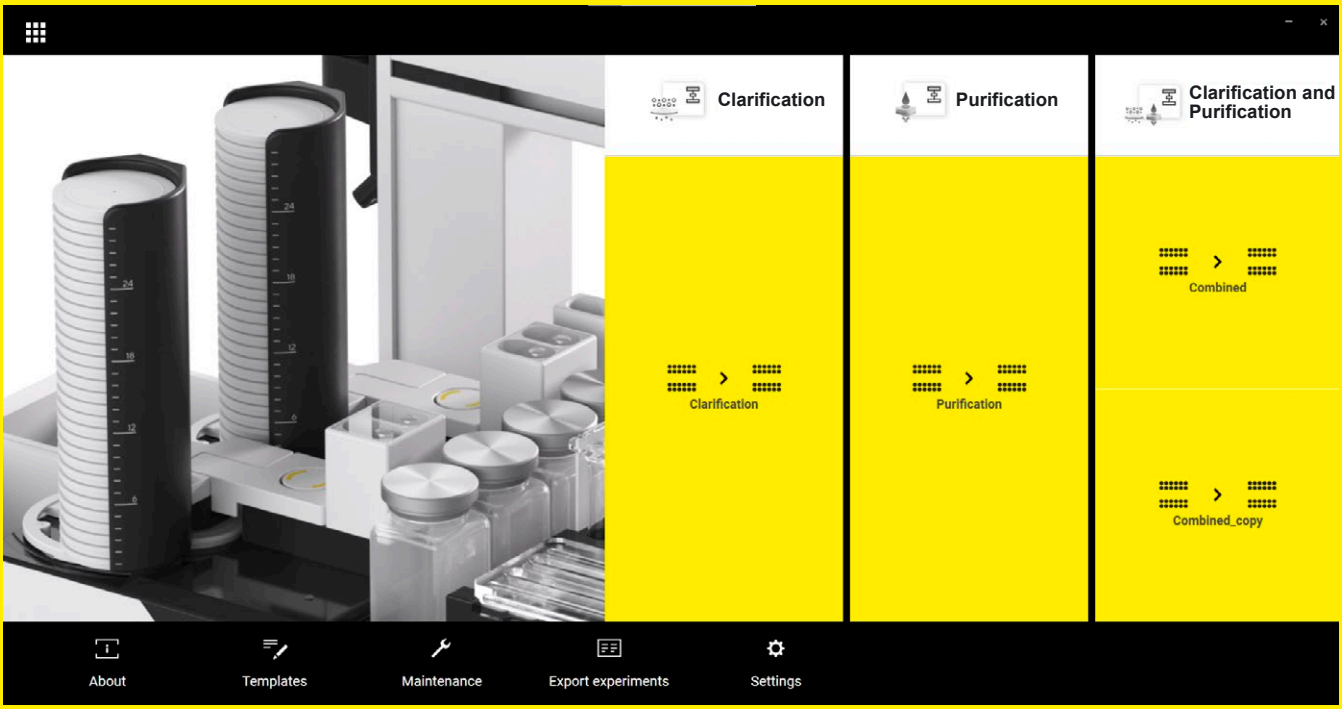
**Operating Instructions**

Original Operating Instructions

# StreamLink® CC 15 Software

Software for Controlling the StreamLink® CC 15 Automated, High-Throughput System




SARTORIUS

# Contents

# 1 About these Instructions

## 1.1 Scope

These instructions are part of the software. These instructions apply to the software in the following versions:

| Software | Version |
|---|---|
| StreamLink® CC 15 software | 20.0.0 and higher |

## 1.2 Related Documents

▶ In addition to these instructions, observe the following documentation:
  – Operating Instructions StreamLink® CC 15

## 1.3 Target Groups

| Target group | Knowledge and qualifications |
|---|---|
| User | The user is familiar with the operation of the software and the associated work processes. The user understands the hazards which may arise when working with the software and knows how to prevent them. The user has been trained in the operation of the product. |
| Operating engineer \| laboratory manager | The operating engineer \| laboratory manager makes decisions about the use and configuration of the product. The operating engineer \| laboratory manager has been trained in the operation of the product. |
| Administrator | The administrator is responsible for integrating the product into a network or a production process. The administrator ensures the reliable functioning of the product. The administrator has been trained in the operation of the product. |

## 1.4 Symbols Used

▶ Required action: Describes activities that must be carried out. The activities in the sequence must be carried out in succession.

▷ Result: Describes the result of the activities carried out.

[ ] Refers to operating and display elements. Indicates status, warning, and error messages.

# 2 Safety Information

## 2.1 Intended Use

The software must be installed on the supplied control unit. The control unit must be connected to the StreamLink® CC 15 device. All process sequences must be controlled on the screen of the control unit.

The device is provided with pre-set templates for clarification only, purification only and combined processes. The user can define their own templates.

## 2.2 Automatic Processes

If automatic processes are executed as part of a template: Automatic actions are performed on the hardware, e. g. rinsing the liquid lines with cleaning solution.

If these automatic sequences are interrupted or changed: The processes may be disrupted. This may have unforeseen consequences, e. g. leakage of fluids. Personnel can be injured, e.g. skin irritation, if fluids escape.

▶ Do **not** interrupt automatic sequences that are being carried out as part of the template.
▶ Do **not** perform any software updates while processes are being carried out on the hardware.

# 3 Introduction

## 3.1 User Interface

After starting the software, the main screen is displayed. All other screens can be opened from this main screen. This screen may differ depending on previous templates run.

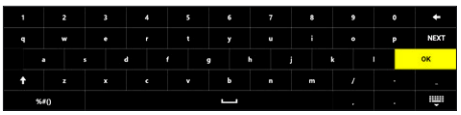

Abb. 1: Main Screen

| Pos. | Name | Description |
|---|---|---|
| 1 | [Home] Button | Opens and closes the main screen. |
| 2 | Quick links | Opens different submenus, e. g. settings. |
| 3 | Last used tiles | Displays latest used templates that enable to access directly to the experiment menu for starting a run. |
| 4 | Last Run Recovery | Is present if the last experiment was stopped unexpectedly before it was fully completed, e.g. when closing the app or after a power failure. Indicates details on the experiment and option to reload in that experiment. |

## 3.2 Navigation

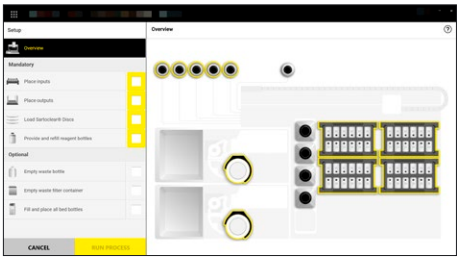
The software can be fully operated by touch. If desired, a mouse and | or keyboard (**not** supplied with the device) can be connected to the control unit.

### Procedure



- ▶ Click on an input field.
- ▷ The keyboard slides up automatically.
- ▶ Confirm your entry with [OK].

- ▶ For navigating in the sub menus you can use the button bars at the top of the page or the arrows at the bottom of the page.



- ▶ Items in the list can be selected to update the mimic | present detailed information | allow updates or the items on the mimic can be clicked to navigate to the same location.
- ▶ Clicking the [Overview] button will bring the mimic back to the high level view.
- ▷ Lists can often be scrolled via the touch screen using the standard Windows drag and let go mechanism.

## 3.3 Opening Operating Instructions from the Software

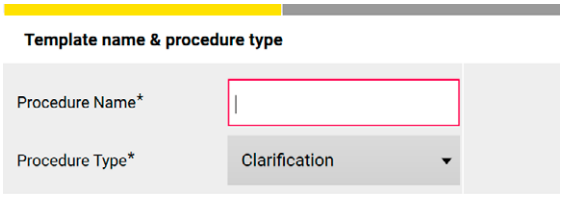
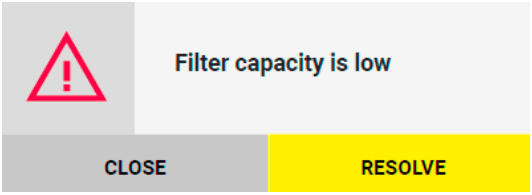
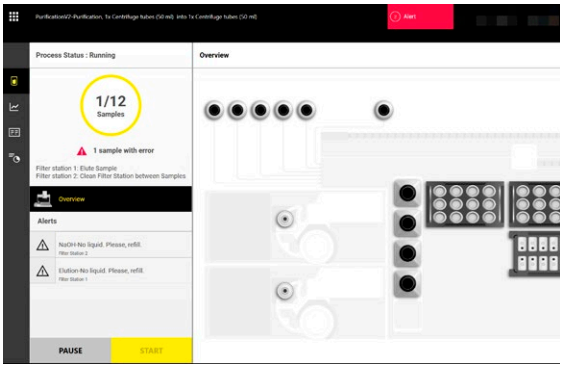
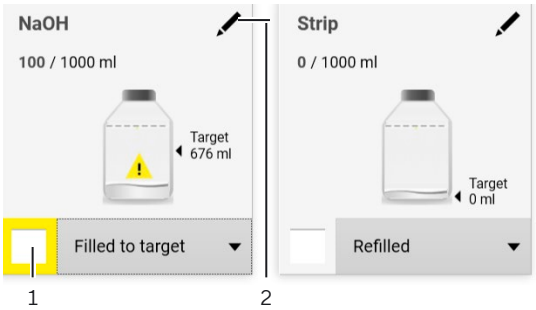
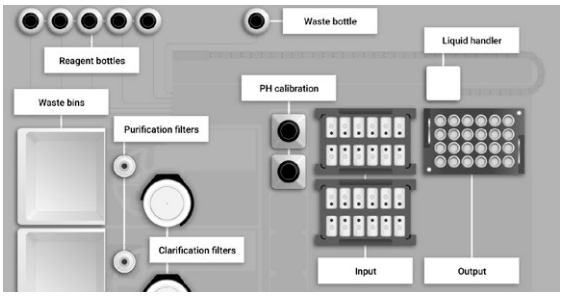
### Procedure

- ▶ In the main screen, click the [About] button to select between the language specific operating instructions for soft- and hardware.

- ▶ Alternatively, use the questionmark symbol in the right corner of each screen to open the operating instructions directly.

## 3.4 Integrated Help | Alerts

The integrated help is displayed at relevant times in the software. They indicate that something needs to be changed in the current settings or that the user needs to confirm a window. The alerts are shown in the upper right corner of the header. Some alerts can be critical resulting in a process stop.

| Help | Procedure |
|---|---|
|  | ▷ If the entry in an input field is invalid: The input field is highlighted \| framed in red, e. g. in the template creation:<br>▶ Change the entry in the input field according to the suggested help text. |
|  | ▷ If a system interaction is needed: A help message will be displayed.<br>▶ Click on [RESOLVE] to see the required actions. |
|  | ▷ If the entry in an input field is invalid: The input field is highlighted \| framed in red and a help text is being displayed.<br>▶ Change the entry in the input field according to the suggested help text (1). |
|  | ▷ If an error on the hardware appears: The item of concern is highlighted red and a warning triangle is shown. Help text is also displayed.<br>▶ Click on the respective item(s).<br>▶ Follow the required actions.<br>▶ Click on [RETRY]. |
|  | ▷ If bottles need to be provided \| refilled: A yellow warning triangle will be displayed.<br>▶ If necessary: Click on the black pencil (2) if more detailed changes are required, e. g. bottle size changes.<br>▶ Refill the respective bottle.<br>▶ The drop down can be changed between “Refilled“ and “Filled to target“.<br>▶ Tick the [Filled to target] (1) checkbox to confirm that the bottles are full. |
|  | ▶ By clicking on the (?) in the right corner of the mimic screen, all hardware components are named in the respective position.<br>▶ By clicking on the (?) in the right corner of the [Templates] screen, a software configured bookmark in this software manual, which has the table of template parameters and their explanation, will open. |

# 4 Operation

## 4.1 Creating a Template

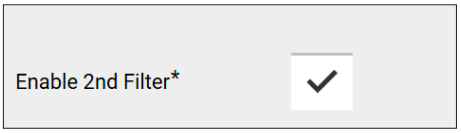
In order to run an experiment, either pre-set templates can be used or a template can be created in which the different phase parameters are defined for each process.

The software guides through the template creation. It leads through different entry fields which need to be filled out.

### Procedure

▶ Navigate to the [Templates] screen and use the [+] button to add a new template, or clone an existing template and edit to change.

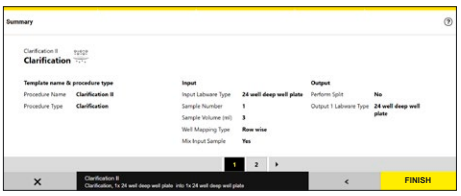
▶ Name the template and select the procedure type.
▶ Fill out the entry fields according to the desired process making sure the template matches the labware | volumes to be loaded.




▷ If desired: Check boxes can be ticked | unticked to enable or disable specific functionality of the template.
▷ Enabling | disabling entry fields may hide or show other parameters to be filled in.

▶ You can always go back and forth using the arrows in the right corner of the screens.
▷ Validation is performed on parameters to ensure a consistent template run. Errors are shown in red highlight and when the edit box is selected the warning will be presented above the on screen keyboard.


▷ The yellow bar (1) indicates the progress.

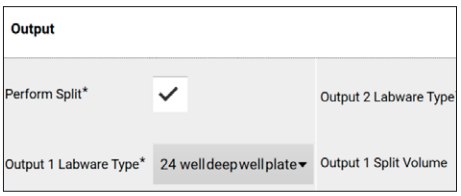



▷ A summary of the defined process is shown.


▶ Click on the [FINISH] button in the template menu to save the template and the user. There is no option save an incomplete template.
▷ If any parameters of the template are invalid, finishing and saving is **not** allowed.
▷ A run can be now created by using the template.

## 4.2 Splitting

When activated, a sample is processed through the clarification and | or purification filters and splits the resulting sample output into 2 fractions, one on output labware 1 | one on output labware 2. These 2 labware types can be different types but each will contain only the 1 fraction of the split.




### Procedure

- ▶ When creating a template: Tick the [Perform Split*] box.
- ▶ When defining labware types for outputs, the number of samples and number of wells in each labware output is checked to ensure that the defined template will be able to run on the device in 1 single run.
- ▷ If a neutralization of the output sample is enabled, it is before the split so both fractions are comparable.

There are 6 labware locations on the device that can be accessed by the liquid handler. The order in which these locations are accessed is controlled by the software and is done as follows:

- Left hand side, back to front for inputs, 1-3. If a 4th input is required then it will be assigned to the back right hand side location.
- Right hand side, back to front for outputs, 1-3. If a 4th output is required then the first location will be the front left location and then 2-4 will be the right hand side back to front order.

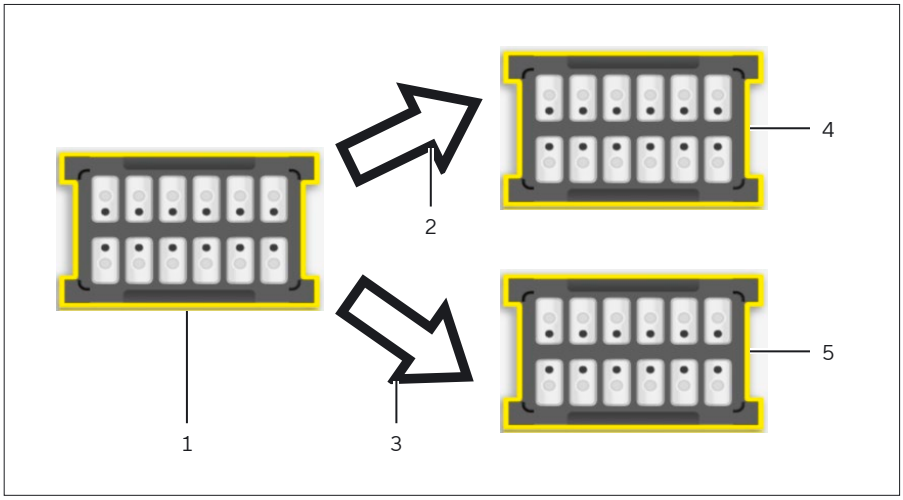



Abb. 2: Bed usage

| Pos. | Labware |
|---|---|
| 1 | Input labware |
| 2 | Output volume – Split volume |
| 3 | Split volume |
| 4 | Output labware 1 |
| 5 | Output labware 2 |

**Template Validation Rules for Creation of Template Parameters**

Clarification:

Output Vol = Sample Volume + (Rinse Volume* No of Rinses)

Purification or Combined:

Output Vol = Neutralization Volume + (max. Elution Volume if Peak Cutting or Elution Volume if not peak cutting)

## 4.3 Editing an Existing Template

It is possible to edit an already existing template. Note that the predefined templates **cannot** be edited, only clones or new ones.

Procedure

▶ Click on the [Edit] button at the top of the [Templates] screen.

▶ Change the entry fields according to the desired process making sure the template matches the labware | volumes to be loaded.

## 4.4 Running an Experiment

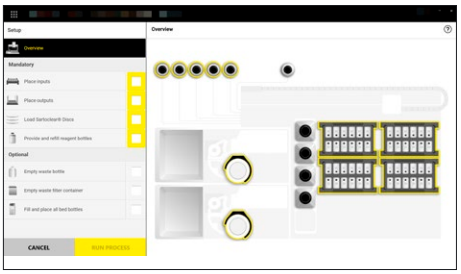
In order to start a process on the hardware an experiment needs to be created. The software will guide through the required actions.

Procedure

▶ Start an experiment by clicking on the desired tile in the main screen.
▶ Alternatively, choose a template in the [Templates] screen.

▶ Click on the [PLAY] button.

▷ The software will prepare to run the experiment based on the template and display actions to be performed before the experiment can be started. Experienced users can now check the check boxes on the main list. New users can select an item and use the detailed guidance information displayed for each item.



**RUN PROCESS**

▶ Execute the tasks which are being displayed on the screen, e. g. refill the reagent bottles, empty the waste filter container.
▶ Execute the tasks in the preferred order.
▷ The mandatory tasks are marked yellow as well as the items on the overview. They will loose the yellow marking once completed.
▶ After a completion: Click on the checkboxes to mark that a task has been fulfilled.

▶ Click on the [RUN PROCESS] button to start a process.

## 4.5 Interrupting | Resuming to a Running Experiment

A running experiment can be paused during operation if necessary.

### Procedure

- ▶ Click on the [PAUSE] button to stop an experiment.
- ▷ Actions will continue until the current in progress samples are fully processed. **No** next samples will be started.
- ▶ Whilst on pause: Items in the [Overview] can be updated, e.g. loading clarification filters | refilling bottles.
- ▶ Once on pause, either close or resume to the experiment.
- ▶ If “close” is chosen, the software will skip the remaining samples and move onto the end of run operations to ensure the device is left in a stable state and all liquid lines are in a good state.

## 4.6 Reports

When a run is completed: You will be prompted to navigate to the [Report] screen. This page can also be navigated to via the left hand side navigation buttons. The left hand side contains information about the experiment as a whole, the table section gives per sample information in more detail.

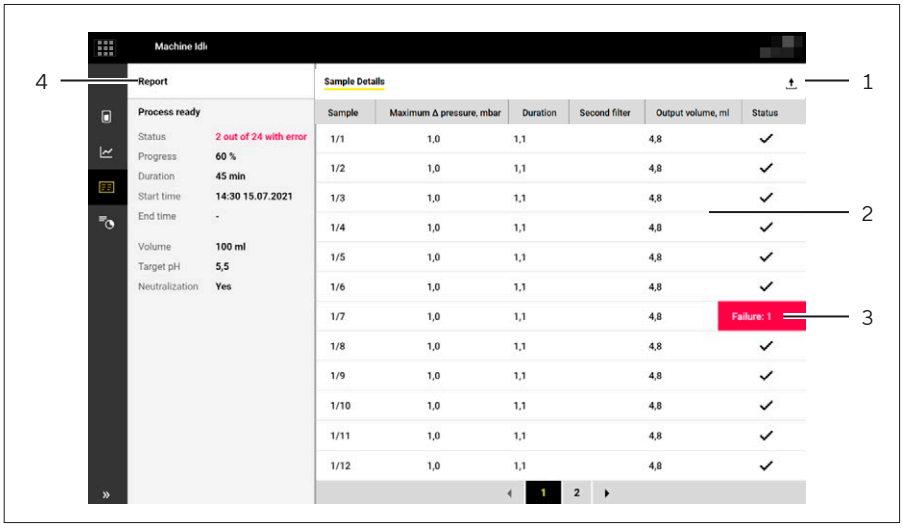



Abb. 3: [Report] screen

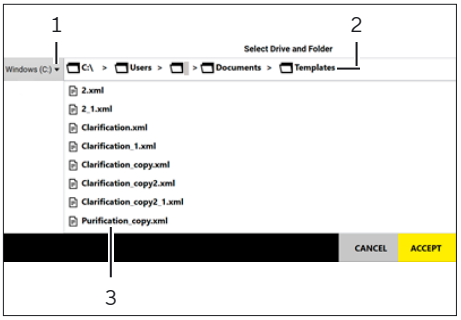
| Pos. | Name | Description |
|---|---|---|
| 1 | Export | Produces a file containing the data shown on this page. |
| 2 | Sample details | Shows a table with the samples listing out the key variable data for each samples processing. |
| 3 | Error message | Faults are indicated per sample. |
| 4 | Report | Shows information about the run, e.g. status \| time started \| samples remaining. |

## 4.7 Exporting Experiments | Templates

The [Export experiments] and [Templates] screen is available from the main screen and will list all the experiments | templates which have been saved on a local device.

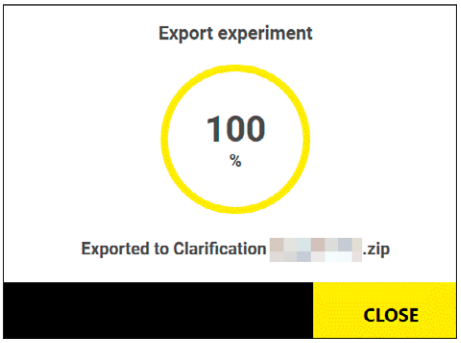
### Procedure

- ▶ In the main screen, click on the [Export experiments] button or select a template in the [Templates] screen.
- ▶ Select an experiment | template and click the [Export] button on the top to zip up the data.




- ▷ The Drive Combo Box (1) shows available mapped drives. Optical drives (CD | DVD) are excluded from the list.
- ▷ The currently selected path (2) will be used if the [ACCEPT] button is pressed. Each element of the path can be touched to select that folder.
- ▶ Use the Drive Combo Box to select a different drive if required. The folder initially shown when the dialog is opened is the default for the requested file export. Each drive remembers the last selected folder on that drive while the dialog is open.
- ▷ Folders and files (3) contained within the currently selected path are shown.
- ▶ To switch to a subfolder, tap on its name.
- ▷ Selecting a file in the folder picker has no effect. System folders and Hidden folders are not shown in the list. If you can see a folder but do not have read access to the contents, an error message will be displayed, and the [ACCEPT] button will be disabled.

- ▶ Click the [ACCEPT] button.




- ▷ The file is exported. The file can be copied off to another machine to be used, e.g. an external data viewer program (see chapter „4.8 Results Viewer“, page 15 ).

## 4.8 Results Viewer

The Results Viewer is an external Sartorius application which can be used to display experiment data from various devices.

Experiment data can be exported from the software onto network or usb drive and loaded up on the external pc system to be imported into the Results Viewer.

The application has a manual containing QuickStart guide which can be referred to. Note that StreamLink® CC 15 data can be used and references to bioreactors can be considered as a sample on the StreamLink CC 15 run.

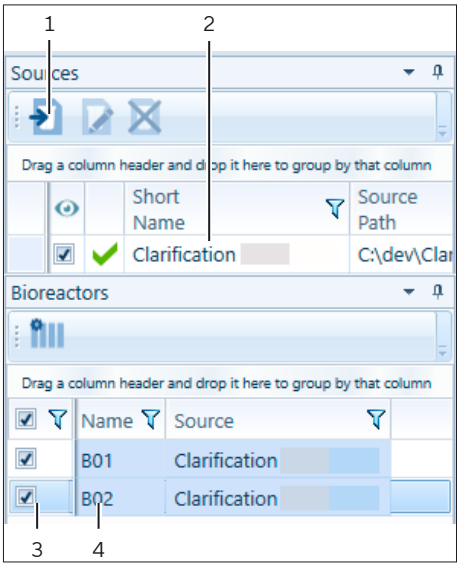
### 4.8.1 Installing the Results Viewer

**Procedure**

- ▶ Go to C:\Program Files\Sartorius\StreamLink CC 15\ResultsViewerInstallers.
- ▶ Copy to and install the application on a desktop pc external to the StreamLink® CC 15 device as this application is designed for a larger monitor and keyboard | mouse use.

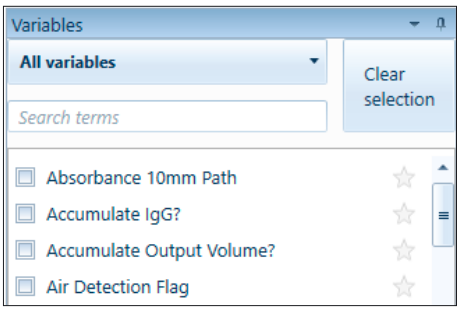
### 4.8.2 Opening Experiments in the Results Viewer

**Procedure**

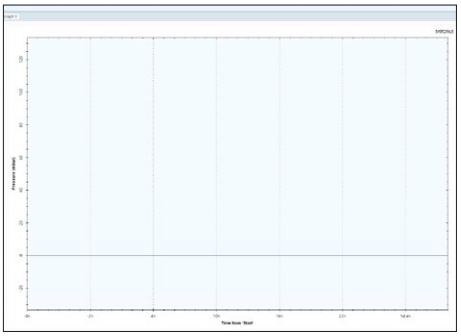



- ▶ Select a folder (1) from a StreamLink® CC 15 experiment run.
- ▷ Selected run names (2) are shown in the table below.

- ▶ Select the samples (3) to plot data for.
- ▷ The list shows the samples (4), indicating which filter station they ran on (e.g. FS01 | FS02) and the sample id (or sample name if it was provided to the system when run).




- ▶ Select the variables from the experiment.



▷ The data will be plotted on the graph for viewing or exporting.

## 4.9 Settings

### 4.9.1 Email Server Setup

In this screen the (single) server details of the preferred email server can be set up. This server is connected to the system pc network.

**Procedure**

▶ Click on the [Settings] menu in the quick links and select [Email Server].
▶ Click on the row and click [UPDATE] button on the bottom of the screen.
▶ Enter the host name.
▷ The name should be a fully qualified domain name which is reachable over the network. It can also be local host or an IP address for local testing.
▶ Enter the port to connect to (usually 25), the user name and password of the mail server to use for sending emails.
▷ This should be created for the StreamLink® CC 15 device to use as its details will be used in emails that are sent from the system.
▷ The Audit folder is for diagnostics only and can be left blank.

### 4.9.2 Email User Setup

This screen allows multiple users to receive emails when the system requires attention, e.g. when a prompt is showing or at the end of a run.

**Procedure**

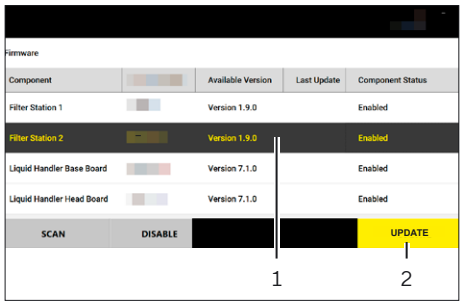
▶ Click on the [Settings] menu in the quick links and select [Email Users].
▶ Click on the [+] icon to add a new user or the pen to edit the selected user row.
▶ Enter an email address to receive the email and specify if the user should receive emails or not (this can be toggled on | off before each run as needed).

In operation, when a prompt or alert is created by the running process, an email will be generated with the current state of the channels as content in the email. The email sending has a small delay (20-30 sec.). So, if a prompt is actioned in that time, the email may be no longer valid and therefore not sent. At the end of the run, if the email settings and users are valid and configured to receive emails, the run report status will be emailed to the user(s).

## 4.9.3 Updating the Firmware

The firmware screen shows the expected firmware system boards and the version reported from the physical system currently installed. If no connection can be made, this is indicated on the column entry.

### Procedure




- ▶ Click on the [SETTINGS] menu and select [Firmware].
- ▷ The screen shows the components, available versions, last updated versions and the component status.
- ▶ Select the required update (1).
- ▶ Click on the [UPDATE] (2) button.
- ▷ The updates are being installed.

### Disabling | Enabling Filter Stations

Filter stations can be disabled in the firmware screen, e.g., when a filter station is known to be non-operational but the device is to be used with just 1 filter station remaining. After a repair, filter stations can be enabled again.

### Procedure

**DISABLE**

- ▶ Click on the [SETTINGS] menu and select [Firmware].
- ▶ Select the required filter station.
- ▶ Click on the [DISABLE] | [ENABLE] button.
- ▷ The “Component Status” is set to “Disabled” | “Enabled”.

### Scanning for Device Components

It is possible to scan for device components in case where a cable was not plugged in first time or a comms issue stops the initial scan.

### Procedure

**SCAN**

- ▶ Click on the [SETTINGS] menu and select [Firmware].
- ▶ Select the required component.
- ▶ Click on the [SCAN] button.
- ▷ The component is scanned for.

## 4.9.4 Licenses

In this menu, “Core“ and “Online Control“ modules are presented with the current status, e.g. expired | licensed.

The software is required to be licensed before it can be used to run experiments. The modules (“Core” | “Online Control”) are required to be licensed. “OPC” is optional and enables data transfer features.

On initial install all will be setup with a demo status which will allows a 30 days running.

Procedure

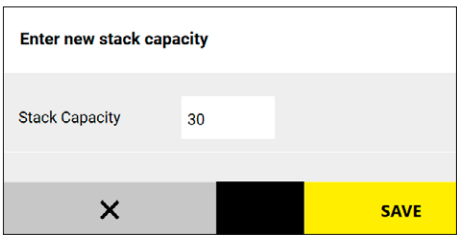
- ▶ Click on the [Settings] menu in the quick links and select [Licenses].
- ▶ To request keys, click on the [GET KEY] button.
  - ▶ If there is connection to the internet and an installed email client: Select [CREATE E-MAIL].
  - ▷ A pop-up opens with all relevant information appears.
  - ▶ Alternatively, click on [COPY] in order to have the relevant information copied.
  - ▶ Send the information to the respective email address.
- ▶ Once the keys are received: Click the [ENTER KEY] button, paste or type in the key and confirm with the [ACTIVATE] button.

## 4.9.5 Updating the Filter Settings

This screen allows setting the capacity of clarification filters that can be stacked.

Procedure

- ▶ Click on the [Settings] menu in the quick links and select [Filter Settings].
- ▶ Select [UPDATE].
- ▶ Enter the desired stack capacity and confirm with the [SAVE] button.



# 5 OPC

## 5.1 Installing the Kepware® OPC server for the OPC Connection

### Requirements

- The personal Windows user profile has administrator rights.
- The "KEPServerEx6.exe" file provided by Sartorius is available.

### Procedure

- ▶ License the OPC module (see chapter „4.9.4 Licenses", page 17) and request the Kepware® license ID from support.
- ▶ Open the "KEPServerEx6.exe" file and launch it as an administrator.
- ▶ Accept defaults for the installation procedure.
- ▶ When the [Vertical Suite Selection] display is shown, select "Custom".
- ▶ When the [Select Features] display is displayed:
  - ▶ Expand the "Communications Server" and "Communication Drivers" area.
  - ▶ Activate the "Custom Interface" selection. This fully installs the driver.
- ▶ Follow the instructions in the installation procedure and accept the default settings.
- ▶ On [User Manager Credentials], set the Kepware® administrator user account password to "S@rt0r1u5B10t3c".

## 5.2 Activating the License for the Kepware® OPC Server

After installation, only a 2-hour demo version can be used. The license for the Kepware® OPC server must be activated.

The license for the Kepware® OPC server is included in the OPC license of the StreamLink® CC 15 software.

### Procedure

- ▶ Open the license program: Start > All Programs > Kepware > KEPServerEX 6 > License > License Utility
- ▶ Enter the 36-digit activation ID.
- ▶ For more information on licenses and transferring licenses to other computers, please see the "License Utility Help" file in the Kepware® installation folder.

## 5.3 Configuring the Kepware® OPC Server (Initial Configuration)

**Procedure**

- ▶ Open the configuration program: Start > All Programs > Kepware > KEPServerEX 6 > KEPServerEX 6 Configuration.
- ▶ Create a channel in the [Edit] > [Connectivity] > [New Channel] menu bar or by right-clicking [Connectivity] > [New Channel].
- ▶ Select the "Custom Interface" selection and switch to the next display.
- ▶ Name the channel "StreamLink CC15" and switch to the next display.
- ▶ Select the default setting for the "Optimization Method" area and switch to the next display.
- ▶ Select the file "StreamLinkCC15_KepwareInterface.xml" from the OPC directory. This saves the configuration files in \Documents\StreamLink CC 15\PegasusSystemConfiguration\OPC configuration.
- ▶ Switch to the next page and finish the configuration.
- ▷ The Kepware® OPC server connects automatically to the OPC interface of the StreamLink® CC 15 software. The data can be viewed in the "Tools" menu in the Kepware® OPC Quick Client.

# 6 Maintenance Operations

The [Maintenance] screen is available from the main screen. Maintenance operations have to be executed outside of an active run.

There are categories available on the left side navigation section. Each section will contain a list of operations in the main table section from which can be chosen. A brief description and "last executed" are shown.

## 6.1 General Maintenance Operations

**Procedure**

- ▶ Select the desired maintenance operation, e.g.:
  - Priming the liquid lines
  - Calibrating the pH probe
  - Draining the liquid lines
  - CIP
  - ...
- ▶ Click the [START] button to activate the desired maintenance operation.
- ▷ A mimic is shown.
- ▶ Execute the tasks which are being displayed on the screen.
- ▷ The automated operation will start once the appropriate step is acknowledged.
- ▶ The estimated time remaining and results at the end will be displayed.

## 6.2 Teaching the Pipette Tip Position

At the initial setup or after a new tip has been installed: The position of the tip needs to be taught by a supervisor or service user.

The teach panel is a standalone application linked to the StreamLink® CC 15 software. Teaching is done with one type of labware. This will allow accessing of all different labware types from the main application.

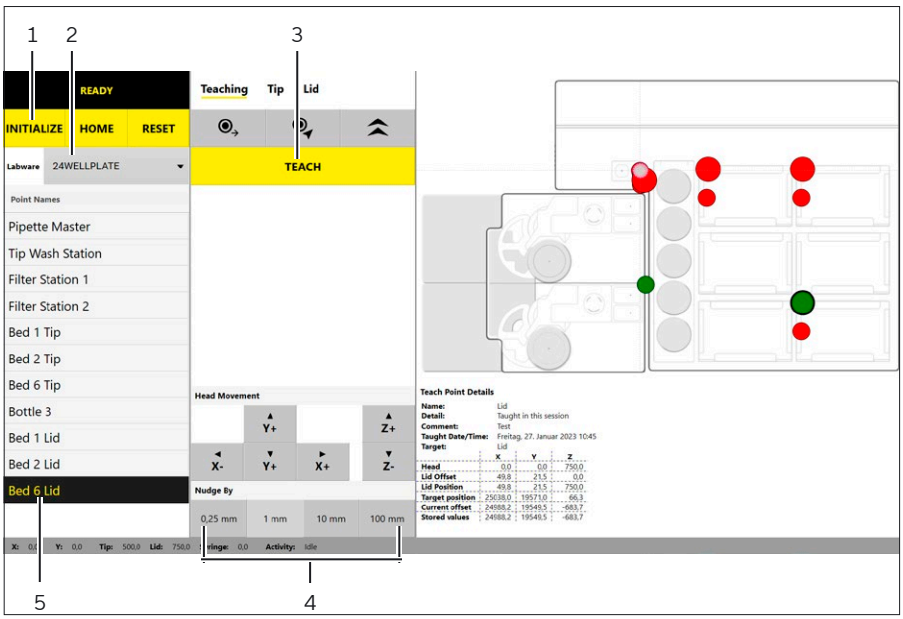
### Requirements

For lid | labware teaching: The labware to be loaded has been selected.

### Procedure


▶ Start the StreamLink® CC 15 Teach Panel.

▶ Check the labware selected (2).
▶ Click the [Initalize] (1) button.
▶ Select the [Pipette Master] teach point first from the visualized map or from the list (5):




▶ Use the respective buttons (4) to change the position.
▷ If a keyboard is present, the arrow keys on it can be used directly to move the head by the selected distance instead of needing to click the screen.
▶ Click the [Teach] (3) button.
▶ Repeat this for any other teach point in any order.
▷ The teach points turn green after being taught and the teach point details are described in the table to the right.
▷ There are options to check teach points by going back to the locations or attempt to pick lids | wells.

# 7 Troubleshooting

## 7.1 Disruptions in Process Sequence

| Fault | Cause | Correction | Chapter, page |
|---|---|---|---|
| A template cannot be started. | The template contains errors or the settings are incorrect. | The software guides through required troubleshooting actions. | |
| | The control unit is **not** connected to the hardware. | Check the connection from the control unit and hardware (how to connect see instructions for the StreamLink® CC 15 hardware). | |
| | The licenses for the product are **not** acitvated. | Activate the licenses. | 4.9.1, 16 |
| A drive does not show up in the drive list. | The drive is **not** mapped and ready at the time the dialog is opened. | – For USB sticks, check the stick is inserted properly, then cancel the dialog and reopen it.<br>– Network drives can sometimes be restored by closing and reopening the dialog. | |
| A folder is missing. | This software does **not** allow for the creation of new folders. | – For USB sticks, use a different computer to create the folder.<br>– For network drives, create the folder on another computer, then move away from the parent folder and back again to force the folder and file list to refresh. | |

## 7.2 Checking Exception Errors

If an exception error occurs, e. g. a template **cannot** be loaded or settings are incorrect: A display containing information on the exception error opens.

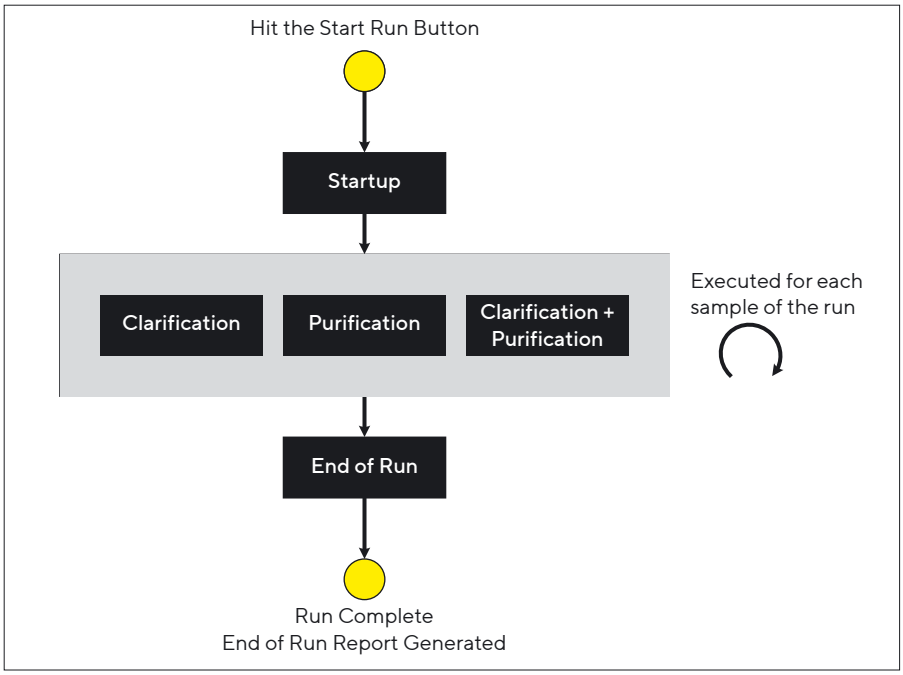
Procedure

▶ Check the description of the exception error in the [EXCEPTION ERROR] display.
▶ If the exception error occurs again: Click on the [DETAILS] button.
▷ The details are shown.
▶ Click on the [Copy] button.
▷ The error description is copied to the clipboard.
▶ Copy the error description into a text processing program or email program, and send to the email address Royston-Support@Sartorius.com.

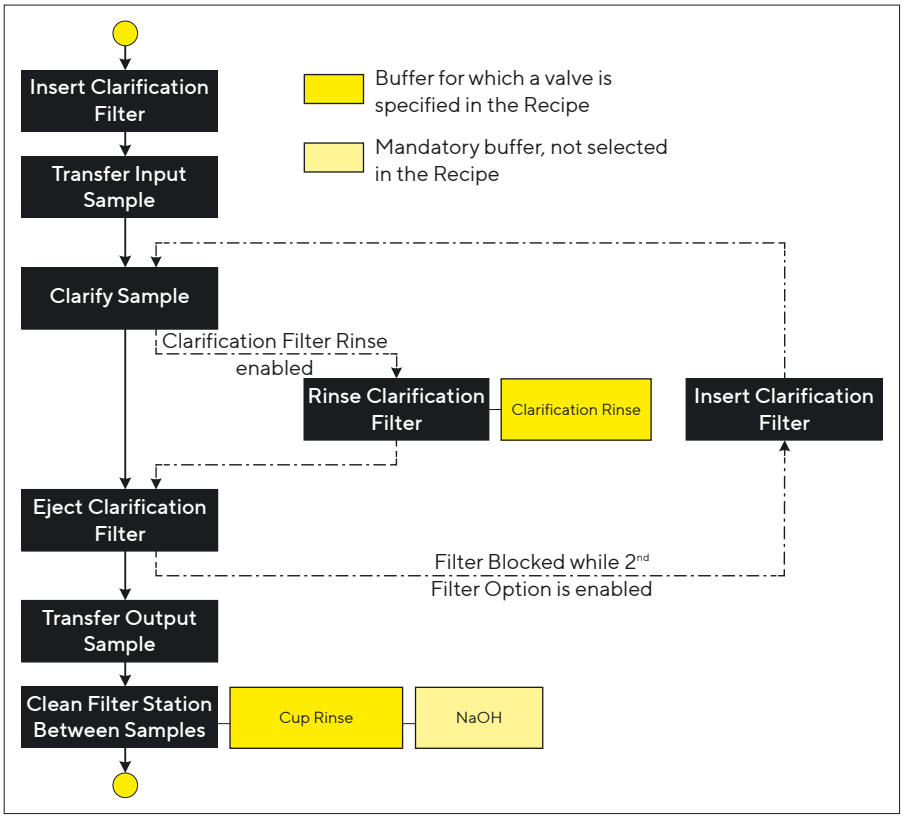
# 8 Appendix

## 8.1 Process Flowcharts

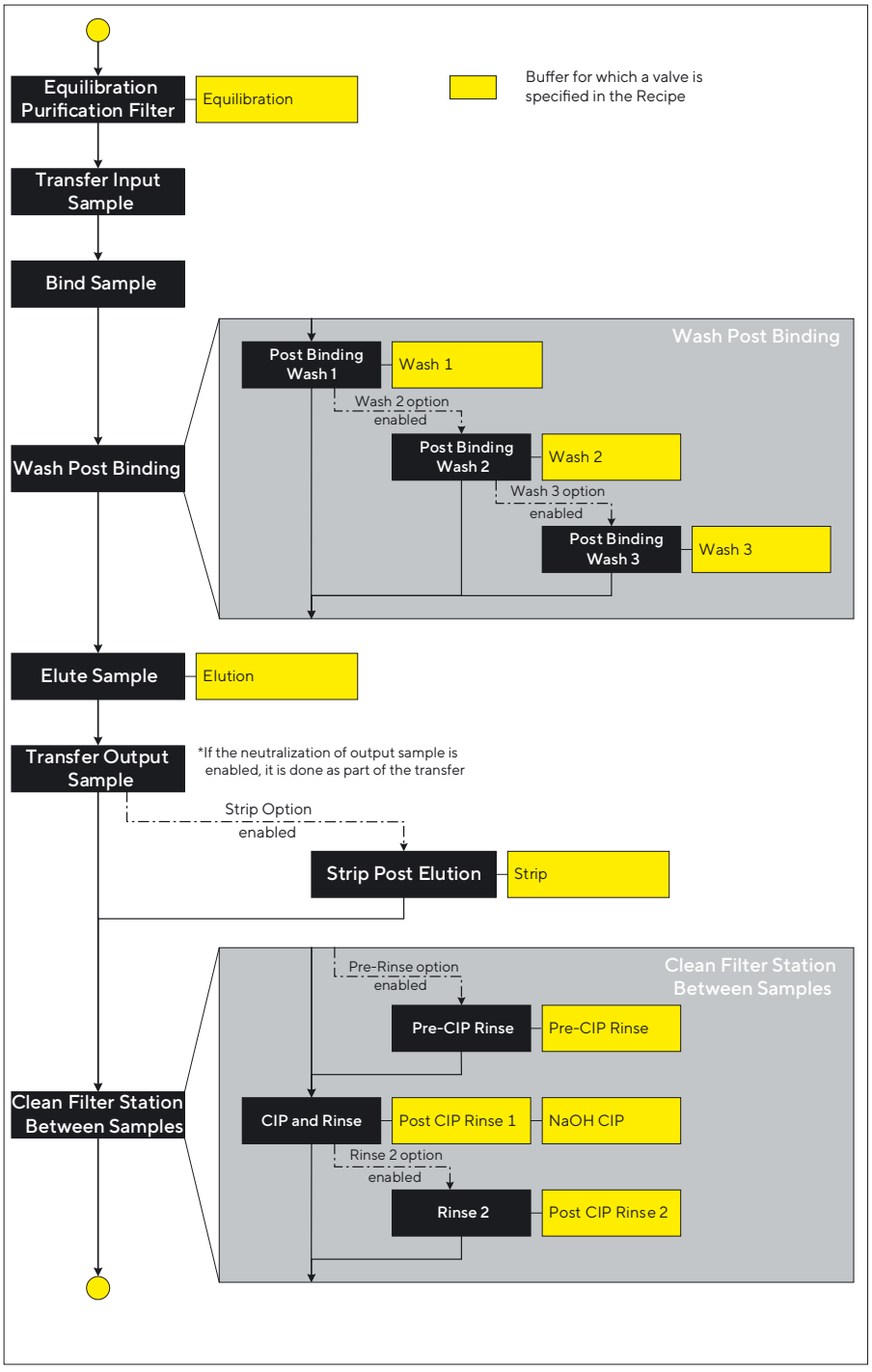
### 8.1.1 Complete Run Process Flowchart



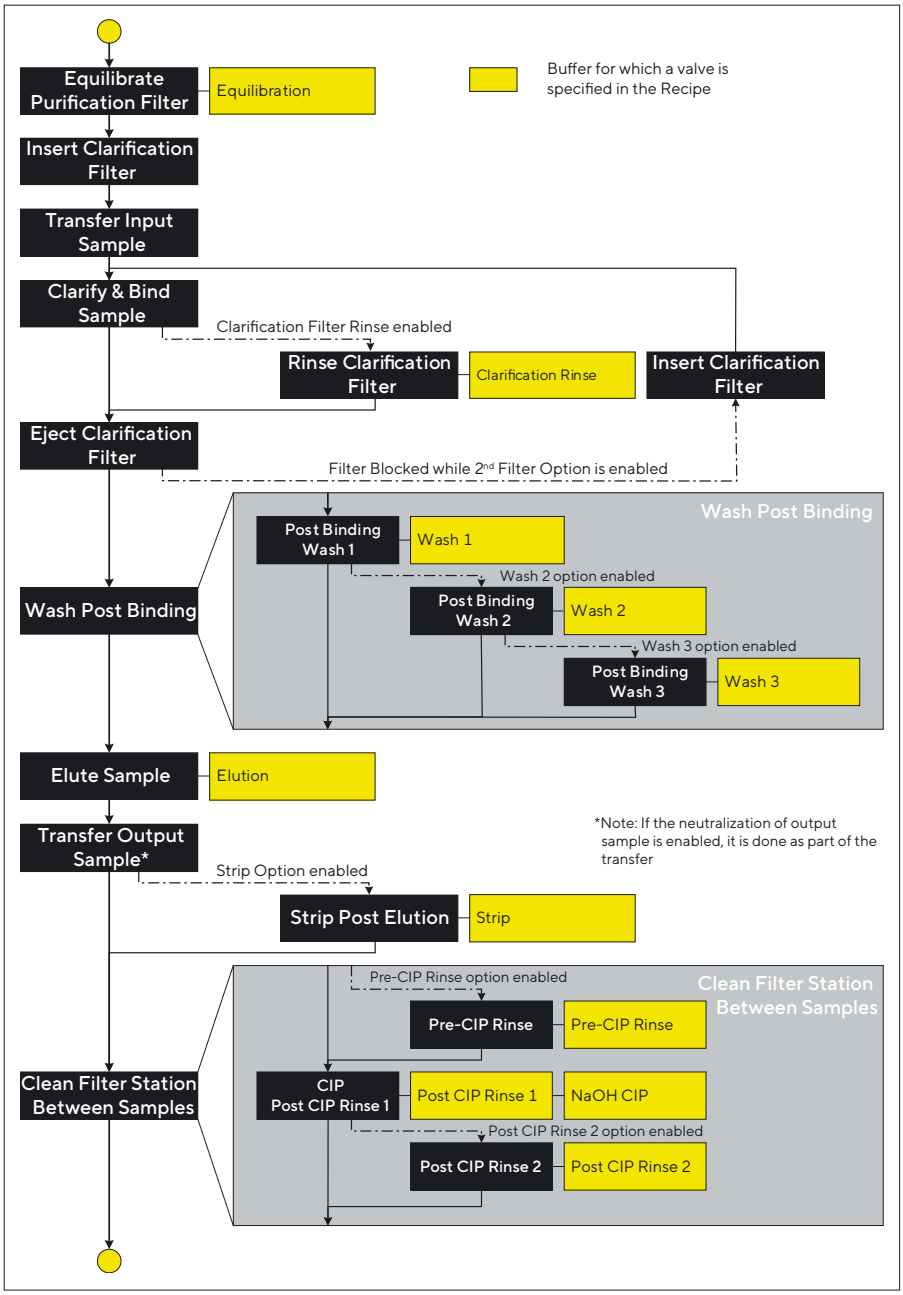

### 8.1.2 Clarification Run Process Flowchart



### 8.1.3 Purification Run Process Flowchart



## 8.1.4 Combined Run Process Flowchart



## 8.2 Description of the User Phases

| User Phase Name | Description | Applicable Template |
|---|---|---|
| Bind Sample | After loading the sample in the filter station, pump it through the purification filter to capture the product. | Purification |
| Clarify and Bind Sample | Pump the sample through the clarification filter to remove large particulate. The filtered sample is directly loaded into the purification device to capture the product. | Clarification + Purification |
| Clarify Sample | Pump the sample through the clarification filter to remove large particulate. | Clarification |
| Clean Filter Station between Sample | Circulate several cycles of buffer and NaOH through the system flowpath, purification device and cups to clean the filter station and avoid carryover between samples. | Clarification<br>Purification<br>Clarification + Purification |
| Eject Clarification Filter | Eject a used clarification filter after a sample has been filtered. It then pushes the clarified sample remaing in the flowpath in the purification device and flush cells from the upstream flowpath to prepare for pumping buffer during purification. | Clarification<br>Clarification + Purification |
| Elute Sample | Pump elution buffer through the purification filter to recover the captured protein. It comes in 2 versions depending if the peak cutting option is selected or not.<br>— No peak cutting selected: The system collects all of the elution as output sample to be collected.<br>— Peak cutting: The collection of the eluted output sample is based on UV absorbance threshold defined by the user to islate a peak of protein concentration. | Purification<br>Clarification + Purification |
| Equilibrate Purification Filter | At the start of a sample process involving purification, flow through equilibration buffer to ensure the purification filter has a stable neutral pH. It also calibrates the UV sensor with the elution buffer absorbance. | Purification<br>Clarification + Purification |
| Insert Clarification Filter | Insert a new clarification filter in the filter station and then, check correct clamping of the clarification filter after insertion via hold up pressure test. | Clarification<br>Clarification + Purification |
| Neutralize Output Sample | Mix neutralization buffer and sample in the output cup, so it is stable before recovery before it is transferred when the output splitting option has been enabled in the template. | Purification<br>Clarification + Purification |
| Pre-Wash Post Binding | After loading the purification filter with sample, pump through the purification filter rinse buffer to wash any remaining waste and particulate other than the product itself (LDH, DNA, HCP...). This an optional post binding wash to enable using another type of buffers. | Purification<br>Clarification + Purification |

| User Phase Name | Description | Applicable Template |
|---|---|---|
| Recover From an Anomaly | Execute an error recovery path after detection of a process anomaly. If it is successfully corrected, automatically or via a manual intervention, the process will continue recording a deviation. If it fails to recover, the sample will be marked as failed, the system will process the next sample if it can. Otherwise it will be stopped. | Clarification<br>Purification<br>Clarification + Purification |
| Rinse Clarification Filter | After pumping the sample through the clarification filter, flush it with buffer to limit product loss because of hold-up volume. It is an optional phase. | Clarification<br>Clarification + Purification |
| Strip Post Elution | After collection of the eluted sample, pump through the purification filter some buffer with low pH to strip any remaining binded and remaining protein from the device. This is an optional phase. | Purification<br>Clarification + Purification |
| Transfer Input Sample | Use the liquid handler to transfer a sample from the input bed location to the input cup of a filter station. | Clarification<br>Purification<br>Clarification + Purification |
| Transfer and Neutralize Output Sample | Transfer the output sample into the output labware, then mix neutralzsation buffer with it to so it is stable before recovery. | Purification<br>Clarification + Purification |
| Transfer Output Sample | Use the liquid handler to transfer a sample from the output cup of a filter station to the dedicated output bed location. | Clarification<br>Purification<br>Clarification + Purification |
| Wash Post Binding | After loading the purification filter with sample, pump through the purification filter rinse buffer to wash any remaining waste and particulate other than the product itself (LDH, DNA, HCP...). It is possible to design 3 separate wash steps that differ in wash solution, wash volume, and wash flow rate. | Purification<br>Clarification + Purification |

## 8.3 Description of the Maintenance Processes

| Name of Maintenance Process | Section | Description | Options |
|---|---|---|---|
| Clean In Place (Configurable) | Cleaning | Process performing a CIP of the selected part of the system following a similar process than the one used at the end of an experiment. | Liquid handler<br>Filter station |
| Filter Station Deep Clean | Cleaning | Process running NaOH and rinse buffers through the filter stations for a prolonged period of time in order to decontaminate it. It includes the cleaning of all input lines. It does not include the purification filter which has its dedicated deep clean process. For this process, it is replaced by a dummy filter. | Filter station |

| Name of Maintenance Process | Section | Description | Options |
|---|---|---|---|
| Liquid Handler Deep Clean | Cleaning | Process running NaOH and rinse buffers through the liquid handler for a prolonged period of time in order to decontaminate it. It includes the cleaning of all input lines. For this process, the pH probe is replaced by a dummy unit. | / |
| Sartobind® Rapid A Nano Regeneration | Cleaning | Process regenerating the binding capacity of the purification filter loaded in the filter station via NaOH soaking \| rinse cycles. | Filter station |
| System Status Check | Diagnostics | Process running a set of self-test on the system in order to verify if it performs as expected. It includes the full range of calibration and checks done at initialization and start-up with stricter parameters to better assess the system status. | Liquid handler<br>Filter station |
| Calibrate pH probe | Setup | Process enabling the calibration of the pH probe without any other actions. | / |
| Full System Installation | Setup | Process initializing a system which has been installed. Users can choose which liquid lines to prime. Equilibration Buffer, Pipette Rinse and NaOH are primed by default. User can also choose to prime newly installed purification filters as part of the process. This process assumes the system is dry. | Filter station<br>Purification filter |
| Filter Station Installation | Setup | Process enabling the initialization of a filter station newly installed on an already initialized system. | Filter station |
| Install new pH probe | Setup | Process enabling the replacing of a pH probe on the liquid handler | / |
| Install a new Sartobind® Rapid A Nano | Setup | Process to install a new purification filter on the selected filter station. The procedure also covers swapping old filters for new ones. | Filter station |
| Prime Liquid Lines | Setup | Process enabling to prime the liquid lines. User can choose which part of the system and which infeed line to prime. Equilibration \| Rinse 1 and Pipette Rinse are primed by default. | Liquid handler<br>Filter station<br>Liquid infeed lines |
| Exchange Supply Buffer(s) | Setup | Process enabling the swapping of a buffer which is already loaded and primed on the system. | Liquid handler<br>Filter station<br>Liquid infeed lines |
| Decommission Filter Station | Storage | Process cleaning and emptying from any liquid a filter station so it can be disconnected from the system to be replac<br>ed or serviced. | Filter station |
| Deprime Liquid Lines | Storage | Process enabling to de-prime an infeed line, so it is emptied of liquid when a buffer bottle is removed or a tube is changed. | Liquid handler<br>Filter station<br>Liquid infeed lines |

| Name of Maintenance Process | Section | Description | Options |
|---|---|---|---|
| Empty System of Storage Solution | Storage | Process flushing the selected part of the system from the storage solution so it is dry. This process assumes the system is in storage solution. It does not dry the purification filters. | Liquid handler<br>Filter station |
| Decommission System | Storage | Process cleaning the system, emptying from any liquid so it can be disconnected and stored for long period of time. After such process once reconnected, an initialize process should be run as if it was installed for the first time. | / |
| Fill System with Storage Solution | Storage | Process storing the selected part of the system in storage solution. This process assumes the system is dry. | Liquid handler<br>Filter station |

## 8.4 Template Parameters

| Name of Parameter | CL | PU | CP | Unit | Min. | Max. | Default | Template Wizard Tab | Description |
|---|---|---|---|---|---|---|---|---|---|
| Sample Volume | X | X | X | mL | 3 | 30* | 10 | Input | Volume of the input sample to be processed by the system. |
| Clarification Flow Rate | X | | X | mL/min | 1 | 50 | 12 | Clarification | Flow rate used to pump the input sample through the clarification filter in order to filter it. In case of a combined process, it is also the flow rate at which the sample is loaded onto the purification filter. The default value is set at 10*MV because it is also the binding flowrate in case of combined process. |
| Clarification Rinse Vol. | X | | X | mL | 0 | 30* | 5 | Clarification | Volume of Rinse 1 buffer used to rinse the clarification filter in order to recover more product. It is pumped at the clarification flow rate. The default value is roughly twice the clarification filter total volume. |
| Enable 2nd Filter | X | | X | | | | FALSE | Clarification | Activate the automatic usage of a second filter during clarification if the current filter is getting blocked. |
| Enable Filter Rinse | X | | X | | | | TRUE | Clarification | After the filtration of the input sample, enable the rinsing of the clarification buffer with buffer in order to recover more product. |

| Name of Parameter | CL | PU | CP | Unit | Min. | Max. | Default | Template Wizard Tab | Description |
|---|---|---|---|---|---|---|---|---|---|
| Max. Clarification ΔP | X | | X | mbar | 250 | 3000 | 1000 | Clarification | During a clarification step, maximum pressure build up in the clarification device. High differential pressure can lead to cell lysis increasing the risk of blocking the filter and impurity of the product. |
| Binding Flow Rate | | X | | mL/min | 0 | 30 | 12 | Purification elution | Flow rate used to pump the input sample through the purification filter during the binding phase to capture the product. The default value is set at 10*MV. |
| Enable Pre-Wash | | X | X | | | | FALSE | Purification binding | After the binding phase, enable a second wash of the purification filter with a different buffer. It is performed before wash 1. |
| Equil. Rate | | X | X | mL/min | 1 | 30 | 12 | Purification binding | Flow rate used to pump the Equilibration buffer through the purification device in order to equilibrate it. The default value is set at 10*MV. |
| Equil. Volume | | X | X | mL | 0 | 50 | 12 | Purification binding | Volume pumped through the purification filter at the start of a sample processing to ensure its pH neutrality and adequate conductivity. The default value is set at 10*MV. |
| Wash Flow Rate | | X | X | mL/min | 1 | 50 | 12 | Purification binding | Flow rate used to pump the Rinse 1 buffer through the purification filter during the wash 1. The default value is set at 10*MV. |
| Pre-Wash Flow Rate | | X | X | mL/min | 1 | 50 | 12 | Purification binding | Flow rate used to pump Rinse 2 buffer through the purification filter during the wash 2. The default value is set at 10*MV. |
| Wash Volume | | X | X | mL | 5 | 50 | 12 | Purification binding | Volume of Rinse 1 buffer used to wash the remaining supernatent or clarified sample out of the purification filter after binding. The default value is set at 10*MV. |
| Wash 1 Valve | | X | X | | | | Equilibration \| Rinse 1 | Purification binding | Valve to use for the wash 1. |
| Wash 2 Valve | | X | X | | | | None | Purification binding | Valve to use for the wash 2. |
| Wash 3 Valve | | X | X | | | | None | Purification binding | Valve to use for the wash 3. |

| Name of Parameter | CL | PU | CP | Unit | Min. | Max. | Default | Template Wizard Tab | Description |
|---|---|---|---|---|---|---|---|---|---|
| Wash 1 Volume | | X | X | mL | 5 | 50 | 12 | Purification binding | Volume pumped through the purification filter to wash the purification filter from supernatant waste after binding the product. The default value is set at 10*MV. |
| Wash 2 Volume | | X | X | mL | 5 | 50 | 12 | Purification binding | Volume pumped through the purification filter to do a second wash of the purification filter. The default value is set at 10*MV. |
| Wash 3 Volume | | X | X | mL | 5 | 50 | 12 | Purification binding | Volume pumped through the purification filter to do a third wash of the purification filter. The default value is set at 10*MV. |
| Wash 1 Flow Rate | | X | X | mL/min | 1 | 50 | 12 | Purification binding | Flow rate used to wash the purification filter with a user-selected buffer during Wash 1. The default value is set at 10*MV. |
| Wash 2 Flow Rate | | X | X | mL/min | 1 | 50 | 12 | Purification binding | Flow rate used to wash the purification filter with a user-selected buffer during Wash 2. The default value is set at 10*MV. |
| Wash 3 Flow Rate | | X | X | mL/min | 1 | 50 | 12 | Purification binding | Flow rate used to wash the purification filter with a user-selected buffer during Wash 3. The default value is set at 10*MV. |
| Elution Flow Rate | | X | X | mL/min | 1 | 30 | 12 | Purification elution | Flow rate used to pump the elution buffer to release the product bound in the purification filter. The default value is set at 10*MV. |
| Max. Elution Volume | | X | X | mL | 1 | 30* | 12 | Purification elution | Maximum volume the system will pump during an elution with the peak cutting activated. It ensures that the output sample is not too big. The default value is set at 10*MV. |
| Min. Elution Volume | | X | X | mL | 1 | 30* | 1.2 | Purification elution | Minimum volume the system will pump during an elution with the peak cutting activated. It ensures that the output sample is not too small. The default value is set at 1 MV. |
| Elution Volume | | X | X | mL | 5 | 30* | 12 | Purification elution | Volume of buffer used to elute the poduct from the purification device. It is also defined as the output sample volume. The default value is set at 10*MV. |

| Name of Parameter | CL | PU | CP | Unit | Min. | Max. | Default | Template Wizard Tab | Description |
|---|---|---|---|---|---|---|---|---|---|
| Neutralization Buffer | | X | X | % | 0 | 100 | 10 | Purification elution | Define the volume of neutralization buffer to mix with the output sample by a ratio with the output sample volume. |
| Neutralization Buffer Vol. | | X | X | mL | 0 | 10 | 0.1 | Purification elution | Define the volume of neutralization buffer to mix with the output sample by an absolute volume value. |
| Enable Peak Cutting | | X | X | | | | FALSE | Purification elution | Activate a feature triggering the collection of the eluted sample based on the absorbance peak measured by the UV sensor @280 nm. Useful for samples with low titer. Sample volume is defined by absorbance peak. |
| Peak Cut End | | X | X | Au | 0 | 50 | 0.5 | Purification elution | Limit value of the absorbance used to determined when to stop collecting the eluted sample. |
| Peak Cut Start | | X | X | Au | 0 | 50 | 0.5 | Purification elution | Limit value of the absorbance used to determined when to start collecting the eluted sample. |
| pH Neutralization | | X | X | | | | FALSE | Extra options | Activate a neutralization step after the sample has been dispensed into the output sample vessel. The sample is mixed by a series aspiration and dispensed:<br>— in the output cup (if split is enabled)<br>— in the output labware well (if split is disabled) |
| Protein Ext. Coef. | | X | X | | 0 | 5 | 1.41 | Purification elution | Qualify the ability of the protein to absorb light @280 nm. It is used to calculate the concentration of product. |
| Low IgG Alarm | | X | X | Mg | 0 | 35 | 1 | Extra options | Amount of IgG under which the system will inform the user about missing IgG in the output sample. |
| Pre-CIP Rinse Flow Rate | | X | X | mL/min | 5 | 30 | 12 | Purification CIP | Flow rate with which the Rinse 1 is pumped through the purification filter during the initial cleaning phase. The default value is set at 10*MV. |

| Name of Parameter | CL | PU | CP | Unit | Min. | Max. | Default | Template Wizard Tab | Description |
|---|---|---|---|---|---|---|---|---|---|
| Pre-CIP Rinse Volume | | X | X | mL | 5 | 50 | 6 | Purification CIP | Volume of Rinse 1 buffer used to do an initial rinse before pumping NaOH through the purification device. It is mandatory if a low pH strip phase was enabled to avoid pH jump in the filter. The default value is set at 5*MV. |
| Post-CIP Rinse Flow Rate | | X | X | mL/ min | 5 | 30 | 12 | Purification CIP | Flow rate with which the Rinse 2 is pumped through the purification filter during the initial cleaning phase. The default value is set at 10*MV. |
| Post-CIP Rinse Volume | | X | X | mL | 5 | 50 | 18 | Purification CIP | Volume of Rinse 2 buffer used to do a final rinse after pumping NaOH through the purification device. It is mandatory to lower the pH in the purification device before starting processing the next sample. The default value is set at 15*MV. |
| Enable Post Elution Strip | | X | X | | | | FALSE | Purification CIP | After elution of the product, enable a washing of the purification filters with a buffer to remove as much residual product in it. This phase comes before the cleaning of the system and purification filter. |
| NaOH CIP Flow Rate | | X | X | mL/ min | 1 | 20 | 6 | Purification CIP | Flow rate used to pump NaOH through the purification filter during the CIP phase. For safety reasons, it has a lower maximum limit at 20 mL/min than other flow rate. It also has a infeed lower maximum pressure at 2 bar. The default value is set at 5*MV. |
| NaOH CIP Volume | | X | X | mL | 0 | 25 | 6 | Purification CIP | Volume of NaOH pumped through the purification device to clean it between samples. The default value is set at 5*MV. |
| Strip Flow Rate | | X | X | mL/ min | 1 | 30 | 12 | Purification elution | Flow rate with which the Strip buffer is pumped through the purification filter during the Strip phase. The default value is set at 10*MV. |

| Name of Parameter | CL | PU | CP | Unit | Min. | Max. | Default | Template Wizard Tab | Description |
|---|---|---|---|---|---|---|---|---|---|
| Strip Volume | | X | X | mL | 0 | 50 | 12 | Purification Elution | Volume of Strip buffer used to wash the purification filter from residual bound product. The default value is set at 10*MV. |
| Enable Pre-CIP Rinse | | X | X | | | | TRUE | Purification CIP | Enable a rinse with equilibration buffer of the purification filter before NaOH is pumped through it. It is done after the Strip phase if a strip was enabled. |
| Perform Split | X | X | X | | | | FALSE | Output | Enable the user to split their output sample in 2 fractions. If it is selected users need to specify the volume for their second fraction while the remaining of the sample is loaded into the primary output labware. |
| Output 2 Split Volume | X | X | X | mL | 0.3 | 30 | 1 | Output | Volume of sample split from the total output sample to create the second fraction. The remaining output sample volume is loaded in the primary output labware. |
| Output 1 Split Volume | X | X | X | mL | 0.5 | 30 | | Output | This template parameter cannot be edited. It is calculated based on the expected output sample volume minus the defined output 2 Split volume. It is displayed for clarity and recorded in the template summary. |

* The actual max can be less based on other template parameters.

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The information and figures contained in these instructions correspond to the version date specified below.
Sartorius reserves the right to make changes to the technology, features, specifications and design of the equipment without notice.
Masculine or feminine forms are used to facilitate legibility in these instructions and always simultaneously denote all genders.



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