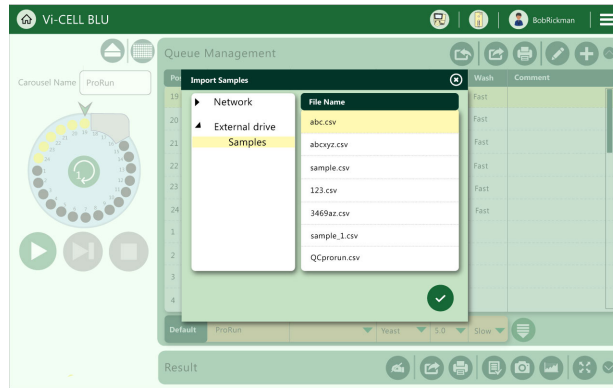


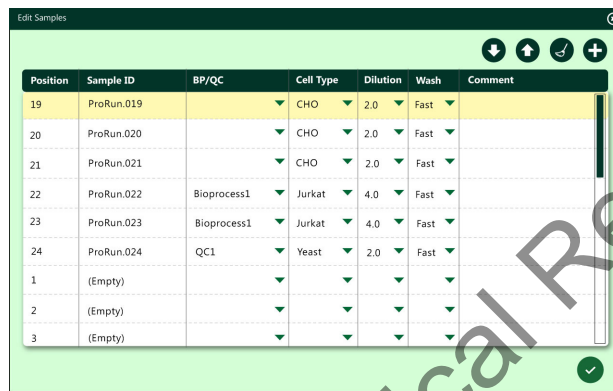
Import Results

Green Screens need to be replaced throughout

- 1 Select  to import results for reanalysis.




- 2 Select the file to reanalyze.

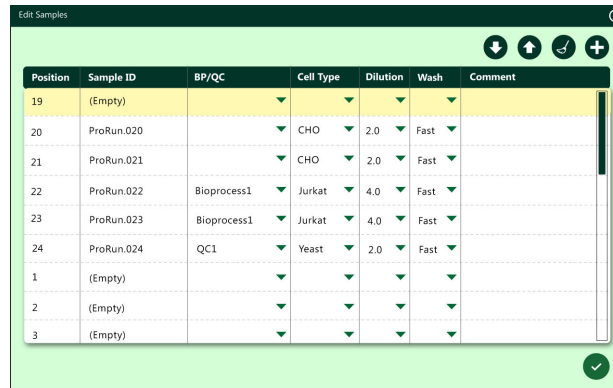


The screenshot shows the 'Edit Samples' window with a table of sample configurations. The table has columns for Position, Sample ID, BP/QC, Cell Type, Dilution, Wash, and Comment. The rows are numbered 19 through 24, followed by three empty rows (1, 2, 3). A green checkmark is visible at the bottom right of the window.


Position	Sample ID	BP/QC	Cell Type	Dilution	Wash	Comment
19	ProRun.019		CHO	2.0	Fast	
20	ProRun.020		CHO	2.0	Fast	
21	ProRun.021		CHO	2.0	Fast	
22	ProRun.022	Bioprocess1	Jurkat	4.0	Fast	
23	ProRun.023	Bioprocess1	Jurkat	4.0	Fast	
24	ProRun.024	QC1	Yeast	2.0	Fast	
1	(Empty)					
2	(Empty)					
3	(Empty)					

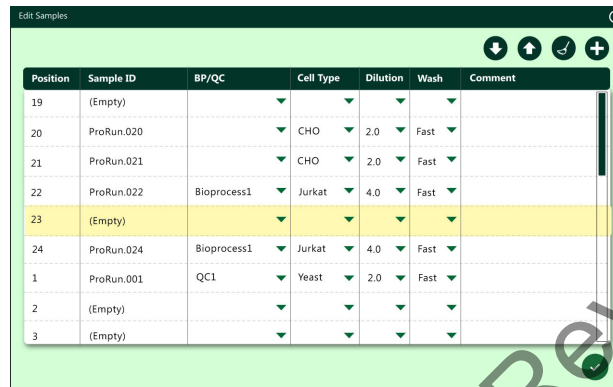
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3 Select  to edit the sample file.



Position	Sample ID	BP/QC	Cell Type	Dilution	Wash	Comment
19	(Empty)					
20	ProRun.020		CHO	2.0	Fast	
21	ProRun.021		CHO	2.0	Fast	
22	ProRun.022	Bioprocess1	Jurkat	4.0	Fast	
23	ProRun.023	Bioprocess1	Jurkat	4.0	Fast	
24	ProRun.024	QC1	Yeast	2.0	Fast	
1	(Empty)					
2	(Empty)					
3	(Empty)					

4 Select  to save the edited sample file.



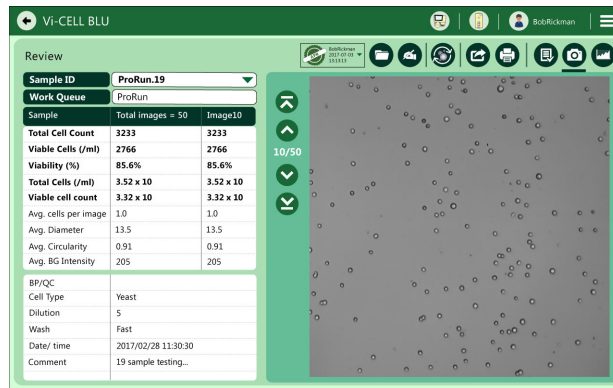
Position	Sample ID	BP/QC	Cell Type	Dilution	Wash	Comment
19	(Empty)					
20	ProRun.020		CHO	2.0	Fast	
21	ProRun.021		CHO	2.0	Fast	
22	ProRun.022	Bioprocess1	Jurkat	4.0	Fast	
23	(Empty)					
24	ProRun.024	Bioprocess1	Jurkat	4.0	Fast	
1	ProRun.001	QC1	Yeast	2.0	Fast	
2	(Empty)					
3	(Empty)					

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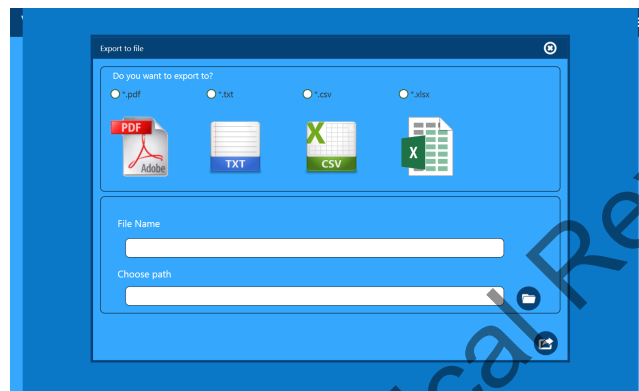
Export Results

Green Screens need to be replaced throughout

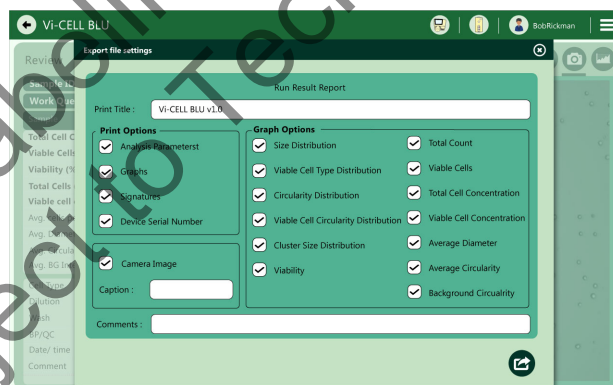
- 1 Select a run and select  to export results.



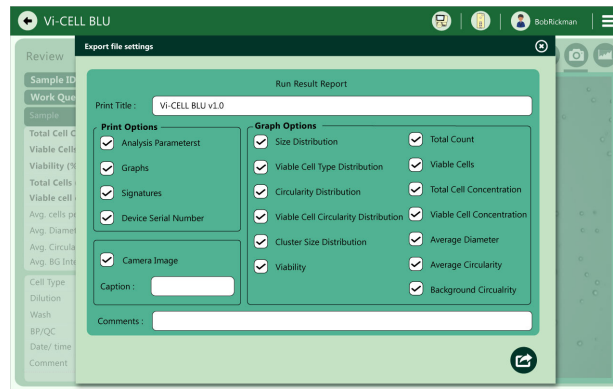
- 2 Select the export destination, enter a file name and file path.



- 3 Select Print, Graph and Camera options to export.



4 If desired, select to Merge with existing excel file.



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Cell Type Administration

What is a Cell Type?

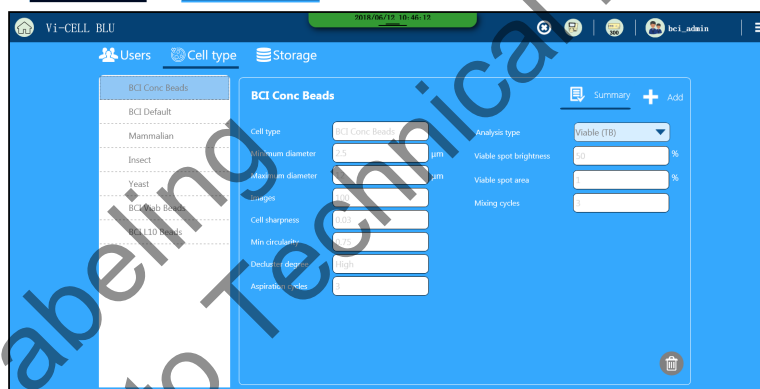
Cell types are files that store the optical settings required to correctly identify and quantify viable versus non-viable cells. Cells will vary in their optical characteristics and understanding how to establish the correct settings is important.


For many cell types, the default cell type values are suitable. In the event any of the parameters must be changed for a given sample, a new cell type may be created or an existing one modified. This section provides the instructions for creating new cell types for use with the software. The Vi-CELL BLU software has 4 cell types predefined, and are intended to be used as starting points for additional customer-defined cell types.

Enter the appropriate information for the particular cell type and dilution factor as necessary. Use the default settings as a starting point if necessary. Use the minimum diameter parameter for excluding cellular debris or unwanted cells. Use the mixing cycle to adjust for cell lines that tend to shear under the stress of mixing. For insect cell lines, a mixing cycle of 1 is found to be suitable.

Cell Type Screen

- 1 Select  >  >  to view the **Cell type** screen.



- 2 Select  to add or edit a Cell type.

BCI Conc Beads
BCI Default
Mammalian
Insect
Yeast
BCI Viab Beads
BCI L10 Beads

- 3 Enter the The **Minimum** and **Maximum** size of cells within the sample.

Minimum diameter	<input type="text" value="2"/>	µm
Maximum diameter	<input type="text" value="60"/>	µm

Any cells that fall outside of this range are ignored. They will appear within the camera image but will not be annotated and will not be included in any of the numerical run results. The minimum diameter can be used to exclude debris and/or unwanted cells. The size range should be used only to specify the expected range of cell sizes within the sample and should not be used to identify sub ranges.

- 4 Enter the number of **Images** (1 to 100).

Images	<input type="text" value="100"/>
--------	----------------------------------

A larger number will give a statistically better result. However a smaller number can be used if cycle time and image storage requirements are more important than absolute accuracy.

- 5 Enter the **Cell Sharpness**.

Cell sharpness	<input type="text" value="0.03"/>
----------------	-----------------------------------

Cell Sharpness the clarity of an image and specifies the minimum sharpness at the outer edge of a cell. This setting affects the focus discrimination algorithm. A higher value will require a more sharply-defined cell, to be accepted. Enter a range from 1 to 200. 1 represents sharpest, 200 unclear. This value also affects the transition from cell boundary (dark) to light (background).

- 6 Enter the **Min circularity**.

Min circularity	<input type="text" value="0.75"/>
-----------------	-----------------------------------

(Least Circular=0, Perfectly Circular=1). This parameter can be used to reject debris that exceeds the minimum cell diameter and are too irregularly shaped to be treated as a real cell. All objects with original (pre-fit) circularity less than this value will be ignored in the analysis. Raise this value to bypass debris more easily.

7 Enter the **Decluster degree**.

The default setting is medium. This function increases the ability of the software to detect cells that are clumped together. Set the de-cluster degree according to how well the cell clusters appear within the images (if not de-clustered properly). Generally, a higher value will identify more cells within a cluster, but a higher value may also split a single non-circular cell into more than one cell. If the cells in a sample are circular, a higher value can be safely used. High will perform the most aggressive declustering; Low will perform the least aggressive declustering. If individual cells are being split into 1 or more cells by the declustering, set this value to Medium or Low.

8 Enter the **Aspiration Cycles**.

In order to ensure that all of the cells are equally dispersed some of the sample is aspirated and then returned to the cup. One cycle is normally sufficient but if the cells are difficult to keep in suspension and have a tendency to attach themselves to the walls of the cup then additional aspirate cycles may be beneficial.

NOTE Cells must be in single cell suspension prior to placement on the system.

9 Select the **Analysis type** from the pull-down menu.

10 Enter the **Viable spot brightness**.

This is the brightness of the center spot of the cell. This is a percentage of the grayscale range. Cell centers must be higher (lighter) than this percent to be counted as viable. This parameter is expressed as a percentage of the background intensity. 75% is a typical value. Pixels in the center of a cell that are brighter than this setting are considered to be part of the center spot. For latex beads the viable cell spot brightness should not be set less than 75%.

NOTE The cell brightness and sharpness help determine whether or not the boundary “dark” pixels belong to a cell or are part of the background. The cell spot brightness and area determine whether or not a cell is viable or non-viable.

11 Enter the **Viable spot area**.

A screenshot of a software interface showing a blue header with the text 'Viable spot area' and a white input field containing the number '1', followed by a '%' symbol.


The cell spot area is a percentage of the total area of the Cell. The bright center spot must be larger than this, as a percent of the total area, to be considered viable. 5 to 10% are typical values. Any extremes in this value will either make the cells all viable or non-viable. If the area of the center spot (as determined from the viable cell spot brightness) is greater than this percentage of the total area contained within the outer edge of the cell (as determined from the cell sharpness), then the cell is considered to be viable.

12 Enter the **Mixing cycles**.

A screenshot of a software interface showing a blue header with the text 'Mixing cycles' and a white dropdown menu with the number '3' selected.

The trypan blue and sample are mixed by sending the mixture back and forth between the sample cup and syringe. This parameter determines the number of times that the mixture is returned to the cup. Normally three times is sufficient but if the sample is immiscible with trypan blue then a higher value may be necessary to achieve good mixing and even background intensities.



This feature is especially useful for cell types, which may shear due to excessive mixing. Lowering the number of mixing cycles will alleviate this situation. For insect cell lines, it has been determined that 1 mixing cycle is most suitable.

13 Select  to save the new or edited Cell type.

Reports Administration

Report Results

Completed Run Summary Reports

1 Select  >  to view the **Report Results** screen.

The **Completed run summary report** screen is displayed by default.

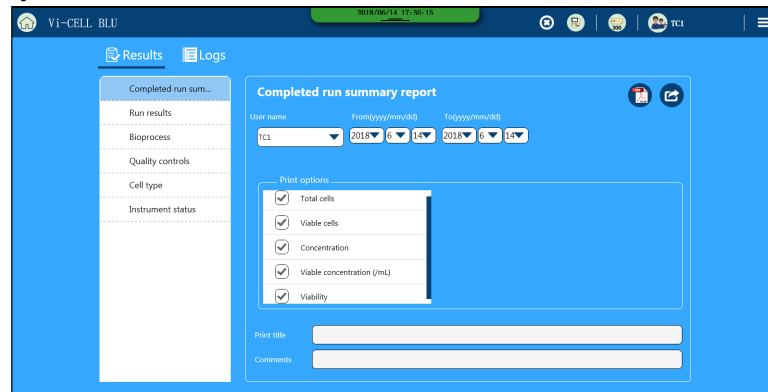
You can choose to create other reports. Use the links below to create other reports.

- [Run Results Reports](#).
- [Bioprocess Reports](#).
- [Quality controls Reports](#)
- [Cell type Reports](#)

- [Instrument Reports](#)

2 On The **Completed run summary report** screen,

- Select the **User name**.
- Select the **From** and **To** dates.
- Select your **Print Options**.
- Enter a **Print title**.
- Enter any additional **Comments**.

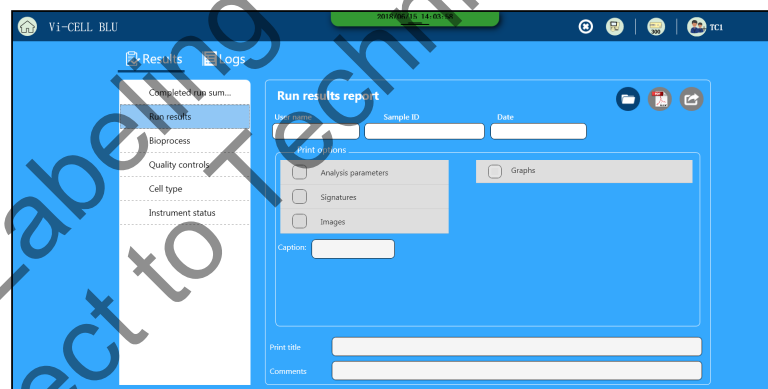



3 Select to save the report as PDF or select to Export the report.


Run Results Reports

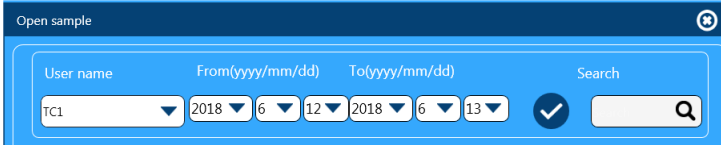
1 Select > to view the **Report Results** screen.


2 Select **Run Results**.

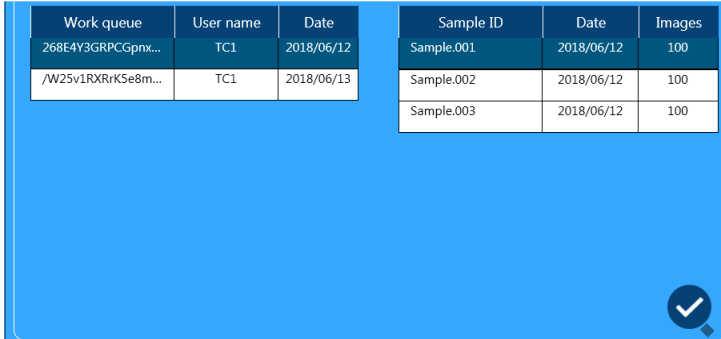


3 Select  to choose a file for the report.

- Select a **User name**.
- Select the **From** and **To** dates.
- Select .



- Select a listing in the **Work Queue**.
- Select a Sample from the **Sample ID** list.
- Select .

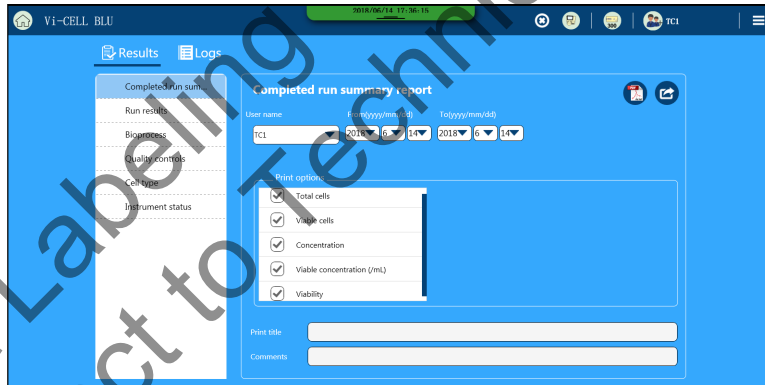


Work queue	User name	Date
268E4Y3GRPCGpnx...	TC1	2018/06/12
/W25vLRXRrK5e8m...	TC1	2018/06/13

Sample ID	Date	Images
Sample.001	2018/06/12	100
Sample.002	2018/06/12	100
Sample.003	2018/06/12	100



4 On The **Run Results** screen,

- Select your **Print Options**.
- Enter a **Caption** if required.
- Enter a **Print title**.
- Enter any additional **Comments**.

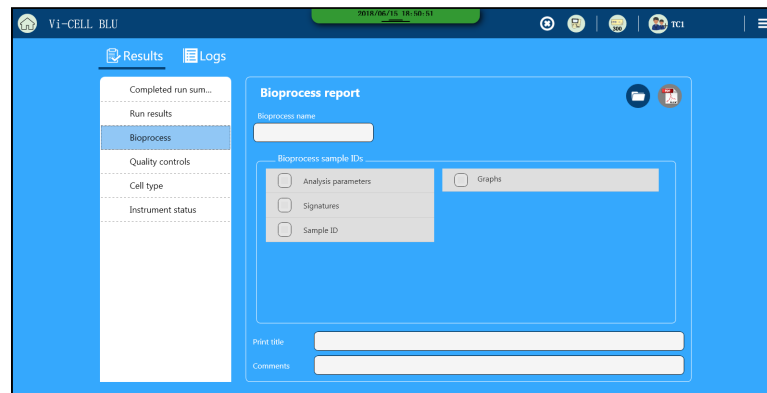




- 5 Select  to save the report as PDF or select  to Export the report.

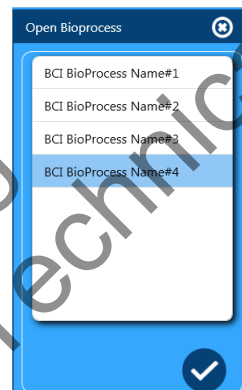
Bioprocess Reports

- 1 Select  >  to view the **Report Results** screen.

- 2 Select **Bioprocess**.

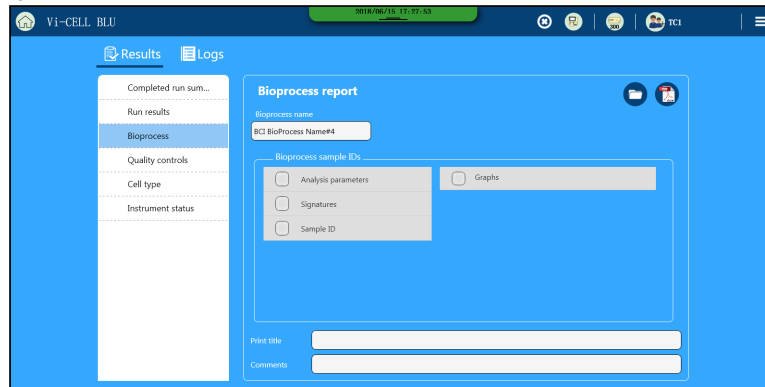


- 3 Select  to choose a Bioprocess file for the report.
 - Select a Bioprocess file.
 - Select .





- 4 On the **Bioprocess report** screen,
 - Select your **Bioprocess sample IDs**.
 - Enter a **Print title**.

- Enter any additional **Comments**.

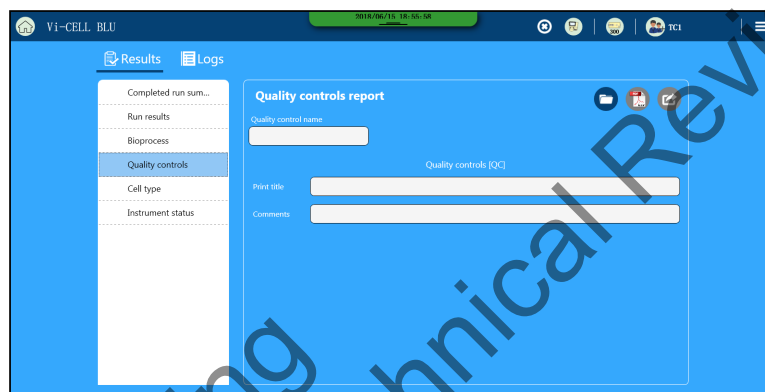


- 5 Select  to save the report as PDF or select  to Export the report.

Quality controls Reports


- 1 Select  >  to view the **Report Results** screen.

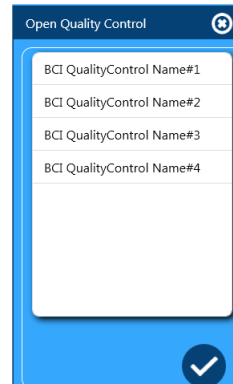
- 2 Select **Quality controls**.



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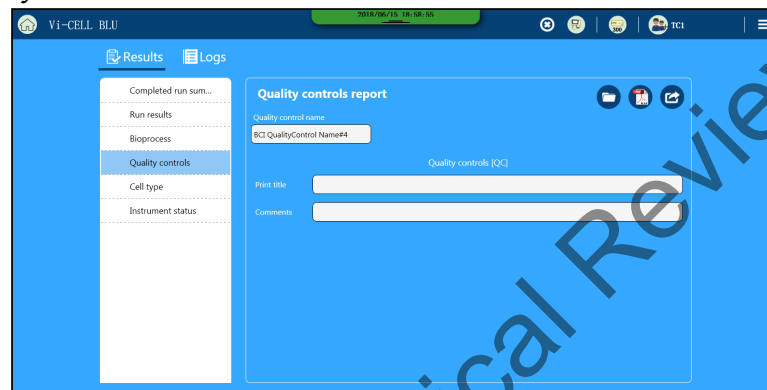
3 Select  to choose a Quality control file for the report.

- Select a Quality control file.
- Select .




4 On the **Quality controls** screen,

- Enter a **Print title**.
- Enter any additional **Comments**.

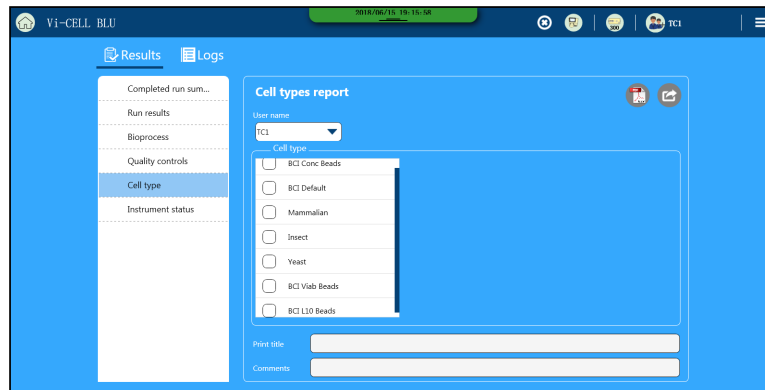


5 Select  to save the report as PDF or select  to Export the report.

Cell type Reports

1 Select  >  Report to view the **Report Results** screen.

2 Select **Cell type**.





3 On The **Cell type** screen,

- Select a **User name**.
- Select your **Cell type** options.
- Enter a **Print title**.
- Enter any additional **Comments**.

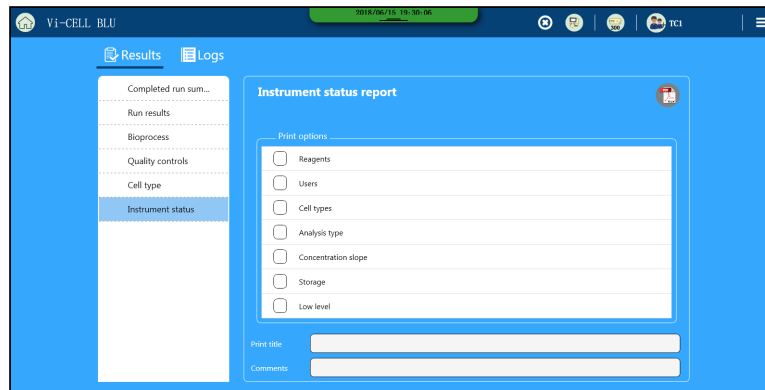
4 Select  to save the report as PDF or select  to Export the report.

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Instrument Reports


1 Select  >  **Report** to view the **Report Results** screen.

2 Select **Instrument status**.



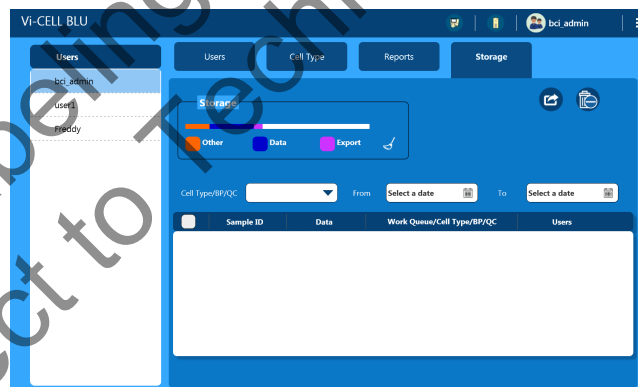
3 On The **Instrument status report** screen,

- Select your **Print Options**.
- Enter a **Print title**.
- Enter any additional **Comments**.

4 Select  to save the report as PDF.

Storage Administration

- Storage Administrations screen.



User Types and Access Levels

The types of user rolls on the instrument are: Normal, Advanced and Admin. When instrument security is disabled, feature availability is as described in the **Security OFF** column and individual user roles are not used.


Refer to [Table 6.1](#) for a list of software features and sub features that are enabled (✓), disabled/read-only (✗), and hidden () for each user type.

Table 6.1 User Types and Access Levels






















Features	Sub Features	Normal User	Advanced User	Admin User	Security OFF
Home	Queue Creation	✓	✓	✓	✓
	Run Results	✓	✓	✓	✓
	Signature	✓	✓	✓	✗
Admin - Users	Add/Edit/Delete			✓	
	Enable/Disable User			✓	
	Change password - Self	✓	✓	✓	
	Reset Password - All Users			✓	
Admin - Cell Types	Add/Edit.Delete		✓	✓	✓
Admin - Storage	View Storage Info	✓	✓	✓	✓
	Delete Shared Folder		✗	✓	✓
	System Backup		✗	✓	✓
	System Cleanup		✗	✓	✓
Reports	Logs		✓	✓	✓
	Results - Self	✓	✓	✓	✓
	Results - All Users		✓	✓	✓
	Instrument Status Report	✓	✓	✓	✓
Review	Reanalyze	✓	✓	✓	✓
	Signature	✓	✓	✓	✗

Table 6.1 User Types and Access Levels

Features	Sub Features	Normal User	Advanced User	Admin User	Security OFF
Bioprocess	Add BP	✗	✓	✓	✓
	Delete BP	✗	✗	✓	✓
	Export Results	👁	✓	✓	✓
	View Results	✓	✓	✓	✓
Quality Controls	Add QC	✗	✓	✓	✓
	Delete QC	✗	✗	✓	✓
	Export Results	👁	✓	✓	✓
	View Results	✓	✓	✓	✓
Settings	Language	✓	✓	✓	✓
	Date & Time	✗	✗	✓	✓
	Security	✗	✗	✓	✓
	Signature Settings	✗	✗	✓	✗
	Run Options - Self	✓	✓	✓	✓
	Show in Results Options - Self	✓	✓	✓	✓
Maintenance	Conc/Size Calibration	✗	✓	✓	✓
	Low Level Controls	👁	👁	👁	👁
	Set Focus	✗	✓	✓	✓
	Dust Reference	✗	✓	✓	✓
	Motor Reg	👁	👁	👁	👁
Reagents	Reagent Containers 1, 2, 3	✓	✓	✓	✓
	Alcohol, CLENZ, Buffer Names	✓	✓	✓	✓
	Alcohol, CLENZ, Buffer Details	✗	✗	✗	✗
My Profile - Self		✓	✓	✓	👁
Help		✓	✓	✓	✓
About		✓	✓	✓	✓

Table 6.1 User Types and Access Levels

Features	Sub Features	Normal User	Advanced User	Admin User	Security OFF
Sign In/Sign Out		✓	✓	✓	 a
Minimize and Exit Software					
Inactivity Timeout/System Lock		✓	✓	✓	N/A

a. Service sign in on long press if security=off.

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What Is The Control Feature?

The control feature monitors Vi-CELL BLU performance. The accuracy of concentration measurements (Total Cells/mL) can be checked using Vi-CELL BLU obtained from Beckman Coulter.

- PN C09148 2 M Concentration Control
- PN C09149 4 M Concentration Control
- PN C09150 10 M Concentration Control
- PN XXXXX L10 size control
- PN C18061 Viability control

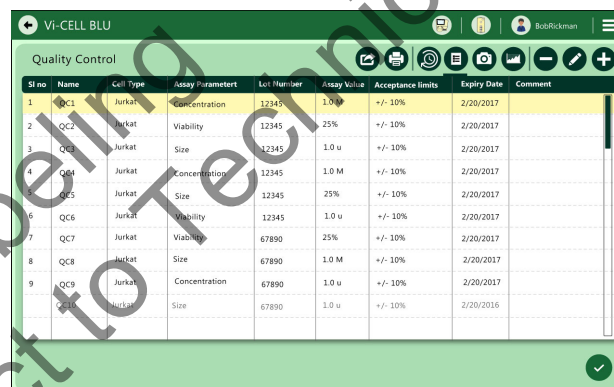
The instrument contains special software that makes it very easy to run the control sample and to store and review the results obtained.

A collection of results from the same control sample are grouped together and can be saved, exported, printed as a single entity called a control (opened, closed etc.). The Vi-CELL BLU is supplied with a control already created to check concentrations.

Run a Concentration Control

[Green Screens need to be replaced throughout](#)

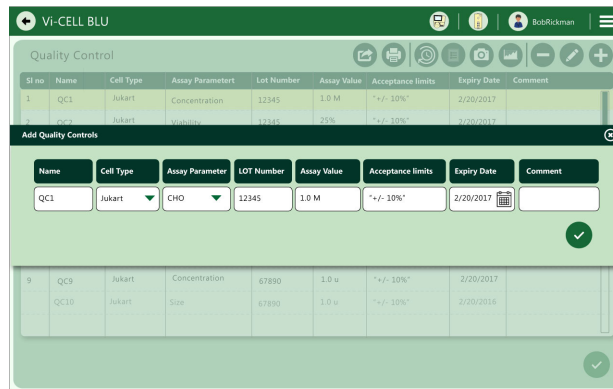
- 1 Select  to display the Quality Control screen and select a control file.




The screenshot shows the 'Quality Control' screen in the Vi-CELL BLU software. The table lists various control samples with their respective parameters and values.

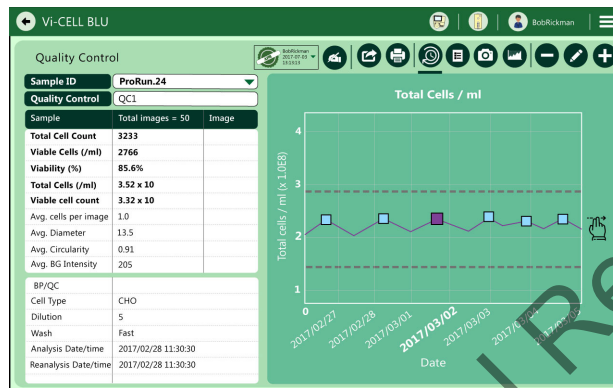
Sl no	Name	Cell Type	Assay Parameter	Lot Number	Assay Value	Acceptance limits	Expiry Date	Comment
1	QC1	Jurkat	Concentration	12345	1.0 u	+/- 10%	2/20/2017	
2	QC2	Jurkat	Viability	12345	25%	+/- 10%	2/20/2017	
3	QC3	Jurkat	Size	12345	1.0 u	+/- 10%	2/20/2017	
4	QC4	Jurkat	Concentration	12345	1.0 M	+/- 10%	2/20/2017	
5	QC5	Jurkat	Size	12345	25%	+/- 10%	2/20/2017	
6	QC6	Jurkat	Viability	12345	1.0 u	+/- 10%	2/20/2017	
7	QC7	Jurkat	Viability	67890	25%	+/- 10%	2/20/2017	
8	QC8	Jurkat	Size	67890	1.0 M	+/- 10%	2/20/2017	
9	QC9	Jurkat	Concentration	67890	1.0 u	+/- 10%	2/20/2017	
10	QC10	Jurkat	Size	67890	1.0 u	+/- 10%	2/20/2016	

2 If desired, select to Add Quality Controls.

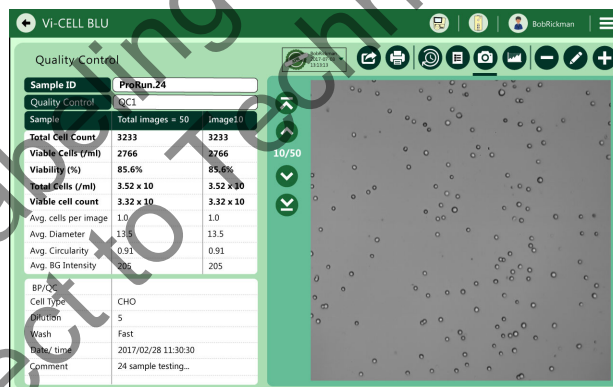


3 Select  to run the Control.

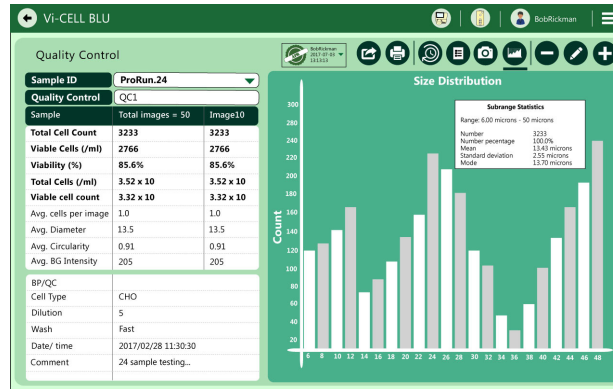
4 Quality Control Total Cells/mL results.



5 Quality Control Camera results.



6 Quality Control Size Distribution results.



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Regulatory Compliance – 21 CFR Part 11

21 CFR Part 11

The Electronic Records and Electronic Signatures Rule (21 CFR Part 11) was established by the FDA to define the requirements for submitting documentation in electronic form and the criteria for approved electronic signatures. This rule, which has been in effect since August 20, 1997, does not stand in isolation; it defines the standards by which an organization can use electronic records to meet its record-keeping requirements. Organizations that choose to use electronic records must comply with 21 CFR Part 11. It is intended to improve an organization's quality control while preserving the FDA's charter to protect the public. Since analytical instrument systems such as the Vi-CELL BLU Cell Viability Analyzer, generate electronic records, these systems must comply with the Electronic Records Rule.

This section describes the relevant portions of the 21 CFR Part 11 regulations and their implementation using the Vi-CELL BLU control software. The implementation and compliance of 21 CFR Part 11 remains the responsibility of the organization or entity creating and signing the electronic records in question. Proper procedures and practices, such as GLP and GMP, are as much part of the overall compliance with these regulations as are the features of the Vi-CELL BLU control software.

Electronic Records

Per Section 11.3 subpart A of 21 CFR Part 11, an electronic record is 'any combination of text, graphics, data, audio, pictorial, or other information representation in digital form that is created, modified, maintained, archived, retrieved or distributed by a computer system'. This refers to any digital computer file submitted to the FDA, or any information not submitted but that needs to be archived. Public docket No. 92S-0251 of the Federal Register (Vol. 62, No. 54) identifies the types of documents acceptable for submission in electronic form and where such submissions may be made.

FDA Requirements

The general comments section of the ruling states that ‘The agency emphasizes that these regulations do not require, but rather permit, the use of electronic records and signatures’. The introduction to the final ruling states that ‘The use of electronic records as well as their submissions to FDA is voluntary’.

If electronic submissions are made, Section 11.2 explains that ‘persons may use electronic records in lieu of paper records or electronic signatures in lieu of traditional signatures provided that: (1) The requirements of this part are met; and (2) The document or parts of a document to be submitted have been identified in public docket No. 92S-0251’.

The Vi-CELL BLU control software has been designed to allow users to comply with the electronic records and signatures rule. Any organization deciding to employ electronic signatures must declare to the FDA their intention to do so.

Implementing Electronic Records and Signatures

Section 11.3 Subpart A describes two classes of systems:

Closed Systems

A closed system is one ‘in which system access is controlled by persons who are responsible for the content of electronic records’. In other words, the people and organization responsible for creating and maintaining the information on the system are also responsible for operating and administering the system.

Open Systems

An open system is one ‘in which system access is not controlled by persons who are responsible for the content of electronic records’.

The Vi-CELL BLU control software is designed to ensure the proper operation, maintenance and administration for system security and data integrity. Anyone who interacts the Vi-CELL BLU, from administrators to users, must abide by these procedures. Therefore the ultimate responsibility is with the organization generating electronic records and signatures. The Vi-CELL BLU software is a component, albeit a vital one, of the overall process.

Controls for Electronic Records

Subpart B, Section 11.10 describes the controls to be applied to a "closed system". Section 11.30 describes the controls for an "open system", which include "those identified in Section 11.10, as appropriate, and additional measures such as document encryption and use of appropriate digital signature standards". Since a typical Vi-CELL BLU system can be regarded as a closed system, additional controls for open systems will not be discussed in this document. The primary thrust of these controls is "to ensure the authenticity, integrity, and, when appropriate, the confidentiality of electronic records, and to ensure that the signer cannot readily repudiate the signed record as not genuine". In other words, to protect the data and to make it difficult for someone to say that

this is not their "signature". Many of the controls described in Section 11.10 refer to written procedures (SOPs) required of an organization by the agency, for the purpose of data storage and retrieval, access control, training, accountability, documentation, record keeping, and change control. The other controls are addressed either by the Vi-CELL BLU software itself, or in combination with end-user procedures.

Of the other controls, perhaps the foremost is described in Section 11.10 Paragraph (a): "Validation of systems to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records." It is the complete and overall validation of the system, as developed by the organization, which ensures the integrity of the system and the data within. It is to this end that the features of the Vi-CELL BLU software comply with the specifications of these regulations.

Establishing an Electronic Record

The Vi-CELL BLU software employs a system of usernames and passwords, consistent with the specifications of Subpart C, Section 11.300, "to ensure that only authorized individuals can use the system, electronically sign a record, access the operation or computer system input or output device, alter a record, or perform the operation at hand".

21 CFR Part 11 Security

To turn on the security option, select.... [TBD](#)

NOTE Inactivity timeout is set to prevent unofficial access to the system, as when the system is left unattended directly after starting the queue.

The system will prompt you to log in. On the **Log In** dialog, enter your user name and password.

New users can only be created and passwords reset by users with Administrator rights. This file is protected with a checksum and for each user name, contains information on when the user was created, by whom, at what level, the user's password in encrypted form and the user's file paths. If this file does not exist or if the checksum is missing or invalid then access to the system will only be possible to a limited number of special users.

File History

The Vi-CELL BLU software also performs data input and "operational checks", as specified in Subpart B, Section 11.10, "to determine, as appropriate, the validity of the source of data input or operational instruction", and "to enforce permitted sequencing of steps and events". These two features ensure that, as much as possible, valid data are being entered into the system, and all required steps have been completed to perform the task at hand.

The purpose of all such data checking and validation is described in Section 11.10, Paragraph (b): "The ability to generate accurate and complete copies of records in both human readable and electronic form suitable for inspection, review, and copying by the agency". Vi-CELL BLU software data files are all automatically saved upon creation and protected with a checksum. Vi-CELL BLU software also allows for the capability for backing up data to mirror directories.

Section 11.10, paragraph (e) requires “use of secure computer-generated, time-stamped audit trails to independently record the date and time of operator entries and actions that create, modify, or delete electronic records. Such audit trail documentation must be retained for a period at least as long that required to for the subject electronic records and must be available for agency review and copying.” The Vi-CELL BLU software complies with this rule by generating an audit trail which records the time a user was logged on. The audit trail is encrypted and checksummed for added security. The audit trail also will record and time-stamp: failed login attempts, switching users, turning security on or off, adding new user, enable/disable user, change password, reset password, lock instrument and failed checksums.

When a data file is created, the Vi-CELL BLU system software provides a computer-generated time-stamped record that documents actions taken to create a record. This information is stored within the actual data file itself, not in the Audit Trail file. Each data file contains a computer-generated time-stamped record, the date and time of operator entries, and the actions taken to create the data file.

The system software does not allow a data record to be modified or deleted within the normal operation of the system software.

If the integrity of a data file is compromised in some way, the file is rendered unusable by the system and it can no longer be used by the Vi-CELL BLU software. Each data file contains an embedded checksum that is used to check the integrity of the file each time the file is loaded. If the data file is compromised, an error message is displayed and the file does not load.

Electronic Signature

In Subpart A, Section 11.3, an electronic signature is defined as "a computer data compilation of any symbol or series of symbols executed, adopted, or authorized by an individual to be the legally binding equivalent of the individual's handwritten signature". Subpart C, Section 11.100 of the regulation defines the general requirements of such a manifestation. Paragraph (a) states that "each electronic signature must be unique to one individual and must not be reused by, or reassigned to, anyone else". These two paragraphs, taken together, mean that an electronic signature is some computer representation of a user's identity, developed to ensure the distinct and unique identity of that user. The procedural aspect of Section 11.100 requires that before any such electronic representation is applied, the organization first must "verify" the identity of that individual. The subsequent use of electronic signatures as the "legally binding equivalent of traditional handwritten signatures" then must be "certified" to the agency in writing.

Subpart C, Section 11.200, refers to biometric and non-biometric forms of electronic signature. Biometric signatures are defined in Subpart A, Section 11.3 as a "a method of verifying an individual's identity based on measurement of the individual's physical feature(s) or repeatable action(s) where those features and/or actions are both unique to that individual and measurable". Biometrics are generally regarded as techniques such as fingerprints or retinal scans, which are considered to be totally unique to each individual and require specific forms of scanning devices to read and interpret. Non-biometric signatures are those that are computer generated and, as per Section 11.200, "Employ at least two distinct identification components such as an identification code and password". It is this form of electronic signature that is supported by the Vi-CELL BLU software.

Generating Electronic Signatures

The Vi-CELL BLU software employs User IDs and passwords to verify the identification of each user logging into the system. When using this technique, Subpart C, Section 11.300 of the regulation requires "maintaining the uniqueness of each combined identification code and password, such that no two individuals have the same combination of identification code and password". This section also requires that the "identification code and password issuances are periodically checked, recalled, or revised". Vi-CELL BLU software supports both of these provisions.

The administration of the system requires that individuals are added to the list of valid Vi-CELL BLU users via the **Add a New User** dialog box. The "identification code" or username of each Vi-CELL BLU user must be unique. No two users on the same Vi-CELL BLU system can have the same user name. It is also required that these users supply a password to access the Vi-CELL BLU software, thus satisfying the requirement to "employ at least two distinct identification components such as an identification code and password". Passwords can be controlled to prohibit the use of duplicates and to force the selection of new passwords after a prescribed period of time.

By the implementation of these features, the Vi-CELL BLU software can satisfy the requirement that "identification code and password issuances are periodically checked, recalled, or revised".

Applying Electronic Signatures

Subpart C, Section 11.200 stipulates several requirements for the control of electronic signatures. Procedurally, the regulations require that electronic signatures "be used only by their genuine owners" and that they "be administered and executed to ensure that attempted use of an individual's electronic signature by anyone other than its genuine owner requires collaboration of two or more individuals". Through the application of Vi-CELL BLU user and password configuration procedures, the system can be configured to "ensure" that inappropriate use of these identifiers can be performed only by the intentional divulgence of security information.

Section 11.200 further specifies the use of electronic signature components during a period "when an individual executes a series of signings during a single, continuous period of controlled system access", and "when an individual executes one or more signings not performed during a single, continuous period of controlled system access". This section of the document represents the "heart" of electronic signature application. To comply with these provisions, the Vi-CELL BLU software uses the application of the username and password to authenticate the user making and saving the changes, in conjunction with file history.

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Data Acquisition

Need to verify these specs

- Operating principle: analysis of video images
- Sample type: spatial data
- Cell size range of 2 microns to 60 microns
- Analysis rate: up to 100 Images in 130 seconds
- Digitizing resolution: 2048x2048

Cell Viability/Concentration/Cell Count

Need to verify these specs

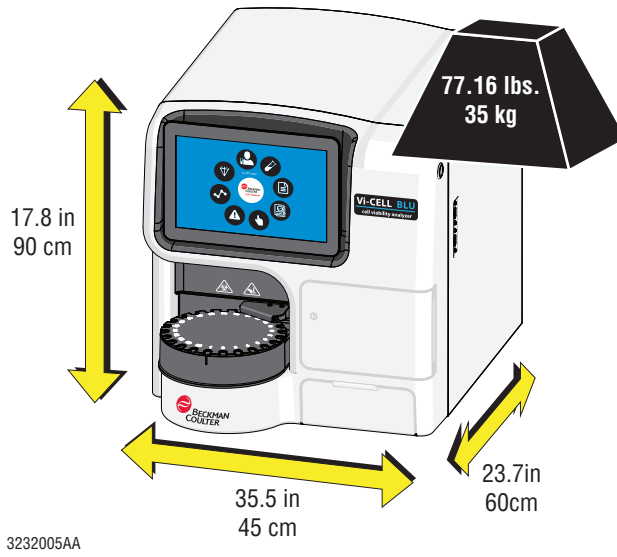
- Concentration Range: 5×10^4 to 15×10^6 Cells/mL
- Viability Range: 0 to 100%
- Mean Recovery Value of 20 replicates of Concentration Control on Vi-CELL BLU compared to the lot assay value used are $\pm 6\%$.

NOTE The results for samples at the low end of the concentration range will not be as statistically accurate due to the low number of measured cells. The accuracy at the high end of the concentration range is affected by the difficulty of declustering groups of cells particularly if the cells are large. The sample should be diluted to bring its concentration into range or to improve the accuracy of the results

Physical Requirements

- Power 50 watts (180 watts max.)
- Voltages 90-264V AC, 47-63 Hz
- Temperature: 13 to 37°C (55 to 99°F)
Temperature Variation of: $\pm 3^\circ\text{C}$ over 8 hours.
- Humidity: 10 to 90%
Humidity Variation of: $\pm 10\%$ over 8 hours

Unit Dimensions



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Service and Maintenance

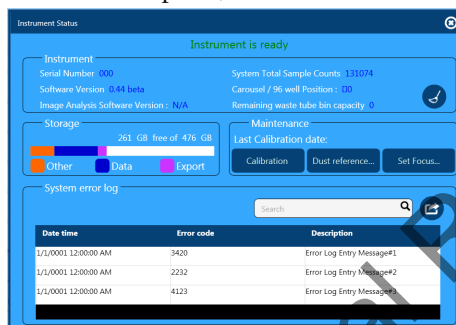
Focusing Wizard

A focusing wizard is provided that automatically checks and if necessary adjusts the focus. Selecting the set focus item in the diagnostic menu and using the Vi-CELL BLU Focus Control that is supplied with the instrument (or can be supplied by Beckman Coulter) begins the process. Focus should be run if images are clearly out of focus or a size control fails specification.

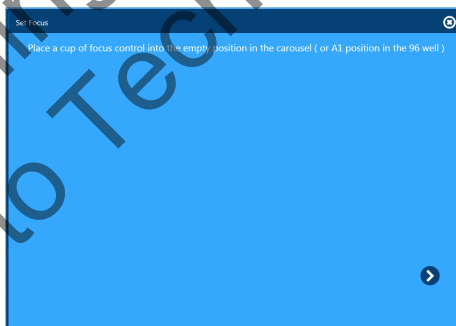
Set Focus



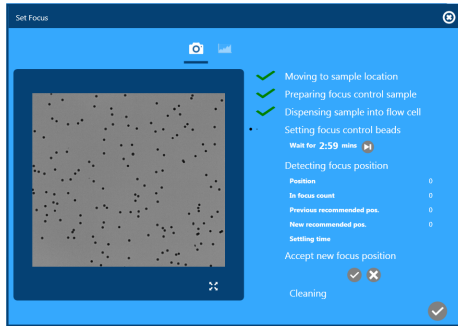
- 1 Select  and  and place a cup of focus control into the empty position in the carousel (or A1 position in the 96 well plate).





- 2 Place a cup of focus control into the empty position in the carousel (or A1 position in the 96 well plate).



- 3 Wait while the Focus Control sample is being processed.




- 4 Choose  to accept the new focus position.

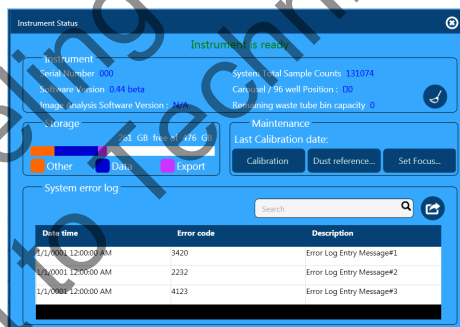
- 5 After cleaning is complete, select  to exit Set Focus.

Calibration Control



NOTE To perform Calibration, you must be logged in as Administrator and have access to a vortexer and a microcentrifuge.

- 1 Select  and **Calibration** and select a control.



- 2 Following the instructions listed on the screen, enter the assay value, lot number, and expiration date for each of the concentrations of Vi-CELL Concentration Control beads.

- 3 To prepare the bead samples, vortex each tube for approximately 10 seconds both right side up and upside down. Place the tubes in a microcentrifuge, ensuring they are evenly spaced so as to keep the centrifuge balanced, and centrifuge them at 2000 rcf for 10 seconds. 10 tubes of the 2M Control, 5 tubes of the 4M Control, and 3 tubes of the 10M Control should be prepared.
- 4 Remove the caps from all of the tubes and load the tubes into the carousel to match the on-screen carousel diagram. The 2M Control will be in positions 1-10, the 4M Control will be in positions 11-15, and the 10M Control will be in positions 16-18.



- 5 Select .
- 6 When all the tubes have been run and the calibration equation has been calculated select to accept the new calibration.
- 7 Review the,
 - Calibration Concentration results screen
 - Calibration Concentration camera screen
 - Calibration Concentration graph screen
 - Calibration Size results screen
 - Calibration Size camera screen
 - Calibration Size graph screen

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Circularity

Verify the definition and equation for circularity are correct

A value from 0 to 1, with 1 representing a perfect circle. Computed as D_a/D_p , where $D_a = \text{square root}(4A/\pi)$, $D_p = P/\pi$; A = pixel area, P = pixel perimeter.

The circularity distribution is based on individual cells, not cells that are part of clusters.

System Performance

Run Statistics

Cell Count — The actual number of cells recorded per frame and for the total number of frames.

Viable Cells — The number of viable cells per image and for the total number of images.

Viability — The percentage of viable cells per image and for the total number of images.

Total Cells/mL — The concentration of cells per mL.

Viable Cells/mL — The concentration of viable or “live” cells per mL.

Avg. Diameter — The average size of cells per image and for total images.

Avg. Circularity — The average “roundness” of the cells.

Images — The total number of images analyzed.

Average Cells/Image — The number of cells captured per image.

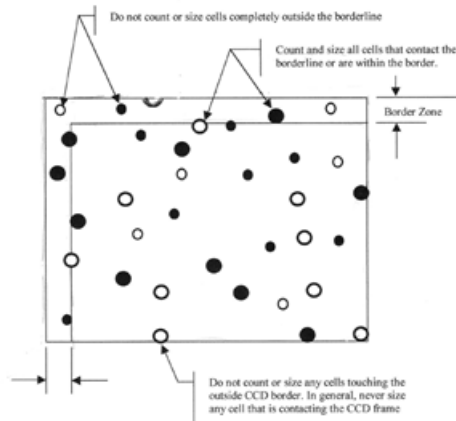
Background Intensity — The average pixel value, from 0 to 255, of the image background.

Effective Field of View

“Effective Field of View” is the size of the area inside the reduced measurement frame, and it most accurately represents the actual counting area. It is the area that should be used in computing cell concentrations.

The Effective Field of View value in the configuration or calibration screens permits you to calculate concentrations to verify them against reported values.

Is this graphic accurate for Vi-CELL BLU?



The border zone indentations on the top and left border of the image are used to correct for the effect whereby larger objects are more likely not to be because of contact with an edge of the image. That effect introduces a bias into size distributions and concentration results, and the indents are a way to correct for it.

Objects intersecting the bottom or right edge are not counted.

Objects that are partially in the main counting area and partially in the border zone are counted.

Objects that are entirely within the border zone are not counted.

With this method, larger objects that would have gotten rejected are now counted.

Smaller objects are not affected (the correction varies in proportion to particle size).

The border indent is 30 microns, which is large enough to handle all actual cell sizes that are encountered.

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Troubleshooting Table

Table D.1 through Table D.6 lists problems that the operator could encounter while running the Vi-CELL BLU instrument, the probable causes of each problem, and the corrective actions. These problems are split into individual tables for each system affected. These problems are listed alphabetically in the Index, under the primary entry “troubleshooting.”

IMPORTANT This troubleshooting table contains the same information given to the instrument operators in the instrument’s Instructions for Use, plus “service only” actions. Links to procedures that are live in the Instructions for Use are replaced in this manual by references to the correct section in the Instructions for Use. Leaving in the action to “[contact us](#)” lets you know how much a customer is expected to do before calling service.

IMPORTANT There are four different severities catalogued by the system:

- Notification. This means no special attention is required.
- Warning. This means the system is operational, but requires special attention.
- Error. This means the system is inoperative, but recoverable.
- Fatal. This means the system is inoperative and the error is not recoverable.

NOTE A particular failure mode can potentially display any level of severity depending on whether or not the system was able to self-correct the problem or not.

Table D.1 Troubleshooting Table - Instrument

Problem	Probable Cause	Corrective Action
Subsystem: General		
<i>Missing component</i>	<ul style="list-style-type: none"> • Loose/disconnected cable • Hardware failure 	Customer 1. Contact us .
<i>Logic error</i>	Software error	Customer 1. Contact us .
Subsystem: Configuration		
<i>Configuration not found</i>	<ul style="list-style-type: none"> • Hard disk corruption • Software error 	Customer 1. Restart the system. 2. If the problem persists, contact us .
<i>Calibration not found</i>	<ul style="list-style-type: none"> • Disk degredation • Software error • Configuration lost because of software update 	Customer 1. Restart the system. 2. Recalibrate the sampler system. Refer to IFU procedure . 3. Refocus the optics. Refer to IFU procedure . 4. If the problem persists, contact us .

Table D.1 Troubleshooting Table - Instrument

Problem	Probable Cause	Corrective Action
Subsystem: Database		
<i>No connection</i>	<ul style="list-style-type: none"> • Disk degradation • Software error 	Customer <ol style="list-style-type: none"> 1. If you are using a remote database, check the network connection. 2. Restart the system. 3. If the problem persists, contact us.
<i>Insert error</i>	<ul style="list-style-type: none"> • Not enough disk capacity • Database is corrupt • Disk drive failure 	Customer <ol style="list-style-type: none"> 1. Navigate to the System Status dialog and verify the available disk capacity. Refer to System Status in Chapter 2, Installation and Verification of the Instructions for Use manual. 2. Backup system data and remove from the system volume. refer to ifu procedure 3. Clear the exported data folders on the instrument. refer to ifu procedure 4. Restart the system. 5. If the problem persists, contact us.
<i>Retrieve error</i>	<ul style="list-style-type: none"> • Invalid reference UUID • Database is corrupt • Disk drive failure 	Customer <ol style="list-style-type: none"> 1. Verify available disk capacity in the System Status dialogs. Refer to IFU procedure 2. Restart the system. 3. If the problem persists, contact us.
Subsystem: Storage		
<i>Read error</i>	<ul style="list-style-type: none"> • Disk drive failure 	Customer <ol style="list-style-type: none"> 1. Restart the system. 2. If the problem persists, contact us.
<i>Write error</i>	<ul style="list-style-type: none"> • Disk drive failure 	Customer <ol style="list-style-type: none"> 1. Restart the system. 2. If the problem persists, contact us.
<i>Near Capacity</i>	System storage is near capacity	Customer <ol style="list-style-type: none"> 1. Backup system data and remove from the system volume. refer to ifu procedure 2. Clear the exported data folders on the instrument. refer to ifu procedure

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Table D.1 Troubleshooting Table - Instrument

Problem	Probable Cause	Corrective Action
Subsystem: Integrity		
<i>Verification on read</i>	<ul style="list-style-type: none"> Disk drive failure 	Customer <ol style="list-style-type: none"> Restart the system. Restore the system from the last archive. Refer to IFU procedure. If the problem persists, contact us.

Table D.2 Troubleshooting Table - Controller Board (Main Board)

Problem	Probable Cause	Corrective Action
Subsystem: General		
<i>Connection Error</i>	Unable to connect to main board.	Customer <ol style="list-style-type: none"> Power cycle the system by unplugging the Analyzer and plugging it back in. Turn on the Analyzer. If the problem persists, contact us.
Subsystem: Communication		
<i>Host Comm Error</i>	<ul style="list-style-type: none"> Main board failure Problem with firmware Problem with communication chips 	Customer <ol style="list-style-type: none"> Contact us.
Subsystem: Firmware		
<i>Firmware Update Error</i>	<ul style="list-style-type: none"> Corrupt firmware update file Main board failure 	Customer <ol style="list-style-type: none"> Contact us.
<i>Firmware Bootup Error</i>	<ul style="list-style-type: none"> Corrupted firmware image on the main board. Main board failure 	Customer <ol style="list-style-type: none"> Contact us.
<i>Invalid Firmware Version</i>	<ul style="list-style-type: none"> Incorrect firmware version 	Customer <ol style="list-style-type: none"> Contact us.

Table D.3 Troubleshooting Table - Reagents

Problem	Probable Cause	Corrective Action
Subsystem: General		
Subsystem: RFID Hardware		
<i>Hardware Error</i>	<ul style="list-style-type: none"> Component failure Loose or faulty wiring between the main board and the RFID board. Main board failure 	Customer <ol style="list-style-type: none"> Restart the system. Replace the reagent pack. Refer to IFU procedure. If the problem persists, contact us.
Subsystem: Bay Hardware		

Table D.3 Troubleshooting Table - Reagents

Problem	Probable Cause	Corrective Action
<i>Sensor Error</i>	<ul style="list-style-type: none"> • Door or pack presence sensor failure • Faulty wiring 	Customer <ol style="list-style-type: none"> 1. Restart the system. 2. Replace the reagent pack. Refer to IFU procedure. 3. If the problem persists, contact us.
<i>Latch Error</i>	<ul style="list-style-type: none"> • Unable to actuate the door latch • Reagent door latch solenoid failure • Faulty wiring to reagent door latch solenoid • Main board failure 	Customer <ol style="list-style-type: none"> 1. Contact us.
Subsystem: Reagent Pack		
<i>Pack Invalid</i>	Corrupted or unprogrammed consumable identification tag	Customer <ol style="list-style-type: none"> 1. Replace the reagent pack. Refer to IFU procedure. 2. If the problem persists, contact us.
<i>Pack Expired</i>	<ul style="list-style-type: none"> • The shelf-life for the reagent pack is past its expiration date. • The in-service life for the reagent pack is past its expiration date Need to align the verbiage for this expiration date nomenclature with the Reagent IFU and customer IFU. 	Customer <ol style="list-style-type: none"> 1. Replace the reagent pack. Refer to IFU procedure.
<i>Pack Empty</i>	<ul style="list-style-type: none"> • The reagent pack is empty 	Customer <ol style="list-style-type: none"> 1. Replace the reagent pack. Refer to IFU procedure.
<i>No Pack</i>	<ul style="list-style-type: none"> • Reagent pack not installed • Failure of the recognition component of the reagent pack 	Customer <ol style="list-style-type: none"> 1. Install the reagent pack. Refer to IFU procedure. 2. Restart the system. 3. If the problem persists, contact us.
<i>Usage Update Fail</i>	<ul style="list-style-type: none"> • Failing RFID module • Failed/corrupt consumable 	Customer <ol style="list-style-type: none"> 1. Replace the reagent pack. Refer to IFU procedure. 2. Restart the system. 3. If the problem persists, contact us.

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Table D.4 Troubleshooting Table - Motion

Problem	Probable Cause	Corrective Action
Subsystem: General		
Subsystem: Sample Deck		
<i>Not Calibrated</i>	<ul style="list-style-type: none"> • Stage/Controller replaced • Software update failed to retain previous settings • Corrupt settings 	Customer 1. Contact us.
<i>Calibration Failure</i>	<ul style="list-style-type: none"> • Failed to correctly follow the calibration sequence • Calibration resulted in invalid values <ul style="list-style-type: none"> — Possible logic error 	Customer 1. Contact us.
Subsystem: Motor		
<i>Operation Timeout</i>	<ul style="list-style-type: none"> • Motor failed to execute operation in the allowed time <ul style="list-style-type: none"> — Motor may be stalled or broken — Main board may have a failing component 	Customer 1. Power cycle the system by unplugging the Analyzer and plugging it back in. 2. Turn on the Analyzer. 3. If the problem persists, contact us.
<i>Homing Failure</i>	<ul style="list-style-type: none"> • The system may not have found homing flag within the allowed time <ul style="list-style-type: none"> — Sensor failure — Encoder failure 	Customer 1. Power cycle the system by unplugging the Analyzer and plugging it back in. 2. Turn on the Analyzer. 3. If the problem persists, contact us.
<i>Positioning Failure</i>	<ul style="list-style-type: none"> • The system did not reach the requested position. <ul style="list-style-type: none"> — Encoder failure — Motor failure — Main board failure — Motion obstructed 	Customer 1. Power cycle the system by unplugging the Analyzer and plugging it back in. 2. Turn on the Analyzer. 3. If the problem persists, contact us.

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Table D.4 Troubleshooting Table - Motion

Problem	Probable Cause	Corrective Action
<i>Thermal</i>	<ul style="list-style-type: none"> • The motor controller chip on board is overheating. <ul style="list-style-type: none"> — Motor travel may be obstructed — Motor wiring may be faulty — Airflow through the instrument may be impeded 	Customer <ol style="list-style-type: none"> 1. Power cycle the system by unplugging the Analyzer. 2. Allow the system to cool down. 3. Plug the system back in. 4. Turn on the Analyzer. 5. If the problem persists, contact us.
<i>Overcurrent</i>	<ul style="list-style-type: none"> • The motor controller chip on board is overheating. <ul style="list-style-type: none"> — Motor travel may be obstructed — Motor wiring may be faulty — Airflow through the instrument may be impeded 	Customer <ol style="list-style-type: none"> 1. Power cycle the system by unplugging the Analyzer and plugging it back in. 2. Turn on the Analyzer. 3. If the problem persists, contact us.

Table D.5 Troubleshooting Table - Fluidics

Problem	Probable Cause	Corrective Action
Subsystem: General		
<i>Hardware Error</i>	<ul style="list-style-type: none"> • Syringe pump failure • Valve controller failure 	Customer <ol style="list-style-type: none"> 1. Power cycle the system by unplugging the Analyzer and plugging it back in. 2. Turn on the Analyzer. 3. If the problem persists, contact us.
<i>Communication Error</i>	<ul style="list-style-type: none"> • Communication fault with the syringe pump mechanism <ul style="list-style-type: none"> — Possible failed pump — Possible failed wiring connection — Possible main board failure 	Customer <ol style="list-style-type: none"> 1. Power cycle the system by unplugging the Analyzer and plugging it back in. 2. Turn on the Analyzer. 3. If the problem persists, contact us.
<i>Nightly Clean Cycle Skipped</i>	<ul style="list-style-type: none"> • Insufficient reagents present to execute the scheduled nightly clean • Other hardware fault 	Customer <ol style="list-style-type: none"> 1. Perform a manual clean. Refer to IFU procedure. 2. Check the reagent status. Refer to IFU procedure. 3. Retry the cleaning cycle at the next interval. Refer to IFU procedure.
Subsystem: Syringe Pump		

Table D.5 Troubleshooting Table - Fluidics

Problem	Probable Cause	Corrective Action
---	<u>??</u>	Customer 1. Power cycle the system by unplugging the Analyzer and plugging it back in. 2. Turn on the Analyzer. 3. If the problem persists, contact us .
Subsystem: Valve Controller		
---	<u>??</u>	Customer 1. Power cycle the system by unplugging the Analyzer and plugging it back in. 2. Turn on the Analyzer. 3. If the problem persists, contact us .

Table D.6 Troubleshooting Table - Imaging

Problem	Probable Cause	Corrective Action
Subsystem: General		
<i>Hardware Error</i>	<ul style="list-style-type: none"> • Camera is disconnected • Camera failure 	Customer 1. Power cycle the system by unplugging the Analyzer and plugging it back in. 2. Turn on the Analyzer. 3. If the problem persists, contact us .
<i>Operation Timeout</i>	<ul style="list-style-type: none"> • The camera failed to trigger • Faulty camera connections • Camera failure 	Customer 1. Power cycle the system by unplugging the Analyzer and plugging it back in. 2. Turn on the Analyzer. 3. If the problem persists, contact us .
Subsystem: Camera		
<i>Hardware Error</i>	<ul style="list-style-type: none"> • Camera is disconnected • Camera failure 	Customer 1. Power cycle the system by unplugging the Analyzer and plugging it back in. 2. Turn on the Analyzer. 3. If the problem persists, contact us .
<i>Operation Timeout</i>	<ul style="list-style-type: none"> • The camera failed to trigger • Faulty camera connections • Camera failure 	Customer 1. Power cycle the system by unplugging the Analyzer and plugging it back in. 2. Turn on the Analyzer. 3. If the problem persists, contact us .
<i>Cannot connect</i>	<u>??</u>	Customer 1. Contact us .
Subsystem: Trigger		


Table D.6 Troubleshooting Table - Imaging

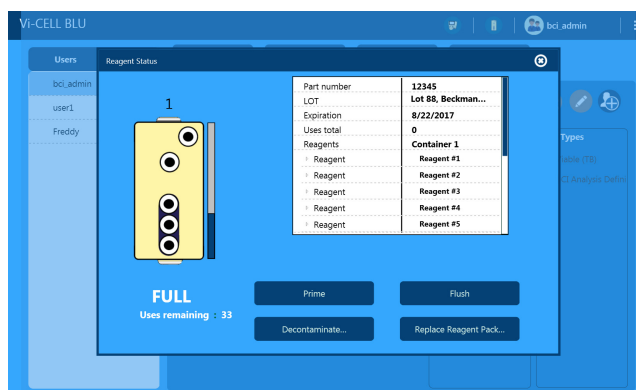
Problem	Probable Cause	Corrective Action
<i>Hardware Error</i>	<ul style="list-style-type: none"> • Problem with the main board • Faulty main board to camera wiring 	Customer <ol style="list-style-type: none"> 1. Power cycle the system by unplugging the Analyzer and plugging it back in. 2. Turn on the Analyzer. 3. If the problem persists, contact us.
<i>Operation Timeout</i>	<ul style="list-style-type: none"> • Problem with the main board • Faulty main board to camera wiring 	Customer <ol style="list-style-type: none"> 1. Power cycle the system by unplugging the Analyzer and plugging it back in. 2. Turn on the Analyzer. 3. If the problem persists, contact us.
Subsystem: LED		
<i>Hardware Error</i>	Connection failure to LED module.	Customer <ol style="list-style-type: none"> 1. Power cycle the system by unplugging the Analyzer and plugging it back in. 2. Turn on the Analyzer. 3. If the problem persists, contact us.

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Replacing Reagents and Decontamination

Reagent Status

Select  to display the Reagent Status screen.



Replace Reagent Pack

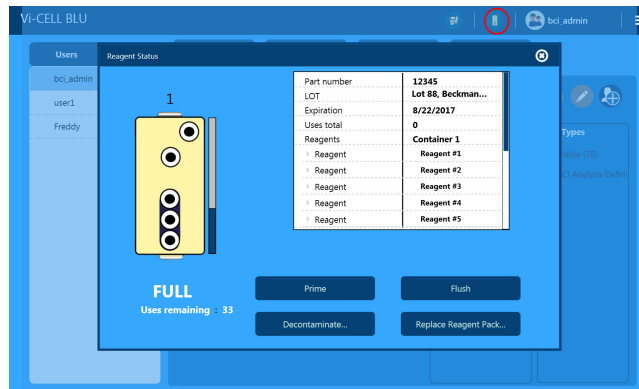



Risk of biohazardous exposure if you have skin contact with the Reagent Pack waste liquid. The Reagent Pack waste bottle has a vent and the Reagent Pack must be upright whenever you are handling a used Reagent Pack in order to prevent waste liquid from leaking out of the Reagent Pack waste bottle. Clean up spills immediately. Dispose of the Reagent Pack and the solid waste in accordance with your local regulations and acceptable laboratory procedures.

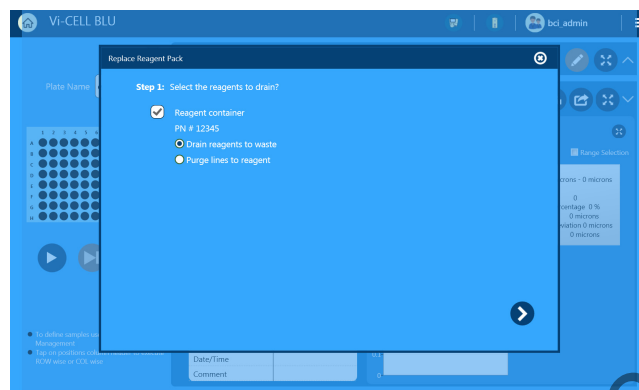
Always use the appropriate Personal Protective Equipment (PPE) when working with biohazardous materials.



- 1 Select  and **Replace Reagent Pack**.

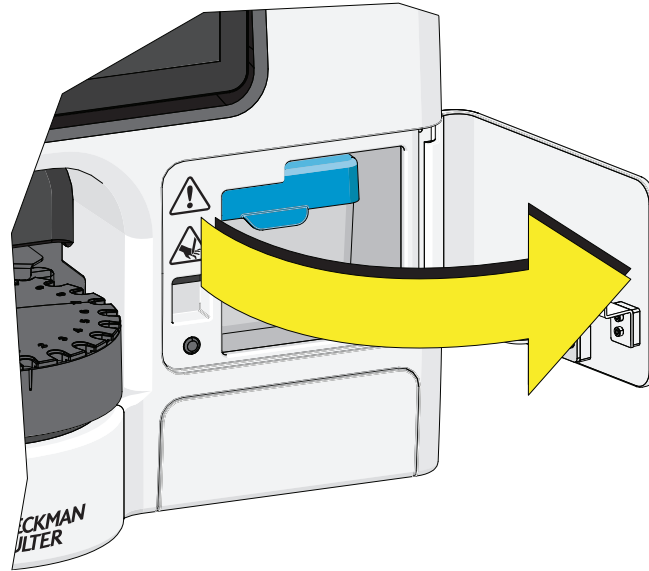


- 2 Select the reagent to drain and select .



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3 The reagent door opens.



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