TERUMO BLOOD AND CELL TECHNOLOGIES

Continuous Mononuclear Cell Collection (Version 12 CMNC) Procedure Training

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Operator’s Manual Information

Spectra Optia Apheresis System

Intended Use

The Spectra Optia Apheresis System, a blood component separator, may be used to perform the following therapeutic apheresis, cell collection, and cell processing procedures*:

- Therapeutic plasma exchange
- Therapeutic plasma exchange with a secondary plasma device
- Red blood cell exchange, depletion, and depletion/exchange
- Mononuclear cell collection from the peripheral blood
- Granulocyte collection from the peripheral blood
- White blood cell depletion‡
- Platelet depletion
- Processing of harvested bone marrow

*Procedure availability varies by country.

‡White blood cell reduction for patients with leukocytosis at risk for leukostasis (Intended Use in the U.S.)

Contraindications for Use

- Leukocytapheresis is contraindicated in AML FAB M3 (APL) because of the accompanying disseminated intravascular coagulation. (Vahdat L, et al., “Early mortality and the retinoic acid syndrome in acute promyelocytic leukemia: impact of leukocytosis, low-dose chemotherapy, PMN/RAR-alpha isoform and CD13 expression in patients treated with all-trans retinoic acid.” Blood 1994; 84: 3843-3849. Daver, et al., “Clinical characteristics and outcomes in patients with acute promyelocytic leukaemia and hyperleucocytosis.” British Journal of Haematology 2015, 168, 646-653.)
- Other contraindications for the use of the Spectra Optia system are limited to those associated with the infusion of solutions and replacement fluids as required by the apheresis procedure, and those associated with all types of automated apheresis systems.

Possible Adverse Events of Apheresis Procedures Include:

- Anxiety, headache, light-headedness, digital and/or facial paresthesia, fever, chills, hematoma, hyperventilation, nausea and vomiting, syncope (fainting), urticaria, hypotension, allergic reactions, infection, hemolysis, thrombosis in patient and device, hypocalcemia, hypokalemia, thrombocytopenia, hypoalbuminemia, anemia, coagulopathy, fatigue, hypomagnesemia, hypogammaglobulinemia, adverse tissue reaction, device failure/disposable failure, air embolism, blood loss/anemia, electrical shock hazard, fluid imbalance, inadequate separation of blood components.

Reactions to Blood Products Transfused During Procedures

- Reactions to transfused blood products can include fever, circulatory overload, shock, allergic reactions, alloimmunization, transfusion-related acute lung injury (TRALI), and graft-versus-host disease (GVHD), as well as transmission of infectious diseases and bacteria. (Sources: *Circular of Information for the Use of Human Blood and Blood Components*, AABB, et al, ed., April, 2006; *Guide to the preparation, use and quality assurance of blood components*, 10th Edition, Council of Europe Publishing; Toy P et al., “Transfusion-Related Acute Lung Injury: Incidence and Risk Factors.” *Blood*, 2012; 119: 1757-1767.)

Restricted to Prescription Use Only:

- Operators must be familiar with the system's operating instructions.
- Procedures must be performed by qualified medical personnel.

Learning Objectives

After completing this training, you will be able to do the following regarding a CMNC procedure using the Spectra Optia system:

- Discuss the principles of the procedure
- Enter and discuss the data needed to perform the procedure
- Discuss how the data you entered affects the procedure and the run targets
- View and change data on the run values screen
- Make changes to data on the data, run, and end run menu screens
- Optimize the run for the desired procedure outcomes
- Troubleshoot issues that may arise

Presentation Overview

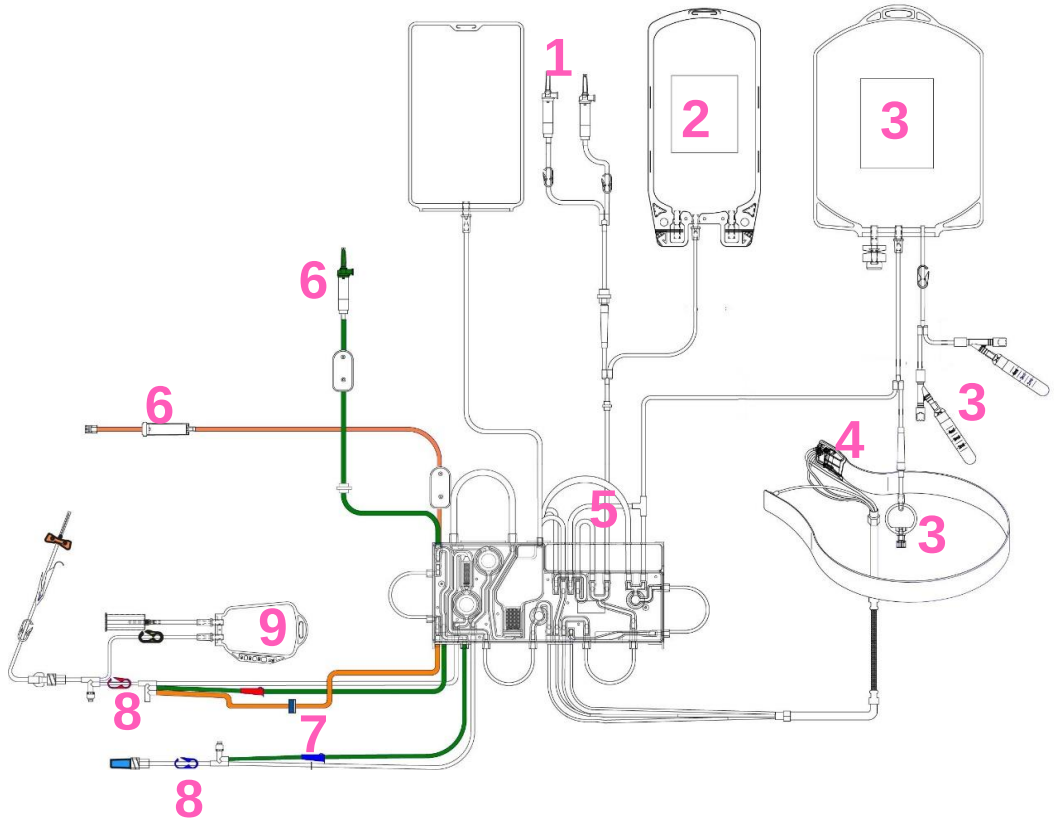
- Introduction
- Preparing to Perform the Procedure
- Monitoring the Run
- Completing the Run
- Making Changes
- Optimization
- Troubleshooting
- Low TBV Patients

Introduction

- IDL Set
- Basic Principles of CMNC Collection
- Cell Separation: Channel
- Cell Separation: Connector
- AIM System Control of Collection
- Collection Preference (CP)

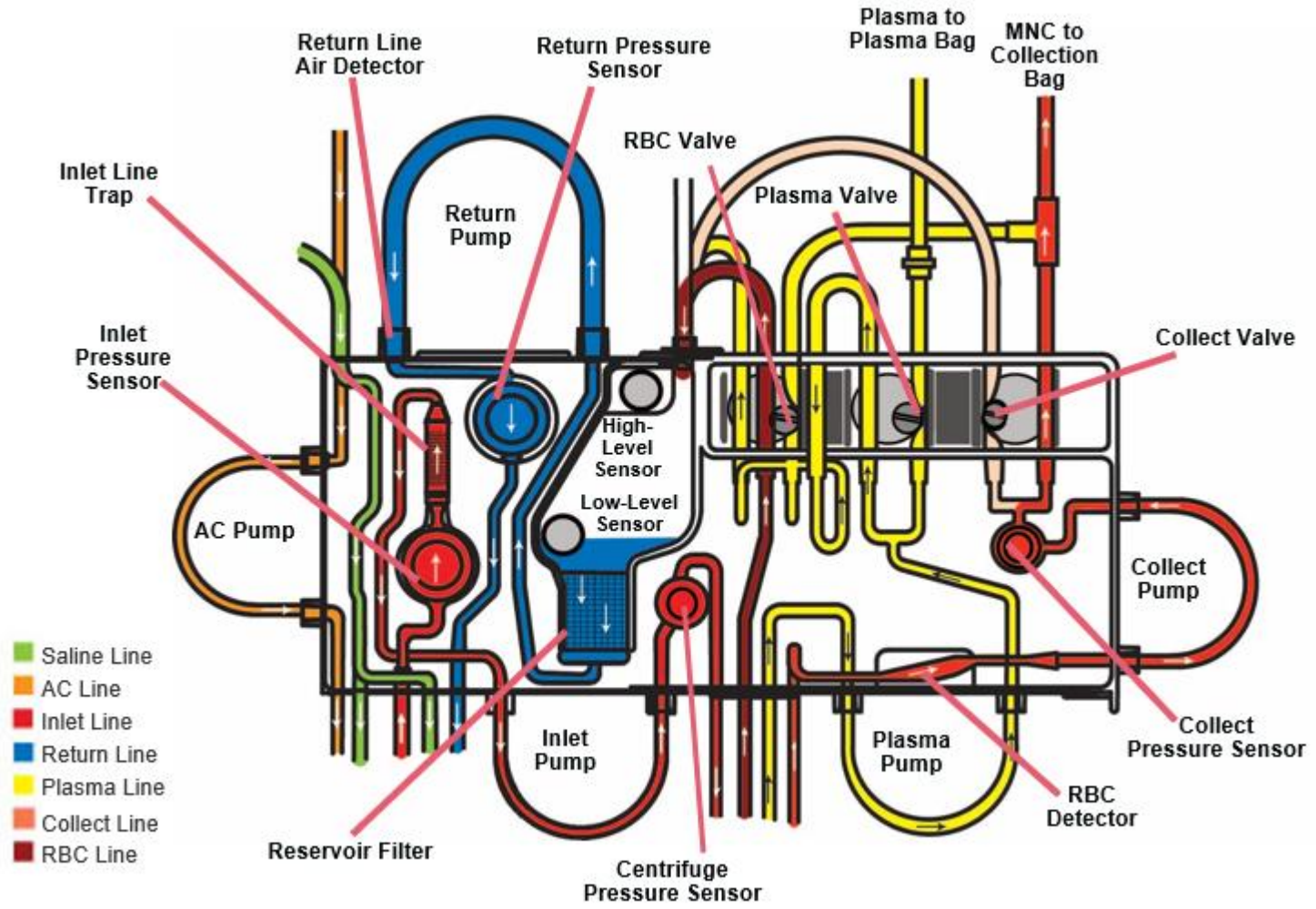
IDL Set

1. Replace line
   - Frangible connector
2. Plasma bag
3. Collection bag
   - Spike port
   - Sample bulbs
   - Sterile barrier filter
4. Connector
5. Cassette
6. AC and saline tubing
   - AC Correct Connect* luer
   - Saline spike
   - Sterile barrier filters
7. AC check valve
8. Colored clamps
9. Diversion bag

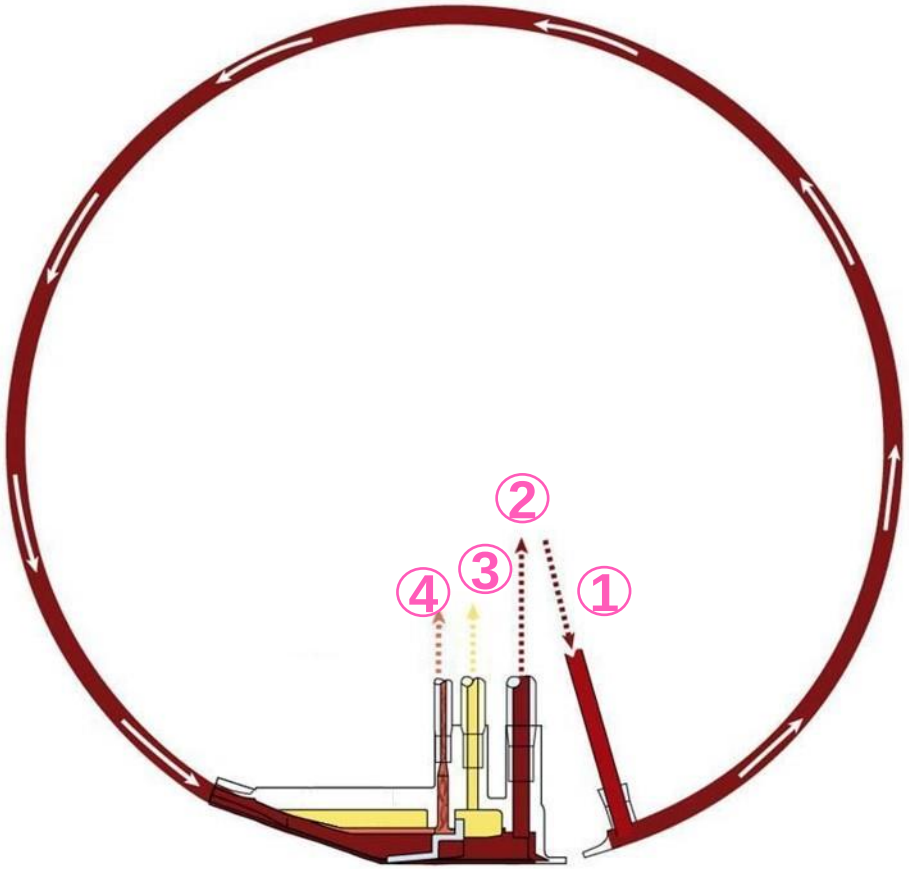


*Correct Connect IDL Set availability is dependent upon regulatory approval

Basic Principles of CMNC Collection



Cell Separation: Channel



1. Whole blood enters the channel.
2. Red blood cells (RBC) flow passively to the reservoir.
3. Plasma is pumped into the reservoir, or it is collected.
4. Cells are continuously pumped into the collection bag.

Cell Separation: Connector

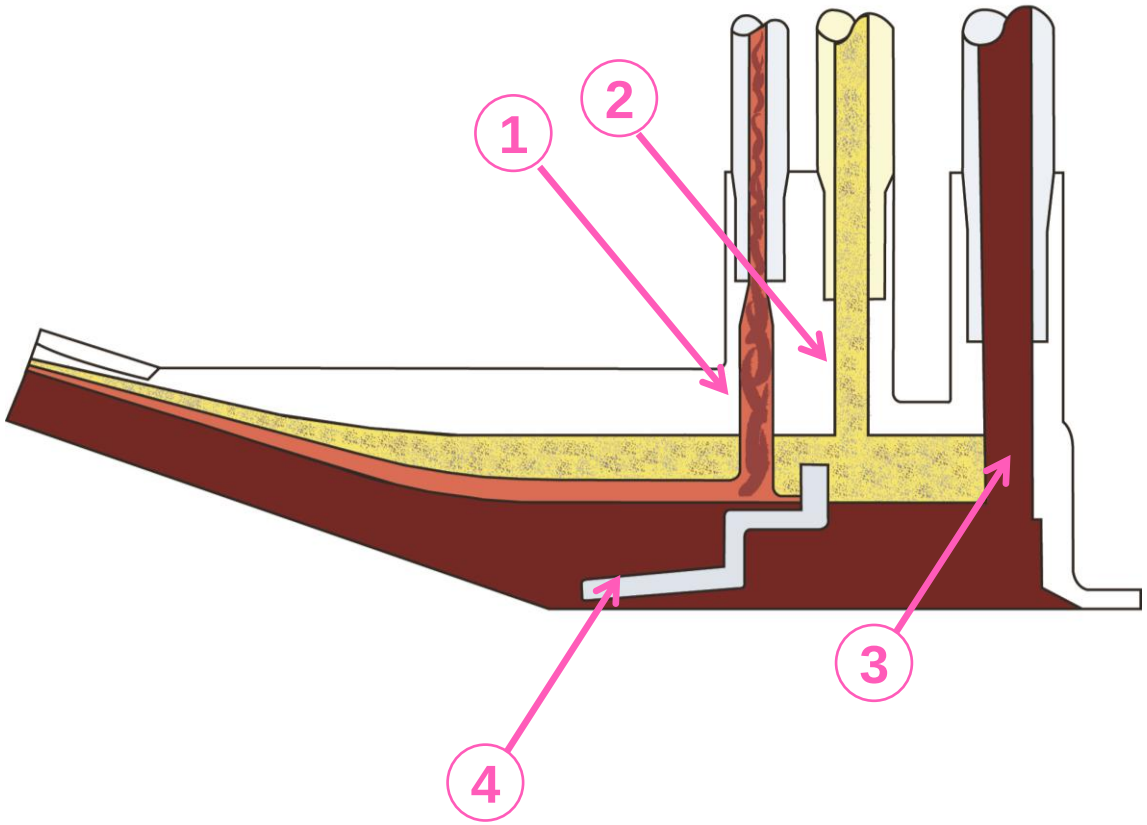
Centrifugal force separates the blood in the connector into layers based on the **specific gravity** of the cells:

Platelets: 1.04 to 1.08

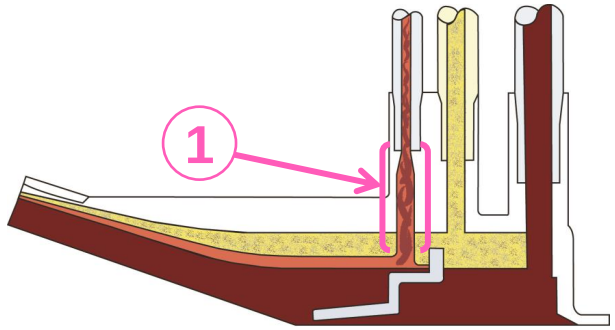
MNC: 1.06 to 1.09

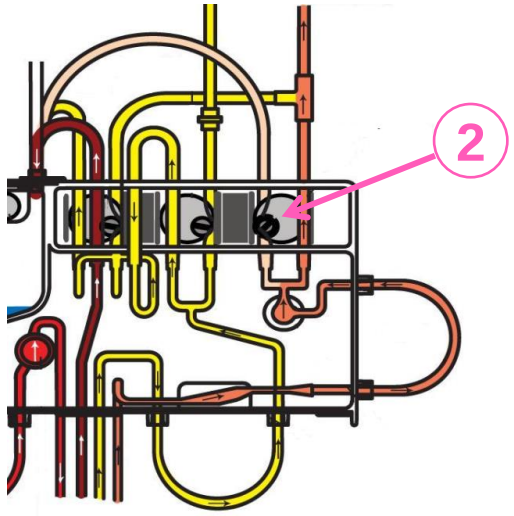
RBC: 1.08 to 1.11

1. Collect port
2. Plasma port
3. RBC port
4. Skimmer dam



AIM System Control of Collection



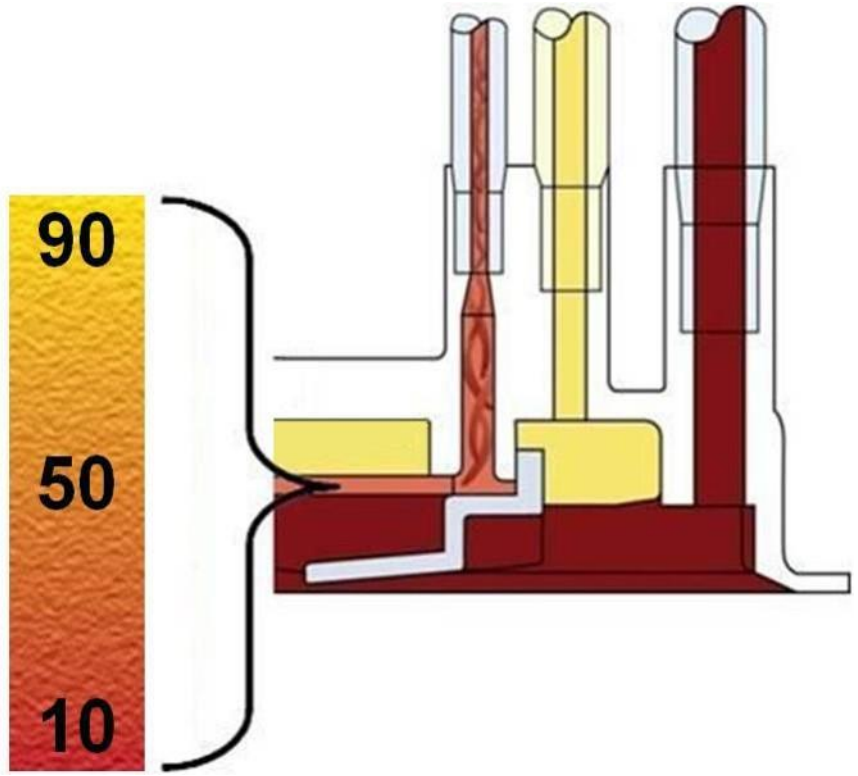


1. The AIM system controls the concentration of cells in the collect port (collection preference).
2. When cells are detected in the collect port the collect valve moves to the collect position.
   - The cells are continuously collected into the collection bag.

Questions?

Collection Preference (CP)

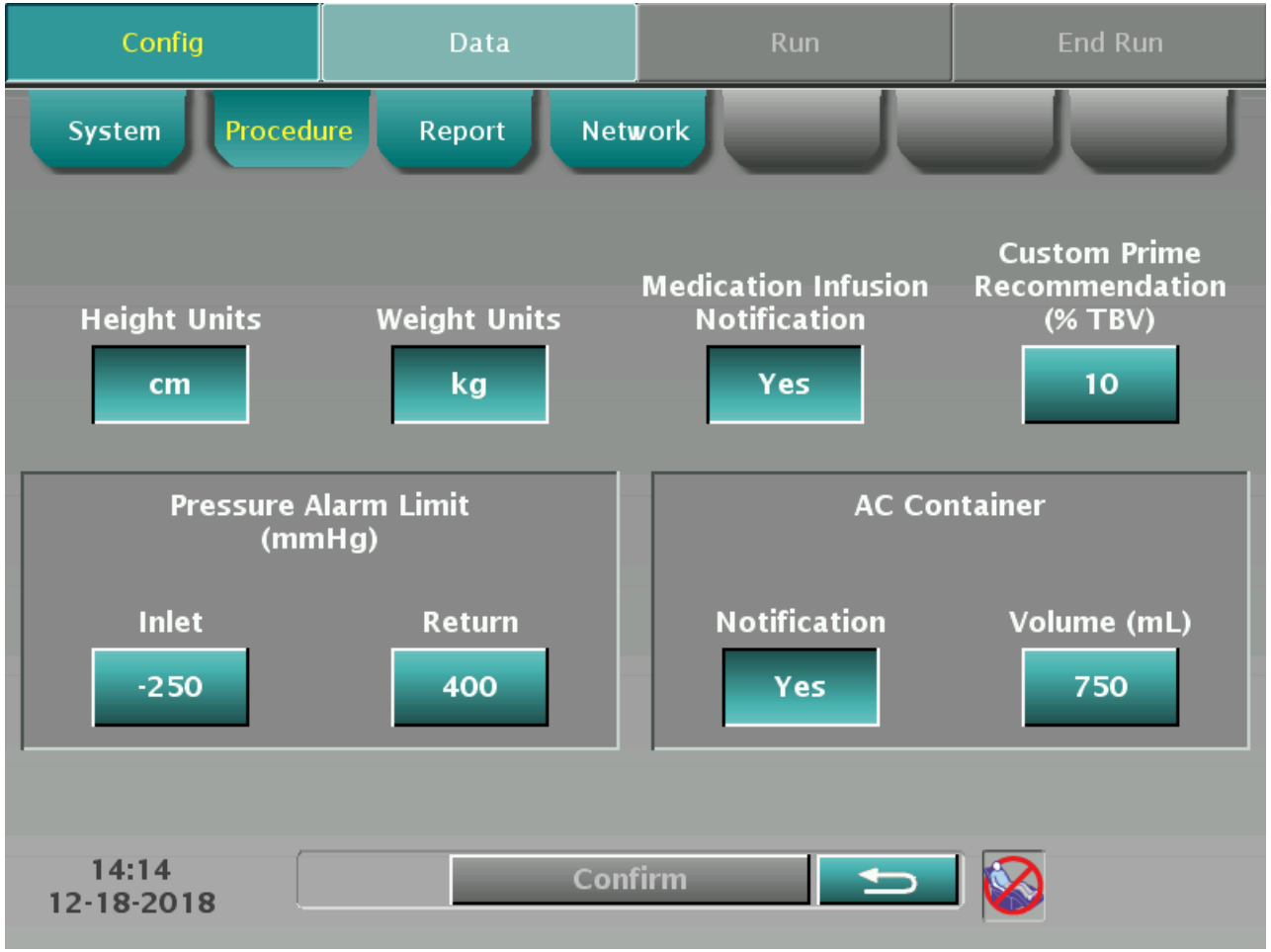
- The AIM system controls the concentration of cells (collection preference) flowing through the collect port by adjusting the plasma pump flow rate.
- The CP will always default to 50.



Preparing to Perform the Procedure

- Configuration: Medication Infusion Notification
- Configuration: CMNC
- Configuration: Blood Warmer and AC
- Channel Loading
- Patient Data
- Run Values
- Patient Connection

Configuration: Procedure

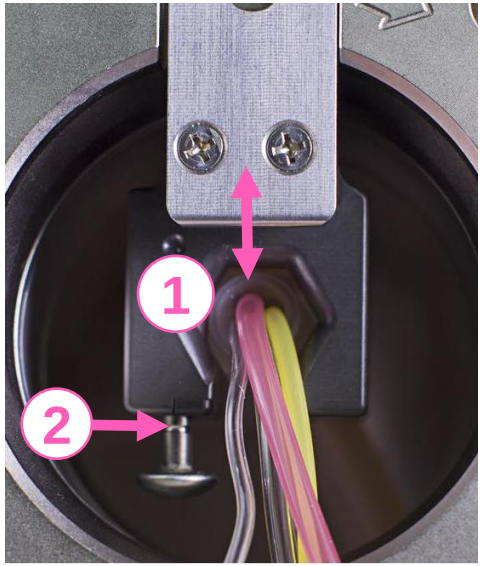


Configuration: CMNC

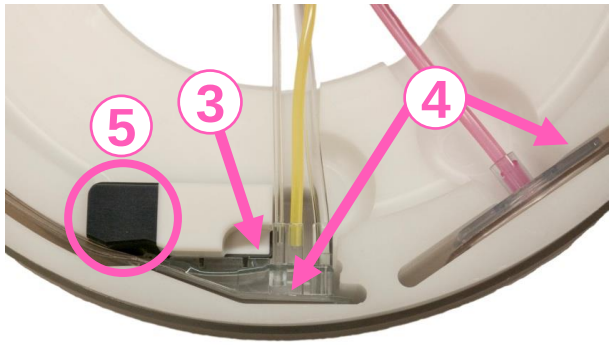
Configuration: Blood Warmer and AC

Channel Loading

1. Centrifuge collar is in the correct position.
2. Notch on locking pin is visible.

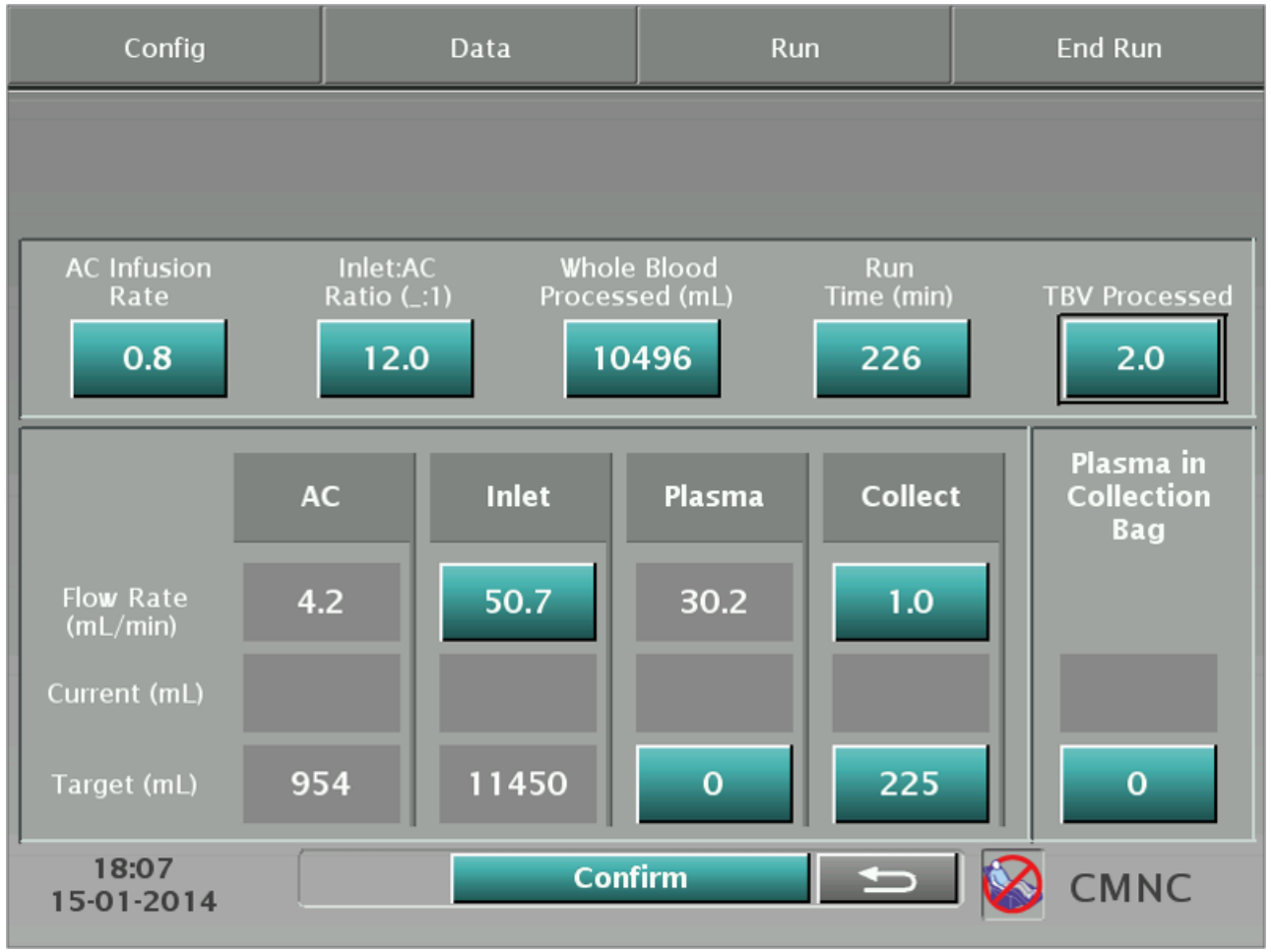


3. Optical reference is visible.
4. Connector and channel sit flush in the filler.
5. Section of IDL filler has a black square.



Patient Data

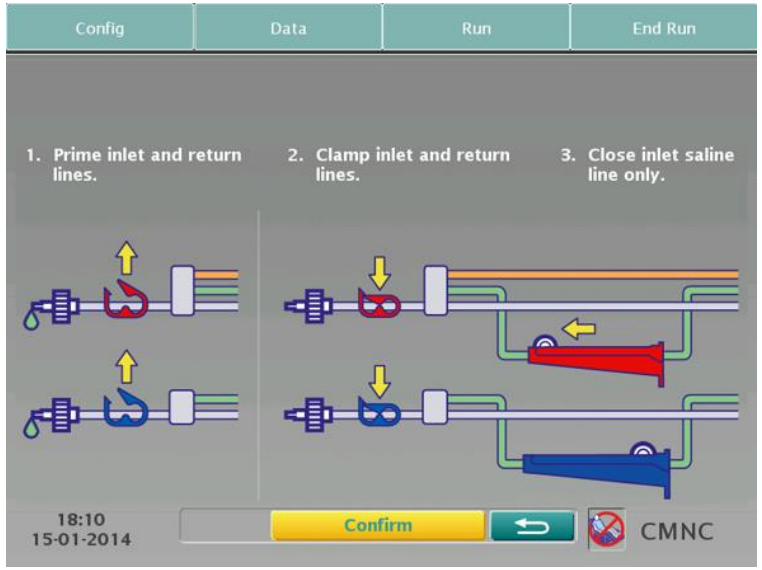
Run Values

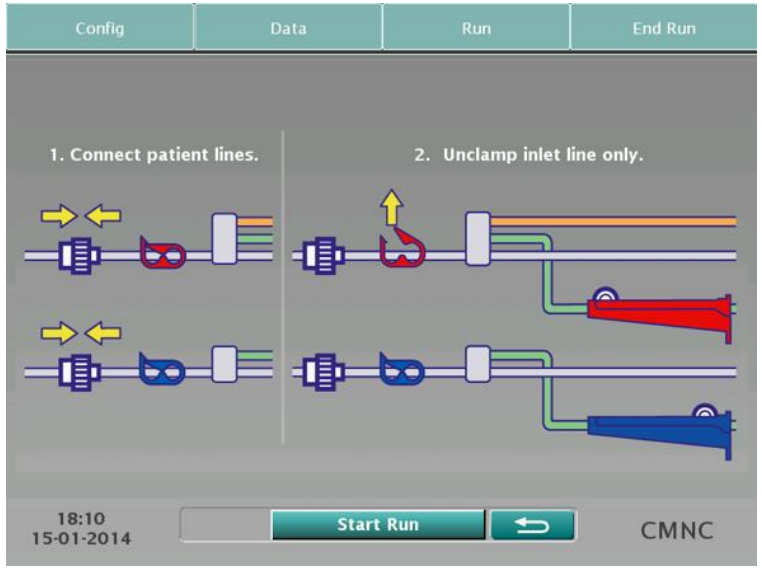

Config
Data
Run
End Run
AC Infusion Rate
0.8
Inlet:AC Ratio (_:1)
12.0
Whole Blood Processed (mL)
10496
Run Time (min)
226
TBV Processed
2.0
AC
Inlet
Plasma
Collect
Plasma in Collection Bag
Flow Rate (mL/min)
4.2
50.7
30.2
1.0
Current (mL)
Target (mL)
954
11450
0
225
0
18:07
15-01-2014
Confirm
CMNC

Patient Connection

Important!

- Unclamp, clamp and close the lines as instructed on the screens.
- Leave the return saline line open at the start of the run to divert the prime saline.



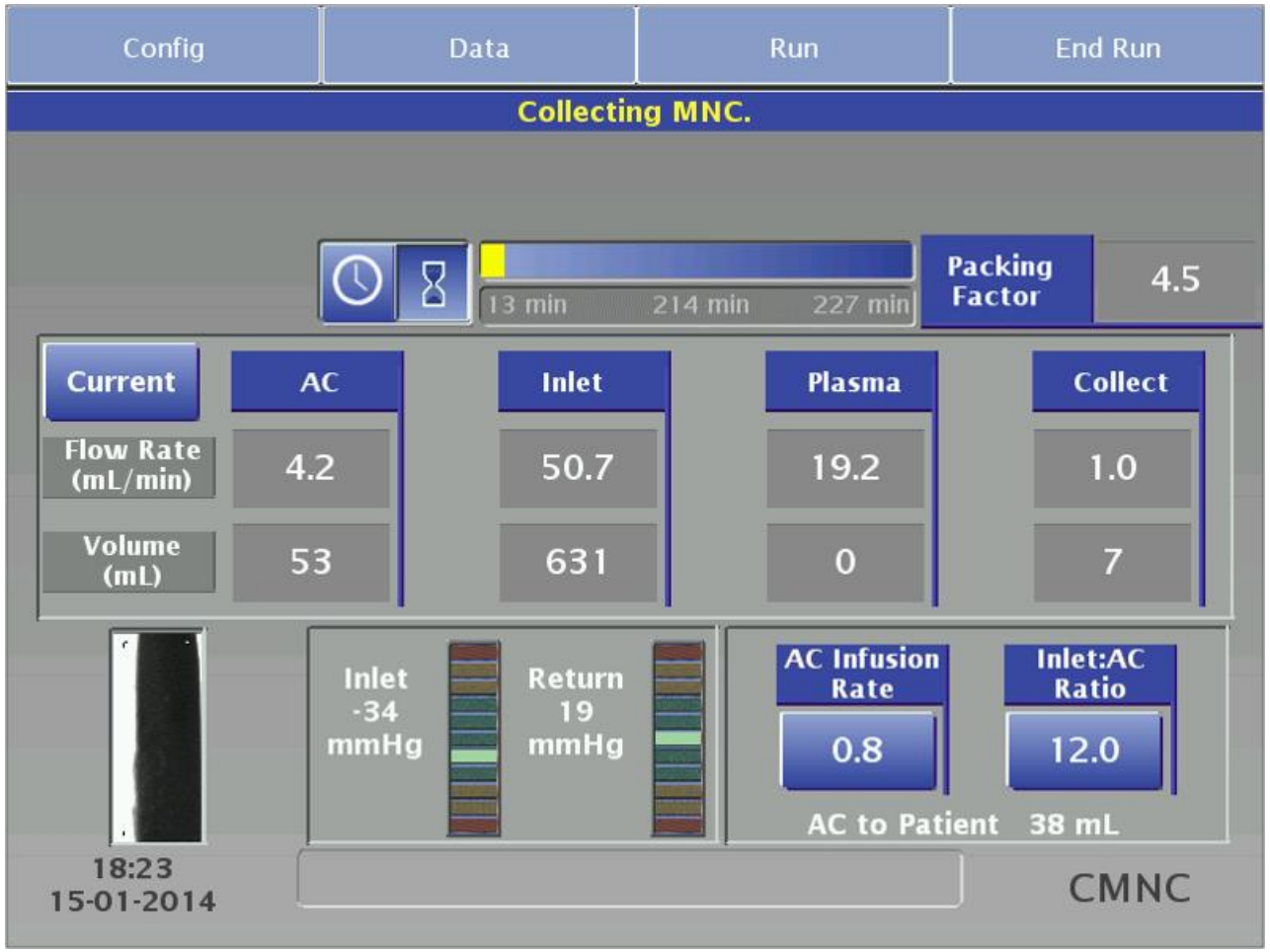


Questions?

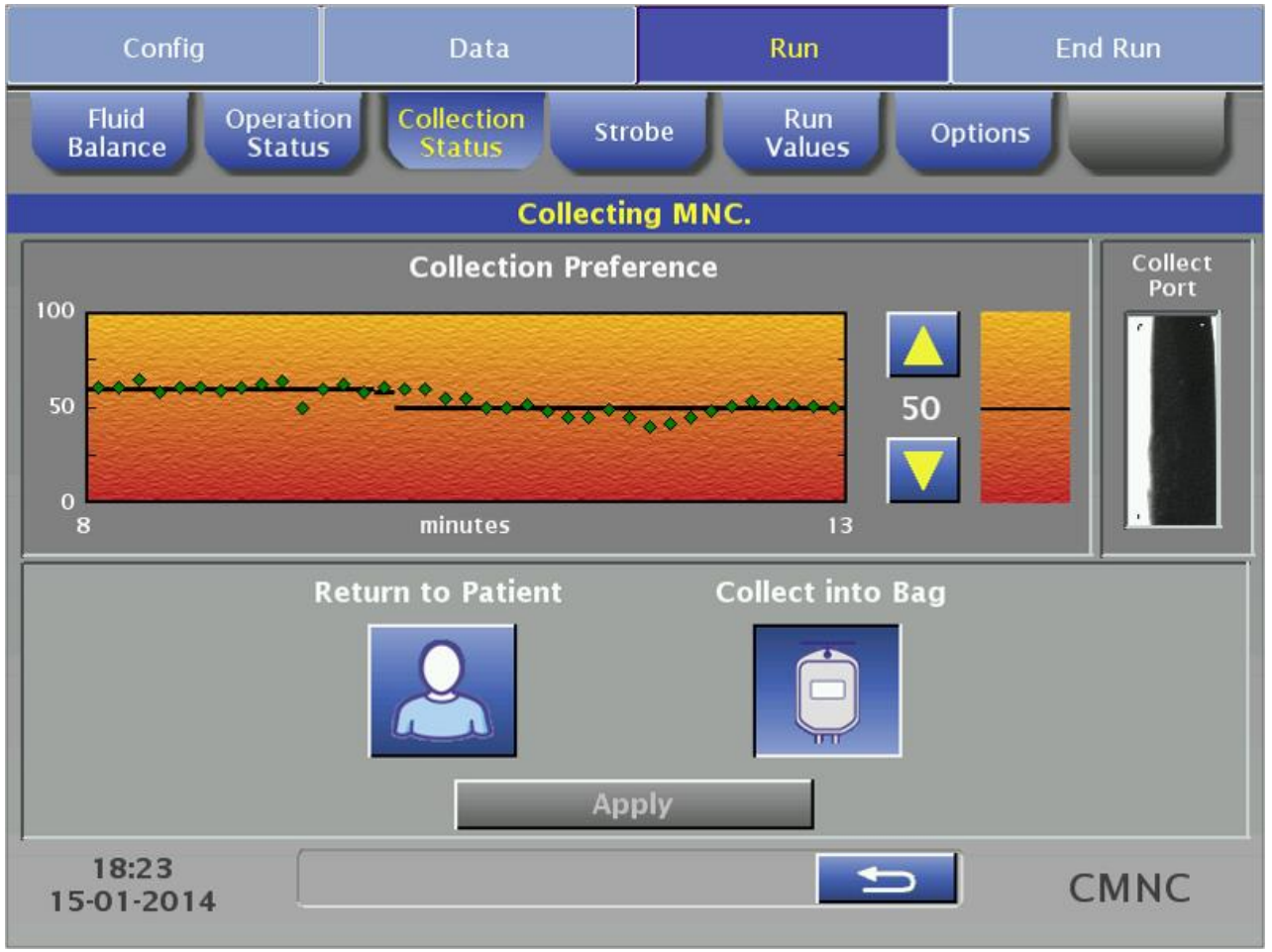
Monitoring the Run

- Main Run
- Collection Status
- Connector
- Collect Line from the Centrifuge
- Caution Status

Main Run

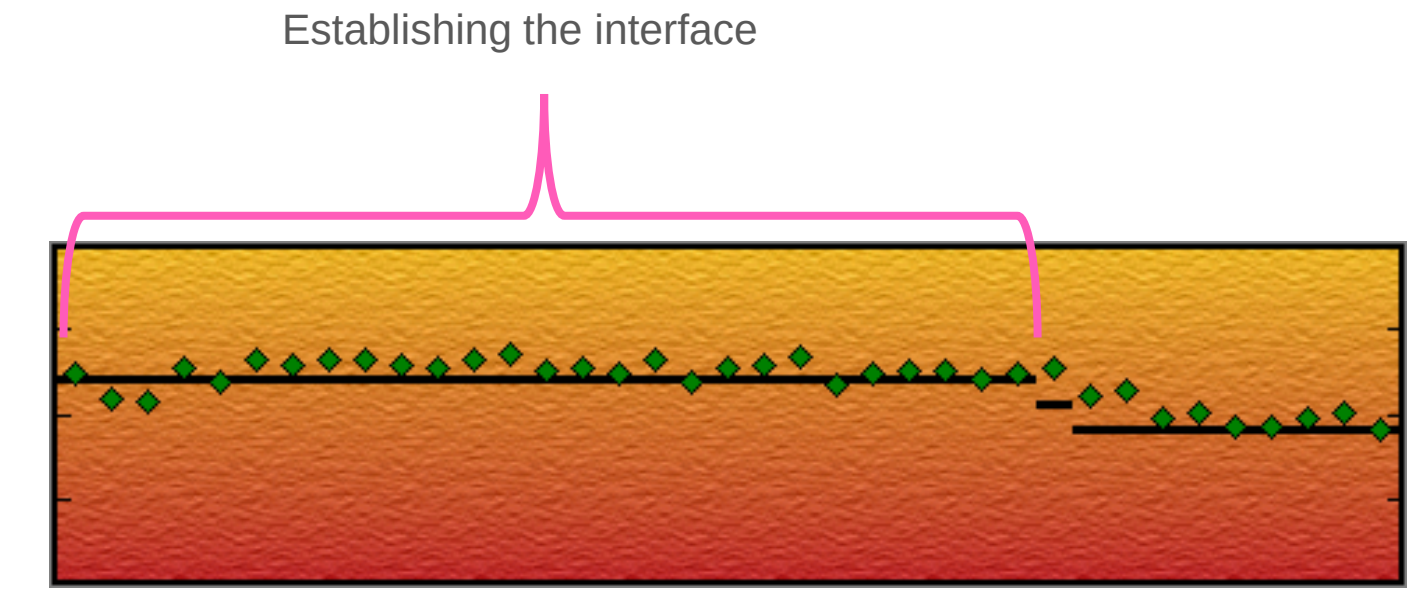

Config
Data
Run
End Run
Collecting MNC.
13 min
214 min
227 min
Packing Factor
4.5
Current
AC
Inlet
Plasma
Collect
Flow Rate (mL/min)
4.2
50.7
19.2
1.0
Volume (mL)
53
631
0
7
Inlet -34 mmHg
Return 19 mmHg
AC Infusion Rate
0.8
Inlet:AC Ratio
12.0
AC to Patient 38 mL
18:23
15-01-2014
CMNC

Collection Status



Collection Status (continued)

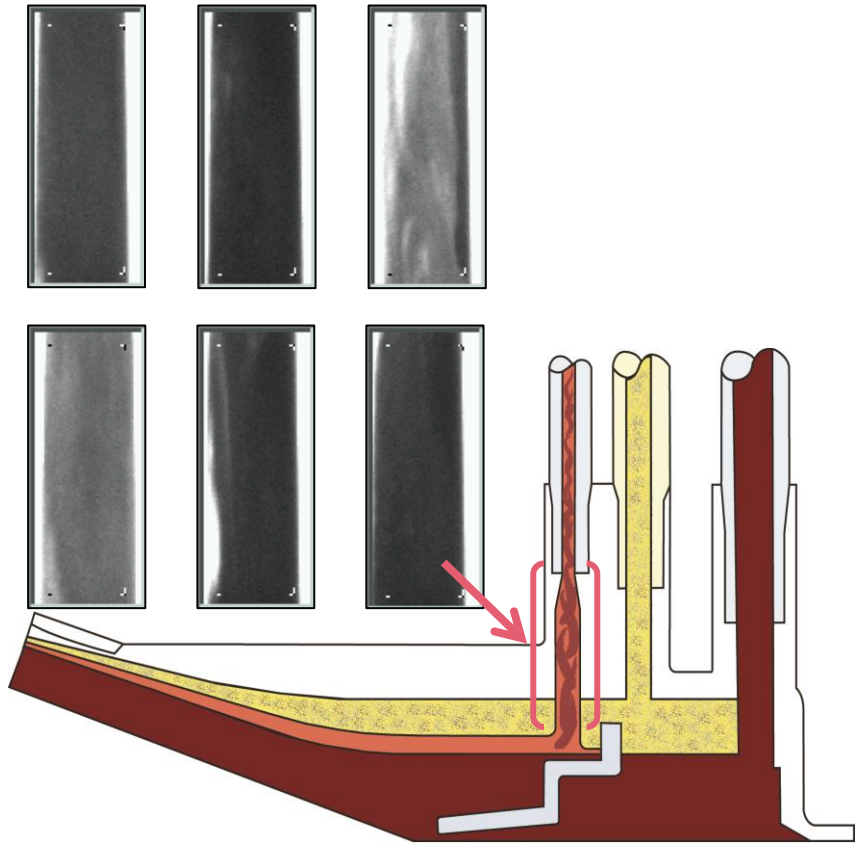
CP trend graph



Targeted CP

Concentration of cells at the collect port

Collection Status (continued)



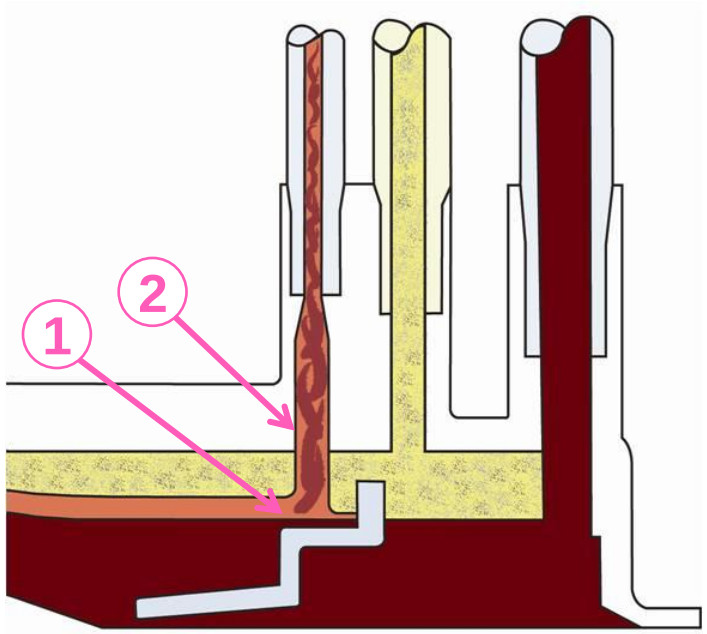
Collect port image:

- The AIM system captures images of the collect port.
- The images show the variation of the concentration of cells in the collect port.

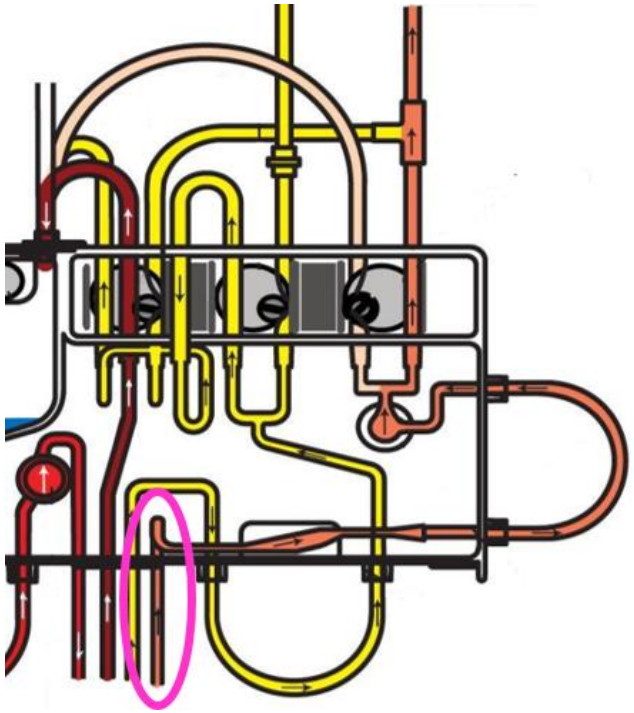
Connector

Monitor the separation of cells in the connector and the concentration of cells in the collect port.

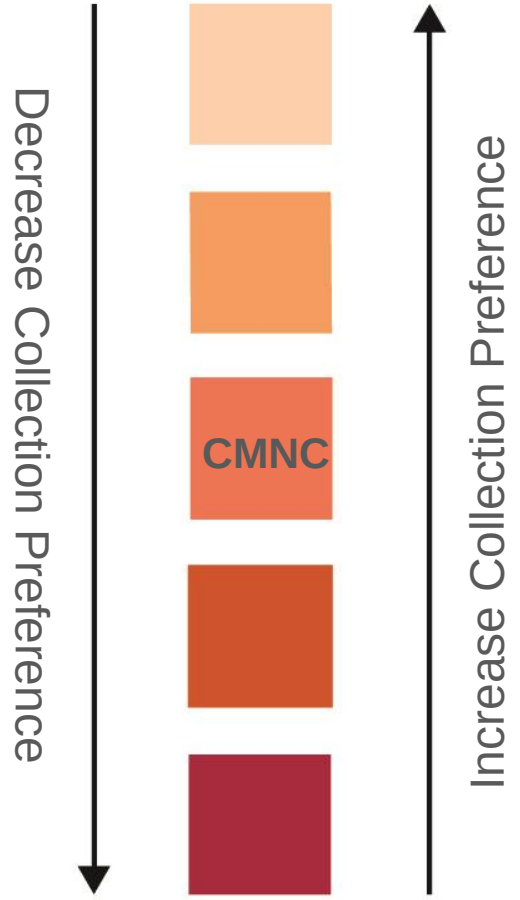
1. The interface should be positioned at the collect port.
2. The cellular concentration in the collect port should be monitored to maintain an appropriate Hct in the collect line.



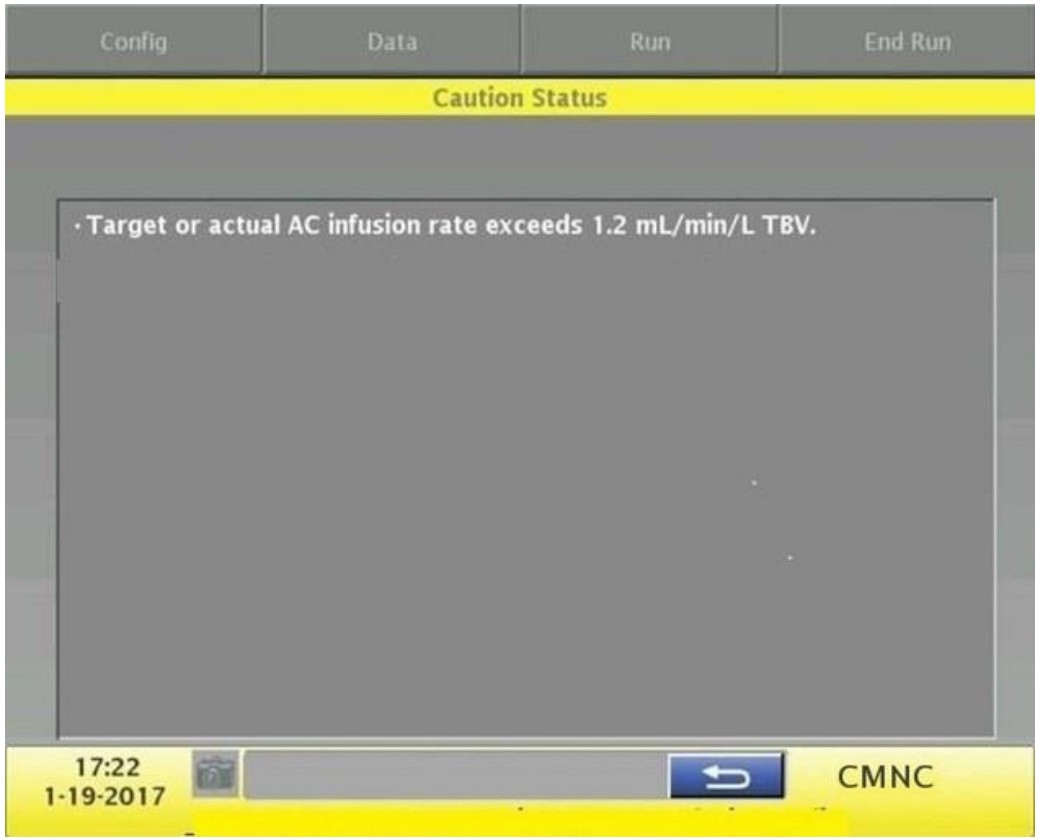
Collect Line From the Centrifuge



Monitor the color in the collect line below the cassette.



Caution Status

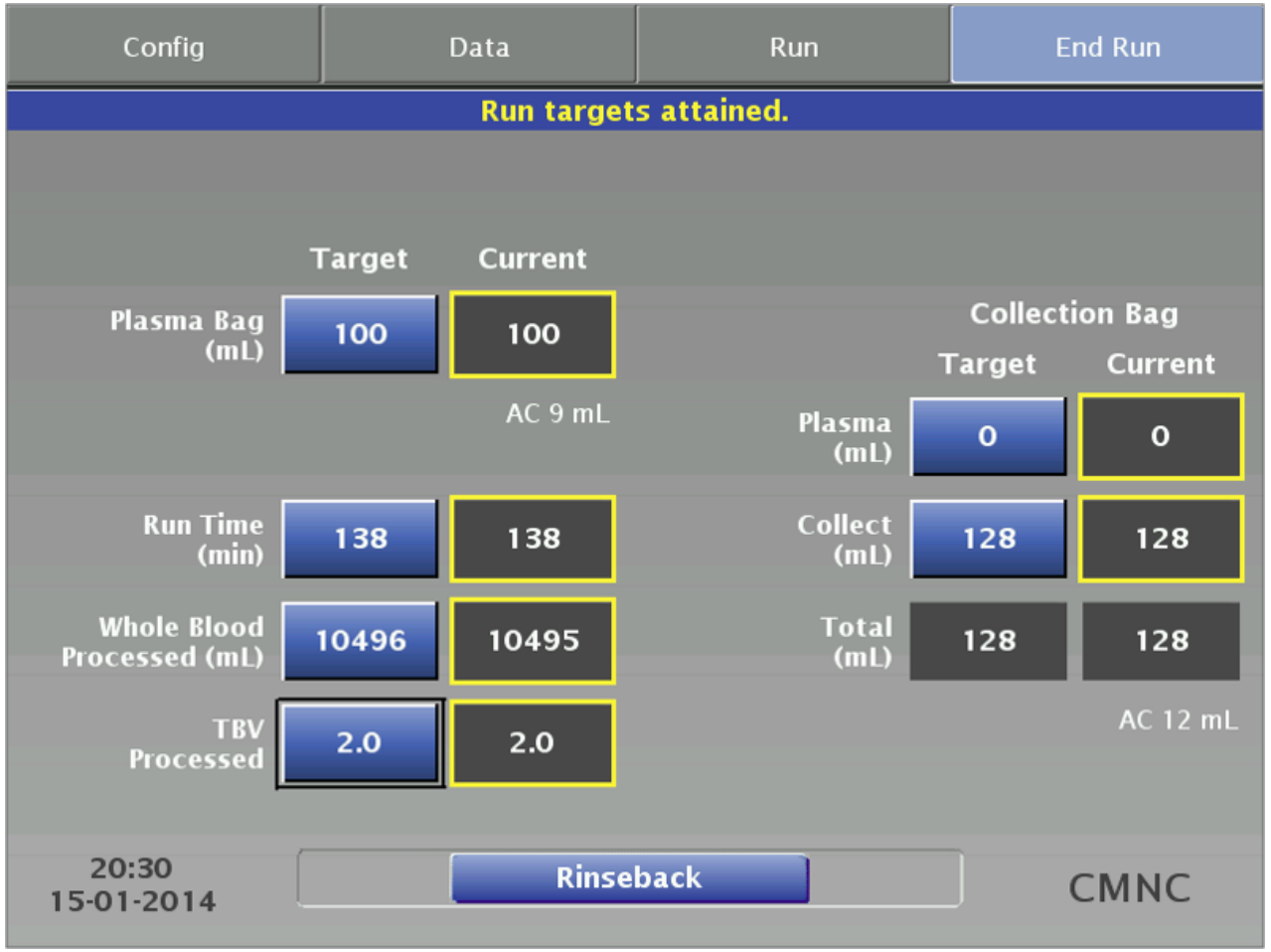


Questions?

Completing the Run

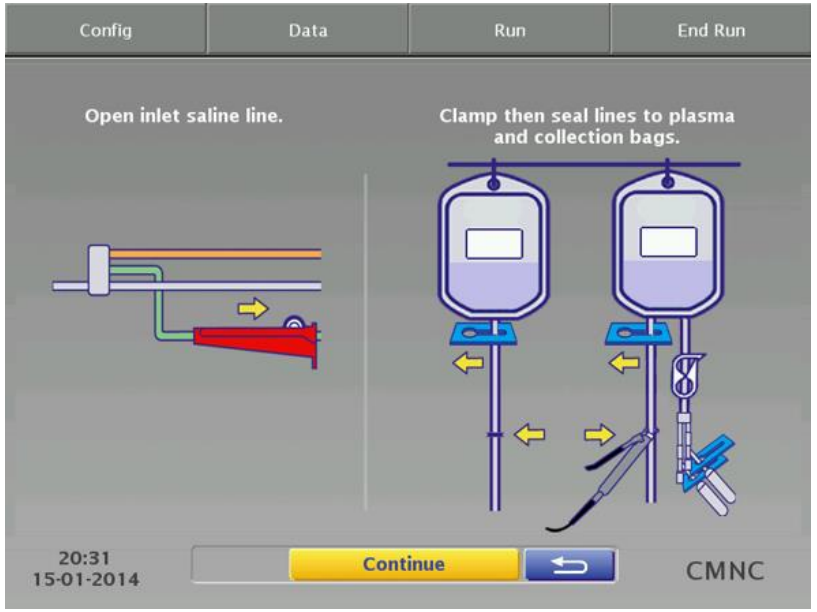
- Run Targets Attained
- Sealing the Product Bags
- Rinseback and Disconnect
- Procedure Summary

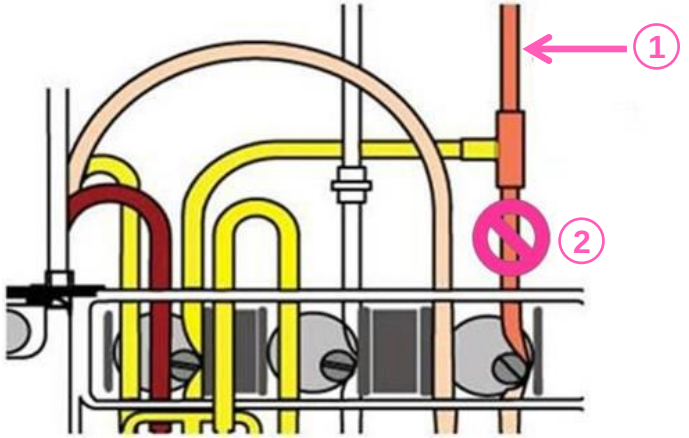
Run Targets Attained



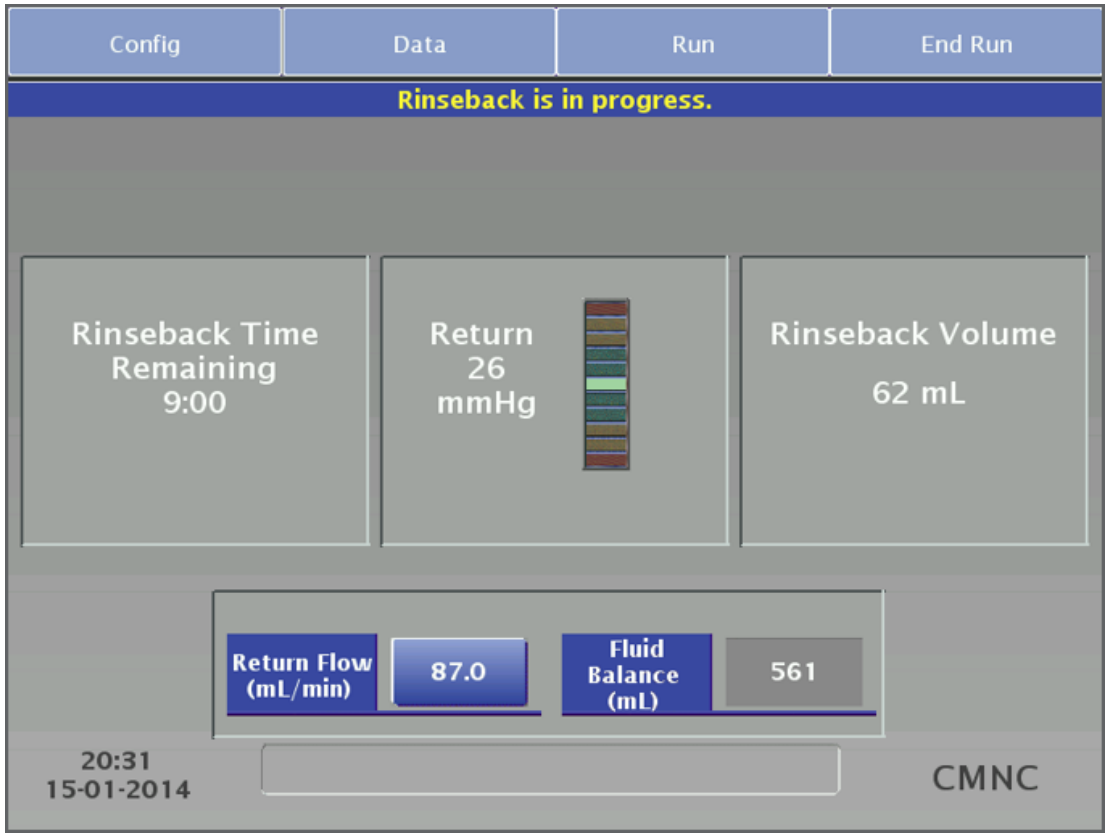
Sealing the Product Bags

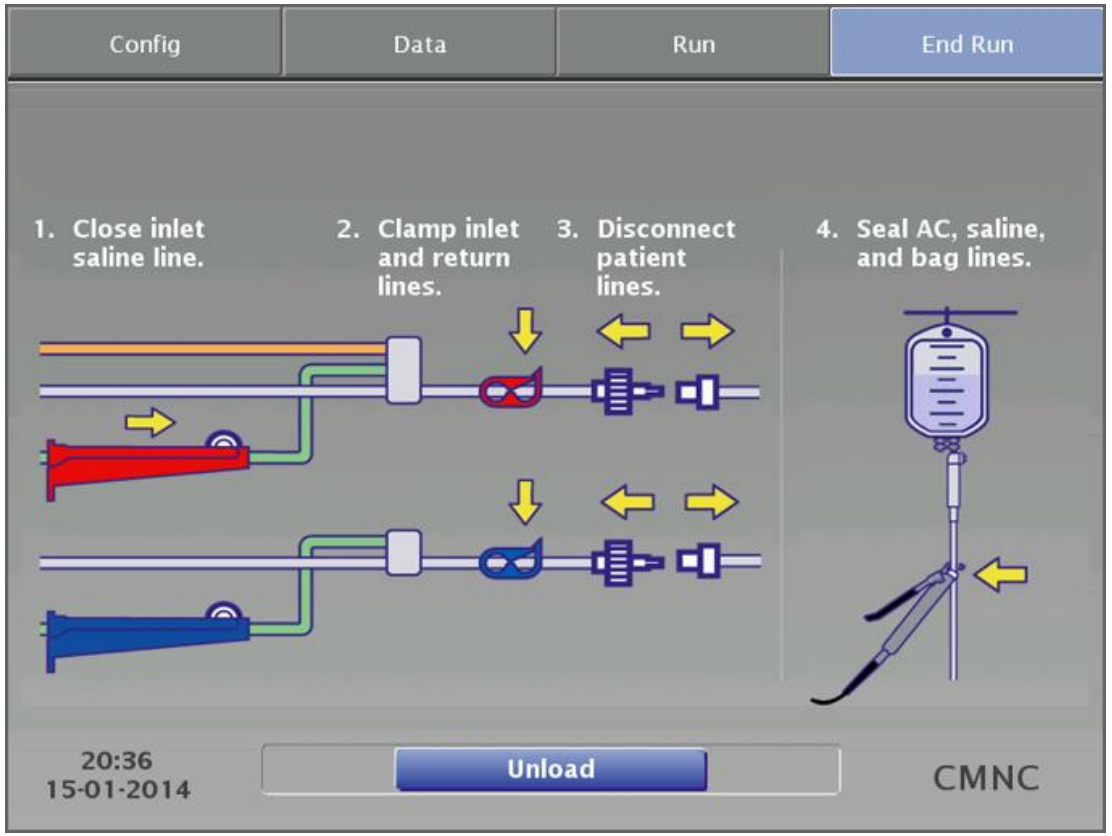
1. Seal the collect line above the T-shaped connector to the plasma line.
2. If you seal the collect line below the connector, the cells in the collection bag could flow back into the tubing set when the system raises the cassette.



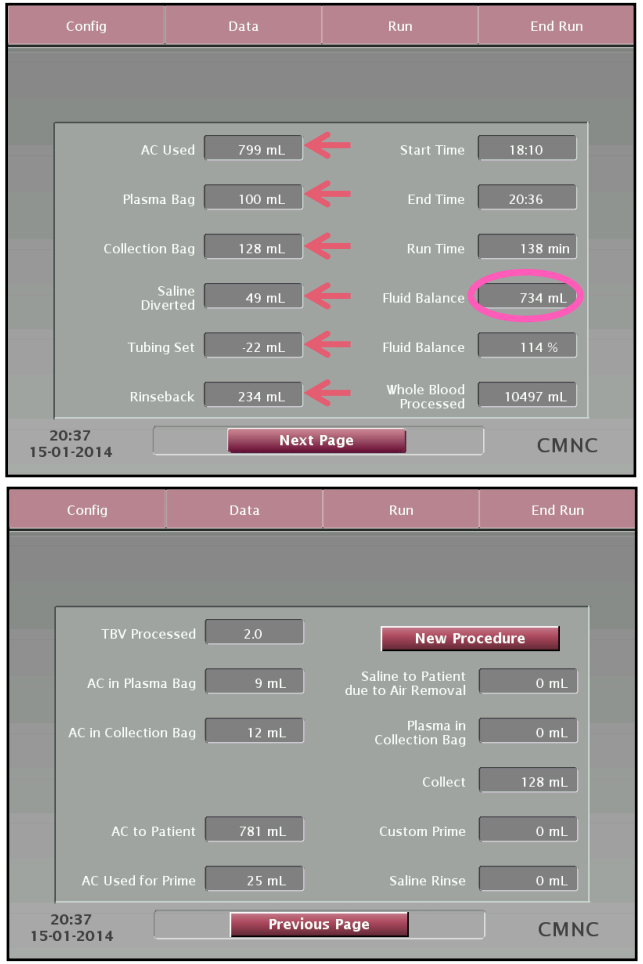


Rinseback and Disconnect





Procedure Summary



To understand the patient's fluid balance, use the values on the procedure summary screen:

+799 mL (AC Used)
–100 mL (Plasma Bag)
–128 mL (Collection Bag)
–49 mL (Saline Diverted)
–22 mL (Tubing Set)
+234 mL (Rinseback)
734 mL (Total)

Questions?

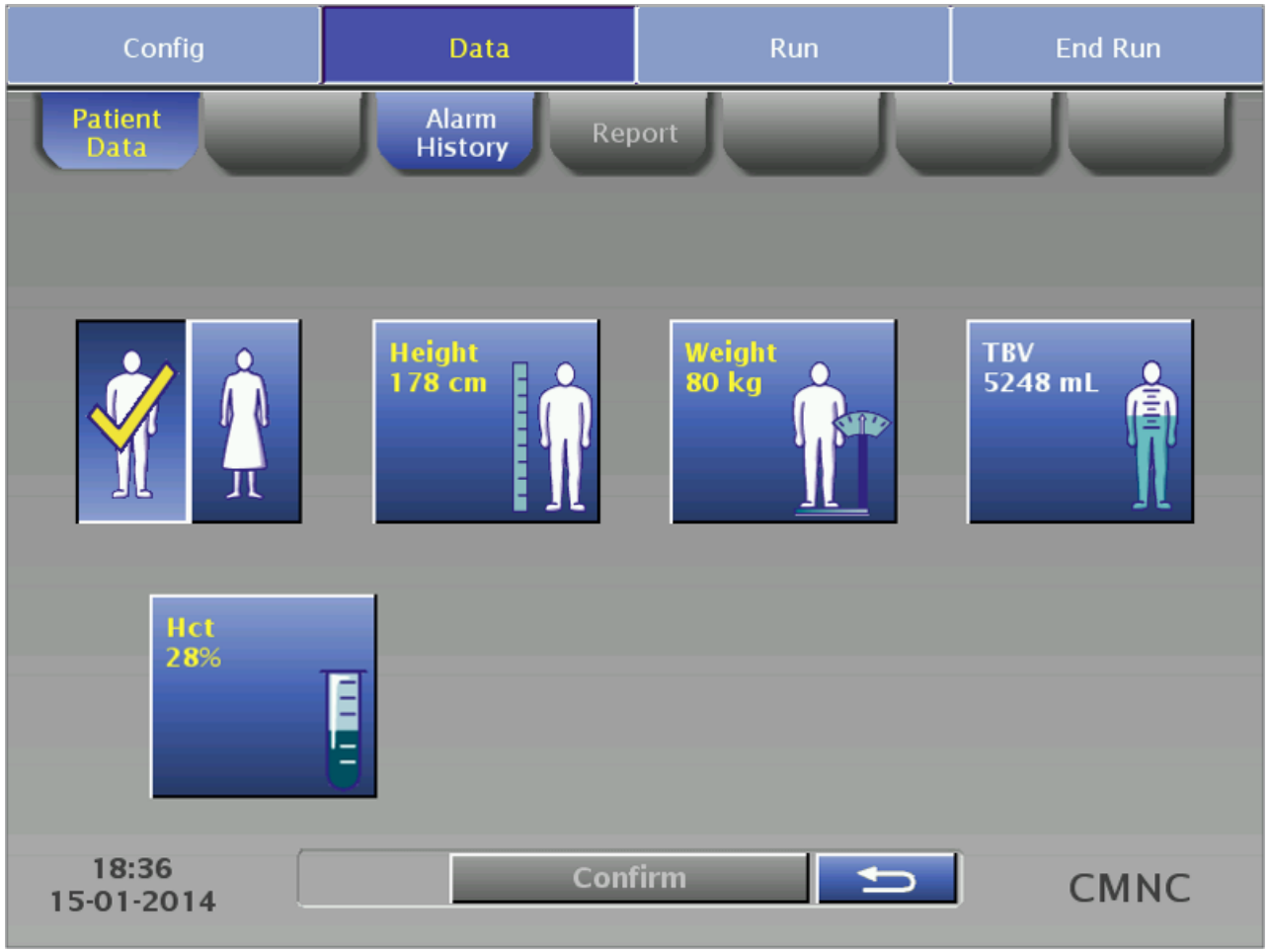
Making Changes

- Data Menu
- Run Menu
- End Run Menu

Data Menu

- Patient Data
- Alarm History
- Report

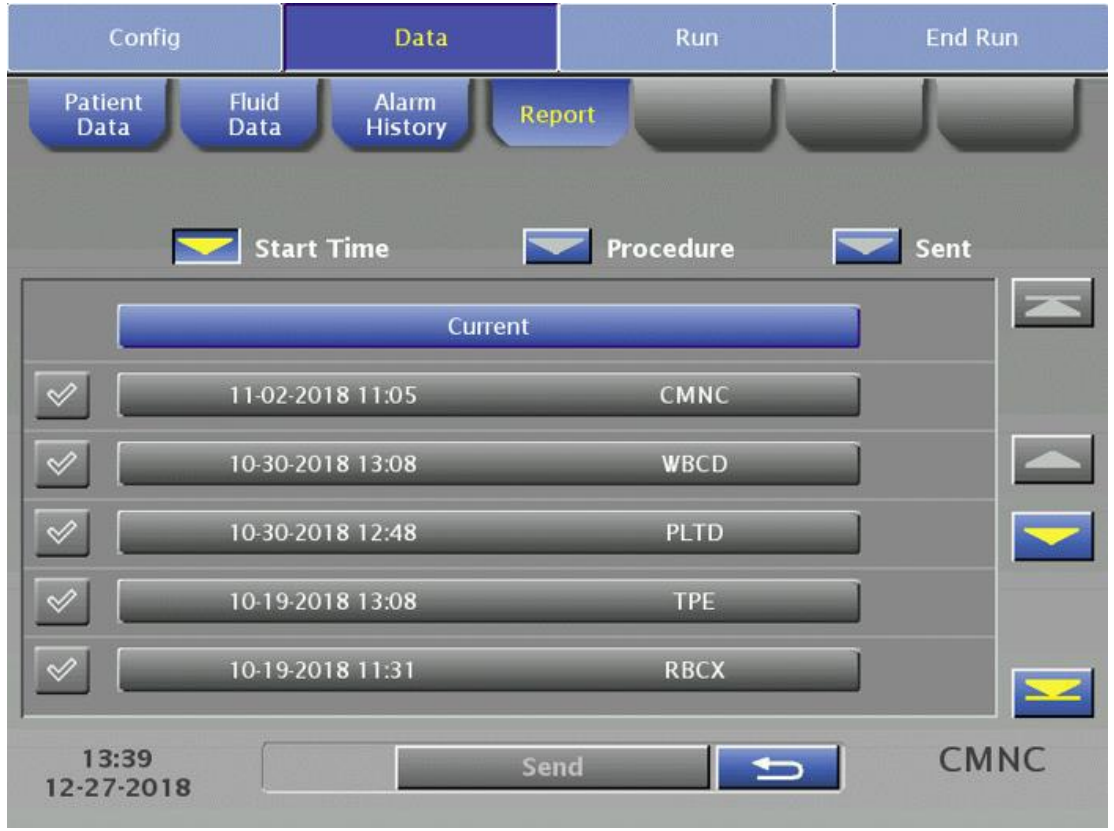
Patient Data



Alarm History

Report

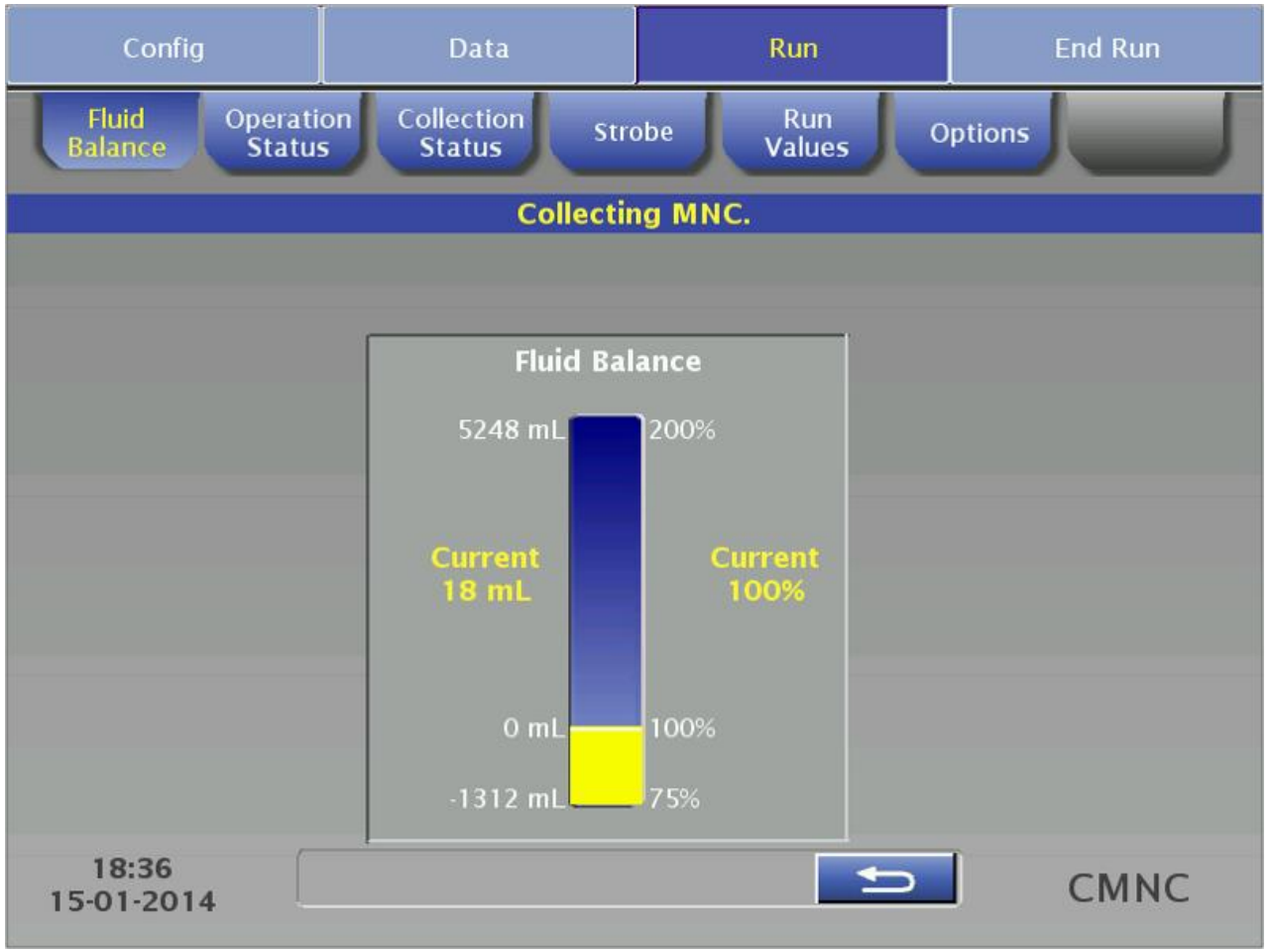
Config
Data
Run
End Run
Patient Data
Alarm History
Report
Start Time
Procedure
Sent
Current
06-19-2019 13:59 WBCD
06-19-2019 12:30 RBCX
06-18-2019 08:31 MNC
03-20-2019 14:05 MNC
03-20-2019 12:16 TPE
13:39
12-27-2018
Send
CMNC


Config
Data
Run
End Run
Patient Data
Fluid Data
Alarm History
Report
Start Time
Procedure
Sent
Current
11-02-2018 11:05 CMNC
10-30-2018 13:08 WBCD
10-30-2018 12:48 PLTD
10-19-2018 13:08 TPE
10-19-2018 11:31 RBCX
13:39
12-27-2018
Send
CMNC

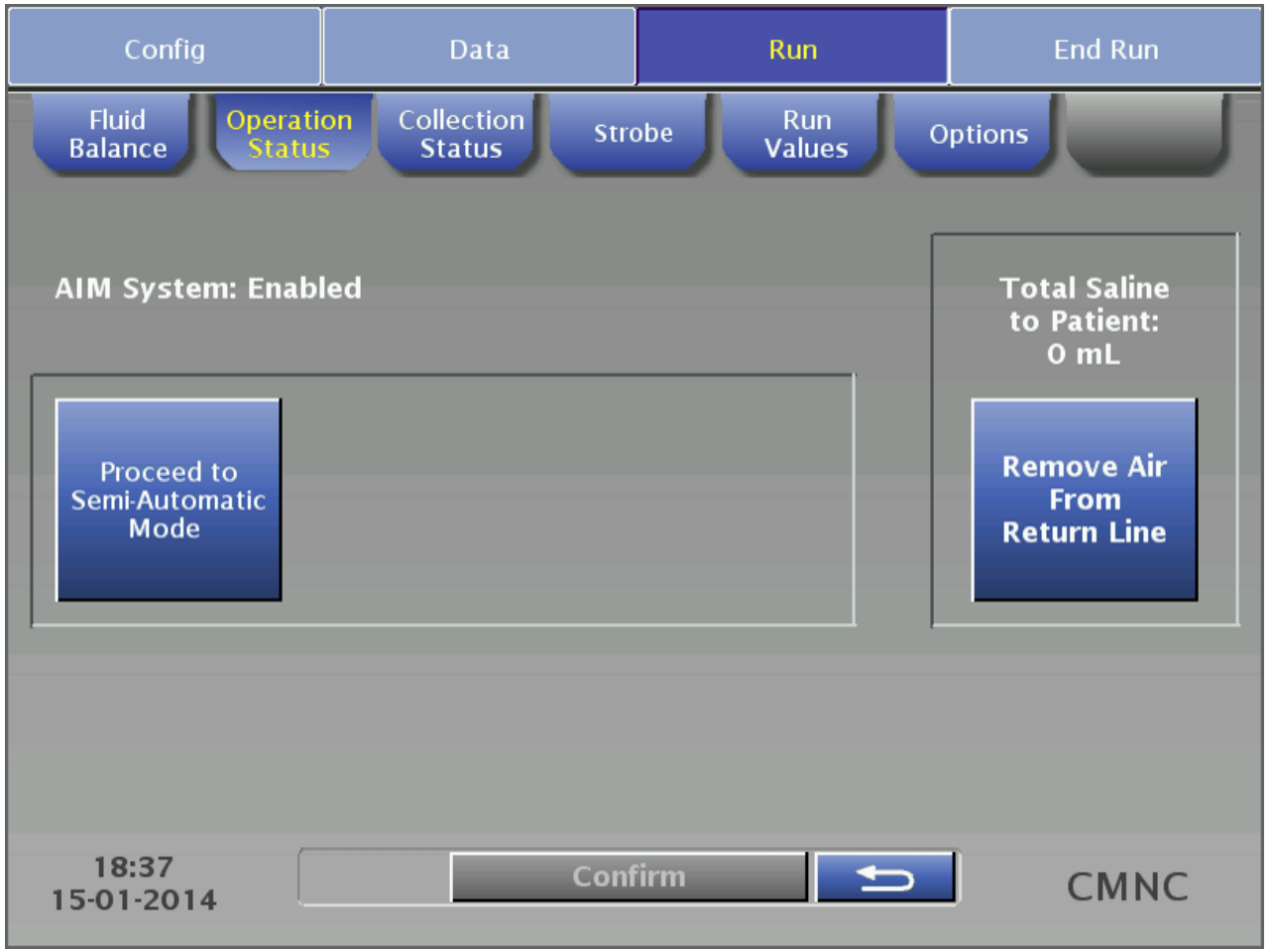
Run Menu

- Fluid Balance
- Operation Status
- Collection Status
- Strobe
- Run Values
- Options

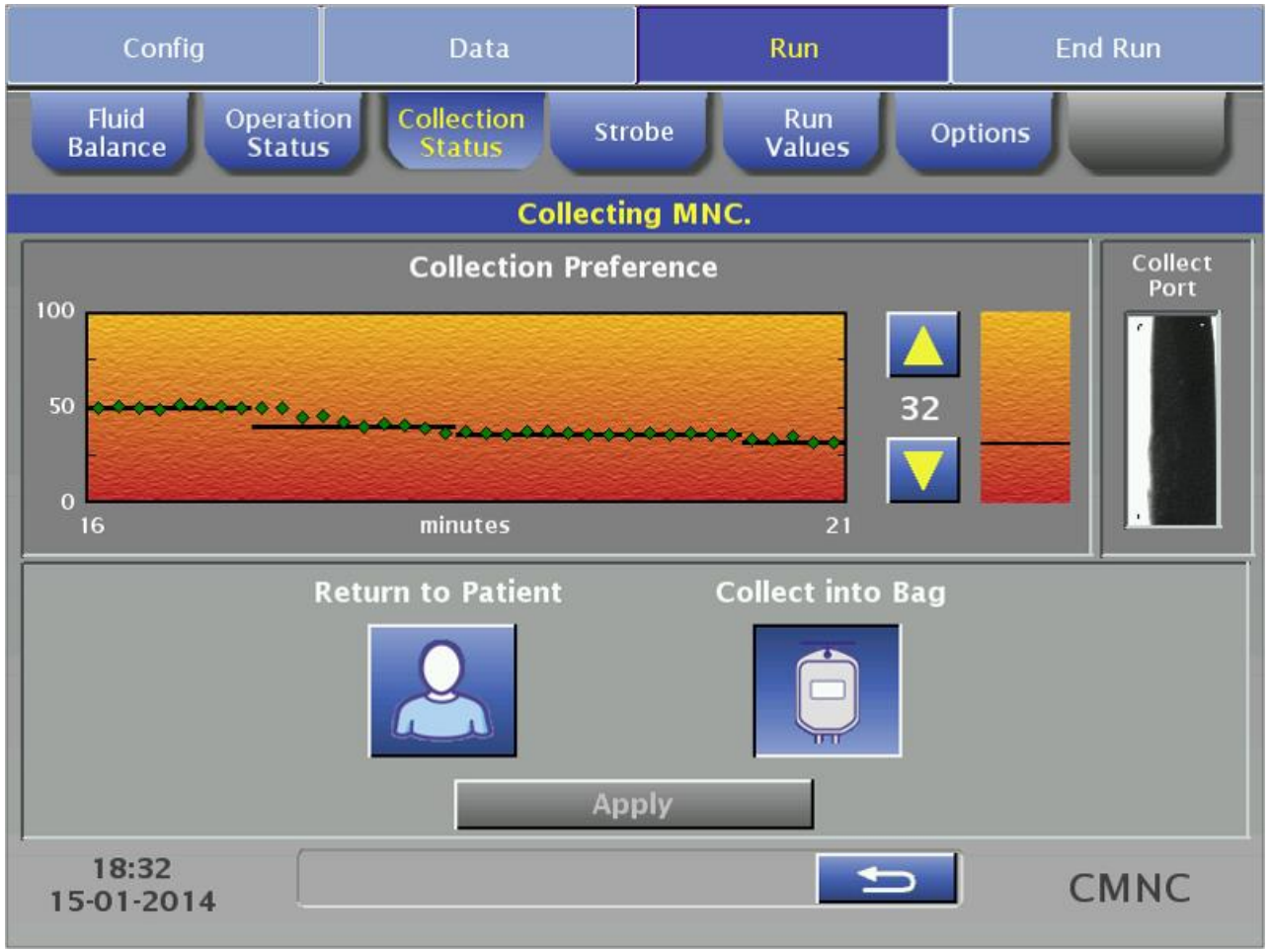
Fluid Balance



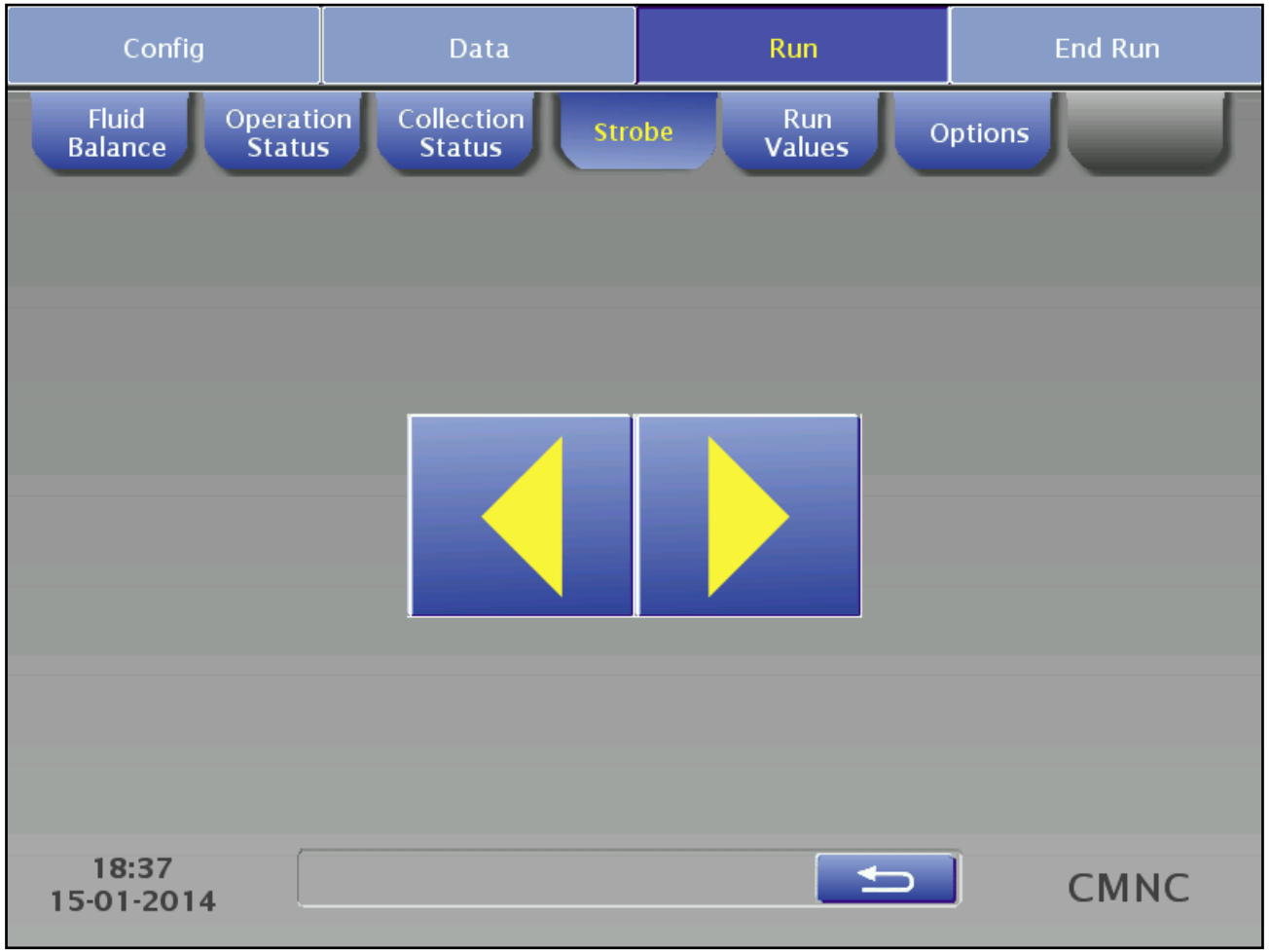
Operation Status



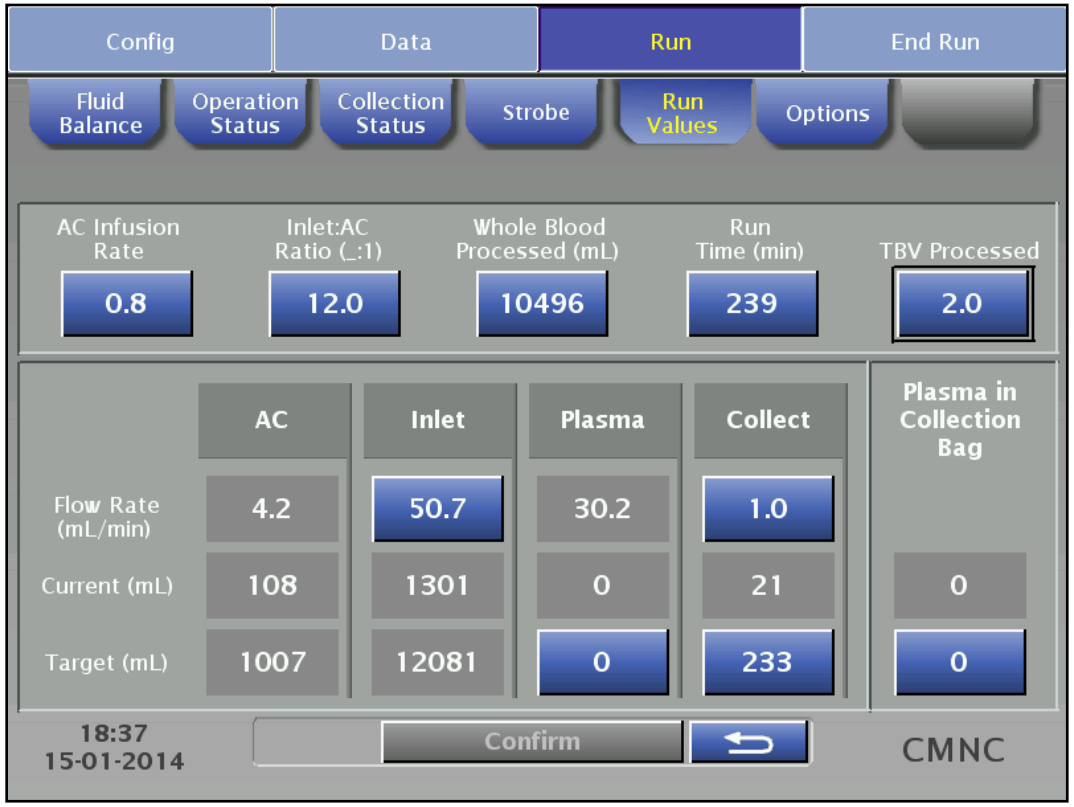
Collection Status

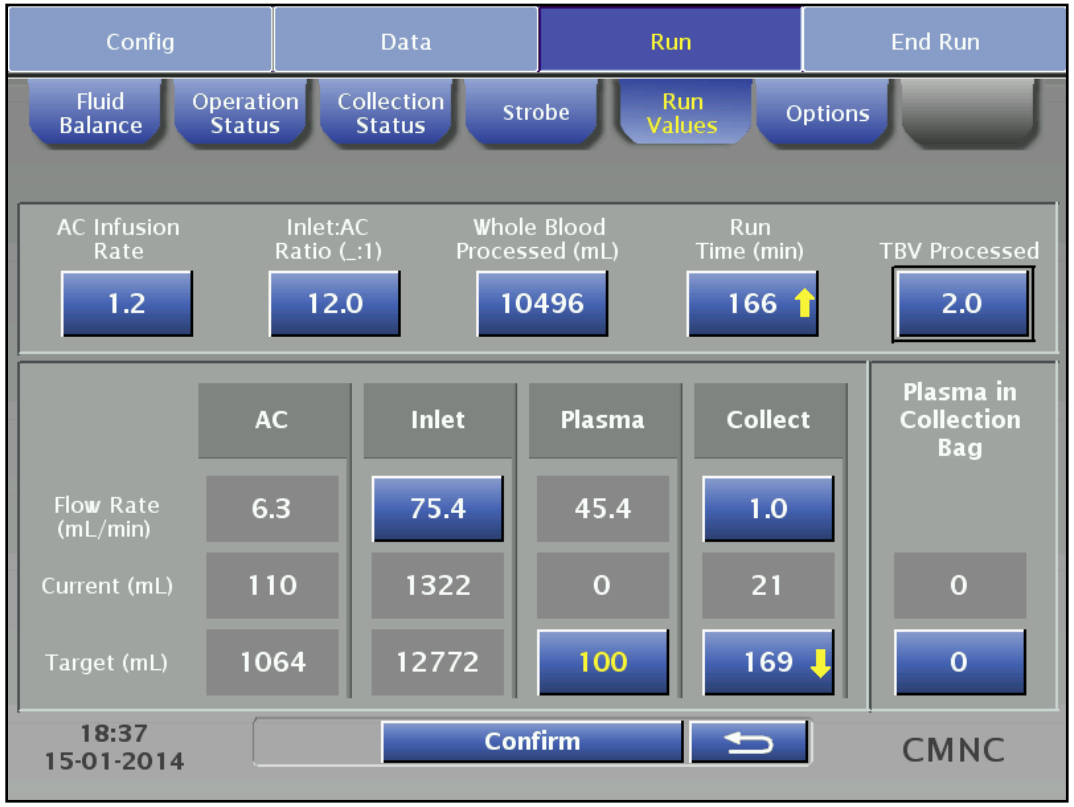


Strobe

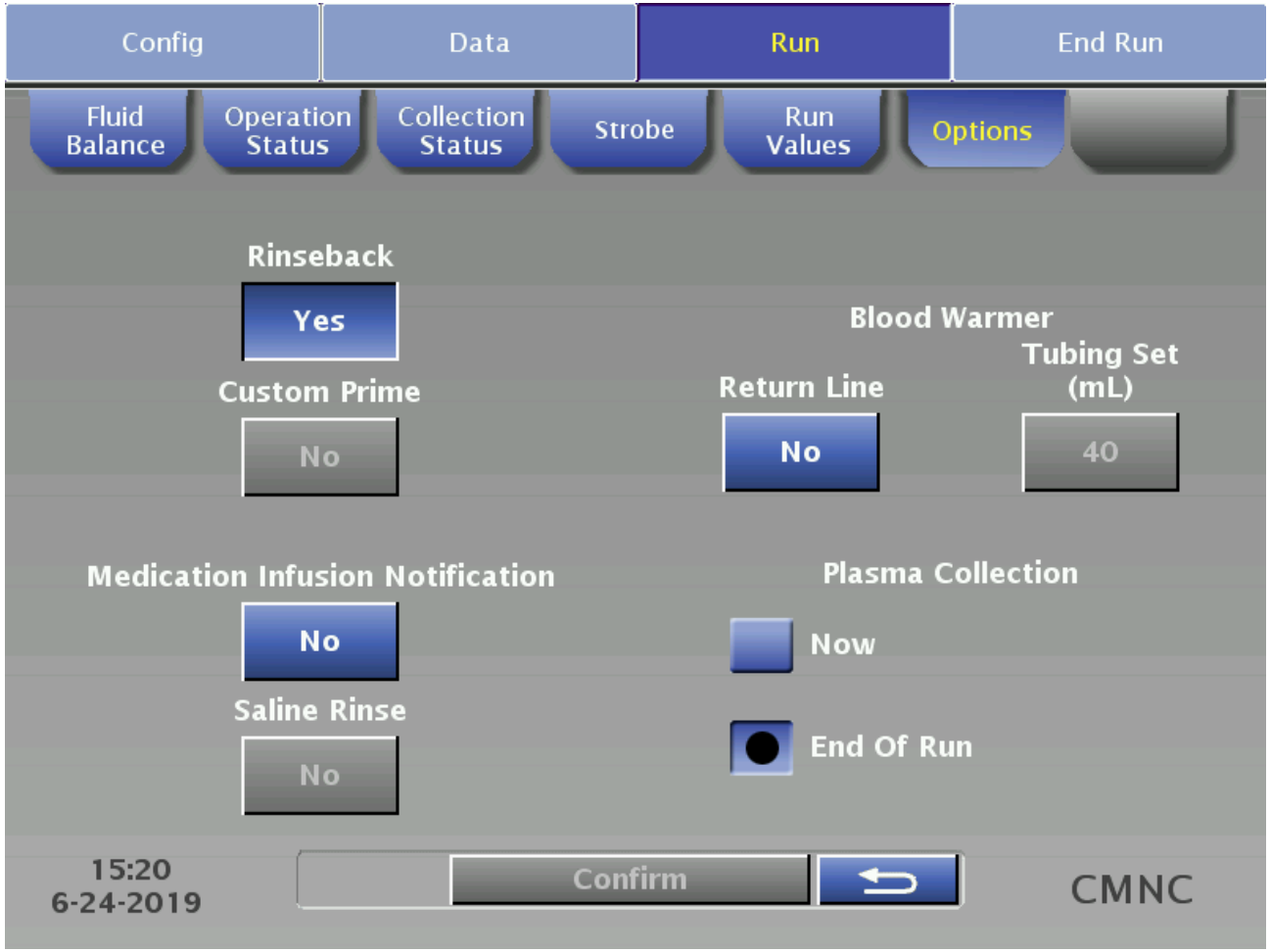

Config
Data
Run
End Run
Fluid Balance
Operation Status
Collection Status
Strobe
Run Values
Options
18:37
15-01-2014
CMNC

Run Values


Config
Data
Run
End Run
Fluid Balance
Operation Status
Collection Status
Strobe
Run Values
Options
AC Infusion Rate
0.8
Inlet:AC Ratio (_:1)
12.0
Whole Blood Processed (mL)
10496
Run Time (min)
239
TBV Processed
2.0
AC
Inlet
Plasma
Collect
Plasma in Collection Bag
Flow Rate (mL/min)
4.2
50.7
30.2
1.0
Current (mL)
108
1301
0
21
0
Target (mL)
1007
12081
0
233
0
18:37
15-01-2014
Confirm
CMNC


Config
Data
Run
End Run
Fluid Balance
Operation Status
Collection Status
Strobe
Run Values
Options
AC Infusion Rate
1.2
Inlet:AC Ratio (_:1)
12.0
Whole Blood Processed (mL)
10496
Run Time (min)
166
TBV Processed
2.0
AC
Inlet
Plasma
Collect
Plasma in Collection Bag
Flow Rate (mL/min)
6.3
75.4
45.4
1.0
Current (mL)
110
1322
0
21
0
Target (mL)
1064
12772
100
169
0
18:37
15-01-2014
Confirm
CMNC

Options


Config
Data
Run
End Run
Fluid Balance
Operation Status
Collection Status
Strobe
Run Values
Options
Rinseback
Yes
Custom Prime
No
Blood Warmer
Return Line
No
Tubing Set (mL)
40
Medication Infusion Notification
No
Saline Rinse
No
Plasma Collection
Now
End Of Run
15:20
6-24-2019
Confirm
CMNC

End Run Menu

- Rinseback
- Disconnect
- Run Targets

Rinseback, Disconnect, Run Targets

Questions?

Optimization

- Collection Preference
- Optimizing the Collection Preference
- Product Purity Versus Yield
- Inlet Pump Flow Rate
- Setting the Run Target
- Collecting Plasma
- Decreasing the Run Time

Collection Preference

CP controls the concentration of cells flowing through the collect port.

1. Low CP (less light can pass through):

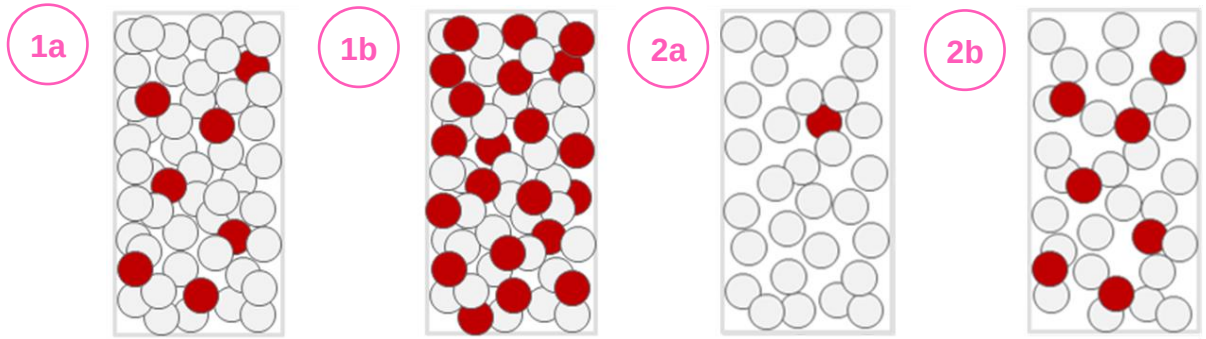
   high concentration of cells

   a. Patient with high MNC
   b. Patient with low MNC

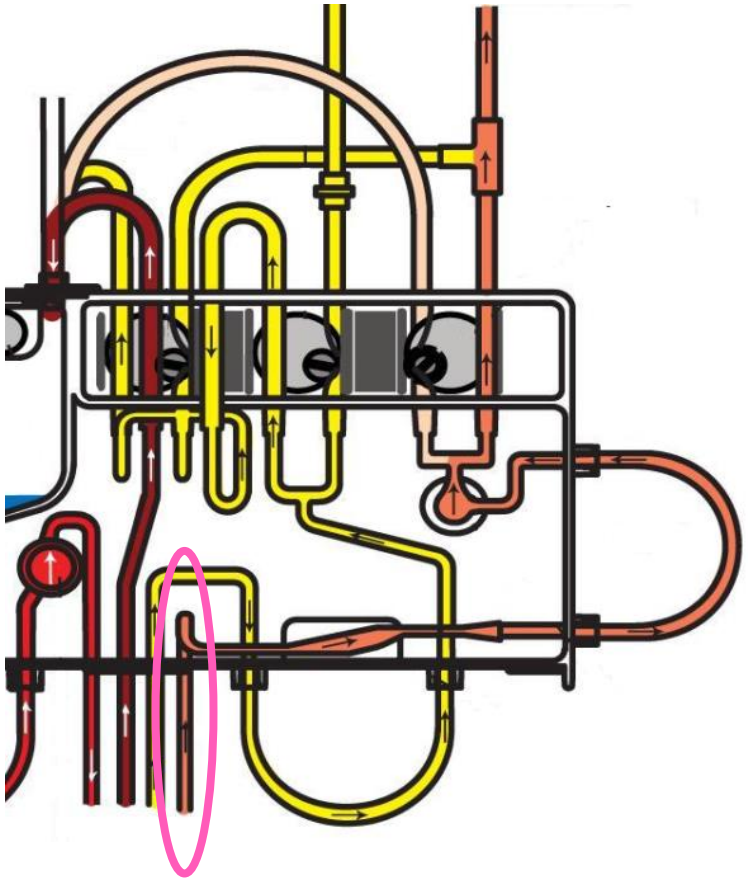
2. High CP (more light can pass through):

   low concentration of cells

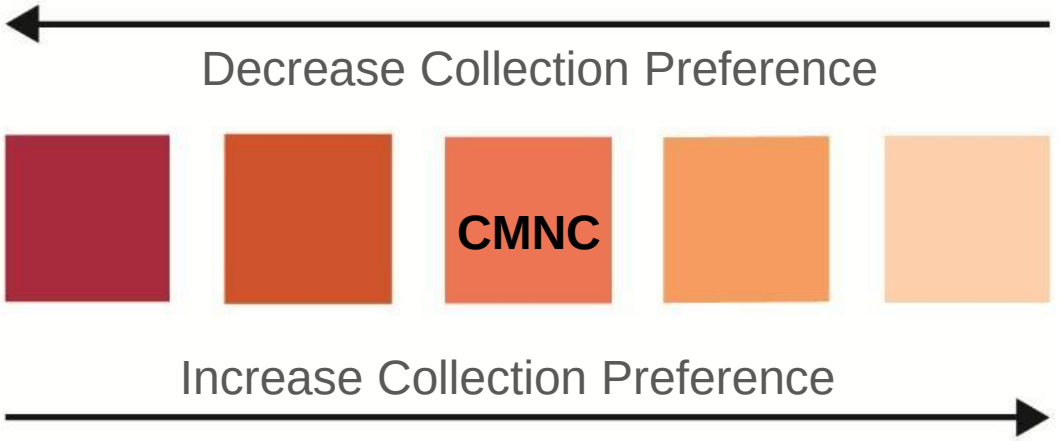
   a. Patient with high MNC
   b. Patient with low MNC



Optimizing the Collection Preference



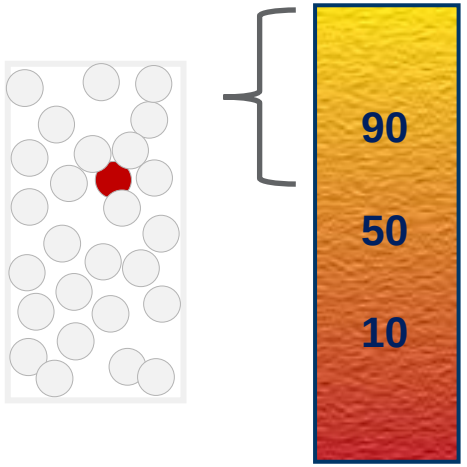
- Periodically monitor the color in the collect line below the cassette.
- Change the CP to maintain the optimal color.



Product Purity Versus Yield

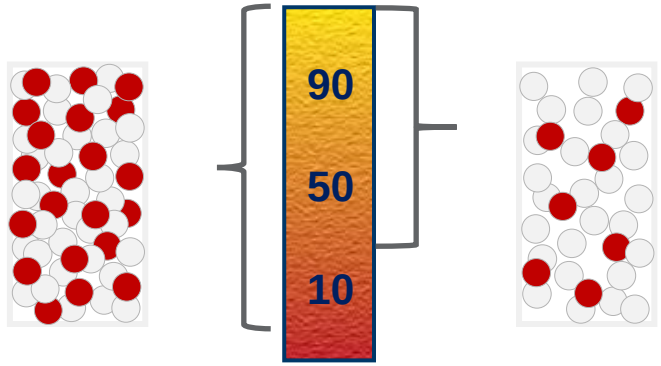
Purity

- Start with a CP ≥50
- Example:
  - ABO-mismatch donor
  - Extracorporeal photochemotherapy



Yield

- Start with a CP ≤50
- Example:
  - Patients with low MNC counts or non-mobilized donors
  - Donor lymphocyte infusion (donor cell counts are also low or normal)

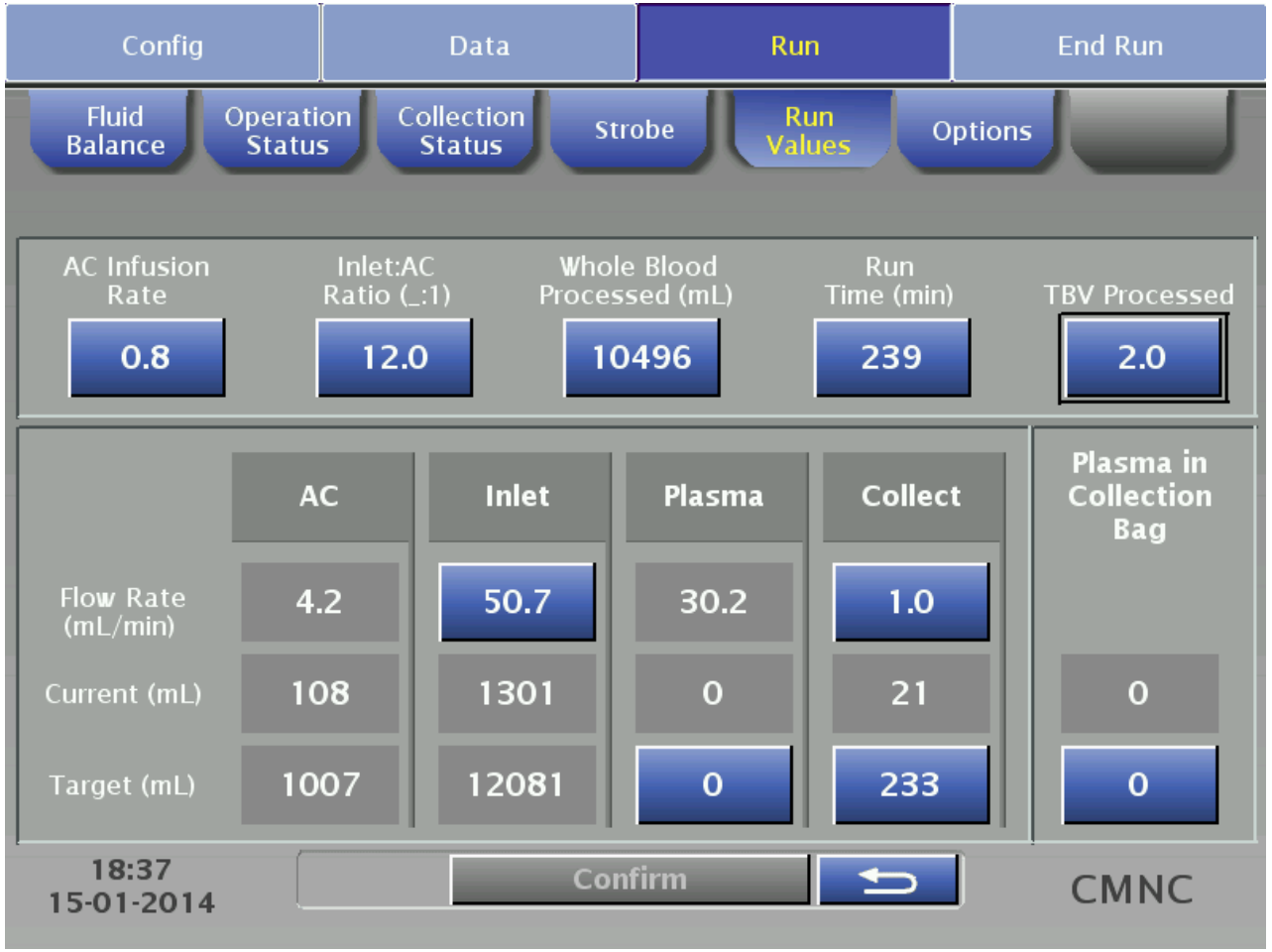


Inlet Pump Flow Rate

Maintaining a steady inlet flow rate allows for a more stable interface position and optimal collection of cells.

- Minimizes the occurrence of pressure alarms.
- Optimizes establishment of the interface and separation of the buffy coat.

Setting the Run Target



Primary Targets:

- Whole Blood Processed
- Run Time
- TBV Processed
- Collect Volume

Secondary Target:

- Plasma Collection

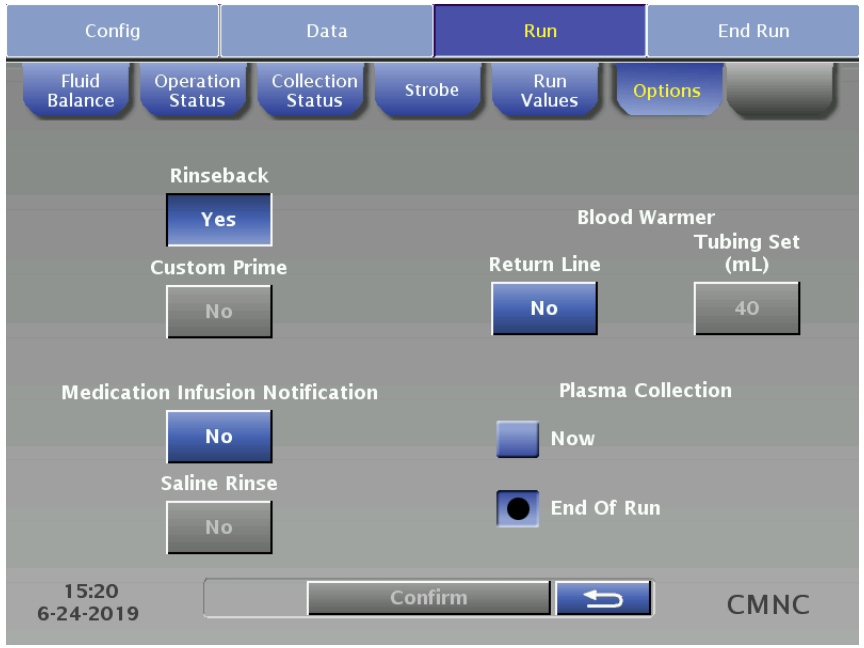
Collecting Plasma

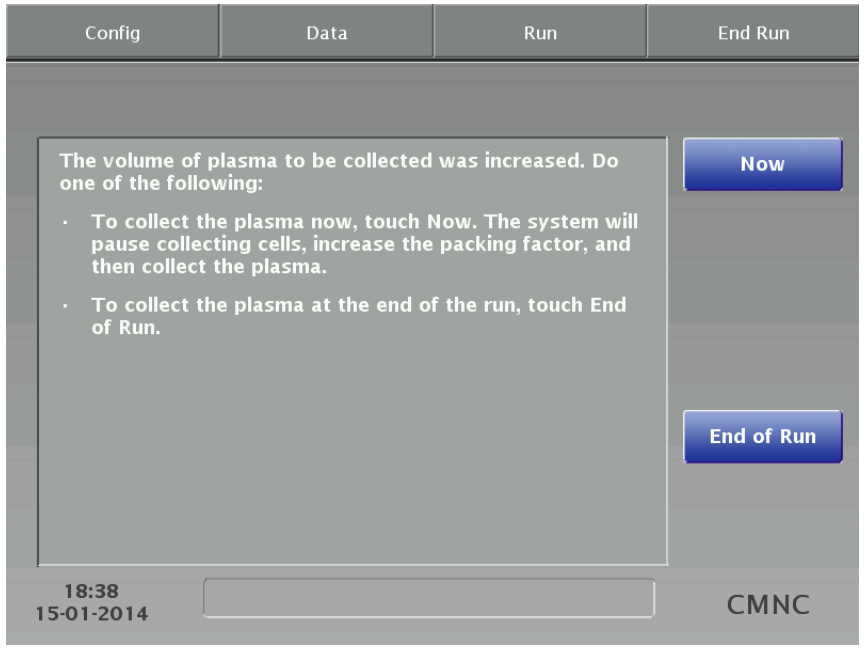
Plasma is collected at a high packing factor. Once plasma collection has been initiated:

- The collect pump stops and the centrifuge speed increases.
- If necessary, the inlet flow rate decreases to 60 mL/min.
- Plasma pump decreases to lower the interface.
- Plasma pump increases.
- Plasma valve moves to collect position.

Collecting Plasma

- Beginning of Run
- End of Run
- Now





Decreasing the Run Time

- Increase the inlet flow rate.
  - This increases the AC infusion rate.
- Increase the AC infusion rate.
  - This increases the inlet flow rate.
- Increase the inlet: AC ratio.
  - This decreases anticoagulation in the extracorporeal circuit and therefore, increases the potential for clumping.
  - This increases the inlet pump flow rate without increasing the AC infusion rate.
- Decrease the target run time.

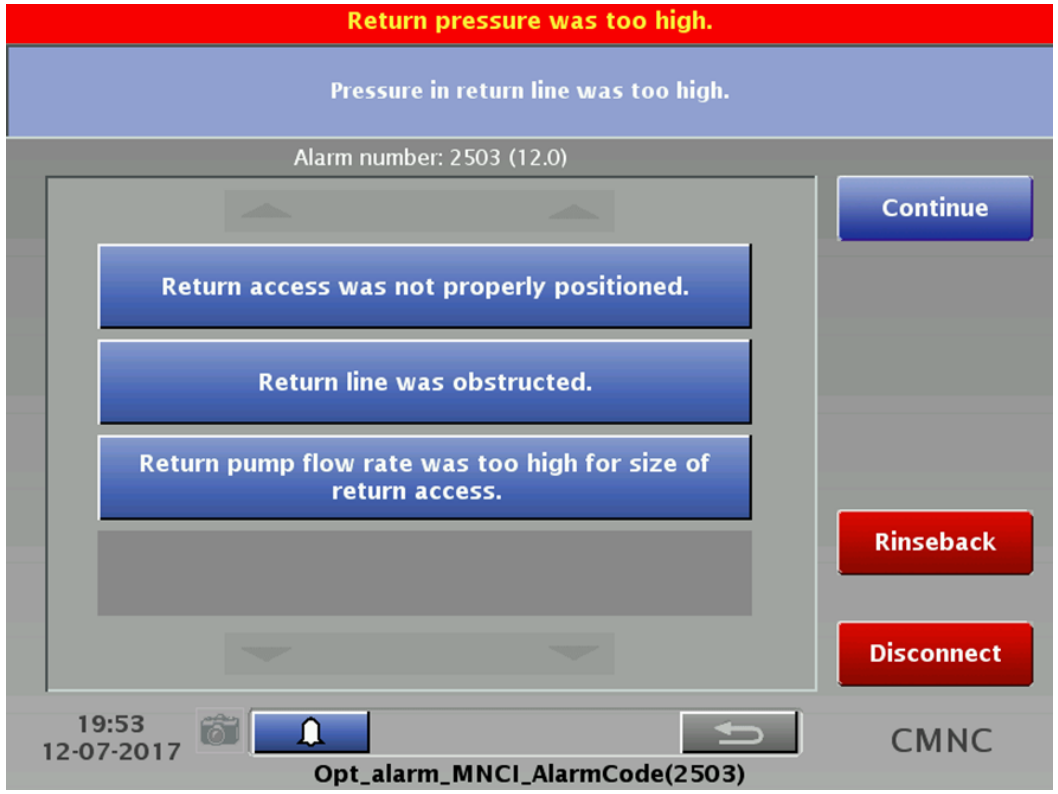
Questions?

Troubleshooting

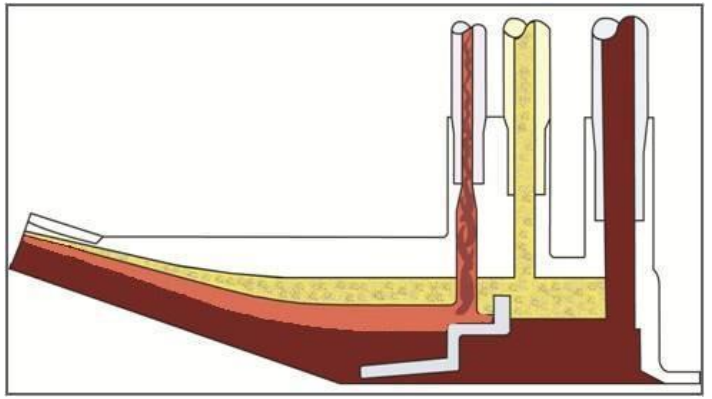
- Alarm Screen
- Inlet and Return Access Alarms
- Accumulation of a Buffy Coat
- Contents in Collect Line Look Too Light
- Contents in Collect Line Look Too Dark
- Clumping in the Collect Port

Alarm Screen

Inlet and Return Access Alarms

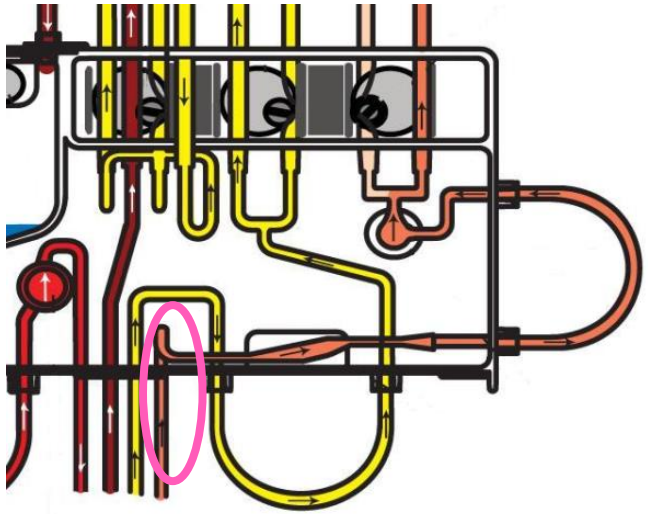


Accumulation of a Buffy Coat



Collect pump flow rate is too slow.	**Increase the collect pump flow rate.**
CP is too high.	**Decrease the CP.**

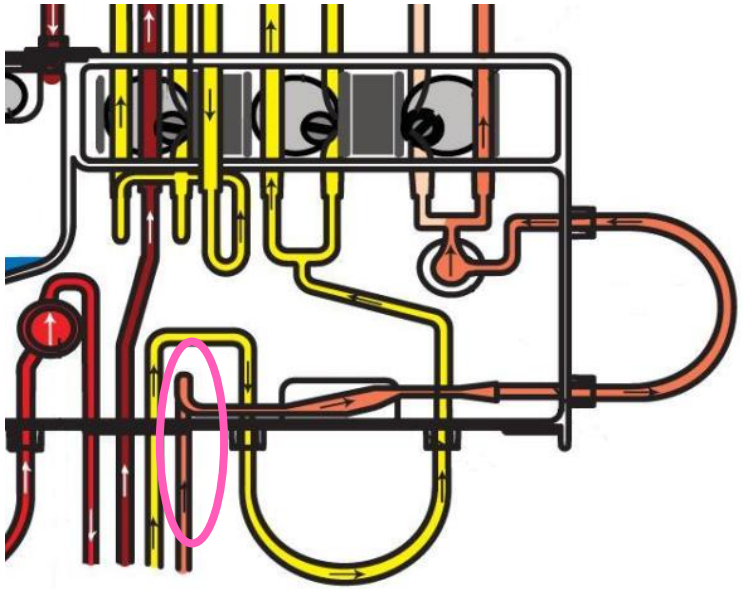
Contents in Collect Line Look Too Light



Contents of the collect line look too light during the run.

CP is too high.	**Decrease the CP to darken the contents.**
Collect pump flow rate is too slow.	**Reset collect pump flow rate to the default value.**

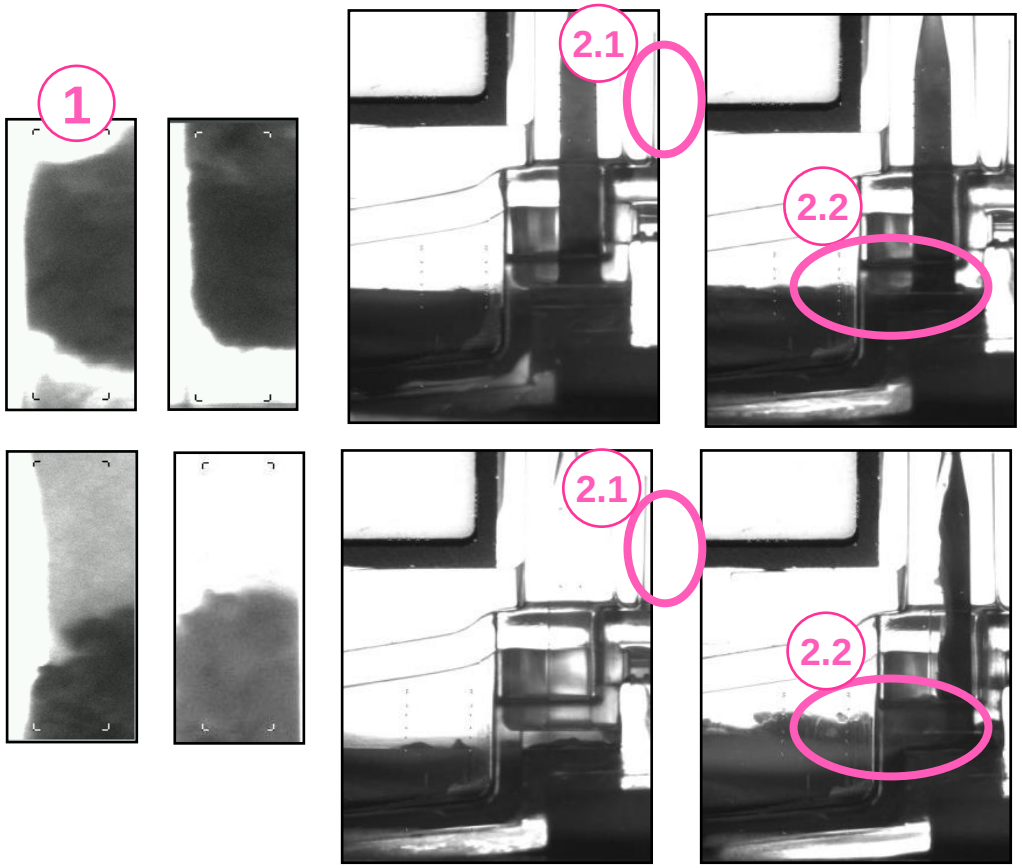
Contents in Collect Line Look Too Dark



Contents of the collect line look too dark.

CP is low.	→	**Increase the CP.**

Clumping in the Collect Port



1. Collect port image alternates between dark and light.
2. Viewport
   (2.1) Collect port
   (2.2) Interface

Inadequate anticoagulation.

Decrease inlet:AC ratio to 8:1.ase the CP.

Low TBV Patients

- Minimum Data Entry Limits
- AC Management
- Fluid Balance
- Custom Prime – RBC
- Custom Prime – RBC (60%)

Minimum Data Entry Limits

- Patient data
  - Height: 12 inches or 30 cm
  - Weight: 5 lbs or 2 kg
  - TBV: 300 mL (The system will not calculate the TBV for weight <25 kg)
- Inlet pump flow rate
  - 5 mL/min

AC Management

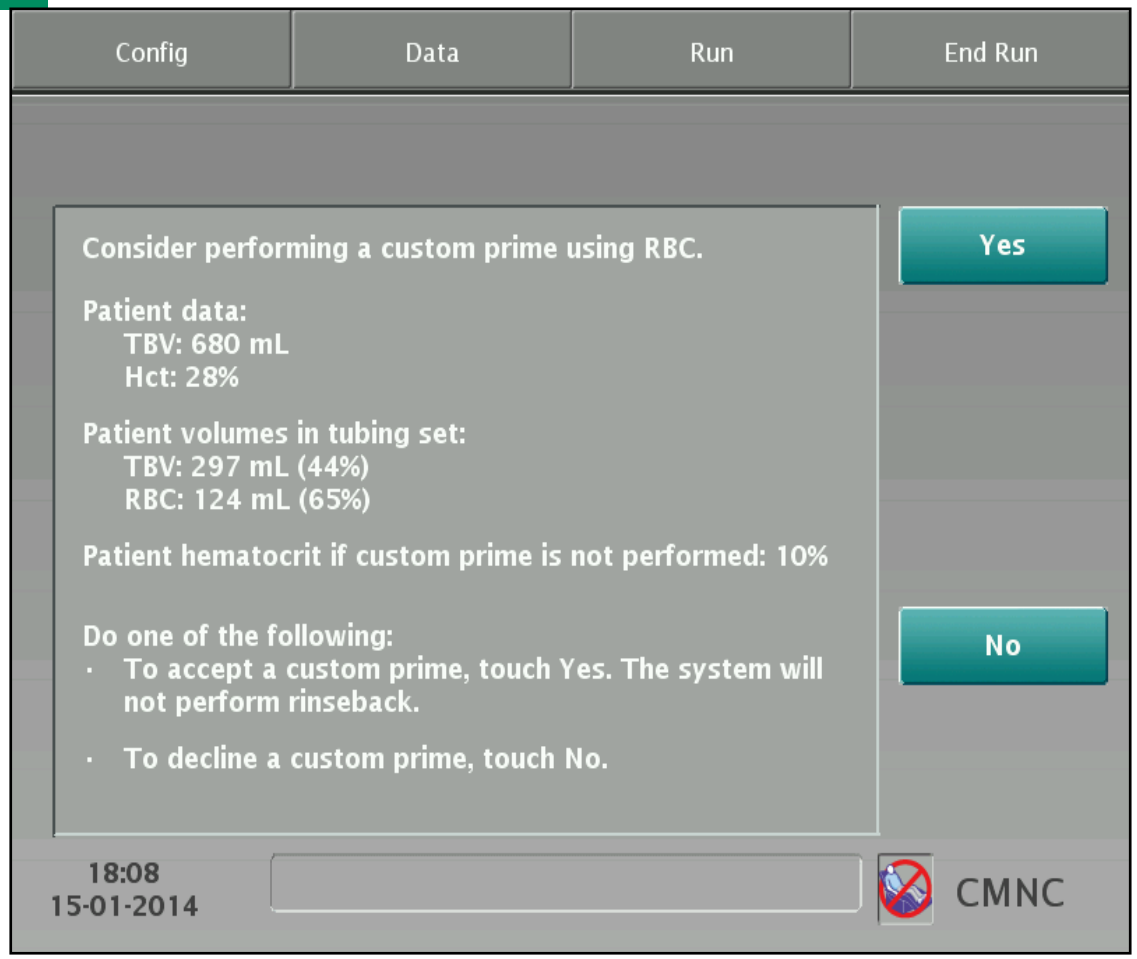
- AC infusion rate
  - The AC infusion rate may need to be increased to achieve an inlet pump flow rate ≥5 mL/min.
- Inlet:AC ratio
  - The Inlet:AC ratio needs to be kept at a value that maintains proper anticoagulation.

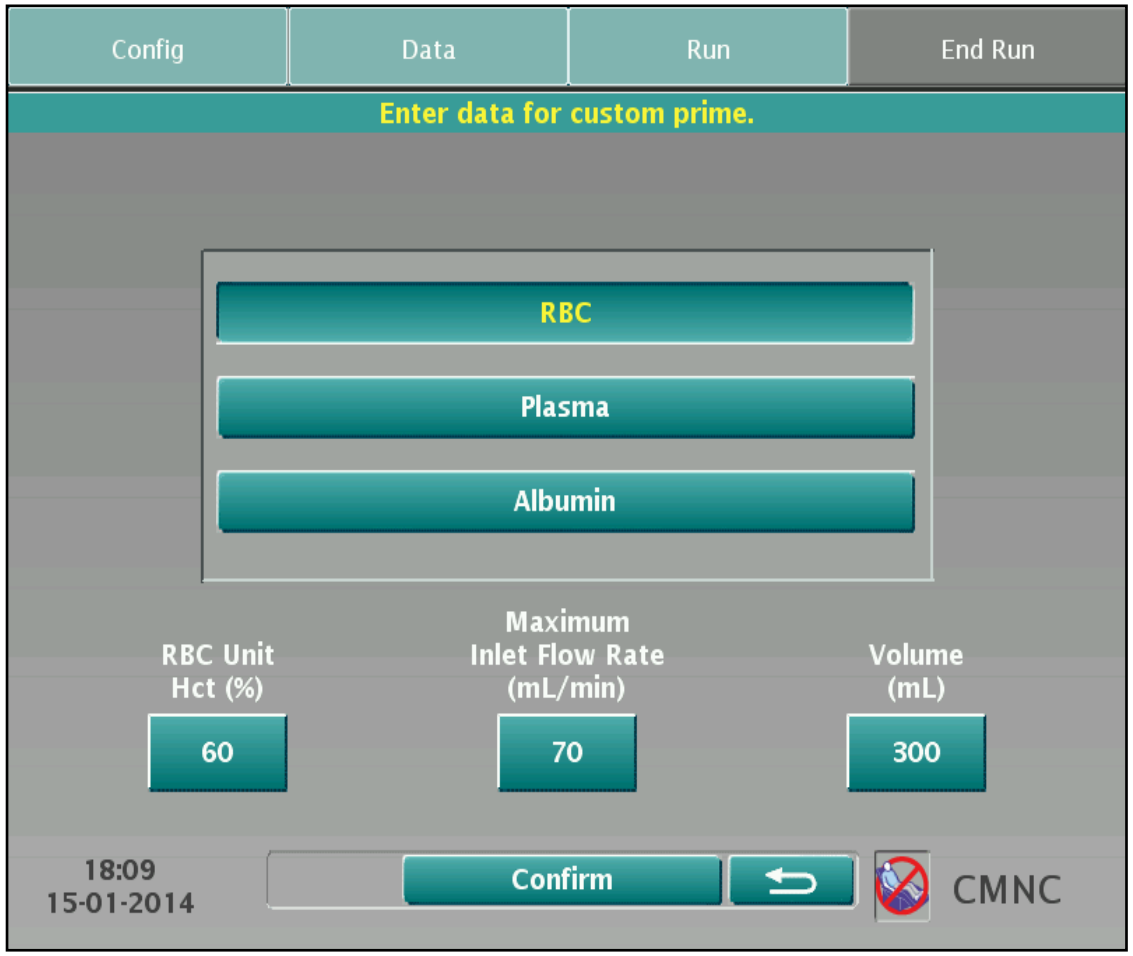
Pt TBV	500	600	700	800	900	1000
Initial inlet pump flow rate	5.4	6.3	7.4	8.4	9.5	10.5
Configured AC infusion rate 0.8 mL/min/L TBV						
If you Increase AC infusion rate	1.8	1.5	1.3	1.1	1.0	1.2
Inlet pump flow rate	10.5	10.5	10.7	10.3	10.5	14.0
Configured inlet:AC ratio 12:1						
If you Increase Inlet:AC ratio	23:1	19:1	17:1	15:1	13:1	15:1
Inlet pump flow rate	10.1	10.0	10.4	10.5	10.3	13.2

Fluid Balance

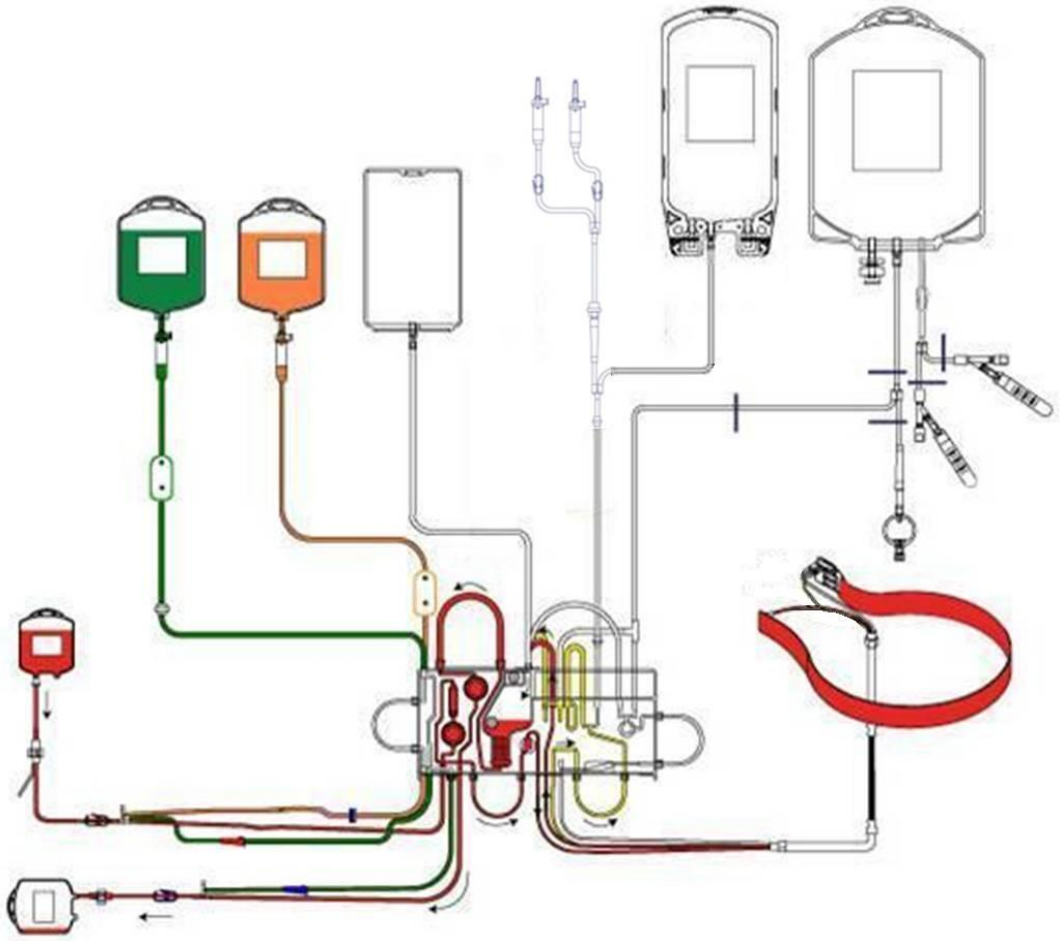
- Managing fluid in and fluid out
  - Volume of AC to the patient versus volume collected
  - Collect pump flow rate
- Blood warmer
  - Patient comfort
- Custom prime
  - Improved tolerance of the volume of the extracorporeal circuit

Custom Prime – RBC





Custom Prime – RBC



Custom Prime – RBC (60% Hct)

This table indicates the calculated estimate of the change in the patient's Hct immediately after the custom prime RBC have been delivered to the patient. This is not an indication of the patient's post procedure Hct since it cannot predict the patient's hemodynamic response to the procedure.

Patient		300 mL RBC	No blood prime	340 mL RBC	No blood prime
		No blood warmer		40 mL blood warmer	
TBV	Hct (%)	Change in patient Hct (%)			
300 mL	25	+11	-22	+13	-22
	30	+10	-26	+12	-26
	35	+9	-27	+10	-28
	40	+8	-28	+9	-29
600 mL	25	+6	-14	+8	-14
	30	+5	-14	+7	-15
	35	+5	-15	+6	-16
	40	+4	-15	+5	-17
1000 mL	25	+4	-9	+5	-9
	30	+3	-9	+4	-10
	35	+3	-9	+4	-10
	40	+3	-10	+3	-11
1500 mL	25	+3	-6	+3	-6
	30	+2	-6	+3	-7
	35	+2	-6	+3	-7
	40	+2	-7	+2	-7

Questions?

Thank You

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