



# Curate<sup>®</sup> Cell Processing System

## Instructions for Use

### Curate System and Associated Products

Curate Cell Processing System – **REF** 455B-10030

Curate Deterministic Cell Separation™ (DCS) Cassette Kit – **REF** 450A-10024



Curate Biosciences, 2715 Loker Avenue West, Carlsbad, CA 92010

**Disclaimers**

The Curate Cell Processing System, and sample preparation protocols in this instruction for use (IFU) have been developed using normal donor apheresis mononuclear cell collections from Spectra Optia® that have been processed within 24 hrs with typical sample handling practices and storage at 2–8°C. Disease and other factors that are known to cause aberrant cell size and/or severe morphological differences and/or otherwise impact cell deformability may impact separation quality. Current programs on the Curate system are not optimized or validated for mobilized samples.

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# 1. NOTIFICATIONS, WARNINGS, AND PRECAUTIONS

## 1.1. SYMBOLS AND DEFINITIONS

Symbol	Meaning
	Biological hazard
	Caution/warning/important. Indicates that the user should pay special attention to the information to avoid personal injury, death, or damage to the equipment or product.
	Reference number
	Sterilized using ethylene oxide (Curate DCS cassette)
	Do not re-use; single use only

## 1.2. SAFETY PRACTICES

The Curate system is designed for safe use when correctly installed, operated by trained staff, and operated in accordance with the general safety practices and instructions in this document.

This document explains the correct operation of the Curate system, potential risks when operating the instrument and provides important safety information to minimize risks. Before using the system, operators should thoroughly familiarize themselves with it by reading this entire document. Follow the instructions carefully to protect yourself, others, and the equipment from potential hazards. Create a safe work environment. Use this instrument only as specified by the manufacturer to avoid damage to equipment and injury to personnel.

Always follow local working area safety instructions and laboratory policies as well as the standards for health, safety, and prevention of accidents. Contact the local authority governing electrical power supply, building constructions, maintenance, and safety for more information about the safe installation and operation of the instrument.



Depending on the biological material used, contamination or infection may lead to severe personal injury or death. If biohazardous material is or has been used, the operator must wear personal safety equipment as indicated in the warnings and precautions for the particular substance.



### WARNING!

Users should not service the Curate instrument themselves. Service should be performed only by trained experts authorized by Curate Biosciences. An improperly serviced instrument may lead to severe personal injury by exposure to mechanical hazards and the risk of electric shock.

Unplug the power cord before cleaning the instrument.

Do not allow fluids or objects to enter the interior of the instrument.

Always wear protective gloves and eyewear to protect against potential biohazard exposure.

Dispose of contaminated tissues and swabs according to their biological security level.

## 2. PRODUCT INFORMATION

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### 2.1. PRODUCT DESCRIPTION

The Curate system is an automated, closed fluidic management system that controls and monitors sample and fluid movement through the Curate Deterministic Cell Separation (DCS) cassette using a combination of peristaltic pumps, valves, gravimetric, bubble and pressure sensors. The system uses a proprietary software, running on an integrated touch screen enabled CPU using a long term support channel (LTSC) Microsoft® Windows IoT operating system. The system has 12 GB of solid state memory to hold records.

#### **Curate DCS Cassette**

The Curate DCS cassette is a single-use consumable, containing a massively parallel microfluidic array that contains over 3.5 million micro-posts, which are less than the width of a human hair, arranged to gently separate and wash cells according to their size.

#### **Curate Software**

The Curate software (version 1.06 or higher) is an integrated and easy-to-navigate software enabling users to process samples on the Curate system with minimal technical knowledge by using optimized pre-defined programs for standardized cell processing. Program customization will be available in future software versions.

#### **Curate Priming Reagent**

The Curate priming reagent is 10% of F-127, a non-lytic, non-ionic copolymer surfactant, in water. The Curate priming reagent is used to make the priming solution for system priming and is flushed from the cassette before sample processing.

#### **Curate QR Code Labels**

The Curate QR code labels are 1.5 inch x 1.5 inch square labels that are attached to all bags prior to loading into the instrument. These labels are an important part of the sample processing procedure because they assist in the correct sequence of instrument loading, help to mitigate human error, and enable run record traceability to the original sample ID.

#### **Curate Documentation**

Users and administrators should familiarize themselves with the Curate documentation before operating the Curate system. Please contact your Curate Sales Representative for additional copies, as needed.

Curate Documentation includes:

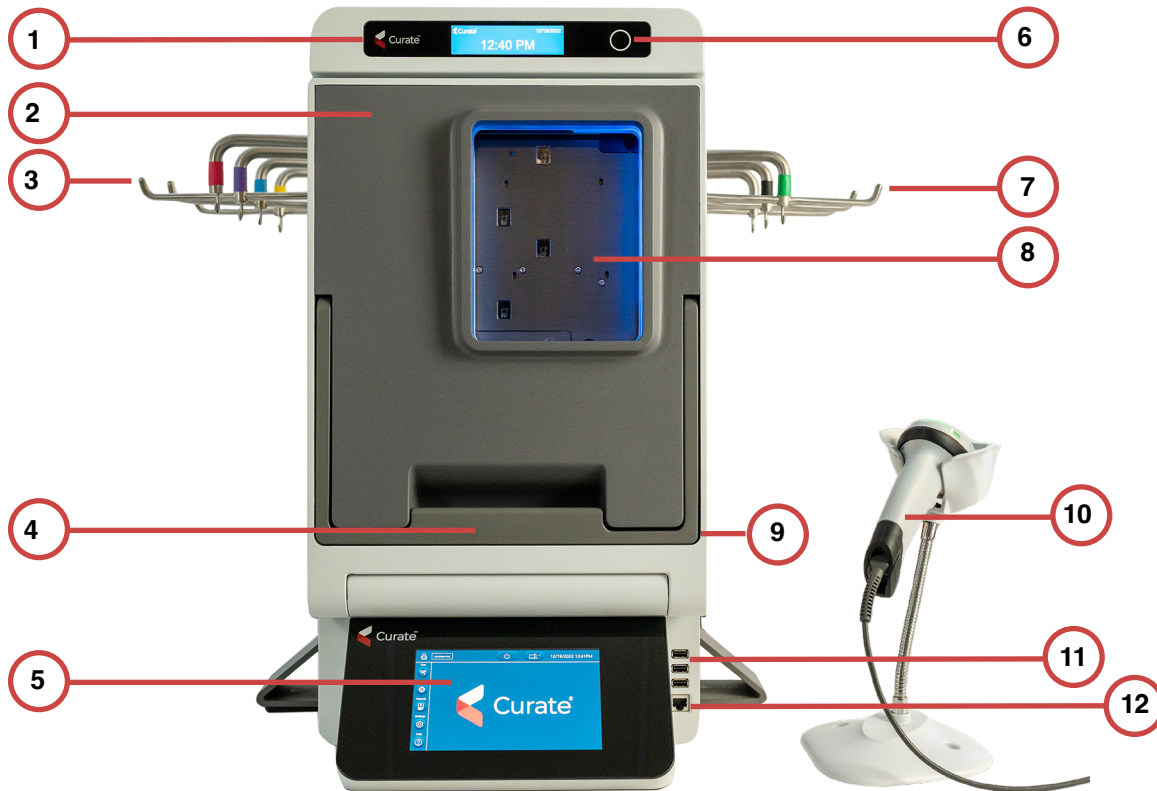
- **Instructions for Use:** This document contains information for administrators and users of the Curate system. Electronic or printed copies of this document should be made available to users during operation.
  - **User Quick Reference Guide:** The User Quick Reference Guide is intended for users who have already read the Instructions for Use and helps remind experienced users of the steps for processing a sample with the Curate system.
  - **Help:** User help screens are available from the Curate instrument touch screen. See “Help Screen” on page 37.
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## 2.2. SYSTEM OVERVIEW

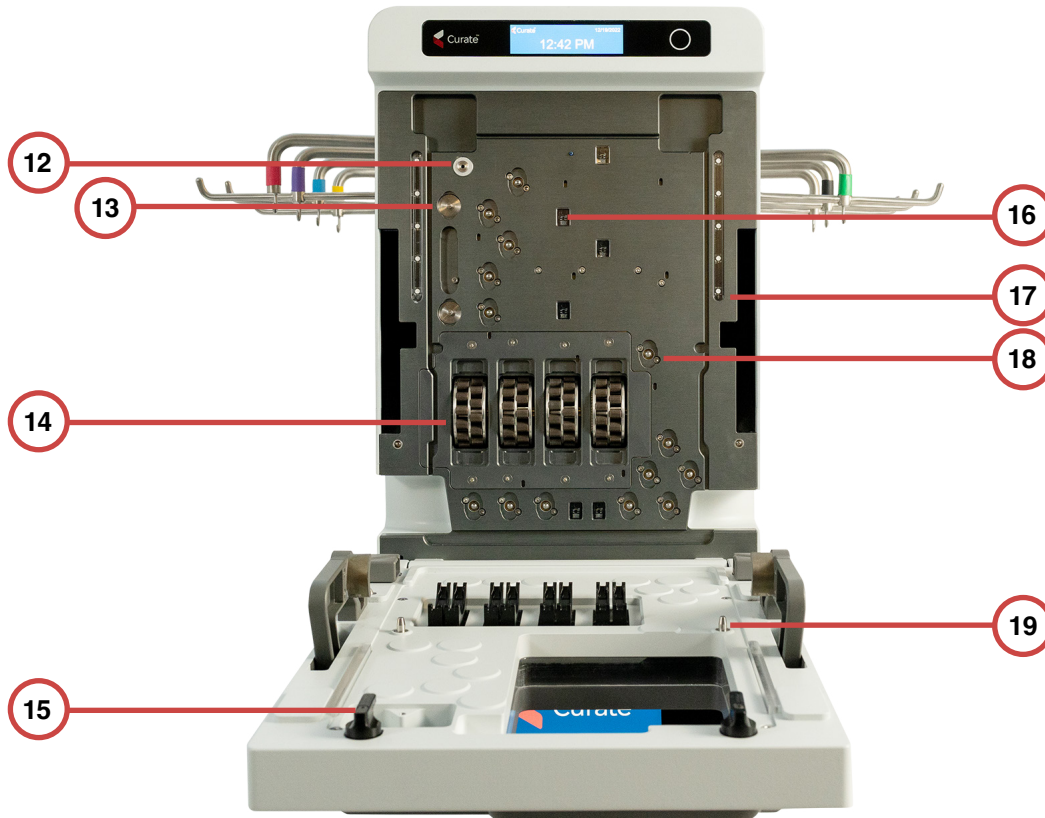
### 2.2.1 Instrument Components

Figure 1. Front view (door closed)



No.	Component	Description
1	Status screen	Displays user prompts, run status, and errors during operation.
2	Door (closed)	Door closed and no cassette loaded. Opened when loading cassette.
3	Bag hangers (left)	Priming solution, buffer, diluent, and sample bag hangers with gravimetric mass sensors.
4	Latching handle	Pull out and lift up to unlatch door.
5	Touch screen	Primary software-user interface for instrument operation.
6	Status screen button	Status screen touch button to advance or confirm prompts.
7	Bag hangers (right)	Waste and product bag hangers with gravimetric mass sensors.
8	Inspection window	Cassette inspection window
9	Emergency stop button	(On side) Stops the system.
10	Bar code scanner	Used to scan bag and cassette bar code labels during instrument loading.
11	USB ports	USB connectivity for peripheral connections, including bar code scanner, and administrator use.
12	CAT6 Ethernet port	Service connector

Figure 2. Front view (door open)



No.	Component	Description
12	De-gasser	Removes dissolved gases and prevents bubble formation.
13	Pressure sensors	Two pressure sensors for monitoring run operations.
14	Peristaltic pumps	Four independently controlled pumps.
15	Cassette locking clips	Two black locking clips for holding the cassette in place.
16	Bubble sensors	Six bubble sensors for air vs fluid detection.
17	Indicator lights	LED colors and patterns indicate operational status. See "Indicator Lights" on page 111.
18	Valves	14 valves control fluid movement through the DCS cassette.
19	Cassette placement pins	Two pins align with cassette to ensure proper placement.

Figure 3. Rear view



No.	Component	Description
20	Vent	For internal ventilation, to exhaust excess heat
21	USB ports	USB connectivity for peripheral connections, including bar code scanner, and administrator use.
22	CAT6 Ethernet port	Service connector
23	Power switch	On/Off Power switch
24	Power cord inlet	120 VAC connects to the power entry module

Figure 4. Top view. Hangers with color coding and numbered in order of the bag loading sequence

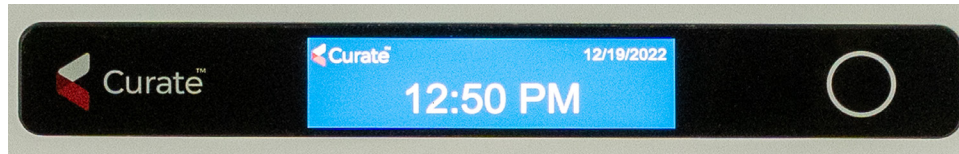


No.	Component	Description	Indicator Band(s)
1	Hanger 1	Priming solution hanger	Yellow
2	Hanger 2	Buffer bag hanger	Blue
3	Hanger 3	Diluent bag hanger	Purple
4	Hanger 4	Sample bag hanger	Red
5	Hanger 5	Secondary waste bag hanger (Reserved for future functionality)	Black Black
6	Hanger 6	Primary waste bag hanger	Black
7	Hanger 7	Product bag hanger	Green

## 2.2.2 Top Panel

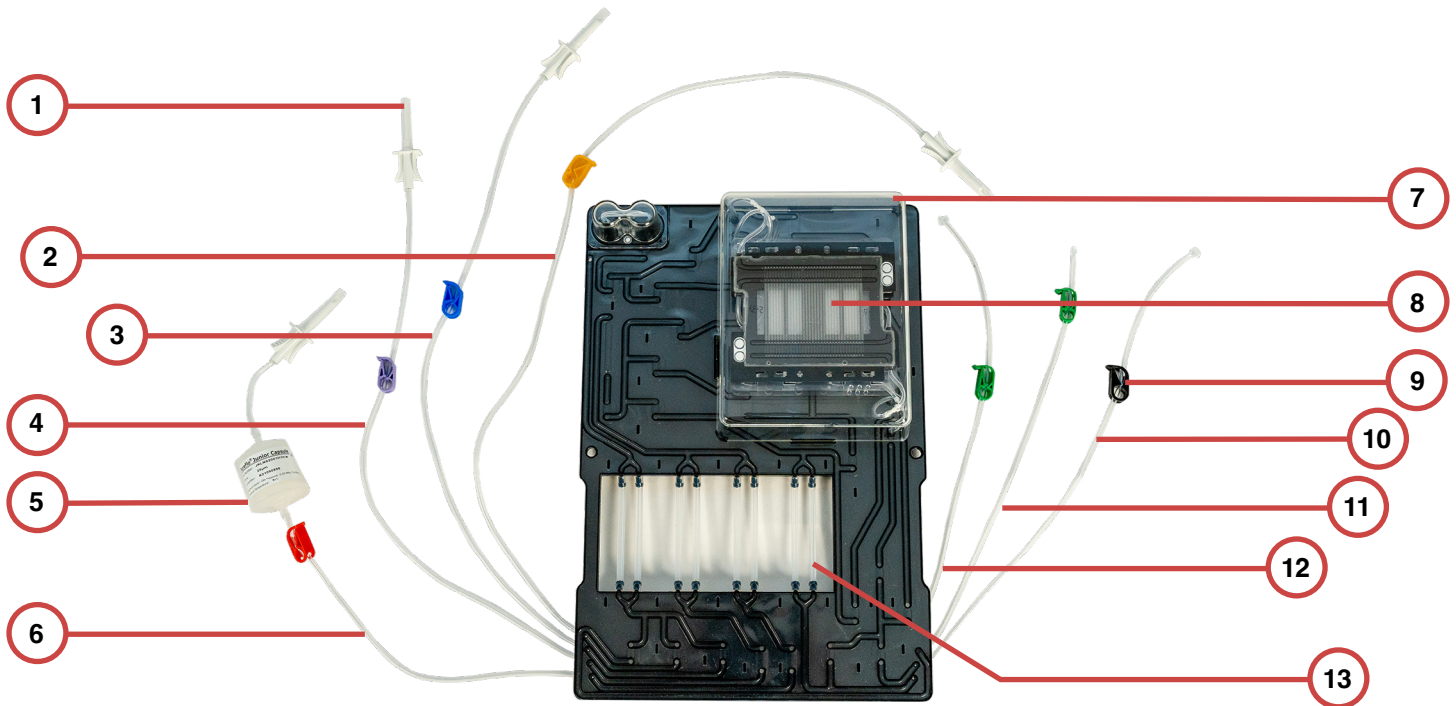
The top panel includes the status screen and a button. The status screen displays error messages and scanning and loading prompts. The button is used during the scanning and loading process.

Figure 5. Detail of top panel showing the status screen and button



## Cassette Components

Figure 6. Curate DCS Cassette



No.	Component	Description
1	Spike tubing connectors	Spikes for connecting to compatible bag spike ports.
2	Priming solution tubing*	Tubing for priming solution bag.
3	Buffer tubing*	Tubing for buffer bag.
4	Diluent tubing*	Tubing for diluent bag.
5	Sample pre-filter	20 $\mu$ m pre-filter
6	Sample tubing*	Tubing for Sample bag.
7	DCS chip protective cover	Prevents damage to DCS chip.
8	DCS chip	Separates and washes cells using patented DCS technology.
9	Color-coded tubing clips	Prevent fluid movement into cassette.
10	Waste tubing*	Tubing for waste bag.
11	Product tubing 1 (collection)*	Collection tubing for product bag.
12	Product tubing 2 (recirculation)*	Recirculation tubing for product bag.
13	Peristaltic pump tubing	Interaction with pumps to move fluid through the cassette.

\*Connection tubing is heat weldable.

### 2.2.3 Curate Priming Reagent

The Curate priming reagent consists of sterile filtered 10% F-127, a non-ionic copolymer surfactant in water. In preparation for processing a sample on the system, Priming reagent is added to a commercially available saline IV bag to make the priming solution (0.5% F-127) for system priming. The priming solution is flushed from cassette before sample processing.

### 2.2.4 Curate QR Code Labels

The Curate QR code labels are 1.5 in x 1.5 inch square labels that are attached to all bags prior to loading into the instrument. These labels are an important part of the sample processing procedure because they enable the following functions:

- Guiding the user through the instrument loading sequence.
- Helping mitigate human error during instrument loading.
- Tracing run records to the original sample ID.



**IMPORTANT!**



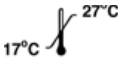
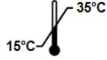
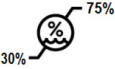

Review “Bags and Corresponding Curate QR Code Labels” on page 74 for details on properly labeling bags with the QR code labels prior to instrument loading.

Figure 7. Curate QR code labels in cassette tray



### 2.3. TECHNICAL SPECIFICATIONS

**Table 1. Curate system technical specifications**

Item	Description	Symbol (if applicable)
Color	Gray and white	
Height	63.4 cm (25 in)	
Width	48.7 cm (19 in) instrument only. 73.8 cm (29 in) with hangers.	
Depth	66.6 cm (26 in)	
Weight	39 kg (86.4 lbs)	
Input voltage	100 – 240 VAC nominal (max 90–264) at 47–63 Hz	
Over-voltage category	II (standard wall receptacle)	
Current	< 4 A (RMS) at 100 – 240 VAC	
Power consumption	< 200 W	
Fuses	T5AH at 250 VAC, 5x20 mm	
Working temperature	17°C to 27°C	
Storage temperature	15°C to 35°C	
Working humidity	30% to 75% humidity	
Pollution degree	2	
Altitude	<1,000 m (3,300 ft) above sea level	



**Table 2. DCS cassette technical specifications**

Item	Description
Pre-filter	20 $\mu\text{m}$ capsule filter pre-connected on sample tubing.
Bag spike connections (qty 4)	Spike connections on sample, diluent, buffer, and priming solution's weldable tubing.
Tubing weld connections (qty 3)	Product tubing (qty 2) and waste tubing (qty 1)
Color coded tubing clips (qty 7)	Clips for sealing tubing. Color-coded for each bag connection.
DCS chip (qty 2)	DCS chip supporting cell sizes ranging 4–22 $\mu\text{m}$

## 2.4. OPERATING LIMITS

**Table 3. Operating limits**

Item	Description
Input sample leukocyte concentration	$\leq 150 \text{ e6 cells/ml}$
Input sample % hematocrit	$\leq 10\% \text{ HCT}$
Mode C 45 maximum input leukocytes	$\leq 7.75 \times 10^9 \text{ cells}$
Mode C 100 maximum input leukocytes	$\leq 17.2 \times 10^9 \text{ cells}$

## 2.5. CURATE SYSTEM PERFORMANCE

**Table 4. Curate system performance\***

Item	Description
Sample processing rate	400 ml/hr**
Maximum cell throughput	$60 \times 10^9 \text{ cells}$
Selected cell size	4–22 $\mu\text{m}$
Cell type	Leukocytes
WBC recovery	$\sim 90\%$ ***
RBC removal	$> 95\%$
Platelet removal	$> 98\%$
Wash efficiency	$> 99.0\%$ ****

\* Performance data is based on the Curate Beta system.

\*\* Sample processing rate of 600 ml/hr, following a 24 minute priming cycle..

\*\*\* Includes a 7% loss to prefiltering.

\*\*\*\* As measured by removal of fluorescently-labeled protein. DNase activity is non-detectable using a standard 2 hour assay.

## 3. INTENDED USE AND CONDITION

**CAUTION!**

Inspect all Curate Biosciences products and product components (power cord and other connectors) as well as all ancillary products and material for damage, hazards, or compromised sterility upon arrival and immediately before use.

### Curate Instrument

The Curate instrument is a multi-use fluid management platform designed to be used indoors under normal environmental conditions and with its corresponding, single-use Curate DCS cassette.

**WARNING!**

Only use Curate consumables and accessories provided for use with the system and that meet the manufacturing specifications. Do not replace the power cord with inadequately rated cords. Only use the barcode scanner supplied by the manufacturer.

### Curate DCS Cassette

**STERILE EO** Curate DCS cassettes are Ethylene Oxide treated.

⊗ Curate DCS cassettes are Single-Use-Only products and should not be reused.

**WARNING!**

Only use Curate DCS Cassettes from Curate Biosciences. Do not use cassettes from unauthorized manufactures, doing so may damage the instrument and result in a failed run and may void the warranty.

### Curate Priming Reagent

**STERILE**

Curate priming reagent is 0.22  $\mu\text{m}$  filtered and bottled into sterile, depyrogenated containers.

⊗ Curate priming reagent is a single-use-only product and should not be reused.

**WARNING!**

Only use Curate priming reagent from Curate Biosciences. Do not use a priming reagent from unauthorized manufacturers, doing so may damage the cassette and result in a failed run.

### Curate QR Code Labels

An assigned set of Curate QR code labels come with each Curate DCS cassette. The Curate QR code labels are attached to all bags by the user before instrument loading and are scanned by the user and recorded by the system during the instrument loading process.

⊗ Curate QR code labels are single-use-only components and should not be reused.

## 4. STORAGE AND HANDLING

If product or product containers are damaged or unintentionally opened before or upon arrival, contact Curate Biosciences Support and set up on-site inspection by Curate Biosciences personnel.

### 4.1. STORAGE

#### Curate Instrument:

Refer to “Table 1. Curate system technical specifications” on page 16 for information regarding Curate instrument’s storage. The Curate Cell Processing System is suitable for usage in ISO-7 14644 classification / US Fed Std. 209E class 10k clean rooms.



#### WARNING!

If the Curate System is used in a manner not specified within this document, protection provided by the system may be impaired and any service contract or warranty agreement may become void.

#### Curate DCS cassette:

Store at room temperature.

#### Curate Priming Reagent:

Store at room temperature.

#### Sample Pretreatment Reagents:

DNase (Ex. benzonase) It is recommended to make and store individual aliquots at -20°C.

### 4.2. HANDLING

#### Curate Instrument:

- Follow instructions for instrument handling and storage.
- Do not place the Curate instrument on its top or sides. Doing so may damage the internal hardware components.
- Avoid unnecessary contact with the Curate bag hangers, as this can result in more frequently needing to calibrate hanger sensors. Do not hang items from the hangers when the system is not in use.
- Do not exceed hanger weight loads greater than their corresponding maximum safe load mass (see Table 5). Exceeding the hanger maximum safe load mass can damage the hanger mass sensor.

**Table 5. Hanger maximum safe loads**

Hanger	Maximum Safe Load (grams)
Hanger 1 (priming solution)	4,500
Hanger 2 (diluent)	4,500
Hanger 3 (buffer)	4,500
Hanger 4 (sample)	4,500

Hanger	Maximum Safe Load (grams)
Hanger 5 (waste)	4,500
Hanger 6 (waste)	4,500
Hanger 7 (product)	900

- When performing any cleaning or aseptic decontamination of the instrument, ensure that the instrument is dried thoroughly. Liquids inside the instrument can cause damage to the system.
- Do not replace detachable power cord by inadequately rated cords.

**Curate DCS Cassette:**

- Ensure Curate cassette sterile package is sealed upon arrival.

**Curate Priming Reagent:**

- Ensure that the bottle cap is sealed upon arrival.

**4.3. SAFE DISPOSAL OF MATERIALS****Curate DCS Cassette:**

- Dispose of Curate DCS cassettes that have processed biologics in appropriate bio hazard waste container.

**Curate Priming Reagent:**

- Dispose of the priming reagent glass bottle in appropriate bio-hazard waste container.

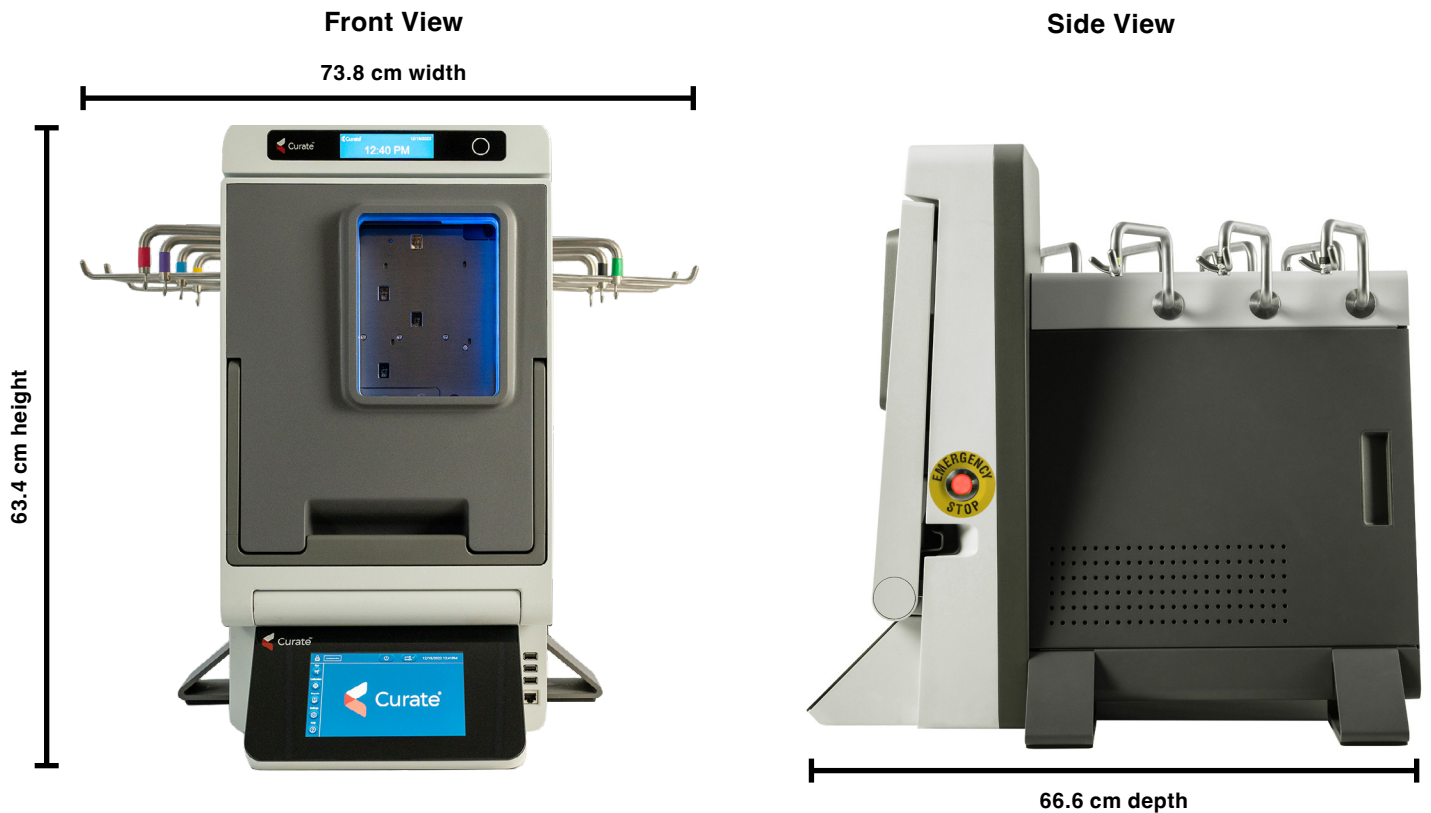
**Unused DNase**

- Excess enzyme should be disposed of in an appropriate bio hazard waste container.
-

## 5. INSTALLATION AND SETUP

### 5.1. DIMENSIONS

Figure 8. Instrument dimensions



### 5.2. WORKING SPACE

#### 5.2.1 Physical Space Requirements

The Curate system is a bench top instrument and can be placed on top a standard laboratory bench with a flat surface. The instrument requires a bench top working space of approximately 68 cm (27 in) height, 84 cm (33 in) width, and 70 cm (28 in) depth.

**NOTE:** Sufficient open space on the left and right sides of the instrument is needed for ventilation and for loading bags onto the hangers. At least 13 cm (5 in) of open space on the left and right sides is recommended.



#### CAUTION!

The Curate instrument should be installed on a stable bench with a flat top surface that is capable of supporting at least 50 kg (110 lbs). If a mobile station is used, the user is responsible for ensuring all safety hazards and risks to instrument operation are properly addressed and functional requirements are met.

### 5.2.2 Power Connection

A power cord is supplied with the instrument and the power connection module is located at the rear of the instrument. See Figure 3 to view the location of the power connection module, which is a recessed, male, 3-pin power connector to which the power cord attaches. Just above the power connector is the ON/OFF switch, on which are two symbols: Bottom symbol (O) is 'OFF' and top symbol (I) is 'ON.'

The power switch must remain accessible after installation. Only use the power cord with the 3-pin plug, provided by Curate Biosciences, plugged into a standard, grounded 3-pin wall receptacle.

## 5.3. INSTALLATION

Installation must be performed by a Curate Biosciences Field Service Technician. As part of the Curate system installation process, Curate Biosciences personnel will perform an install check to verify that all sensors and systems are functional. Each sensor will be re-calibrated, as needed, to establish the calibration curves necessary for the Curate system. A system test will then be performed to test the system performance over an hour-long run, with all sensors actively in-use and monitoring progress. The results of this performance test will verify that the system is ready for sample processing. The performance test results will be shared before proceeding to training. The system test should be used to assess initial installation qualification (IQ) as well as any subsequent operational qualification (OQ).

The Curate Biosciences personnel will create a user profile for the system and install location as well as confirm that all relevant programs for operating the system are accessible and functional from the user profile.

For information about calibrating the system, see "Calibration Procedures" on page 103.

## 5.4. HANDLING AND SAFETY


**IMPORTANT!**

Before lifting instrument, review these handling and safety instructions.

The instrument requires two persons for lifting and must be installed on a flat surface. Use the instrument legs and bottom front frame when lifting. DO NOT use the bottom touch screen panel on the front of the instrument to lift the instrument, since excess force may damage the panel. The instrument is heaviest at the front, so extra support should be placed at the front of the instrument when lifting. See Figure 9 for proper hand placement when lifting the instrument.

Figure 9. Proper hand placement when lifting the instrument



 **WARNING!**  
DO NOT use the front touch screen panel to lift the instrument, since excess force may damage the panel.

## 6. SOFTWARE OVERVIEW

### 6.1. ABOUT AND INTENDED USE

The Curate software manages and controls all physical operations of the system to support reproducible cell processing. The software accommodates multiple user classes. Reports are generated on individual runs and on reports across multiple runs. All operator data entry, selection, and controls are tracked and traced. To ensure optimal system performance, the software guides users through maintenance and calibration processes.

### 6.2. SOFTWARE TECHNICAL SPECIFICATIONS

Relevant system software and database updates may be updated, as needed, by Curate Biosciences technical staff to improve performance or add functionality. This documentation is applicable to the initial release only.

**Table 6. Software technical specifications**

Item	Description
Operating system	Windows Hardened IoT, OS10
Software version	V1.06 or higher
Database version	V1.017 or higher



**WARNING!**

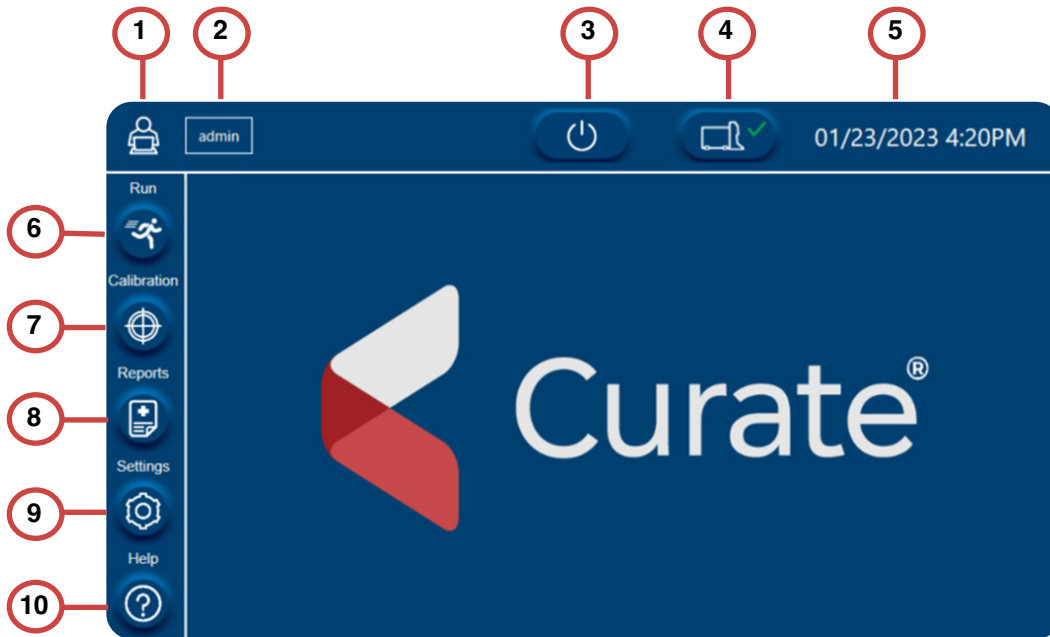
**Warning! The Curate System is sensitive to electrical fast transient signals and bursts at 1000 V/-1000 V, which may decrease sensitivity of the main touch screen. Should this occur when the system is not in use, restart the instrument to regain touch screen functionality. If the issue occurs during a run, connect a mouse to any of the available USB ports. Only if an error message appears during a run and a mouse is unavailable, press the Emergency STOP button on the side of the instrument and close all the clips. Restart the unit to regain touch screen functionality. For how to proceed after an emergency stop, see “12.12. Emergency Stop Button” on page 102.**



### 6.3. GUI DASHBOARD

The software's Graphical User Interface (GUI) dashboard is the user's control center for the system and is accessed through the touchscreen on the instrument's bottom panel. All system operational functions, settings, and information are accessed through the dashboard.

Figure 10. Software GUI dashboard with all functional and information components highlighted



No.	Component	Description
1	Log in/log out	Logs out user and returns to login screen.
2	User status	Indicates current user logged onto system.
3	Power	Powers down system.
4	System status	Indicates system status. A green check ( ✓ ) indicates system ready/no errors. A red warning symbol ( ⚠ ) indicates an error. Users can touch the icon to view error messages, sensor status, and system information.
5	Date and Time	Displays current date and time.
6	Run button	Opens the Run Mode Selection screen.
7	Calibration button	Opens the Calibration Selection screen.
8	Reports button	Opens the Report screen.
9	Settings button	Opens the Settings screen.
10	Help button	Opens the Help section.

## 6.4. LOGIN AND USER MANAGEMENT

### 6.4.1 Login

User can log into the system when starting the instrument and software. Once instrument startup is complete, the login screen will appear, and the user can enter a pre-assigned user name and password.

During installation, users can log in with a user name and password pre-assigned by Curate Biosciences personnel. After the initial log in during installation, users can edit their user name and password within the system settings.

### 6.4.2 User Management

The user classes range from limited to maximum access: Operator, Supervisor, and Engineer. The user migration path is setup such that an Operator can advance to a Supervisor, and a Supervisor can advance to become an Engineer. An Administrator has full autonomy over user access. The software allows a maximum of three administrators.

**Table 7. Recommended permission settings**

Function	Operator	Supervisor	Engineer	Administrator
View System Test	✓	✓	✓	✓
Hanger calibration		✓	✓	✓
Export Location		✓	✓	✓
View Run History			✓	✓
Manage Users			✓	✓
View Log			✓	✓
Printer			✓	✓
Access Connectivity			✓	✓
Delete Records				✓
Export Raw Data				✓

Create new users or modify permissions for existing users within the Settings screen. See "Creating a New User" on page 30.

**Table 8. Locked user access settings**

Function	Operator	Supervisor	Engineer	Administrator
Log in	✓	✓	✓	✓
Select Run Modes	✓	✓	✓	✓
Run Samples	✓	✓	✓	✓
Site Information	✓	✓	✓	✓
Script Database Version Upgrade			✓	✓
Add New Media				✓
Set Reminders				✓

## 6.5. RUN MODE SELECTION SCREEN

The system comes with these pre-defined processing run modes:

1. **Separation and Wash (Mode A)**
2. **Separation and Wash plus Concentration (Mode C)**
3. **System Test (Mode E)**

Users can select a specific run mode by selecting **Run** on the left side of the screen to navigate to the **Run Mode Selection** screen.

The system test mode allows the user to qualify the instrument throughout the full range of the instrument's capability. A system test mode run is identical to an actual sample run, except performed using saline in all relevant bags instead of run buffer and a biological sample. For more information about the system test, see "Performing a System Test" on page 51.

Figure 11. Run Mode Selection screen

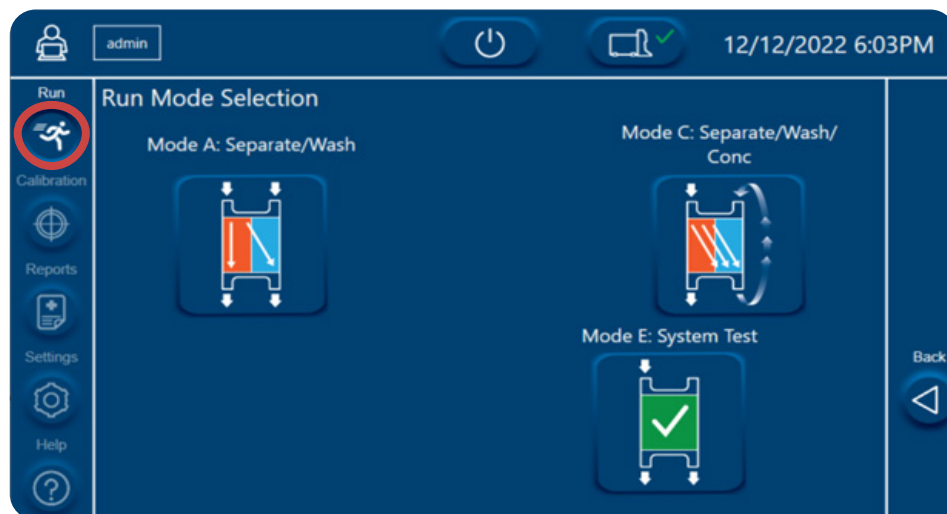
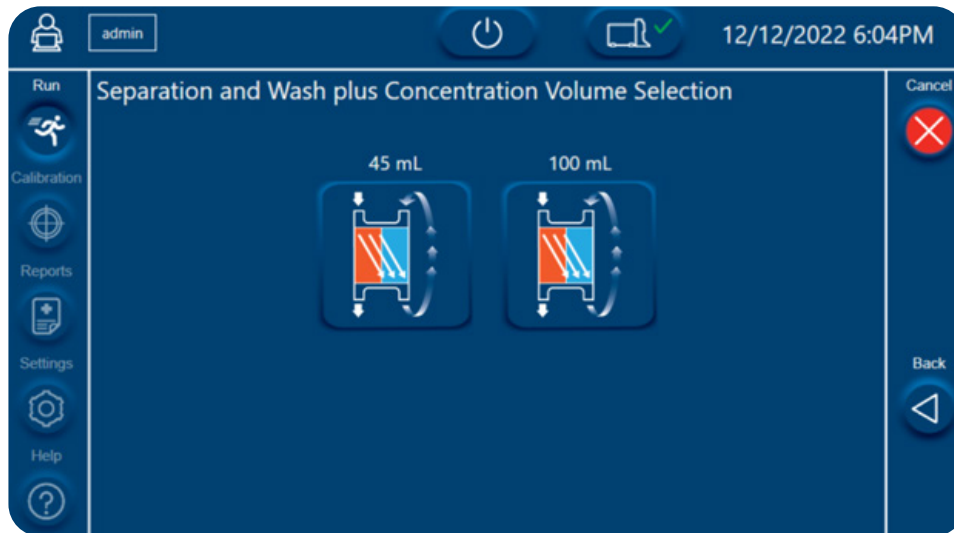


Figure 12. Separation and Wash plus Concentration Volume Selection screen



## 6.6. CALIBRATION SELECTION SCREEN

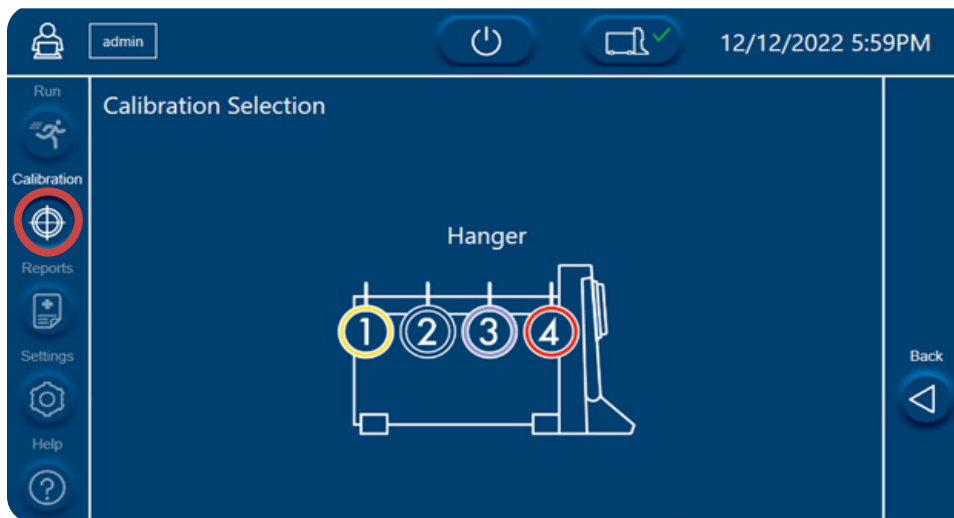
To ensure optimal system performance, the instrument must be routinely calibrated as per your organization’s quality control requirements. Within the software’s Calibration Selection screen, users can calibrate the instrument’s seven hanger sensors.



**IMPORTANT!**

Users should review “Hanger Calibration” on page 29 and “Calibration Procedures” on page 103 for more detailed information on Curate system calibration schedules and procedures.

Figure 13. Calibration Selection screen



**NOTE: Only Curate Biosciences qualified personnel can calibrate the pressure sensors and bubble sensors and inspect the instrument valves.**

### 6.6.1 Hanger Calibration

The system's pumps are controlled by the software and respond to feedback from the hanger gravimetric sensors. Since proper feedback from the hanger sensors requires accurate measurements from the sensors, calibration of these sensors is critical for optimal performance.

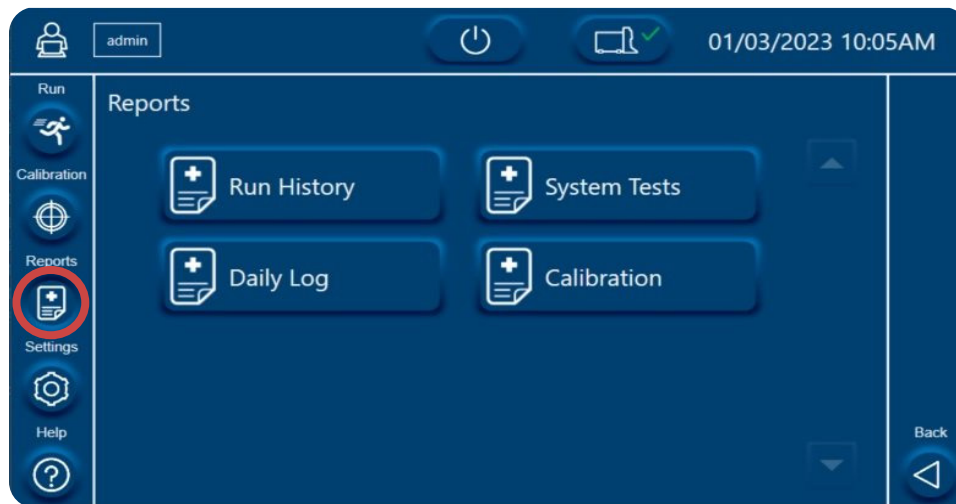
See "Hanger Calibration" on page 104 for detailed instructions for hanger sensor calibration.

## 6.7. REPORTS SCREEN

Run reports maintain a copy of the original file name, which is not overwrite-able, to allow for complete post run re-creation of all parameters. The system can report upon all tracking, tracing, and run metrics, associated error conditions and any system related parameters. The software can verify, calibrate, configure, and record data within a run, track across runs, and generate reports. The software can measure, calculate, and change parameters during a run to ensure run quality as well as report deviations beyond established limits. Access to view and download reports is controlled by the administrator.

To access reports, select the **Reports** button on the left side of the screen.

Figure 14. Reports screen



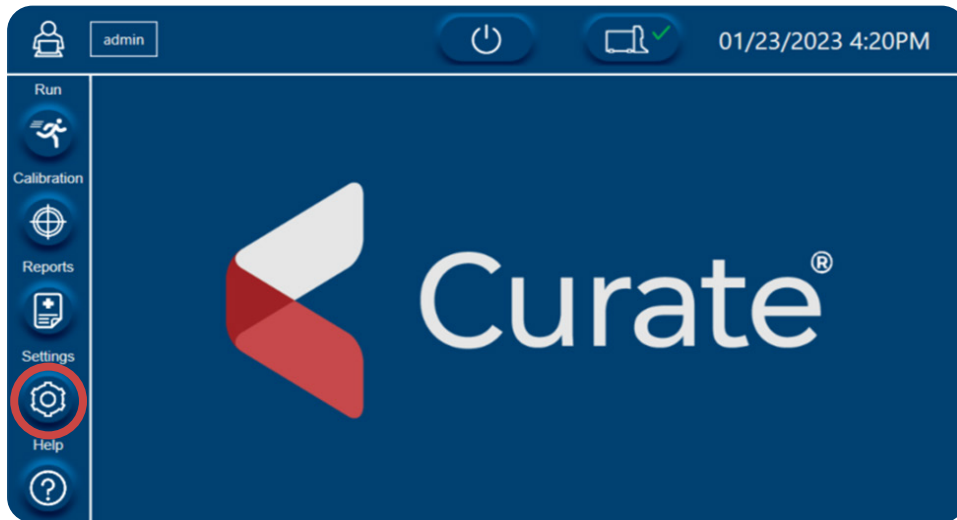
## 6.8. SETTINGS SCREEN

In the Settings screen, depending on the user's permission level and details, users can modify user class details, change data export, and import locations, edit the system's location, date and time, as well as set preventative maintenance, system test, and weight calibration schedules.

### 6.8.1 Creating a New User

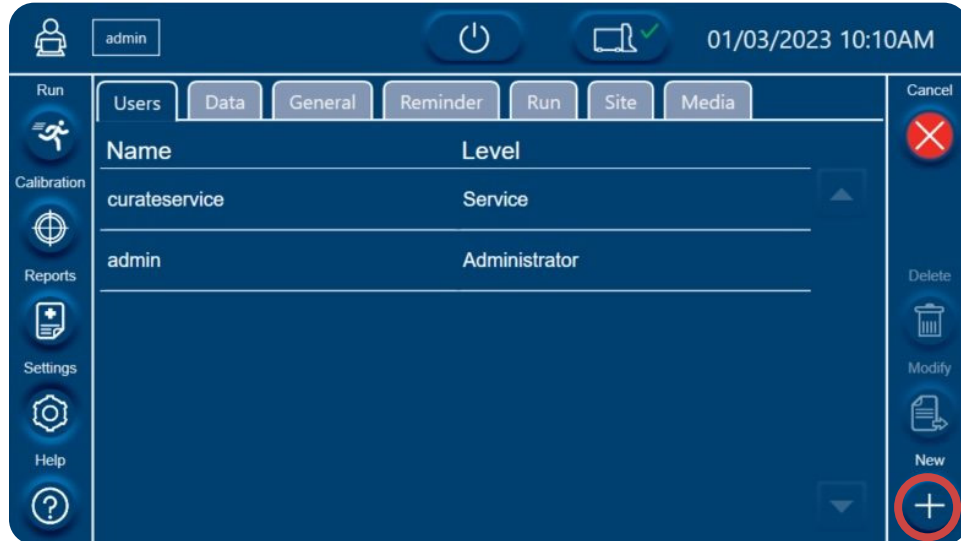
1. Select **Settings** on the left side of the screen.

Figure 15. Curate dashboard with the Settings button highlighted



2. Create a new user by selecting **New** on the right side of the screen.

Figure 16. Users tab



3. Choose a **User Type** and **Name**, create a **Password**, select permissions for the user, and then **Save** the new user's settings. For recommendations for each user type, see "Table 7. Recommended permission settings" on page 26.

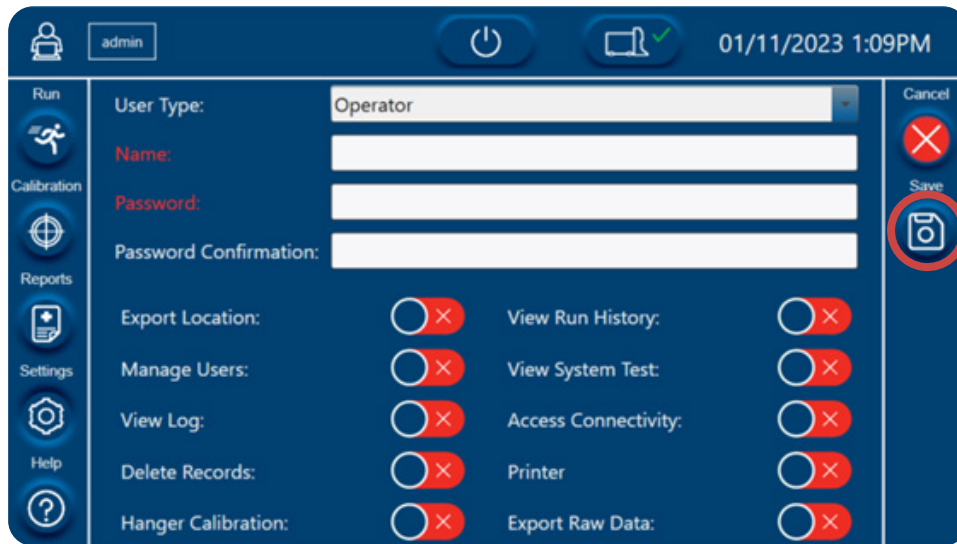
#### Name requirements:

- Minimum number of characters = 5.
- Maximum number of characters = 20.
- User with same username must not exist.

#### Password requirements:

- Minimum number of characters = 8.
- Cannot contain the user name.
- Must include at least 1 upper case character.
- Must include at least 1 lower case character.
- Must include at least 1 number.
- Maximum of 4 repeating characters.

Figure 17. Setting the user information

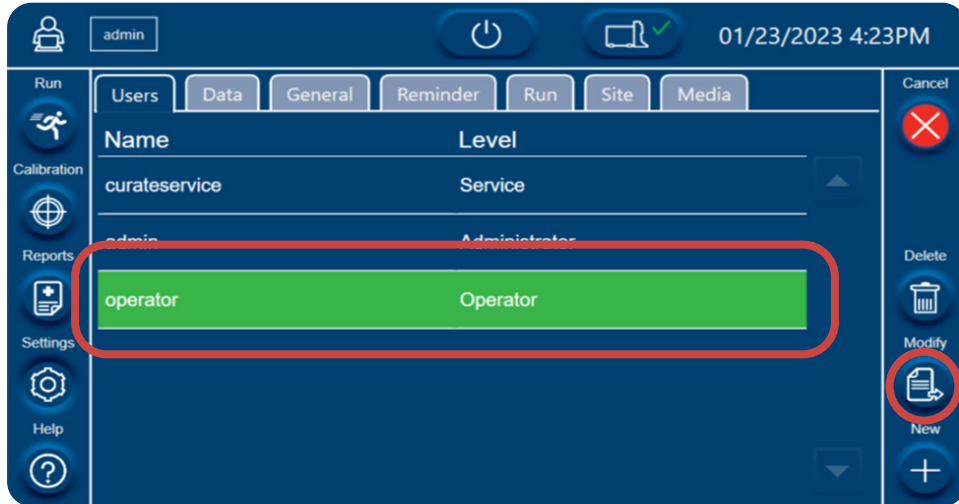




## 6.8.2 Modifying Existing Users

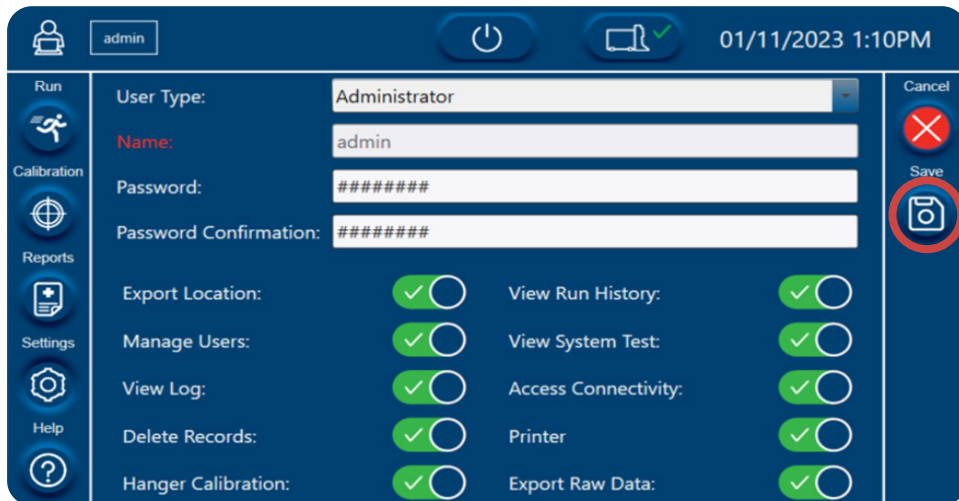
1. Select the existing user and then press **Modify** on the right side of the screen.

Figure 18. Selecting the user



2. Edit **User Type** and **Name**, **Password**, and permissions for this user and **Save** the user's settings.

Figure 19. Editing the user information



### 6.8.3 Setting Data Export and Import Locations

Within the Settings screen, users can set a default export location, import run scripts as well as turn on the auto export run data function. The auto export run data function enables automatic export of run data to the chosen default export location when the sample run is complete.

**Note: Software versioning shall be controlled by Curate Biosciences in accordance with IEC 62304 policy.**

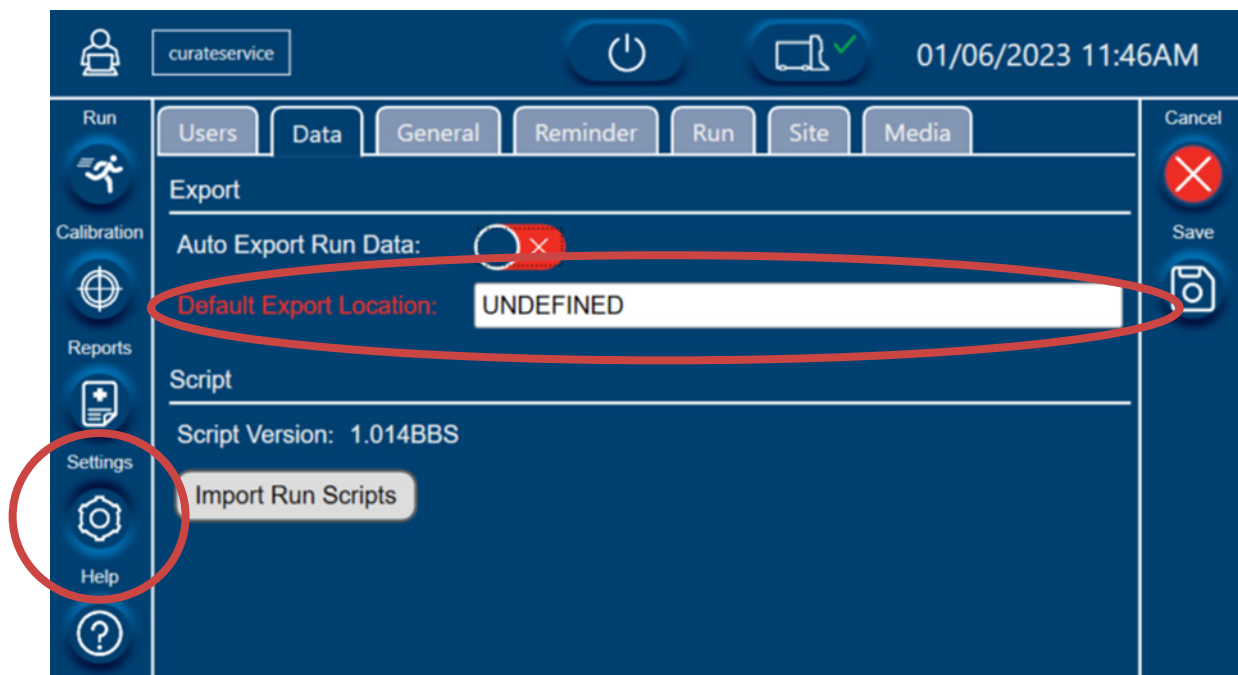


**IMPORTANT!**

An empty, external USB drive that is dedicated to the Curate System can be used for exporting data. For data connections to off-system servers, please contact Curate Technical Support for assistance regarding security policies.

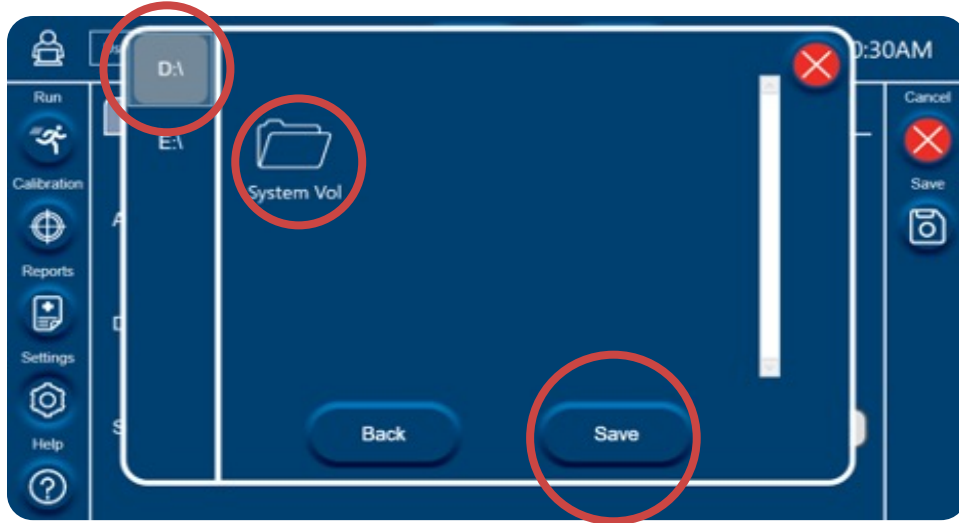
1. To set a default export location, navigate to the **Data** tab within the **Settings** screen and press the **Export Location** field to open a browser and choose a location.

Figure 20. Data tab within the settings screen



2. Select a **Default Export Location** and **Save**.

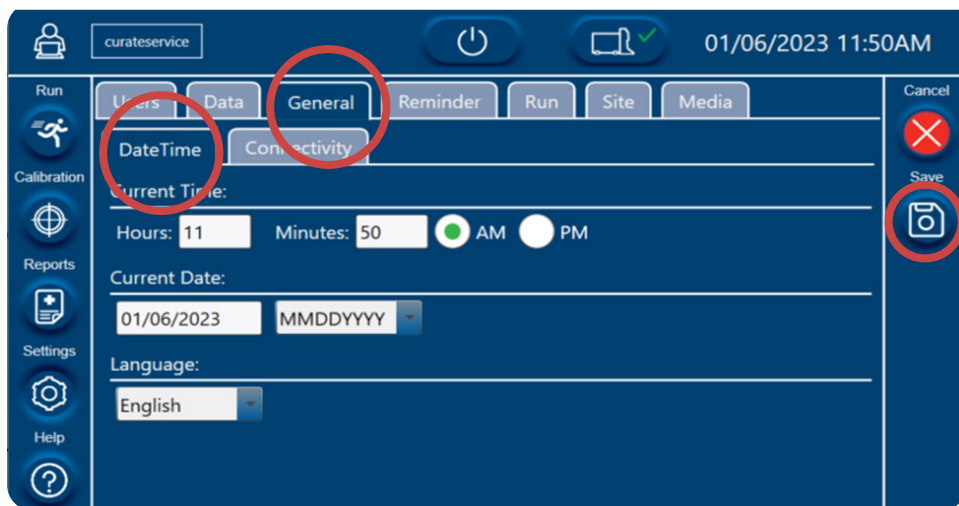
Figure 21. Setting the default export location



#### 6.8.4 Setting the Date, Time, and Maintenance Schedules

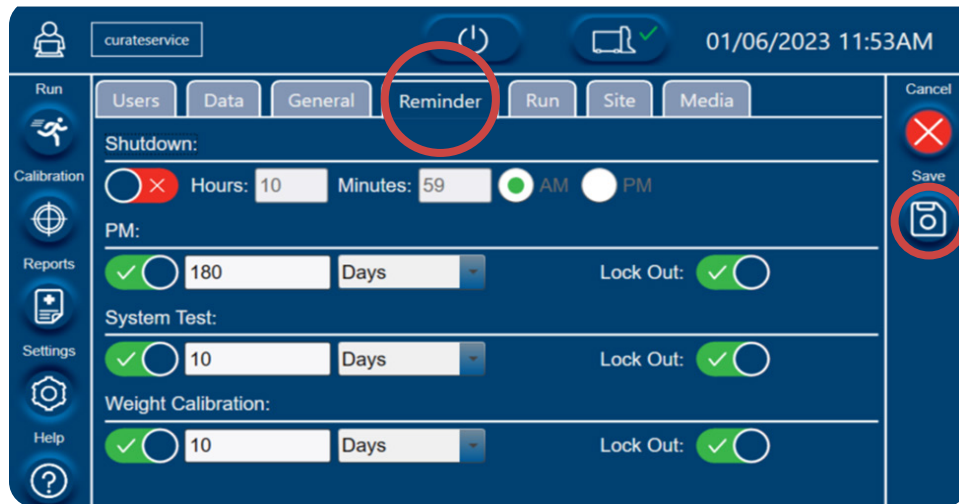
1. Navigate to the **General** tab within the **Settings screen** to edit the following features:
  - Current Time
  - Current Date
  - Date Format
  - Language (English is the only selection for the initial release)
2. Press **Save** after making any edits or selections.

Figure 22. DateTime sub-tab of the General tab



- Navigate to the **Reminder** tab within the **Settings** screen to edit the following features:
  - Shutdown time
  - Preventative Maintenance (PM) schedule (default: 180 days)
  - System Test schedule (default: 10 days)
  - Weight Calibration schedule (default: 10 days)
- Press **Save** after making any edits or selections.

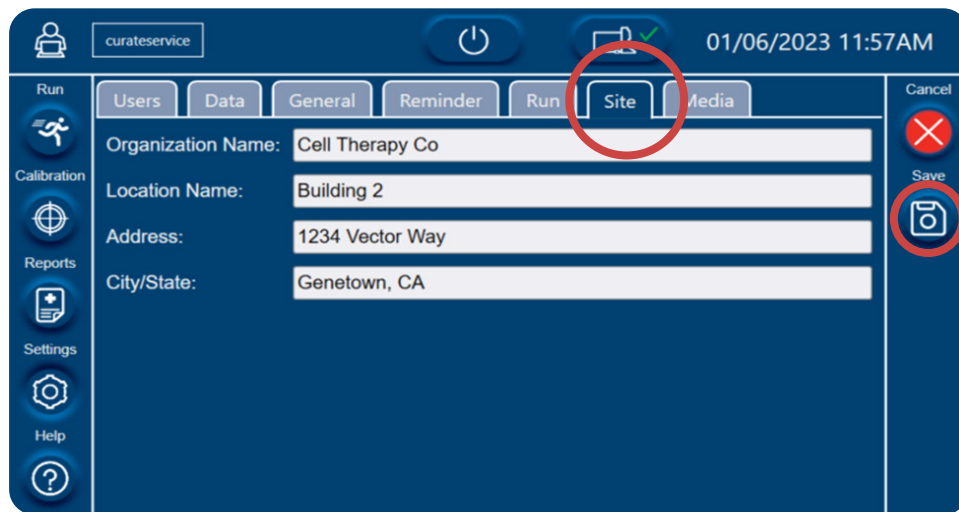
Figure 23. Reminder tab



### 6.8.5 Entering the Site Information

- To enter information for the site at which the instrument is located, navigate to the **Site Information** tab within the **Settings** screen to enter the following information:
  - Organization Name
  - Location Name
  - Address
  - City/State
- Press **Save** after entering the site information.

Figure 24. Site Information tab within the Settings screen

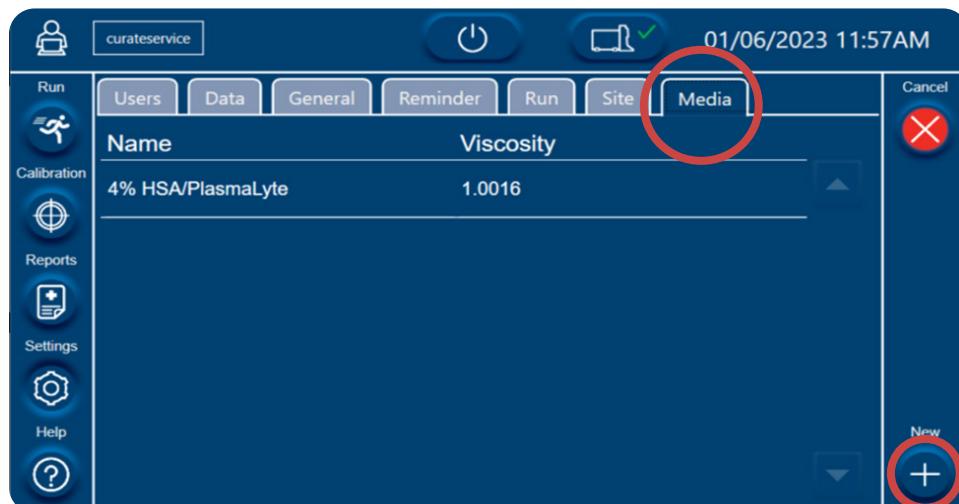


### 6.8.6 Adding New Media

Only users with administrator access can add new media. See “Recommended permission settings” on page 26.

1. To add new media, navigate to the **Media** tab within **Settings** to enter the following information:
  - Media Name
  - Media Viscosity
2. **Save** after adding the media information.

Figure 25. Media Tab



## 6.9. HELP SCREEN

The help section contains information on the system components, operational processes (reagents and disposables usage and instrument loading), error messages, and Curate Biosciences Support details, as well as service engineering functions when user is logged in at the service user level.

Where applicable, you can use the **Next** and **Back** buttons to navigate through the screens within each tab.

Figure 26. Help screen showing Curate tab



Figure 27. Help screen showing Curate tab, screen 2

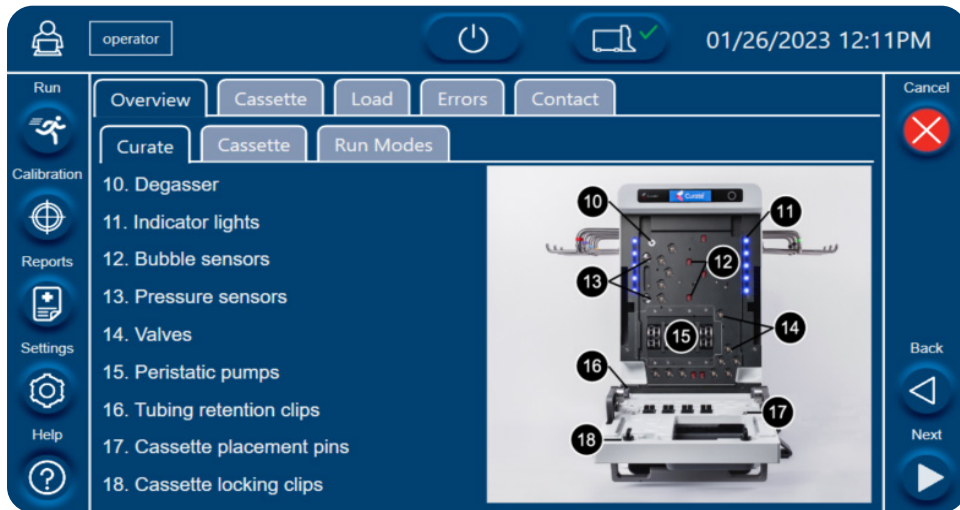


Figure 28. Help screen showing Curate tab, screen 3

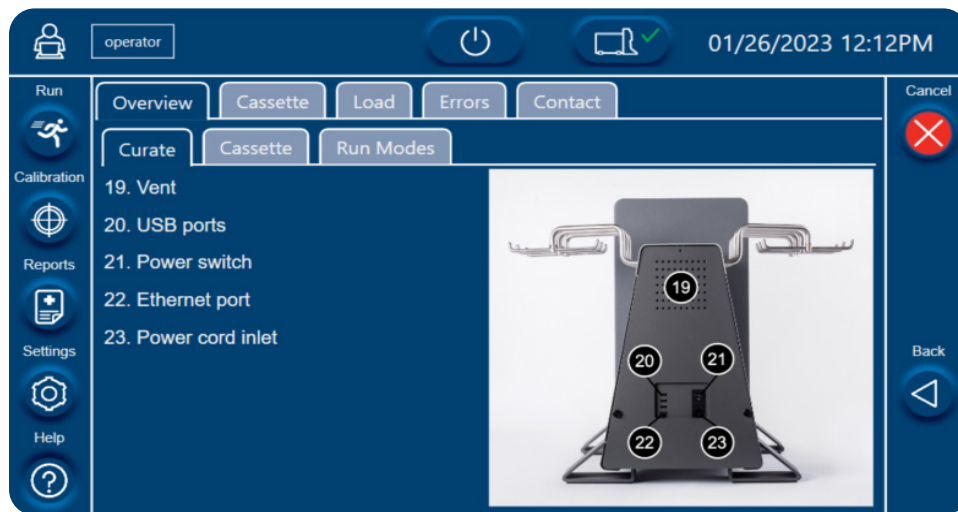


Figure 29. Help screen showing Cassette tab

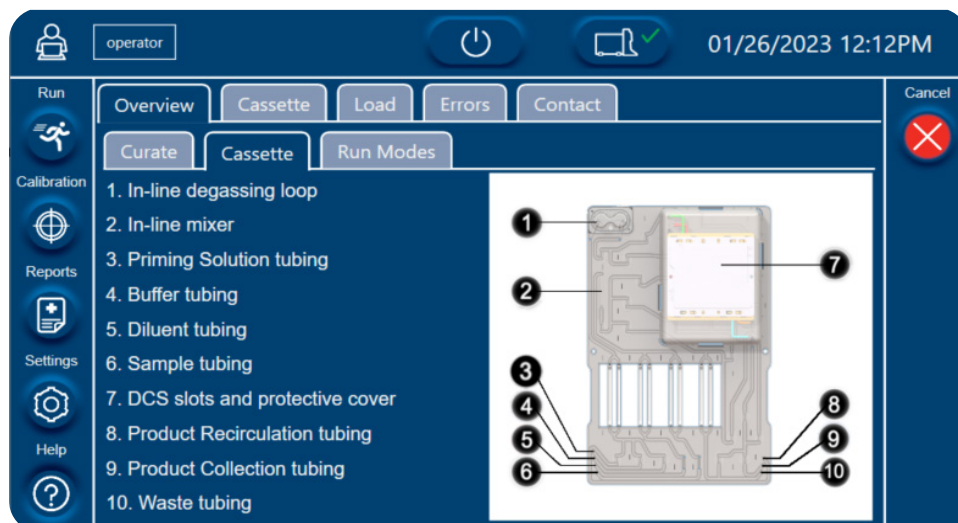


Figure 30. Help screen showing the Run Modes tab

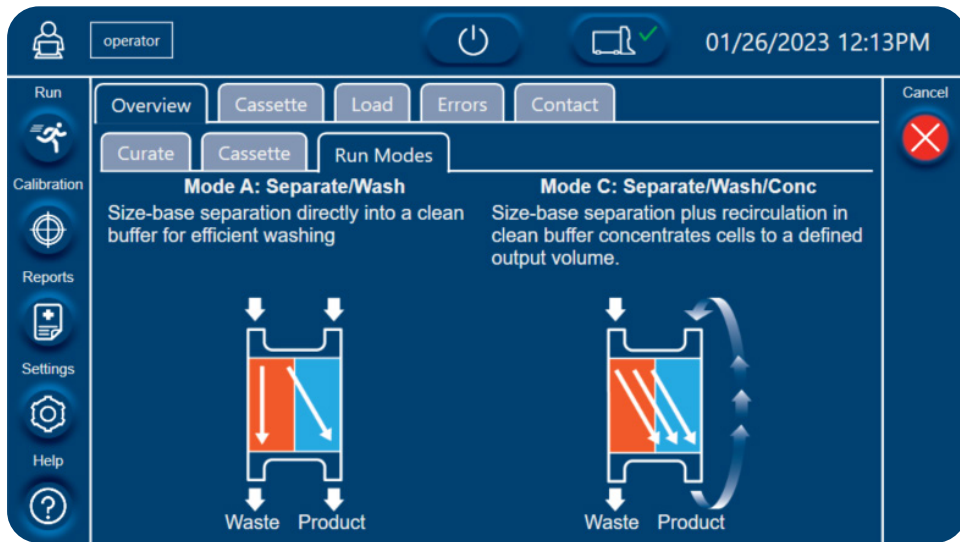


Figure 31. Help screen showing the Cassette Connections tab, screen 1

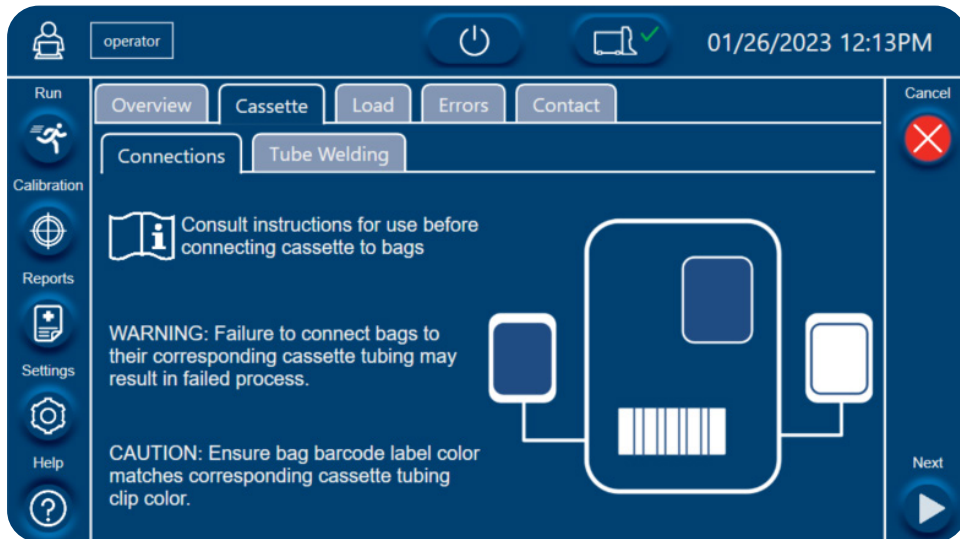




Figure 32. Help screen showing the Cassette Connections tab, screen 2

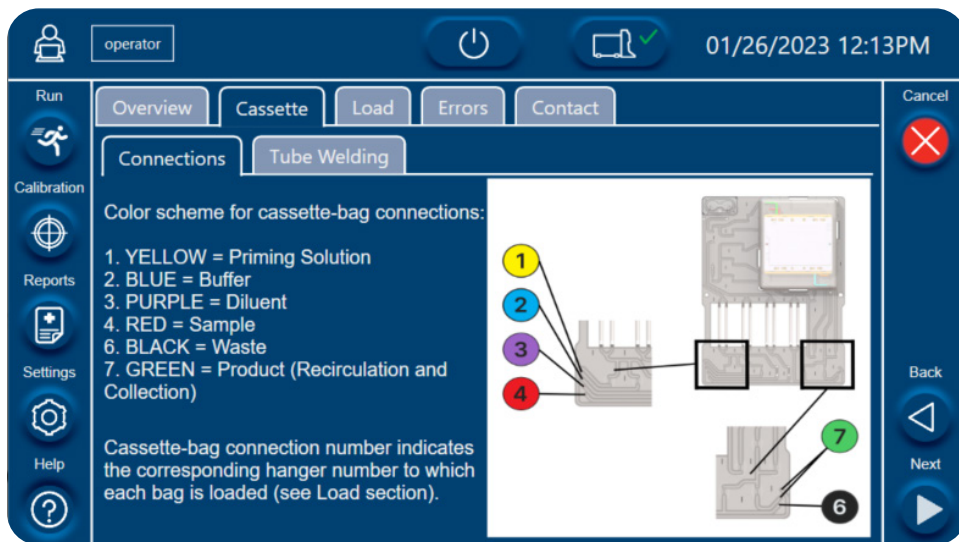


Figure 33. Help screen showing the Cassette Connections tab, screen 4

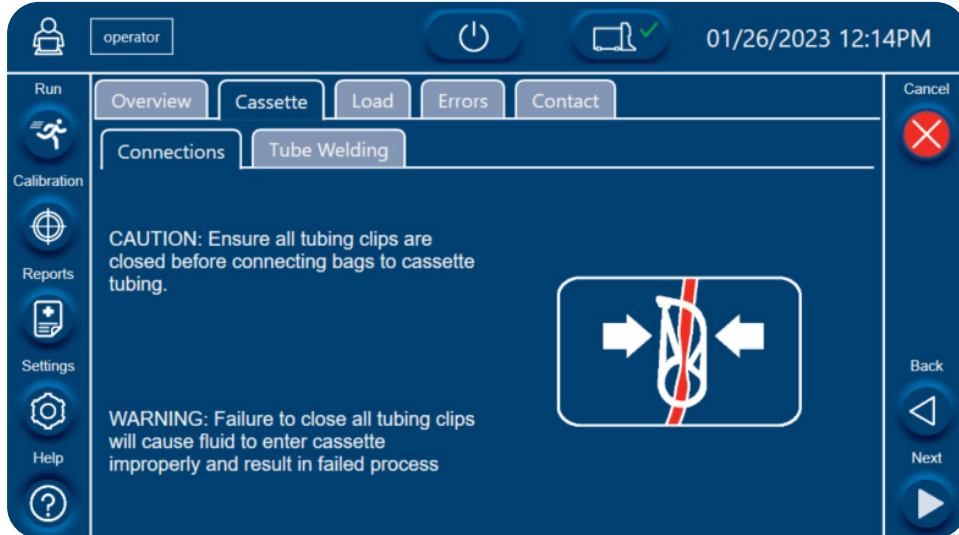


Figure 34. Help screen showing the Cassette Connections tab, screen five

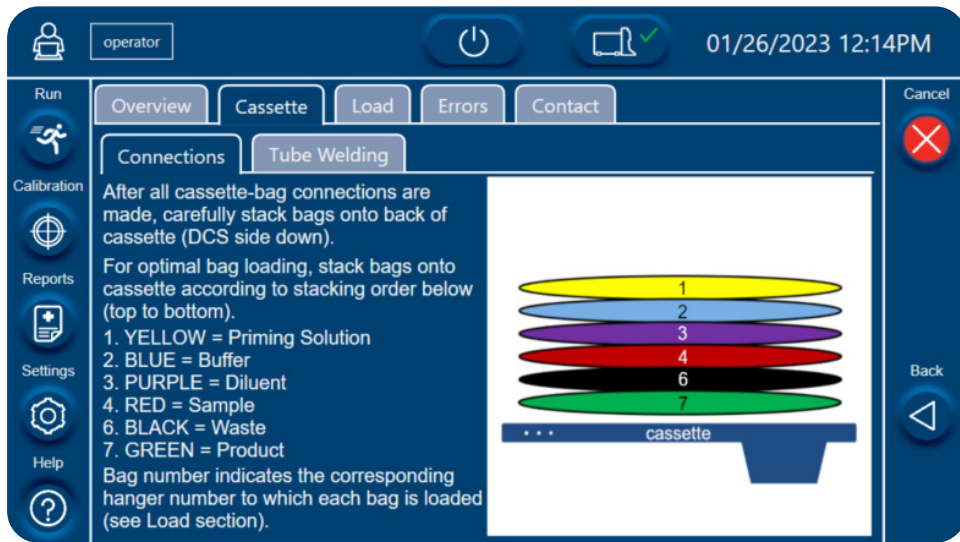


Figure 35. Help screen showing the Tube Welding tab

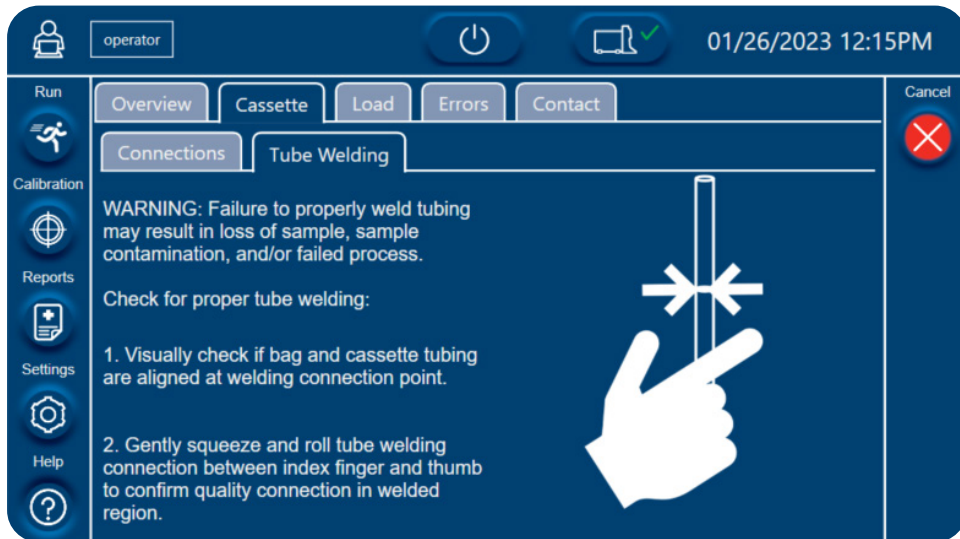


Figure 36. Help screen showing the Load tab, screen 1

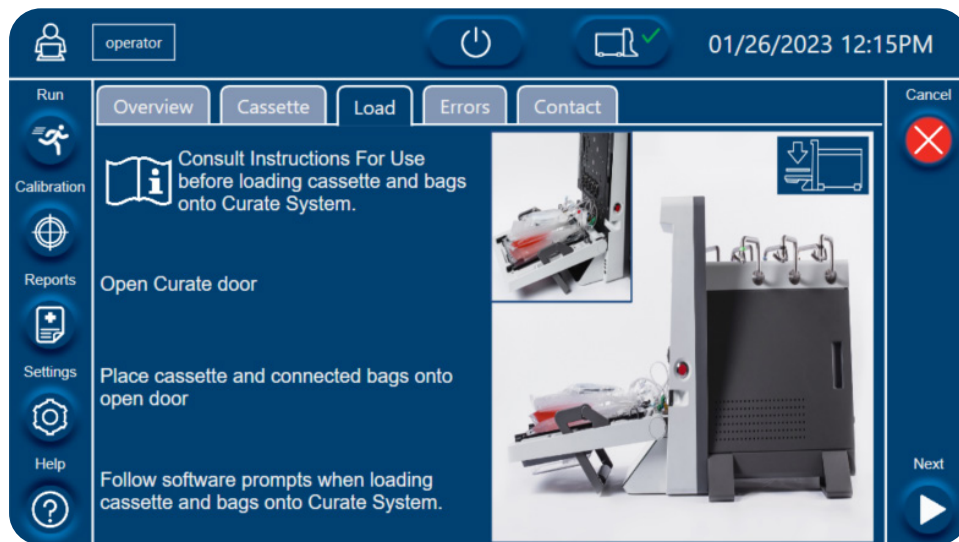


Figure 37. Help screen showing Load tab, screen 2



Figure 38. Help screen showing Load tab, screen 3

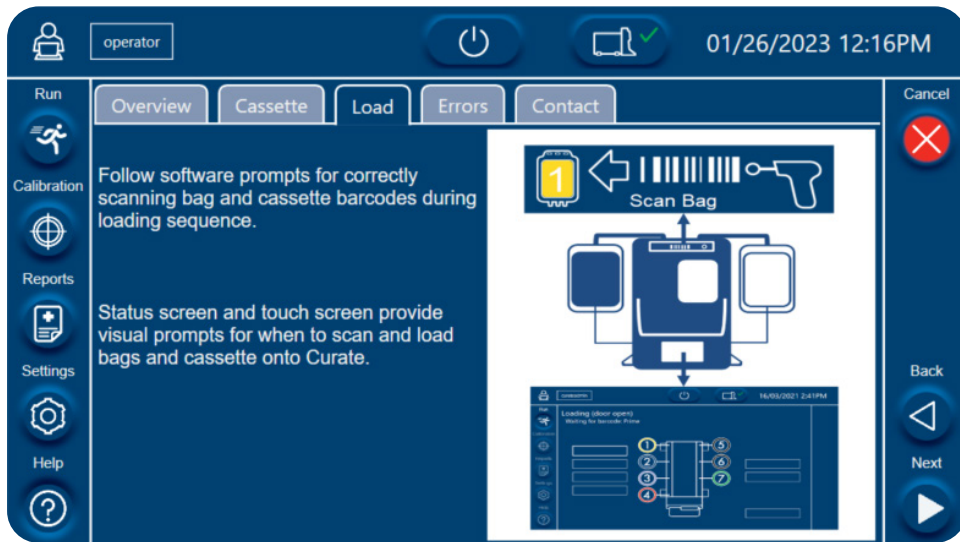


Figure 39. Help screen showing Load tab, screen 4

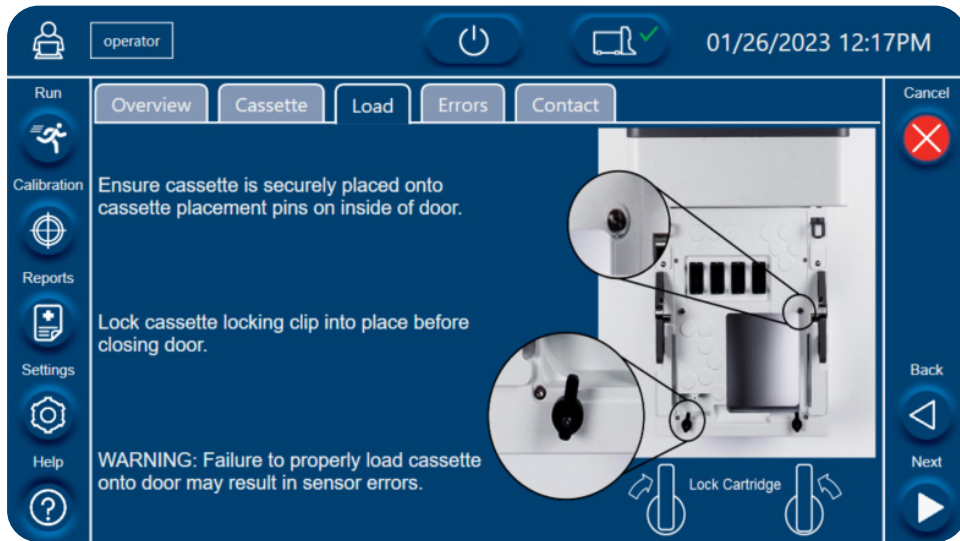


Figure 40. Help screen showing Load tab, screen 5



Figure 41. Help screen showing the Errors tab

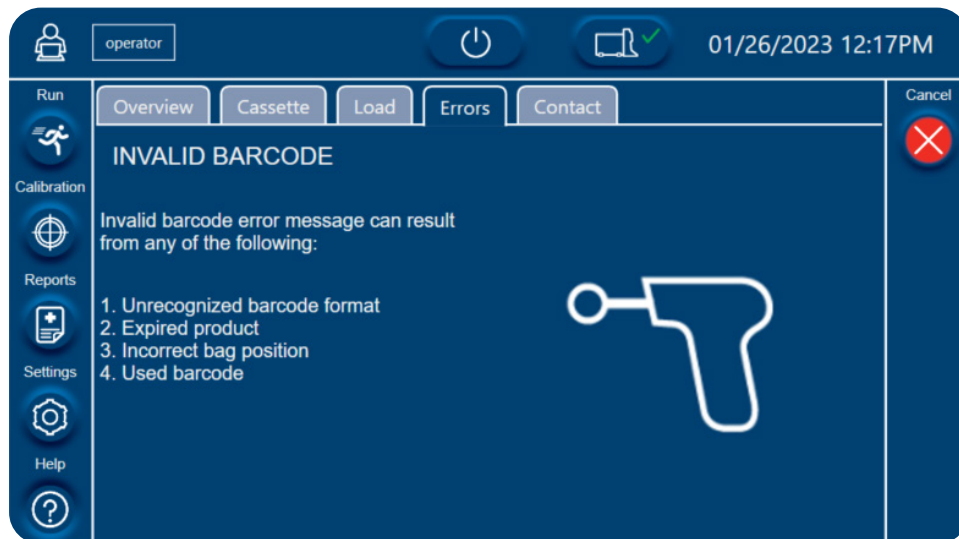


Figure 42. Help screen showing the Contact information tab



## 6.10. SOFTWARE UPGRADES

The software is upgradeable only by a secure download by a Curate Biosciences field service engineer. Software versioning shall be controlled by Curate Biosciences in accordance with IEC 62304 policy.

Contact Curate Biosciences Support for information on software upgrades (See “Technical Support” on page 121).

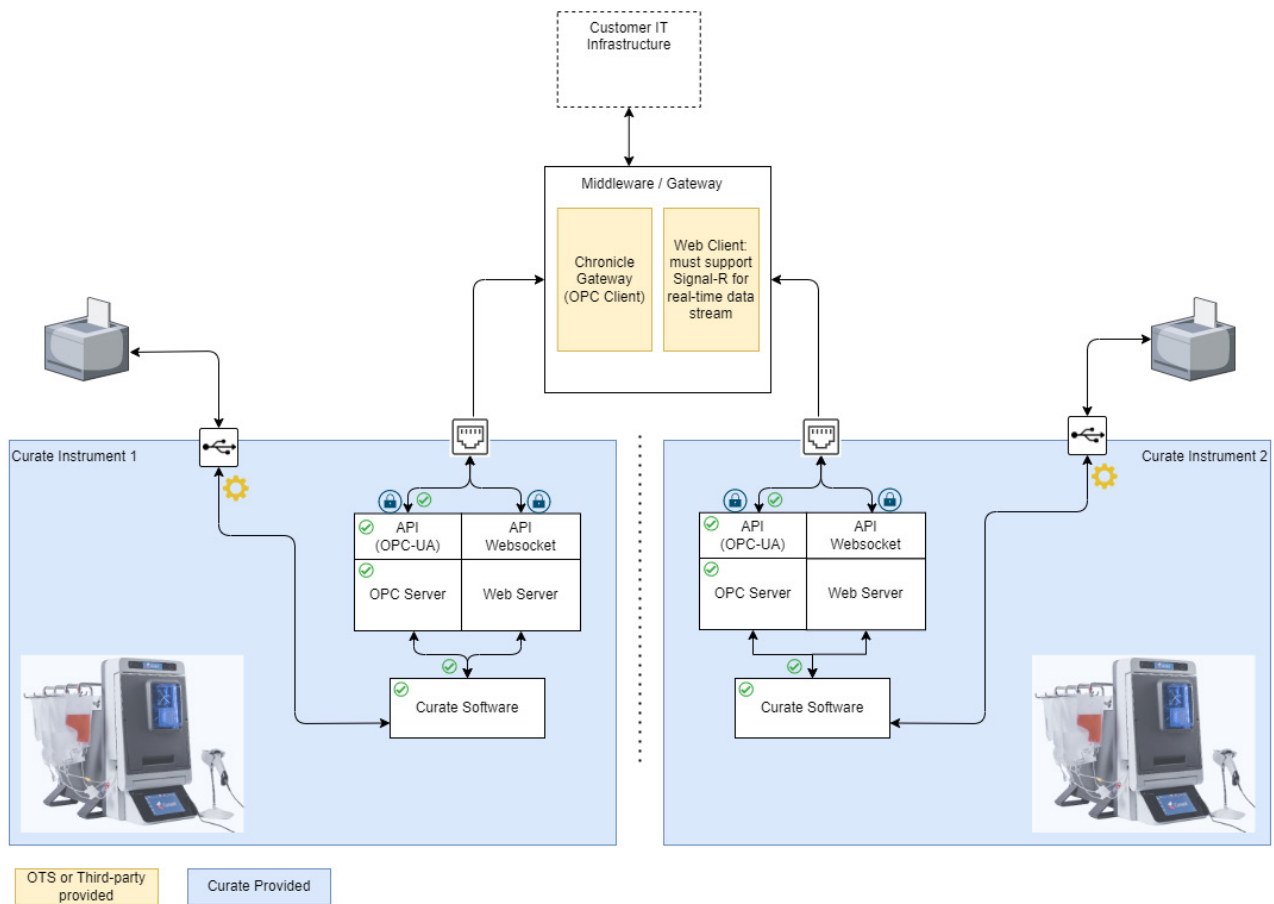
## 7. DATA MANAGEMENT

The Curate system software is designed to ensure the authenticity, integrity, and, as appropriate, the confidentiality of electronic records from the point of their creation by the software to the to the point of their receipt. All user data entry, selection, and controls are tracked and traced in compliance with 21-CFR-11 and are encrypted via TLS 1.2 encryption.

Designed to reside behind a firewall, the system collects time stamped status and any error codes for all parameters every 0.1 seconds, allowing for high resolution monitoring. The system has a 12 GB local hard drive capable of storing several years of data, however, it is highly recommended that all collected data be archived regularly. To facilitate network access and to support modern device gateways, the system uses an Ethernet connection to support both web API and OPC/UA in a unidirectional manner (Curate to gateway). In addition, the system supports secure FTP (sFTP) data transfer. Data transfer and connections for peripheral devices via USB 3.0 is also supported (three ports at the rear, and three ports at the front of the system). During an on-site service call a Curate Bioscience Tech Support Technician will require access to the system via a USB and Ethernet connection.

To obtain more specific information on connectivity to data-secure access to internal systems using these interfaces, please contact [techsupport@curatebio.com](mailto:techsupport@curatebio.com).

Figure 43. General network architecture, using Chronicle as the OPC client example



## 7.1. STORAGE

The system stores several types of exportable data including proprietary raw run data logs as .csv and run reports as PDF format files.

Logs are stored as proprietary \_Usr.curate files. They contain all sensor data, stored every 1 second, as well as the run mode, QR bar-code IDs, and errors.

For user run data, the system creates PDF reports (see “Reports Screen” on page 29 for more details).

The system hard drive can retain at least a year of data generated by the system. This data includes:

- Raw data files
- Run data
- Logs

Run records are maintained as a copy of the original file, which cannot be over-written and contain all the information necessary to reconstruct an entire run with all conditions that may have affected the run.

Run file data is appended to a file during a run to ensure rapid response in situations where an emergency stop is initiated and such that none of the data collected prior to the emergency stop is at risk of loss.

## 7.2. PRINTING

To print reports, users must export reports to an external USB drive and then print from the USB drive using a computer connected to a printer.

## 7.3. DATA TRANSFER

Transferring data, such as reports, to other devices, such as the user’s computer or a network server, must be done using an external USB drive. Users can export data from the instrument to a specific USB drive by inserting the USB drive into the instrument’s USB port, navigating to **Settings>Data** screen, and then selecting the USB drive as the **Default Export Location**.

See section “Setting Data Export and Import Locations” on page 34 for detailed instruction on exporting data.

**NOTE: Batch records are preserved as individual PDFs with associated edit protection and document signature security.**

## 7.4. SAMPLE ID TRACEABILITY

Full traceability and association of all Curate Bioscience provided consumables, operator, system, and metrics for each run are secured by use of 2D QR code data linkage to system data logging information.



### IMPORTANT!

It is the user’s responsibility to implement a data management process that traces and records the user’s original sample ID to the Curate Sample bag QR code ID.

Before loading the instrument and starting a sample run, all bags and the cassette are labeled with Curate QR code labels (see “Bags and Corresponding Curate QR Code Labels” on page 74) with a unique QR code for each bag. As each bag’s label is scanned during the instrument loading process, the QR code is automatically recorded along with all other processing data associated with the sample run. The user’s sample ID can then be traced to the Sample bag QR code, which is also displayed as the Sample ID in the Sample Run Report (see Figure 44).



Figure 44. Example of Curate System Run Report PDF with the Sample ID highlighted and displaying the unique Sample Bar code ID for the Sample bag

## Curate System Run Report



[1] Prime: YELLOW, Wash: RED, Flush: BLUE

## 7.5. RESULTS FILES

Results generated files are export-only files and are not sharable between instruments. The results data files are divided into these categories:

- **Run Summary report:** The Run Summary report file is auto-generated as a locked PDF (edits not permissible) at the end of the run. Each PDF file is timestamped, and marked with the instrument serial number and the operator name at the time of creation. Users can export this report as a PDF to an external USB drive. Please contact Curate Biosciences technical support for more information about network access for the system.
- **Run Raw log:** The Run Raw log is auto-generated as a .curate file during the run. The .curate file is a binary formatted file that contains an encrypted and compressed version of the raw log data which is in .csv format. Each .curate file is timestamped, and marked with the instrument serial number and the operator name at the time of creation. The .curate file is encrypted and can only be exported by users with export privileges.
- **Daily Log:** The Daily Log is auto-generated as a PDF file on each calendar day. Each day's PDF file tracks user activities on the Curate system. The Daily Log can be exported by users with export privileges and is overwritten at the end of the day.
- **Calibration Log:** The Calibration Log is auto-generated as a .csv file, storing the Curate system's prior hanger calibration results. The Calibration Log can be exported by users with export privileges.

## 7.6. SCRIPTS

Scripts are series of defined action sequences to be executed during a run and are stored in a password protected database file (.db). The database file can only be imported from an external USB drive by administrators and engineer users. The .db file format ensures authenticity, and integrity of the generated data. Password protection ensures that only the Curate software, and the service app can access the database.

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## 8. PERFORMING A SYSTEM TEST

The system test mode allows the user to qualify the instrument throughout the full range of the instrument's capability. The process for preparing a system test is the same as that for running a sample, except that the test is performed using 0.9% saline or Plasma-Lyte A in all relevant bags (instead of run buffer and a biological sample). Similar to a standard run process, the software guides users through the entire system test protocol. A test report showing performance metrics is generated and saved upon completion. This test and report are designed for the Incoming quality and operational quality purposes.

### 8.1. PREPARING THE SYSTEM TEST CASSETTE

**Table 9. Recommendations for system test run**

Item	Recommended bag	Vendor	Part Number
Priming Solution	Sodium chloride 0.9% Injection USP, 250 ml IV	VWR (or equivalent)	95037-774
Run Buffer	Plasma-Lyte A Injection, pH 7.4, 1000 ml	VWR (or equivalent)	80089-818
Diluent	Sodium chloride 0.9% Injection USP, 250 ml IV	VWR (or equivalent)	95037-774
Sample	Sodium chloride 0.9% Injection USP, 250 ml IV	VWR (or equivalent)	95037-774
Waste	EXP-PAK™ Cell Expansion Bio-Container 1L	Charter Medical	EXP-1L
Product	EXP-PAK™ Cell Expansion Bio-Container, 500 ml	Charter Medical	EXP-500

1. Prepare the priming solution using the method described in “Preparing Priming Solution” on page 68.
2. Prepare the cassette by following the method described in “Connecting Bags to the Cassette” on page 72.

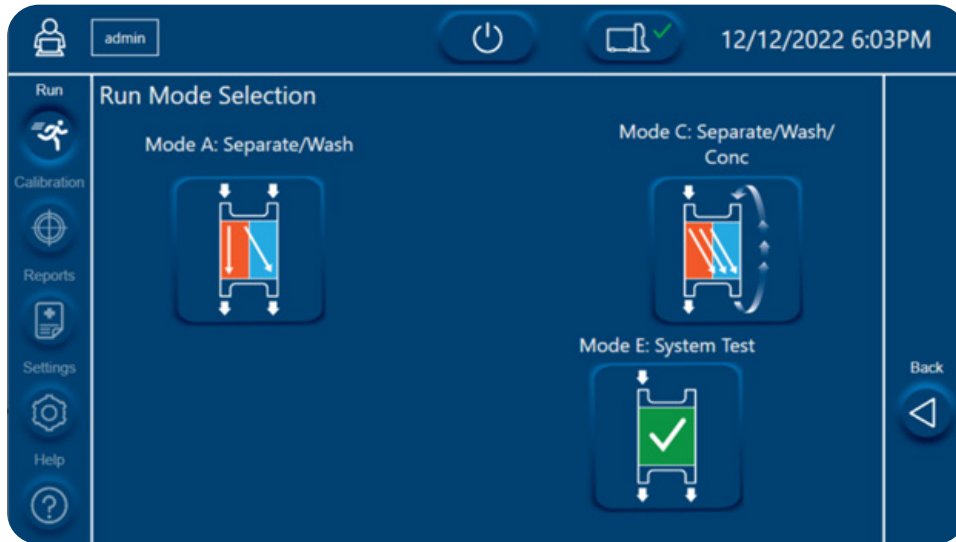
Use the recommended reagent, product, and waste bags listed in Table 9.

**NOTE: A biological sample is not used during a system test run. 250 ml 0.9% saline and 1,000 ml PlasmaLyte-A bags are used for the sample and run buffer, respectively.**

## 8.2. PERFORMING THE SYSTEM TEST RUN

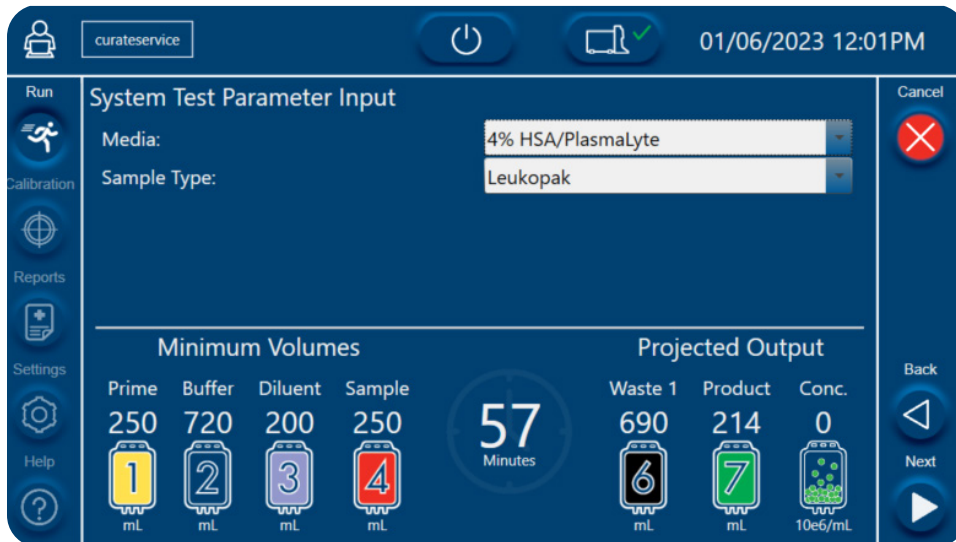
1. In the **Run Mode Selection** screen, press the **Mode E: System Test** icon

Figure 45. Run Mode Selection screen, showing the System Test icon



2. Confirm that the attached bags contain the minimum volumes shown in Figure 46 and press the **Next** button.

Figure 46. System Test Parameter Input screen

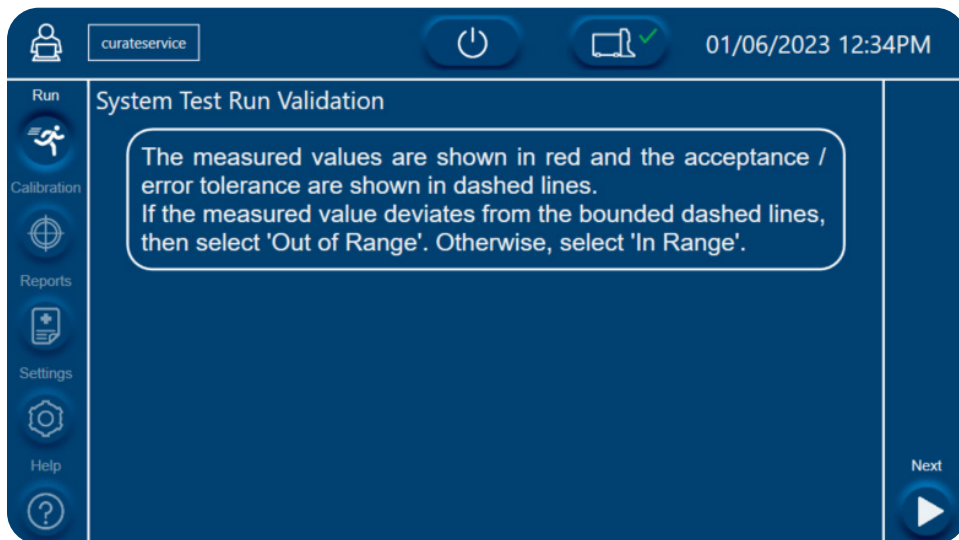


**NOTE: You cannot change the values for the Media or Sample Type for the system test.**

3. Proceed with the accessioning process using the method shown in “Starting the Protocol” on page 84. Once the System Test run is complete, the indicator lights will change to solid white to indicate that the run is complete.

4. Press **Next** to review the System Test Run Validation screens, showing the measured Flow Rate and Pressure Sensor readings.

Figure 47. System Test Run Validation screen



5. Evaluate the flow rate and pressure validation screens. For each screen, if the measured value (red line) deviated from the bounded, dashed lines, then select **Out of Range**. Otherwise, select **In Range**. Use the **Next** button to advance through all the validation screens.

Figure 48. PRIME Flow Rate Validation screen

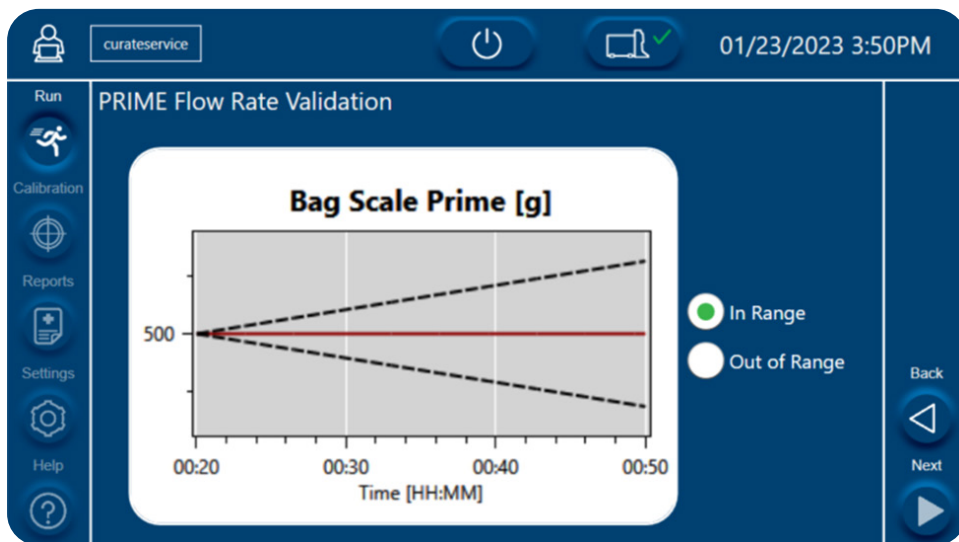


Figure 49. Buffer Flow Rate Validation screen

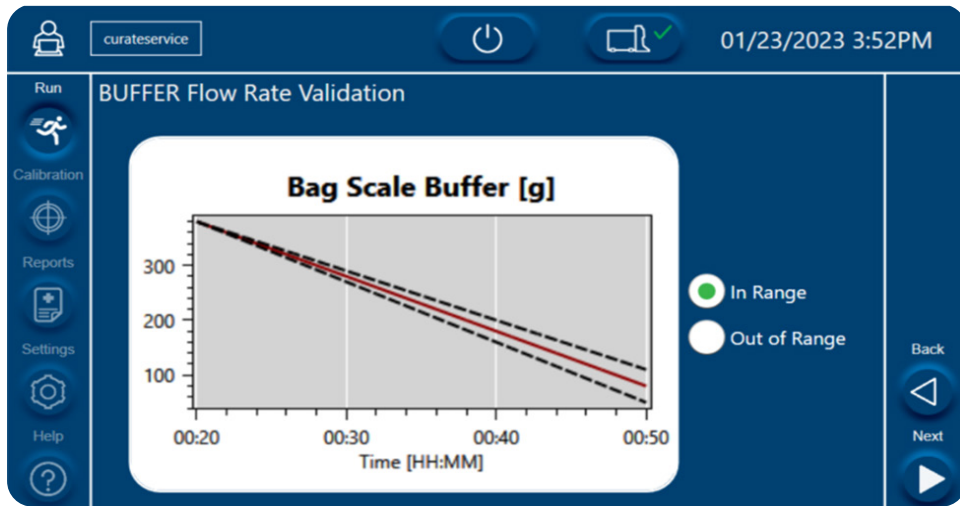


Figure 50. Diluent Flow Rate Validation screen

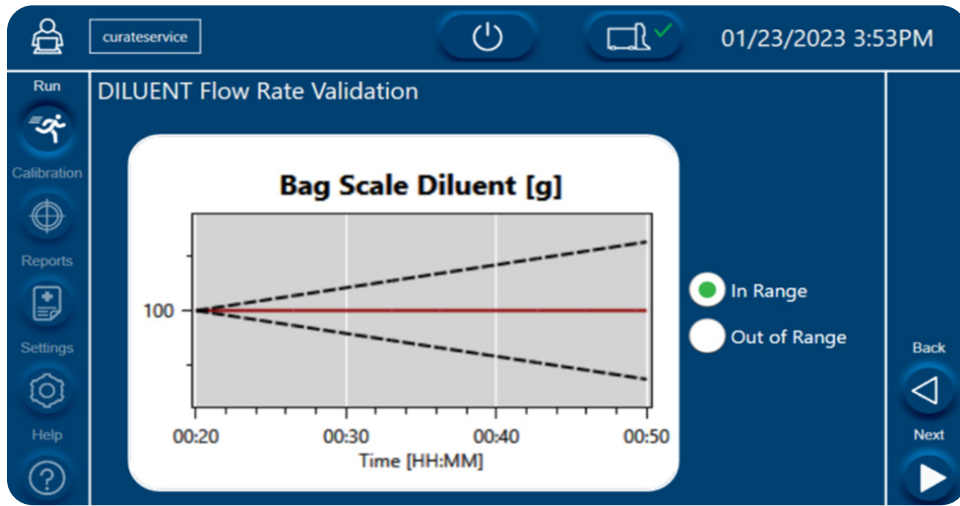


Figure 51. SAMPLE Flow Rate Validation screen

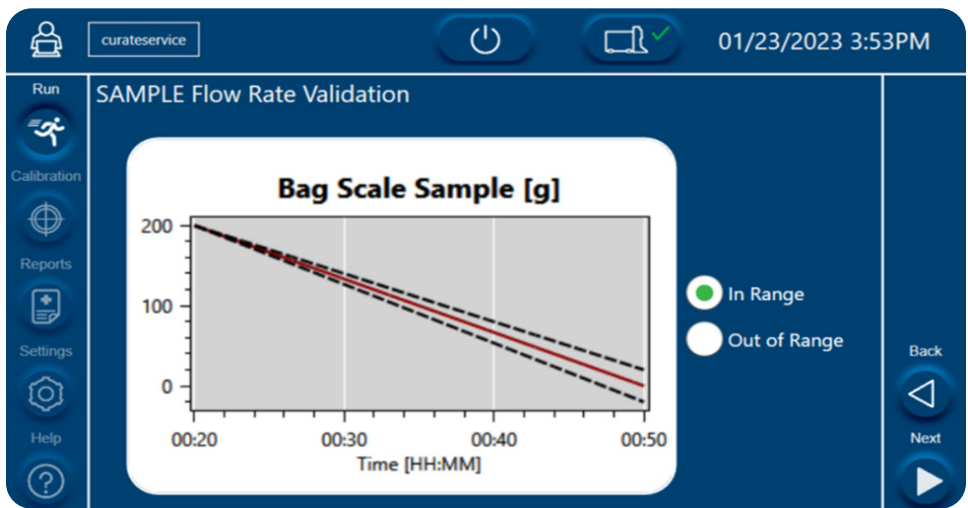


Figure 52. Waste Flow Rate Validation screen

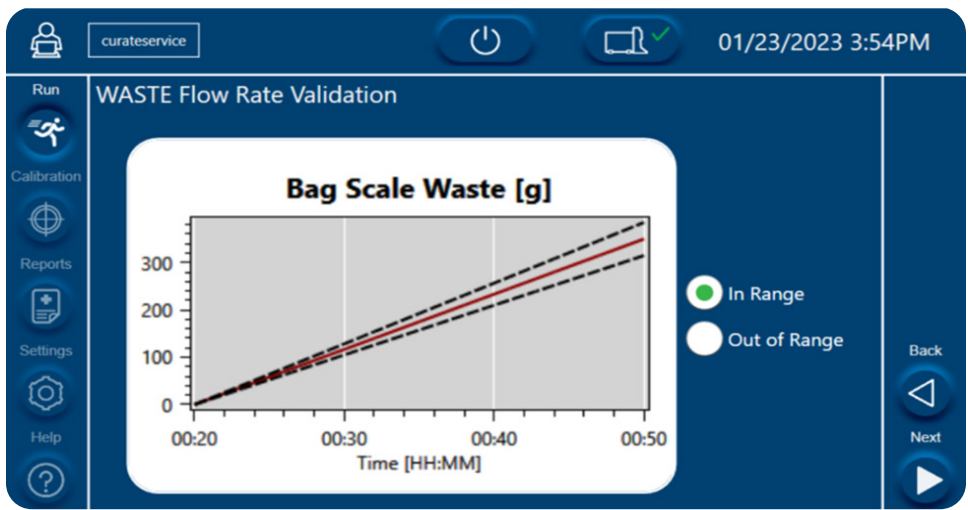


Figure 53. Product Flow Rate Validation screen

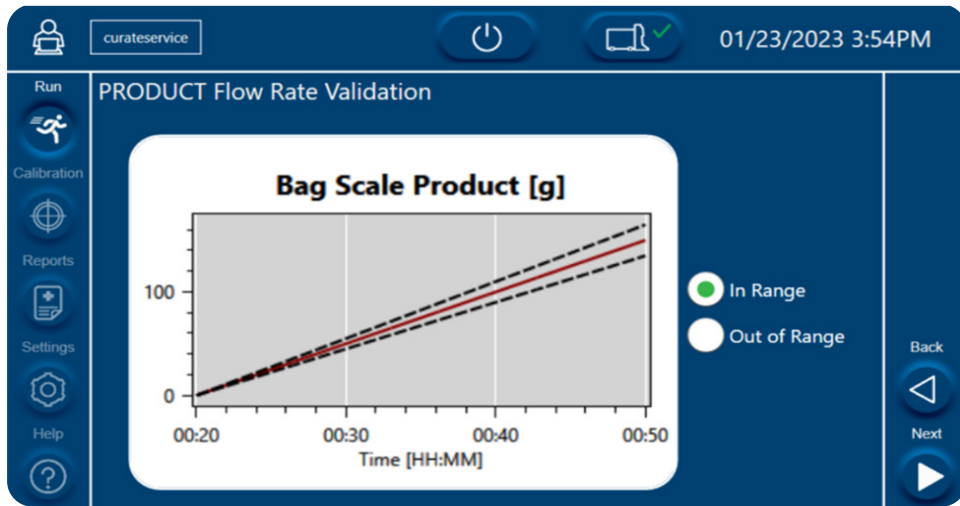


Figure 54. Pressure 1 Validation screen

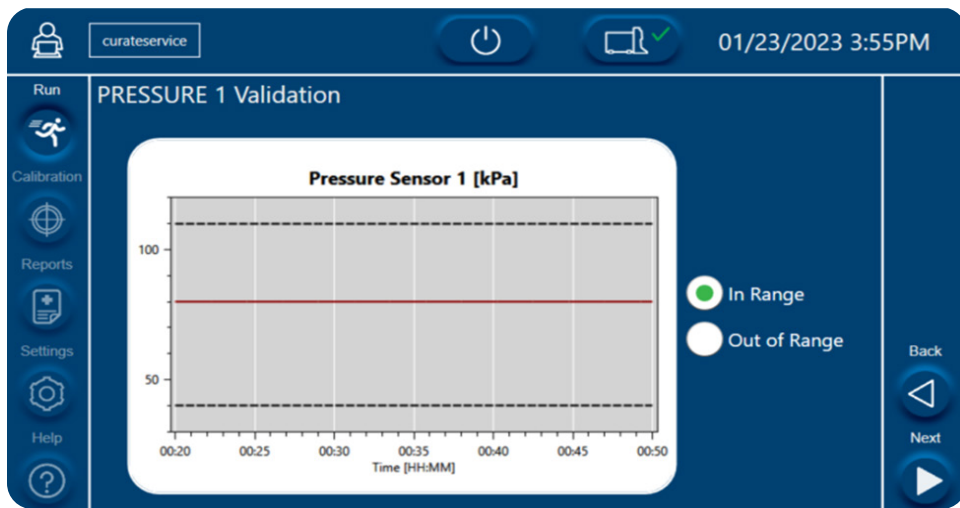
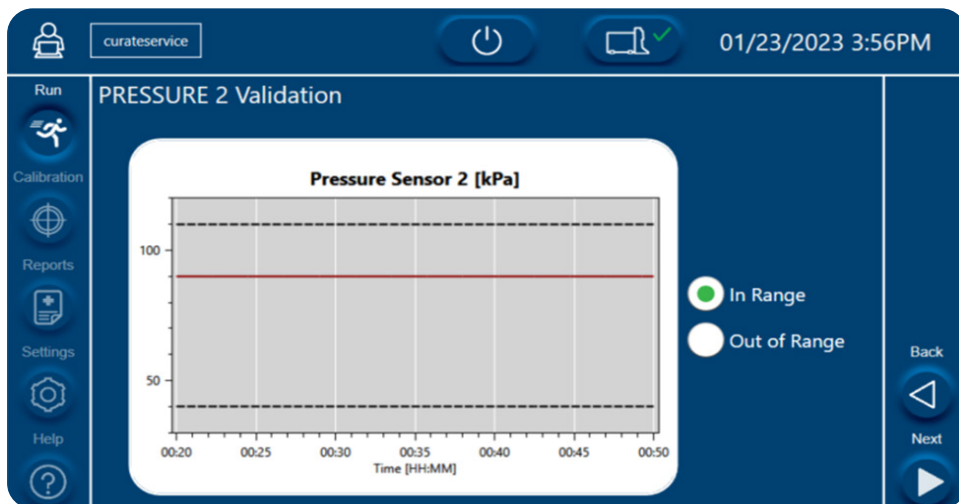


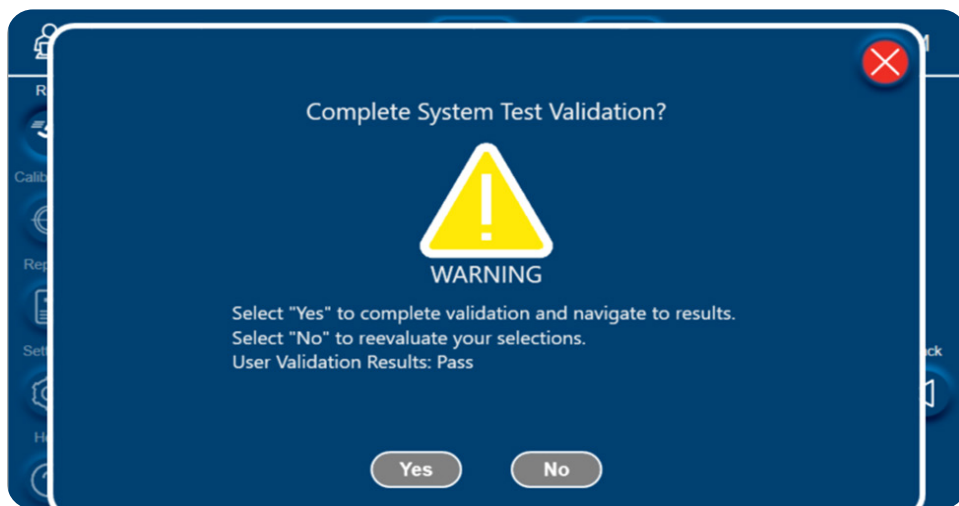


Figure 55. Pressure 2 Validation screen



- When you reach the **Complete System Test Validation** prompt, select **Yes** to confirm your validation and complete the system test validation. Select **No** if you want to re-evaluate the validations.

Figure 56. System test completion prompt



- View and export the **System Test Results Summary**.

Figure 57. System Test Run Results Summary

System Test Run Results Summary			
Operator:	curateservice	Run Duration:	00:00:07
Run Type:	Mode E:	Product FlowRate:	Pass
	System Test	Pressure 1:	Pass
Prime FlowRate:	Pass	Pressure 2:	Pass
Buffer FlowRate:	Pass	Results:	Pass
Diluent FlowRate:	Pass	Export Status:	-----
Sample FlowRate:	Pass		
Waste FlowRate:	Pass		

Press next or open door to return to home screen.

Figure 58. System Test Report, page one

## System Test Run Report

<b>Run ID</b>	5	<b>Organization</b>	Cell Therapy Co
<b>Protocol ID</b>	Mode E: System Test	<b>Location Name</b>	
<b>Sample Barcode ID</b>	10999-L60000-L1004-R58265-437001-030032-021031	<b>Location Address</b>	1234 Vector Way
		<b>Location City/State</b>	Genetown, CA

### Run Information

<b>Operator</b>	Admin	<b>Run Status</b>	Pass
<b>Curate SN</b>	2235-003	<b>Start Time</b>	1/23/2023 1:23:22 PM
<b>Software Version</b>	V01.07.000_c9340fbc	<b>End Time</b>	1/23/2023 2:34:51 PM
		<b>Time Zone</b>	(UTC-08:00) Pacific Time (US & Canada)
<b>Protocol Description</b>	System Test		

### Results and Estimations

<b>Prime FlowRate [mL/hr]</b>	0.0	<b>Sample FlowRate [mL/hr]</b>	-600.0
<b>Buffer FlowRate [mL/hr]</b>	-900.0	<b>Waste FlowRate [mL/hr]</b>	1050.0
<b>Diluent FlowRate [mL/hr]</b>	0.0	<b>Product FlowRate [mL/hr]</b>	450.0
<b>Pressure Range [kPa]</b>	(75.0, 125.0)		
<b>Total Procedure Duration (HH:MM:SS)</b>	01:11:29		

### Performance Metrics

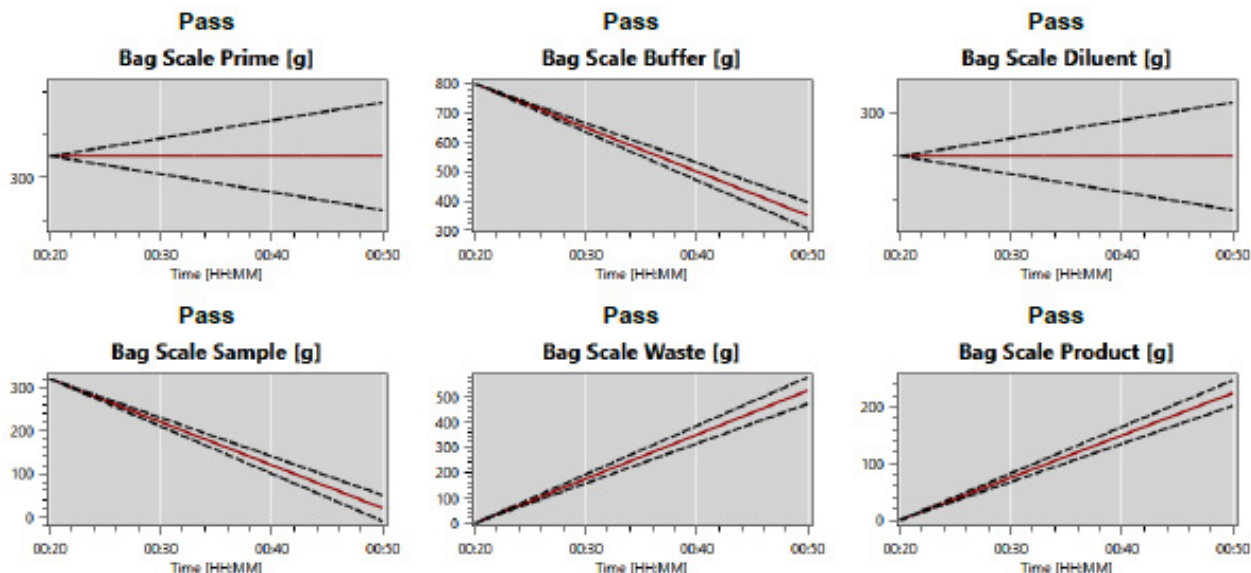
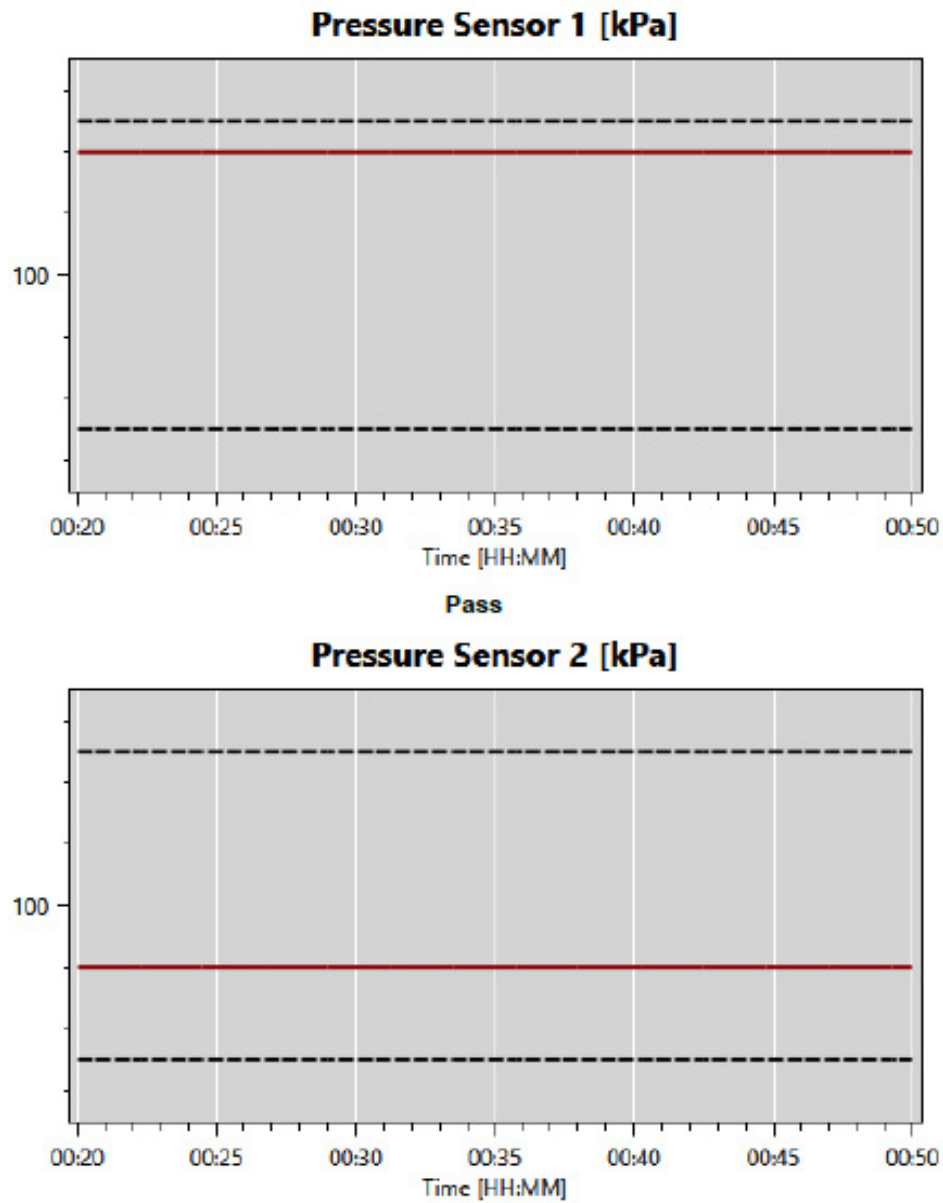


Figure 59. System Test Report, page two



## 9. LEUKOPAK COLLECTION AND HANDLING

The Curate Cell Processing System has been validated with leukopaks that have been primarily collected using Spectra Optia® and then processed within 24 hrs of collection. Additionally, the leukopak must be treated with additional sodium citrate, as described in this section, within 60 minutes of collection. Be sure your collection site is aware of these requirements.

The brief summary described in this section outlines the general, hands-on process only and does not reflect any modifications that may be required by your institution. Further, it assumes that the person performing the tasks has had appropriate bio-safety and aseptic live cell handling training and is wearing the appropriate equipment (PPE) in an appropriate workspace.

Please contact your local sales representative or Curate Biosciences techsupport@curatebio.com to obtain the leukopak collection and handling procedure in full, as a generic and editable standard operating procedure (SOP) document.

### 9.1. SAMPLE COLLECTION PREREQUISITES

To reduce sample degradation and cell death during transit, Curate Biosciences has determined that leukopaks should be collected with additional sodium citrate (4%) to ensure that the samples can be effectively processed using high performance microfluidic deterministic cell separation.

#### 9.1.1 Post-MNC or CMNC Apheresis Citrate Addition Instructions

After the completion of the mononuclear (MNC) or continuous mononuclear (CMNC) apheresis collection, an additional bolus of sodium citrate anticoagulant must be added to the product bag according to the instructions summarized here.

##### **Bolus requirements:**

- 1.0 ml of 4% sodium citrate solution per 10.0 ml of final leukopak product weight
- 50 cc syringe
- 70% ethanol
- Luer connection (recommended)

##### **Procedure for adding sodium citrate:**



##### **IMPORTANT!**

This procedure must be performed under aseptic conditions and within 60 minutes of collection.

1. Wipe and spray sterilize a bio-safety hood with 70% ethanol.
2. Place syringes/needles as needed inside the hood.  
A 50 cc syringe is recommended to avoid multiple additions.
3. Weigh the leukopak product to determine the amount of sodium citrate to add.
4. Record the initial weight on the product bag.
5. Use ethanol wipes to wipe and directly transfer the product bag and the sodium citrate bag into the bio-safety hood

without touching any other objects.

6. Aspirate the required volume of sterile sodium citrate.
  - a. Use 1.0 ml of 4% sodium citrate per 10.0 ml of leukopak product weight.
  - b. Record the volume of 4% sodium citrate.
7. Re-wipe the leukopak bag access port with 70% alcohol and inject the sodium citrate into the product bag.
8. Mix the leukopak bag by inverting it three times.
9. Seal the port and dispose of sharps.
10. Wipe the leukopak bag port and protect, as appropriate.
11. Remove the product bag from the bio-safety hood, reweigh it and record the final weight and time of the addition.

### **9.1.2 Shipping and Storage Requirements for Leukopaks**

1. Pack and ship at 2–8 °C on an insulated cold pack, or using some other temperature-controlled shipping method, with appropriate spill protection.
  2. If overnight storage is necessary, store at 2–8 °C on a rocking and waving shaker equipped with a wire rack to maximize gas exchange at 2–8 °C.
  3. Do not exceed 24 hours from the time of the collection to the completion of processing.
-

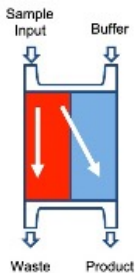
# 10. RUNNING THE SYSTEM

## 10.1. GENERAL OVERVIEW

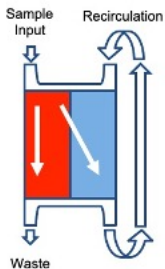
Prior to running biological samples for the first time, the system should be calibrated and have a system test performed to ensure that it has been installed properly (Installment Qualification (IQ)). To confirm full operational function (Operational Qualification (OQ)), see “Performing a System Test” on page 51 for a description of a test routine processing liquids.

### 10.1.1 Modes of Operation

The Curate system can perform two different sample processing functions, improving cell yields and quality across the cell manufacturing workflow, and also supports a self-test routine to support system validation.



**Separation and Wash** – Gentle separation of cells based on size, while operating under laminar flow conditions, producing two fluid streams: one with larger cells that have passed into a clean buffer, and the other with smaller cells retained in the original sample matrix. The size-determined lateral movement of cells or particles directly into a parallel second fluid stream of clean buffer results in efficient washing and with no physical “dead” volume or possibility for carry-over.



**Separation and Wash plus Concentration** – By recirculating the desired cells in the same microfluidic device, the system can concentrate the cells into a defined output volume of clean buffer fluid. This recirculation occurs in parallel to the cell separation, enabling collection of the product cells in clean buffer, and in a specified volume. This process does not affect the run time as the operation takes place in parallel.



**System Test** – This mode allows the user to perform a system test without the need to consume a leukopak. The routine proceeds through all steps of a normal run while assessing all system functions. All sensors are monitored throughout the run to confirm proper performance of both the subsystems as well as the unit as a whole. In addition, at the end of the run, the user is shown the relevant sensor data as well as the boundaries of expected performance and is directed to step through each test to determine a pass/fail. The system test generates both a user-friendly and detailed technical report that may be required by the user to assist in technical support calls.

### 10.1.2 Sample Processing Workflow Overview

1. Prepare the Priming Solution.  
See “Preparing Priming Solution” on page 68.
2. Prepare the bags.  
See “Bags and Fluids Needed for System Run” on page 71.
3. Pretreat the Leukopak sample.  
See “Sample Pretreatment” on page 66.

**NOTE: Place the Leukopak sample on a rocker if preparation steps 1 and 2 were not completed before pretreatment of the Leukopak sample bag.**


4. Connect the prepared bags to cassette.  
See “Connecting Bags to the Cassette” on page 72.
  5. Turn the Curate system on.  
See “Starting the Instrument and Software” on page 65.
  6. Run the protocol.
    - a. “Starting the Protocol” on page 84.
    - b. “Loading the Cassette onto the System” on page 87.
    - c. “Load Verification and Starting the Run” on page 95.
    - d. “Completing the Protocol” on page 100.
-



### 10.1.3 Starting the Instrument and Software

1. Turn on the Curate instrument using the power switch at the rear of the instrument. The instrument does not need to warm up before use.
2. Log in using the touch screen. Logging in will automatically open the Curate GUI dashboard.

Figure 60. Login screen



**NOTE: The system will automatically lock a user out after six incorrect password attempts. The user will be locked out for 30 minutes. Passwords can be reset by the administrator by modifying the user information.**

3. Navigate through the dashboard to start sample run, calibrate instrument, view reports, change settings, or to view the Help content.

# 11. SAMPLE PRETREATMENT

## 11.1. SAMPLE PRETREATMENT

To maximize the performance of the highly efficient microfluidic deterministic cell separation array, a single cell suspension is required. As noted in “Leukopak Collection and Handling” on page 61, even with storage and careful shipment at 2-8 °C, >25% leukocyte loss can still occur during transit. This cell death releases DNA that can cause cells to loosely associate.

To ensure that DNA-cell associations do not impact the robust processing, a DNase pre-treatment protocol is required for optimal recovery and performance benefits. The high efficiency of the Curate system’s intrinsic washing process has shown that, under typical operating modes, there is no detectable DNase activity using a standard 2 hour assay.

Please contact your local sales representative or Curate Biosciences techsupport@curatebio.com to obtain the Sample Pretreatment procedure as a generic and editable standard operating procedure (SOP) document, along with a Microsoft® Excel calculator worksheet.

**IMPORTANT!**

Prior to beginning processing, allow the sample adequate time to achieve room temperature (approx. 15 min. at ambient temperature) while on a rocking and waving shaker equipped with a wire rack).

**Required materials that are not provided**

- Magnesium Chloride
- Benzonase Enzyme

**Prior to entry into a sterile environment:**

1. Confirm and record the volume of the leukopak product to determine the amount of enzyme to add. (Note this may also be done once within the clean environment).
2. Calculate the volume of Magnesium Chloride and Benzonase needed to achieve final concentrations of 7.5 mM and 100 U/ml, respectively. (See the Microsoft® Excel calculator worksheet, available from your Curate sales representative.)
3. Use your institute’s decontamination protocol to ensure appropriate care before entry into a clean environment. Minimally spray the container and leukopak with 70% ethanol and wait one minute before removing contents and transferring through a pass-through window or other approved, clean transfer protocol.

**Once the bag is within the clean environment (i.e. within a suitably specified clean room or within a suitable bio-safety hood):**

1. Assemble all needed fluid transfer materials (reagents, syringes, ports, etc.)
2. Wipe and spray sterilize the bag in preparation for the addition of enzyme.
3. Add required volumes through an appropriate fluid port using a syringe/Luer.
4. Mix bag by inversion 3 times.
5. Record the volumes added.
6. Add the weights of the leukopak product, and Magnesium Chloride. Record this value.

**NOTE:** The sum of all fluid additions plus the initial sample volume are used as the input sample volume for data entry during the Curate run. The system will automatically subtract an average bag weight from the total bag mass to verify the loaded sample volume.

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## 12. PROCESSING A SAMPLE



### IMPORTANT!

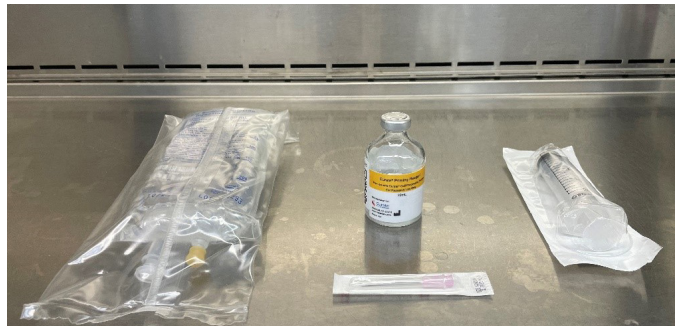
Use proper aseptic techniques throughout the entire Curate process, including but not limited to, preparation of the sample, running the sample on the Curate system, collecting the product, and the proper disposal of waste and the entire cassette assembly at end of run.

### 12.1. PREPARING PRIMING SOLUTION

The Curate cassette must be primed before processing a biological sample. The priming process ensures removal of all air from the fluid path and prepares the system to receive the sample.

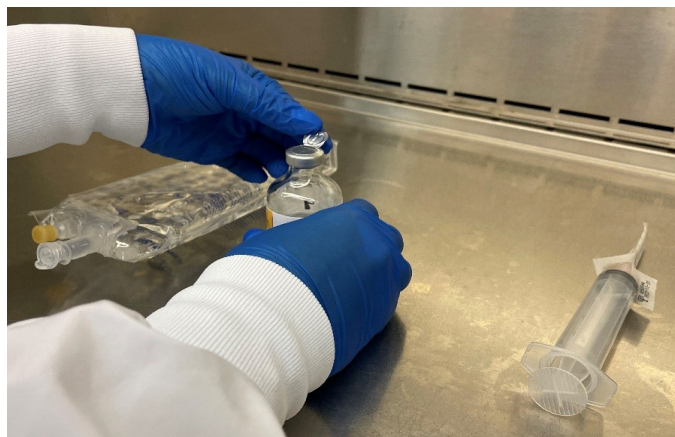
1. Use your institute's decontamination protocol to ensure appropriate care before entry into a clean environment. Minimally spray the Curate priming reagent bottle, 250 ml 0.9% saline bag and other necessary materials with 70% ethanol and wait one minute before transferring items into a laminar flow hood/clean room area.
2. Gently mix the Curate priming reagent by inverting the vial three times. DO NOT shake the vial.

Figure 61. Curate priming reagent vial with a 20 cc syringe, a 1" needle and a 250 ml 0.9% saline bag



3. Carefully lift the center disk of the aluminum crimp seal to expose the septum.

Figure 62. Exposing the septum



4. Using a 20 cc syringe and a 1" sterile needle (18–24 gauge), pierce the rubber septum.

5. With the needle still inside the bottle, slowly turn the bottle upside down and adjust the end of the needle so its tip is immersed within the liquid.
6. Pull back the syringe stopper and withdraw 15 ml of the Curate priming reagent.

*Figure 63. Drawing the Curate priming reagent into the syringe*



7. Wipe the 250 ml 0.9% saline bag's injection port with 70% ethanol.
8. Inject 15 ml of the Curate priming reagent into the bag.

*Figure 64. Adding the Curate priming reagent to the saline*

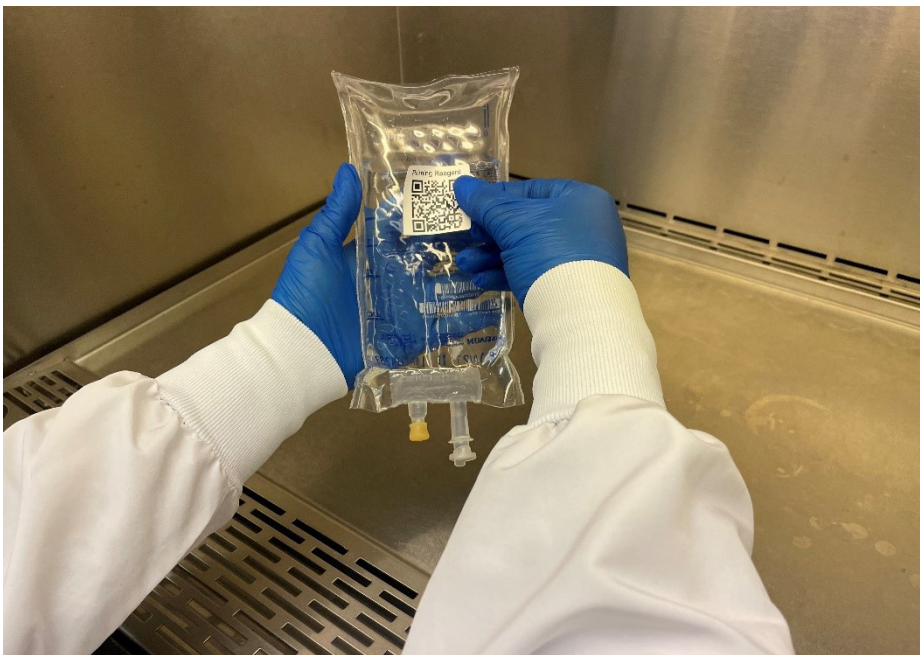


9. Invert the bag three times to ensure proper mixing of the priming solution. DO NOT shake the bag. After mixing, the solution should look clear and colorless.
10. Transfer the peel-off Curate QR code label on the Curate priming reagent bottle to the priming solution bag.

Figure 65. Removing the label



Figure 66. Adding the label to the saline bag



## 12.2. BAGS AND FLUIDS NEEDED FOR SYSTEM RUN

### Requirements:

- 250 ml priming solution (0.9% saline containing 0.5% F-127, a non-ionic copolymeric surfactant) bag with spike port.
- 1000 ml run buffer (Plasma-Lyte containing 4% HSA) bag with a spike port.
- 250 ml diluent (0.9% saline) bag with a spike port.
- Sample bag with an available spike port for connecting to cassette tubing.
- 1 L waste bag with weld-compatible tubing.
- Product bag with two lengths of weld-compatible tubing for sample collection.
- Curate QR code labels.

### Optional:

- Charter Medical 4" PVC with spike adapter and Luer. Catalog # 03-220-90.

**NOTE: These bags and fluids must be fully prepared before beginning the preparation of the Curate DCS cassette.**

**Table 10. Recommended commercially-available fluids, product, and waste bags**

Item	Recommendation	Vendor	Part Number
Priming solution (For priming reagent)	Sodium chloride 0.9% Injection USP, 250 ml IV	VWR (Or equivalent)	95037-774
Human serum albumin	25% human serum albumin for injection	Grifols (Or equivalent)	N/A
Run buffer	Plasma-Lyte® A Injection, pH 7.4, 1000 ml, (modified to contain 4% Human Serum Albumin (HSA))	VWR (Or equivalent)	80089-818
Diluent	Sodium chloride 0.9% Injection USP, 250 ml IV	VWR (Or equivalent)	95037-774
Sample	Provided by user	N/A	N/A
Waste	EXP-PAK™ Cell Expansion Bio-Container 1L	Charter Medical	EXP-1L
Product, separation, and wash	EXP-PAK™ Cell Expansion Bio-Container 500 ml	Charter Medical	EXP-500
Product, separation and wash plus concentration	Custom VueLife FEP Bag 197-C	Saint Gobain	SGS07422 Rev A



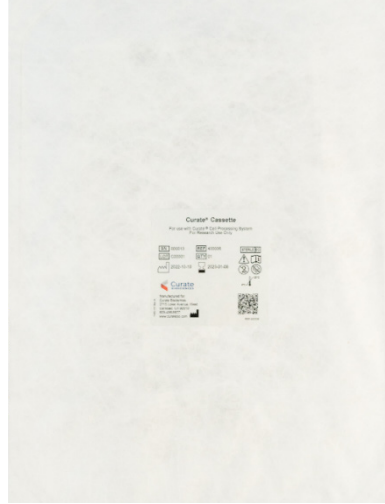
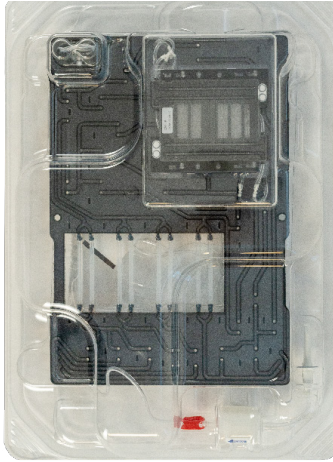
#### Caution!

Use of non-validated bags has been shown to lead to sub-optimal separation quality.

### 12.3. CONNECTING BAGS TO THE CASSETTE

The Curate DCS cassette is provided in a sealed, EO sterilized package.

Figure 67. Curate DCS cassette in a sealed and EO sterilized package



#### 12.3.1 Connection Protocols

There are two protocol options for connecting the bags to the cassette:

- “Protocol A - Using provided Connections (Spike and Sterile Weld)” on page 73
- “Protocol B - Using Sterile Weld Connections Only” on page 79

For all spike connections and additional sampling, it is highly recommended that aseptic procedure is followed under sterile conditions (i.e. in a laminar flow hood).



## 12.4. PROTOCOL A - USING PROVIDED CONNECTIONS (SPIKE AND STERILE WELD)

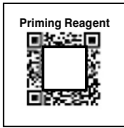






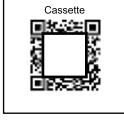
1. When required, record the lot number and use-by-date of the Curate DCS cassette
2. Minimally spray the packaging and fluid bags with 70% ethanol and wait one minute before transferring to a sterile environment.
3. Remove the Tyvek® lid using sterile technique.

Figure 68. Curate DCS cassette packaging tray with the lid removed



4. Before assembling cassette and bags, place all color-coded Curate QR code labels on their corresponding bags. See “Bags and Corresponding Curate QR Code Labels”.

**Table 11. Bags and Corresponding Curate QR Code Labels**

Bag	Curate QR Code Label
Priming Reagent (White) <div style="border: 1px solid black; border-radius: 10px; padding: 2px; display: inline-block; background-color: white;">White</div> (Label is added to priming solution bag)	
Priming Solution (Yellow) <div style="background-color: yellow; border-radius: 10px; padding: 2px; display: inline-block;">Yellow</div>	
Buffer (Blue) <div style="background-color: blue; border-radius: 10px; padding: 2px; display: inline-block; color: white;">Blue</div>	
Diluent (Purple) <div style="background-color: purple; border-radius: 10px; padding: 2px; display: inline-block; color: white;">Purple</div>	
Sample (Red) <div style="background-color: red; border-radius: 10px; padding: 2px; display: inline-block; color: white;">Red</div>	
Waste (Black) <div style="background-color: black; border-radius: 10px; padding: 2px; display: inline-block; color: white;">Black</div>	
Product (Green) <div style="background-color: green; border-radius: 10px; padding: 2px; display: inline-block; color: white;">Green</div>	
Curate Cassette (CLEAR)	

5. Close all seven color-coded clips. If necessary, move the clips away from the spike end to ensure there is enough tubing length remaining for welding.

**IMPORTANT!**

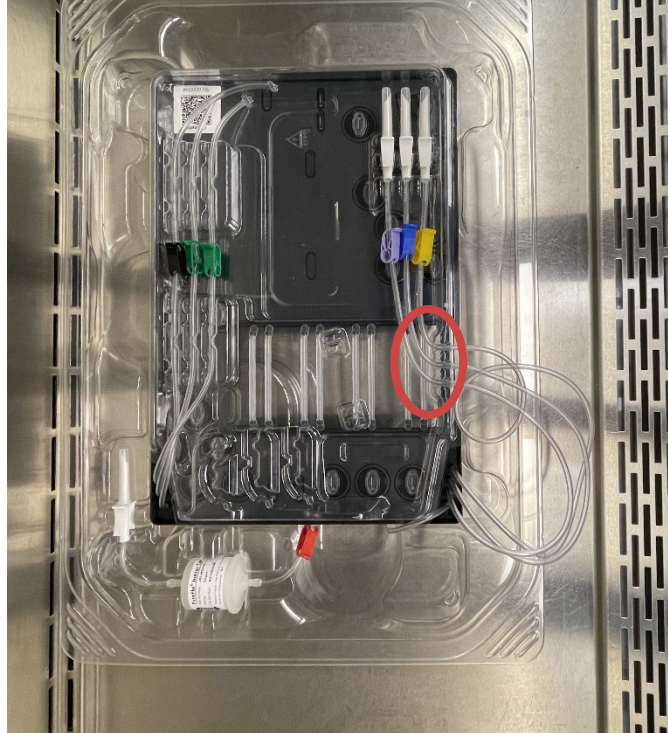
Failure to close the clips will cause improper flow of fluid into cassette, causing a failed process.

Figure 69. Closing the clips



6. Remove the looped tubing from the inner tray's central retention features and secure them to the retention feature on the right side of the tray. This will allow better access to the tubing during loading.

*Figure 70. Purple, blue, and yellow clip tubing removed from the center of the inner tray and secured to the tray's retention features on the right*



**IMPORTANT!**

Proper tube welding is critical for a successful sample run. For Charter Medical bags (product and waste bags), the bag tubing is weldable **ONLY** below the branch, but not above the branch.

Failure to make the correct connections will cause a failed process.

**TIP: Connecting and stacking the bags in the order given in these instructions will facilitate the loading of bags on the Curate instrument.**

7. Remove the tubing with green clips from the tray's retention features. Sterile weld the two tubes marked with green to the product bag with the green Curate QR code label. Place the product bag on top of the cassette.

**IMPORTANT!**

Do not weld the green tubing to product bag's tubing meeting at a Y-junction.

The use of a custom Saint Gobain VueLife 197-C bag is recommended for Curate's Separation and Wash plus Concentration mode of operation. Weld the two Curate cassette tubing with green clips to the two tubing extensions on each side of the bag.

8. Remove the tubing with the black clip from the retention feature and weld to the waste bag with the black Curate QR code label. Place the waste bag on top of the cassette.
9. Remove the in-line filter by lifting the filter from the top and bottom ends and remove the attached spike from its retention snap.

**WARNING!**

Do not pull the tubing to release the in-line filter or spike from their retention features.

When the cassette and bags are correctly assembled, the pre-filter should be between the sample bag and the cassette. The filter should be within 10 cm of the sample bag.

Figure 71. In-line filter lifted from the retention snap



10. Connect the sample tubing (red clip and in-line filter) to the sample bag (red Curate QR code label) by using the sterile spike at the end the cassette tubing and a spike port on the sample bag.
11. Place the connected sample bag on top of the cassette.
12. Remove the diluent spiked tubing with the purple clip from the retention feature.
13. Connect the diluent tubing (purple clip) to the diluent bag (purple Curate QR code label) using the sterile spike at the end of the cassette tubing and a spike port on the diluent bag.
14. Place the diluent bag on top of the cassette.
15. Remove the run buffer spiked tubing with the blue clip from the retention feature.
16. Connect the run buffer tubing (blue clip) to the run buffer bag (blue Curate QR code label) using the sterile spike at the end of the cassette tubing and spike port on the run buffer bag.
17. Place the run buffer bag on top of the cassette.
18. Remove the priming solution spiked tubing with the yellow clip from the retention feature.
19. Connect the priming solution tubing (yellow clip) to the priming solution bag (yellow and clear Curate QR code labels) using the sterile spike at the end of the cassette tubing and the spike port on the priming solution bag.
20. Place the priming solution bag on top of the cassette.
21. Release the tubing from the tray's right hand side retention features.
22. The cassette is now ready for use. Carry the tray with the bags on top to the Curate instrument.

The bags should now be in the correct order on the cassette. Correct bag stacking order facilitates accessioning and loading.

Figure 72. Tray with bags



## 12.5. PROTOCOL B - USING STERILE WELD CONNECTIONS ONLY

1. When required, record the lot number and use-by-date of the Curate DCS cassette.
2. Place the cassette into a sterile environment.
3. Remove the Tyvek® lid using sterile technique.

Figure 73. Curate DCS Cassette packaging tray with lid removed



4. Before assembling cassette and bags, place all color-coded Curate QR code labels on their corresponding bags. See “Bags and Corresponding Curate QR Code Labels” on page 74.
5. Close all seven color-coded clips. If necessary, move the clips away from the spike end to ensure there is enough tubing length remaining for sterile welding.



### IMPORTANT!

Failure to close the clips will cause improper flow of fluid into cassette, causing a failed process.

Figure 74. Closing the clips



6. Use a sterile tubing sealer to seal the red, purple, blue, and yellow cassette tubing immediately below the attached spikes, and detach the sealed-off spikes from the cassette tubing.

You may detach the sealed-off spikes by pulling the sealed-off sections apart.



**WARNING!**

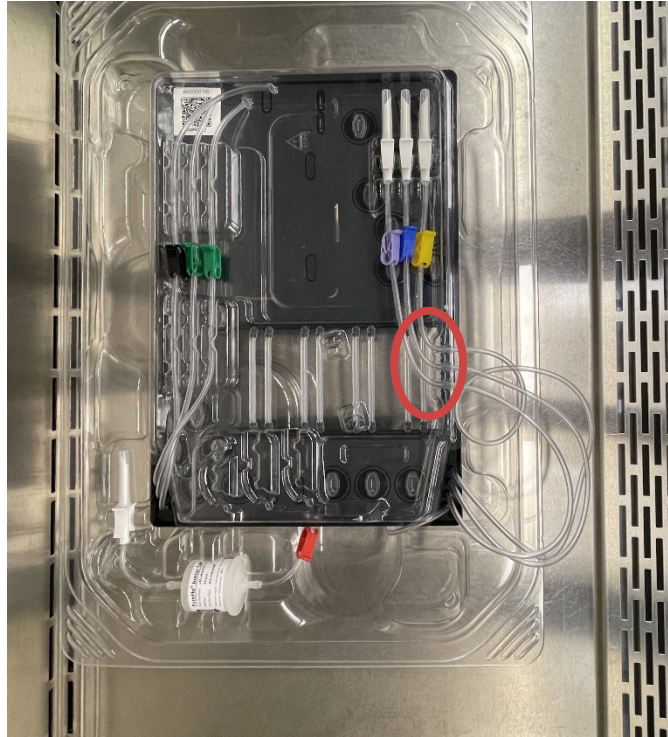
Always remove (or seal off) ALL spikes immediately below the spike. Shortening and/or lengthening the cassette tubing during the welding process will result in a failure.

Removing (or sealing off) the color-coded clips or the inline filter will result in a failure.

7. Spike the diluent bag and the prepared priming solution and run buffer bags using a sterile spike and tubing adapter (e.g. Charter Medical Catalog #03-220-90).
8. Once all cassette tubing has been sterile sealed, you may remove the packaging tray and cassette from the sterile environment. All bags will be sterile welded to the Curate DCS cassette.
9. Remove the looped tubing from the inner tray's central retention features and secure them to the retention feature on the right side of the tray. This will allow better access during loading.



Figure 75. Purple, blue, and yellow looped tubing removed from the center of the inner tray and secured to the tray's retention features (highlighted) on the right



**IMPORTANT!**

Proper tube welding is critical for a successful sample run. For Charter Medical bags (product and waste bags), the bag tubing is weldable **ONLY** below the branch, but not above the branch.

Failure to make the correct connections will cause a failed process.

**TIP:** Connecting bags in the order outlined in these instructions will facilitate the loading of bags on the Curate instrument.

10. Remove the tubing with green clips from the tray's retention features. Sterile weld the two tubes marked with green to the product bag with the green Curate QR code label. Place the product bag on top of the cassette.



**IMPORTANT!**

Do not weld the green tubing to product bag's tubing meeting at a Y-junction.

The use of a custom Saint Gobain VueLife 197-C bag is recommended for Curate's Separation and Wash plus Concentration mode of operation. Weld the two Curate Cassette tubing with green clips to the two tubing extensions on each side of the bag.

11. Remove the tubing with the black clip from the retention feature and weld to the waste bag with the black Curate QR code label. Place the waste bag on top of the cassette.
12. Remove the in-line filter from the retention features by lifting the filter from the top and bottom ends.



**WARNING!**

Do not pull the tubing to release the in-line filter. This will result in a failure.

Figure 76. In-line filter lifted from the retention snap



13. Weld the sample bag tubing to the stub of cassette tubing (red clip) that remains above the filter (where you removed the spike) and place the sample bag on top of the cassette.

When welded correctly, the filter should be within 10 cm of the bag.



**WARNING!**

Sealing-off and/or detaching the inline filter when sterile welding cassette tubing (red clip) to sample bag tubing (red Curate QR code label) will result in a failure.

Welding the cassette tubing to the wrong portion of the tubing will result in a failure.

Figure 77. Correct attachment of the in-line filter



14. Remove the diluent tubing (purple clip) from the retention feature and sterile weld to the diluent bag (purple Curate QR code label). Place the diluent bag on top of the cassette.
15. Remove the run buffer tubing (blue clip) from the retention feature and sterile weld to the run buffer bag (blue Curate QR code label). Place the run buffer bag on top of the cassette.
16. Remove the priming solution tubing (yellow clip) from the retention feature and sterile weld to the prepared priming solution bag (yellow and clear Curate QR code label). Place the priming solution bag on top of the cassette.
17. Release the tubing from the tray's right hand side retention features.
18. The cassette is now ready for use. Carry the tray with the bags on top to the Curate instrument. Bag stacking order corresponds with bag accessioning and loading order.

Figure 78. Fully assembled tray with bags located in the bag organizer



## 12.6. STARTING THE PROTOCOL

1. Transport the cassette with the connected bags to the instrument. Log into the Curate system as described in “Login” on page 26.

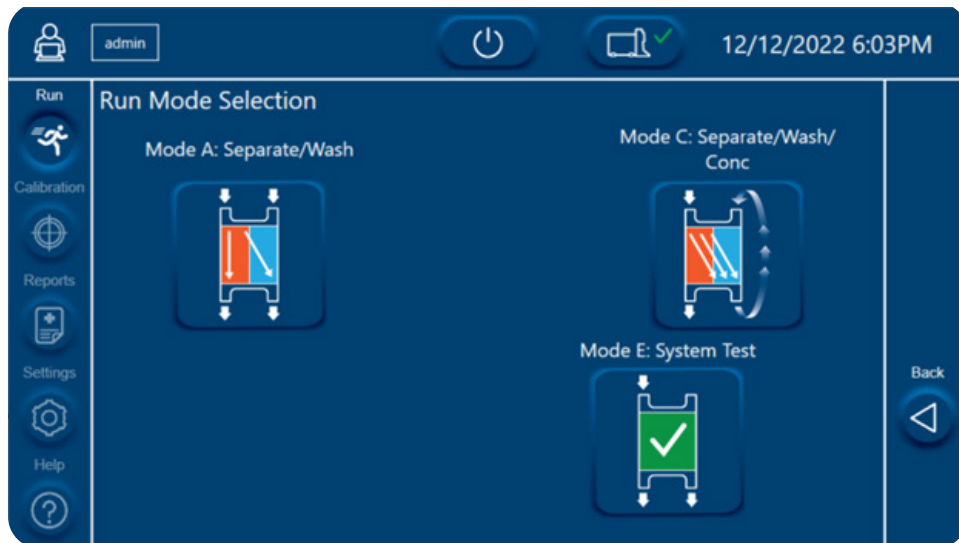


**IMPORTANT!**

Refer to “Operating limits” on page 17 before selecting a run mode. Do not select ‘Mode C: Separation and Wash + Concentration 45 or 100 mL’ if the input sample’s total leukocyte count exceeds 7.75 and 17.2 billion, respectively.

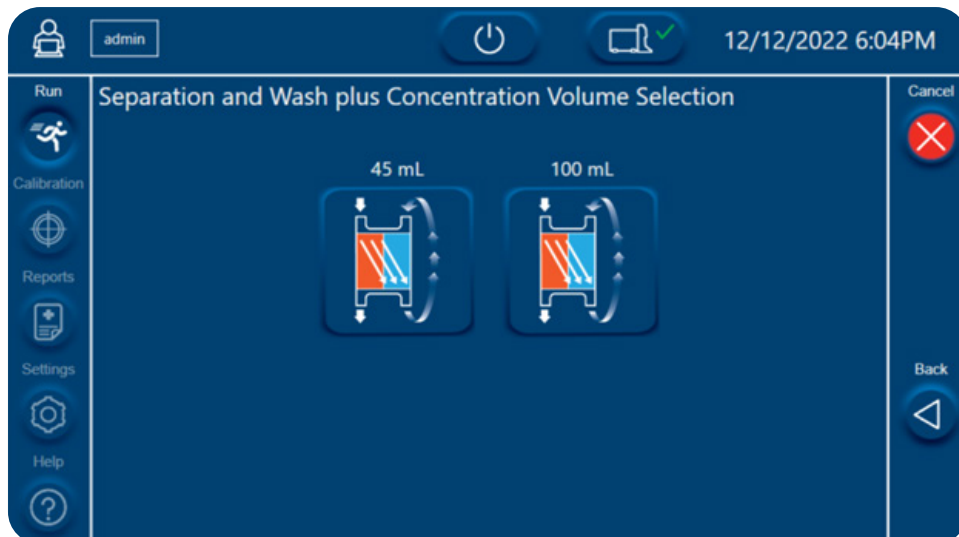
2. Select a run mode by pressing a run mode icon.

Figure 79. Run Mode Selection screen



3. For Separation and Wash Plus Concentration mode, select the desired output volume.

Figure 80. Separation and Wash plus Concentration Volume Selection screen



4. Enter sample input parameters (**Media**, **Sample Volume**, and **WBC Concentration**)

Sample processing completion time is calculated based on input parameters and shown at the bottom of touch screen.

5. Press **Next** on the right side of the screen to advance to next step.

Figure 81. Separation and Wash Parameter Input screen

Minimum Volumes				Projected Output		
Prime	Buffer	Diluent	Sample	Waste 1	Product	Conc.
250	420	200	50	340	90	9
1 mL	2 mL	3 mL	4 mL	6 mL	7 mL	10e6/mL

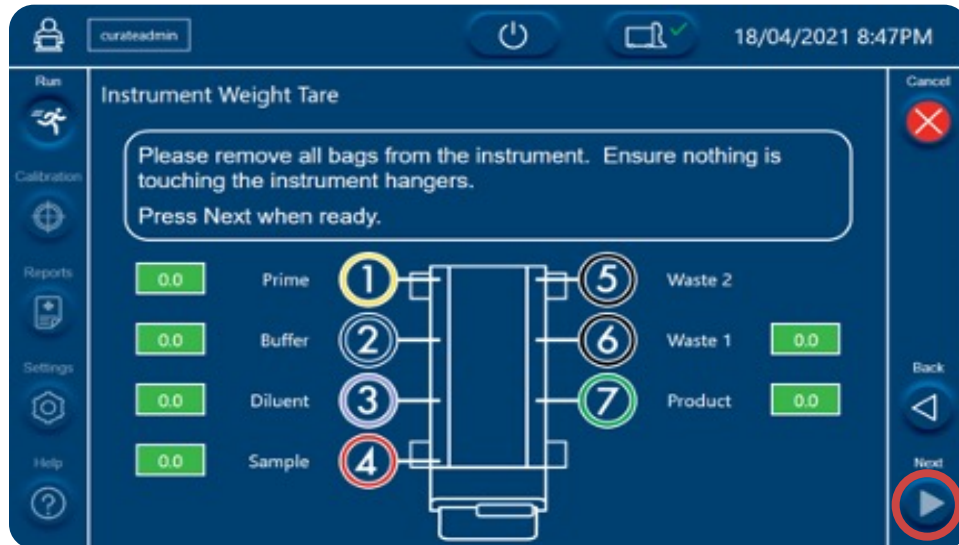
Figure 82. Separation and Wash plus Concentration Parameter Input

Minimum Volumes				Projected Output		
Prime	Buffer	Diluent	Sample	Waste 1	Product	Conc.
250	420	200	50	340	45	18
1 mL	2 mL	3 mL	4 mL	6 mL	7 mL	10e6/mL

**NOTE:** In the parameter input screens, the volumes are displayed below the bag names. Prime, Buffer, Diluent, and Sample volumes are automatically calculated, based on the input sample volume. Volumes for Waste 1, Product, and Conc (product concentration) are estimates based on input volume and concentration.

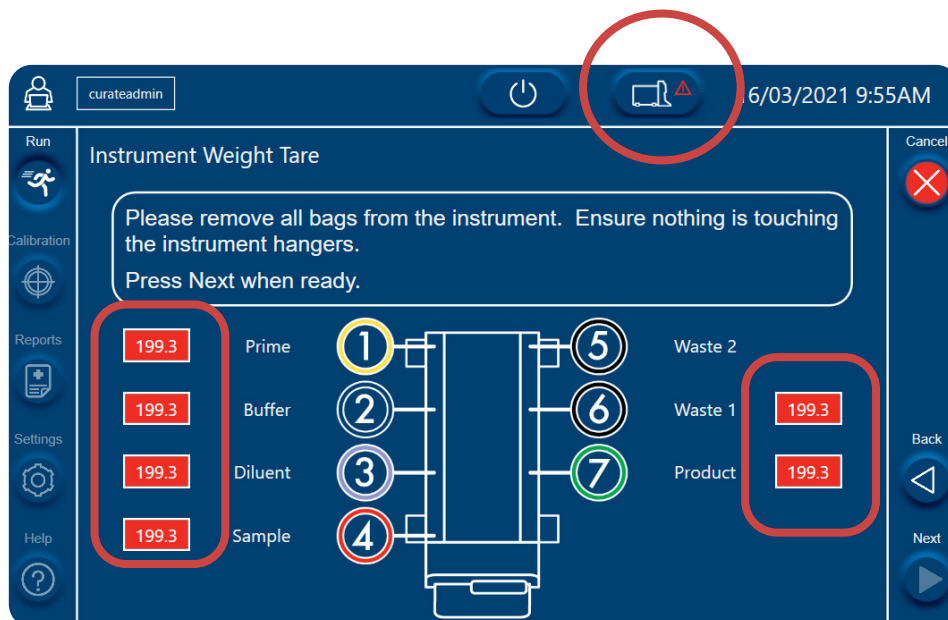
6. Wait for the instrument to tare the hanger weight sensors. All hangers should be empty when taring. Hanger mass boxes will turn green when the tare is complete and successful.

Figure 83. Instrument Weight Tare screen



If the instrument weight tare fails for any hanger, a red warning symbol (⚠) will appear in the System Status button and the mass value box will turn red and display the out of range value.

Figure 84. Instrument Weight Tare screen showing out of range values



A weight tare error can occur for the following reasons:

- Bags placed on the hangers prematurely
- Loose hanger
- Hanger is incorrectly calibrated

- Hanger contacting surrounding objects on the bench top

In the event of a weight tare error, ensure the following:

- All hangers are stable and not moving
- Nothing is placed on the hangers
- Hangers are not in contact with anything on the bench top
- Hangers are correctly attached to the instrument

If these corrective actions do not resolve the error, exit and recalibrate the hanger sensors. See “Calibration Procedures” on page 103. If the issue persists after recalibration, contact Curate Biosciences Technical Support at [techsupport@curatebio.com](mailto:techsupport@curatebio.com).

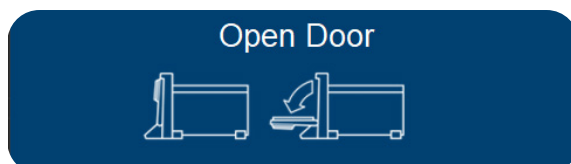
7. Press **Next** to advance to the next step.

## 12.7. LOADING THE CASSETTE ONTO THE SYSTEM

Users are guided through the loading process by prompts on the status screen.

**NOTE:** Before loading the instrument, Curate QR code labels must be added to all bags and the cassette, as described in “Bags and Corresponding Curate QR Code Labels” on page 74. The Curate QR code labels are scanned during instrument loading to reduce the chance of human error during loading and to support process traceability.

1. Ensure all the color-coded clips are closed and open the instrument door.



**NOTE:** During the cassette loading process, the user can proceed to the next step by pressing the blinking, round button on the instrument top panel. During sample accessioning, the user can proceed by either scanning the bar-code displayed on the status screen, or by pressing the round button.

2. Follow the instructions in the prompts and unlock the cassette locking clips.



3. Remove the assembled cassette and bags from the bottom packaging tray and load it onto the instrument door.



Figure 85. Open Curate Instrument door with cassette and bags










4. Load the bags by following the instructions given by the prompts, as detailed in this step.

Be sure to scan and hang the bags in the order detailed in Table 12, according to the prompts detailed in this step. For an illustration of the hanger positions see Figure 4 on page 12.



**Table 12. Bag load order**

Load order	QR Label Color and Text	Item	Clip Color	Hanger Position and Band Color	Notes
1	White Priming Reagent	Priming solution bag	Yellow	1 	
2	Yellow Priming Solution	Priming solution bag	Yellow	1 	
3	Blue Run Buffer	Run buffer bag	Blue	2 	
4	Purple Diluent	Diluent bag	Purple	3 	
5	Red Sample	Sample bag	Red	4 	Confirm that the pre-filter is hanging vertically below the Sample bag with only 10 cm of tubing between the bag and pre-filter (see Figure 24 on page 37).
6	Black Waste	Waste bag	Black	6 	Note: Hanger position 5 (double black bands) is reserved for future upgrades.
7	Green Product	Product bag	Green	7 	
8	Clear Cassette	DCS Cassette	N/A	N/A	

5. Follow the prompts to scan and hang the priming solution bag:

**Prompt 1.** Scan the white Curate priming reagent QR code label on the priming solution bag.

This is the label that was transferred from the reagent bottle to the priming solution bag when preparing the priming solution.



**Prompt 2.** Scan the yellow Curate QR code label on the priming solution bag.



**Prompt 3.** Load the priming solution bag onto the hanger with the yellow indicator band (hanger position 1).



**Prompt 4.** Scan the bar code on the screen or press the round button on the instrument top panel when prompted. The instrument will not proceed to the next step until the bag is loaded onto the correct hanger.



6. Follow the prompts to scan and hang the run buffer bag.

**Prompt 1.** Scan the blue Curate QR code label on the buffer bag.



**Prompt 2.** Load the buffer bag onto the hanger with the coordinating blue indicator band (hanger position 2).



**Prompt 3.** Scan the bar-code on the screen or press the round button on the instrument top panel when prompted.

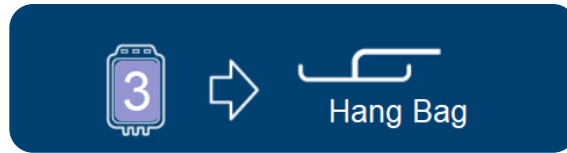


7. Follow the prompts to scan and hang the diluent bag.

**Prompt 1.** Scan the purple Curate QR code label on the diluent bag.



**Prompt 2.** Load the diluent bag onto the hanger with the purple indicator band (hanger position 3).



**Prompt 3.** Scan the bar code on the screen or press the round button on the instrument top panel when prompted.



8. Follow the prompts to scan and hang the sample bag.

**Prompt 1.** Scan the red Curate QR code label on the sample bag.



**Prompt 2.** Mix the sample bag by inversion 3 times. Load the sample bag onto the hanger with the red indicator band (hanger position 4).



**Prompt 3.** Scan the bar code on the screen or press the round button on the instrument top panel when prompted.



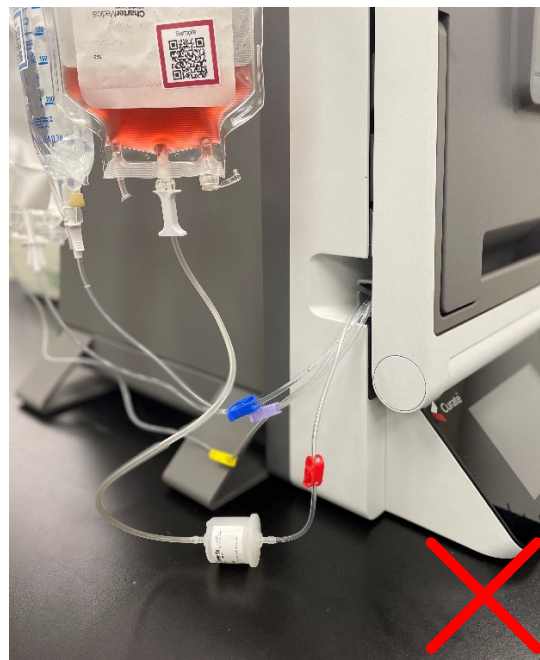
**CAUTION!**

When the sample bag and in-line filter are correctly assembled, the in-filter should be hanging below the sample bag. The filter **SHOULD NOT** be on the tabletop next to the instrument as this will result in an error.

Figure 86. Correct filter placement



Figure 87. Incorrect filter placement



9. Follow the prompts to scan and hang the waste bag.

**Prompt 1.** Scan the black Curate QR code label on the waste bag.



**Prompt 2.** Load the waste bag onto the hanger with the single black indicator band (hanger position 6).



**Prompt 3.** Scan the bar code on the screen or press the round button on the instrument top panel when prompted.



10. Follow the prompts to scan and hang the product bag.

**Prompt 1.** Scan the green Curate QR code label on the product bag.



**Prompt 2.** Load the product bag onto the hanger with the green band (position 7).



**Prompt 3.** Scan the bar code on the screen or press the round button on the instrument top panel when prompted.



11. Remove the packaging tray's plastic, inner lid/bag organizer from the top of the cassette.

12. Scan the clear Curate Cassette QR code label after loading all the bags.

Scan Cassette



13. Lock the Curate cassette locking clips.

Lock Cassette



14. Secure the color-coded cassette tubing in the clips on both sides of the door.

Secure Tubing



15. When closing the door, confirm that no tubing is trapped behind the cassette or pinched.

Do Not Pinch Tubing



16. Close the instrument door.

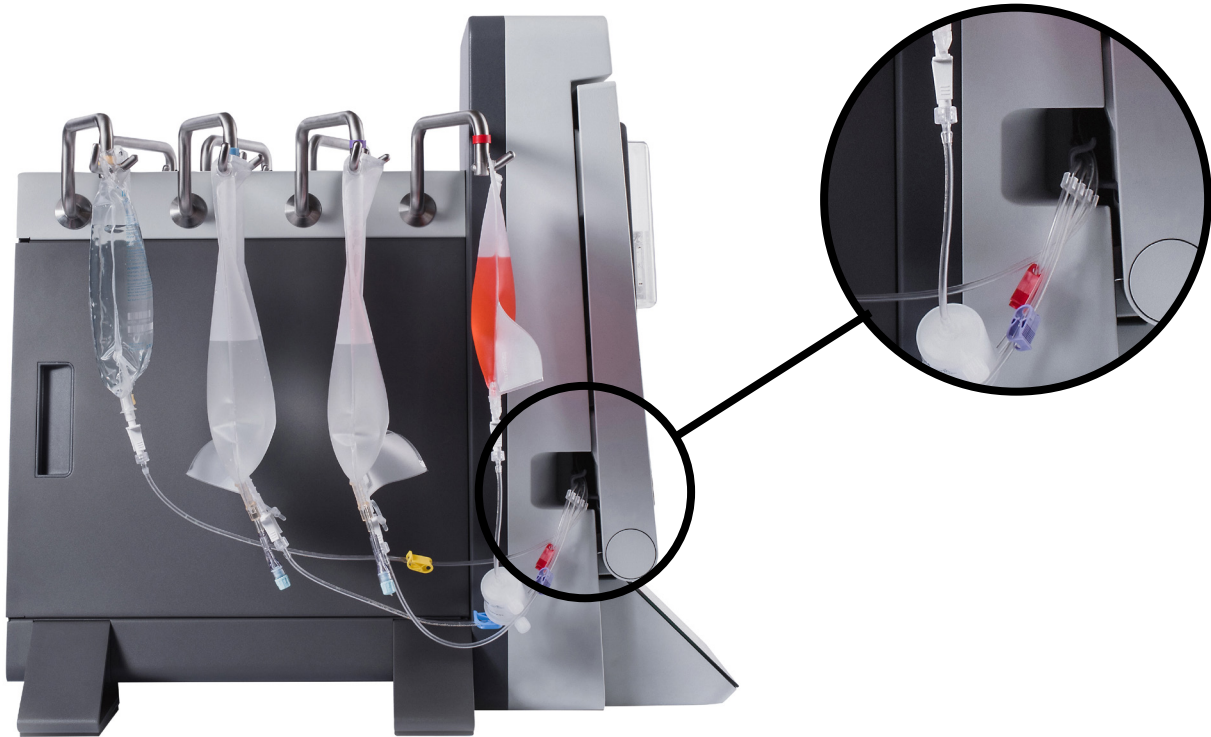
**WARNING!**

When closing the door, confirm that all tubing is exiting the instrument through the retainer clips and pockets on either side of the door hinge, and that no tubing is trapped behind the cassette or pinched when door is closed (see Figure 88).

Close Door



Figure 88. Side view of the instrument with the door closed and the cassette tubing correctly passing through the pocket



## 12.8. LOAD VERIFICATION AND STARTING THE RUN

1. The instrument will perform a load verification once the door is closed. The weight display boxes will be displayed as gray and then turn green once the expected weight range is detected and stable. Press **Next** to advance.

Figure 89. Load Verification screen

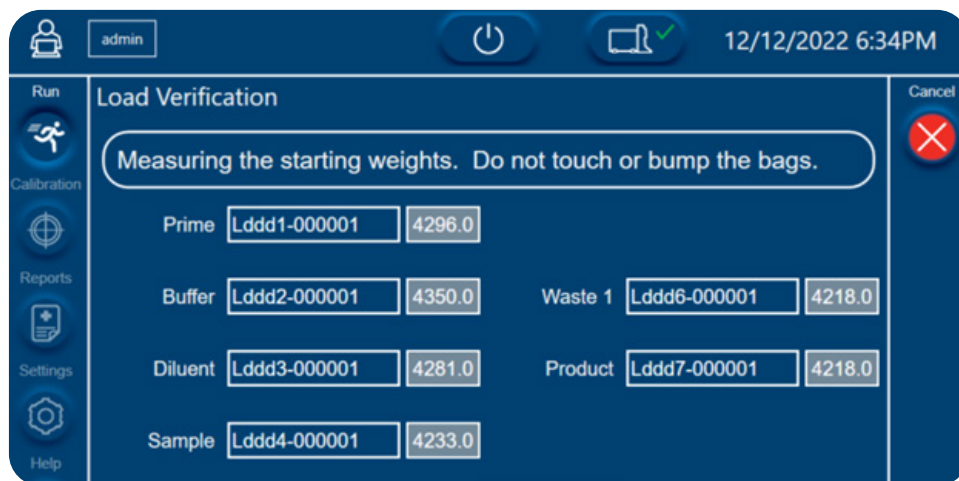


Figure 90. Load Verification screen showing expected weight range

The screenshot shows the 'Load Verification' screen in the Curate Cell Processing System. The interface is dark blue with white text. At the top, there is a user profile icon for 'curateservice', a power button, a checkmark icon, and the date/time '01/05/2023 1:03PM'. Below this is a navigation sidebar with icons for Run, Calibration, Reports, Settings, and Help. The main area is titled 'Load Verification' and contains a message: 'Please verify the bag weights and barcode serial numbers before continuing.' Below the message are several input fields for component weights and serial numbers. The weights are displayed in green boxes, indicating they are within the expected range. The serial numbers are in white boxes. At the bottom, there is a 'Cassette ID' field with the value 'C46988-370001'. On the right side, there are 'Cancel' and 'Next' buttons.

Component	Serial Number	Weight
Prime	L1001-370001	410.0
Buffer	L1002-370001	500.0
Diluent	L1003-370001	280.0
Sample	L1004-370001	110.0
Waste 1	L1006-370001	0.0
Product	L1007-370001	0.0

Cassette ID: C46988-370001

If an error occurs during load verification, the weight value box(s) will turn red and an error will appear.

Figure 91. Invalid Weights error message

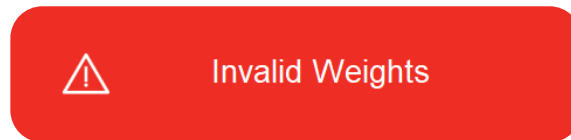


Figure 92. Load Verification screen showing invalid weights

The screenshot shows the 'Load Verification' screen in the Curate Cell Processing System. The interface is dark blue with white text. At the top, there is a user profile icon for 'admin', a power button, a warning triangle icon, and the date/time '12/12/2022 6:36PM'. Below this is a navigation sidebar with icons for Run, Calibration, Reports, Settings, and Help. The main area is titled 'Load Verification' and contains a message: 'Please verify the bag weights and barcode serial numbers before continuing.' Below the message are several input fields for component weights and serial numbers. The weights are displayed in green boxes, indicating they are within the expected range. The serial numbers are in white boxes. At the bottom, there is a 'Cassette ID' field with the value 'C00000-000001'. On the right side, there are 'Cancel' and 'Next' buttons.

Component	Serial Number	Weight
Prime	Lddd1-000001	320.0
Buffer	Lddd2-000001	500.0
Diluent	Lddd3-000001	270.0
Sample	Lddd4-000001	110.0
Waste 1	Lddd6-000001	60.0
Product	Lddd7-000001	60.0

Cassette ID: C00000-000001



A load verification error can occur for the following reasons:

- Bags moving during load verification process.
- Bag volume outside of expected range.
- Loose hanger.
- Hanger not properly calibrated.

In the event of a load verification error, ensure the following:

- All bags are stable and not moving.
- All bag volumes are within acceptable range (no more than +/-10% from the specified value).
- Hangers are correctly attached to the instrument.

If these corrective actions do not resolve the error, exit and recalibrate the hanger sensors. See “Calibration Procedures” on page 103. If the issue persists after recalibration, contact Curate Biosciences Technical Support at [techsupport@curatebio.com](mailto:techsupport@curatebio.com).

2. The Run Preview screen will appear following successful load verification. Ensure that all clips remain closed and press **Next** to advance.

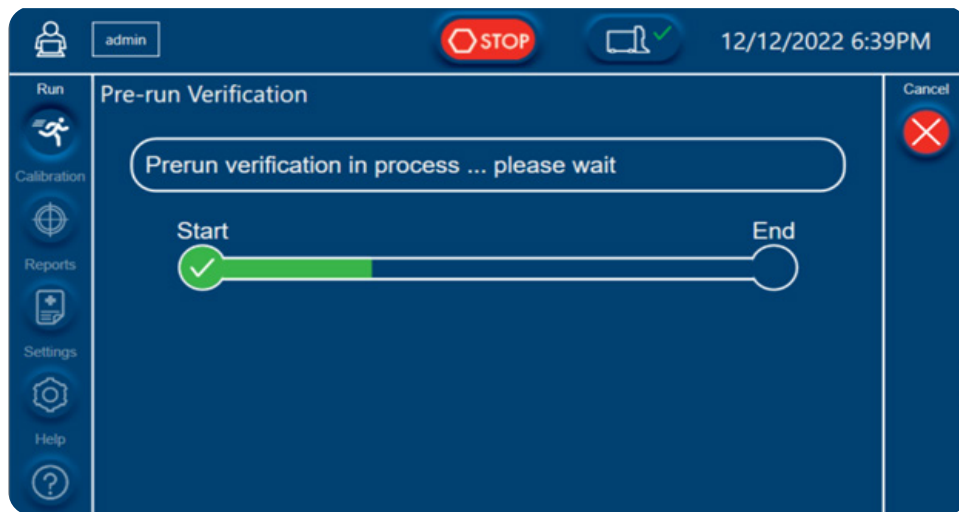
Figure 93. Run Preview screen



3. Pre-run Verification will start automatically.

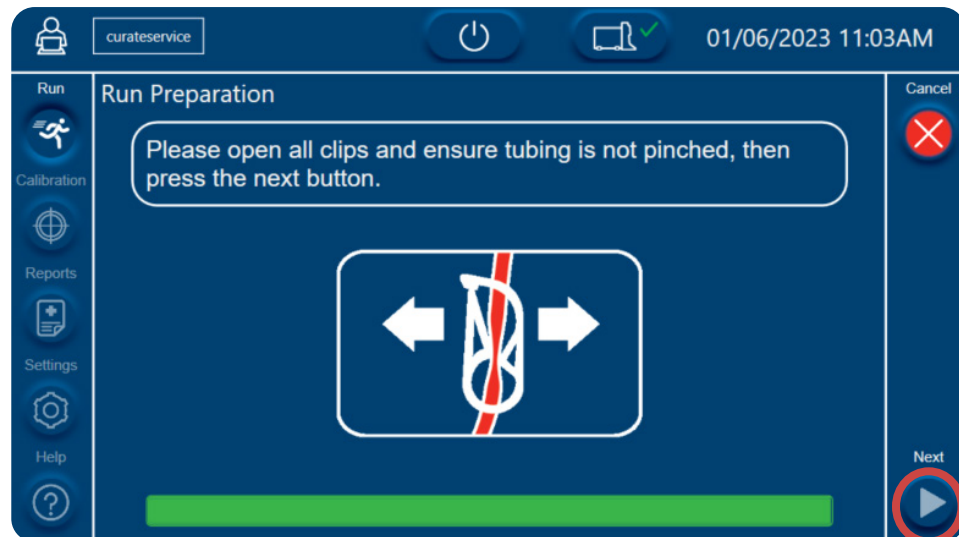
Pre-run Verification

Figure 94. Pre-run Verification screen showing progress bar



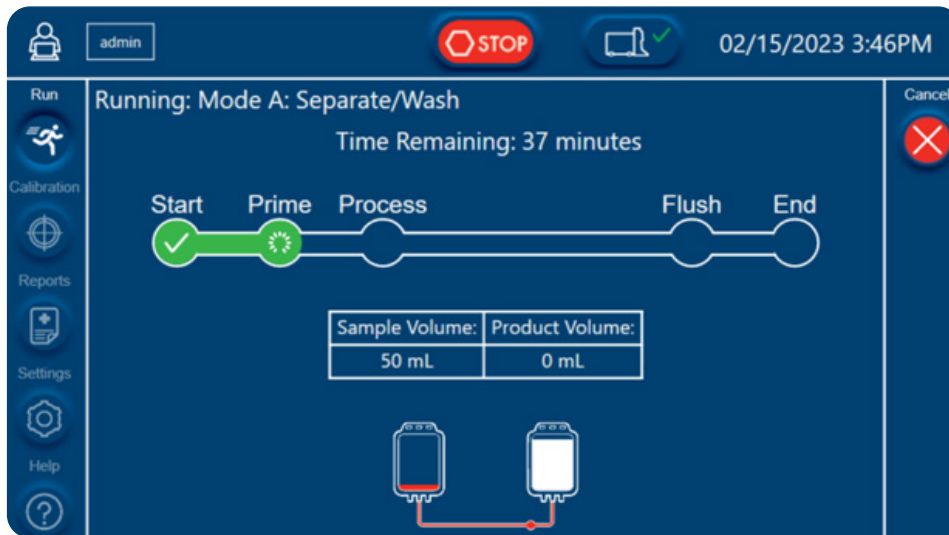
4. Open all the tubing clips after pre-run verification has passed. Then press **Next** to advance to the next step.

Figure 95. Run Preparation screen showing prompt to remove clips



All the remaining steps (start, prime, process, and flush) are automated. The screen will show the progress of the run, the time remaining and the estimated sample volume processed and product volume produced.

Figure 96. Sample running screen showing the progress of the run



## 12.9. COMPLETING THE PROTOCOL

Once the run is complete, the LED lighting will change to white to indicate that the run is complete, and the prompt will display a message saying the run was successful.

1. Use a tube sealer to seal the product bag collection and recirculation tubing as close as possible to the original weld points.

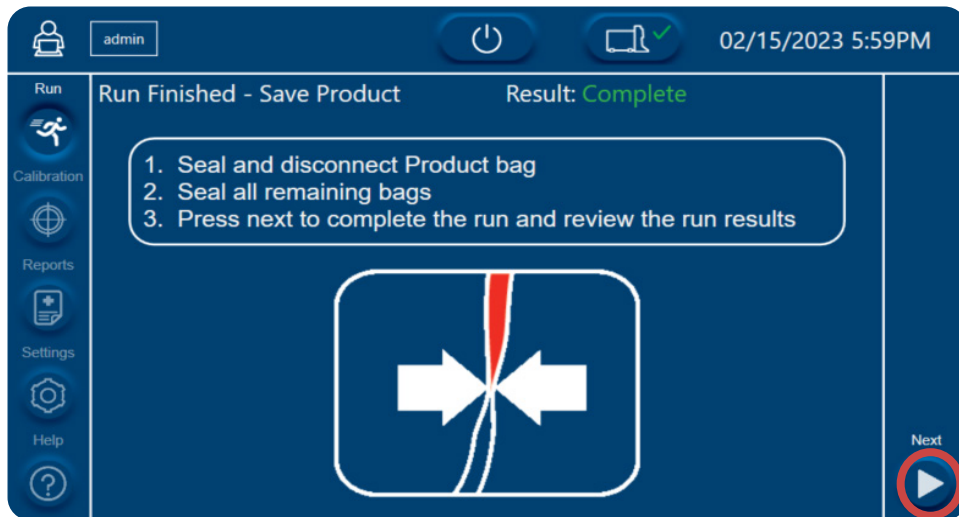


**IMPORTANT!**

When sealing the tubing and disconnecting the product bag, make the seal close to the weld line. This helps prevent the seal from leaking and improves the accuracy of measuring the final product volume.

2. Press **Next** to review run results.

Figure 97. Run completion screen



3. View and export the run results summary.

Figure 98. Run Results Summary



4. Press **Next** or open the door to return to home screen.
5. Proceed to “12.10. Securing the Product and Disposables After the Run” on page 101.

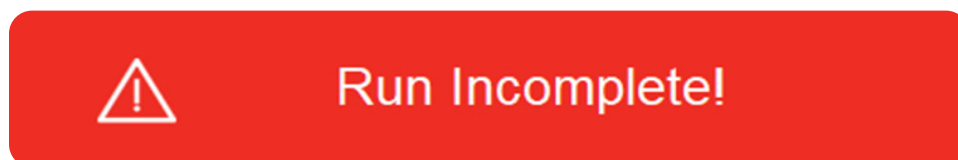
## 12.10. SECURING THE PRODUCT AND DISPOSABLES AFTER THE RUN

1. Close all the clips on all the bags.
2. Pull the tubing seals apart to disconnect the product bag and remove from the hanger. The product is ready for downstream processing.
3. Use a tube sealer to seal the waste bag tubing. Pull the seal apart and remove the waste bag from hanger.
4. Dispose of the waste using proper techniques for the disposal of human blood and tissues.
5. Use a tube sealer to seal the diluent, buffer, and priming solution bags.
6. Pull the tubing seals apart and remove the diluent, buffer, and priming solution bags from hangers. Buffer, diluent, and priming solution can all be disposed per standard aqueous waste disposal practices.
7. Open the door with the cassette remaining loaded.
8. Remove the sample bag from hanger and place the bag and sealed tubing on the cassette.
9. Lift the cassette and the bags off the door and dispose in bio hazard waste receptacle.

## 12.11. INCOMPLETE RUNS

When a run must stop prematurely, the Curate instrument will display the Run Incomplete prompt in the System Status screen.

Figure 99. Run Incomplete prompt



### 12.11.1 Pre-Processing Errors

If an error occurs during the pre-run verification and priming steps, the Curate system will preserve the sample and product cells by sealing all the valves and stopping the run. The instrument may require user intervention to resolve errors. See “Troubleshooting” on page 111.

If the corrective actions do not resolve the error, the instrument will automatically abort the run. The LED lighting will change to solid red and the screen will display the *Run Incomplete!* prompt to indicate that the run is incomplete.

### 12.11.2 Processing Errors

If an error, such as a high pressure error, occurs during the processing and flush steps, the instrument will require the user to press continue before aborting the run and flushing the remaining input cells as well as the collected product cells into their corresponding bags. The LED lighting will automatically change to solid red and the screen will display the *Run Incomplete!* prompt.

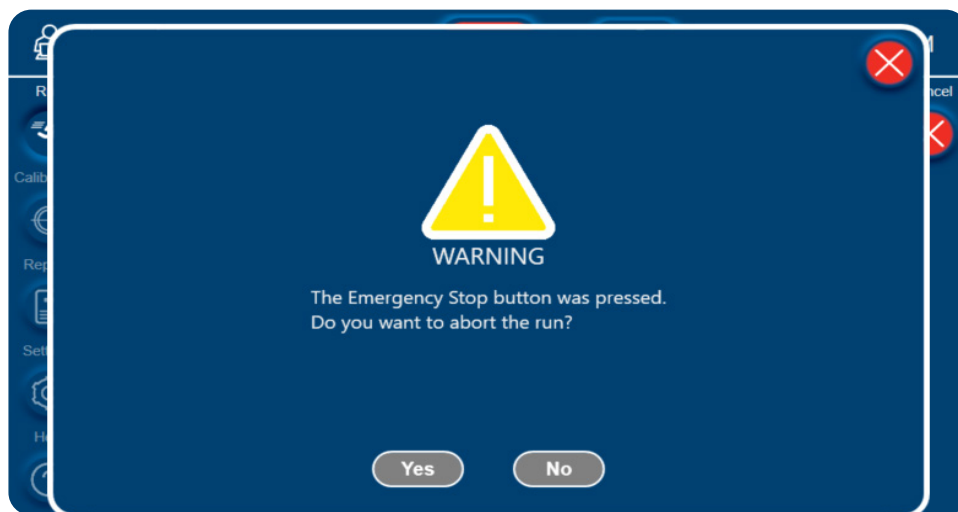
### 12.11.3 Resolving Incomplete Runs

1. Follow the steps in “12.10. Securing the Product and Disposables After the Run” on page 101 to detach the product bag as well as the remaining input.
2. Dispose of the consumable and reagent bags.
3. To process the remainder of the input sample, re-start the process with a new DCS Curate cassette.

### 12.12. EMERGENCY STOP BUTTON

1. In the event of an emergency, press the Emergency Stop Button on the right side of the instrument to abort the run. The Emergency Stop button prompt will appear on the screen.

Figure 100. Emergency Stop button prompt



2. Select **Yes** to abort the run.  
(Selecting **No** will resume the run automatically.)
3. Follow the steps in “Securing the Product and Disposables After the Run” on page 101 to detach the product bag as well as the remaining input. Dispose of the consumable and reagent bags.
4. To process the remainder of the input sample, re-start the process with a new DCS Curate cassette.

### 12.13. TURNING OFF INSTRUMENT

1. Ensure that all the hangers are free of bags.
2. Close the door and secure the handle in the locked position.
3. Power down the Curate software.  
Wait until the touchscreen goes dark before proceeding to the next step.
4. Turn off the power switch at rear of instrument.

# 13. MAINTENANCE

## 13.1. INSTRUMENT MAINTENANCE

It is the user's responsibility to ensure routine instrument maintenance is performed and to set a maintenance schedule that meets the user's organization quality control requirements.

**WARNING!**

Do not service the instrument yourself. Service should be performed only by trained personnel authorized by Curate Biosciences. An improperly serviced instrument may lead to severe personal injury or death by exposure to mechanical hazards and the risk of electric shock.

Users with administrator- or engineer-level authorization, can set routine system test and hanger weight sensors calibration schedules by navigating to the General tab within the Settings screen (see "Setting the Date, Time, and Maintenance Schedules" on page 35).

## 13.2. SPARE PARTS

The Curate system does not require spare parts.

## 13.3. CLEANING AND DECONTAMINATION

The outer surface of the Curate instrument should be cleaned on regular intervals and after each use with an antiseptic solution. Dry the instrument after cleaning and ensure no excess liquid remains on the instrument. When decontaminating peristaltic pumps, use a 70% ethanol wipe. Do not pour or spray liquid directly into the pumps or the instrument panels. Do not press against the sensors on the instrument panels when cleaning. It is not necessary to remove the hangers when cleaning the Curate instrument. Verify the hanger calibration after the cleaning process. See "Hanger Calibration" on page 29.

**WARNING!**

Unplug the power cord before any cleaning or maintenance of the instrument. Do not allow fluids or objects to enter the interior of the instrument.

**WARNING!**

Always wear protective gloves and eyewear to protect against potential biohazard exposure. Dispose of contaminated tissues and swabs according to their biological security level.

## 13.4. CALIBRATION PROCEDURES

To ensure optimal system performance, the instrument should be routinely calibrated as per the organization's quality control requirements. Within the software's Calibration screen, users can calibrate the instrument's seven hanger sensors.

**NOTE:** Only a Curate Biosciences qualified service engineer can calibrate the pressure sensors and bubble sensors and inspect the instrument valves.

### 13.4.1 Hanger Calibration

The system's pumps are controlled by the software and respond to feedback from the hanger gravimetric sensors. Since proper feedback from the hanger sensors requires accurate measurements from the sensors, calibration of these sensors is critical for optimal performance.

Hanger sensors are calibrated using a series of certified calibration weights with known masses and recording the values measured by each sensor as incremental mass is added. The software guides the user through the hanger calibration process.

There are two options for calibration weights:

- Option A: Calibration with standard weights
- Option B: Calibration with bags of water

#### Option A: Calibration with standard weights

**NOTE: Organizations need to provide their own set of certified calibration weights. The weights should be 100, 200, and 500 grams.**

Figure 101. Calibrating with standard weights



#### Option B: Calibration with bags of water

This method involves using bags of water of known masses

1. Place an empty bag on a calibrated lab scale.  
Do not tare the scale.
2. Inject water into the bag until the mass is 100 g.  
I.e. the total mass of the bag and fluid should be 100 g.
3. Repeat steps 1 and 2, but creating bags of water with a total mass of 200 g and 500 g.

**Note: The bags must be within 1-2% of the expected masses. If reusing bags, always verify the mass before using.**



Figure 102. Calibrating with bags of water



### Calibration Order

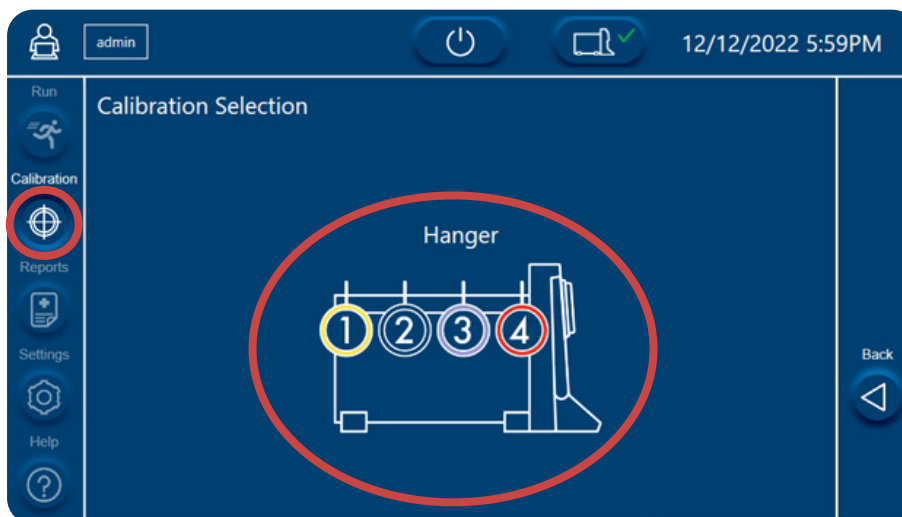
Hangers are calibrated in the following sequence:

1. Priming solution hanger 1 (yellow) Yellow
2. Buffer hanger 2 (blue) Blue
3. Diluent hanger 3 (purple) Purple
4. Sample hanger 4 (red) Red
5. Waste hanger 5 (double black) Black Black
6. Waste hanger 6 (black) Black
7. Product hanger 7 (green) Green

### Calibration steps

1. Select **Calibration** on the left side of the screen and then select the **Hanger** icon.

Figure 103. Calibration Selection screen with the Hanger icon highlighted



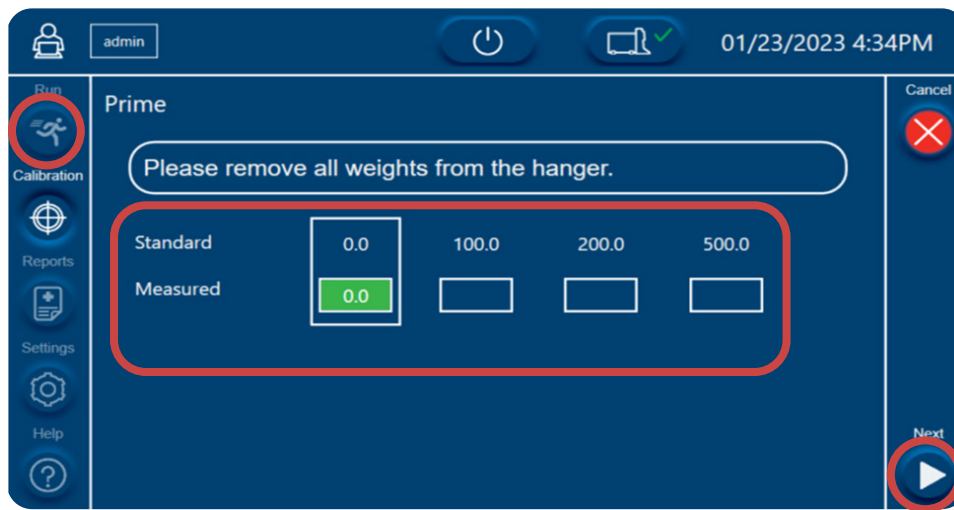
2. Select **New** on the right side of the screen to calibrate the hangers.

Figure 104. Hangers Calibration screen



3. Follow the instructions on the touch screen to calibrate each hanger, starting with the priming solution hanger (hanger 1, yellow). For each hanger, the user is instructed to apply a known standard weight to the hanger, wait 3–5 seconds for the hanger sensor to measure the weight, and then select **Next** to add the next standard weight.

Figure 105. Prime screen



4. Remove weight before adding next weight to hanger.
5. Once all weights are successfully measured by the hanger sensor, all measured value boxes turn green, the slope is reported, and the system registers a pass for the hanger sensor. Select **Next** to advance to the next hanger.

Figure 106. Prime screen with green value boxes, indicating successful calibration



6. Repeat steps 3–4 for remaining hanger sensors.
7. When all hanger sensors are calibrated, the slope and result summary will display in the Hanger Calibration screen. The hanger sensors are now calibrated.

Figure 107. Hangers Calibration screen showing slopes and results

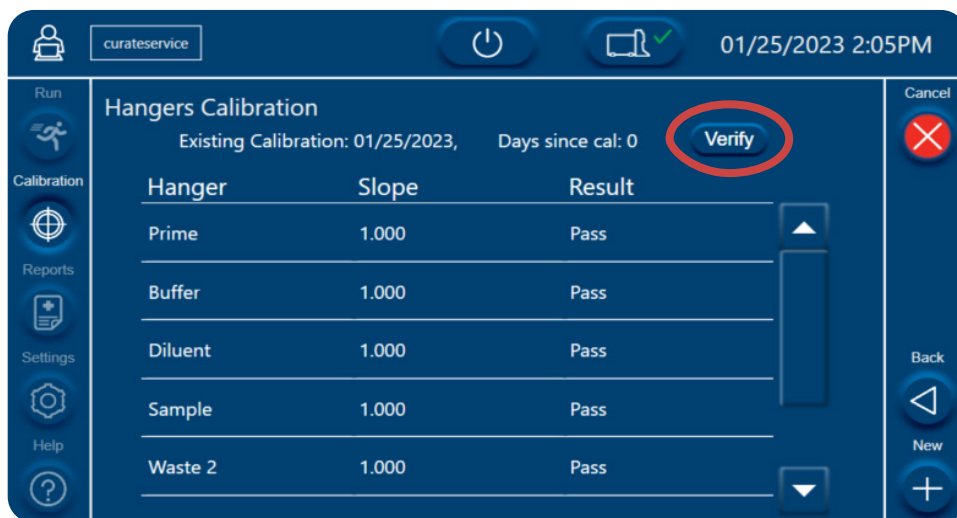


### 13.4.2 Hanger Calibration Verification

Users can verify that the hangers are calibrated by the hanger calibration verification feature on the software.

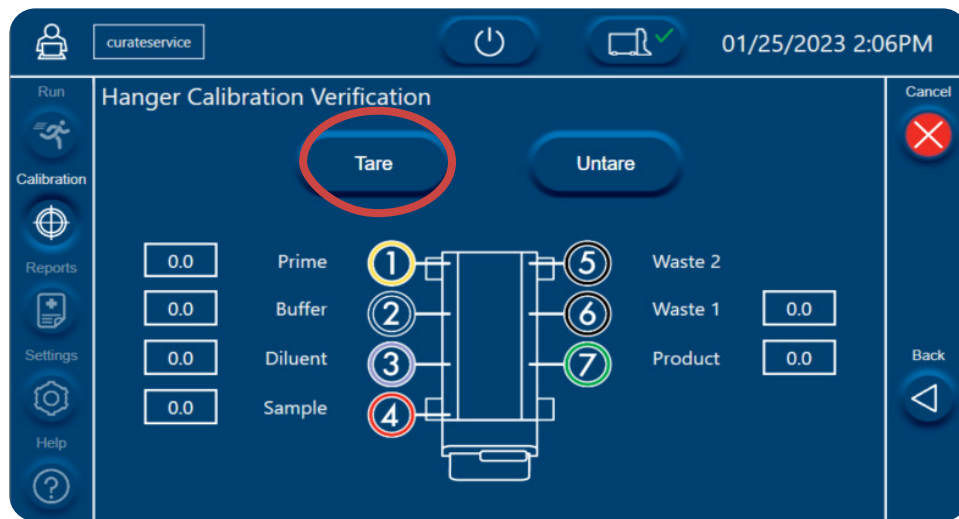
1. Select **Verify** within the **Hanger Calibration** screen.

Figure 108. Hangers Calibration screen with the Verify button highlighted



2. With all hangers empty, select **Tare** to tare all hanger sensors. Then hang weights of known mass to check if the system detects the correct weight.

Figure 109. Hanger Calibration Verification screen with Tare button highlighted



## 14. FREQUENTLY ASKED QUESTIONS

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### **Do I need to turn on the machine in advance? Does it need a warming up time before use?**

**No.** The Curate Biosciences instrument does not need to be running to warm up before use. You can turn on the Curate just before starting the process of an actual samples run.

### **Does the Curate Priming reagent contact the cells?**

The Curate priming reagent is flushed from the cassette by >100 ml of run buffer during the priming process prior to introduction of cells. The sample and product lines are not exposed to the Curate priming reagent as part of the priming process.

### **What bags are recommended for use with the Curate system?**

See “Table 10. Recommended commercially-available fluids, product, and waste bags” on page 71

### **What is the recommended run Buffer?**

4% HSA in Plasma-Lyte is recommended for processing samples on the Curate system. Addition of 2 mM EDTA to this buffer may be preferred for protocols that go directly to cell specific selections as the next step.

### **Is there a recommended tube welder?**

A sterile tube welder allows you to sterilely connect the weld compatible bag tubing to the cassette tubing by welding the tubes together. An example is the Terumo Sterile Tubing Welder.

### **Do I need to buy a 20 cc syringe and 1” sterile needle, or are these included with the Curate cassette or priming reagent?**

Users will need to purchase the 20 cc syringe and a 1 inch (18–24 gauge) sterile needle.


### **Is there a recommended tube sealer?**

A tube sealer allows you to disconnect the bags from the cassette while sealing the tubing to prevent fluid from leaking out. An example is the Sebra® 2600 OMNI™ sealer with hand-held sealing head.

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# 15. TROUBLESHOOTING

## 15.1. TROUBLESHOOTING THE CURATE SYSTEM

The Curate system indicates issues through error messages on the touchscreen, the status screen and through indicator lights on the front of the instrument. The touchscreen indicates an error with a red warning icon (). Users can touch the warning icon to view error messages, sensor status, and system information.

## 15.2. INDICATOR LIGHTS

**Table 13. Indicator light key**

LED State	Status
Solid blue	Instrument is on and the door is closed without a cassette present.
Pulsing blue	Instrument is processing sample
Solid red	“Post error” system check failure
Pulsing red	All run errors
Solid white	Door is closed with cassette present
Pulsing yellow	User interaction is needed

## 15.3. COMMON ERROR CODES AND SYSTEM ISSUES

Issues and errors are organized in tables according to when they are likely to be detected by the user.

### 15.3.1 Pre-processing Issues

Pre-processing includes issues that occur during the sample preparation, loading the instrument, pre-run verification, and priming steps.

**Table 14. Pre-processing Issues**

Error Code	Observation	Reason(s) for issue	Remediation
N/A	The touchscreen displays the following message during system start-up:  <i>Please use the power button to shutdown the software before turning off the instrument.</i>	The software was not properly shut down before the system was powered off.	1) Follow steps in “Turning Off Instrument” on page 102 to turn the software off first and the system second. 2) If the issue persists, contact Curate Biosciences Technical Support at techsupport@curatebio.com.
N/A	The touchscreen displays the following message during accessioning process:  <i>The door was opened unexpectedly, please close it before continuing.</i>	User opened door during the accessioning process causing a minor delay in process.	1) Ensure that all color-coded clips remain closed. 2) Close instrument door. The system will automatically continue with the accessing process.

Error Code	Observation	Reason(s) for issue	Remediation
N/A	<p>The touchscreen displays the following message during a Mode C 45 or Mode C 100 accessioning process:</p> <p><i>The input value(s) exceeds the system's specified maximum WBC Concentration output limit of the product: 150 x10<sup>6</sup>/mL. The system may not produce the concentration that you want. Press Continue to proceed at your own risk or Cancel to change your volume.</i></p>	<p>Sample input parameters exceed Mode C 45 or Mode C 100 maximum input leukocyte limits of 7.75x10<sup>9</sup> cells or 17.2x10<sup>9</sup> cells, respectively.</p>	<p>1) Press <b>Cancel</b> to exit the run screen. 2) Follow steps in "Starting the Protocol" on page 84 to begin the run again. 3) Choose the appropriate run mode per the Curate system's operating limits as defined in Table 3.</p>
N/A	<p>Status screen displays the following message during the accessioning process:</p> <p><i>Remove Bags</i></p>	<p>A bag was removed from a hanger in the middle of the accessioning process.</p> <hr/> <p>A hanger was pulled out of its position and inserted back in place in the middle of the accessioning process.</p>	<p>1) Ensure that all color-coded clips are closed. 2) Open the instrument door and release the cassette tubing from the clips on both sides of the door. 3) Remove the bags from all hangers. 4) Replace the bags on the cassette in the original order (green, black, red, purple, blue, yellow, from bottom to top) 5) Remove the cassette and bags from the instrument door. 6) Ensure that the hangers are correctly installed. 7) Follow steps in "Starting the Protocol" on page 84 to begin the run and re-load the cassette.</p>
N/A	<p>Status screen indicates a weight tare error. Mass value boxes turn red and display an out of range value.</p>	<p>System cannot tare the hangers prior to loading bags due to one of the following errors:</p> <ul style="list-style-type: none"> <li>•Bags placed on the hangers prematurely.</li> <li>•Loose hanger.</li> <li>•Hanger is incorrectly calibrated.</li> <li>•Hanger contacting surrounding objects on the bench top</li> </ul>	<p>Ensure the following:</p> <ul style="list-style-type: none"> <li>•All hangers are stable and not moving.</li> <li>•Nothing is placed on the hangers.</li> <li>•Hangers are not in contact with anything on the bench top.</li> <li>•Hangers are correctly attached to the instrument.</li> <li>•If these corrective actions do not resolve the error, exit and recalibrate the hanger sensors. See "Calibration Procedures".</li> <li>•If the issue persists after recalibration, contact Curate Biosciences Technical Support at techsupport@curatebio.com.</li> </ul>



Error Code	Observation	Reason(s) for issue	Remediation
N/A	Status screen indicates an invalid or expired QR code. QR code serial number boxes turn red.	<p>QR code is scanned incorrectly</p> <hr/> <p>Cassette or priming reagent is expired</p> <hr/> <p>•QR code was scanned in the incorrect sequence •The QR code is on the incorrect bag</p> <hr/> <p>QR code is misprinted</p>	<p>Rescan QR code</p> <hr/> <p>Perform the following steps:</p> <ol style="list-style-type: none"> <li>1) Ensure that all color-coded clips are closed.</li> <li>2) Seal off all bags from the cassette tubing while ensuring the sample and reagents remain sterile.</li> <li>3) Remove bags from all hangers.</li> <li>4) Release cassette tubing from the clips on both sides of the door.</li> <li>5) Remove cassette from instrument door.</li> <li>6) Dispose of the expired cassette and priming solution bag.</li> <li>7) Use an unexpired bottle of priming reagent to prepare a new priming solution bag. Follow steps in "Preparing Priming Solution" on page 68.</li> <li>8) Follow steps in section "Connecting Bags to the Cassette" on page 72 to re-start the process using an unexpired Curate DCS cassette.</li> </ol> <hr/> <p>•Confirm that barcode being scanned matches the color of the bar-code displayed on the top screen. •Confirm correct bar-code is on correct bag (bar-code color should match clip color).</p> <hr/> <p>Contact techsupport@curatebio.com or call +1-888-784-6618</p>
N/A	Status screen indicates an insufficient weight when loading priming solution, run buffer, and/or diluent bags. Mass value boxes turn red and display an out of range value.	<p>User has incorrectly prepared priming solution and diluent by filling bags with sterile saline.</p> <hr/> <p>User is re-using bags.</p> <hr/> <p>Insufficient volume of run buffer to process the indicated sample volume.</p>	<ol style="list-style-type: none"> <li>1) Ensure that all color-coded clips are closed.</li> <li>2) Seal off the indicated bag with insufficient reagent volume.</li> <li>3) Open the instrument door and release the cassette tubing from the clips on both sides of the door.</li> <li>4) Remove bags from all hangers.</li> <li>5) Replace the bags on the cassette in the original order (green, black, red, purple, blue, yellow, from bottom to top)</li> <li>6) Remove cassette and bags from the instrument door.</li> <li>7) Ensure that the hangers are correctly installed.</li> <li>8) Prepare new bags with sufficient volumes (see "Bags and Fluids Needed for System Run" on page 71).</li> <li>9) Transfer the old QR labels to the new reagent bags.</li> <li>10) Follow steps in "Starting the Protocol" on page 84 to begin the run and re-load the cassette.</li> </ol>

Error Code	Observation	Reason(s) for issue	Remediation
N/A	<p>Status screen gives the following message when loading the sample bag:</p> <p><i>Insufficient Weight</i></p> <p>The weight value boxes will remain red and display an out of range value.</p>	User entered the incorrect sample volume at the start of accessioning.	<ol style="list-style-type: none"> <li>1) Ensure that all color-coded clips are closed.</li> <li>2) Open the instrument door and release the cassette tubing from the clips on both sides of the door.</li> <li>3) Remove bags from all hangers.</li> <li>4) Replace the bags on the cassette in the original order (green, black, red, purple, blue, yellow, from bottom to top)</li> <li>5) Remove cassette and bags from the instrument door.</li> <li>6) Ensure that the hangers are correctly installed.</li> <li>7) Follow steps in "Starting the Protocol" on page 84 to begin the run and re-load the cassette.</li> <li>8) Confirm the sample volume loaded and enter the correct value when starting a run.</li> </ol>
N/A	Instrument door does not close properly	<ul style="list-style-type: none"> <li>•Misalignment of the cassette with the door's alignment pins.</li> <li>•Damaged cassette.</li> </ul>	<ol style="list-style-type: none"> <li>1) Ensure that all color-coded clips are closed.</li> <li>2) Seal off all bags from the cassette tubing while ensuring the sample and reagents remain sterile.</li> <li>3) Remove bags from all hangers.</li> <li>4) Release cassette tubing from the clips on both sides of the door.</li> <li>5) Remove cassette from instrument door.</li> <li>6) Dispose of the damaged cassette and priming solution bag.</li> <li>7) Follow steps in section "Preparing Priming Solution" on page 68 to prepare a new priming solution bag .</li> <li>8) Follow steps in "Connecting Bags to the Cassette" on page 72 to re-start the process using a new Curate DCS cassette.</li> </ol>
16	<p>Status screen and Daily Log indicate:</p> <p><i>Error Code 16 Degasser fault detected!</i></p> <p>Run and Calibration buttons are disabled.</p>	Faulty degasser connection.	<ol style="list-style-type: none"> <li>1) Follow steps in "Turning Off Instrument" on page 102 to turn the system off and back on.</li> <li>2) If the issue persists, contact Curate Biosciences Technical Support at techsupport@curatebio.com.</li> </ol>
N/A	Curate door is difficult to close	<p>Cassette locking tabs are rotated &gt;90 degrees to the unlock position</p> <hr/> <p>System has a mechanical issues</p>	<p>Open door and rotate tabs to locked position</p> <hr/> <p>Contact Curate Biosciences Technical Support at techsupport@curatebio.com.</p>

### 15.3.2 PROCESSING ISSUES

Processing includes the all the issues that occur during the run/process and flush steps.

**Table 15. Processing issues**

Error Code	Observation	Reason(s) for Issue	Remediation Required
24	Status screen and Run Report indicate:  <i>Error Code 24. Pump Stall Detected!</i>	<ul style="list-style-type: none"> <li>•Cassette peristaltic tubing is not run in properly.</li> <li>•Pump malfunction.</li> </ul>	<ol style="list-style-type: none"> <li>1) Ensure that all color-coded clips are closed.</li> <li>2) Open instrument's door and release the cassette tubing from the clips on both sides of the door.</li> <li>3) Remove bags from all hangers.</li> <li>4) Replace the bags on the cassette in the original order (green, black, red, purple, blue, yellow, from bottom to top)</li> <li>5) Remove cassette and bags from the instrument door.</li> <li>6) Ensure that the hangers are correctly installed.</li> <li>7) Follow steps in "Starting the Protocol" section to begin the run and re-load the cassette.</li> <li>8) If the issue persists, follow steps in section "Performing a System Test" to complete a System Test run.</li> <li>9) In case of a system test failure, contact Curate Biosciences Technical Support at techsupport@curatebio.com.</li> </ol>
121	Status screen and Run Report indicate:  <i>Error Code 121. Open door was detected during the run. Please close the door immediately and engage all of the clips.</i>	User opened door during the run and the system automatically aborted the run.	<ol style="list-style-type: none"> <li>1) Ensure that all color-coded clips are closed.</li> <li>2) Seal off all bags from the cassette tubing while ensuring the sample and reagents remain sterile.</li> <li>3) Remove bags from all hangers.</li> <li>4) Release cassette tubing from the clips on both sides of the door.</li> <li>5) Remove cassette from instrument door.</li> <li>6) Dispose of the cassette and priming solution bag.</li> <li>7) Use a new bottle of priming reagent to prepare a new priming solution bag. Follow steps in "Preparing Priming Solution" on page 68.</li> <li>8) Follow steps in "Connecting Bags to the Cassette" on page 72 to re-start the process using a new Curate DCS cassette.</li> </ol>
2000	Status screen and Run Report indicate:  <i>Error Code 2000: Priming Error. No fluid detected at Bubble Sensor 1. Please check that clips and connections on Buffer bag are open and press continue to resume, or abort to end the run.</i>	<p>No fluid detected at bubble sensor 1 during priming due to one of the following:</p> <ul style="list-style-type: none"> <li>•Blue Buffer clip was left open during cassette assembly leading to improper flow of fluid in cassette prior to Curate run.</li> <li>•Blue Buffer clip left closed after the pre-run verification step.</li> <li>•Weld connections on blue buffer tubing left closed after cassette preparation.</li> </ul>	<ol style="list-style-type: none"> <li>1) Check that the blue buffer clip or weld connection is open after pre-run verification.</li> <li>2) Without opening the door, Check that the blue buffer tubing is not caught in the door.</li> <li>3) Press <b>Continue</b> to proceed with run.</li> <li>4) If error cannot be cleared, system will abort the run. Follow steps in section "Connecting Bags to the Cassette" on page 72 to move bags to a new cassette and re-start the process.</li> </ol>

Error Code	Observation	Reason(s) for Issue	Remediation Required
2001	<p>Status screen and Run Report indicate:</p> <p><i>Error Code 2001: Priming Error.</i>  <i>No fluid detected at Bubble Sensor 1. Please check that clips and connections on Prime bag are open and press continue to resume, or abort to end the run.</i></p>	<p>No fluid detected at bubble sensor 1 during priming due to one of the following:</p> <ul style="list-style-type: none"> <li>•Yellow priming solution clip was left open during cassette assembly leading to improper flow of fluid in cassette prior to Curate run.</li> <li>•Yellow priming solution clip left closed after the pre-run verification step.</li> <li>•Weld connections on yellow prime solution tubing left closed after cassette preparation</li> </ul>	<ol style="list-style-type: none"> <li>1) Check that the yellow priming solution clip or weld connection is open after pre-run verification.</li> <li>2) Without opening the door, Check that yellow priming solution tubing is not caught in the door.</li> <li>3) Press <b>Continue</b> to proceed with run.</li> <li>4) If error cannot be cleared, system will abort the run. Follow steps in section “Connecting Bags to the Cassette” on page 72 to move bags to a new cassette and re-start the process.</li> </ol>
2002	<p>Status screen and Run Report indicate:</p> <p><i>Error Code 2002:</i>  <i>No fluid detected at Bubble Sensor 4. Please check that clips and connections on Prime bag are open and press continue to resume, or abort to end the run.</i></p>	<p>No fluid detected at bubble sensor 4 during priming due to one of the following:</p> <ul style="list-style-type: none"> <li>•Yellow priming solution clip was left open during cassette assembly leading to improper flow of fluid in cassette prior to Curate run.</li> <li>•Yellow priming solution clip left closed after the pre-run verification step.</li> <li>•Weld connections on yellow priming solution tubing left closed after cassette preparation</li> </ul>	<ol style="list-style-type: none"> <li>1) Check that the yellow priming solution clip or weld connection is open after pre-run verification.</li> <li>2) Without opening the door Check that yellow priming solution tubing is not caught in the door.</li> <li>3) Press <b>Continue</b> to proceed with run.</li> <li>4) If error cannot be cleared, system will abort the run. Follow steps in “Connecting Bags to the Cassette” on page 72 to move bags to a new cassette and re-start the process.</li> </ol>
2003	<p>Status screen and Run Report indicate:</p> <p><i>Error Code 2003: Priming Error.</i>  <i>No fluid detected at Bubble Sensor 2. Please check that clips and connections on Prime bag are open and press continue to resume, or abort to end the run.</i></p>	<p>No fluid detected at bubble sensor 2 during priming due to one of the following:</p> <ul style="list-style-type: none"> <li>•Yellow priming solution clip was left open during cassette assembly leading to improper flow of fluid in cassette prior to Curate run.</li> <li>•Yellow priming solution clip left closed after the pre-run verification step.</li> <li>•Weld connections on yellow priming solution tubing left closed after cassette preparation</li> </ul>	<ol style="list-style-type: none"> <li>1) Check that the yellow priming solution clip and weld connection is open after pre-run verification.</li> <li>2) Without opening the door, Check that yellow priming solution tubing is not caught in the door.</li> <li>3) Press <b>Continue</b> to proceed with run.</li> <li>4) If error cannot be cleared, system will abort the run. Follow steps in “Connecting Bags to the Cassette” on page 72 to move bags to a new cassette and re-start the process.</li> </ol>
2004	<p>Status screen and Run Report indicate:</p> <p><i>Error Code 2004: Priming Error.</i>  <i>No fluid detected at Bubble Sensor 3. Please check that clips and connections on Prime bag are open and press continue to resume, or abort to end the run.</i></p>	<p>No fluid detected at bubble sensor 3 during priming due to one of the following:</p> <ul style="list-style-type: none"> <li>•Yellow priming solution clip was left open during cassette assembly leading to improper flow of fluid in cassette prior to Curate run.</li> <li>•Yellow priming solution clip left closed after the pre-run verification step.</li> <li>•Weld connections on yellow priming solution tubing left closed after cassette preparation</li> </ul>	<ol style="list-style-type: none"> <li>1) Check that the yellow priming solution clip or weld connection is open after pre-run verification.</li> <li>2) Without opening the door, Check that the yellow priming solution tubing is not caught in the door.</li> <li>3) Press <b>Continue</b> to proceed with run.</li> <li>4) If error cannot be cleared, system will abort the run. Follow steps in “Connecting Bags to the Cassette” on page 72 to move bags to a new cassette and re-start the process.</li> </ol>

Error Code	Observation	Reason(s) for Issue	Remediation Required
2005	Status screen and Run Report indicate:  <i>Error Code 2005: Priming Error.</i> <i>No fluid detected at Bubble Sensor 1/4. Please check that clips and connections on Buffer bag are open and press continue to resume, or abort to end the run.</i>	No fluid detected at bubble sensor 1/4 during priming due to one of the following: •Blue Buffer clip was left open during cassette assembly leading to improper flow of fluid in cassette prior to Curate run. •Blue Buffer clip left closed after the pre-run verification step. • Weld connections on blue buffer tubing left closed after cassette preparation.	1) Check that the blue buffer clip or weld connection is open after pre-run verification. 2) Without opening the door, Check that the blue buffer tubing is not caught in the door. 3) Press <b>Continue</b> to proceed with run. 4) If error cannot be cleared, system will abort the run. Follow steps in “Connecting Bags to the Cassette” on page 72 to move bags to a new cassette and re-start the process.
2006	Status screen and Run Report indicate:  <i>Error Code 2006: Priming Error.</i> <i>No fluid detected at Bubble Sensor 5. Please check that clips and connections on Sample and Buffer bags are open and press continue to resume, or abort to end the run.</i>	No fluid detected at bubble sensor 5 during priming due to one of the following: •Red sample and/or blue buffer clips were left closed after the pre-run verification step. •Weld connections on red sample and blue buffer tubing left closed after cassette preparation.	1) Check that the red sample clip or weld connection is open after pre-run verification. 2) Check that the blue buffer clip or weld connection is open after pre-run verification. 3) Without opening the door, check that the red sample tubing and blue buffer tubing is not caught in the door. 4) Press <b>Continue</b> to proceed with run. 5) If error cannot be cleared, system will abort the run. Follow steps in “Connecting Bags to the Cassette” on page 72 to move bags to a new cassette and re-start the process.
2007	Status screen and Run Report indicate:  <i>Error Code 2007: Priming Error.</i> <i>No fluid detected at Bubble Sensor 4/6. Please check that clips and connections on Diluent bag are open and press continue to resume, or abort to end the run.</i>	No fluid detected at bubble sensor 4/6 during priming due to one of the following: •Purple diluent clip was left open during cassette assembly leading to improper flow of fluid in cassette prior to Curate run. •Purple diluent clip left closed after the pre-run verification step. •Weld connections on purple diluent tubing left closed after cassette preparation.	1) Check that the purple Diluent clip or weld connection is open after pre-run verification. 2) Without opening the door Check that the purple diluent tubing is not caught in the door. 3) Press Continue to proceed with run. 4) If error cannot be cleared, system will abort the run. Follow steps in section “Connecting Bags to the Cassette” to move bags to a new cassette and re-start the process.
2011	Status screen and Run Report indicate:  <i>Error Code 2011: Priming Error.</i> <i>No fluid detected at Bubble Sensor 5. Please check that clips and connection on Sample bag are open and press continue to resume, or abort to end the run.</i>	No fluid detected at bubble sensor 5 during priming due to one of the following: •Red sample clip was left closed after the pre-run verification step. •Weld connections on red sample tubing left closed after cassette preparation.	1) Check that the red sample clip or weld connection is open after pre-run verification. 2) Without opening the door, Check that red sample tubing is not caught in the door. 3) Press Continue to proceed with run. 4) If error cannot be cleared, system will abort the run. Follow steps in section “Connecting Bags to the Cassette” to move bags to a new cassette and re-start the process.

Error Code	Observation	Reason(s) for Issue	Remediation Required
2142	Status screen and Run Report indicate:  <i>Error Code 2142: High Pressure Warning. High pressure detected during prime phase. Please check that clips and connections on Product bag are open and press continue to resume, or abort to end the run.</i>	Green product blockage detected in product bag due to one of the following: •Green tubing clip was left closed after the pre-run verification step. •Weld connections on green product tubing left closed after cassette preparation.	1) Check that the green product clip or weld connection is open after pre-run verification. 2) Without opening the door, Check that green product tubing is not caught in the door. 3) Press Continue to proceed with run. 4) If error cannot be cleared, system will abort the run. Follow steps in section “Connecting Bags to the Cassette” to move bags to a new cassette and re-start the process.
2133	Status screen and Run Report indicate:  <i>Error Code 2133: Low Pressure Warning. Lower pressure threshold crossed during prime phase. Press continue to resume, or abort to end the run.</i>	Leakage detected during priming due to damaged cassette.	1) Press Continue to proceed with run or abort to end the run. 2) If error cannot be cleared, system will abort the run. Follow steps in section “Connecting Bags to the Cassette” to move bags to a new cassette and re-start the process.
2351-2359	Status screen and Run Report indicate:  <i>Error Code 2351: Flow rate out of tolerance. Prime hanger flow rate out of tolerance during run phase. Please confirm all bags are hanging freely from the correct hangers. Please press continue to resume, or abort to end the run.</i>	Incorrect flow rate detected during the run phase due to one of the following: •User has touched the bag during the run. •User has removed the bag from a hanger during the run. •Bag is in contact with an item on the bench top. •Product bag is leaning on the waste.	Ensure the following: •All hangers are stable and not moving. •All bags are stable and not moving. •Bags are not in contact with anything on the bench top. •Bags are not in contact with each other.
N/A	Run Stops Prematurely	•The leukopak collection center is missing or not properly following instructions. See “Leukopak Collection and Handling” on page 61  •The user did not correctly pretreat the sample with benzonase prior to the run  •The total leukopak volume on the sample was reported incorrectly by the leukopak collection center.  The benzonase has been improperly stored, causing loss of activity.	Contact your leukopak collection center. Confirm that the correct procedural steps are provided and followed.  Always follow the steps in “Sample Pretreatment” on page 66 before beginning the run.  Contact your leukopak collection center. Confirm that the correct procedural steps are provided and followed.  Use only freshly-thawed benzonase.

Error Code	Observation	Reason(s) for Issue	Remediation Required
N/A	Run is aborted. System is turned off in the middle of the run. Collected product may be contaminated.	Power interruption	<ol style="list-style-type: none"> <li>1) Ensure that all color-coded clips are closed.</li> <li>2) Seal off all bags from the cassette tubing while ensuring the sample and reagents remain sterile.</li> <li>3) Remove bags from all hangers.</li> <li>4) Release cassette tubing from the clips on both sides of the door.</li> <li>5) Remove cassette from instrument door.</li> <li>6) Dispose of the cassette and priming solution bag. 7) Use a new bottle of priming reagent to prepare a new priming solution bag. Follow steps in "Preparing Priming Solution" on page 68.</li> <li>8) Follow steps in "Connecting Bags to the Cassette" on page 72 to re-start the process using a new Curate DCS cassette.</li> </ol>
N/A	<p>Touchscreen indicates:</p> <p><i>Please perform the following service(s) prior to a run.</i></p> <p>The run button is disabled.</p>	<p>Hanger calibration is expired.</p> <hr/> <p>System test run is due.</p>	<p>Follow the steps in "Hanger Calibration" on page 29 to calibrate the hangers.</p> <hr/> <p>Follow the steps in section "Performing a System Test" on page 51 to complete a system test run.</p>

### 15.3.3 Post-processing Issues

Post-processing includes all the issues that occur after the run has finished.

**Table 16. Post-processing issues**

Error Code	Observation	Issue cause	Remediation required
301	<p>Touchscreen indicates:</p> <p><i>Error 301.</i></p> <p><i>Missing default export location!</i></p>	<ul style="list-style-type: none"> <li>•User has not defined an export location</li> <li>•The export location does not exist anymore.</li> </ul>	Follow steps in "Setting Data Export and Import Locations" on page 34 to set an export location on a USB drive.
N/A	Cell viability is low	<p>Improper storage of the product bag after the run. Cells settling in the bag tubing and injection ports may lead to localized regions where cells are less viable.</p> <hr/> <p>Improper mixing of the product bag prior to removing the aliquot for analysis. Cells settling in the bag tubing and injection ports may lead to localized regions where cells are less viable.</p>	<ul style="list-style-type: none"> <li>•Place the product bag on a rocker immediately after the Curate run.</li> <li>•Ensure bag is being fully mixed. Periodic inversion of the bag may be beneficial to redistribute cells in any areas that are not mixing well.</li> <li>•Adjust the mixing speed, avoiding generation of bubbles.</li> <li>•Ensure even air-flow around the bag while rocking (use wire grate if needed).</li> </ul> <hr/> <p>Mix bag properly by hand, and then withdraw/expel from a syringe to mix any product in the tubing. Then remove an aliquot for sampling.</p>
N/A	Low % White Blood Cell (WBC) recovery in product	<p>User is inaccurately measuring the product volume.</p> <hr/> <p>Incorrect cell counts are used for input material.</p>	<p>Refer to the Curate Run Report for the accurate final volume.</p> <hr/> <p>Use the cell counts of input material after treating with benzonase, and immediately prior to loading the Curate system.</p>

Error Code	Observation	Issue cause	Remediation required
N/A	The Run Report, Daily log and/ or Calibration Log screens are missing information.	Software error	Contact Curate Biosciences Technical Support at techsupport@curatebio.com.

### 15.3.4 Issues That Can Occur at Any Time

Table 17. Issues That Can Occur at Any Time

Error Code	Observation	Issue cause	Remediation required
1	Status screen indicates:  <i>Error Code 1 Software cannot establish communication with the instrument (firmware).</i>  System is disconnected and touchscreen is disabled.	System was idle for too long.	1) Follow steps in sections “Turning Off Instrument” on page 102 to turn the system off and back on. 2) If the issue persists, contact Curate Biosciences Technical Support at techsupport@curatebio.com.
2	Status screen indicates:  <i>Error Code 2 The Firmware failed the POST tests. Please contact service.</i>	Instrument firmware error	1) Follow steps in “Turning Off Instrument” on page 102 to turn the system off and back on. 2) If the issue persists, contact Curate Biosciences Technical Support at techsupport@curatebio.com.
5	Status screen and Daily Log indicate:  <i>Error Code 5 Instrument hardware failure detected! Valves</i>  Run and Calibration buttons are disabled.	One or multiple valves is not actuating due to one of the following: • Valve cannot actuate due to sticking. • Power-up issue.	1) Follow steps in “Turning Off Instrument” on page 102 to turn the system off and back on. 2) If the issue persists, contact Curate Biosciences Technical Support at techsupport@curatebio.com.



# 16. TECHNICAL SUPPORT


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**Technical Assistance:**

If assistance is required, contact Curate Biosciences Technical


**Curate Biosciences Technical Support**

	techsupport@curatebio.com
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	+1-888-784-6618
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**Curate Biosciences Customer Service**

	customerservice@curatebio.com
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	+1-888-784-2297
	+1-805-456-8977

**When contacting Technical Support, please have the following information available:**

- Any error messages
  - Any recent log or run files
  - Details of recent system performances
  - Product name and serial number
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# 17. COMPLIANCE

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## 17.1. STANDARDS

The Curate system and software have been designed to comply in substantial accordance with the following standards:

1. ISO 13485:2016
2. ISO 14971: 2019
3. IEC 61010-1:2010
4. IEC 61326-1:2012
5. IEC 62304: 2006
6. 21 CFR Part 11
7. EU Directive 2014/30/EU European Union EMC Directive
8. Directive 2012/19/EU European Union “WEEE Directive” - Waste electrical and electronic equipment

## 17.2. ELECTROMAGNETIC INTERFERENCE (EMI) STATEMENT (CLASS A)

US: This equipment has been tested and found to comply with the limits for a Class A digital device, pursuant to part 15 of the FCC rules. These limits are designed to provide reasonable protection against harmful interference when the equipment is operated in a commercial environment. This equipment generates, uses, and can radiate radio frequency energy and, if not installed and used in accordance with the instruction manual, may cause harmful interference to radio communications. Operation of this equipment in a residential area is likely to cause harmful interference, in which case the user will be required to correct the interference at his own expense.

Canada: This class A digital apparatus complies with Canadian ICES-003. Cet appareil numérique de la classe A est conforme à la norme NMB[1]003 du Canada.

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