: | <input checked="" type="radio"/> Customer Number | <input type="radio"/> US Patent Practitioner | <input type="radio"/> Limited Recognition (37 CFR 11.9) |
| Customer Number    | 86738                                            |                                              |                                                         |

**Domestic Benefit/National Stage Information:**

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, 365(c), or 386(c) or indicate National Stage entry from a PCT application. Providing benefit claim information in the Application Data Sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78.

When referring to the current application, please leave the "Application Number" field blank.

|                          |                 |                          |                                    |
|--------------------------|-----------------|--------------------------|------------------------------------|
| Prior Application Status | Pending         | <a href="#">Remove</a>   |                                    |
| Application Number       | Continuity Type | Prior Application Number | Filing or 371(c) Date (YYYY-MM-DD) |
|                          | Continuation of | 16/931333                | 2020-07-16                         |

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

|                                                                                                                       |                         |                                         |                          |               |                         |
|-----------------------------------------------------------------------------------------------------------------------|-------------------------|-----------------------------------------|--------------------------|---------------|-------------------------|
| <b>Application Data Sheet 37 CFR 1.76</b>                                                                             |                         | Attorney Docket Number                  |                          | 130670-80104  |                         |
|                                                                                                                       |                         | Application Number                      |                          |               |                         |
| Title of Invention                                                                                                    |                         | SYSTEM AND METHOD FOR COLLECTING PLASMA |                          |               |                         |
| Prior Application Status                                                                                              |                         | Patented                                |                          | Remove        |                         |
| Application Number                                                                                                    | Continuity Type         | Prior Application Number                | Filing Date (YYYY-MM-DD) | Patent Number | Issue Date (YYYY-MM-DD) |
| 16/931333                                                                                                             | Continuation of         | 15/793339                               | 2017-10-25               | 10792416      | 2020-10-06              |
| Prior Application Status                                                                                              |                         | Patented                                |                          | Remove        |                         |
| Application Number                                                                                                    | Continuity Type         | Prior Application Number                | Filing Date (YYYY-MM-DD) | Patent Number | Issue Date (YYYY-MM-DD) |
| 15/793339                                                                                                             | Continuation in part of | 15/608183                               | 2017-05-30               | 10758652      | 2020-09-01              |
| Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the <b>Add</b> button. |                         |                                         |                          |               | Add                     |

## Foreign Priority Information:

This section allows for the applicant to claim priority to a foreign application. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55. When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX)<sup>i</sup> the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(i)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

|                                                                                                        |                      |                          |                                          |
|--------------------------------------------------------------------------------------------------------|----------------------|--------------------------|------------------------------------------|
|                                                                                                        |                      |                          | Remove                                   |
| Application Number                                                                                     | Country <sup>i</sup> | Filing Date (YYYY-MM-DD) | Access Code <sup>i</sup> (if applicable) |
|                                                                                                        |                      |                          |                                          |
| Additional Foreign Priority Data may be generated within this form by selecting the <b>Add</b> button. |                      |                          | Add                                      |

## Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

☐ This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.

NOTE: By providing this statement under 37 CFR 1.55 or 1.78, this application, with a filing date on or after March 16, 2013, will be examined under the first inventor to file provisions of the AIA.

|                                           |                                         |                        |              |
|-------------------------------------------|-----------------------------------------|------------------------|--------------|
| <b>Application Data Sheet 37 CFR 1.76</b> |                                         | Attorney Docket Number | 130670-80104 |
|                                           |                                         | Application Number     |              |
| Title of Invention                        | SYSTEM AND METHOD FOR COLLECTING PLASMA |                        |              |

## Authorization or Opt-Out of Authorization to Permit Access:

When this Application Data Sheet is properly signed and filed with the application, applicant has provided written authority to permit a participating foreign intellectual property (IP) office access to the instant application-as-filed (see paragraph A in subsection 1 below) and the European Patent Office (EPO) access to any search results from the instant application (see paragraph B in subsection 1 below).

Should applicant choose not to provide an authorization identified in subsection 1 below, applicant **must opt-out** of the authorization by checking the corresponding box A or B or both in subsection 2 below.

**NOTE:** This section of the Application Data Sheet is **ONLY** reviewed and processed with the **INITIAL** filing of an application. After the initial filing of an application, an Application Data Sheet cannot be used to provide or rescind authorization for access by a foreign IP office(s). Instead, Form PTO/SB/39 or PTO/SB/69 must be used as appropriate.

### 1. Authorization to Permit Access by a Foreign Intellectual Property Office(s)

**A. Priority Document Exchange (PDX)** - Unless box A in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the State Intellectual Property Office of the People's Republic of China (SIPO), the World Intellectual Property Organization (WIPO), and any other foreign intellectual property office participating with the USPTO in a bilateral or multilateral priority document exchange agreement in which a foreign application claiming priority to the instant patent application is filed, access to: (1) the instant patent application-as-filed and its related bibliographic data, (2) any foreign or domestic application to which priority or benefit is claimed by the instant application and its related bibliographic data, and (3) the date of filing of this Authorization. See 37 CFR 1.14(h)(1).

**B. Search Results from U.S. Application to EPO** - Unless box B in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the EPO access to the bibliographic data and search results from the instant patent application when a European patent application claiming priority to the instant patent application is filed. See 37 CFR 1.14(h)(2).

The applicant is reminded that the EPO's Rule 141(1) EPC (European Patent Convention) requires applicants to submit a copy of search results from the instant application without delay in a European patent application that claims priority to the instant application.

### 2. Opt-Out of Authorizations to Permit Access by a Foreign Intellectual Property Office(s)

☐ A. Applicant **DOES NOT** authorize the USPTO to permit a participating foreign IP office access to the instant application-as-filed. If this box is checked, the USPTO will not be providing a participating foreign IP office with any documents and information identified in subsection 1A above.

☐ B. Applicant **DOES NOT** authorize the USPTO to transmit to the EPO any search results from the instant patent application. If this box is checked, the USPTO will not be providing the EPO with search results from the instant application.

**NOTE:** Once the application has published or is otherwise publicly available, the USPTO may provide access to the application in accordance with 37 CFR 1.14.

|                                           |                                         |                        |              |
|-------------------------------------------|-----------------------------------------|------------------------|--------------|
| <b>Application Data Sheet 37 CFR 1.76</b> |                                         | Attorney Docket Number | 130670-80104 |
|                                           |                                         | Application Number     |              |
| Title of Invention                        | SYSTEM AND METHOD FOR COLLECTING PLASMA |                        |              |

## Applicant Information:

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                          |                                                  |                |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|--------------------------------------------------|----------------|
| Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                          |                                                  |                |
| <b>Applicant</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 1                                        | <a href="#">Remove</a>                           |                |
| <p>If the applicant is the inventor (or the remaining joint inventor or inventors under 37 CFR 1.45), this section should not be completed. The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46. If the applicant is an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest) together with one or more joint inventors, then the joint inventor or inventors who are also the applicant should be identified in this section.</p> |                                          |                                                  |                |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                          | <a href="#">Clear</a>                            |                |
| <input type="radio"/> Assignee                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Legal Representative under 35 U.S.C. 117 |                                                  | Joint Inventor |
| Person to whom the inventor is obligated to assign.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                          | Person who shows sufficient proprietary interest |                |
| If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                          |                                                  |                |
| <div> <div></div> <div></div> </div>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                          |                                                  |                |
| Name of the Deceased or Legally Incapacitated Inventor: <input type="text"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                          |                                                  |                |
| If the Applicant is an Organization check here. <input checked="" type="checkbox"/>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                          |                                                  |                |
| Organization Name                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Haemonetics Corporation                  |                                                  |                |
| <b>Mailing Address Information For Applicant:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                          |                                                  |                |
| Address 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 125 Summer Street                        |                                                  |                |
| Address 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                          |                                                  |                |
| City                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Boston                                   | State/Province                                   | MA             |
| Country                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | US                                       | Postal Code                                      | 02110          |
| Phone Number                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                          | Fax Number                                       |                |
| Email Address                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                          |                                                  |                |
| Additional Applicant Data may be generated within this form by selecting the Add button. <a href="#">Add</a>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                          |                                                  |                |

## Assignee Information including Non-Applicant Assignee Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

|                                           |                                         |                        |              |
|-------------------------------------------|-----------------------------------------|------------------------|--------------|
| <b>Application Data Sheet 37 CFR 1.76</b> |                                         | Attorney Docket Number | 130670-80104 |
|                                           |                                         | Application Number     |              |
| Title of Invention                        | SYSTEM AND METHOD FOR COLLECTING PLASMA |                        |              |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                      |                      |                      |                                       |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|----------------------|---------------------------------------|
| <b>Assignee</b>   1                                                                                                                                                                                                                                                                                                                                                                                                                                    |                      |                      |                      |                                       |
| Complete this section if assignee information, including non-applicant assignee information, is desired to be included on the patent application publication. An assignee-applicant identified in the "Applicant Information" section will appear on the patent application publication as an applicant. For an assignee-applicant, complete this section only if identification as an assignee is also desired on the patent application publication. |                      |                      |                      |                                       |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                      |                      |                      | <input type="button" value="Remove"/> |
| If the Assignee or Non-Applicant Assignee is an Organization check here.                                                                                                                                                                                                                                                                                                                                                                               |                      |                      |                      | <input type="checkbox"/>              |
| Prefix                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Given Name           | Middle Name          | Family Name          | Suffix                                |
| <input type="text"/>                                                                                                                                                                                                                                                                                                                                                                                                                                   | <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="text"/>                  |
| <b>Mailing Address Information For Assignee including Non-Applicant Assignee:</b>                                                                                                                                                                                                                                                                                                                                                                      |                      |                      |                      |                                       |
| Address 1                                                                                                                                                                                                                                                                                                                                                                                                                                              |                      | <input type="text"/> |                      |                                       |
| Address 2                                                                                                                                                                                                                                                                                                                                                                                                                                              |                      | <input type="text"/> |                      |                                       |
| City                                                                                                                                                                                                                                                                                                                                                                                                                                                   | <input type="text"/> | State/Province       | <input type="text"/> |                                       |
| Country i                                                                                                                                                                                                                                                                                                                                                                                                                                              | <input type="text"/> | Postal Code          | <input type="text"/> |                                       |
| Phone Number                                                                                                                                                                                                                                                                                                                                                                                                                                           | <input type="text"/> | Fax Number           | <input type="text"/> |                                       |
| Email Address                                                                                                                                                                                                                                                                                                                                                                                                                                          | <input type="text"/> |                      |                      |                                       |
| Additional Assignee or Non-Applicant Assignee Data may be generated within this form by selecting the Add button.                                                                                                                                                                                                                                                                                                                                      |                      |                      |                      | <input type="button" value="Add"/>    |

**Signature:**

**NOTE:** This Application Data Sheet must be signed in accordance with 37 CFR 1.33(b). **However, if this Application Data Sheet is submitted with the INITIAL filing of the application and either box A or B is not checked in subsection 2 of the "Authorization or Opt-Out of Authorization to Permit Access" section, then this form must also be signed in accordance with 37 CFR 1.14(c).**

This Application Data Sheet **must** be signed by a patent practitioner if one or more of the applicants is a **juristic entity** (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, **all** joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of **all** joint inventor-applicants.

See 37 CFR 1.4(d) for the manner of making signatures and certifications.

|                                                                                     |                                      |           |                   |                                    |
|-------------------------------------------------------------------------------------|--------------------------------------|-----------|-------------------|------------------------------------|
| <b>Signature</b>                                                                    | Jonathan C. Lovely, Reg. No. 60,821/ |           | Date (YYYY-MM-DD) | 2021-03-18                         |
| First Name                                                                          | Jonathan                             | Last Name | Lovely            | Registration Number                |
|                                                                                     |                                      |           |                   | 60,821                             |
| Additional Signature may be generated within this form by selecting the Add button. |                                      |           |                   | <input type="button" value="Add"/> |

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

|                                           |                                         |                        |              |
|-------------------------------------------|-----------------------------------------|------------------------|--------------|
| <b>Application Data Sheet 37 CFR 1.76</b> |                                         | Attorney Docket Number | 130670-80104 |
|                                           |                                         | Application Number     |              |
| Title of Invention                        | SYSTEM AND METHOD FOR COLLECTING PLASMA |                        |              |

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

## Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.



## **SYSTEM AND METHOD FOR COLLECTING PLASMA**

### **Priority**

**[0001]** This application is a continuation of and claims priority from co-pending U.S. Application No. 16/931,333, entitled “System and Method for Collecting Plasma,” filed July 16, 2020, attorney docket number 130670-80103, and naming Michael Ragusa as inventor, the disclosure of which is incorporated herein, in its entirety, by reference.

**[0002]** U.S. Application No. 16/931,33, in turn, is a continuation of and claims priority from U.S. Application No. 15/793,339, entitled “System and Method for Collecting Plasma,” filed October 25, 2017, now U.S. Patent No. 10,792,416, attorney docket number 130670-80102 (formerly 1611/C86), and naming Michael Ragusa as inventor, the disclosure of which is incorporated herein, in its entirety, by reference.

**[0003]** U.S. Application No. 15/793,339 is a continuation-in-part of and claims priority to U.S. Patent Application No. 15/608,183, entitled “System and Method for Collecting Plasma,” filed May 30, 2017, now U.S. Patent No. 10,758,652, attorney docket number 130670-08002 (formerly 1611/C80), and naming Michael Ragusa as inventor, the disclosure of which is incorporated herein, in its entirety, by reference.

### **Technical Field**

**[0004]** The present invention relates to systems and methods for blood apheresis, and more particularly system and methods for collecting a plasma product.

### **Background Art**

**[0005]** Apheresis is a procedure in which individual blood components can be separated and collected from whole blood temporarily withdrawn from a subject. Typically, whole blood is withdrawn through a needle inserted into a vein of the subjects arm and into a cell separator, such as a centrifugal bowl. Once the whole blood is separated into its various components, one or more of the components (e.g., plasma) can be removed from the centrifugal bowl. The remaining components can be returned to the subject along with optional compensation fluid to make up for the volume of the removed component. The

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process of drawing and returning continues until the quantity of the desired component has been collected, at which point the process is stopped. A central feature of apheresis systems is that the processed but unwanted components are returned to the donor. Separated blood components may include, for example, a high density component such as red blood cells, an intermediate density component such as platelets or white blood cells, and a lower density component such as plasma.

**[0006]** Many jurisdictions have regulations regarding the amount of whole blood and/or blood components that can be removed from a donor. For example, the U.S. Food and Drug Administration (“the FDA”) sets both an upper limit on the volume of plasma that may be collected (e.g., 800 ml for an adult weighing more than 175 pounds) as well as an upper limit on the total collection volume (e.g., 880 ml for an adult weighing more than 175 pounds). Prior art plasma collection systems are unable to determine the total volume of plasma that has been collected (e.g., because the product collected is a mixture of plasma and anticoagulant) and, therefore collect based on the total collection volume, even if the total volume of plasma that has been collected is below the limit prescribed by the FDA. Additionally, prior art collection systems do not tailor the amount of plasma collected to the individual (e.g., other than what weight group they fall into) and, therefore, the percentage of the patient’s plasma that is collected varies widely from patient to patient (e.g., only 23% percent of the plasma is collected for some patients and 29% - or greater – of the plasma is collected for others).

### **Summary of the Invention**

**[0007]** In accordance with some embodiments of the present invention, a method for collecting plasma includes determining the weight and hematocrit of a donor, and inserting a venous-access device into the donor. Once the venous access device is inserted, the method may withdraw whole blood from the donor through the venous-access device and a draw line that is connected to a blood component separation device. The method may then introduce anticoagulant into the withdrawn whole blood through an anticoagulant line and separate, using the blood component separation device, the withdrawn whole blood into a plasma component and at least a second blood component. Once separated, the plasma component

may be collected from the blood component separation device and into a plasma collection container. During processing, the method may calculate (1) a percentage of anticoagulant in the collected plasma component, and (2) a volume of pure plasma collected within the plasma collection container. The volume of pure plasma may be based, at least in part, on the calculated percentage of anticoagulant in the collected plasma component. The method may continue the process (e.g., withdrawing whole blood, introducing anticoagulant into the whole blood, separating the blood, collecting the plasma, and calculating the percentage of anticoagulant and volume of pure plasma) until a target volume of pure plasma is collected within the plasma collection container.

**[0008]** In some embodiments, the method may determine a change in volume within an anticoagulant container, and the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the change in volume within the anticoagulant container. Additionally or alternatively, the method may determine a volume of anticoagulant introduced into the whole blood based on a number of rotations of an anticoagulant pump. In such embodiments, the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the number of rotations of the anticoagulant pump. The method may also determine a volume of anticoagulant within the blood component separation device, and the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the volume of anticoagulant within the blood component separation device.

**[0009]** In further embodiments, the method may monitor the volume and/or weight of the plasma component collected within the plasma collection container (e.g., using a weight sensor), and the calculated volume of pure plasma collected within the plasma collection device may be based, at least in part, on the monitored volume and/or weight of the collected plasma component. Additionally or alternatively, determining the hematocrit of the donor may include monitoring a volume of red blood cells collection within the blood separation device. In such embodiments, the determined hematocrit of the donor may be based, at least in part, on the monitored volume of red blood cells collected within the blood separation device and the volume of whole blood withdrawn from the donor.

**[0010]** The target volume of pure plasma may be based, at least in part, on the weight of the donor. The percentage of anticoagulant in the collected plasma component may include at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant that is added to the system during a priming step. After collecting at least a portion of the target volume of pure plasma, the method may return the second blood component to the donor through a return line.

**[0011]** In accordance with additional embodiments, a system for collecting plasma includes a venous-access device for drawing whole blood from a subject and returning blood components to the subject, and a blood component separation device for separating the drawn blood into a plasma component and a second blood component. The blood component separation device has an outlet and is configured to send the plasma component to a plasma container. The system may also include a blood draw line fluidly connected to the venous-access device and an anticoagulant line connected to an anticoagulant source. The blood draw line transports drawn whole blood to the blood component separation device, and the flow through the blood draw line may be controlled by a blood draw pump. The anticoagulant line may introduce anticoagulant into the drawn whole blood.

**[0012]** Additionally, the system may include a controller that controls the operation of the centrifuge bowl. The controller may also calculate (1) a percentage of anticoagulant in the collected plasma component, and (2) a volume of pure plasma collected within the plasma container. The volume of pure plasma may be based, at least in part, upon the percentage of anticoagulant in the collected plasma component. The controller may stop the blood draw pump when a target volume of pure plasma (e.g., based, at least in part, on the weight of the donor) is collected within the plasma container. In some embodiments, the percentage of anticoagulant in the collected plasma component may be based, at least in part, on the volume of anticoagulant added to the drawn whole blood and the subject's hematocrit.

**[0013]** The system may also include an anticoagulant source weight sensor that measures the weight of the anticoagulant source. The controller may monitor the change in volume within the anticoagulant container based on the measured weight of the anticoagulant source, and the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the change in volume within the anticoagulant source. Additionally or

alternatively, the controller may monitor the number of rotations of an anticoagulant pump to determine a volume of anticoagulant introduced into the whole blood. In such embodiments, the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the number of rotations of the anticoagulant pump.

**[0014]** In some embodiments, the system may include an optical sensor located on the blood component separation device. The optical sensor may 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 percentage of anticoagulant in the collected plasma may be based, at least in part, on the volume of anticoagulant within the blood component separation device.

**[0015]** In additional embodiments, the system may also include a plasma container weight sensor that monitors a volume and/or weight of the plasma component collected within the plasma collection container. The calculated volume of pure plasma collected within the plasma collection container may be based, at least in part, on the monitored volume and/or weight of collected plasma component. The system may also have an optical sensor located on the blood component separation device. The optical sensor may monitor the volume of red blood cells collected within the blood separation device. The controller may then determine the subject's hematocrit based, at least in part, upon on the monitored volume of red blood cells collected within the blood separation device and the volume of whole blood withdrawn from the donor. The percentage of anticoagulant in the collected plasma component may include at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant added to the system during a priming step.

**[0016]** In accordance with additional embodiments, a method for collecting plasma determines the weight, height, and hematocrit of a donor, and calculates a donor plasma volume based, at least in part, on the weight, height and hematocrit of the donor. The method then calculates a target plasma collection volume based, at least in part, on the calculated donor plasma volume and a target percentage of plasma (e.g., between 26.5 and 29.5 percent of the donor's plasma volume), and withdraws whole blood from the donor through the venous-access device and a first line that is connected to a blood component separation

device. As the whole blood is withdrawn, the method may introduce anticoagulant into the withdrawn whole blood through an anticoagulant line.

**[0017]** The blood component separation device separates the withdrawn whole blood into a plasma component and at least a second blood component, and the method may collect the plasma component from the blood component separation device and into a plasma collection container. During processing, the method may calculate a volume of pure plasma collected within the plasma collection container. The method continues the withdrawing, introduction of anticoagulant, separating, collecting, and calculating steps until the volume of pure plasma collected within the plasma collection container equals the target plasma collection volume.

**[0018]** In some embodiments, after collecting at least a portion of the target plasma collection volume, the method may return the contents of the blood component separation device to the donor through the first line. Additionally or alternatively, the method may calculate an intravascular deficit based, at least in part on, the volume of pure plasma collected and the volume of the contents of the blood component separation device that are returned to the donor. The method may also return a volume of saline to the donor to obtain a target intravascular deficit. The target intravascular deficit may be between -250 and 500 milliliters (e.g., it may be 0 milliliters or 250 milliliters). The donor plasma volume may be calculated based, at least in part, on the donor's body mass index that, in turn, is calculated based on the donor's weight and height.

**[0019]** In further embodiments, the method may include calculating a percentage of anticoagulant in the collected plasma component. In such embodiments, the volume of pure plasma may be based, at least in part, on the calculated percentage of anticoagulant in the collected plasma component. The calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on a change in volume within the anticoagulant container, the number of rotations of the anticoagulant pump, and/or the volume of anticoagulant within the blood component separation device. The method may determine the change in volume within the anticoagulant container, the volume of anticoagulant introduced into the whole blood, and/or the volume of anticoagulant within the blood component separation device. The percentage of anticoagulant in the collected plasma component may

include at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant added during a priming step.

**[0020]** In some embodiments, the method may include monitoring a volume or and/or weight of the plasma component collected within the plasma collection container. In such embodiments, the calculated volume of pure plasma collected within the plasma collection device may be based, at least in part, on the monitored volume and/or weight of collected plasma component. To determine the donor's hematocrit, the method may monitor the volume of red blood cells collected within the blood separation device. The hematocrit of the donor may be based, at least in part, on the monitored volume of red blood cells collected within the blood separation device and the volume of whole blood withdrawn from the donor.

**[0021]** In accordance with still further embodiments, a system for collecting plasma includes a venous-access device for drawing whole blood from a subject and returning blood components to the subject, and a blood component separation device for separating the drawn blood into a plasma component and a second blood component. The blood component separation device may have an outlet and may send the plasma component to a plasma container. The system may also have a first line and an anticoagulant line. The first line may be fluidly connected to the venous-access device and may (1) transport drawn whole blood to the blood component separation device and (2) return fluid within the blood component separation device to the subject. The flow through the first line may be controlled by a first pump. The anticoagulant line may be connected to an anticoagulant source and may introduce anticoagulant into the drawn whole blood.

**[0022]** The system may also include a controller that controls the operation of the centrifuge bowl and the first pump. The controller may calculate (1) a donor plasma volume, (2) a target plasma collection volume, and (3) a volume of pure plasma collected within the plasma container. The donor plasma volume may be based, at least in part, on a weight and height of the donor and a hematocrit of the donor. The target plasma collection volume may be based, at least in part, on the calculated donor plasma volume and a target percentage of plasma. The volume of pure plasma collected within the plasma container may be based, at least in part, upon a percentage of anticoagulant in the collected plasma component. The

controller may stop the first pump when the calculated volume of pure plasma collected within the plasma collection container equals the target plasma collection volume.

**[0023]** In further embodiments, the controller may return, after collecting at least a portion of the target plasma collection volume, fluid remaining within the blood component separation device via the first line. Additionally or alternatively, the controller may calculate an intravascular deficit based, at least in part on, the volume of pure plasma collected and the volume of the contents of the blood component separation device returned to the donor. The system may also include a saline line that fluidly connects to a saline source and the blood component separation device. The controller may return a volume of saline to the donor to obtain a target intravascular deficit (e.g., between -250 and 500 milliliters).

**[0024]** The controller may calculate the donor's body mass index based, at least in part, on the weight and height of the donor. The donor plasma volume may, in turn, be calculated based, at least in part, on the donor's body mass index. The target percentage of plasma may be between 26.5 and 29.5 percent (e.g., 28.5 percent) of the donor's plasma volume.

**[0025]** In additional embodiments, the controller may calculate the percentage of anticoagulant in the collected plasma component, for example, based on the volume of anticoagulant added to the drawn whole blood, and the subject's hematocrit. The system may also include an anticoagulant source weight sensor that measures the weight of the anticoagulant source. The controller may then monitor a change in volume within the anticoagulant container based on the measured weight of the anticoagulant source. The calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the change in volume within the anticoagulant source. Additionally or alternatively the controller may monitor a number of rotations of the anticoagulant pump to determine the volume of anticoagulant introduced into the whole blood. In such embodiments, the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the number of rotations of the anticoagulant pump.

**[0026]** The system may also include an optical sensor and/or a plasma container weight sensor. The optical sensor may be located on the blood component separation device and may monitor the contents of the blood component separation device to determine if a



volume of anticoagulant remains within the blood component separation device. The calculated percentage of anticoagulant in the collected plasma may then be based, at least in part, on the volume of anticoagulant within the blood component separation device. The plasma container weight sensor may monitor a volume and/or weight of the plasma component collected within the plasma container. The calculated volume of pure plasma collected within the plasma collection device may then be based, at least in part, on the monitored volume and/or weight of collected plasma component. The optical sensor may also monitor the volume of red blood cells collected within the blood separation device, and the controller may determine the subject's hematocrit based, at least in part, upon on the monitored volume of red blood cells collected within the blood separation device and the volume of whole blood withdrawn from the donor. The percentage of anticoagulant in the collected plasma component may include at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant added during a priming step.

#### **Brief Description of the Drawings**

[0027] The foregoing features of the invention will be more readily understood by reference to the following detailed description, taken with reference to the accompanying drawings, in which:

[0028] Fig. 1 schematically shows a perspective view of a blood processing system in accordance with some embodiments of the present invention.

[0029] Fig. 2 schematically shows a top view of the blood processing system of Figure 1, in accordance with some embodiments of the present invention;

[0030] Fig. 3 schematically shows a disposable set installed within the blood processing system of Figure 1, in accordance with some embodiments of the present invention.

[0031] Fig. 4 is a flowchart depicting a method of collecting plasma, in accordance with embodiments of the present invention.

[0032] Fig. 5 is a flowchart depicting an alternative method of collecting plasma, in accordance with further embodiments of the present invention.

**Detailed Description of Specific Embodiments**

[0033] Illustrative embodiments of the present invention provide blood processing systems and methods for collecting a target volume of pure plasma. The system and method calculate a percentage of anticoagulant collected within a plasma collection container (e.g., in addition to the plasma that is collected within the container) based on the amount of anticoagulant added to the system and the hematocrit of the donor. The system/method may then calculate the volume of pure plasma (e.g., plasma without anticoagulant) that has been collected within the container. Further embodiments may tailor the volume of plasma collected based on the donor's plasma volume and a target percentage of plasma to collect. Details of the illustrative embodiments are discussed below.

[0034] As shown in Figures 1 and 2, the blood processing system 100 includes a cabinet 110 that houses the main components of the system 100 (e.g., the non-disposable components). Within the cabinet 110, the system 100 may include a first/blood pump 232 that draws whole blood from a subject, and a second/anticoagulant pump 234 that pumps anticoagulant through the system 100 and into the drawn whole blood. Additionally, the system 100 may include a number of valves that may be opened and/or closed to control the fluid flow through the system 100. For example, the system 100 may include a donor valve 120 that may open and close to selectively prevent and allow fluid flow through a donor line 218 (e.g., an inlet line; Fig. 3), and a plasma valve 130 that selectively prevents and allows fluid flow through an outlet/plasma line 222 (Fig. 3). Some embodiments may also include a saline valve 135 that selectively prevents and allows saline to flow through a saline line 223.

[0035] To facilitate the connection and installation of a disposable set and to support the corresponding fluid containers, the system 100 may include an anticoagulant pole 150 on which the anticoagulant solution container 210 (Fig. 3) may be hung, and a saline pole 160 on which a saline solution container 217 (Fig. 3) may be hung (e.g., if the procedure being performed requires the use of saline). Additionally, in some applications, it may be necessary and/or desirable to filter the whole blood drawn from the subject for processing. To that end, the system 100 may include blood filter holder 170 in which the blood filter (located on the disposable set) may be placed.

**[0036]** As discussed in greater detail below, apheresis systems 100 in accordance with embodiments of the present invention withdraw whole blood from a subject through a venous access device 206 (Fig. 3) using the blood pump 232. As the system 100 withdraws the whole blood from the subject, the whole blood enters a blood component separation device 214, such as a Latham type centrifuge (other type of separation chambers and devices may be used, such as, without limitation, an integral blow-molded centrifuge bowl, as described in U.S. Patent Nos. 4,983,158 and 4,943,273, which are hereby incorporated by reference). The blood component separation device 214 separates the whole blood into its constituent components (e.g., red blood cells, white blood cell, plasma, and platelets). Accordingly, to facilitate operation of the separation device 214, the system 100 may also include a well 180 in which the separation device 214 may be placed and in which the separation device 214 rotates (e.g., to generate the centrifugal forces required to separate the whole blood).

**[0037]** To allow the user/technician to monitor the system operation and control/set the various parameters of the procedure, the system 100 may include a user interface 190 (e.g., a touch screen device) that displays the operation parameters, any alarm messages, and buttons which the user/technician may depress to control the various parameters. Additional components of the blood processing system 100 are discussed in greater detail below (e.g., in relation to the system operation).

**[0038]** FIG. 3 is a schematic block diagram of the blood processing system 100 and a disposable collection set 200 (with an inlet disposable set 200A and an outlet disposable set 200B) that may be loaded onto/into the blood processing system 100, in accordance with the present invention. The collection set 200 includes a venous access device 206 (e.g., a phlebotomy needle) for withdrawing blood from a donor's arm 208, a container of anti-coagulant 210, a centrifugation bowl 214 (e.g., a blood component separation device), a saline container 217, and a final plasma collection bag 216. The blood/inlet line 218 couples the venous access device 206 to an inlet port 220 of the bowl 214, the plasma/outlet line 222 couples an outlet port 224 of the bowl 214 to the plasma collection bag 216, and a saline line 223 connects the outlet port 224 of the bowl 214 to the saline container 217. An anticoagulant line 225 connects the anti-coagulant container 210 to the inlet line 218. In

addition to the components mentioned above and as shown in Figure 3, the blood processing system 100 includes a controller 226, a motor 228, and a centrifuge chuck 230. The controller 226 is operably coupled to the two pumps 232 and 234, and to the motor 228, which, in turn, drives the chuck 230. The controller 226 may be operably coupled to and in communication with the user interface 190.

**[0039]** In operation, the disposable collection set 200 (e.g., the inlet disposable set 200A and the outlet disposable set 200B) may be loaded onto/into the blood processing system 100 prior to blood processing. In particular, the blood/inlet line 218 is routed through the blood/first pump 232 and the anticoagulant line 225 from the anti-coagulant container 210 is routed through the anticoagulant/second pump 234. The centrifugation bowl 214 may then be securely loaded into the chuck 230. Once the bowl 214 is secured in place, the technician may install the outlet disposable set 200B. For example the technician may connect a bowl connector 300 to the outlet 224 of the bowl 214, install the plasma container 216 into the weight sensor 195, run the saline line 223 through valve 135, and run the plasma/outlet line 222 through valve 130 and the line sensor 185. Once the disposable set 200 is installed and the anticoagulant and saline containers 210/217 are connected, the system 100 is ready to begin blood processing.

**[0040]** Figure 4 is a flowchart depicting an exemplary method of collecting plasma in accordance with various embodiments of the present invention. Prior to connecting the donor to the blood processing device 100, it is beneficial (and perhaps necessary in some instances) to obtain/determine some information regarding the donor, namely, the donor's weight (Step 410) and hematocrit (Step 415). Not only does this information help determine if the individual is a viable donor and the volumes of blood components that may be withdrawn/collected (e.g., per the FDA guidelines), the hematocrit may be used during processing to help collect a target volume of plasma. The technician may obtain/determine the donor's weight by weighing the donor (e.g., on a scale). To obtain/determine the donor's hematocrit, the technician may draw a blood sample from the donor and test the sample of blood. Additionally or alternatively, as discussed in greater detail below, the system may determine the hematocrit during blood processing. For example, the blood processing device 100 may include a hematocrit sensor (not shown) that determines the hematocrit of the blood

flowing into the blood processing device 100 and/or the system 100 may determine the hematocrit based on a volume of red blood cells collected within the bowl 214.

**[0041]** Once the lines 222/223 are in place and the technician has determined the donor's weight and/or hematocrit (if needed), the user/technician may insert the venous access device 206 into the donor's arm 208 (Step 420). Next, the controller 226 activates the two pumps 232, 234 and the motor 228. Operation of the two pumps 232, 234 causes whole blood to be drawn from the donor (step 425), anticoagulant from container 210 to be introduced into the drawn whole blood (step 430), and the now anticoagulated whole blood to be delivered to the inlet port 220 of the bowl 214.

**[0042]** It should be noted that the anticoagulant line 225 may also include a bacteria filter (not shown) that prevents any bacteria in the anticoagulant source 210, the anticoagulant, or the anticoagulant line 225 from entering the system 100 and/or the subject. Additionally, the anticoagulant line 225 may include an air detector 140 that detects the presence of air within the anticoagulant. The presence of air bubbles within any of the system 100 lines can be problematic for the operation the system 100 and may also be harmful to the subject if the air bubbles enter the blood stream. Therefore, the air detector may be connected to an interlock that stops the flow within the anticoagulant line 225 in the event that an air bubble is detected (e.g., by stopping the anticoagulant pump 234), thereby preventing the air bubbles from entering the subject.

**[0043]** As the anti-coagulated whole blood is withdrawn from the subject and contained within the blood component separation device 214, the blood component separation device 214 separates the whole blood into several blood components (Step 435). For example, the blood component separation device 214 may separate the whole blood into a first, second, third, and, perhaps, fourth blood component. More specifically, the blood component separation device 214 (and the centrifugal forces created by rotation of the separation device 214) can separate the whole blood into plasma, platelets, red blood cells ("RBC"), and, perhaps, white blood cells ("WBC"). The higher density component, i.e., RBC, is forced to the outer wall of the bowl 214 while the lower density plasma lies nearer the core. A buffy coat is formed between the plasma and the RBC. The buffy coat is made up of an inner layer of platelets, a transitional layer of platelets and WBC and an outer layer

of WBC. The plasma is the component closest to the outlet port and is the first fluid component displaced from the bowl 214 via the outlet port 224 as additional anticoagulated whole blood enters the bowl 214 through the inlet port 220.

**[0044]** As shown in Figure 3, the system 100 may also include an optical sensor 213 that may be applied to a shoulder portion of the bowl 214. The optical sensor monitors each layer of the blood components as they gradually and coaxially advance toward the core from the outer wall of the bowl 214. The optical sensor 213 may be mounted in a position (e.g., within the well 180) at which it can detect the buffy coat and/or the red blood cells reaching a particular radius, and the steps of drawing the whole blood from the subject/donor and introducing the whole blood into the bowl 12 may be altered and/or terminated in response to the detection.

**[0045]** Additionally, in some embodiments, the optical sensor 213 may be used to determine the hematocrit of the donor during processing. For example, as the bowl 214 fills with red blood cells and the optical sensor 213 detects the layer of red blood cells, the system 100 (e.g., the controller) can determine the volume of red blood cells within bowl 214 based on the location of the red blood cell layer and the fixed/known bowl volume. The system 100 may then calculate the donor hematocrit based on the volume of red blood cells within the bowl and the volume of whole blood that has been processed to that point.

**[0046]** Once the blood component separation device 214 has separated the blood into the various components, one or more of the components can be removed from the blood component separation device 214. For instance, the plasma may be removed to a plasma container 216 (e.g., a plasma bottle) through line 222 (Step 440). As noted above, some embodiments of the system 100 may include a weight sensor 195 (Fig. 1) that measures the amount of plasma collected. The plasma collection process may continue until a target volume of pure plasma (discussed in greater detail below) is collected within the plasma collection container 216. Although not shown, if the blood processing system 100 and/or the disposable set 200 include platelet, red blood cell, and/or white blood cell bags, each of the bags/containers may include similar weight sensors (e.g., load cells).

**[0047]** In some embodiments, the system 100 may also include a line sensor 185 (mentioned above) that can determine the type of fluid (e.g., plasma, platelets, red blood cells

etc.) exiting the blood component separation device 214. In particular, the line sensor 185 consists of an LED which emits light through the blood components leaving the bowl 214 and a photo detector which receives the light after it passes through the components. The amount of light received by the photo detector is correlated to the density of the fluid passing through the line. For example, if plasma is exiting the bowl 214, the line sensor 185 will be able to detect when the plasma exiting the bowl 214 becomes cloudy with platelets (e.g., the fluid exiting the bowl 214 is changing from plasma to platelets). The system 100 may then use this information to either stop the removal of blood components from the bowl 214, stop drawing whole blood from the subject, or redirect the flow by, for example, closing one valve and opening another.

**[0048]** It is important to note that during processing, the osmolarity of the red blood cells prevents the anticoagulant introduced into the whole blood from entering/remaining with the red blood cells (e.g., within the bowl 214). Rather, the anticoagulant mixes with the plasma component. Therefore, the anticoagulant exits the bowl 214 with the plasma and is collected within collection container 216 along with the plasma. In other words, the weight of the product measured by the weight sensor 195 is the weight of the plasma, as well as any anticoagulant that is mixed with the plasma – the weight provided by the weight sensor 195 is not the weight of pure plasma.

**[0049]** Additionally, whole blood contains a variable amount of plasma, as determined by the donor's hematocrit. The hematocrit for typical donors can vary from 38% to 54%, which means that for 100 ml of whole blood, the volume of plasma can vary from 36 to 62 ml. Furthermore, the amount of anticoagulant added to the withdrawn whole blood is fixed (e.g., it does not depend on the hematocrit of the donor), meaning that the percentage of anticoagulant in the collected plasma may vary from 9.7% to 12.7% for donor hematocrits between 38% to 54%, respectively. Therefore, not only does the volume measured by the weight sensor 195 include the volume of anticoagulant, that volume of anticoagulant may vary from donor to donor based on the hematocrit.

**[0050]** As mentioned above, some embodiments of the present invention continue the blood processing/separation procedure until a target volume of pure plasma (e.g., plasma only – without the volume of any anticoagulant mixed with the plasma included in the target

volume) is collected within the plasma collection container 216. To that end, some embodiments of the present invention may calculate the volume of pure plasma within the plasma collection container 216. For example, the technician or the system 100 (e.g., the controller) may calculate the percentage of anticoagulant within the collected plasma (Step 455) (e.g., the plasma contained within the plasma collection container 216) based on the amount of anticoagulant added/metered into the whole blood and the hematocrit of the donor. The technician and/or system can calculate the percentage of anticoagulant according to the following equation, where AC is the amount of anticoagulant added to the system 100. As noted above, 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.

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

**[0051]** The amount of anticoagulant that is added to the system 100 can be determined in a number of ways. For example, the system 100 can base the amount of anticoagulant (e.g., the value of “AC” in the above equation) on the predetermined ratio of anticoagulant per unit of anticoagulated whole blood. In some embodiments, the value of “AC” may be the inverse of the predetermined ratio (e.g., “AC” would be 16 if the ratio of anticoagulant to anticoagulated whole blood was 1:16). Additionally or alternatively, the technician/system 100 can monitor the volume of anticoagulant added to the system. In such embodiments, the technician/system can monitor the volume of anticoagulant added to the system 100 based on the number of rotations of the anticoagulant pump (e.g., each rotation of the anticoagulant pump introduces a set volume of anticoagulant into the system 100) and/or based on the change in weight of the anticoagulant container 210 as measured by a weight sensor (discussed in greater detail below).

**[0052]** Once the technician/system 100 has calculated the percentage of anticoagulant within the plasma collection container 216, the technician/system 100 may then use this information to calculate the volume of pure plasma within the plasma collection container 216 (Step 465). For example, the technician/system 100 may determine the volume of



anticoagulant within the container (based on the percentage of anticoagulant within the container 216) and subtract this volume from the total volume of fluid within the container 216 as measured by the weight sensor 195. The system 100 may continue to monitor the volume of pure plasma collected within the container 216 and continue processing whole blood (e.g., continue performing Steps 425, 430, 435, 440, 455, 460 and 465) until a target volume of pure plasma is collected within the plasma collection container 216 (Step 470) (e.g., 800 mL for an adult donor weighing more than 175 pounds or other limit prescribed by the FDA or similar governing body).

**[0053]** Once the system 100 has collected the target volume of pure plasma within the plasma collection container 216, the system 100 can return the remaining components (e.g., the components remaining within the bowl 214) to the subject (Step 475). For example, when all the plasma has been removed and the bowl 214 is full of RBCs (and any other blood component not collected), the controller 226 stops the draw of whole blood from the subject and reverses the direction of the blood/first pump 232 to draw the RBCs (and other components) from the bowl 214 directly back to the subject. Alternatively, if the system 100 is so equipped, the system may return the components to the subject via a dedicated return line.

**[0054]** In addition to the non-collected blood components (e.g., the components remaining in the bowl 214), the system 100 may also return saline to the patient/subject. The saline may be used as a compensation fluid to make up for the volume of the blood component (e.g., plasma) that was removed and collected, and is not being returned to the patient. To that end, during the return step (e.g., Step 475), the saline valve 135 may be opened to allow saline from the saline container 217 to flow through the saline line 223 and into the bowl 214 (via outlet 224), where it can be returned to the patient/donor with or after the remaining blood components.

**[0055]** It should be noted that some embodiments may perform some additional and optional steps to help determine the volume of pure plasma within the plasma collection container 216. For example, as mentioned above, some embodiments may monitor the change in weight of the anticoagulant container 210 (e.g., as measured by a weight sensor/load cell on the anticoagulant container 210) (step 445). This measurement provides

an indication of the volume of anticoagulant that has been added to the system 100, and may be used help determine the percentage of anticoagulant within the plasma collection container 216. Additionally or alternatively, some embodiments may similarly, monitor the change in weight and/or volume of the plasma and anticoagulant collected within the plasma collection container 216 (e.g., via weight sensor 195) (step 450). This measurement may be used to calculate of the total volume of pure plasma collected within the plasma collection container 216 (e.g., to obtain the total weight from which to subtract the calculated volume of anticoagulant).

**[0056]** Some embodiments may also (optionally) monitor the volume of anticoagulant remaining in the bowl 214 (step 460) (e.g., anticoagulant that did not mix with the plasma and/or otherwise remained in the bowl). For example, the system 100 may utilize the optical sensor on the bowl 214 to determine whether any anticoagulant remains within the bowl 214. If it does, the method 400/system 100 may modify the calculation of the amount of pure plasma collected within the plasma collection container (e.g., either increase the calculated amount or decreased the calculated amount), based on the volume of anticoagulant remaining within the bowl 214.

**[0057]** The various embodiment of the present invention described above provide numerous benefits over prior art plasma collection systems. In particular, as noted above, prior art plasmapheresis devices end plasma collection based on a total volume of anticoagulated plasma (e.g., pure plasma plus the added anticoagulant). Although this is the easiest method because it requires only that the product collection container be weighed, the amount of true product – the pure plasma – is dependent on the donor's hematocrit. In other words, prior art systems will collect more plasma from low hematocrit donors than from high hematocrit donors because of the variation of the percentage of anticoagulant in the product. Various embodiments of the present invention address the issues of prior art systems by collecting a standard volume (e.g., a target volume) of pure plasma from each donor. As noted above, embodiments of the present invention accomplish this by using knowledge of the donor's hematocrit and the amount of anticoagulant collected within the plasma collection container 216 (e.g., by counting pump rotations and/or using scale/weight sensors, etc.) to determine the percentage of anticoagulant in the product. Additionally, by stopping

the plasma collection process based on a volume of pure plasma collected, embodiments of the present invention are able to collect a greater volume of plasma as compared to prior art systems that stop based on a plasma/anticoagulant mixture.

**[0058]** Figure 5 shows an alternative method for collecting plasma, using the system (or similar system) shown within Figures 1-3, that bases the total volume of plasma to collect on the individual donor (e.g., based on their height, weight, hematocrit, blood volume and/or plasma volume). In a manner similar to that described above for the method shown in Figure 4, prior to connecting the donor to the blood processing device 100, the system/method may obtain/determine some information regarding the donor, namely, the donor's weight and height (Step 505) and hematocrit (Step 510). For example, the technician may obtain/determine the donor's weight by weighing the donor (e.g., on a scale) and the donor's height by measuring the donor. To obtain/determine the donor's hematocrit (e.g., in a manner similar to that described above), the technician may test a blood sample or the system may determine the hematocrit during blood processing using a hematocrit sensor and/or based on the volume of red blood cells collected within the bowl 214.

**[0059]** Using the donor height and weight, and the hematocrit, the system 100/method 500 may calculate the donor's plasma volume (e.g., the volume of plasma within the donor's blood) (Step 515). For example, the system 100/method 500 may calculate the donor/subject's body mass index ("BMI") using the donor's height and weight (e.g.,  $BMI = \text{weight}/\text{height}^2$ ), and then the total blood volume within the donor/subject using the calculated BMI (e.g., see Lemmens et al., *Estimating Blood Volume in Obese and Morbidly Obese Patients*, Obesity Surgery, 2006:16, 773-776, the subject matter incorporated herein by reference). The total blood volume may be calculated using the following equation:

$$\text{[0060]} \text{ InBV} = \frac{70}{\sqrt{BMI_p/22}}$$

**[0061]** In the above equation, InBV is the indexed blood volume (e.g., the donor's total blood volume), BMI<sub>p</sub> is the patient's BMI (e.g., kg/ m<sup>2</sup>), 22 is the BMI value (e.g., also in kg/m<sup>2</sup>) for an ideal body weight (IBW), and 70 is the total blood volume (in mL/kg) for a donor at their ideal weight (BMI = 22 kg/ m<sup>2</sup>). Once the system 100 has calculated the total

blood volume within the donor/subject, the system 100 (e.g., the controller) may then determine/calculate the volume of plasma within the donor's blood (Step 515) based, for example, on the donor's hematocrit.

**[0062]** As mentioned above, the embodiment shown in Figure 5 bases the volume of plasma to collect on the individual donor. To that end, once the system 100/method 500 has determined the donor's plasma volume, the system 100/method 500 may then calculate the target volume of plasma to collect (Step 520). For example, the system 100/method 500 may multiply the total plasma volume within the patient by a target percentage of plasma to collect to obtain the target plasma volume to collect (e.g., if the total plasma volume is 2700 ml and the target percentage to collect is 28.5%, then the target plasma volume to collect is 769.5 ml). The target percentage of plasma to collect may depend on the application and/or the donor, and may be input directly into the system 100 (e.g., using the user interface 190) or may be preset from the factory. In some embodiments, the target percentage may be between 26.5 and 30%, and preferably may be 28.5%. However, in other embodiments, the target percentage may be below 26.5% or above 30%.

**[0063]** Once the lines 222/223 are in place and the system 100/method 500 has calculated the target plasma volume, the user/technician may insert the venous access device 206 into the donor's arm 208 (Step 525). Next, in a manner similar to that described above for the method shown in Figure 4, the controller 226 activates the two pumps 232, 234 and the motor 228. Operation of the two pumps 232, 234 causes whole blood to be drawn from the donor (step 530), anticoagulant from container 210 to be introduced into the drawn whole blood (step 535), and the now anticoagulated whole blood to be delivered to the inlet port 220 of the bowl 214.

**[0064]** As the anti-coagulated whole blood is withdrawn from the subject and introduced into the blood component separation device 214, the blood component separation device 214 separates the whole blood into the respective blood components (e.g., into plasma, platelets, RBC, and, perhaps, WBC) (Step 540). As discussed above, the higher density component, i.e., RBC, is forced to the outer wall of the bowl 214 and the plasma is the component closest to the outlet port and, therefore, is the first fluid component displaced from the bowl 214 via the outlet port 224 as additional anticoagulated whole blood enters the

bowl 214 through the inlet port 220. During separation and processing, the optical sensor 213 monitors each layer of the blood components as they gradually and coaxially advance toward the core from the outer wall of the bowl 214, and the steps of drawing the whole blood from the subject/donor and introducing the whole blood into the bowl 12 may be altered and/or terminated in response to the detection. Additionally, as discussed above, the optical sensor 213 may be used to determine the hematocrit of the donor during processing (e.g., if it is not known and/or determined prior to the start of processing).

**[0065]** Once the blood component separation device 214 has separated the blood into the various components, the plasma may be removed to a plasma container 216 (e.g., a plasma bottle) through line 222 (Step 545). As noted above, some embodiments of the system 100 may include a weight sensor 195 (Fig. 1) that measures the amount of plasma collected. The plasma collection process may continue until the target plasma collection volume (discussed in greater detail below) is collected within the plasma collection container 216. If equipped with the line sensor 185, the system 100 may then use the information from the sensor 185 to either stop the removal of blood components from the bowl 214, stop drawing whole blood from the subject, or redirect the flow by, for example, closing one valve and opening another.

**[0066]** As mentioned above, some embodiments of the present invention continue the blood processing/separation procedure until a target plasma collection volume is collected. In order to ensure that this volume does not include the volume of any anticoagulant collected within the container 216, the target plasma collection volume should only include the volume of pure plasma (e.g., plasma only – without the volume of any anticoagulant mixed with the plasma included in the target volume). To that end and in a manner similar to that described above, some embodiments of the present invention may calculate the volume of pure plasma within the plasma collection container 216. To determine the volume of pure plasma, the technician or the system 100 (e.g., the controller) may calculate the percentage of anticoagulant within the collected plasma (Step 560) (e.g., the plasma contained within the plasma collection container 216) based on the amount of anticoagulant added/metered into the whole blood and the hematocrit of the donor (see equation provided above). The amount of anticoagulant that is added to the system 100 can be determined in any of the ways

mentioned above (e.g., based on the predetermined ratio of anticoagulant per unit of anticoagulated whole blood, by monitoring the volume of anticoagulant added to the system, etc.).

**[0067]** Once the technician/system 100 has calculated the percentage of anticoagulant within the plasma collection container 216, the technician/system 100 may then use this information to calculate the volume of pure plasma within the plasma collection container 216 (Step 570). For example, as discussed above, the technician/system 100 may determine the volume of anticoagulant within the container (based on the percentage of anticoagulant within the container 216) and subtract this volume from the total volume of fluid within the container 216 as measured by the weight sensor 195. The system 100 may continue to monitor the volume of pure plasma collected within the container 216 and continue processing whole blood (e.g., continue performing Steps 530, 535, 540, 545, 560, 570 and, possibly, steps 550, 555 and 565) until the volume of pure plasma collected within the plasma collection container 216 reaches the target plasma volume (Step 575) (e.g., as calculated based on the individual plasma volume of the donor and the target percentage of plasma to collect).

**[0068]** Once the system 100 has collected the target plasma volume within the plasma collection container 216, the system 100 can return the remaining components (e.g., the components remaining within the bowl 214) to the subject (Step 580) by stopping the draw of whole blood from the subject and reversing the direction of the blood/first pump 232 to draw the RBCs (and other components) from the bowl 214 and back to the subject (e.g., directly via the blood/inlet line 218 or, if so equipped, via a dedicated return line).

**[0069]** It is important to note that, because the system 100/method 500 collect and do not return some of the blood components (e.g., the plasma), the volume of fluid that is returned to the donor/subject is less than the volume that was removed. This, in turn, creates an intravascular deficit that is equal to the amount of plasma collected (e.g., the volume of whole blood removed from the donor minus the volume of plasma collected/not returned). In instances in which the intravascular deficit is too large, the donor is at risk of fainting when the procedure is complete and they get up to leave the facility. To reduce the intravascular deficit (and the risk of donor injury), as noted above, some embodiments of the present

invention return saline to the patient/subject (Step 585). The saline may be used as a compensation fluid to make up for the volume of the blood component (e.g., plasma) removed. To that end, during the return step (e.g., Step 580), the controller 226 (or the technician) may open the saline valve to allow saline from the saline container 217 to flow through the saline line 223 and into the bowl 214 (via outlet 224), where it can be returned to the patient/donor with or after the remaining blood components.

**[0070]** As mentioned above, the volume of plasma that is collected from the donor varies from donor to donor (e.g., because it is based on the donor's height, weight, hematocrit, and blood volume). Therefore, the volume of saline that is returned to the donor to reduce the intravascular deficit may similarly be dependent on the donor. To that end, when returning the contents of the separation device and the saline (Steps 580 and 585) to the donor, the system 100/method 500 may calculate the intravascular deficit (Step 590) based on the total volume of whole blood removed from the donor and the volume of blood components and saline that has been returned (or based on the volume of plasma collected and the volume of blood components and saline that have been returned). The system 100/method 500 may continue returning saline until the donor's intravascular deficit reaches a target intravascular deficit (Step 595).

**[0071]** The target intravascular deficit may be any intravascular deficit that reduces the donor's risk for fainting and may be the same for each donor. For example, the target intravascular deficit may be set to 0 mL or 250 mL for each donor. Alternatively, like the target plasma volume to collect, the target intravascular deficit may be different for each donor. In other words, the target intravascular deficit may be set to 0 mL for some donors and 250 mL for others. It should be noted that 0 and 250 mL are provided as examples only and other embodiments may have target intravascular deficits between 0 and 250, or greater than 250 mL. Additionally, in some instances, it may be beneficial to return more fluid to the donor than was removed/collected. In such instances, the target intravascular deficit may be set less than zero (e.g., -1 to -250 mL) so that the donor has more fluid/volume after the procedure than they did before the procedure.

**[0072]** Like the method 400 shown in Figure 4, the method 500 may similarly perform some additional and optional steps to help determine the volume of pure plasma

within the plasma collection container 216. For example, some embodiments may monitor the change in weight of the anticoagulant container 210 (e.g., as measured by a weight sensor/load cell on the anticoagulant container 210) (step 550). This measurement provides an indication of the volume of anticoagulant that has been added to the system 100, and may be used help determine the percentage of anticoagulant within the plasma collection container 216. Additionally or alternatively, some embodiments may similarly, monitor the change in weight and/or volume of the plasma and anticoagulant collected within the plasma collection container 216 (e.g., via weight sensor 195) (step 555). This measurement may be used to calculate of the total volume of pure plasma collected within the plasma collection container 216 (e.g., to obtain the total weight from which to subtract the calculated volume of anticoagulant). Also, some embodiments may also monitor the volume of anticoagulant remaining in the bowl 214 (step 565) (e.g., anticoagulant that did not mix with the plasma and/or otherwise remained in the bowl) using the optical sensor on the bowl 214 to determine whether any anticoagulant remains within the bowl 214 and modify the calculation of the amount of pure plasma collected within the plasma collection container (e.g., either increase the calculated amount or decreased the calculated amount), based on the volume of anticoagulant remaining within the bowl 214.

**[0073]** As noted above, prior art systems that follow the current FDA nomogram for plasma collection collect a volume of plasma product (e.g., anticoagulant and plasma mixed together) based solely on the weight of the donor – the same volume is collected from every donor at the same weight. However, the total blood volume and plasma volume for two donors may vary greatly. For example, when comparing two donors in the same weight grouping according to the FDA nomogram – one obese and one not obese – the obese donor will effectively have a lower blood volume that the non-obese donor. Furthermore, with respect to the total plasma volume, donors with high hematocrit will have lower plasma volumes. In other words, because the total blood volume and total plasma volume vary from donor to donor (even among donors that weight the same), the percentage of the donor's plasma that is ultimately collected may vary widely from donor to donor. By tailoring the plasma collection to the donor (e.g., based on the donor's height, weight, BMI, hematocrit, total blood volume, and/or total plasma volume) and collecting a predetermined percent of



plasma from each donor, embodiments of the preset invention are able to collect a greater volume of plasma (e.g., pure plasma) from some donors but less plasma from more vulnerable donors (e.g., smaller donors with high hematocrit, donors with lower plasma volume, etc.), as compared to systems that do not base the collection volume on the individual donor.

**[0074]** Similarly, current systems do not tailor the saline return volume to the patient (e.g., each donor at a given level receives the same volume of saline, for example, if the target plasma product volume is 800 mL, the donor will receive 500 mL of saline). However, because prior art systems collect based on the volume of the plasma product (which includes both plasma and anticoagulant) and the volume of pure plasma that is actually collected (and therefore, the volume removed from the donor) varies based on the donor hematocrit, the intravascular deficit for each donor will vary. In other words, the volume of saline returned to the donor may be sufficient for some, but insufficient for others. By tailoring the saline return to the individual donor, embodiments of the present invention are able to ensure that each donor has the same intravascular deficit (if any) once the procedure is complete. This, in turn, allows embodiments of the present invention to achieve isovolemia for each donor and greatly reduce any adverse reactions that the donor may experience (e.g., falling, fainting, light-headedness, vasovagal reactions, etc.).

**[0075]** It is also important to note that, although the various embodiments discussed above are in relation to a blood processing system that collects plasma, the features discussed herein may be applied to any type of blood processing system. For example, the features described herein may be implemented on blood processing systems that collect and/or process red blood cells, platelets and/or white blood cells.

**[0076]** The embodiments of the invention described above are intended to be merely exemplary; numerous variations and modifications will be apparent to those skilled in the art. All such variations and modifications are intended to be within the scope of the present invention as defined in any appended claims.

What is claimed is:

1. A system for collecting plasma, comprising:

a venipuncture needle configured to draw whole blood from a donor;

a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;

a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the blood separator, flow through the donor line being controlled by a first pump;

an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;

a touchscreen configured to receive input from an operator; and

a controller programmed to control operation of the system, the controller coupled to the touchscreen and programmed to receive at least a donor's weight and hematocrit, to determine a target volume for plasma product and/or raw plasma, to control the system to operate a draw and return cycle to withdraw the whole blood from the donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor, to establish a current value of the hematocrit of the donor and a new target volume for plasma product and/or raw plasma, and to control the system to operate a subsequent draw and return cycle, whereby the donor's changing hematocrit is taken into account in calculating the new target volume for plasma product and/or raw plasma.

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

3. The system of claim 2, wherein the controller is programmed to repeat draw and return phases until the target volume of plasma product and/or raw plasma is collected, wherein the

target volume for plasma product and/or raw plasma is redetermined prior to the start of each draw phase.

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

5. The system of claim 1, wherein the controller is programmed to determine the target volume for plasma product and/or raw plasma based on the donor's total blood volume and the donor's plasma volume.

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

7. A system for collecting plasma, comprising:

a venipuncture needle configured to draw whole blood from a donor;

a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;

a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the blood separator, flow through the donor line being controlled by a first pump;

an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;

a touchscreen configured to receive input from an operator; and

a controller programmed to control operation of the system, the controller coupled to the touchscreen and programmed to receive at least a donor's weight, height, sex and

hematocrit, to determine a target volume for plasma product and/or raw plasma based at least in part on the weight, height, sex and hematocrit, to control the system to operate draw and return phases to withdraw whole blood from the donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor.

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

9. The system of claim 8, wherein the controller is further programmed to account for anticoagulant introduced into the plasma collection container separate from the plasma product attributable to a priming or other pre-processing step.

10. A system for collecting plasma, comprising:

- a venipuncture needle configured to draw whole blood from a donor;

- a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;

- a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the blood separator, flow through the donor line being controlled by a first pump;

- an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;

- a touchscreen configured to receive input from an operator; and

- a controller programmed to control operation of the system, the controller coupled to the touchscreen and programmed to receive at least a donor's weight, height and hematocrit and to determine a target volume for plasma product comprising raw plasma and

anticoagulant, wherein the target volume for plasma product is determined prior to withdrawing the whole blood from the donor based at least in part on an anticoagulant ratio, the donor's weight, height and the donor's hematocrit, the controller programmed to then control the system to operate a plurality of draw and return cycles to withdraw whole blood from the donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor.

11. The system of claim 10, wherein the controller is programmed to determine the target volume for plasma product based on the donor's total blood volume and the donor's plasma volume.

12. The system of claim 11, wherein the controller is programmed to determine the donor's total blood volume based on multiple parameters selected from the group consisting of the weight, height, sex, age, and morphology of the donor.

13. The system of claim 10, wherein the controller is configured to receive the donor's weight and hematocrit electronically.

14. The system of claim 10, wherein the controller is programmed to control the system to collect the plasma product in the plasma product collection container until the plasma product in the plasma product collection container reaches the determined target volume.

15. The system of claim 10, wherein the controller is programmed to perform the draw and return cycles at least three times and the controller is programmed to determine a volume of whole blood to be drawn in a final draw phase which is different than a volume drawn in a prior draw phase.

16. A system for collecting plasma, comprising:

a venipuncture needle configured to draw whole blood from a donor;

a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;

a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the separator, flow through the donor line being controlled by a first pump;

an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;

a touchscreen configured to receive input from an operator; and

a controller programmed to control operation of the system, the controller coupled to the touchscreen and programmed to receive donor parameters electronically, to determine a target volume for plasma product and/or raw plasma based at least in part on the donor parameters and to control the system to operate draw and return phases to withdraw whole blood from a donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor.

17. The system of claim 16, wherein the controller is programmed to control the system to collect the plasma product in the plasma product collection container until a collected volume of plasma product reaches the target volume for plasma product and/or raw plasma.

18. The system of claim 16, further comprising a control system, wherein the control system is in electronic communication with the controller.

19. The system of claim 18, wherein the control system is programmed to calculate the target volume for plasma product and/or raw plasma and the controller is programmed to determine a target volume for plasma product and/or raw plasma by receiving the target volume for plasma product and/or raw plasma from the control system.

20. The system of claim 16, wherein the controller determines the target volume for plasma product and/or raw plasma by calculating the target volume for plasma product and/or raw plasma and wherein the controller is local to and coupled to the blood separator.

21. The system of claim 16, wherein the donor parameters received electronically comprise a donor weight, wherein the controller is programmed to determine the target volume for plasma product and/or raw plasma based at least in part on the donor weight.

22. The system of claim 21, wherein the donor parameters received electronically comprise a donor hematocrit, wherein the controller is programmed to determine the target volume for plasma product and/or raw plasma based at least in part on the donor hematocrit.

23. The system of claim 22, wherein the controller is programmed to determine a target volume for plasma product based on the donor's total blood volume and the donor's plasma volume.

24. The system of claim 23, wherein the controller is programmed to determine the donor's total blood volume based on the weight and height of the donor.

25. The system of claim 24, wherein the controller is programmed to determine the donor's total blood volume before whole blood is withdrawn from the donor during a donation.

26. The system of claim 25, wherein the controller is programmed to determine the target volume for plasma product comprising raw plasma and anticoagulant, wherein the target volume for plasma product is determined prior to withdrawing the whole blood from the donor based at least in part on an anticoagulant ratio, the donor's weight and the donor's hematocrit.

27. The system of claim 16, further comprising a reservoir separate from the blood separator for receiving concentrated red blood cells.

**Abstract**

A method for collecting plasma includes determining the weight, height, and hematocrit of a donor, and calculating a donor plasma volume and a target plasma collection volume. The target plasma collection volume is based on the donor plasma volume and a target percentage of plasma. The method then withdraws blood from the donor through a line connected to a blood component separation device, and introduces anticoagulant into the withdrawn blood. The blood component separation device separates the blood into a plasma component and a second blood component, and the plasma component is collected from the blood component separation device and into a plasma collection container. The method may then calculate the volume of pure plasma collected within the plasma collection container, and continue processing/collecting until the calculated volume of pure plasma equals the target plasma collection volume.



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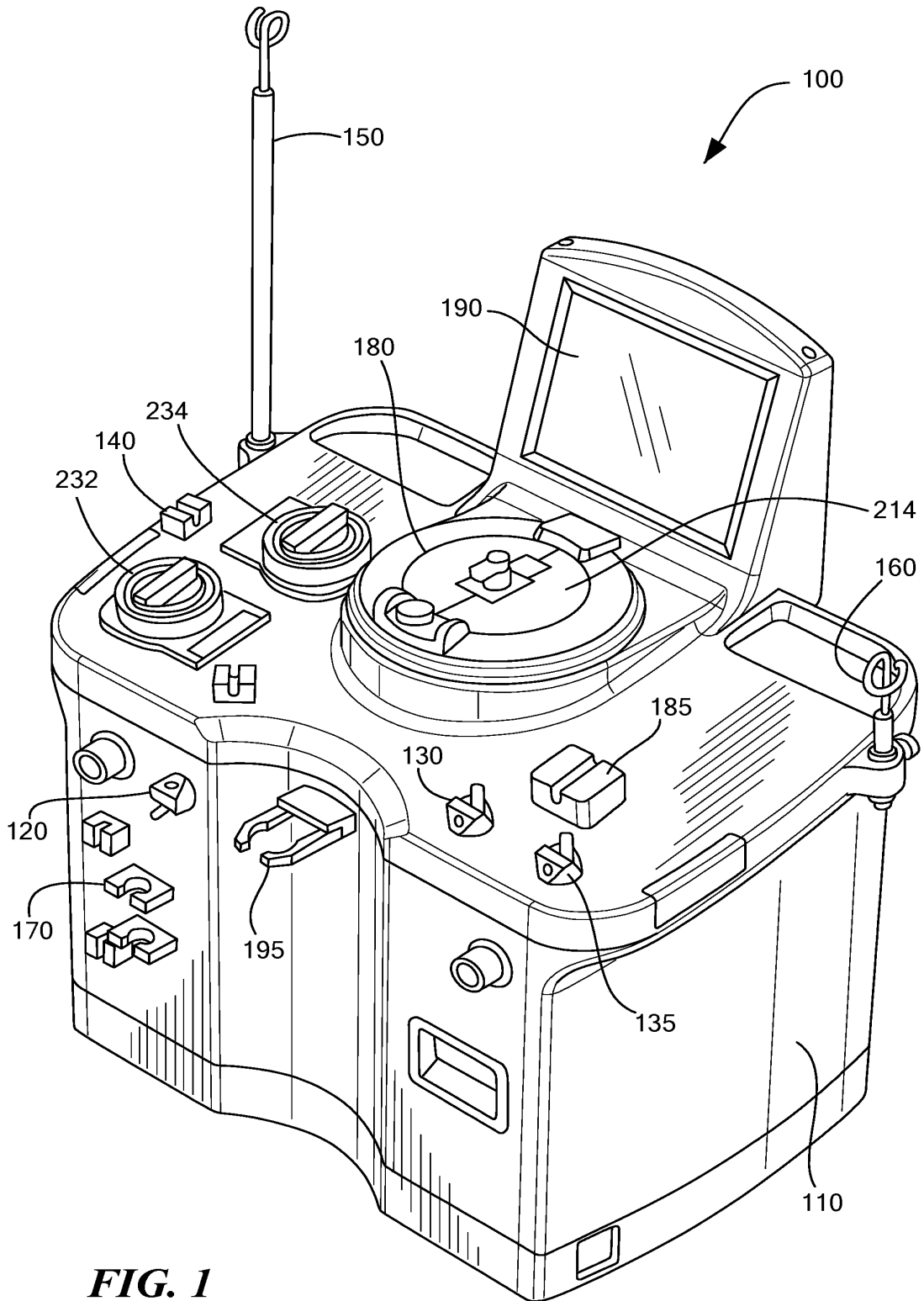
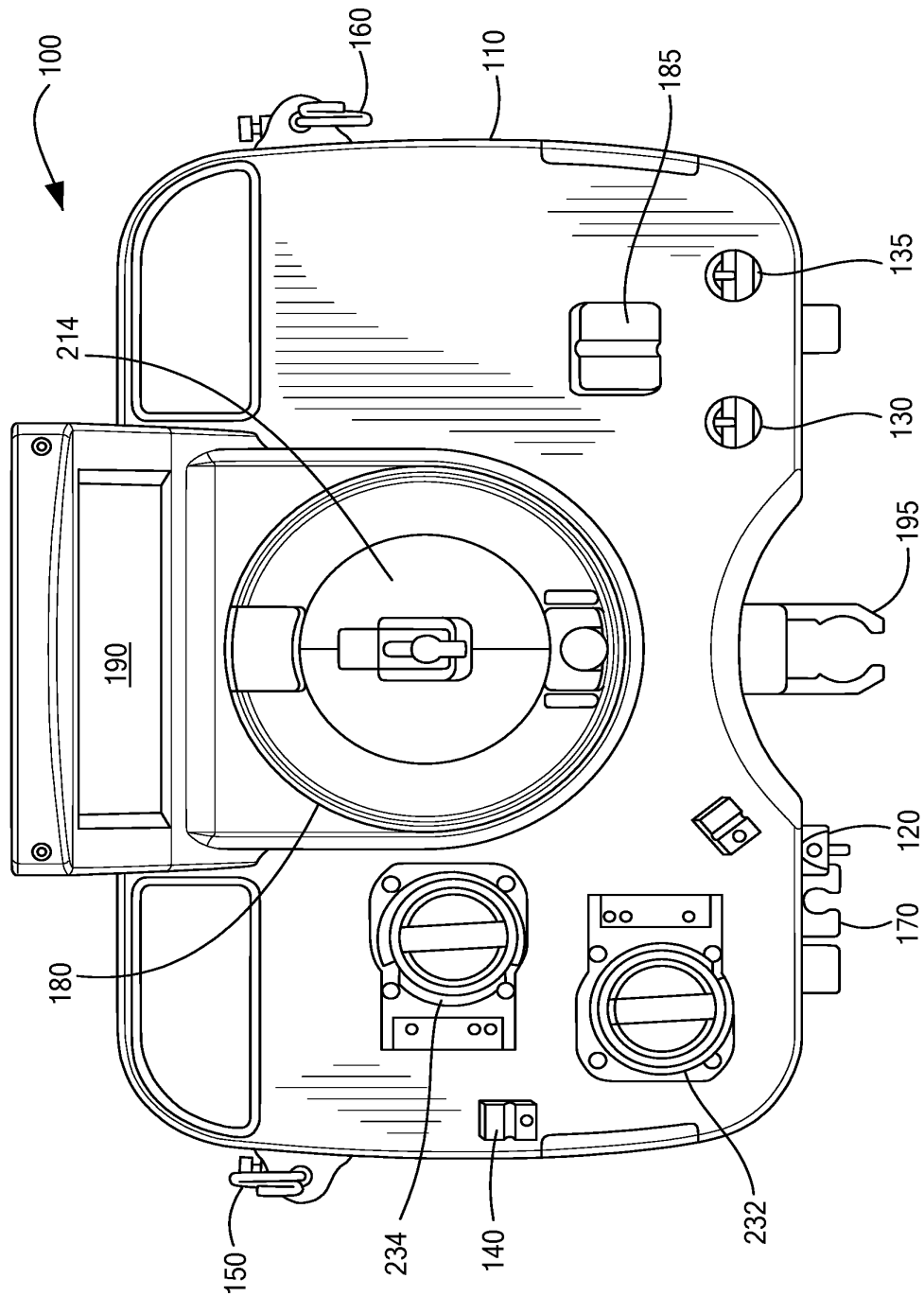
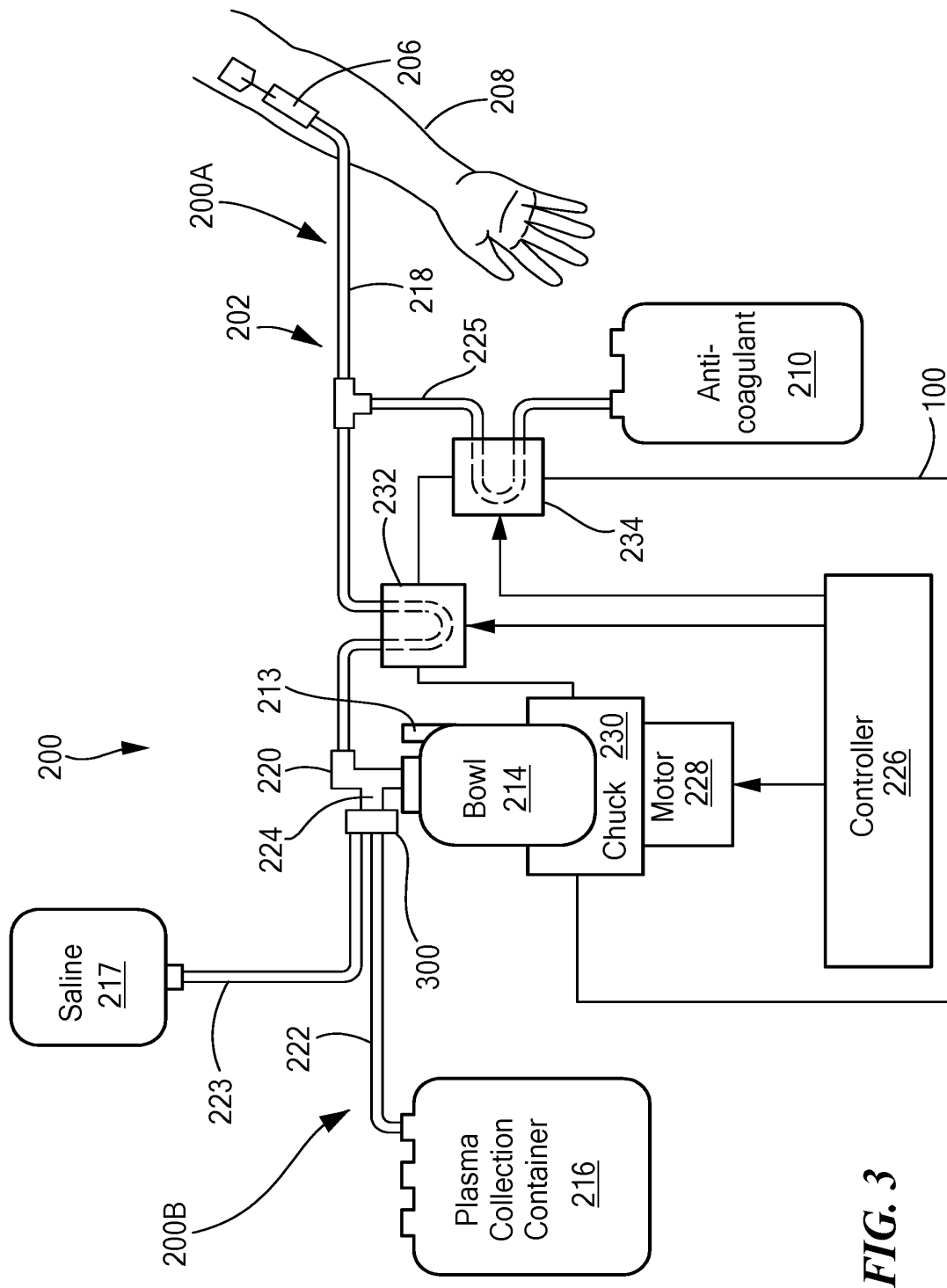


**FIG. 1**

**FIG. 2**

**FIG. 3**

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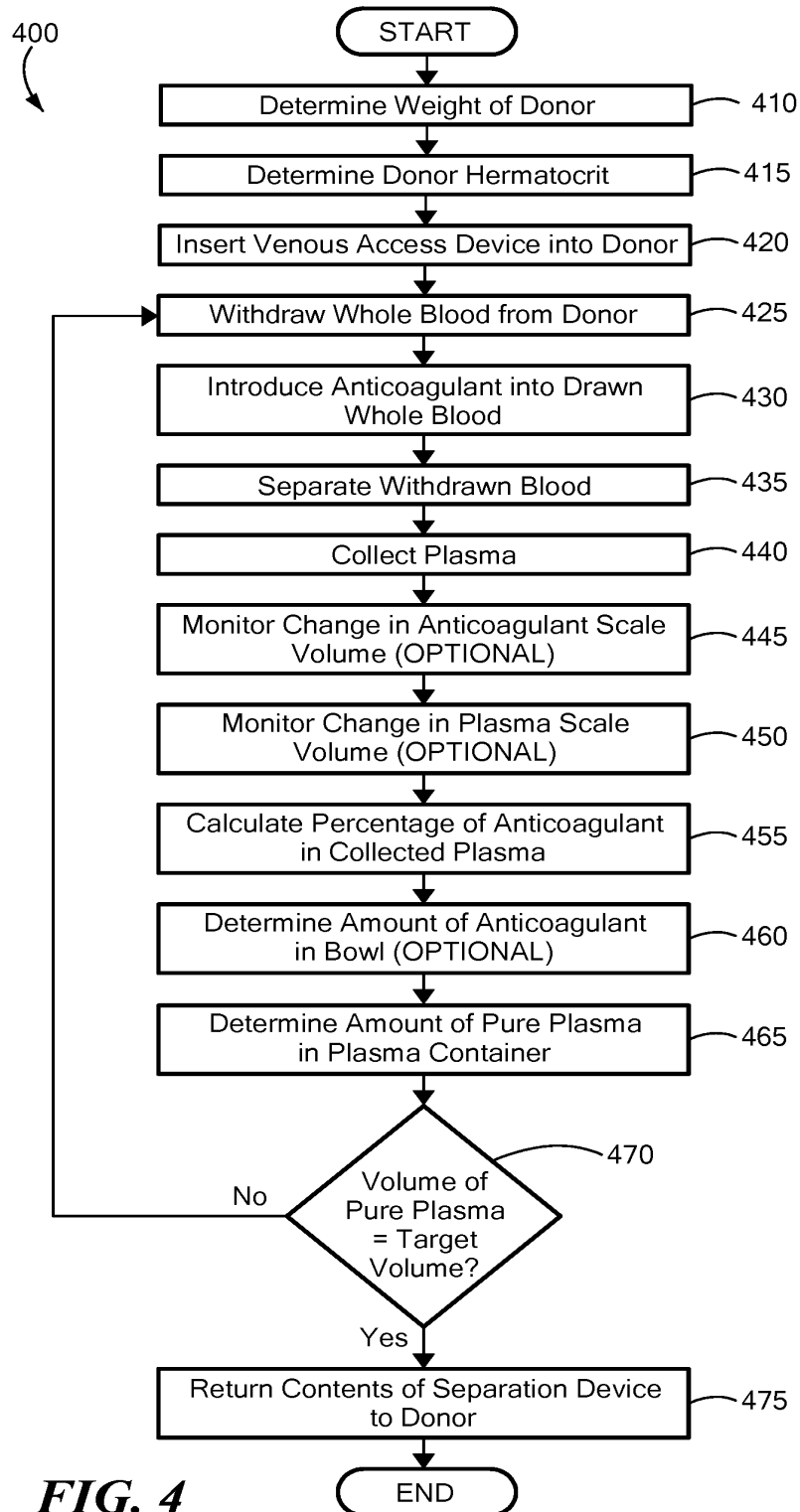


**FIG. 4**

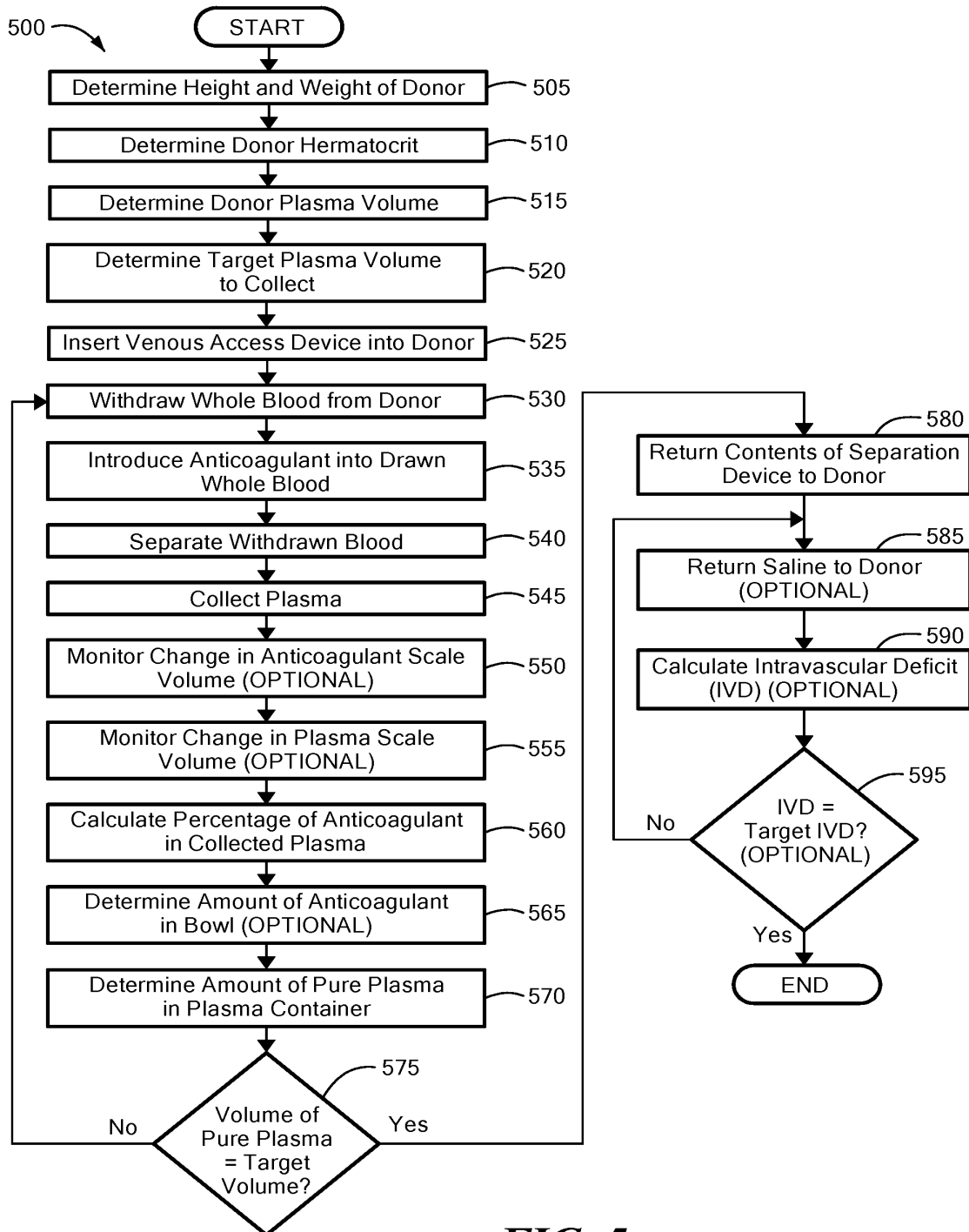


FIG. 5

| Electronic Patent Application Fee Transmittal |          |                                         |        |                      |
|-----------------------------------------------|----------|-----------------------------------------|--------|----------------------|
| Application Number:                           |          |                                         |        |                      |
| Filing Date:                                  |          |                                         |        |                      |
| Title of Invention:                           |          | SYSTEM AND METHOD FOR COLLECTING PLASMA |        |                      |
| First Named Inventor/Applicant Name:          |          | Michael Ragusa                          |        |                      |
| Filer:                                        |          | Jonathan Lovely/Tricia Troup            |        |                      |
| Attorney Docket Number:                       |          | 130670-80104                            |        |                      |
| Filed as Large Entity                         |          |                                         |        |                      |
| Filing Fees for Utility under 35 USC 111(a)   |          |                                         |        |                      |
| Description                                   | Fee Code | Quantity                                | Amount | Sub-Total in USD(\$) |
| <b>Basic Filing:</b>                          |          |                                         |        |                      |
| UTILITY APPLICATION FILING                    | 1011     | 1                                       | 320    | 320                  |
| UTILITY SEARCH FEE                            | 1111     | 1                                       | 700    | 700                  |
| UTILITY EXAMINATION FEE                       | 1311     | 1                                       | 800    | 800                  |
| <b>Pages:</b>                                 |          |                                         |        |                      |
| <b>Claims:</b>                                |          |                                         |        |                      |
| CLAIMS IN EXCESS OF 20                        | 1202     | 7                                       | 100    | 700                  |
| INDEPENDENT CLAIMS IN EXCESS OF 3             | 1201     | 1                                       | 480    | 480                  |
| <b>Miscellaneous-Filing:</b>                  |          |                                         |        |                      |

| Description                              | Fee Code | Quantity | Amount | Sub-Total in USD(\$) |
|------------------------------------------|----------|----------|--------|----------------------|
| <b>Petition:</b>                         |          |          |        |                      |
| <b>Patent-Appeals-and-Interference:</b>  |          |          |        |                      |
| <b>Post-Allowance-and-Post-Issuance:</b> |          |          |        |                      |
| <b>Extension-of-Time:</b>                |          |          |        |                      |
| <b>Miscellaneous:</b>                    |          |          |        |                      |
| <b>Total in USD (\$)</b>                 |          |          |        | <b>3000</b>          |

| Electronic Acknowledgement Receipt          |                                         |
|---------------------------------------------|-----------------------------------------|
| <b>EFS ID:</b>                              | 42217530                                |
| <b>Application Number:</b>                  | 17205400                                |
| <b>International Application Number:</b>    |                                         |
| <b>Confirmation Number:</b>                 | 4686                                    |
| <b>Title of Invention:</b>                  | SYSTEM AND METHOD FOR COLLECTING PLASMA |
| <b>First Named Inventor/Applicant Name:</b> | Michael Ragusa                          |
| <b>Customer Number:</b>                     | 86738                                   |
| <b>Filer:</b>                               | Jonathan Lovely                         |
| <b>Filer Authorized By:</b>                 |                                         |
| <b>Attorney Docket Number:</b>              | 130670-80104                            |
| <b>Receipt Date:</b>                        | 18-MAR-2021                             |
| <b>Filing Date:</b>                         |                                         |
| <b>Time Stamp:</b>                          | 14:30:20                                |
| <b>Application Type:</b>                    | Utility under 35 USC 111(a)             |

### Payment information:

|                                                                                                                |                  |
|----------------------------------------------------------------------------------------------------------------|------------------|
| Submitted with Payment                                                                                         | yes              |
| Payment Type                                                                                                   | DA               |
| Payment was successfully received in RAM                                                                       | \$ 3000          |
| RAM confirmation Number                                                                                        | E20213HE30521724 |
| Deposit Account                                                                                                |                  |
| Authorized User                                                                                                |                  |
| The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: |                  |



|                                                                                                                                                                                                            |                                                     |                                                        |                                          |                  |                  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|--------------------------------------------------------|------------------------------------------|------------------|------------------|
|                                                                                                                                                                                                            |                                                     |                                                        |                                          |                  |                  |
| File Listing:                                                                                                                                                                                              |                                                     |                                                        |                                          |                  |                  |
| Document Number                                                                                                                                                                                            | Document Description                                | File Name                                              | File Size(Bytes)/ Message Digest         | Multi Part /.zip | Pages (if appl.) |
| 1                                                                                                                                                                                                          | Transmittal of New Application                      | Utility_Patent_Application_Transmittal.pdf             | 31981                                    | no               | 1                |
|                                                                                                                                                                                                            |                                                     |                                                        | 58b42fad3de4f1add55d1740029e81f9fea63dbf |                  |                  |
| Warnings:                                                                                                                                                                                                  |                                                     |                                                        |                                          |                  |                  |
| Information:                                                                                                                                                                                               |                                                     |                                                        |                                          |                  |                  |
| 2                                                                                                                                                                                                          | Power of Attorney                                   | Haemonetics_Corporation_GPOA.pdf                       | 169121                                   | no               | 2                |
|                                                                                                                                                                                                            |                                                     |                                                        | 09ee38ef68619178cdfdd9414ff838c961ad68ff |                  |                  |
| Warnings:                                                                                                                                                                                                  |                                                     |                                                        |                                          |                  |                  |
| The page size in the PDF is too large. The pages should be 8.5 x 11 or A4. If this PDF is submitted, the pages will be resized upon entry into the Image File Wrapper and may affect subsequent processing |                                                     |                                                        |                                          |                  |                  |
| Information:                                                                                                                                                                                               |                                                     |                                                        |                                          |                  |                  |
| 3                                                                                                                                                                                                          | Oath or Declaration filed                           | Executed_Declaration_-_Michael_Ragusa_15_793339.PDF    | 99922                                    | no               | 1                |
|                                                                                                                                                                                                            |                                                     |                                                        | f914d7ceee82b879229fe014d8c786c9b07b56bd |                  |                  |
| Warnings:                                                                                                                                                                                                  |                                                     |                                                        |                                          |                  |                  |
| Information:                                                                                                                                                                                               |                                                     |                                                        |                                          |                  |                  |
| 4                                                                                                                                                                                                          | Application Data Sheet                              | 130670-80104_-_Application_Data_Sheet_Fillable_PDF.pdf | 1255635                                  | no               | 8                |
|                                                                                                                                                                                                            |                                                     |                                                        | ee615962ab710a7ee4ccda32d9d17e4e25bbcb6b |                  |                  |
| Warnings:                                                                                                                                                                                                  |                                                     |                                                        |                                          |                  |                  |
| Information:                                                                                                                                                                                               |                                                     |                                                        |                                          |                  |                  |
| 5                                                                                                                                                                                                          |                                                     | Application.pdf                                        | 118192                                   | yes              | 32               |
|                                                                                                                                                                                                            |                                                     |                                                        | fbed5c8693772fec657a6ad04d5c72b586bbaaa5 |                  |                  |
|                                                                                                                                                                                                            | Multipart Description/PDF files in .zip description |                                                        |                                          |                  |                  |
|                                                                                                                                                                                                            | Document Description                                |                                                        | Start                                    | End              |                  |
|                                                                                                                                                                                                            | Specification                                       |                                                        | 1                                        | 25               |                  |
|                                                                                                                                                                                                            | Claims                                              |                                                        | 26                                       | 31               |                  |

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| <b>Warnings:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                             |              |                                          |    |
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                             |              |                                          |    |
| 6                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Drawings-only black and white line drawings | Figures.PDF  | 140972                                   | no |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                             |              | 417f9009a2bdf6044427fd31c78e93c58890f348 |    |
| <b>Warnings:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                             |              |                                          |    |
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                             |              |                                          |    |
| 7                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Fee Worksheet (SB06)                        | fee-info.pdf | 37802                                    | no |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                             |              | 35e5cd1904466ae3e4b6468c8412f9a950a0e1db |    |
| <b>Warnings:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                             |              |                                          |    |
| <b>Information:</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                             |              |                                          |    |
| <b>Total Files Size (in bytes):</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                             |              | 1853625                                  |    |
| <p><b>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</b></p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b><br/> <b>If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</b></p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b><br/> <b>If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</b></p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b><br/> <b>If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</b></p> |                                             |              |                                          |    |

Under the Paperwork Reduction Act of 1995 no persons are required to respond to a collection of information unless it displays a valid OMB control number.

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|---------------------------------------------------------------------------------------------------------------------------------------------|--|-------------------------------------|-----------------------------------------|
| <b>UTILITY<br/>PATENT APPLICATION<br/>TRANSMITTAL</b><br><br><small>(Only for new nonprovisional applications under 37 CFR 1.53(b))</small> |  | Attorney Docket No. 130670-80104    |                                         |
|                                                                                                                                             |  | First Named Inventor Michael Ragusa |                                         |
|                                                                                                                                             |  | Title                               | SYSTEM AND METHOD FOR COLLECTING PLASMA |
|                                                                                                                                             |  | Priority Mail Express® Label No.    |                                         |

|                                                                                                                    |                                                                                           |
|--------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| <b>APPLICATION ELEMENTS</b><br><small>See MPEP chapter 600 concerning utility patent application contents.</small> | <b>ADDRESS TO:</b> Commissioner for Patents<br>P.O. Box 1450<br>Alexandria, VA 22313-1450 |
|--------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|

|                                        |                                                                                                                                                                                                            |
|----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>ACCOMPANYING APPLICATION PAPERS</b> | <b>10. <input type="checkbox"/> Assignment Papers</b><br><small>(cover sheet &amp; document(s))</small><br><br>Name of Assignee<br><div style="border: 1px solid black; height: 30px; width: 100%;"></div> |
|----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

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| 1. <input type="checkbox"/> <b>Fee Transmittal Form</b><br><small>(PTO/SB/17 or equivalent)</small><br>2. <input type="checkbox"/> <b>Applicant asserts small entity status.</b><br><small>See 37 CFR 1.27</small><br>3. <input type="checkbox"/> <b>Applicant certifies micro entity status.</b> See 37 CFR 1.29.<br><small>Applicant must attach form PTO/SB/15A or B or equivalent.</small><br>4. <input checked="" type="checkbox"/> <b>Specification</b> [Total Pages <u>32</u> ]<br><small>Both the claims and abstract must start on a new page.<br/>         (See MPEP § 608.01(a) for information on the preferred arrangement)</small><br>5. <input checked="" type="checkbox"/> <b>Drawing(s)</b> (35 U.S.C. 113) [Total Sheets <u>5</u> ]<br>6. <input type="checkbox"/> <b>Inventor's Oath or Declaration</b> [Total Pages <u>1</u> ]<br><small>(including substitute statements under 37 CFR 1.64 and assignments<br/>         serving as an oath or declaration under 37 CFR 1.63(e))</small><br>a. <input type="checkbox"/> Newly executed (original or copy)<br>b. <input checked="" type="checkbox"/> A copy from a prior application (37 CFR 1.63(d))<br>7. <input checked="" type="checkbox"/> <b>Application Data Sheet</b> * See note below.<br><small>See 37 CFR 1.76 (PTO/AIA/14 or equivalent)</small><br>8. <input type="checkbox"/> <b>CD-ROM or CD-R</b><br><small>in duplicate, large table, or Computer Program (Appendix)</small><br><input type="checkbox"/> Landscape Table on CD<br>9. <input type="checkbox"/> <b>Nucleotide and/or Amino Acid Sequence Submission</b><br><small>(if applicable, items a. – c. are required)</small><br>a. <input type="checkbox"/> Computer Readable Form (CRF)<br>b. <input type="checkbox"/> Specification Sequence Listing on:<br>i. <input type="checkbox"/> CD-ROM or CD-R (2 copies); or<br>ii. <input type="checkbox"/> Paper<br>c. <input type="checkbox"/> Statements verifying identity of above copies | 11. <input type="checkbox"/> <b>37 CFR 3.73(c) Statement</b><br><small>(when there is an assignee)</small> <input checked="" type="checkbox"/> <b>Power of Attorney</b><br>12. <input type="checkbox"/> <b>English Translation Document</b> (if applicable)<br>13. <input type="checkbox"/> <b>Information Disclosure Statement</b><br><small>(PTO/SB/08 or PTO-1449)</small><br><input type="checkbox"/> Copies of citations attached<br>14. <input type="checkbox"/> <b>Preliminary Amendment</b><br>15. <input type="checkbox"/> <b>Return Receipt Postcard</b><br><small>(MPEP § 503) (Should be specifically itemized)</small><br>16. <input type="checkbox"/> <b>Certified Copy of Priority Document(s)</b><br><small>(if foreign priority is claimed)</small><br>17. <input type="checkbox"/> <b>Nonpublication Request</b><br><small>Under 35 U.S.C. 122(b)(2)(B)(i). Applicant must attach form PTO/SB/35<br/>         or equivalent.</small><br>18. <input type="checkbox"/> <b>Other:</b> <div style="border: 1px solid black; height: 40px; width: 100%;"></div> |
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**\*Note:** (1) Benefit claims under 37 CFR 1.78 and foreign priority claims under 1.55 **must** be included in an Application Data Sheet (ADS).  
 (2) For applications filed under 35 U.S.C. 111, the application must contain an ADS specifying the applicant if the applicant is an assignee, person to whom the inventor is under an obligation to assign, or person who otherwise shows sufficient proprietary interest in the matter. See 37 CFR 1.46(b).

|                                                                                                                                                               |  |                                       |  |                                   |  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------|--|---------------------------------------|--|-----------------------------------|--|
| <b>19. CORRESPONDENCE ADDRESS</b>                                                                                                                             |  |                                       |  |                                   |  |
| <input checked="" type="checkbox"/> The address associated with Customer Number: <u>86738</u> <b>OR</b> <input type="checkbox"/> Correspondence address below |  |                                       |  |                                   |  |
| Name                                                                                                                                                          |  |                                       |  |                                   |  |
| Address                                                                                                                                                       |  |                                       |  |                                   |  |
| City                                                                                                                                                          |  | State                                 |  | Zip Code                          |  |
| Country                                                                                                                                                       |  | Telephone                             |  | Email                             |  |
| Signature                                                                                                                                                     |  | /Jonathan C. Lovely, Reg. No. 60,821/ |  | Date                              |  |
| Name (Print/Type)                                                                                                                                             |  | Jonathan C. Lovely                    |  | Registration No. (Attorney/Agent) |  |
|                                                                                                                                                               |  |                                       |  | March 18, 2021                    |  |
|                                                                                                                                                               |  |                                       |  | 60,821                            |  |