



TruBio Bioprocess Control Software Version 5.0 User's Guide

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How to use this guide

Scope of this publication

This user's guide contains information about the Thermo Scientific™ TruBio™ Bioprocess Control Software (version 5.0), powered by Emerson's DeltaV™ Distributed Control Platform, including product design verification methods, installation, operation, and specifications. It is intended for use by people who may or may not have experience with Thermo Scientific systems, but who have some knowledge of bioproduction processes and large-scale mixing systems.

Document change information

Rev.	Date	Section	Change made	Author
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Questions about this publication

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Document	Document number
TruBio Discovery Bioprocess Control Software	COL010192 0919
TruBio bioprocess automation software	COL010087 0819

Abbreviations/acronyms

See the list below for definitions of abbreviations used in this publication.

AI/AO	Analog Input/Analog Output
ARW	Anti-Reset Windup
BPC	BioProcess Container
cGMP	Current Good Manufacturing Process
DO	Dissolved Oxygen
DV	DeltaV
FRS	Functional Requirement Specification
KBA	Knowledge-Based Article
MFC	Mass Flow Controller
MSA	Motor Safety Alarm
OPU	Online Parameter Update
PHV	Process History View
PV	Process Value (or Process Variable)
P/V	Power Input to Volume
PWM	Pulse Width Modulation
QC	Quality Control
SOP	Standard Operating Procedure
SP	Setpoint
S.U.B.	Single-Use Bioreactor
S.U.F.	Single-Use Fermentor
TCU	Temperature Control Unit
UPS	Uninterrupted Power Supply
VFD	Variable Frequency Drive
W/m ³	Watts per Meters Cubed



TruBio Software overview

Chapter contents

- 1.1 Introduction
- 1.2 Operational description
- 1.3 Hardware overview
- 1.4 User interface
- 1.5 Setup information

1.1 Introduction

The Thermo Scientific TruBio Bioprocess Control Software powered by DeltaV™ distributed control system from Emerson™ is an open, fully-configurable software solution designed to provide a flexible system for the control of bioprocesses. TruBio Software is powered by DeltaV from Emerson Process Management™, and is fully compatible with DeltaV version 12.3.1. TruBio Software has been developed according to GAMP5 methods and conforms to regulatory requirements for use in current good manufacturing practice (cGMP)-compliant processes. It is optimized to allow easy scaling to accommodate R&D, process development, and manufacturing.

TruBio Software must be installed on all of the DeltaV workstations controlling/viewing bioreactor/fermentor or mixing operations. The exceptions are the Application station, used for history storage, and the Plant Web Messenger station. Refer to the Emerson Process Management publication AK-1000-0144 for a list of PCs/servers currently recommended and supported. TruBio Software requires a DeltaV MD+, MQ, MX, SQ, or SX controller with an associated 2-wide power supply and 8-wide carrier. For R&D purposes (using Thermo Scientific Hyperforma G3Lab Controllers), TruBio can be run on the DeltaV Discovery platform (referred to as TruBio Discovery Bioprocess Control Software), which allows the use of the workstation as a controller (to execute control logic). The workstation also runs a virtual I/O card that interfaces with the G3Lab Controllers using Modbus over TCP/IP. See Appendix L for further details regarding the differences and limitations between TruBio Discovery and TruBio run on traditional DeltaV controllers.

Neither Emerson Process Management or Thermo Fisher Scientific recommend or support installation of any third-party software. Downloading files from the Internet is not recommended. See Emerson KBA (knowledge based article) AP-0800-0025.

TruBio Software is intended for use by personnel with a reasonable familiarity with bioprocesses and systems. We recommend that you become familiar with the manuals included on the ETP to obtain maximum performance from the system.

The contents of this guide may be copied into customer documents such as standard operating procedures (SOPs) as needed, but only for use with Thermo Scientific equipment. However, the customer takes full responsibility for the accuracy of the copy and its use in such documentation.

Every effort has been made to ensure the accuracy of the information in this document. However, Thermo Fisher Scientific reserves the right to change its products without notice.

TruBio Software is designed to provide the user with the ability to use a wide range of bioreactor/fermentor or mixing vessels, from small tabletop development systems to high-volume manufacturing vessels. It also allows the user to:

- Use different bioreactor/fermentor vessels in the same network with no change in the operator interface
- Use up to three probes for pH and DO if available on the controller
- View total pump and gas delivery volume on the Main Screen instead of a separate screen
- Integrate data from offline equipment, such as chemistry analyzers
- Display the full record of the last vessel load performed
- Set alarm notification parameters: email, building horn
- Save and load vessel settings
- Calibrate analog devices

In addition, TruBio Software allows the user to include third-party data and build sophisticated process control strategies. Other updates include more flexibility in calibrations and more informative displays.

1.2 Operational description

TruBio Software provides a control solution for upstream processes that is independent of process-control hardware. It can be configured by end users without having to learn process control programming, and resides on the DeltaV system by Emerson Process Management.

1.2.1 Licenses

TruBio Software is licensed per vessel, via proprietary license files. The license becomes active when the software activation key is installed on the required workstation(s). Additional licenses for DeltaV may be required by Emerson Process Management.

Locating TruBio Software license information

Use the following steps to locate license information.

1. From any screen (Main Screen is shown as an example), select **TruBio** at the bottom of the screen (Figure 1.1). The TruBio splash screen will display.

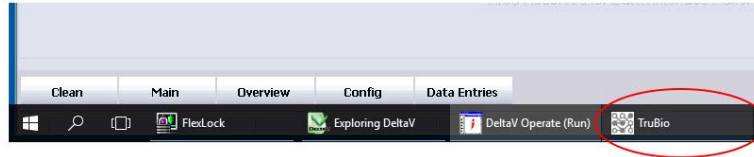


Figure 1.1. TruBio button shown on Main Screen.

2. Select **License Info** (Figure 1.2) to display the current licensing information for the system.

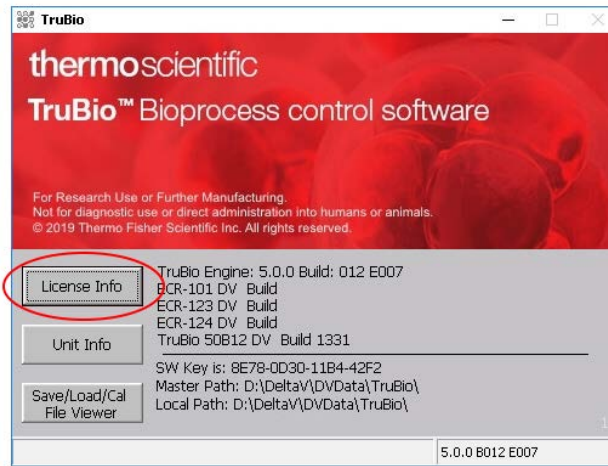


Figure 1.2. "License Info" button.

Locating the DeltaV license information

Use the following steps to locate license information.

1. To find DeltaV licensing information, click **Exploring DeltaV** from the toolbar at the bottom of the screen (Figure 1.3).

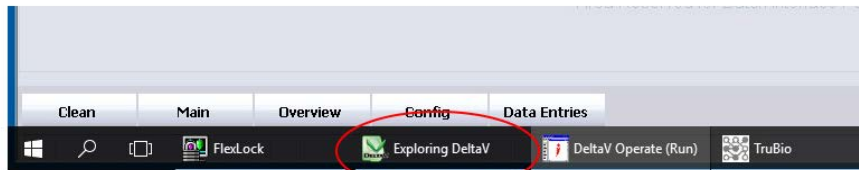


Figure 1.3. Exploring DeltaV button.

- From the File menu in the Exploring DeltaV window, choose **Licensing**, then **Licensing Report** (Figure 1.4).

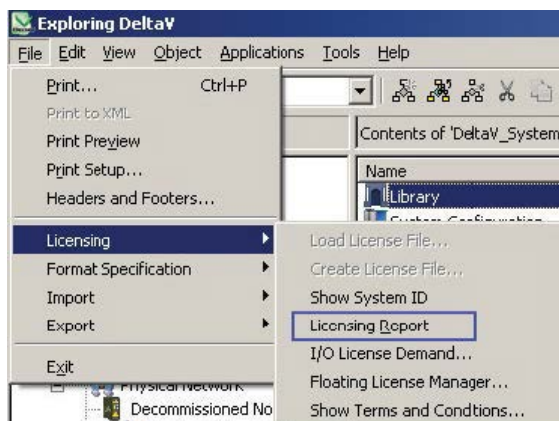


Figure 1.4. Selecting File > Licensing > Licensing Report.

Figure 1.5 shows a sample Licensing Report. Licensing information can be printed, or a screenshot can be copied into another program for email convenience.

 A screenshot of the 'Licensing Report' dialog box. It contains a table with three columns: 'Node', 'Assigned License Features:', and '# Configured:'. The table lists various license features for different nodes, including 'System', 'ALT-VAS-VS-BEX', 'ALT-VAS-VS-BH', and 'ALT-VAS-VS-CH'. At the bottom of the dialog, there are buttons for 'Print', 'Help', and 'Exit', along with a checkbox for 'Show discrepancies only'.

Node:	Assigned License Features:	# Configured:
System	(System Size: 0 DSTs)	275!
	(DeltaV Version 0)	12!
	(Advanced Unit Management 0 Units)	27!
	(Discrete Input Software: 0 DSTs)	45!
	(Discrete Output Software: 0 DSTs)	99!
	(Analog Input Software: 0 DSTs)	23!
ALT-VAS-VS-BEX	(Analog Output Software: 0 DSTs)	108!
	(Workstation Common Services)	1!
	(Batch Level: <none>)	Basic!
ALT-VAS-VS-BH	(Batch Units Capacity: 0 Units)	25!
	(Workstation Common Services)	1!
	(Batch Level: <none>)	Professional!
ALT-VAS-VS-CH	(Batch Units Capacity: 0 Units)	25!
	(Workstation Common Services)	1!
	(DeltaV Continuous Historian: 0 Pmtrs)	317!
	(Event Chronicle)	1!

Figure 1.5. Sample licensing report.

1.2.2 Definitions

BioProcess Container (BPC)

A plastic bag used to contain bioreactor media. BPCs are generally sterilized by the manufacturer, and have ports for the insertion of probes and spargers. BPCs must be placed in a solid containment vessel, such as a Single-Use Bioreactor (S.U.B.), for support.

DeltaV Books Online

A set of help files included with DeltaV systems. These files comprise the official documentation of the standard DeltaV system and include parameter and feature definitions.

G3 Gateway

A device that connects the G3Lab Controller to a TruBio Discovery Software Workstation.

Headspace

The space between the top of the media and the top of the S.U.B. or fermentor vessel.

Load file/log file

A file created when performing a Vessel Load; a record of the vessel load.

Parameter list

A file containing a list of all parameter paths, the values of which are to be written to and saved during a vessel save.

Process value

Also referred to as **process variable** or **measured variable**. In process control, a measurable quality or quantity that, if changed, can cause other changes in the process or make such changes possible. Common process values are temperature, pH, dissolved oxygen (DO), and pressure. Reflects the current state of the system.

SaveFile/configuration file

A snapshot of the current system configurations, created from a Vessel Save. The file is then used by the Vessel Load function to load all the saved parameters into the DeltaV system.

Setpoint

An input variable that reflects the desired value for a process value. Control loop algorithms compare the process value with the setpoint to determine an appropriate output.

TruBio Discovery BioProcess Control Software

TruBio Discovery Software provides the power of TruBio for non-production, non-GMP laboratory applications, within a single workstation. Connection to the HyPerforma G3Lab Controller is via a G3 Gateway. Control modules are executed within the DeltaV Workstation instead of a TruLogic.

TruBio Engine

A software application that interacts with DeltaV Operate and DeltaV control module logic. This provides functions enhancing the standard capabilities of a DeltaV system, and provides additional capabilities for bioprocess applications. TruBio utilizes the DeltaV control platform from Emerson Process Management.

Vessel load

A function in which parameter values that have been saved in a SaveFile are written to the selected vessel's parameters.

Vessel save

A function in which the current parameter values of a vessel are saved in a SaveFile.

1.2.3 Toolbar buttons

Table 1.1. Toolbar button icons and functionality descriptions.















Icon	Function
	Exits operator interface.
	Prints current page.
	Opens a control module faceplate, but requires manual entry of the module name. Same function as clicking the control box.
	Opens the detail screen for a control module, but requires manual entry of the module name. Also accessed on the control module faceplate.
	Resets the Operator Interface in case of graphics error.

Table 1.2. Toolbar button icons and functionality descriptions (continued).

Icon	Function
	Select a graphic page from the graphics root directory. Limited access as errors may crash the Operator Interface.
	Return to the previous Main Screen.
	Opens the Main Overview graphic, with links to each tower and vessel graphic. An easy way to navigate quickly between vessels.
	Opens the Alarm Summary, showing all active and unacknowledged alarms.
	Opens the Alarm Filter page, excluding alarms from inactive vessels and showing only alarms from active vessels.
	DeltaV Utilities, provides access to Emerson Process Management functions.
	DeltaV logon, logs user into DeltaV workstation.
	Opens the Diagnostics screen to facilitate troubleshooting.
	Opens the Process History View.

1.3 Hardware overview

TruBio Software operates on a ProfessionalPLUS PC/Server and requires a DeltaV dongle. The ProPlus should be connected to a TruLogic Controller that includes DeltaV cards. The ProPlus, TruLogic, and G3 Controller (G3Lab, G3Lite, and G3Pro) form a control network with the G3 Controller providing input/output (I/O) connections for sensors, agitator drives, and pumps. Scales/load cells may be connected directly to the TruLogic or through the G3 Controller.

Note: TruBio Discovery Software does not require the use of TruLogic Controllers. See Appendix L for further details.

1.3.1 Instrumentation

The field instrumentation associated with the bioprocess unit that is monitored and/or controlled depends on the specific bioprocess application.

TruBio Software and the associated TruLogic-DeltaV hardware are designed for upstream processes, namely bioreactor/fermentor vessel control. The TruBio system includes pH and DO, and pressure sensors and can include other sensors, such as CO₂.

1.3.2 New features of TruBio Software, version 5.0

A TruBio licensing dongle is no longer required for operations. Licensing information is embedded in the software. The Chart Builder function will be embedded in each graphic object. Setting up alarms and limits is now done on one screen instead of having separate screens. The screens are configured using low contrast colors in accordance with the Emerson Human-Centered Design philosophy.

1.3.3 Software change tracking

- TruBio Software, version 4.0: Original release. Compatible with DeltaV 10.3. Run on Windows™ XP, 1 GHz Pentium III.
- TruBio Software, version 4.5: Developed on DeltaV 10.3.1 and validated on versions 10.3 and 11.3.1. Runs on Windows 7. Automatic or manual pump calibration option, pump dosing, gas manifold interlock option, redundant pressure sensors, user-selectable pressure units, totals on main screen, availability of up to 3 pH and DO sensors, pH deadband.
- TruBio Software, version 4.6: Developed on DeltaV 11.3 and runs on Windows 7. Adds MultiFeed capability, new pump calibration, support for G3Lab Universal.
- TruBio Software, version 4.7: Developed and validated on DeltaV 11.3.1 and 12.3.x; runs on Windows 7 and Server 2008 software. Adds Total Dose Strategy, reversible agitator control. Rev2 of the user's guide adds perfusion and licensing information.
- TruBio Software, version 5.0: Developed and validated on DeltaV 12.3.1; runs on Windows 7 Professional SP1 64 bit and Windows Server 2008 R2 64 bit.

1.4 User interface

The user interface consists of a number of screens that enable the user to calibrate sensors, configure the system, and set up key parameters. These screens are:

- Splash/opening screen
- Overview screen
- Main bioreactor/fermentor screen
- Configuration screen
- Online parameter update screen
- Individual parameter faceplates
- Data entry screen (for offline information)
- Cleaning screen

1.4.1 Splash screen

The splash screen (Figure 1.6) contains the alarm banner and toolbar. The user can enter the program by clicking anywhere in this screen.

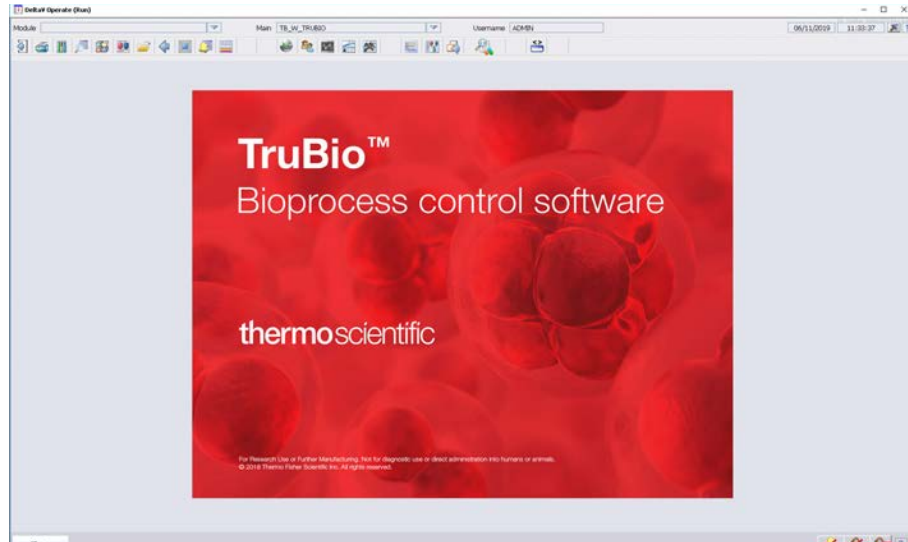


Figure 1.6. Splash screen.

1.4.2 Overview screen

The rectangles shown in Figure 1.7 represent individual bioreactor/fermentor vessels. Clicking in any rectangle will open the main screen for that vessel. The numbers shown in the following illustration are user-selected key parameters, which is discussed in section 4.11, “Key parameter setup.”

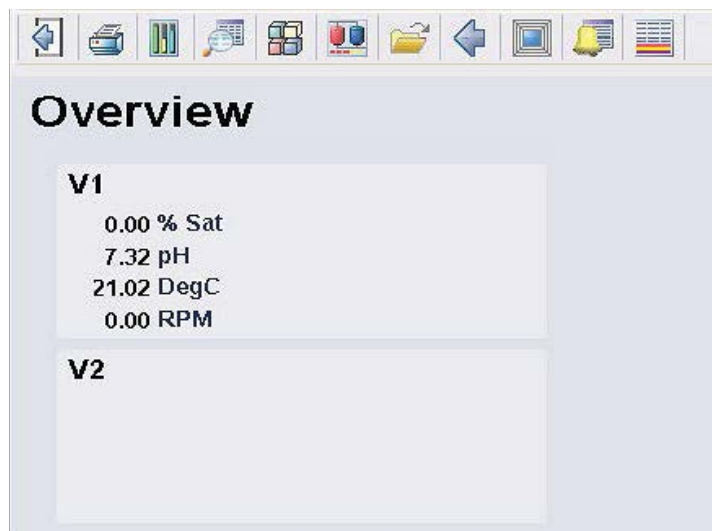


Figure 1.7. Overview screen.

TruBio Software, version 5.0 supports many types of bioreactors/fermentors, including small R&D glass vessels, cell culture rockers, and large manufacturing vessels. Different types of vessels may be used on one network. Three sample types are shown below, illustrating the features common to all vessel types.

1.4.3 Main screen—vessel without SaveFile

The illustration in Figure 1.8 is of a vessel that has not had a Save (parameter) file loaded.

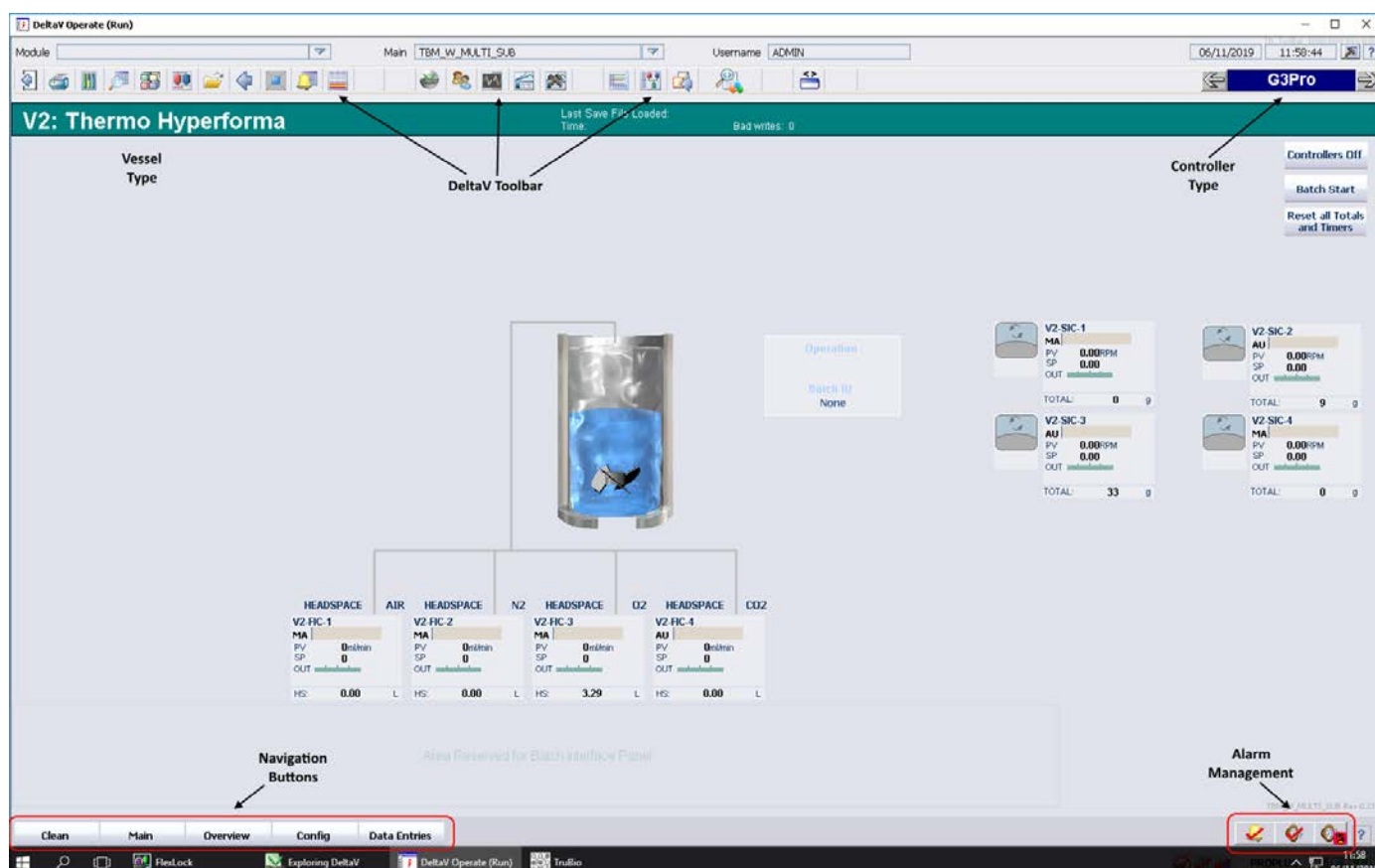


Figure 1.8. Main screen (vessel without SaveFile).

Note the following features:

- The **controller identification box** (blue box, top right corner) identifies which controller is in use. Clicking the forward or back arrows changes the graphic display.
- The **DeltaV Tool Bar** provides rapid access to such features as the alarm list, diagnostics, and Process History View. See the “Toolbar Buttons” section for a description of the buttons.

- The **vessel type** and number is displayed in a banner across the top of the screen, just below the toolbar. This indicates which type of vessel is in use. When a SaveFile has been loaded the type of file and the date loaded will also be displayed on this banner.
- The “**Navigation**” buttons allow the user to access vessel and overview graphic screens quickly and easily.
- The **Alarm Management** toolbar enables the user to acknowledge alarms, silence the horn, or disable the horn. Alarms are discussed in the “Alarms and Limits” section.

1.4.4 Main screen—SaveFile loaded

This screen (Figure 1.9) displays buttons and control boxes for control loop and measurement values. These will be discussed more fully in the context of establishing control loops.

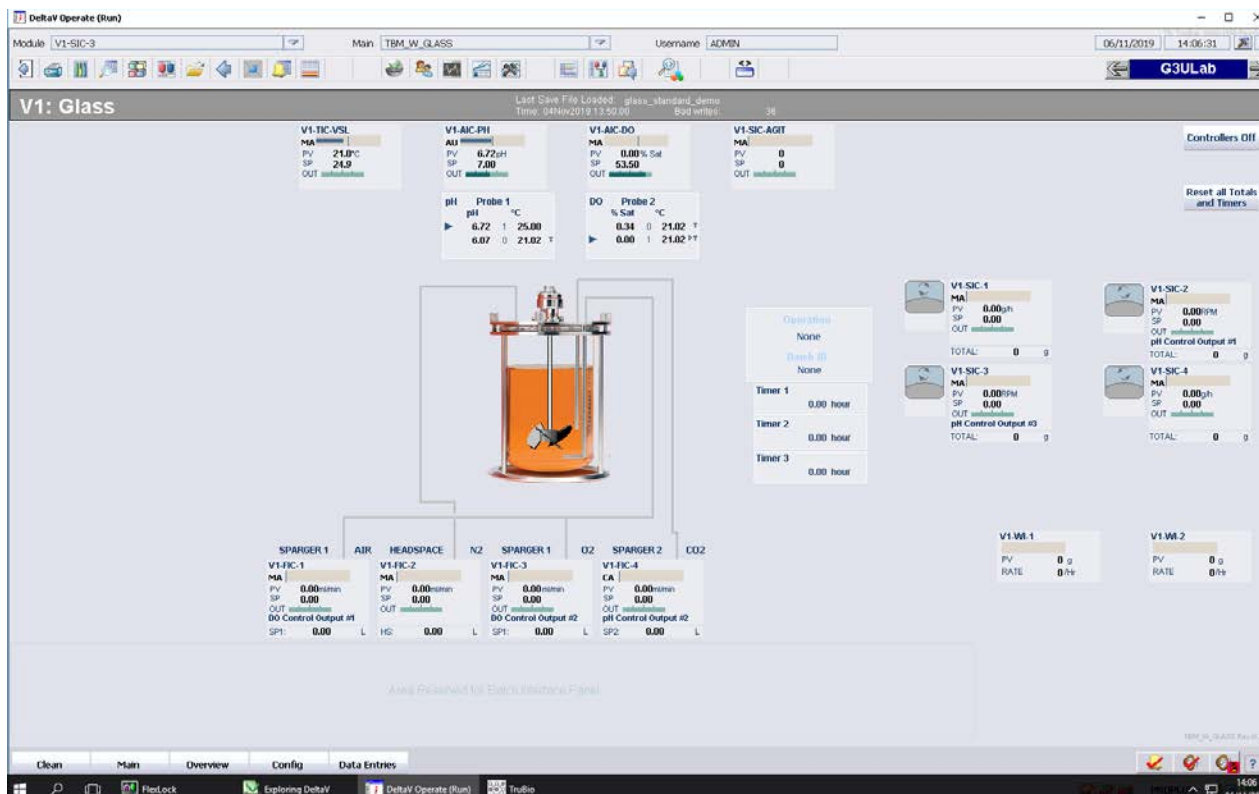


Figure 1.9. Main screen (SaveFile loaded).

There are several new features for version 5.0 that are shown on this screen. In the upper right corner of the screen, a box is labeled “Reset all totals and timers.” This is an option in version 5.0 and is set up by Thermo Fisher Scientific. It allows the user to set all timers and totals back to zero (0). The “Controllers Off” button will be discussed below. The name of the vessel is shown at the top left of the screen. Note in Figure 1.10 that there are two pH and DO boxes.



Figure 1.10. pH and DO boxes.

The upper box, the control box, displays the setpoint, the process value, and the output of the relevant controller. The top line (shown as MA) indicates the mode the controller is in: MANual in this illustration. The lower box displays the raw probe data, with the blue arrow indicating the probe from which the controller is reading the PV. Clicking on the box will open the controller faceplate.

Also note the display of gases at the bottom of the screen. The user can see the flow path for each gas fed into the vessel; there are up to three possible flow paths. The total gas added for each path is shown in the lower part of the display box for the specific gas.

The control box also displays the selected remote setpoint at the bottom of the box. In Figure 1.11, pH Control Output #1 provides the setpoint for the CO₂ control.

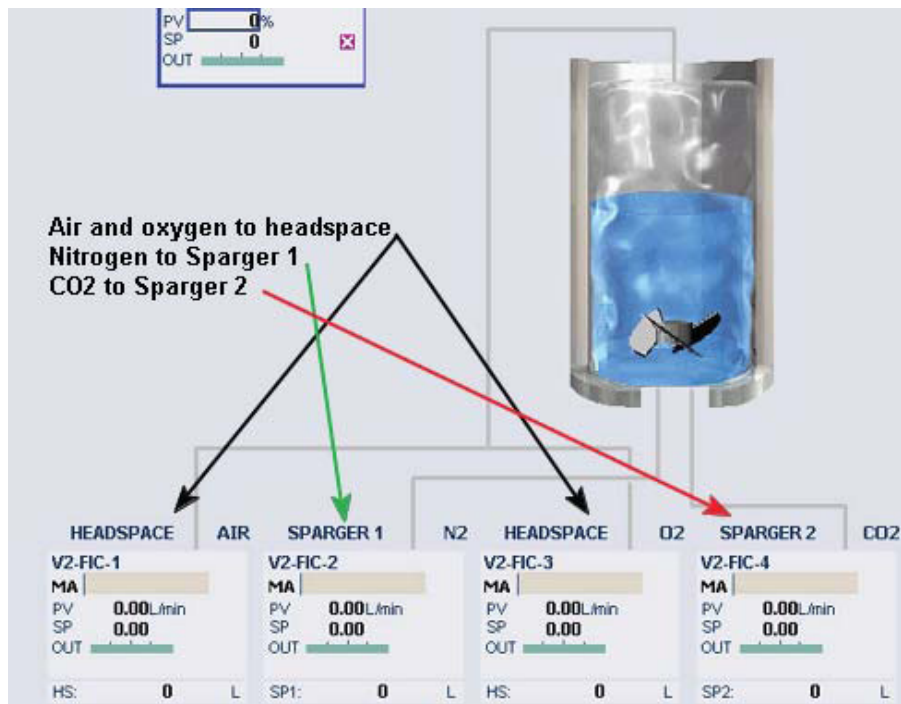


Figure 1.11. Control box on main screen.



Figure 1.12. Control box Sparger 2 detail on main screen.

The control box (for gases and pumps) is a totalizer box (Figure 1.13). Clicking it opens the Totals faceplate.

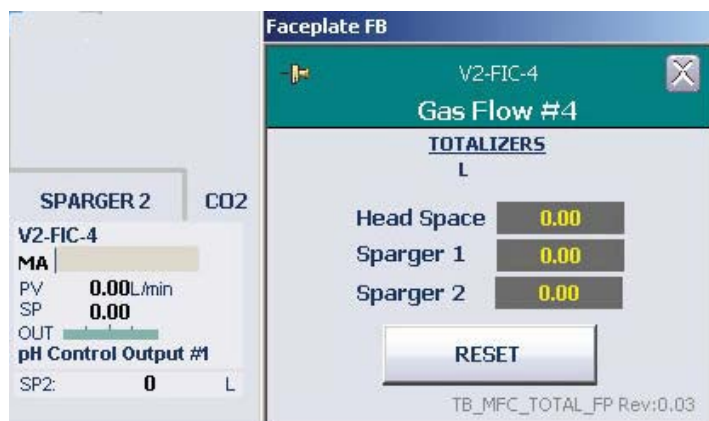


Figure 1.13. Totalizer box.

Clicking **Reset all Totals and Timers** (Figure 1.14) will set all values to zero (0).



Figure 1.14. Reset all Totals and Timers button.

Batch Start button

It is possible to have a button on the Main screen that will start the batch timer at the user's discretion. It will NOT start the batch, but will start the batch timer, and is required if using XL Report or DreamReport. To make this button visible on the screen, use the following protocol.

Note: The **Batch Start** button will start the batch timer ONLY, not the batch itself. The batch starts when all control loops have been set up and the appropriate faceplates set to AUTO mode.

1. To access the Batch Start button, open the Online Parameter Update.
2. Verify that the correct vessel is displayed at the top of the pop-up screen.
3. In the first column (Module), click on **VX-COMMON**, where X indicates the vessel number (Vessel 1 shown in example).
4. In the second column (Category) click **Default**.
5. In the third column (Parameters) locate and click on the string **/USE_START_STOP.F_CV**. The Value for this string can be either 0 or 1. If it is 1, the button will be displayed on the Main screen. Set the Value to either 0 or 1 and click **Update** to save the change.

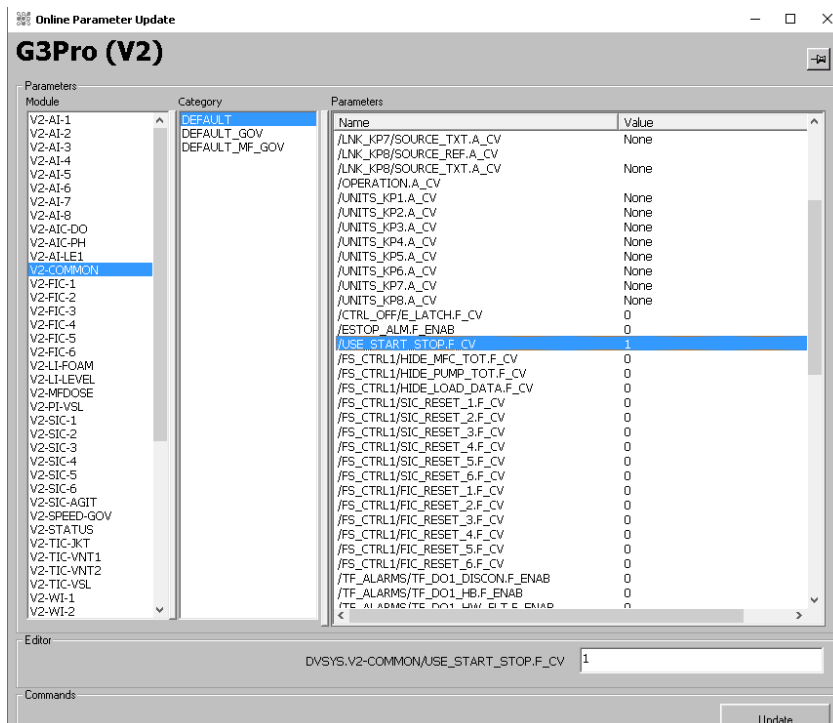


Figure 1.15. Selecting Batch Start option.

The **Batch Start** button will be displayed at the upper right corner of the Main screen, as shown in Figure 1.16.



Figure 1.16. Batch Start button.

Tag Display settings

It is possible to change the labels on the control boxes on the Main screen, if desired. To change the labels, click the box on the toolbar shown in Figure 1.17.



Figure 1.17. Tag Display settings box.

The Module Tag is the name string found in the Online Parameter Update (OPU) lists, e.g. F450_UI_FLT1-P.

The Description and Friendly Name tags are very similar, and use common terminology to describe the module, e.g. pH control.

Use the Tag Display settings to change the tags on the Main screen. The module identification number will remain the same, regardless of the display choice. The options are:

- Module Tag
- Description
- Friendly Name
- No Display

Figure 1.18 shows examples of the Module Tag, Description, and Friendly Name tags, respectively. If No Display is selected there will be no label on the control box.

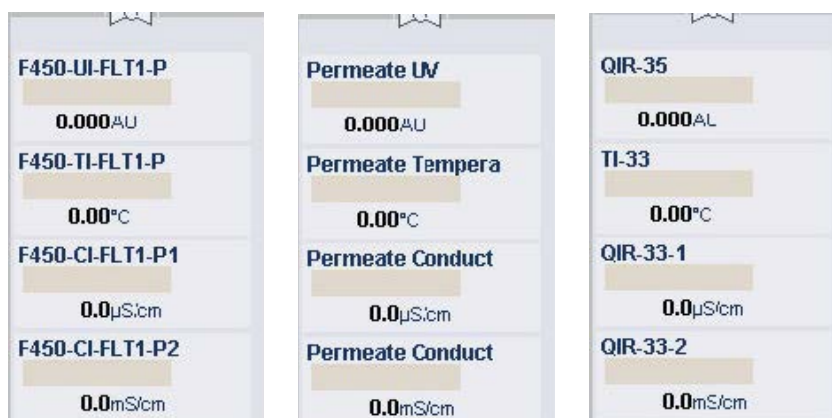


Figure 1.18. Examples of Module Tag (left), Description tag (center), and Friendly Name tag (right).

1.4.5 Main screen—rocker

The Rocker screen is arranged in the same manner as the other vessel screens, with the addition of the agitation control located immediately above the image of the rocker. The rocker settings also include the rock angle and the rock speed, circled in Figure 1.19.

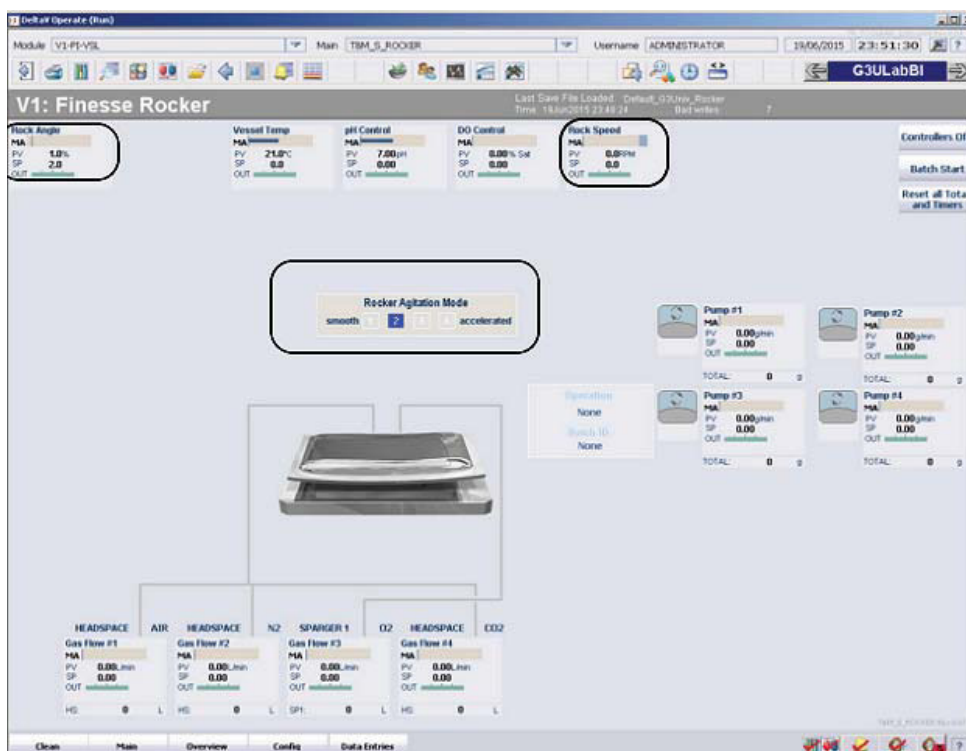


Figure 1.19. Main screen rocker.

1.4.6 Configuration screen

The Configuration screen (Figure 1.20) allows the user to configure control loops, signal conditioning, vessel type selection, define measurement parameters, and set up control loop strategies.

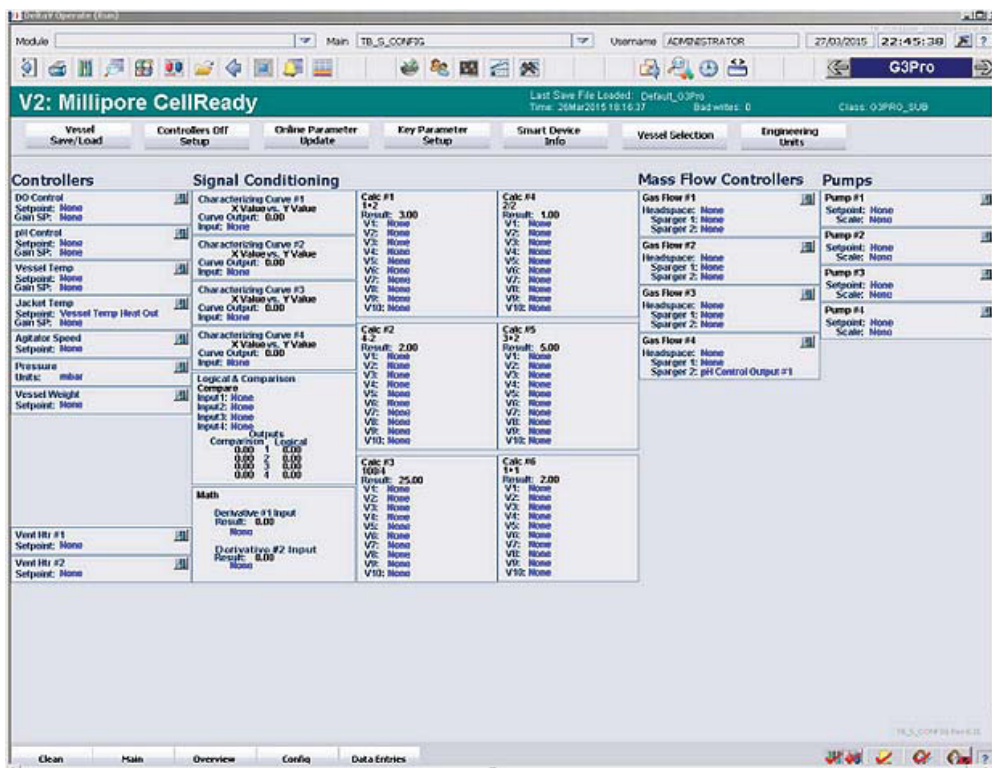


Figure 1.20. Configuration screen.

The screen is divided as follows:

- Controllers, Mass Flow Controllers (MFCs), And Pumps: control loop and measurement definitions only.
- Signal Conditioning; customized calculations and control tactics to be applied to the control loops.

A number of parameters have been moved from the screen area to the top of the screen, just below the colored band with the vessel information.

- **Vessel Save/Load:** Allows the user to load or save the configuration input on this screen.
- **Controllers Off setup:** Allows the user to define the controller mode, output, or setpoint established for the controllers when the “Controllers Off” button on the Main screen is activated.
- **Online Parameter Update:** Provides a detailed list of parameters used for each Control Module. Faceplates for the Control Modules can be opened from the Main screen or from the Faceplate icon in the toolbar.

- **Key Parameters setup:** Defining those parameters to be displayed on the Overview screen box.
- **Smart Device Information:** Provides model and serial numbers for connected SmartMFC gas controllers and SmartPumps.
- **Vessel Selection:** Allows the user to define the vessel type being controlled.
- **Engineering Units:** A list of the units available in the software, such as gm/hr or rpm.

1.4.7 Online Parameter Update

The Online Parameter Update (OPU) function (Figure 1.21) is the interface between TruBio software and Emerson DeltaV. The OPU screen displays the online parameter values for all control modules. Users can view the current value of a selected parameter and enter a new value, as desired. A new value can only be written if the user has the correct security privilege. This function is used to customize a vessel configuration. When parameter changes have been made, they can be saved by using Vessel Load/Save on the Configuration screen. This screen will be discussed further in the context of pump setup.

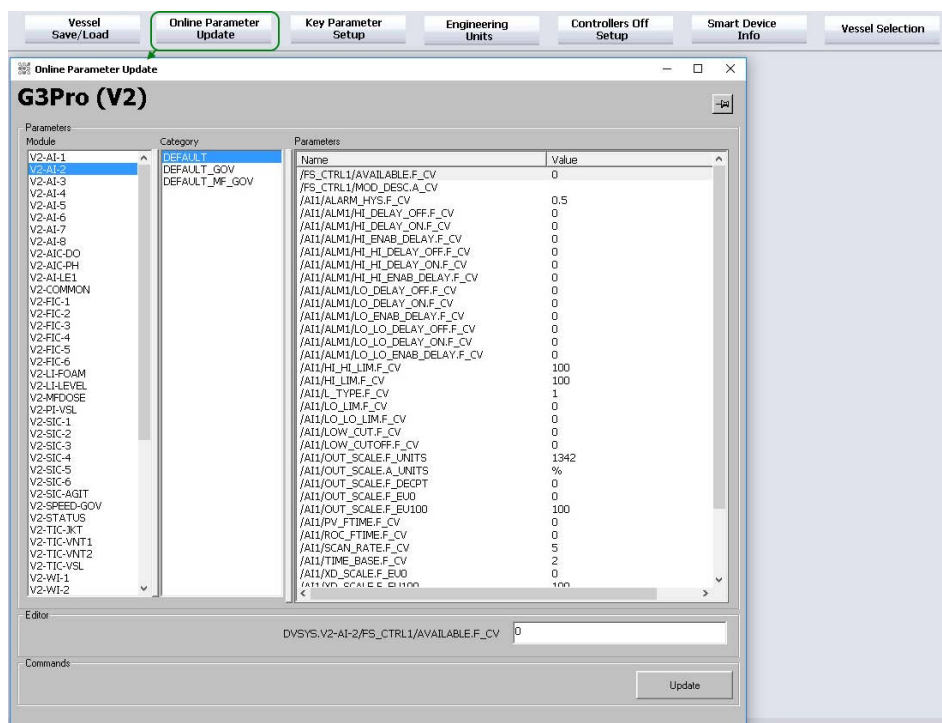


Figure 1.21. Online Parameter Update screen.

1.4.8 Faceplates

Clicking on any of the control or measurement boxes opens its faceplate (Figure 1.22). The most commonly-used aspects of the faceplates are noted here. For a full description, see Appendix A.

The vertical bars represent the current process value for the parameter on the right (yellow bar) and the controller output on the left (blue). The numbers at the top and bottom of the vertical bars represent maximum and minimum range values. The large white arrow and the box on the right side represent the setpoint.

The number in the box at the top of the yellow bar is the process value. Clicking on the Detail icon enables the user to access probe selection, calibration, and alarm settings.

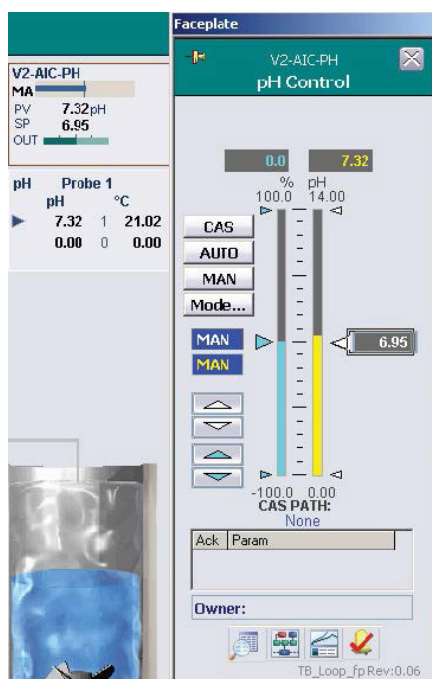


Figure 1.22. Faceplate example.

Next to the Detail icon are links to parameter trending charts, the DeltaV Control Studio, the Process History View, and alarm acknowledgement (Figure 1.23).

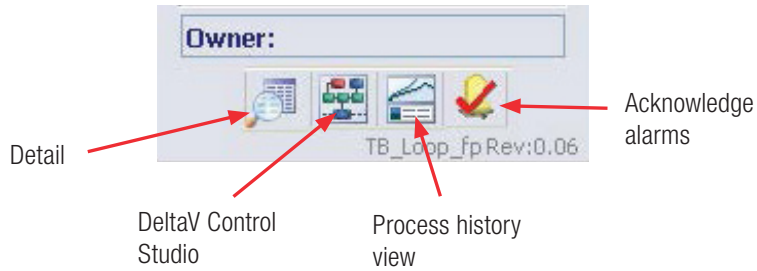


Figure 1.23. Options on bottom of faceplate.

1.4.9 Data Entry screen

The Data Entry screen is accessed from the alarm banner, located under the main graphic (Figure 1.24). Click **Data Entries** to open the following screen, shown in Figure 1.25.



Figure 1.24. Data Entries button located under main graphic.

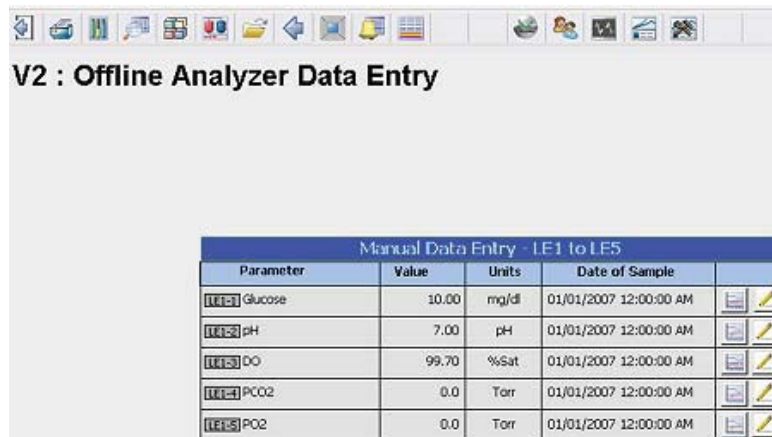


Figure 1.25. Offline analyzer data entry screen.

This screen enables the user to input offline test data. To enter data, click on the pencil icon in the appropriate line. This will open a pop-up screen, as shown in Figure 1.26.

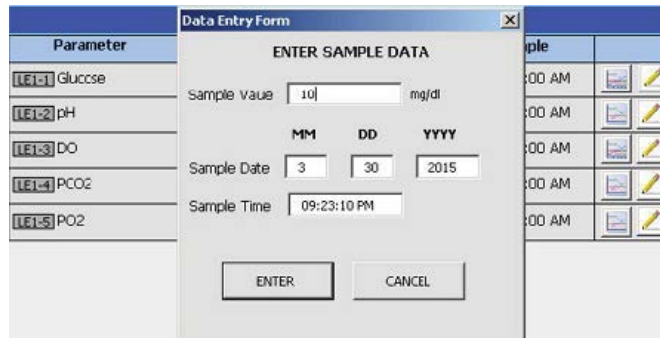


Figure 1.26. Pop-up screen to enter sample data.

Enter the data in the appropriate boxes, then click **Enter**. Once entered, data cannot be deleted (to preserve batch record integrity). To view data trends, click on the graph icon next to the pencil icon.

1.4.10 Cleaning screen

Clicking **Clean** on the Main screen opens the Cleaning screen (Figure 1.27). This screen enables the user to clean a touchscreen at any time while preventing the accidental entry of erroneous data or interference with an ongoing process.

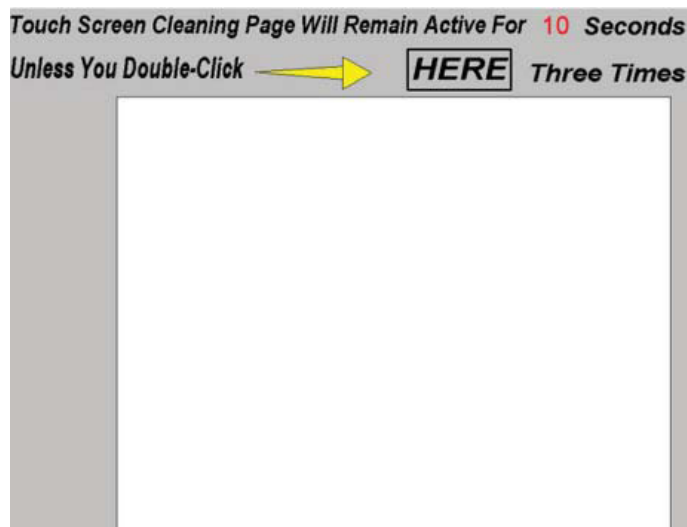


Figure 1.27. Cleaning screen.

The “Clean” button opens the cleaning page for 21 seconds. The page displays a countdown in the top right corner (Figure 1.27) and can be opened repeatedly, if necessary, to provide adequate time to complete the cleaning. Double click three times in the **Here** box to close the screen before the countdown ends.

1.5 Setup information

Many bioreactor/fermentor systems, especially those that are large or complex, are set up by Thermo Fisher Scientific service personnel. Smaller systems may come pre-configured. However, users may find it necessary or desirable to modify an existing system or to set up a new system.

Pump setup

Open the cover to install the tubing in the pumps. For the series 100 and 300 pumps, this is done by lifting the cover. The series 500 pumps require the use of a screwdriver to turn the cover release.

To install tubing in the series 100 and 300 pumps, put the tubing into place before closing the cover (Figure 1.28), pressing down until the cover snaps into place. In the series 500 pumps, the tubing is looped over the pump and the pump turned manually to pull the tubing into place.



Figure 1.28. Tubing placed into peristaltic pumps.

Check the Main screen of the selected vessel. If the pumps have been configured, the control boxes will be shown on the right side of the screen.

If the control boxes are not displayed, proceed as follows:

1. From the Configuration screen, click **Online Parameter Update**. This opens the display shown in Figure 1.29. Refer to Figure 1.29 for the following steps.

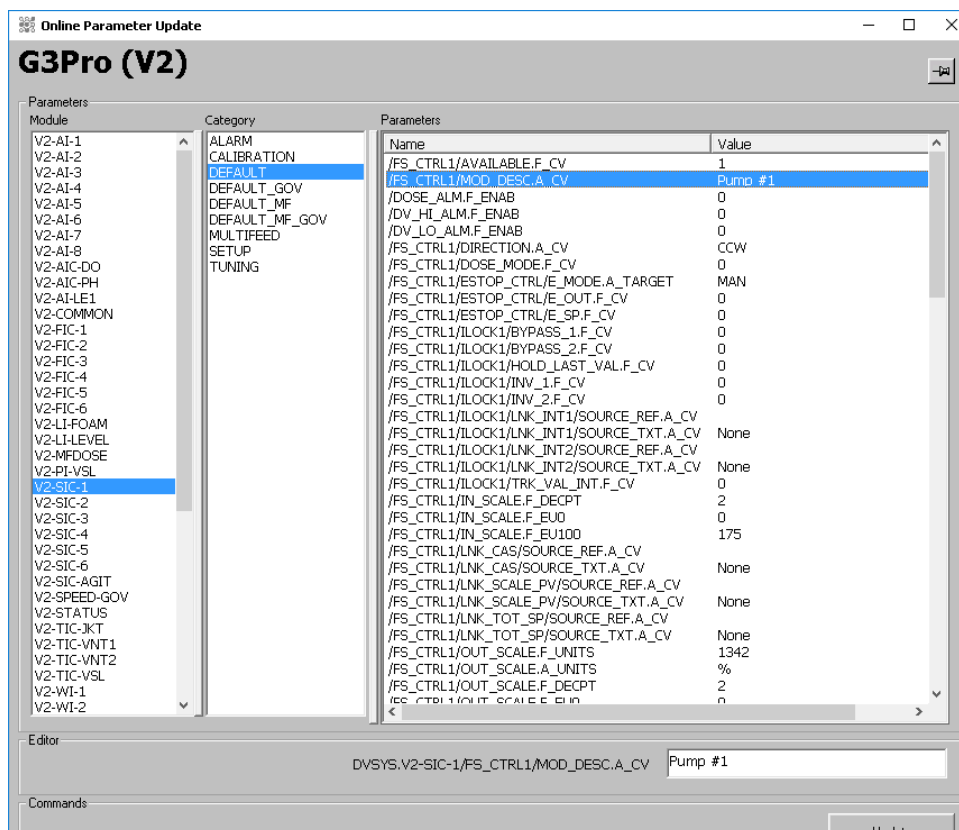


Figure 1.29. Online Parameter Update screen for pumps.

2. Verify that the correct vessel is displayed (Figure 1.29 shows “Vessel 2”) and click **Default** in the “Category” column (see the second column in Figure 1.29).
3. In the “Module” column (first column in Figure 1.29), locate and click the string that reads **Vy-SIC-x**, with y being the vessel number and x being the pump number to be set up.
4. Click **Default** in the “Category” column again.

5. In the “Parameters” column (third column in Figure 1.29), locate and click the Name string, **/FS_CTRL1/AVAILABLE.F_CV**.

The available values for this Parameter tag are 0 and 1. If the pump is inactive, the Value will be 0. If the pump is active, the Value will be 1. Smart pumps are automatically activated when installed and working correctly.

In addition, on this screen the user can create a name or description for the pump, such as “Pump 1” or “Base Pump,” and select the delivery units over time.

To name the pump, click to highlight the Name string, **/FS_CTRL1/MOD_DESC.A_CV**. Enter the desired name (Value), up to 28 characters. Press **Enter** or click **Update**.

2

General system operation

Chapter contents

- 2.1 User login
- 2.2 Vessel selection
- 2.3 Calibrating sensors

Select the vessel to be used. Run “Vessel Load” if a default save (parameter) file has not been set up, then set up the process control loops. **Note:** Sensors and pumps must be calibrated before use, and pumps must be calibrated using the same tubing as will be used for the process.

2.1 User login

Click the user login icon on the toolbar (Figure 2.1). Enter a valid user name and password in the pop-up box. If using Domain in the first line, it is very important to use the correct domain name.

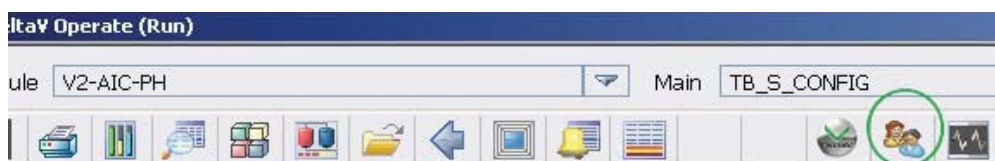


Figure 2.1. User login icon on toolbar.

The list of users and available actions is given in Table 2.1 below. Contact your Thermo Scientific sales representative for a list of default passwords.

Table 2.1. Available actions for each user level.

Action	Operator	Maintainer	Supervisor	Administrator
Access Window desktop	×	×	×	✓
Exit DeltaV Operate	×	×	×	✓
Access overview page	✓	✓	✓	✓
Access configuration page	✓	✓	✓	✓
View Smart Device info	✓	✓	✓	✓
Vessel select	×	×	×	✓
Vessel save/load	✓	✓	✓	✓
OPU access	×	×	×	✓
Access control module configuration forms	×	×	×	✓
Key parameter setup	×	×	×	✓

Table 2.1. Available actions for each user level (continued).

Action	Operator	Maintainer	Supervisor	Administrator
Controllers off setup	✗	✗	✗	✓
Controllers off access	✗	✗	✓	✓
Change modes on faceplate: bypass to normal and normal to bypass	✓	✗	✓	✓
Change modes on faceplate: manual, auto, cascade	✓	✗	✓	✓
Enter setpoint	✓	✗	✓	✓
Enter output	✓	✗	✓	✓
Access Details displays	✓	✓	✓	✓
Access Control Studio	✗	✗	✗	✓
Access Process History view	✓	✓	✓	✓
Calibrate	✗	✓	✗	✓
Change alarm limits	✓	✓	✓	✓
Change limits (ARW, setpoint hi/lo)	✗	✗	✓	✓
Change conditional alarm settings	✗	✗	✓	✓
Enable/disable alarms	✓	✗	✓	✓
Set alarm priority	✗	✗	✓	✓
Acknowledge alarms	✓	✓	✓	✓
Bypass interlocks	✗	✗	✓	✓
Change tuning parameters/gain scheduling	✗	✗	✓	✓
Access Diagnostics	✓	✗	✓	✓
Probe selection	✗	✗	✓	✓
Pump functions: change direction, set dosing	✗	✗	✓	✓
Start/stop/reset timers	✓	✗	✓	✓
Enter data on Data Entry screen	✓	✗	✓	✓

To add, change, or delete a user or group, click the link “Exploring DeltaV” in the Windows toolbar (bottom of the screen), then click on the “User Manager” icon. For more information on the user manager, refer to DeltaV Books Online.

2.2 Vessel selection

Although one controller controls only one vessel at any given time, up to seven vessel types may be programmed into the software to allow for ease of switching between vessels. The number of available vessels depends on the controller that is being used: the HyPerforma G3Lab Controller only controls tabletop vessels, such as the Thermo Scientific™ HyPerforma™ Glass or Rocker Bioreactors, and larger vessels are controlled by the G3Lite, or G3Pro.

Vessel types are programmed into the software at the factory, according to customer specifications.

A feature in the TruBio Software allows the user to change the type of vessel assigned to a particular controller and expands the number of vessel types available for selection. For example, if Vessel 2 is currently a Mobius™ CellReady and the user wishes to change the vessel to a Thermo S.U.B., this can be done with the Vessel Selection option.

The option is accessed from the Configuration page. Clicking **Vessel Selection** opens the pop-up box (Figure 2.2), allowing the user to switch to a different vessel type. **Note:** Vessel selection is only available on the G3Lab Universal and G3Pro Universal Controllers.

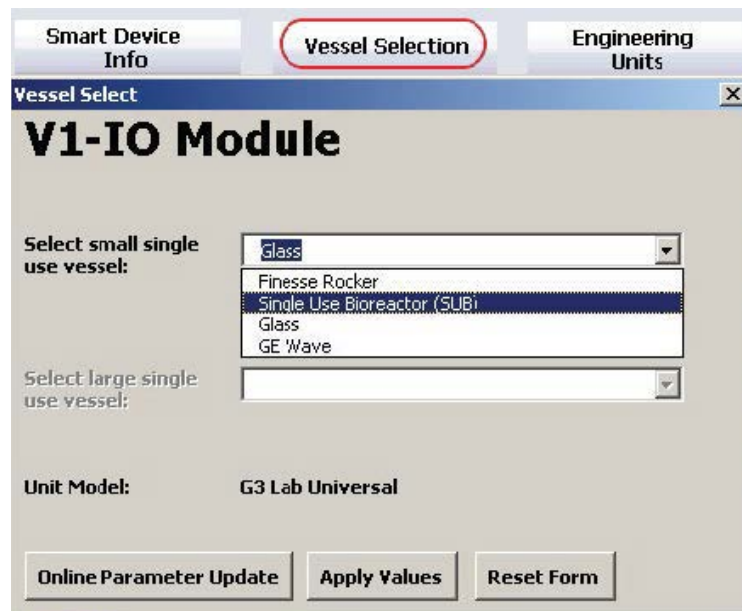


Figure 2.2. Vessel Selection pop-up window.

The menu available depends on the size of the controller. If a smaller controller (such as the G3Lab Controller) is in use, the menu will be for the vessel types listed above. For a larger controller, such as the G3Pro Controller, there will be a different menu of available vessels (Figure 2.3).

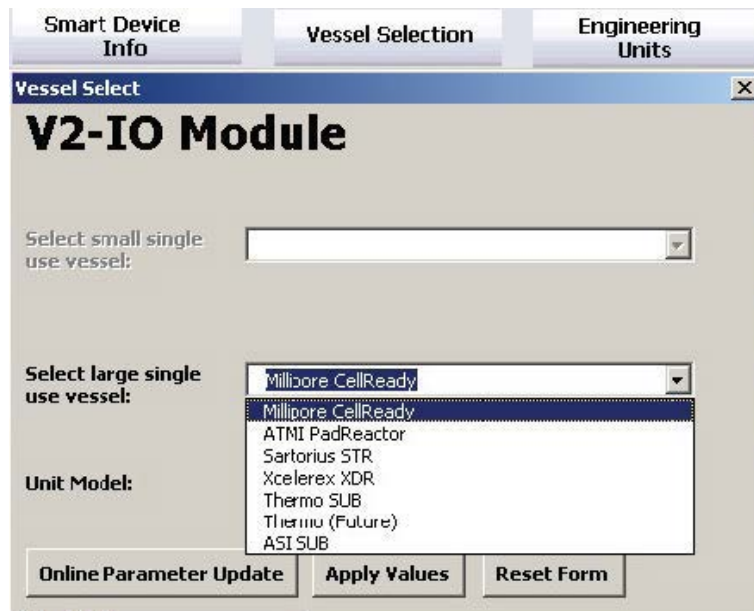


Figure 2.3. Vessel Selection pop-up window for large vessels.

Select the type of vessel to be added (substituted) and click **Apply Values**. Another pop-up window will ask the user to confirm the change (Figure 2.4), as all values will be reset to allow configuration of a new vessel type.

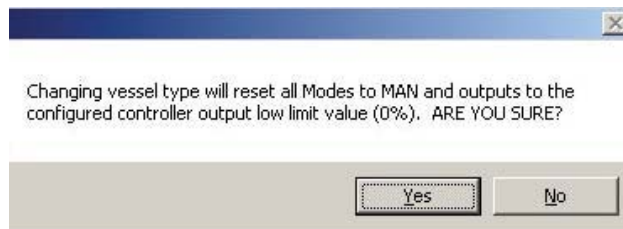


Figure 2.4. Vessel Selection confirmation pop-up window.

Click **Yes** to confirm the change in vessel type. **Note:** The Vessel Selection feature should only be used to change the assigned vessel type, e.g. changing Vessel 2 from a Thermo S.U.B. to a Sartorius™ STR. The selection box in the toolbar is used to change the number of the vessel to be viewed.

2.3 Calibrating sensors

After the SaveFile is loaded, the individual parameters can be adjusted for the particular run. For more information, see section 4.2, Loading and saving a vessel file.

TrupH or TruDO electrochemical sensors, if used, must be calibrated prior to insertion into the sterile bag. TruFluor pH and DO sheaths are factory calibrated. The sheaths are inserted into a sterile bag at the manufacturer before the assembly is sterilized.

After calibration, the entire sterilizable sensor is autoclaved and inserted into the sterile bioreactor/fermentor vessel, using appropriate technique to avoid introducing contamination.

Factory-calibrated sheaths of single-use sensors are inserted into a sterile bag by the manufacturer, who then ships the sterilized assembly to the user. Therefore, the user needs only to insert the appropriate reader into the sheath and attach the cables.

When a S.U.B. assembly is shipped with sterilized sheaths in place, pH calibration is most easily verified by removing an aliquot of the media and verifying the TruFluor reading by using a separate instrument calibrated with NIST-traceable standards.

Calibration of all sensors can be verified post-run, if desired, to bracket the run data with pre- and post-run calibration data.

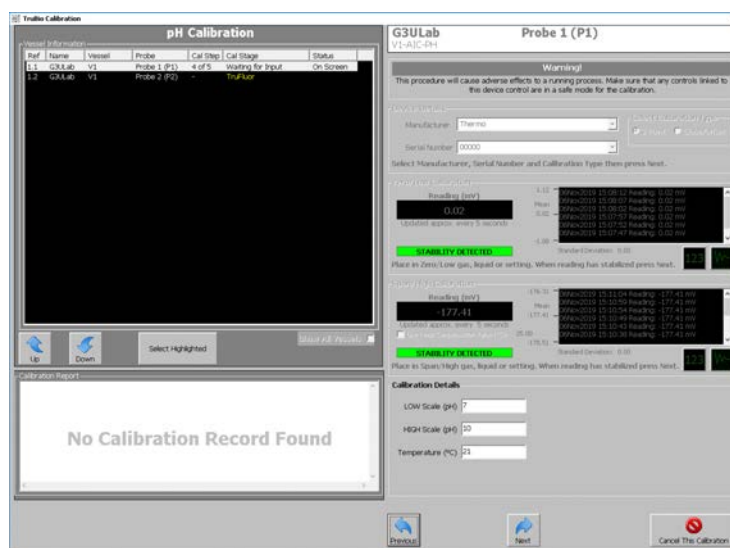


Figure 2.5. Adjusting parameters of sensors.

Both the single-point standardization and full calibration will be discussed below.

2.3.1 pH calibration

To open the pH faceplate, click the pH control box on the Main screen, located just above the bioreactor/fermentor vessel (Figure 2.6). To open the Detail window, click the Detail icon in the lower left corner of the faceplate.

In the Detail window, click the **Calibration** tab.

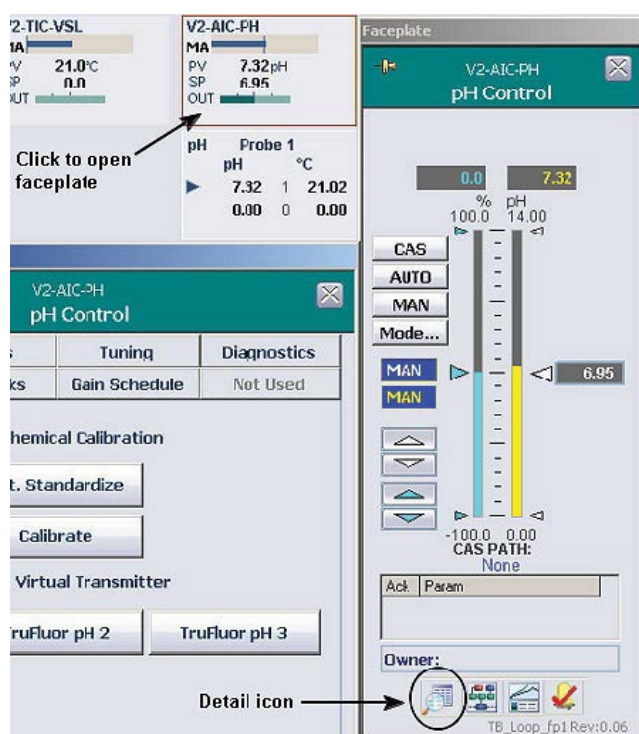


Figure 2.6. Opening pH control box.

Single-point standardization

Using sterile procedure as defined in the facility, remove an aliquot of media from the bioreactor/fermentor. Using a standard pH meter that has been calibrated with NIST-traceable standards, determine the pH of the media.

Click the “1pt Standardization” box in the calibration tab of the detail window, which opens the following screen (Figure 2.7).

Figure 2.7. 1pt Standardization box.

Select the appropriate transmitter by clicking the radio button, enter the pH value obtained by testing the aliquot and click **Enter**. The pH curve will be updated.

Two-point calibration

From the “Calibration” tab of the Detail window, click **Calibrate**. This opens a series of screens that will guide the user through the process. The right-hand portion of the following screen displays the ongoing calibration information. The left-hand side, called the Vessel Information screen, displays the vessel and the probes selected for calibration. **Note:** In the TruBio Software, multiple probes can be calibrated concurrently.

Enter the manufacturer and the serial number of the probe to be calibrated. If the probe has previously been calibrated, you can select the serial number from the drop-down menu. Click **Next**.

The display advances to the Zero/Low Calibration screen. Place the probe in the calibration buffer and observe the screen. The display updates every five seconds, and when the standard deviation of the displayed points is less than 1%, the “Stability Detected” message appears (Figure 2.8).

The display can be either numeric or graphic. Both display options are labeled in Figures 2.8 and 2.9.

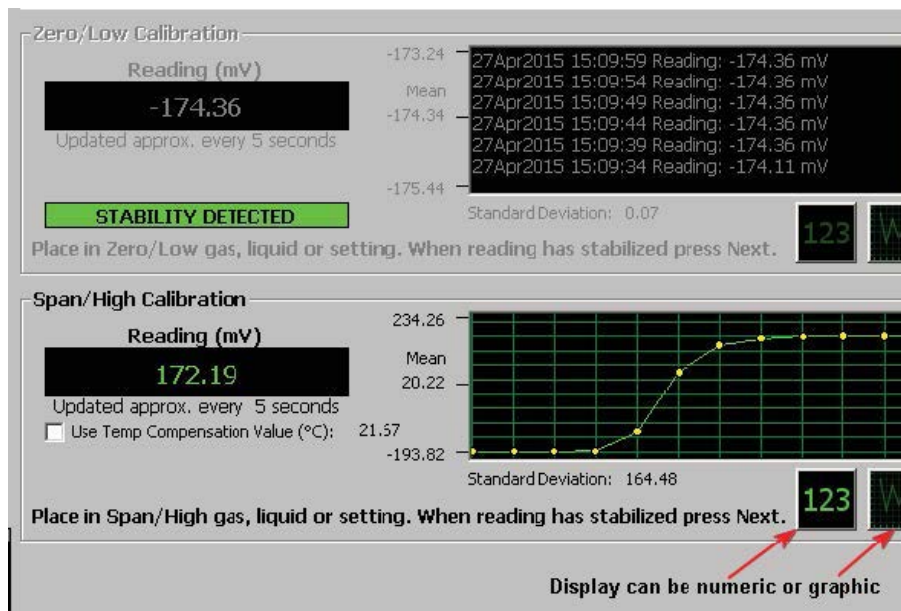


Figure 2.8. “Stability Detected” message for first calibration point.

When “Stability Detected” appears, click **Next** at the bottom of the screen to lock in the first buffer value. The display will advance to the Span/High Calibration screen.

Repeat the procedure with the second buffer. Again, the screen will show when the readings are stable and display both readings. In Figure 2.9, both the numeric display and the graphic display are shown.

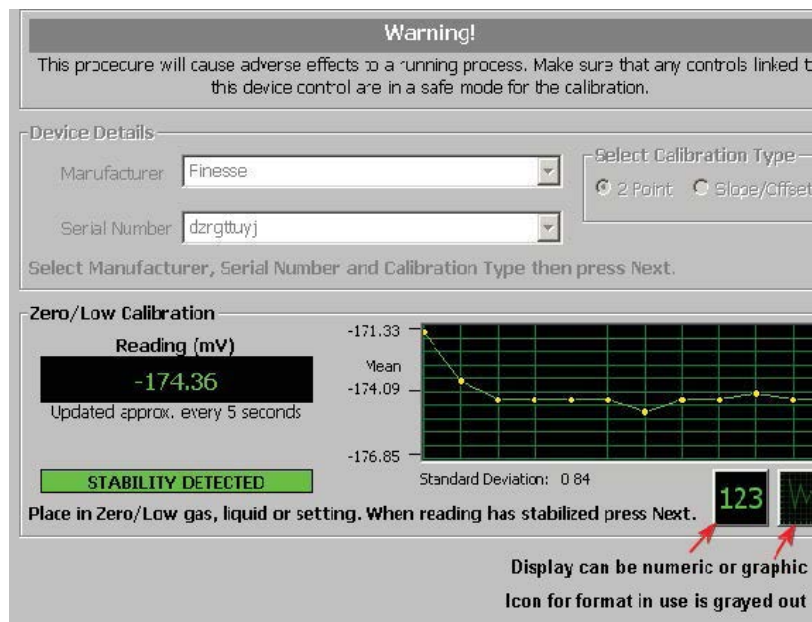


Figure 2.9. “Stability Detected” message for second calibration point.

The graphic display auto adjusts to the pH range of the buffer being read. After the second reading stabilizes, click **Next** and the display will request the calibration details.

Temperature compensation

To use temperature compensation, either use a probe that incorporates temperature measurement or a separate temperature probe/sensor.

Click the **Use Temperature Compensation Value** check box, place the temperature probe (if separate) in the buffer along with the pH probe, and the system will integrate the temperature reading from the probe.

If you use an external temperature device that is not connected to the control system, leave the check box unchecked and enter the temperature with the buffer values.

Enter the buffer values used and the temperature, if not using temperature compensation, before clicking **Next**. The entire calibration record will be displayed for review (Figure 2.10). Comments may also be entered on this screen. A username and password are required to save the calibration.

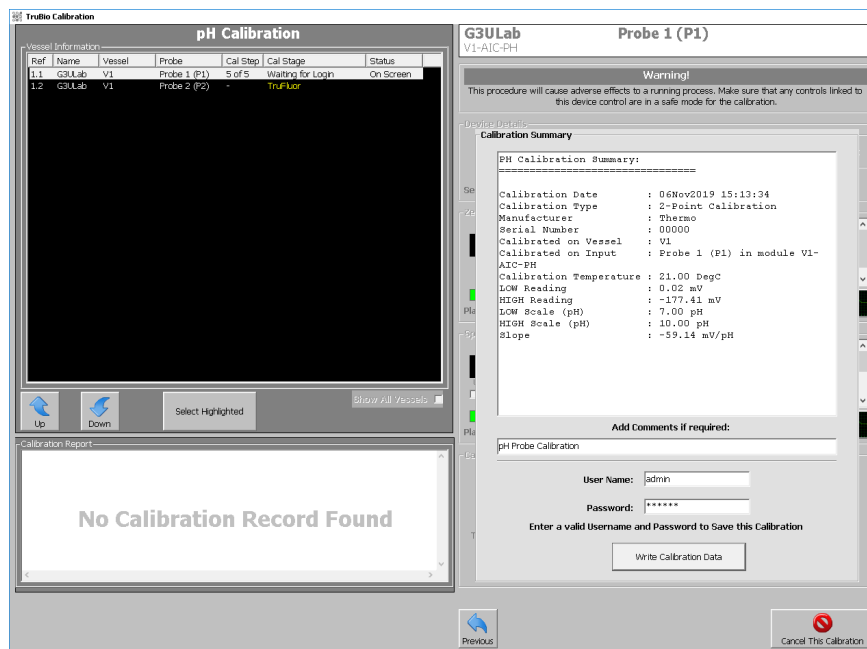


Figure 2.10. Temperature compensation—calibration record.

Click **Write Calibration Data** to save the calibration. Then click **OK**. A second pop-up window will confirm that the calibration has been saved.

Calibration records can be reviewed by selecting the desired vessel and probe on the Vessel Information screen. Clicking the vessel and probe number will bring up the first calibration screen. Enter the probe information and click **Next**. The Calibration Report window will display the detailed calibration history for the probe (Figure 2.11). Once written into the file, records cannot be modified or deleted.

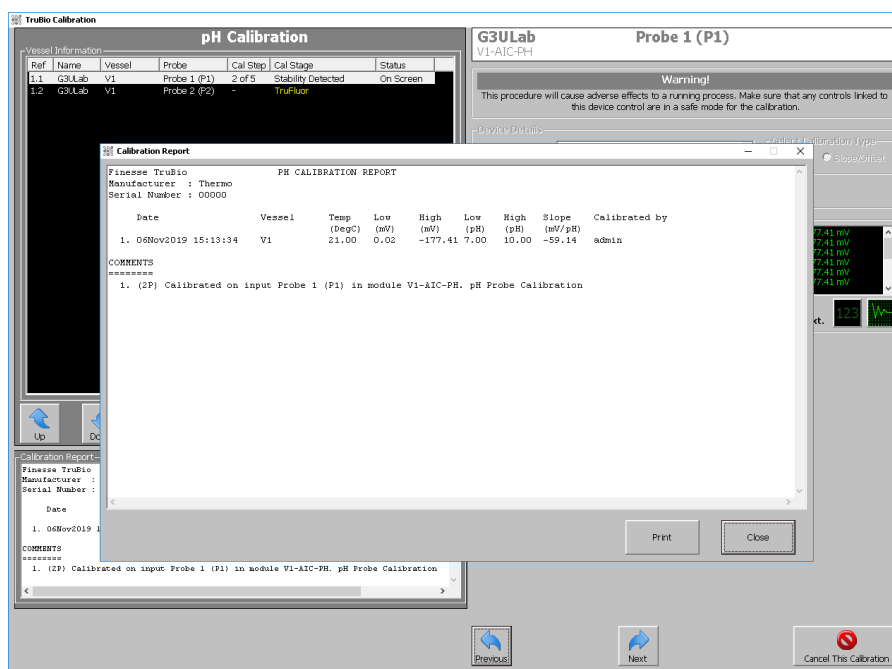


Figure 2.11. Calibration saved confirmation window.

When the calibration process or review is completed, close the calibration screen by clicking the **X** in the upper right corner of the screen.

Calibration of TruFluor sensors using a virtual transmitter

If you are using TruFluor pH and DO probes, and the system incorporates a virtual transmitter, the calibration process will display different screens, but will be performed in the same manner.

For TruFluor pH sensors, two-point calibration is recommended. For TruFluor DO sensors, no calibration is required, but one-point calibration may be used, if necessary.

Open the Detail screen as described above and click on the “Calibration” tab. Then click the appropriate **TruFluor pH** button for the TruFluor pH sensor being used: 1, 2, or 3 (Figure 2.12).

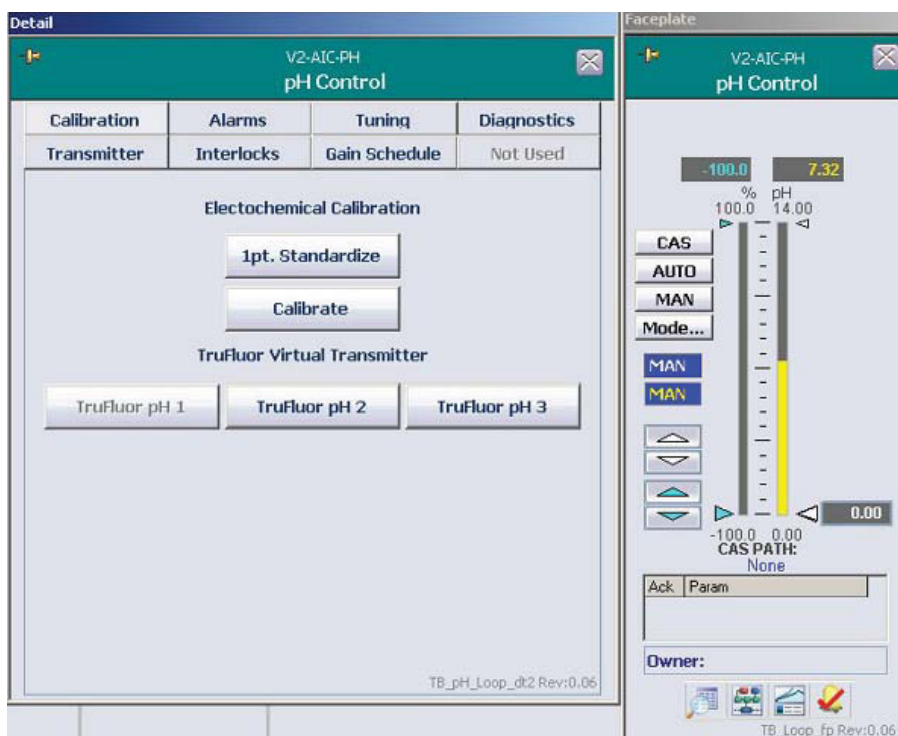


Figure 2.12. Selecting TruFluor pH sensor for calibration.

Note: For the remainder of the calibration procedure, you can only navigate by using the arrow keys and the named buttons with your mouse.

Use the following steps to complete TruFluor pH sensor calibration.

1. In the TruFluor pH window, click **Menu** (Figure 2.13).

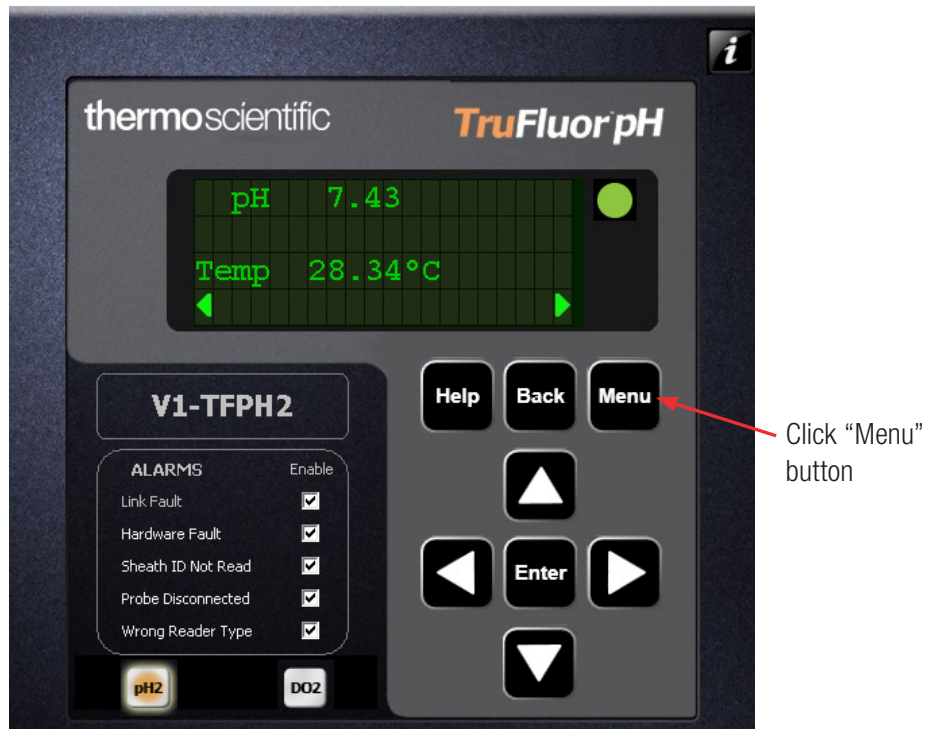


Figure 2.13. TruFluor pH window.

2. In the Main menu, use the arrow keys to navigate to "Calibrate" (Figure 2.14). Then click **Enter**.



Figure 2.14. Selecting "Calibrate" from Main menu.

- In the Calibrate menu, navigate to “pH” (Figure 2.15). Then click **Enter**.



Figure 2.15. Selecting “pH” from Calibrate menu.

- In the pH Cal Type menu, navigate to “One Point” (Figure 2.16) and click **Enter**.



Figure 2.16. Selecting “One Point” from pH Cal Type menu.

5. Remove an aliquot of media from the bioreactor/fermentor BPC according to facility-specific aseptic methodology.
6. Check the pH of the aliquot using a separate pH meter that has been calibrated using NIST-traceable standards.
7. Use the left/right arrows to position the cursor to the “Buffer1 pH” field. Then use the up/down arrows to adjust the number to the proper setting (Figure 2.17). Click **Enter** when you have finished.



Figure 2.17. Adjusting Buffer1 pH setting.

8. At the “Please authenticate” prompt, click **Enter** to accept the calibration (Figure 2.18).



Figure 2.18. “Please authenticate” screen.

9. At the “Calibration Summary” page, enter any notes in the Comment field, if desired. Then, enter a valid username and password, and click **Apply** (Figure 2.19).

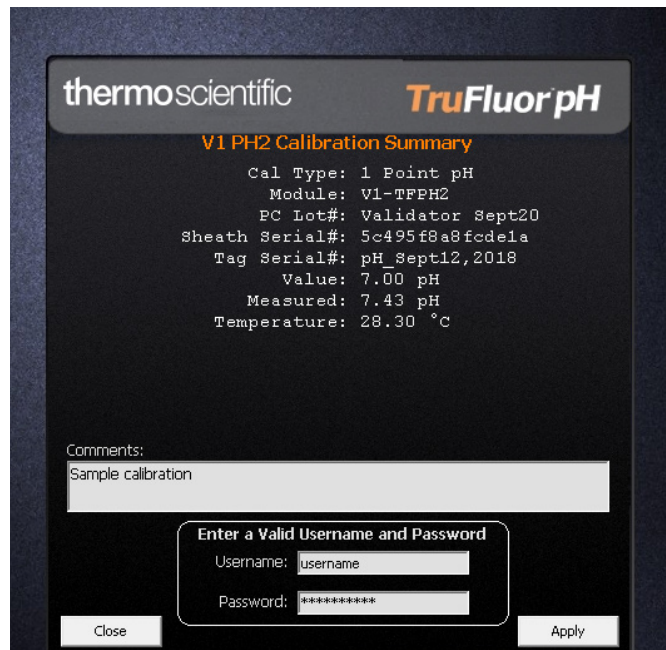


Figure 2.19. Calibration summary page.

- Click **Menu** twice to return to the display of pH and temperature. This is the recommended display when a run is in progress.

Note: It is recommended to return the display to the Main screen when the calibration is completed.

An asterisk (*) appears next to a parameter name, as shown in Figure 2.20, to indicate a non-factory calibration is in use.



Figure 2.20. Asterisk next to parameter name, indicating non-factory calibration in use.

Two point calibration of TruFluor pH

We recommend two point calibration for TruFluor pH sensors. Because it is not possible to remove the TruFluor sheaths from a sterilized S.U.B. BPC, the following procedure is suggested.

- IMPORTANT:** Fill the BPC with the media that will be used in the process. Set up the temperature control and allow 4–6 hours for the temperature to equilibrate. The pH is registered by the TruFluor pH sensor.
- Aseptically remove a small aliquot of media from the BPC. Verify the pH using a pH meter calibrated with NIST-traceable standards.
- Compare the readings with the desired pH setpoint of the system and note the value of the deviation and whether it is above or below the desired setpoint.
- Add CO₂ (or acid) and/or base to the system until the reading is approximately the same deviation from the desired value on the opposite end of the pH scale.
- Remove another aliquot and verify the pH as above.
- Adjust the pH to the desired setpoint and allow 30–60 minutes to equilibrate.

7. Inoculate the media and start the process.
8. During the process, the TruFluor pH sensor reading can be checked by reading an aliquot at facility-specified intervals.

Accessing TruFluor calibration records

TruFluor calibration records cannot be accessed through the faceplate. They can be accessed easily through the TruBio screen.

1. From any screen (Figure 2.21 shows the Main screen), click the TruBio icon (indicated with the arrow) on the Windows toolbar at the bottom of the screen.

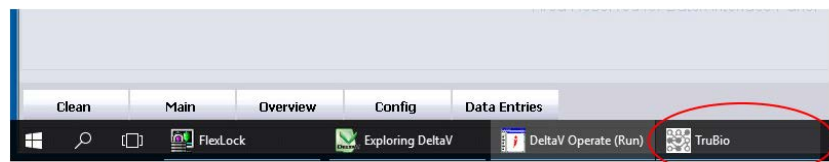


Figure 2.21. TruBio icon on Windows toolbar.

2. When the TruBio screen appears, click **Save/Load/Cal File Viewer** on the lower left (Figure 2.22).

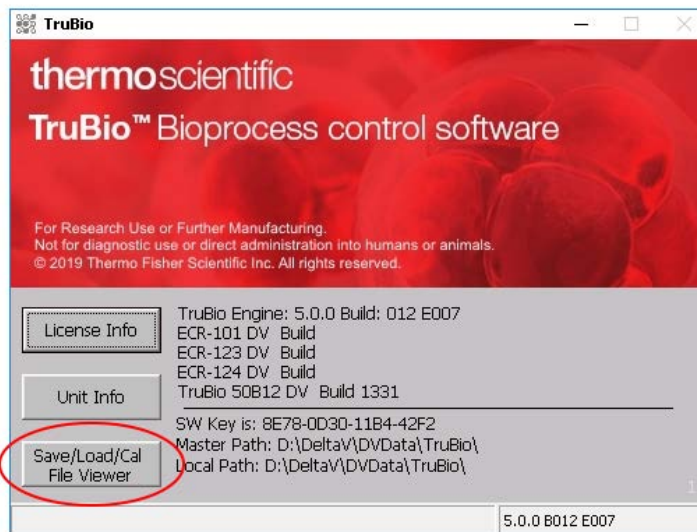


Figure 2.22. “Save/Load/Cal File Viewer” button.

3. Click **View Cal File** button (Figure 2.23).

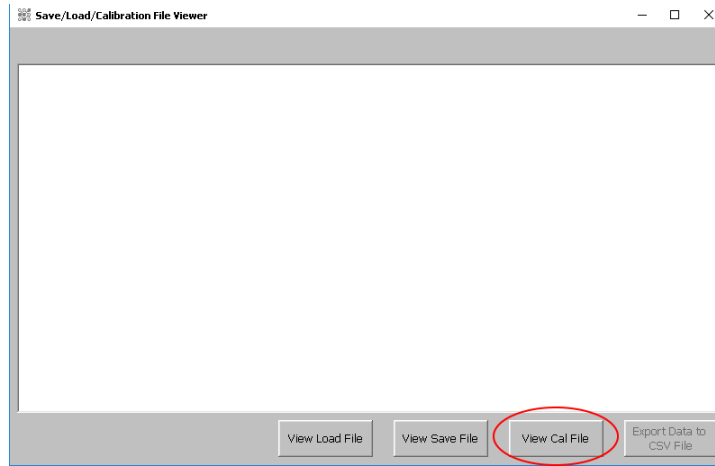


Figure 2.23. “View Cal File” button.

4. Select either pH or DO, select the TruFluor option, and select the probe to see the calibration files (Figure 2.24).

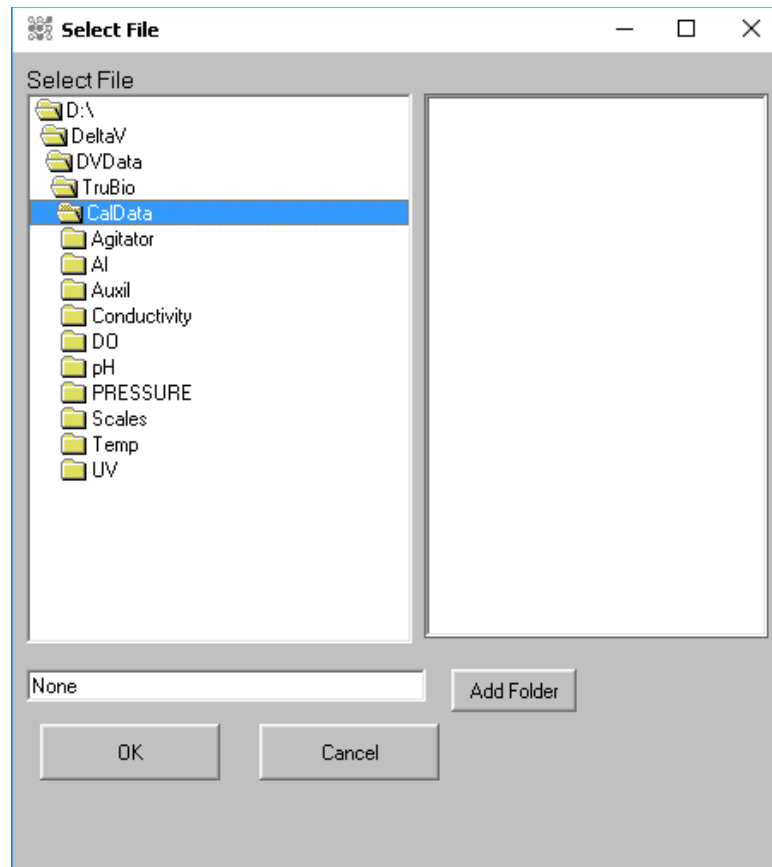


Figure 2.24. Calibration files under probe heading.

5. Select the desired file from the drop-down menu (Figure 2.25) to view the calibration data (Figure 2.26).

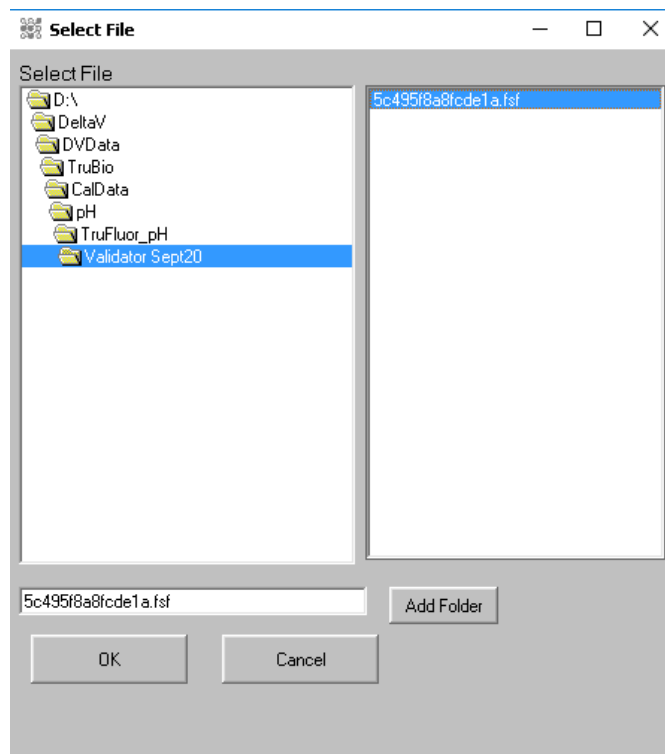


Figure 2.25. Selecting desired sensor file.

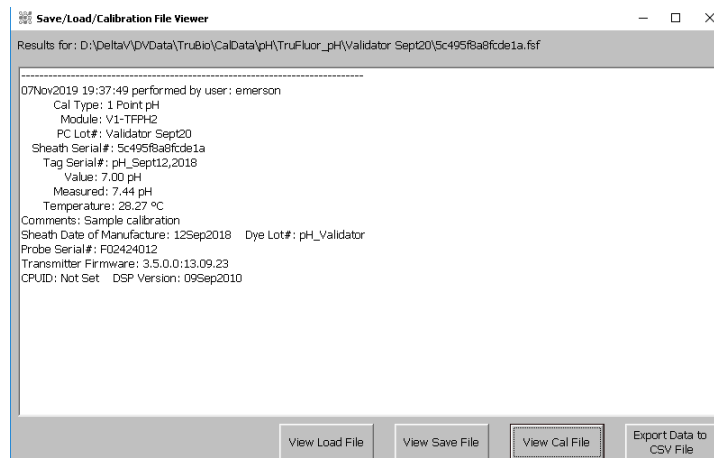


Figure 2.26. Save Load file results.

2.3.2 DO calibration

In the TruBio Software, version 5.0, the steps for calibrating dissolved oxygen (DO) are essentially the same as for calibrating pH.

The single-use TruFluor DO sensor is factory-calibrated and may be used directly without further calibration. However, users may wish to verify calibration in order to satisfy regulatory requirements.

1. Click the DO Control box above the picture of the bioreactor/ fermentor vessel on the main screen.
2. Click the Detail icon in the lower left corner of the faceplate to open the Detail pop-up window.
3. Click the “Cal” tab.
4. Select either the Electrochemical Calibration (calibration of electrochemical sensors) or the TruFluor Virtual transmitter (if available). The screens will be the same as those seen in the pH calibration.

Note: In calibrating DO, the low (zero) calibrator is generally a flow of nitrogen, and the high calibrator open air. It takes slightly longer for the readings to stabilize.

Single-point verification

To perform a single-point verification, select either electrochemical or TruFluor and follow the instructions on the screen, as for pH single-point verification. For DO single-point verification, ambient air is generally used.

Temperature calibration

To apply temperature compensation to TruFluor calibrations, the temperature must be calibrated in order for the compensation to be correct.

To calibrate the temperature, set up the calibration as for pH or DO, but select “Temperature” and follow the instructions as shown on the screen.

Calibration of electrochemical sensors

1. Click **Calibrate** to open the calibration screen (Figure 2.27).

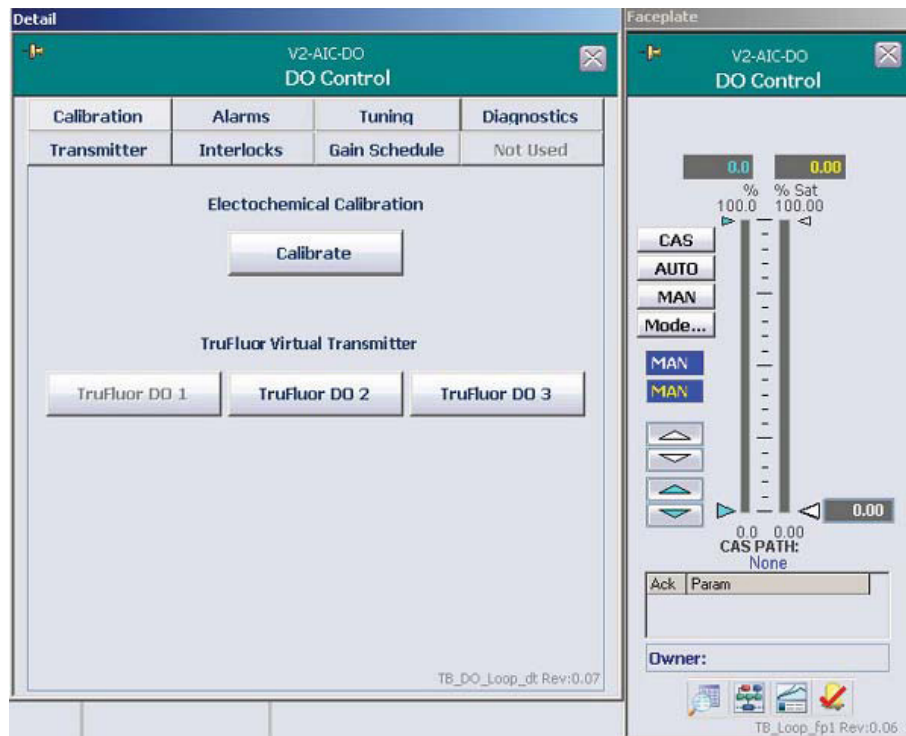


Figure 2.27. DO electrochemical calibration.

2. Enter the probe manufacturer and serial number either manually or using the drop-down menu (Figure 2.28) and click **Next**.

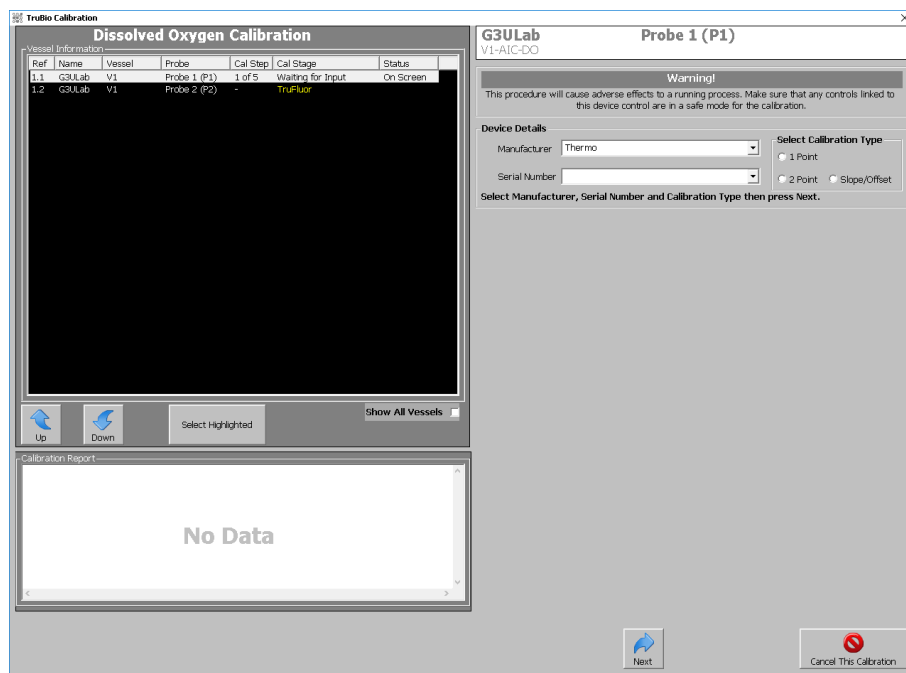


Figure 2.28. Enter probe manufacturer and serial number for DO calibration.

The zero calibrator for DO is usually a flow of nitrogen. A length of tubing sufficient to enclose the terminal 6–8 cm (2–3 in.) of the probe to deliver a flow of nitrogen into one end works as well, as does a 50 mL conical tube. The DO reading may require more time to stabilize than the pH.

3. Once the negative reading is stable, click **Next**.
4. Remove the probe from the nitrogen flow and allow 2–3 minutes for the nitrogen to dissipate. The high reading (100% saturation) is generally taken with the probe exposed to ambient air. If a sterilizable bioreactor/fermentor tank is in use, it might be necessary to use a pressure compensation for the DO reading. Contact your sales representative for further information.

2.3.3 Temperature calibration

Temperature calibration follows the same pattern as pH and DO calibration. The calibration standards are water baths that are set to a known temperature and then verified by calibrated thermometers.

2.3.4 Agitator calibration

Calibration of the agitator follows the same pattern as the other calibrations.

1. When calibrating the agitator, be sure to set the mode to “Manual.”
2. Clicking **Agitator** on the main screen will open the faceplate (Figure 2.29).

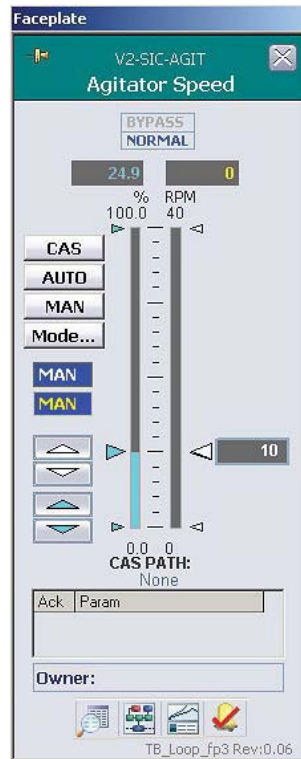


Figure 2.29. Agitator faceplate.

3. Click **Detail** to open the detail pop-up window.
4. Open the “Calibration” tab. Click **Calibrate** and then move the screen so that the faceplate can be accessed (Figure 2.30).

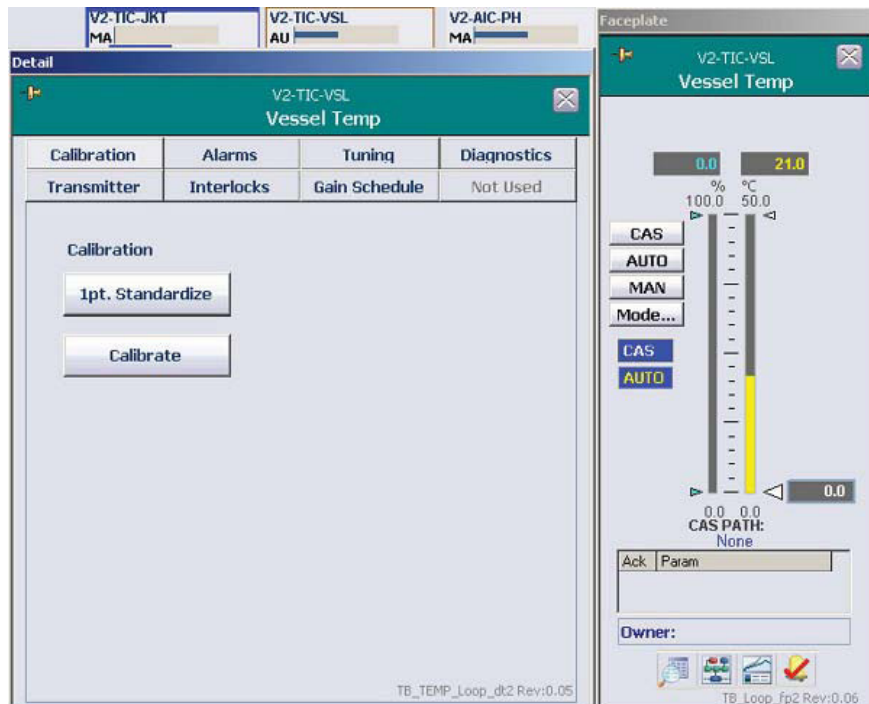


Figure 2.30. Vessel Temp faceplate.

5. Enter the agitator manufacturer and serial number either by typing in or selecting from the drop-down menu (Figure 2.31). Then click **Next**.

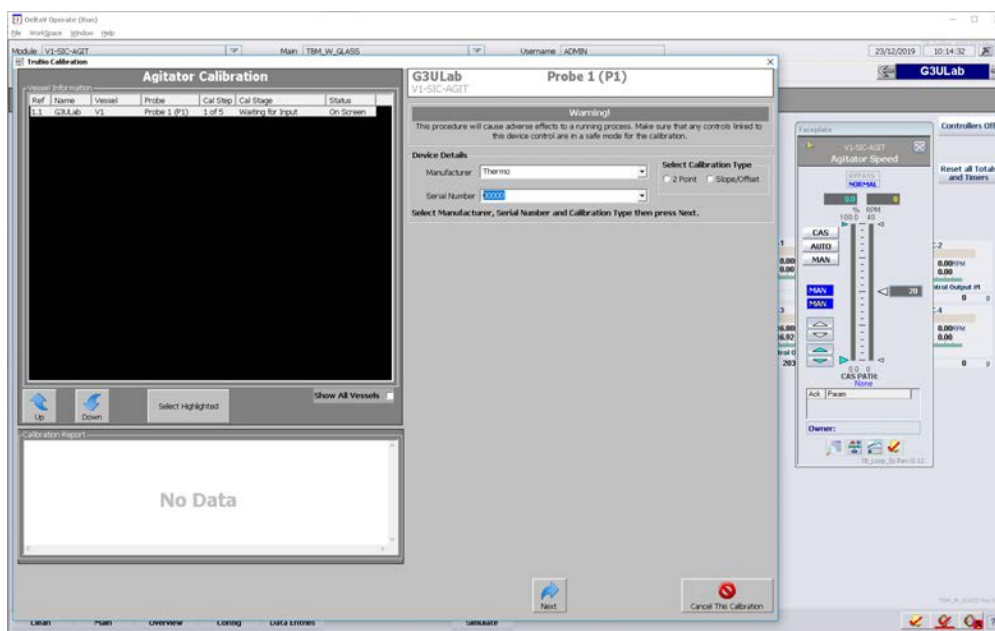


Figure 2.31. Entering manufacturer and serial number.

6. Use the agitator faceplate to set the agitator speed (blue number) to 0 rpm or a number in a range lower than the intended speed to be used during the run. This is done by typing in the value desired as a percentage of the maximum agitator speed. For example, if the maximum agitator speed is 250 rpm and the desired value is 75 rpm, type 30 into the box, which is 30% of 250 or 75.
7. Ensure that the agitator PV (right side column) comes to the value set above. Then click **Next**.
8. Set the agitator to a higher level by typing in a higher percentage value. Allow the speed to stabilize and click **Next**.
9. Once the second reading has been accepted, turn the agitator off by setting the value to zero.
10. Follow the screen instructions to finish the calibration and close the screen. **Note:** The only way to control the agitator speed in this process is by entering a number that represents a percentage of the maximum agitator speed.

2.3.5 Pressure calibration

The TruTorr II pressure sensor is factory calibrated and requires no further verification by the user. If desired, the user may perform a one point (zero) calibration with no pressure on the sensor.

The TruBio Software enables the user to program two pressure sensors and to use units other than the TruTorr II pressure sensor. Preferred units may be selected from a pop-up menu accessed from the Configuration screen (Figure 2.32).

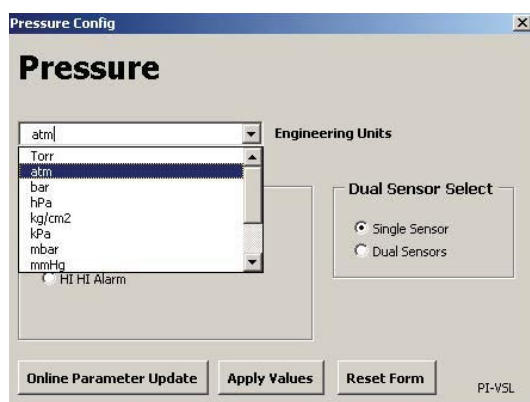


Figure 2.32. Selecting preferred units for pressure configuration.

If you make a change to the Engineering Units value, click **Apply Values** when you are done.

2.3.6 Pump calibration

Updated pump features in the TruBio Software include either manual or automatic calibration, and the ability to calibrate using either forward or reverse pump direction—onto or off of a scale.

Note: Pumps must be calibrated using the same tubing as will be used in the process. Using different tubing will result in inaccurate pump delivery.

Manual calibration

1. Install the tubing in the pump head(s) as illustrated in the “Pump setup” section.
2. Click the appropriate Pump box at the right-hand side of the Main screen to open the faceplate.

- Click **Detail** open the Detail pop-up screen (Figure 2.33). Click the “Calibration” tab if it is not already open.

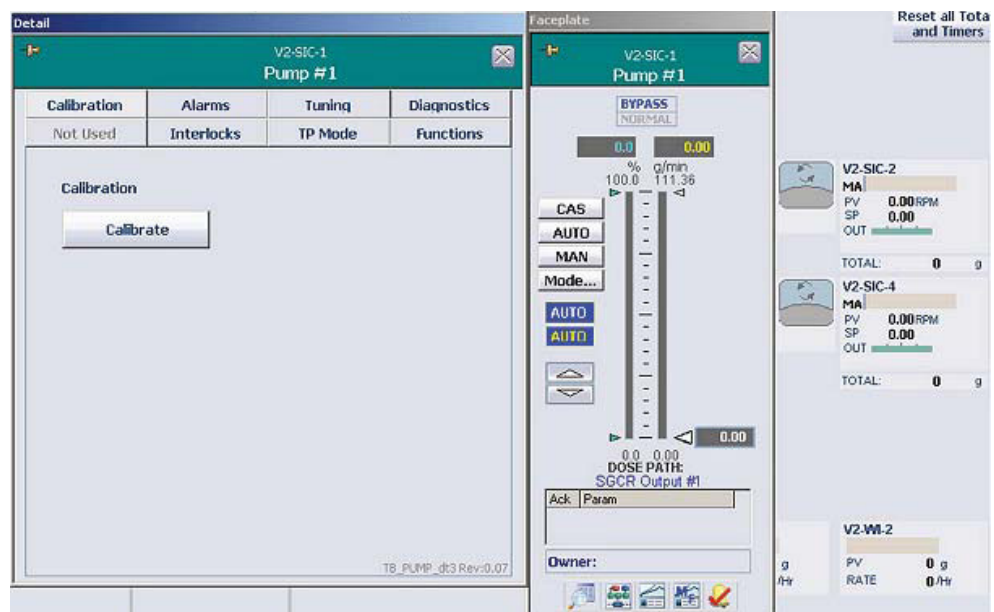


Figure 2.33. Pump #1 detail pop-up screen.

- Click **Calibrate**, which opens the screen shown in Figure 2.34. The screen displays the default settings for the calibration.

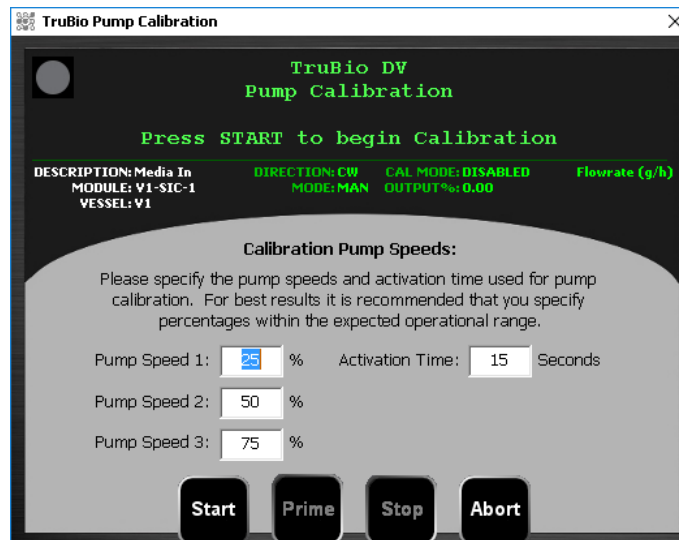


Figure 2.34. Calibration pump speeds screen.

5. Modify the settings as desired. Then click **Start**.
6. At the warning screen (Figure 2.35), ensure that the device is in a safe mode and click **Start** again.

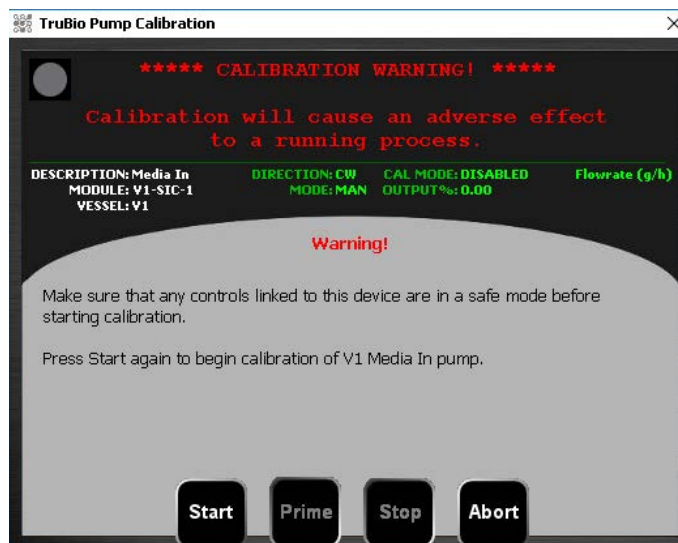


Figure 2.35. Calibration warning screen.

Note: If the pump calibration is performed at below the minimum speed set in the TP, the calibration time must be a multiple of the cycle time. For more information, see the Time Proportioning of Pumps section.

7. Select the method (manual or automatic) and the pump direction (Figure 2.36). Then, click **Start**.

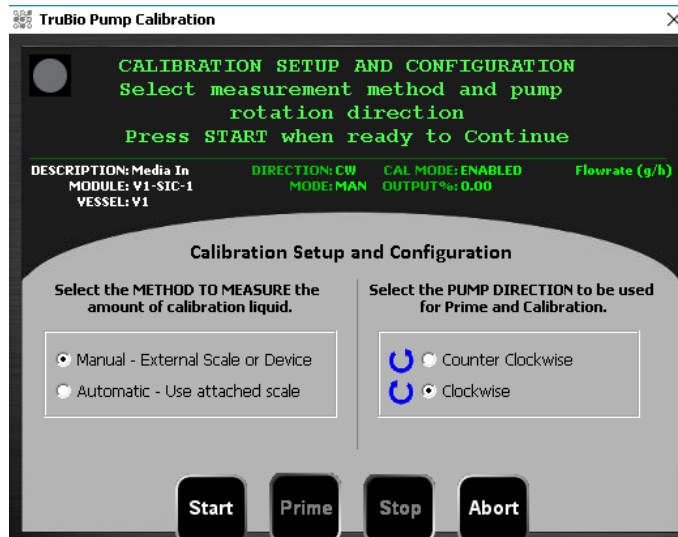


Figure 2.36. Selecting method and pump direction for calibration.

8. Follow the instructions on the “Calibration Step 1/3” screen to complete the calibration (Figure 2.37).

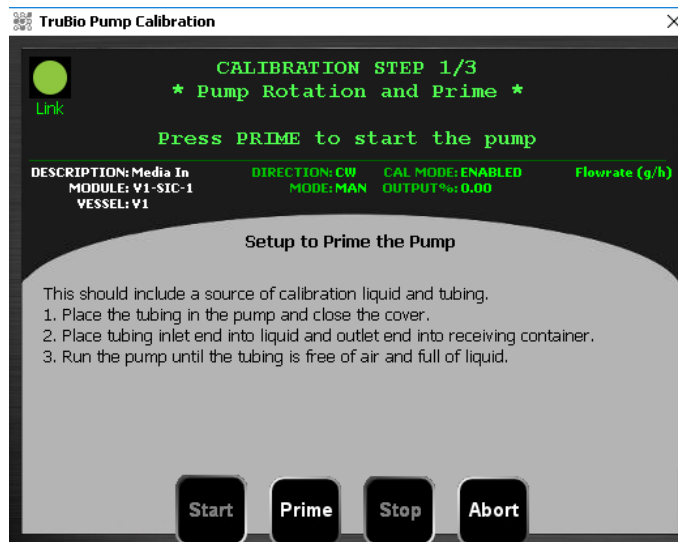


Figure 2.37. Calibration step 1 of 3: Setup to prime the pump.

The default program will run the pumps for 15 seconds at 25%, 50%, and 75% of maximum speed. If desired, you can set the desired speed and time to more closely match the pump speed(s) to be used during processing.

9. At the end of the pump activations (the default is 15 seconds), the user will be prompted to enter the weight recorded on the scale (Figure 2.38). **DO NOT** tare or zero the scale between measurements. Do not empty the receiver container between measurements.

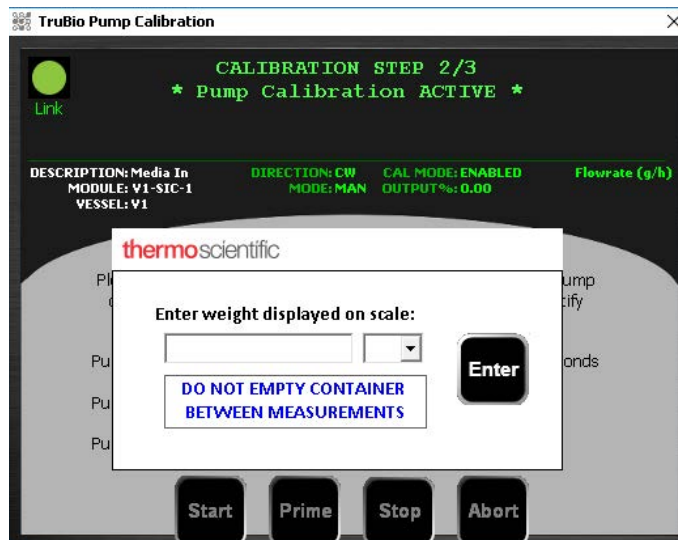


Figure 2.38. Screen for entering weight displayed on scale.

- At the end of the three runs, a prompt appears for a username and password (Figure 2.39). You can also add comments. To write the calibration to the record, click **Apply**.

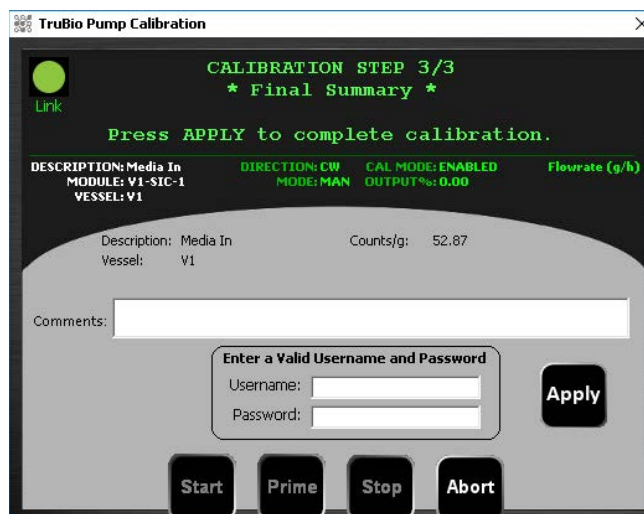


Figure 2.39. Prompt for username and password.

- Repeat these steps for any other pumps to be used.

Automated calibration

An automated pump calibration may be run if a scale has been assigned to the pump. The pump will be calibrated in units of weight/time. Therefore, the pump must have a PV range consistent with the scale, meaning g/hr or g/min instead of rpm.

- To change a pump's operating mode from speed control to flow control, open the Configuration screen. Verify that the correct vessel number is displayed. Then click the pump to open the "Pump Configuration" form (Figure 2.40).

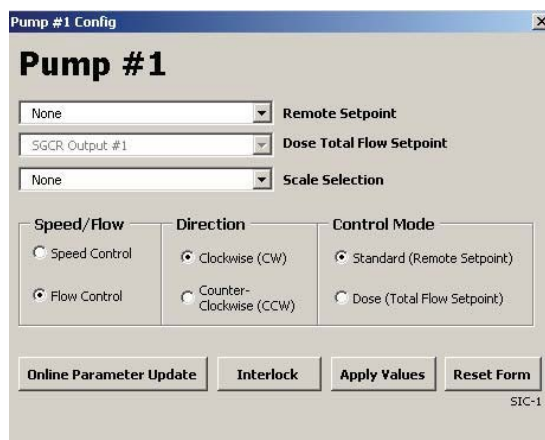


Figure 2.40. "Pump Configuration" form.

2. Under the Speed/Flow heading, select **Speed Control** or **Flow Control**.
3. Click **Apply Values** to save the mode selection.
4. In the calibration setup screen, select **Automatic**.

A liquid reservoir must be provided. The pump will be activated for three speeds (default is 25%, 50%, and 75% of maximum speed for 15 seconds). The weight transferred during each run will be automatically recorded.

2.3.7 Analog inputs

Analog inputs may be calibrated in the same way as other calibratable modules in the system.

2.3.8 Vent heaters

Vent filters are heated to prevent condensation of escaping vapor from the bioreactor, which could wet the vent filter and cause an unsafe rise in vessel pressure.

Some vent heaters lack a thermostat and cannot be calibrated. Refer to the instruction manual for the specific heater or contact your customer service representative for more information.

Heaters with thermostatic control can be calibrated through the TruBio Software. The usual procedure is to calibrate at either end of a range around the desired value. Calibration is done in the same way as the vessel temperature calibration.

1. Open the faceplate and the detail screen (Figure 2.41). Place a calibrated thermometer into the vent.



Figure 2.41. Vent heater detail screen.

2. Select either the single point standardization or the full (two-point) calibration.
3. If the single point calibration is used, allow the temperature to equilibrate, and read the value from the thermometer. Then type the value into the pop-up window (Figure 2.42) and click **Enter**.

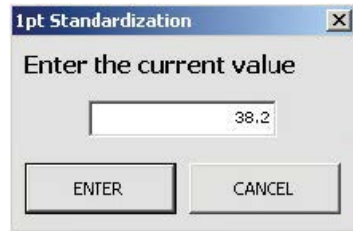


Figure 2.42. Vent heater 1 pt standardization.

4. If you are running a two-point calibration, first set the temperature to the lower point of the desired range (Figure 2.43). This can be done from the faceplate either by sliding the right-side pointer to the desired temperature, or clicking the box and typing in the value. The white up/down arrows also change the value.

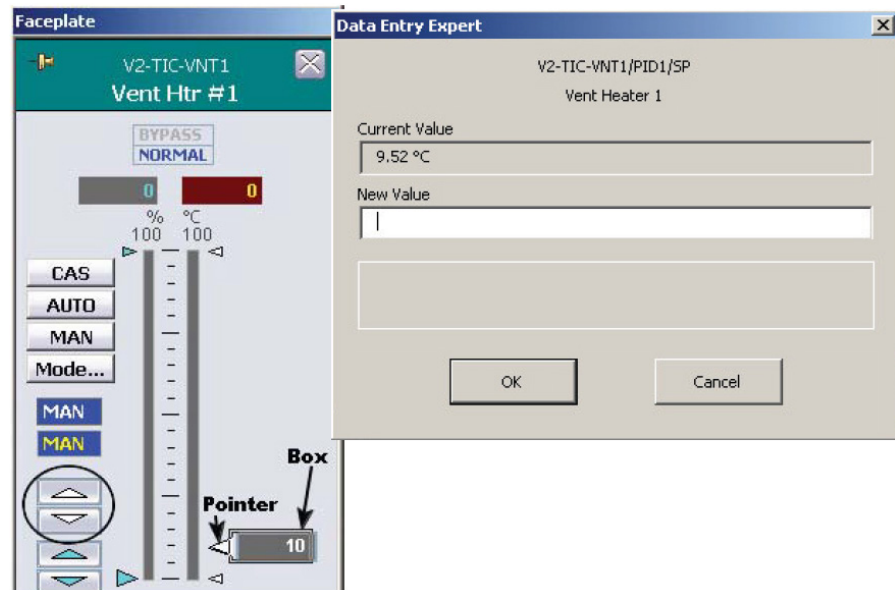


Figure 2.43. Entering temperature value to lower point of desired range.

5. After the value is set, allow time for the temperature to equilibrate.
6. Click **Calibrate** to open the Calibration screen.
7. Fill in the information, then move the screen to one side so the faceplate can be seen to one side so the faceplate can be seen at the side of the calibration screen as shown in the “Agitator Calibration” section.
8. On the Calibration screen, click **Next**. When the display reads “Stability Detected,” click **Next** again.
9. Set the temperature to the higher value using one of the methods described in step 4. Allow the temperature to equilibrate.
10. At the “Stability Detected” message, click **Next**.
11. Follow the screen prompts to finish the calibration.

2.3.9 Jacket temperature

The thermal control unit (TCU) is tested and verified before being sent to customers, and again while being set up at the customer’s facility. This means that a calibration should not be necessary. However, if calibration is necessary due to regulatory requirement or facility protocol, it may be done by measuring the temperature of liquid flowing from the TCU into the jacket of the tank.

To do this, prime the unit before using a short piece of tubing to connect the inlet and outlet connectors on the back of the TCU. Connect an RTD sensor to the tubing, or insert into the tubing. Run the calibration as for any other temperature calibration.

2.3.10 Vessel weight

The vessel weight calibration is done as for any other calibration, except it is recommended that the serial number be entered as the vessel number and WIC-VSL.

1. In the Scale Control tab, select **Gross** and tare the scale.
2. The first reading is always zero (0), so record the weight with the vessel empty.
3. Once the reading is stable, add a known weight to the vessel. This second weight should be about 80% of the scale range. If no calibrated weights are available, weigh containers of water on a calibrated scale and add to the vessel.
4. Complete the calibration as directed on the screen.

3

Alarms and limits

Chapter contents

- 3.1 Explanation of alarms and limits
- 3.2 Alarm management
- 3.3 Other limits

3.1 Explanation of alarms and limits

A general scheme for alarms and limits in relation to the setpoint is shown in Figure 3.1 below.



Figure 3.1. Alarms/limits in relation to setpoint.

- The **Setpoint** is the desired value for the parameter, e.g. pH of 7.2 or DO of 40%.
- The **Deadband** is the area around the setpoint over which the pH or DO process value (PV) will normally fluctuate, and within which no alarms are set. Setting up a deadband allows these normal fluctuations to resolve without triggering the control loops.
- The **Dev Lo** and **Dev Hi** limits are deviation limits from the setpoint. They can be used for triggering a warning when the PV deviates from the setpoint by more than these limits.
- The **Hi Limit** and **Lo Limit** are limits on the PV that should not be exceeded. They can be set at limits which are of concern but will not threaten the health of the cells in the vessel.
- The **Hi-Hi Limit** and **Lo-Lo Limit** are limits that require immediate action by the operator. They may be used with automatic interlocks to shut down the controller action. For example, they could be set where health of the culture is threatened, which should prompt immediate action.

- The **SP Hi Limit** and **SP Lo Limit** are limits that are set just at the point at which the culture will be irrevocably compromised. Establishing these values also ensures that the setpoint cannot be set or changed to a value outside these settings, preventing an accidental change of the setpoint.
- To set control limits and alarms for any parameter, open the faceplate for that parameter, click **Detail**, and then select the “Alarms” tab. Figure 3.2 shows the alarm settings for pH control, as an example.

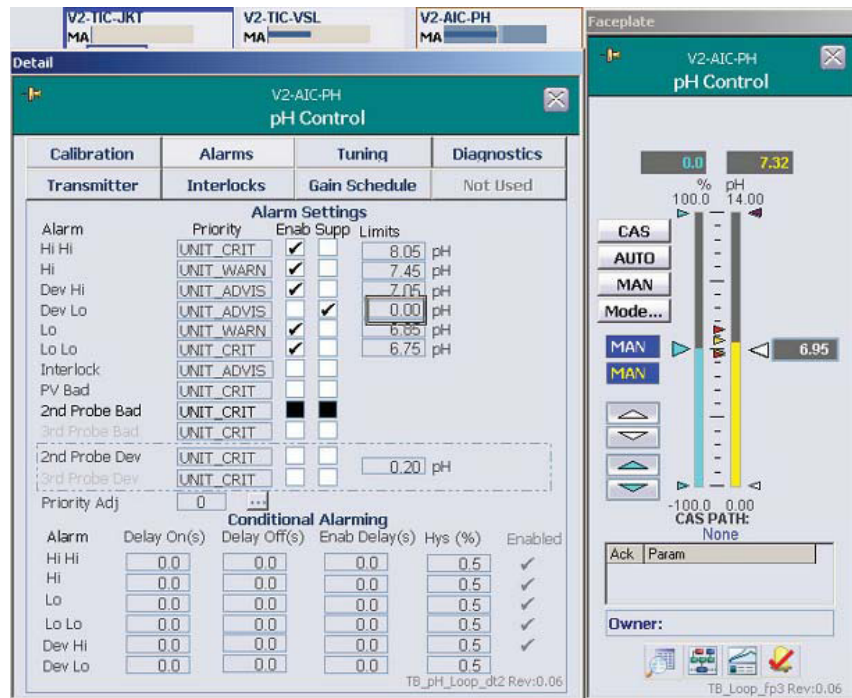


Figure 3.2. Alarm settings screen for pH control.

- If “Enable” is checked, an alarm box will appear in the alarm banner, and an audible alarm will sound if provided in the hardware. The control box on the Main screen will show a colored, blinking outline to match the severity of the alarm.
- If “Suppress” is checked, there will be no notification to the operator that an alarm condition has developed.
- If both “Enable” and “Suppress” are checked, there will be no notice on the alarm banner, and no audible alarm, but the box on the Main screen will display a blue outline. This is further discussed later in this section.

Note: It is recommended that alarms not be enabled until the system has stabilized, with all parameters within limits. Otherwise, the alarms would mean nothing more than a parameter has not yet reached the target level.

2. Set the limits by typing in the values (Figure 3.3), then confirm the entry by pressing **Enter** on the keyboard.

Detail			
V2-AIC-PH pH Control			
Calibration	Alarms	Tuning	Diagnostics
Transmitter	Interlocks	Gain Schedule	Not Used
Limits			
Out Hi Lim	100.00	%	
Out Lo Lim	-100.0	%	
ARW Hi Lim	100.00	%	
ARW Lo Lim	-100.0	%	
SP Hi Lim	14.00	pH	
SP Lo Lim	0.00	pH	
Tuning			
Gain	1.00		
Reset	150.0		
Rate	0.0	s	
PV Filter TC	0.0	s	
SP Filter TC	0.0	s	
SP Rate DN	0.00	EU/s	
SP Rate UP	0.00	EU/s	
Structure	PI action on error, D action on PV		
Controller Action: Increasing Error Decreases Output (Indirect Action)			
ENABLE DeadBand Local Override	<input type="checkbox"/>	Note: Acid - Base split must be on Output Scale 1 and Output Scale 2 on Config. Page	
HI Deadband	1.50	HI Gap	0.00
LO Deadband	1.50	LO Gap	0.00
TB_pH_Loop_dt Rev:0.06			

Figure 3.3. SP Hi and Lo limits for pH control.

An additional alarm on the “Alarms” tab is PV Bad. If the probe signal is bad, the display box will have a red background. If the PV Bad alarm is enabled, an alarm message will show on the faceplate.

The “Priority Adj” function will lower the priority of alarms (e.g. from Hi-Hi to Hi) and should not be used unless under direction of your service representative.

The TruBio Software systems allow the user to disable the TruFluor alarms if a transmitter is configured, but the system will automatically reset the alarm. In Trubio Software, version 5.0, the alarm can be permanently disabled, if desired. **Note:** Consult your customer service representative for more information. New in the TruBio Software, version 5.0, the conditional alarm settings are now on the main page. The alarm delays can be set to the user’s preference.

Hysteresis

The last block of settings is marked “Hys,” an abbreviation for “Hysteresis.” This is calculated as the percent of the parameter range. The PV must change by the calculated value before the alarm will be retriggered. For example, assume that the SP of the pH is 7.0, the Hi Limit alarm is set to 7.15, and the Hysteresis is set to the recommended 0.5% value.

If the PV exceeds 7.15, the alarm is triggered. In order for the alarm to be retriggered, the pH must drop by 0.5% of the range, or 14 (pH range) times 0.5% (Hysteresis value), which is 0.07 pH units. So the alarm will not be retriggered unless the PV drops below a pH of 7.08 and then rises again.

The purpose of the hysteresis setting is to prevent the alarm from being continuously sounded while the condition that triggered the alarm is addressed.

3.2 Alarm management

Enabling and suppressing alarms

As noted earlier, the “Alarms” tab offers the option of enabling or suppressing specific alarms by clicking the appropriate box.

In the examples shown, the Hi Limit for Pump #1 has been set to 95 and the Hi-Hi Limit to 100. In Figure 3.4, the alarms have not been enabled, and the rate has been set above 100. Note that there is only a thin brown line around the Pump #1 control box outline and no alarm message in the faceplate. If the “Suppress” boxes are checked, the display will look the same as when the “Enable” boxes are not checked.

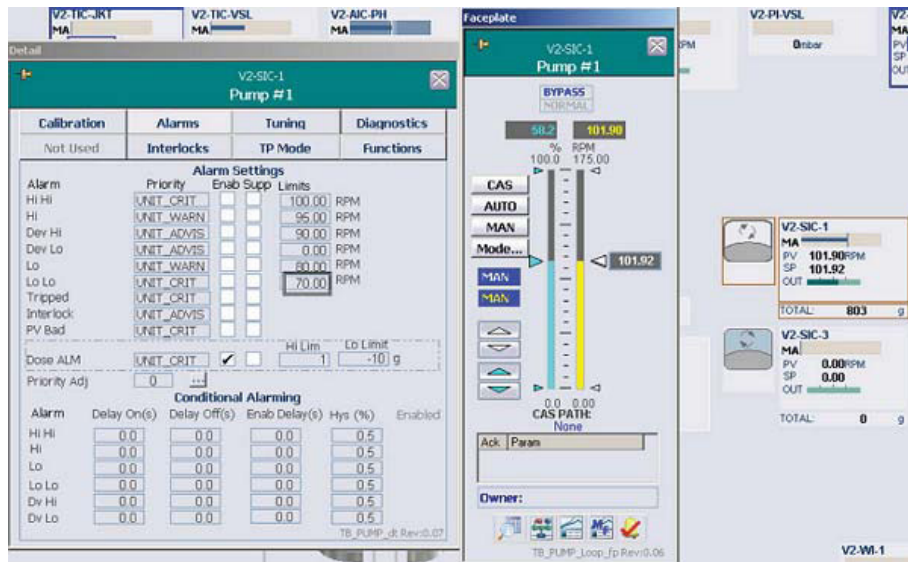


Figure 3.4. Alarm settings screen for Pump #1.

When the “Enable” boxes are checked, the limits are displayed on the faceplate and the Hi alarm will be displayed in Figure 3.5.

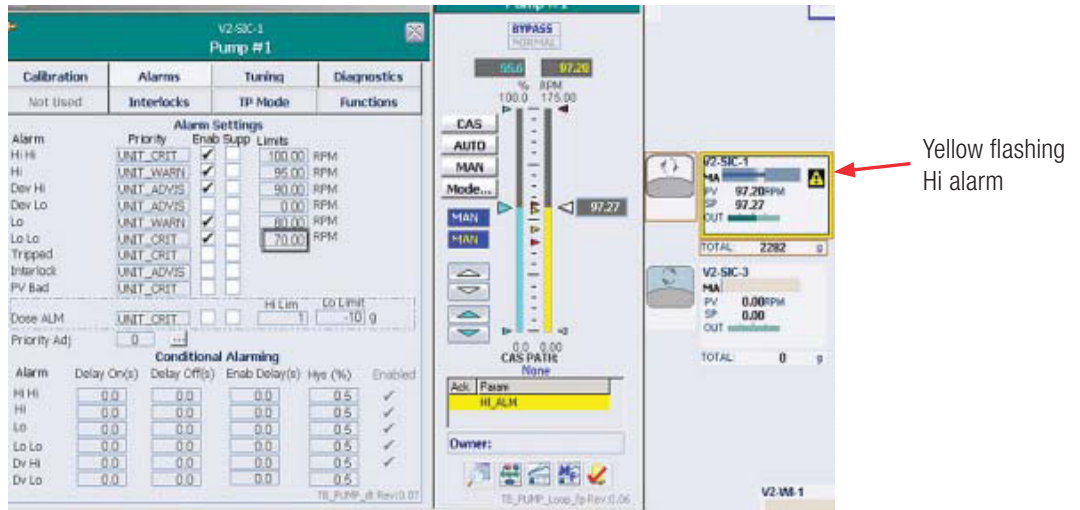


Figure 3.5. Hi alarm (yellow) for Pump #1.

The Hi-Hi alarm will look very much the same, except that the alarm bar and the border of the control box will be red (Figure 3.6).

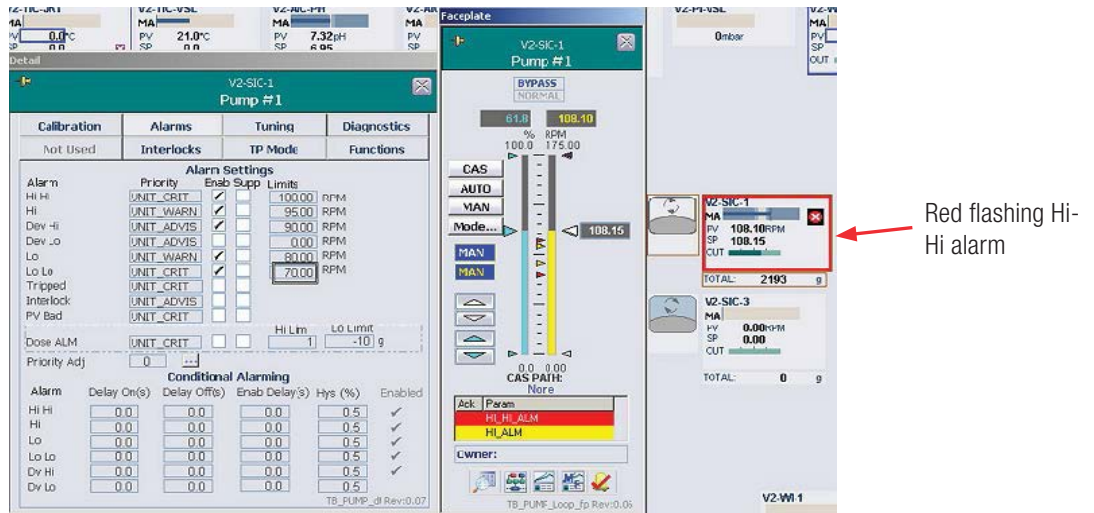


Figure 3.6. Hi-Hi alarm (red) for Pump #1.

If both the “Enable” and “Suppress” boxes for an alarm are checked, the limits will be shown on the faceplate, but there will not be an alarm notification, either visual or audible. The border of the control box will turn blue (Figure 3.7).

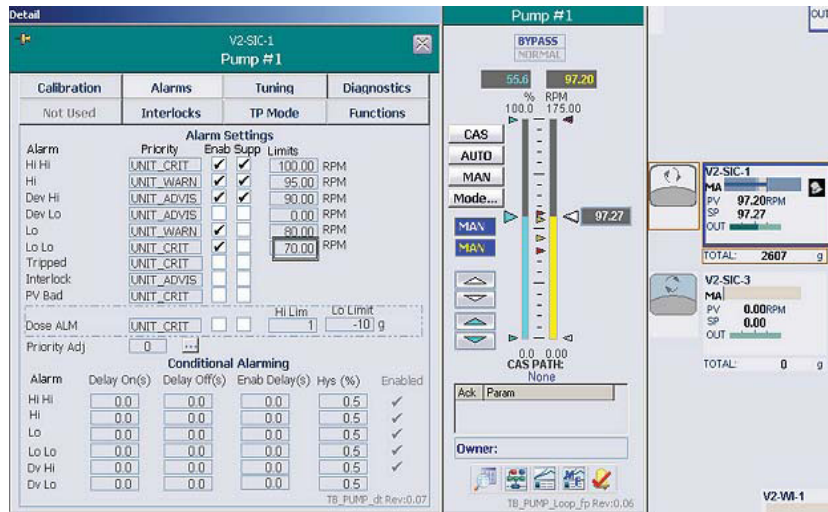


Figure 3.7. Alarms both enabled and suppressed.

Alarms may also be suppressed from the Alarm page. To do so, use the following instructions.

1. Click the alarm button in the toolbar, which will open the list of alarms (Figure 3.8).

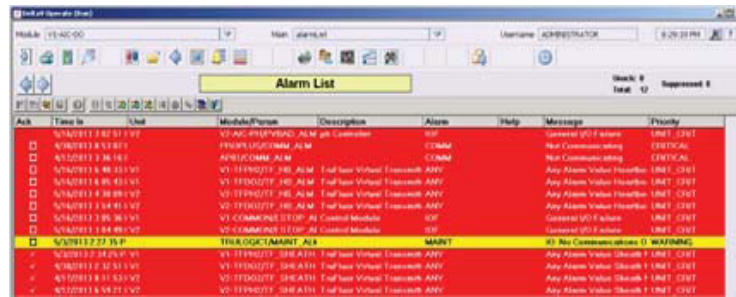


Figure 3.8. Alarm list.

2. Right click an alarm to suppress it. The line for the selected alarm turns black and a menu displays.
3. From the menu, select **Suppress Alarm** (Figure 3.9).

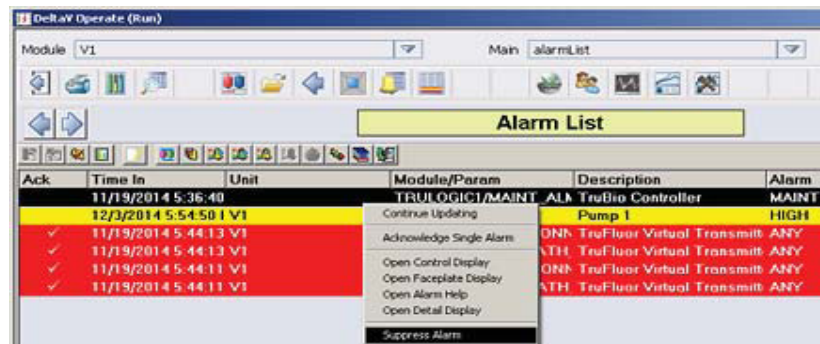


Figure 3.9. Selecting “Suppress Alarm” from menu.

When an alarm is suppressed, an icon displays on the toolbar, and the status display notes the suppressed alarm (Figure 3.10).

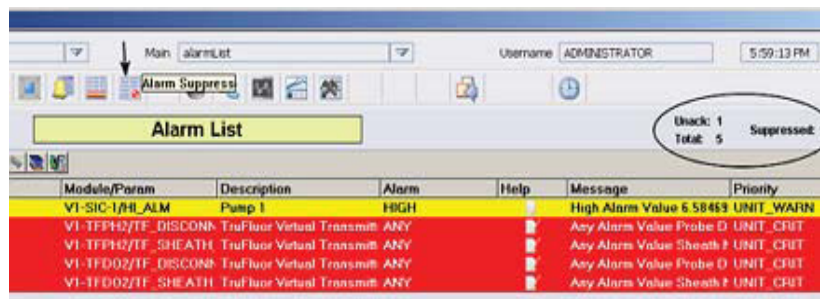


Figure 3.10. Status display noting suppressed alarm.

Suppression for an alarm may be disabled, either from the “Alarms” tab in the Detail screens or by clicking **Alarm Suppress** on the toolbar.

When **Alarm Suppress** is clicked, the list of suppressed alarms displays. Right click the selected alarm to display the menu that includes the “Unsuppress Alarm” option (Figure 3.11).

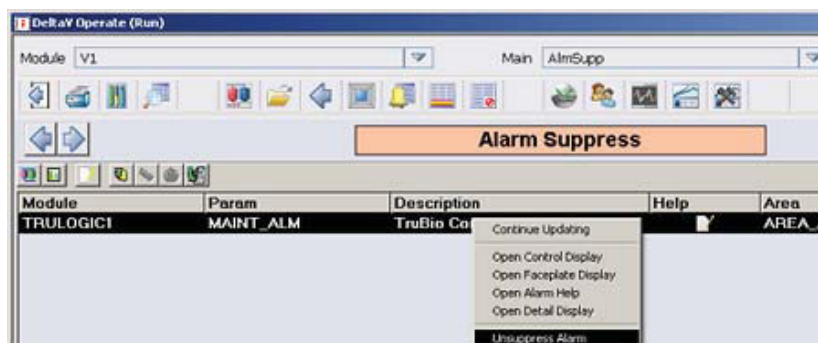


Figure 3.11. Selecting “Unsuppress Alarm” option.

Acknowledging and silencing alarms

At the bottom of all screens except the Cleaning screen is an alarm banner.

If the alarm is triggered when the PV is above the Hi limit but below the Hi-Hi limit, or below the Lo limit but above the Lo-Lo limit the box will be yellow. If the PV is above the Hi-Hi limit or below the Lo-Lo limit the box will be red.

An audible alarm sounds if that function has been enabled and the system provides a speaker for the alarm. To turn off the audible alarm, click the icon on the lower right corner of the screen (Figure 3.12).

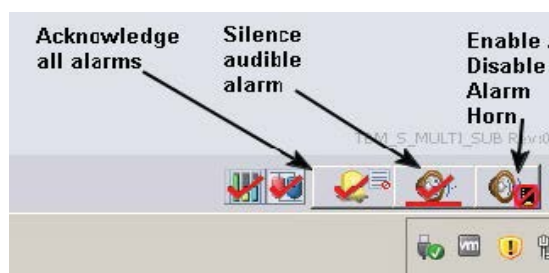


Figure 3.12. Icons for controlling alarms.

If there is an active, unacknowledged alarm, the banner displays a flashing box, as seen on Vessel 2 (V2) in Figure 3.13. If the alarm is active, but has been acknowledged, the alarm logo displays with the vessel number but no box, as seen on V2 (red shown for visibility).

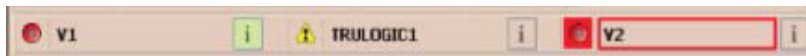


Figure 3.13. Active unacknowledged alarm in banner.

Clicking the box in the alarm banner opens the alarm faceplate for the relevant vessel. An active alarm shows flashing boxes (shown on the left in Figure 3.14), plus an alarm acknowledgement box (shown on the right).



Figure 3.14. Active alarm showing flashing boxes (left) and acknowledgement box (right).

An alarm that is active and has been acknowledged will not flash and will not display an acknowledgement box. For a complete list of active and inactive alarms, click **Alarm** on the toolbar.

3.3 Other limits

Setpoint Hi/Lo limits: These are high and low limits that the setpoint cannot exceed. These limits are used to prevent an accidental change of setpoint beyond the point at which the culture might be irrevocably compromised.

Output Hi/Lo limits: These restrict controller output to the set high and low limits.

Anti-Reset Windup (ARW) limits: The ARW parameter is set to reduce controller integral action. When the controller output exceeds the high ARW limit then integral action is reduced by a factor of 16. This parameter is typically used when a setpoint is changed and the controller needs to quickly drive the PV to the new setpoint. The ARW limits should be less than the Output Hi/Lo limits. Consult your customer service representative before changing this parameter from the default limits.

Deadband local override: When the PV is within the Deadband, the system is in local override and the “LO” indicator appears on the faceplate. As long as any PV deviation is less than the Deadband, the control loops will be inactive.

Gain Scheduling Deadband: When controller gain scheduling is used, the transition from one set of control gains to the next is made after the Gain Reference value is exceeded by the Gain Scheduling Deadband value. This prevents the gains from changing back and forth when near the reference value. Consult your customer service representative for use of the Gain Scheduling option.

4

Setting up a run

Chapter contents

- 4.1 Attaching probes
- 4.2 Loading and saving a vessel file
- 4.3 Setting up control loops
- 4.4 Pump setup—pre-programmed pump functions
- 4.5 Pump total flow dosing strategy
- 4.6 Pump MultiFeed strategy
- 4.7 Locking and unlocking pumps
- 4.8 Setting up MultiFeed dosing
- 4.9 Weight control setup (S.U.B. vessels only)
- 4.10 Foam/level control setup
- 4.11 Key parameter setup
- 4.12 Saving the file
- 4.13 Starting the run

Setting up a bioprocessing run involves establishing setpoints and alarm limits, setting up control loops, and creating a Vessel SaveFile.

4.1 Attaching probes

4.1.1 Attaching single-use probes

If using a S.U.B. that has had TruFluor sheaths sterilized with the S.U.B., attach the readers and cables to the appropriate sheaths.

4.1.2 Attaching sterilizable probes

If using sterilizable probes, insert the sterile probe into the bioreactor/fermentor vessel, according to facility-specified procedure, and then attach the cables.

4.1.3 Attaching other devices

Attach the gas lines to the sparger(s) and headspace and attach pump tubing to the appropriate ports. Attach any auxiliary equipment, such as scales. If using an agitator, follow the vendor's installation guidelines. **Note:** When setting up pump connections, ensure that the tubing is not kinked and is protected from occlusion by chairs, other equipment, etc.

4.2 Loading and saving a vessel file

1. From the Configuration page, open "Vessel Settings Management." Then click **Vessel Load** (Figure 4.1).

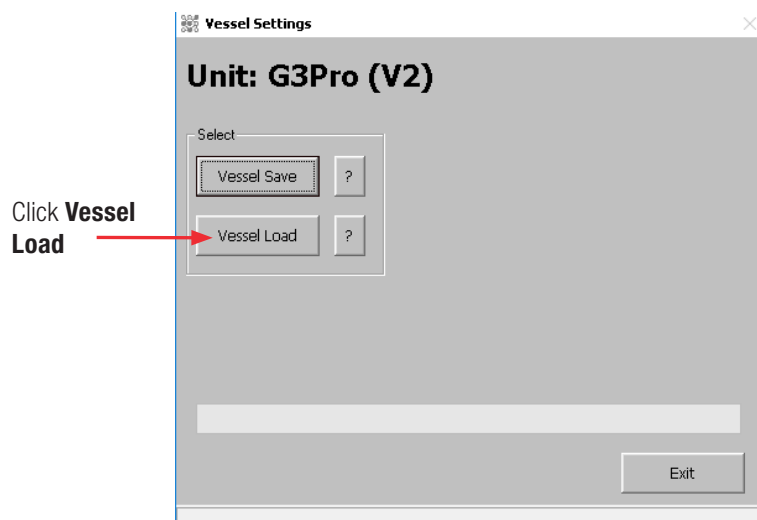


Figure 4.1. "Vessel Load" option on Vessel Settings.

- The best way to create a new configuration is to load an existing save file. Select the appropriate file from the drop-down menu (Figure 4.2).

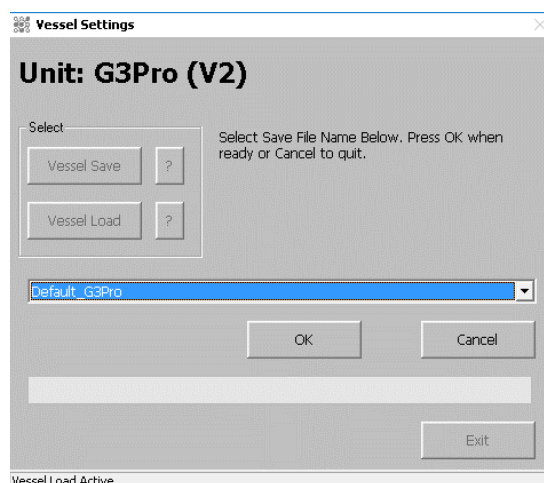


Figure 4.2. Loading an existing file to create a new file.

Note: The selected file MUST be from the same vessel as the one being used. For example, if setting up a Thermo Scientific S.U.B., any file that is chosen must have been used to load the Thermo Scientific S.U.B.

The only exception to this rule is in a circumstance when all vessels and peripherals on a system are identical. Otherwise, parameters designed for a 500 L vessel may be applied to a 10 L vessel with potential damage to the system.

All TruBio systems are sent from the factory with a “default” save file available; if the vessel is new on the system, this default file may be used (Figure 4.3).

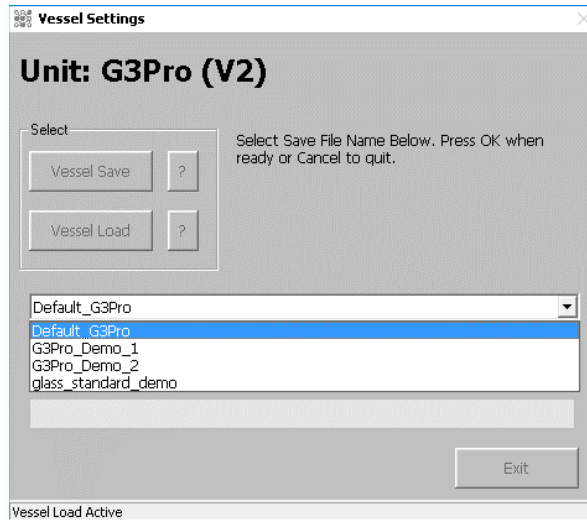


Figure 4.3. Selecting default file.

The system will request a new name for a load (log) file. This file contains a log of all parameters loaded and if there were any errors during the load.

3. Name the file according to facility protocol and click **OK**.

Loading the file requires a few seconds, during which the activity displays in the message bar (Figure 4.4).

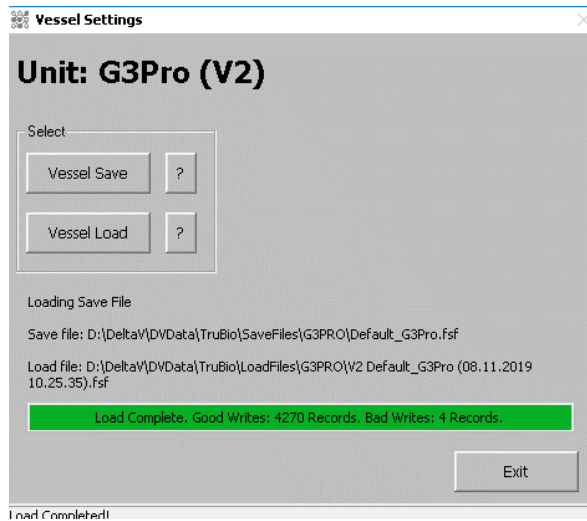


Figure 4.4. Loading progress shown in green bar.

Note: During the load, a message may flash about “bad writes.” These are less problematic than they may appear; TruBio will rewrite them up to five times. If there are still bad writes after the five attempts, a notification is generated. If this occurs, consult your customer service representative.

4. Save/Configuration Files are handled in the same way. Select the category to be used for the save file (Figure 4.5). The “DEFAULT” category may be used.

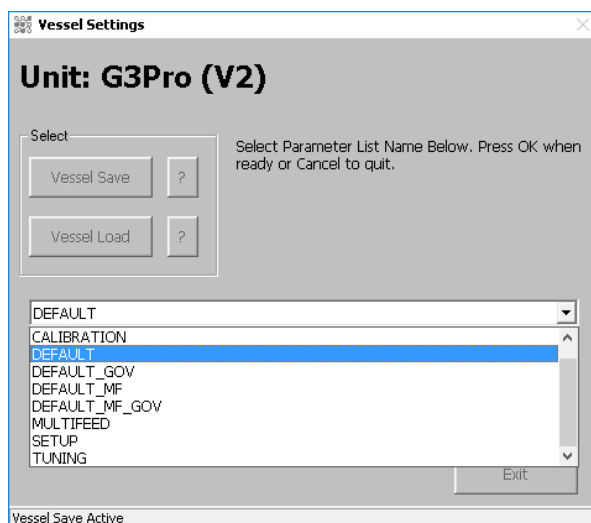


Figure 4.5. Selecting a category to use as save file.

5. After selecting the category, specify a new save file name according to facility protocol. Click **OK** to save the file, as described in the previous section.

Note: Save Files can be emailed from one facility to another only if the TruBio version, the vessels, and all auxiliaries are identical on both sides, including instrument ranges. Consult your customer service representative for more information.

6. After the Vessel Save completes, click **Exit**.
7. In the Main screen, set up the run parameters and control loops.

Note: If the Vessel Save process produces “bad reads” at approximately 30% or greater, check to ensure that the operator is logged into the DeltaV system. The operator must be logged into both the DeltaV and Trubio systems in order to load and save Vessels. If the operator is logged into the DeltaV system and bad reads continue, contact your service representative.

4.3 Setting up control loops

4.3.1 Gas manifold

The gas supplies that are connected to the TruFlow mass flow controllers (MFCs) must be set at the appropriate level to avoid damage. If these supplies are too high, damage to the internal parts of the MFCs or solenoids could result in incorrect delivery of gas or gases to the S.U.B.

Pressure to each MFC should be regulated at 30–35 psi, or 2–2.4 bar.

CAUTION: Supply of gases to the TruFlow should not exceed 35 psi or 2.4 bar. Excess pressure will damage the internal components.

4.3.2 pH control

Controlling pH is done by adding an acid and/or a base to maintain the pH at the optimum level for the process. The two substances most frequently used are a NaOH (which is added via pump) and CO₂ (via sparging).

Note: Liquids added for the control of pH must be figured into the total bioreactor/fermentor volume to avoid overfilling the vessel.

Configuring the pH setpoint

1. Click **pH Control** located at the top of the Main screen to open the faceplate.
2. Use the sliding box on the right-hand side of the faceplate to set the desired pH setpoint. Alternatively, click the box, type the value in the pop-up window, and click **OK**.

Setting pH control alarms

1. On the pH Control faceplate, click **Detail** to open the Detail screen (Figure 4.6).

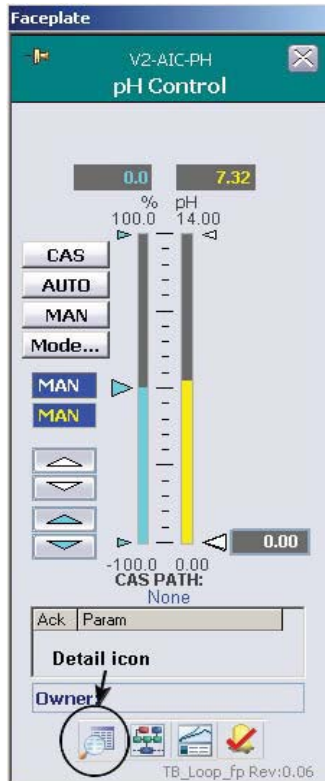


Figure 4.6. Detail icon on pH Control faceplate.

2. Click the “Alarms” tab. Set the Hi-Hi limit, Hi limit, Lo limit, and Lo-Lo limit (Figure 4.7).

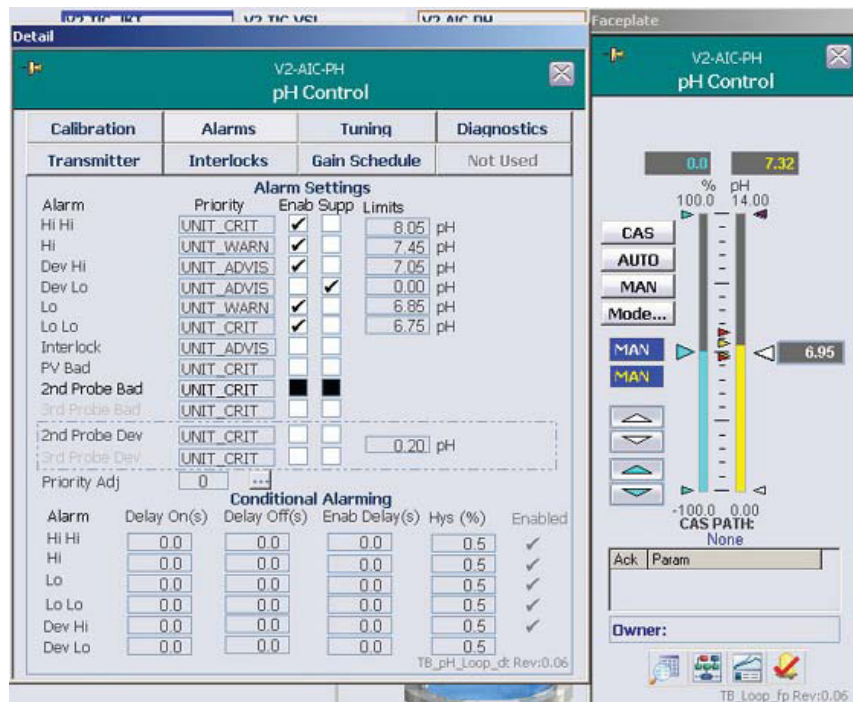


Figure 4.7. Hi-Hi, Hi, Lo, and Lo-Lo alarms set for pH control.

These are the levels at which an alarm will be generated, assuming the user has enabled alarms. The ranges for alarms should be narrow enough to provide optimum growth conditions, yet wide enough to prevent excessive alarms.

3. When setting the alarm values, the **Enter** key must be pressed on the keyboard to set up the value. **Note:** If the **Tab** key is pressed in order to proceed to the next box, the values will NOT be saved.
 - a. The user may also wish to set the “SP Hi” limit and the “SP Lo” limit. These represent the range of the setpoint, to prevent accidental altering of the setpoint, and are found on the “Tuning” tab.
 - b. As the values are set, small triangles will appear around the setpoint arrow. The SP limit will be indicated by small white arrows on the right side of the column, and the other limits by red and yellow arrows on the left side of the column.
 - c. The “Out” limits are to limit the output of the controller, and the ARW is generally set to a smaller range.
4. (Optional) If desired, set a deadband at the bottom of the “Tuning” tab.
 - a. A deadband applies to the pH and DO only, and is a value above and below the setpoint in which the control loops are not active. It is intended to accommodate transient variations around the setpoint.
5. (Optional) If desired, set a gap above and below the deadband.
 - a. This will allow extra time for equilibration if the control loop has been activated. Figure 4.8 illustrates the operation of a control loop, with the deadband and the gap shown.

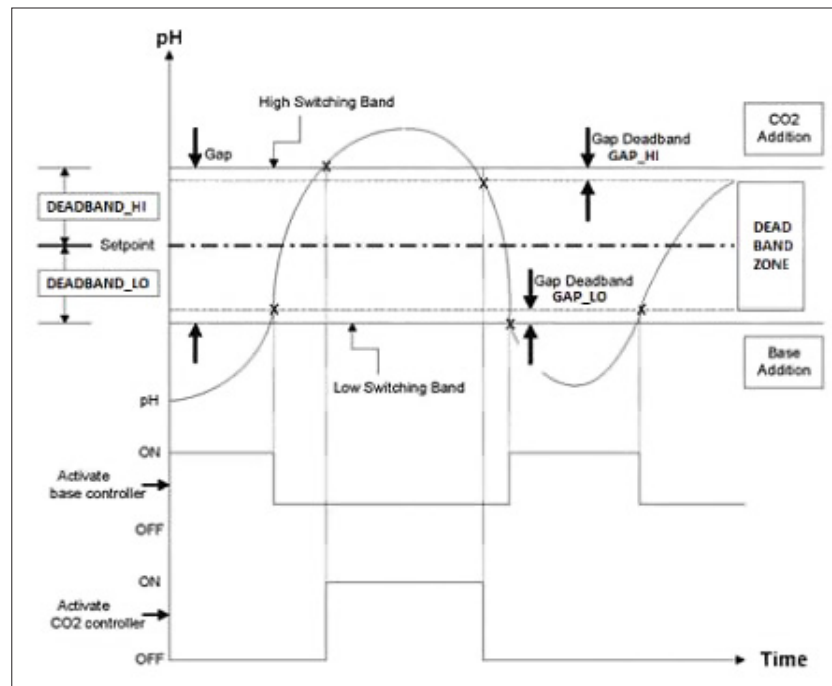


Figure 4.8. Operation of control loop with deadband and gap.

2. Close the “Detail” window.

On the faceplate, note that the range of the Control output (left column) is -100 to 100, so that zero is in the middle of the range. This is important when setting up the control loops.

Adjusting pH control settings

1. On the “Configuration” screen, click **pH Control** on the left-hand side of the screen to open the “pH Control” screen (Figure 4.9).

Figure 4.9. pH Control screen.

The remote setpoint is used only if the setpoint has not been set on the faceplate.

2. Enter the probe types being used and select the priority of reading.
3. Thermo Scientific TruFluor pH and DO sensors may also read temperature. If so, set the pH Temp Comp as appropriate. Otherwise, select the compensation sensor from the drop-down menu.

The values under the Controller Output heading are in percentages. In Figure 4.9, Output Scale #1 is for the base addition and Output Scale #2 is for the CO₂ supply. The settings will vary according to the user's preference.

In Figure 4.10, the faceplates for the base pump and the CO₂ MFC (used for gas flow) note the maximum ranges on the right-hand column. In this example, the pump maximum is 175 rpm and for the MFC, maximum is 0.25 liters per minute (lpm).

Using maximum input rates for pH control is not advised, as a sudden influx of either CO₂ (or acid) and/or base can kill cells in the area of the sparger or pump port before adequate mixing can take place. In Figure 4.10, the Controller Output for the base pump is 150 rpm instead of the maximum rate of 175.

As the MFC in Figure 4.10 has a maximum range of 0.25 lpm, the maximum output has been set to 0.20.

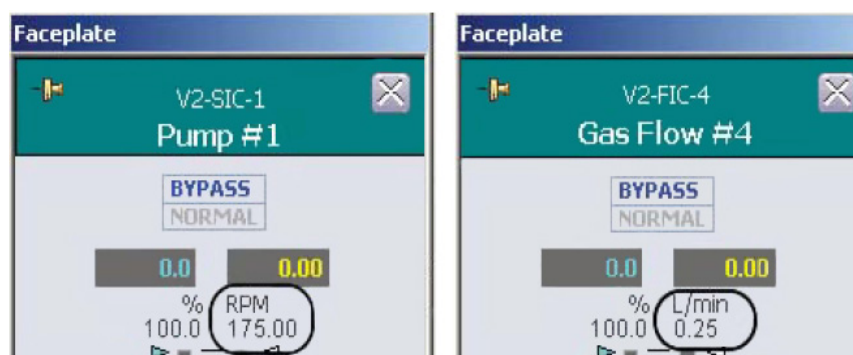


Figure 4.10. Faceplates for base pump (Pump #1) and CO₂ MFC (Gas Flow #4).

The pH controller output range is -100 to +100, with the -100 to 0 range being acid (pH of 0–7) and the 0 to +100 range being base (pH of 7–14). The remainder of the form will not be used here.

4. Close the pH Control form.
5. Still on the Configuration screen, click the pump to be used for base.
6. Set the remote setpoint to “pH Control Output #1.” Select the “Speed Control” radio button to set and the correct pump direction to flow into the vessel (usually “clockwise”) (Figure 4.11).
7. Click **Apply Values** to save the settings and close the screen.

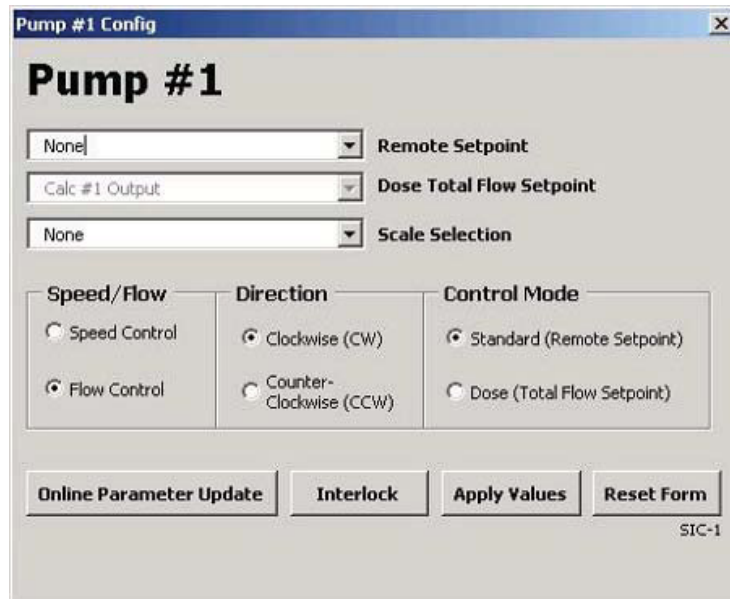


Figure 4.11. Pump #1 Config screen with Speed/Flow, Direction, and Control Mode options.

Adjusting mass flow controller settings

1. Click the MFC box that you have assigned for CO₂ output (Figure 4.12). In Figure 4.12, Gas Flow #4 is selected.

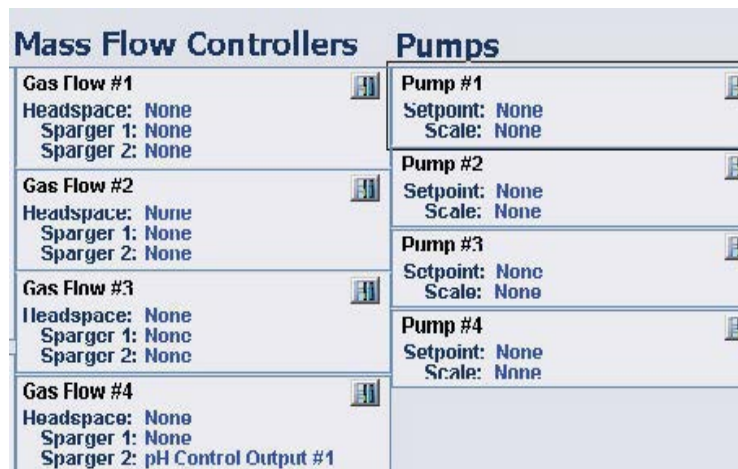


Figure 4.12. Mass Flow Controller boxes.

2. Set the appropriate flow setpoint to “pH Control Output #2.” Set the “Allowed Flowpaths” and “Selected Flowpaths” radio buttons to the same output (Figure 4.13). Then click **Apply Values** to save the settings and close the window.

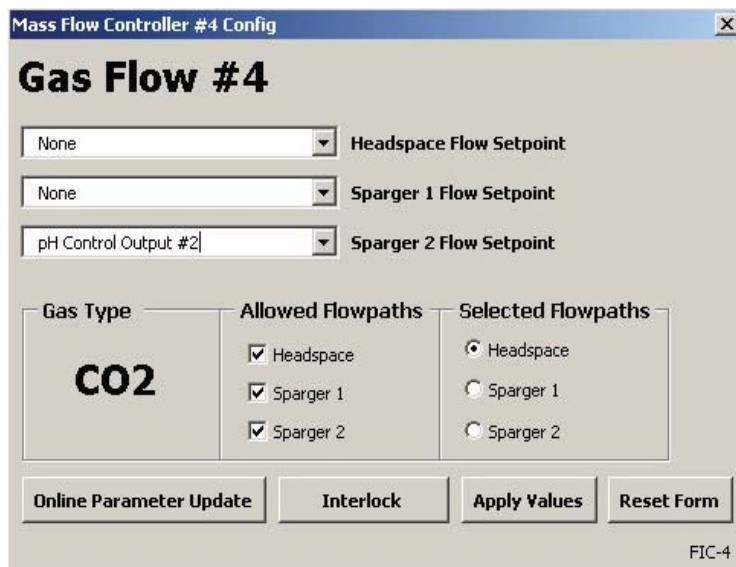


Figure 4.13. MFC Configuration for Control Output #2.

3. Return to the Main screen. Then click the control box for the MFC that is attached to the CO₂ to open the faceplate.
4. At the top of the MFC faceplate, click **Bypass** to have TruBio bypass the CO₂ controller and apply the setpoint as the controller output.

IMPORTANT: Failure to set the MFC to “Bypass” will prevent TruBio from managing the delivery.

5. On the left side of the faceplate, click **Cascade (CAS)** to set the pH Output Scale #2 as the CO₂ remote setpoint. The cascade path should read “pH Control Output #_.”
6. Close the faceplate.
7. Click the control box for the base delivery pump. On the left side of the faceplate, click **Cascade (CAS)** to set the pump into the cascaded pH control loop. The cascade path below the two columns should change to “pH Control Output #_.”
8. Close the faceplate.
9. Click the pH Control box to open the faceplate.
10. On the left side of the faceplate, confirm that the pH Setpoint is accurate. Then click “Auto” to enable auto control. **Note:** The control loop will not operate unless the system is set to “Auto” mode on the faceplate.
11. Close the faceplate.

4.3.3 DO control

Inadequate oxygen will inhibit cell growth, while excessive oxygen will either inhibit growth or kill cells. Therefore, a balance must be maintained for optimal cell growth.

Nitrogen is used to remove excessive oxygen from the media by formation of nitrogen oxides. If the cells being grown are strict anaerobes, nitrogen will be the only gas supplied to the vessel.

Normal atmospheric oxygen concentration is about 20%. Most aerobic cells growth best at a slightly lower value.

However, in the TruBio Software, ambient air is assumed to be 100% saturated, so the usual setpoint for DO is about 40%, depending on the cell requirements.

Oxygen is generally supplied to the bioreactor/fermentor vessel by a flow of air across the surface of the media. The oxygen is absorbed both passively and through the action of the agitator, and by bubbling air and/or oxygen through the vessel from a sparger at the bottom of the tank or bag.

Oxygen demand is assumed to increase over time as the cells multiply. As demand increases, air will not be a sufficient source of oxygen, and pure oxygen will be needed to replace air as the source.

If pure oxygen is insufficient to maintain an adequate DO level, the agitator speed can be increased to enhance distribution and also to enhance oxygen absorption from the headspace. However, this method has only limited value.

On the Main screen, click **DO Control** at the top of the screen to open the faceplate (Figure 4.14).

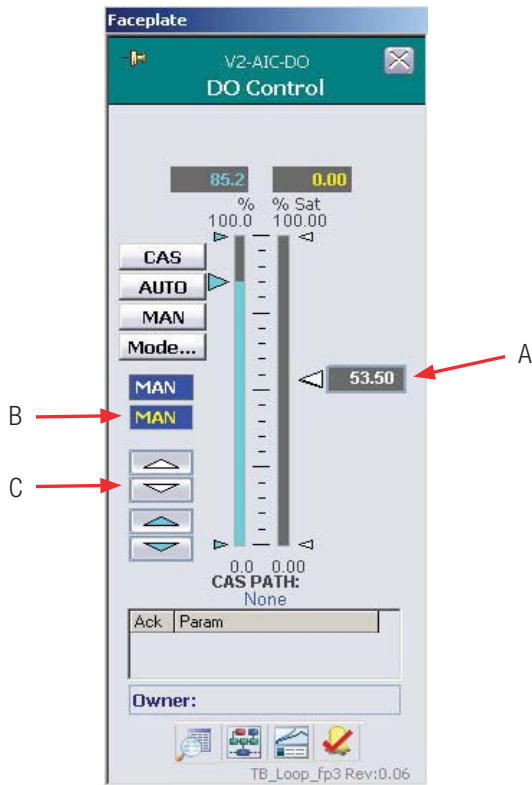


Figure 4.14. DO Control faceplate.

The desired DO setpoint may be set in any of the following ways:

- A. Dragging the slider on the right to the desired level
- B. Clicking the box, entering the new value in the pop-up window and clicking **OK**
- C. Using the white up/down arrows on the left side of the faceplate

Adjusting DO control settings

1. On the Configuration screen, click the **DO Control** box on the left side of the page. The remote setpoint is used only if the setpoint has not been set on the faceplate. Consult your customer service representative for the use of the Gain Schedule Aux Input.
2. Set up the DO probes by entering the manufacturer name from the drop-down menus. If more than one probe is being used, select the priority for each probe. Click the appropriate radio button for the number of probes in use.

- Temperature compensation input may be from the pH probe, the DO probe, or the vessel temperature. Select according to facility standards.
- Pressure compensation is used with sterilizable tanks. Consult your customer service representative for use of this function.
- Input scaling is usually percent saturation, so ensure that the appropriate radio button is clicked.

In Figure 4.15, the Controller Outputs have been defined as follows:

- Output #1 is air
- Output #2 is oxygen
- Output #3 is the agitator, with the maintenance speed assumed to be 75 rpm
- Output #4 is nitrogen

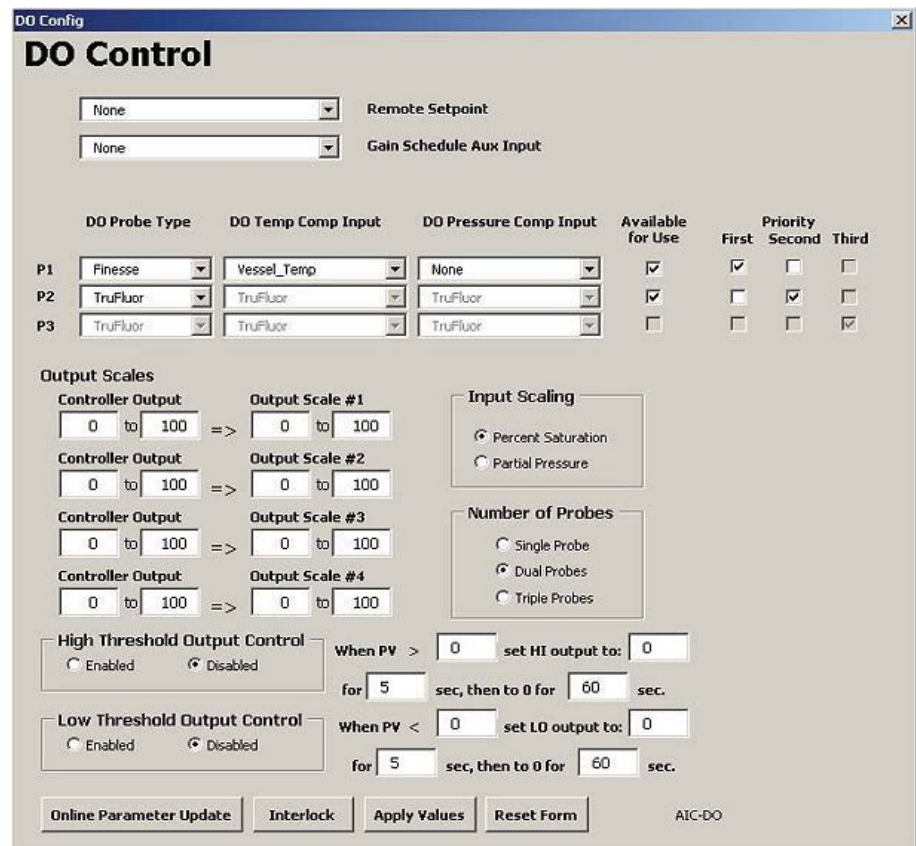


Figure 4.15. DO Control screen.

The limit of the sparger is assumed to be 25 lpm. Excessive bubbling can kill cells, so only one sparger will be used at less-than-full capacity, instead of using two spargers for separate delivery of oxygen and air.

Some users may prefer to set the agitator as Output #1 to bring more air into the media, but it should be kept in mind that a too-rapid agitator speed can damage or kill cells.

Logically, as oxygen demand increases and oxygen is added to air, the air flow must be decreased as the oxygen flow is increased, to avoid overload of the sparger.

3. On the “Configuration” screen, open an unused Calculation box (Figure 4.16).

Signal Conditioning			
Characterizing Curve #1 X Value vs. Y Value Curve Output: 0.00 Input: None	Calc #1 1+2 Result: 3.00 V1: None V2: None V3: None V4: None V5: None V6: None V7: None V8: None V9: None V10: None	Calc #4 2/2 Result: 1.00 V1: None V2: None V3: None V4: None V5: None V6: None V7: None V8: None V9: None V10: None	
Characterizing Curve #2 X Value vs. Y Value Curve Output: 0.00 Input: None		Calc #2 4-2 Result: 2.00 V1: None V2: None V3: None V4: None V5: None V6: None V7: None V8: None V9: None V10: None	Calc #5 3+2 Result: 5.00 V1: None V2: None V3: None V4: None V5: None V6: None V7: None V8: None V9: None V10: None
Characterizing Curve #3 X Value vs. Y Value Curve Output: 0.00 Input: None		Calc #3 100/4 Result: 25.00 V1: None V2: None V3: None V4: None V5: None V6: None V7: None V8: None V9: None V10: None	Calc #6 1+1 Result: 2.00 V1: None V2: None V3: None V4: None V5: None V6: None V7: None V8: None V9: None V10: None
Logical & Comparison Compare Input1: None Input2: None Input3: None Input4: None Outputs Comparison Logical 0.00 1 0.00 0.00 2 0.00 0.00 3 0.00 0.00 4 0.00			
Math Derivative #1 Input Result: 0.00 None Derivative #2 Input Result: 0.00 None			

Figure 4.16. Opening unused Calculation box.

For this calculation (Calc #1 in Figure 4.17), only “Variables” will be needed.

Free Form Equation #1 Config

Calc #1

Formula = Calculation Steps Remaining: 9

Constants

C1	1	C6	0
C2	2	C7	0
C3	0	C8	0
C4	0	C9	0
C5	0	C10	0

Operators

Buttons: +, exp(^), sin, (,)
 -, sqr, cos, Delete
 *, log, tan, Clear
 /, ln, e, abs

Enter formula using buttons. Press Apply when complete

Variables

Note: Trig functions are in degrees, not radians

V1	None	V6	None
V2	None	V7	None
V3	None	V8	None
V4	None	V9	None
V5	None	V10	None

Buttons: Online Parameter Update, Apply Values, Reset Form

XY-FUNC1

Figure 4.17. Calc #1 configuration.

- Use the drop-down menus to set V1 to “DO Control Output #1” and V2 to “DO Control Output #2.”
- To set up the formula, click the appropriate Operator buttons. Click **V1**, then - (minus symbol), and **V2**.
- Click **Apply Values** to save the calculation. Then close the Calculation screen.

Adjusting DO mass flow controllers

- Click the MFC box for the air supply (Figure 4.18).

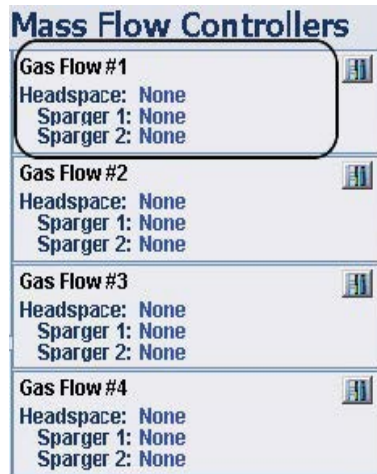


Figure 4.18. Mass Flow Controller box for air supply.

2. Use the dropdown menu for the sparger that is connected to the air supply. Set the “Flow Setpoint” to “Calc #x Output,” where x is the calculation box used. Ensure that the radio buttons for “Allowed” and “Selected Flowpaths” are set for the sparger being used.
3. Click **Apply Values** to save the setting.
4. Click the MFC box for the oxygen supply.
5. Set the appropriate sparger to “DO Control Output #2” (Figure 4.19) and verify that the appropriate sparger is selected. Then click **Apply Values**.

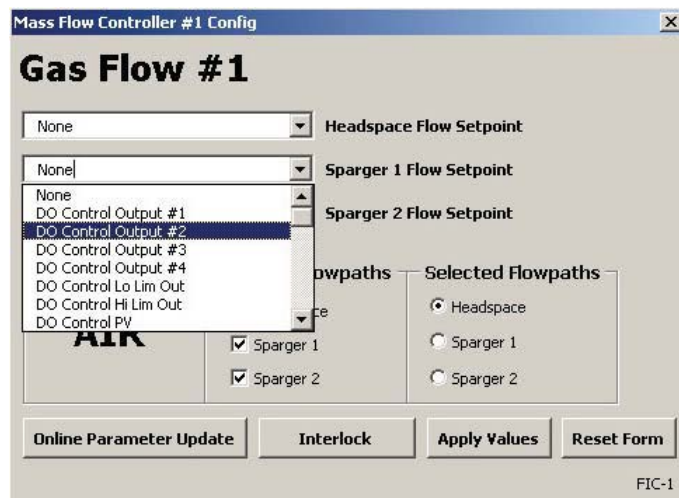


Figure 4.19. Selecting “DO Control Output” from “Sparger 1 Flow Setpoint” dropdown list.

6. Click the MFC box for the nitrogen supply and set it up as for oxygen and air, selecting as the Sparger Flow Setpoint “DO Control Output #4.” Then click **Apply Values**.

Adjusting the agitator

The agitator will be operating during the run, so this time a remote setpoint will be used to increase the agitator speed, when required.

1. Open the agitator control box. Note that only a remote setpoint is offered, as the agitator speed is usually set from the Main screen. Use the dropdown menu to select “DO Control Output #3.”
2. Return to the Main screen and open the MFC faceplate for oxygen.
3. Verify that the system is in “BYPASS” mode, which is the default setting. Click **CAS** to set the cascade mode and put oxygen into the DO control loop. Close the faceplate.
4. Open the MFC faceplate for air, ensure that “Bypass” is highlighted, and set to “Cascade” mode. Close the faceplate.
5. Open the MFC faceplate for nitrogen, highlight “Bypass,” and set to “Cascade” mode. Close the faceplate.
6. Open the DO Control faceplate. On the left side of the faceplate, click **Auto** to set the DO Control to “Automatic” mode. Close the faceplate.

Note: The MFCs must be set to “Bypass” mode (the default), rather than “Normal” mode. If set to “Normal” mode, the MFC will not respond correctly.

4.3.4 Temperature control

Temperature can be controlled in bioreactor/fermentor vessels in two ways. The most common method is the jacket that is built into the stainless-steel vessel that holds the S.U.B. Water circulates in the jacket through a separate temperature control unit (TCU).

The second method, which is used in 250 L or smaller systems, is a thermal blanket that is wrapped around the vessel. The control of the jacket will be shown first, followed by the control of the blanket.

1. On the Main screen, click **Vessel Temperature** at the top of the screen to open the faceplate (Figure 4.20).

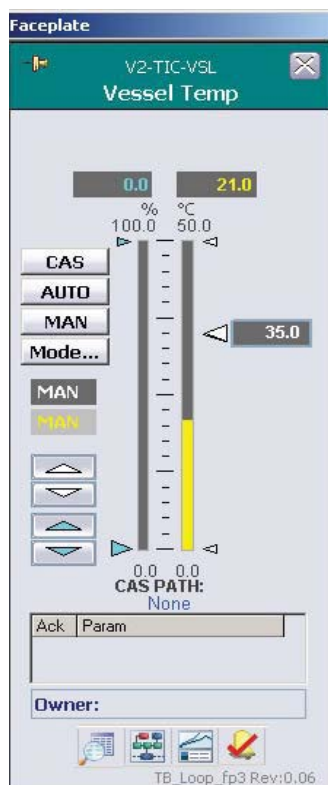


Figure 4.20. Vessel Temperature faceplate.

2. Set the desired temperature setpoint with one of the following methods:
 - Click the white up/down arrows at the left side of the faceplate
 - Slide the box on the right up or down
 - Click the box, enter the desired value, and clicking **OK**
3. Open the Detail screen, click the “Alarms” tab (Figure 4.21), and set the Hi-Hi, Hi, Lo, and Lo-Lo limits. Set the setpoint limits appropriate to the process.

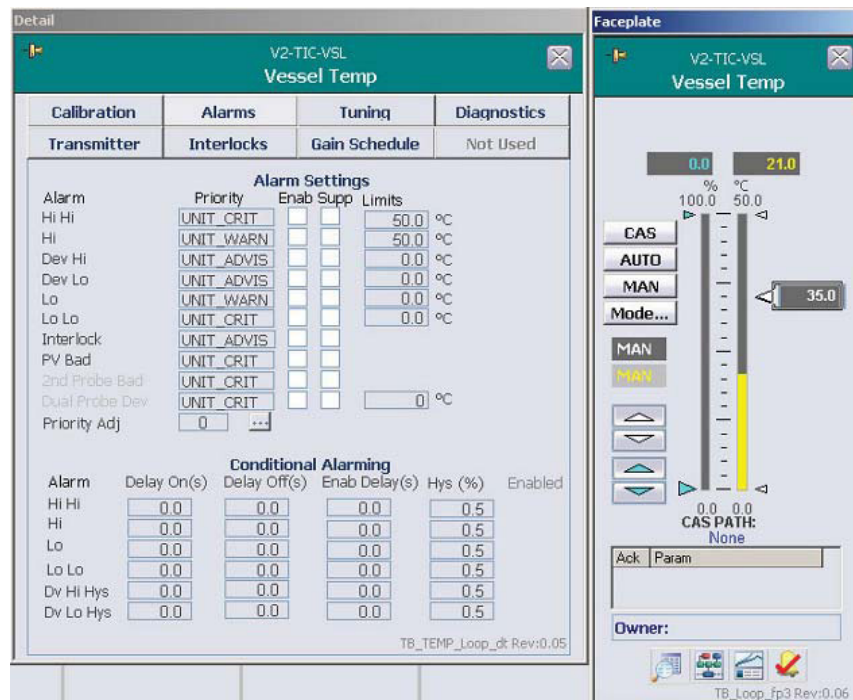


Figure 4.21. Alarms tab for Vessel Temp.

Note: Do not set the SP Lo Limit to 0 if water is used in the TCU, as the TCU will freeze. An SP Lo Limit of ≥ 5 is recommended. If glycol is used, the SP Lo Limit can be set to 0.

4. Close the faceplate.
5. On the Configuration screen, click **Jacket Temperature** control on the left side of the screen.
6. Set the Remote Setpoint to “Vessel Temp Heat Out.” The Gain Schedule should be set to “None.”
7. Set the Control Modes and Available Outputs to “Heat Only,” and click the radio button for the correct number of probes. “Discrete Output Settings” will not be used (Figure 4.22).

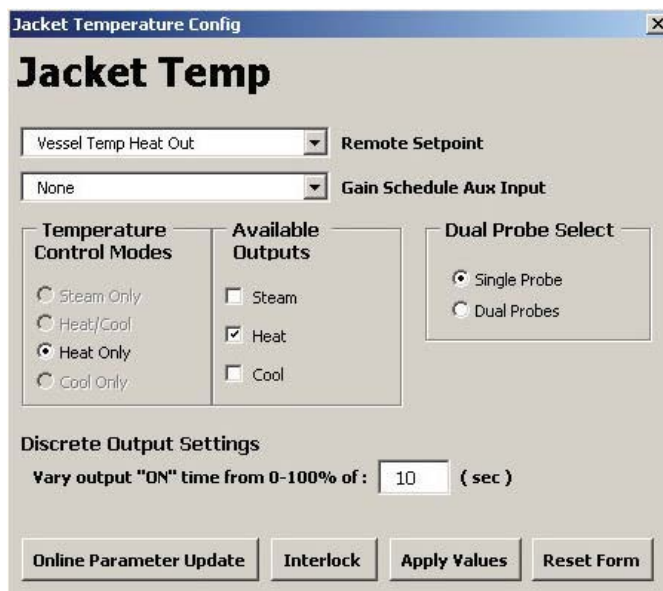


Figure 4.22. Jacket Temperature Configuration screen.

8. Click **Apply Values** to save the settings and close the screen.
9. Click the **Vessel Temperature** control. Set the Remote Setpoint and Gain Schedule to “None” and set Temperature Control and Available Outputs to “Heat Only.” Click the radio button for the appropriate number of probes and close the screen.
10. Return to the Main screen and open the “Jacket Temperature” faceplate.
11. Click **CAS** to set the control into “Cascade” mode, and link the jacket and vessel controls. The Cascade path will read “Vessel Temp Heat Out.” Close the faceplate.
12. Click the **Temperature** control box to open the temperature faceplate again. Click **AUTO** to set the temperature control to “Automatic Control” mode.
13. When using a thermal blanket, there is no TCU. Therefore, the temperature is set on the Vessel Temp faceplate and the mode is set to “AUTO.”
14. On the Configuration screen, the Vessel Temperature Control will show “None” for Remote Setpoint or Gain Schedule. The Modes and Outputs will be “Heat,” and the Discrete Output Settings must be a number greater than 0. The default time of 10 seconds works well in most applications.

Remote start/stop for TCU units

An additional feature in the TruBio Software has been designed for TCU units that are located remotely from the S.U.B. vessel, and that require remote start/stop control (Figure 4.23). For information on this feature, contact your customer service representative.

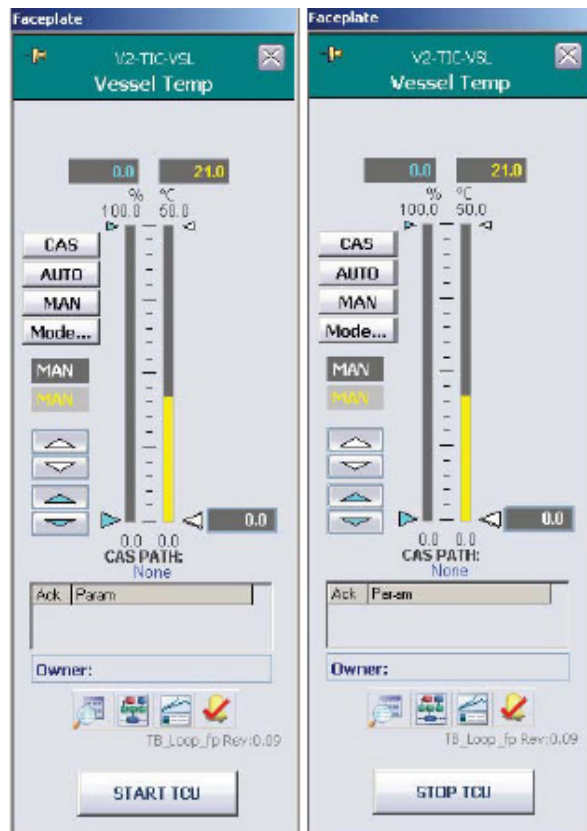


Figure 4.23. Vessel Temperature remote start/stop faceplate.

4.3.5 Agitator control

The agitator is easily set, as it runs continuously and is remotely controlled only in the DO loop.

1. On the Main screen, click **Agitator Speed** on the upper right of the screen.
2. To set the agitator speed, click the blue up/down arrows on the left of the faceplate (Figure 4.24).

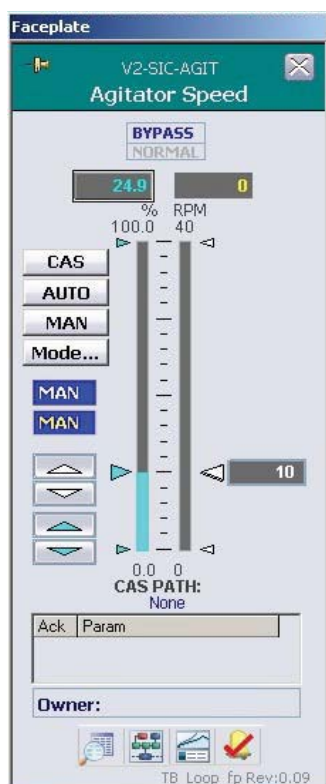


Figure 4.24. Setting the agitator speed using arrows on left.

3. Set the mode to “AUTO.”

Note: Thermo Fisher Scientific recommends that the agitator be run in Bypass mode, which will provide better performance, as it allows the agitator to reach the setpoint faster.

4.3.6 Agitator reverse function

This feature allows the user to reverse the rotational direction of the agitator, either as a single occurrence or as a configured part of the agitator programming.

To use this function, use the following steps.

1. Open the Agitator faceplate and click **Detail** to open the “Detail” window. Then click the **Functions** tab (Figure 4.25).

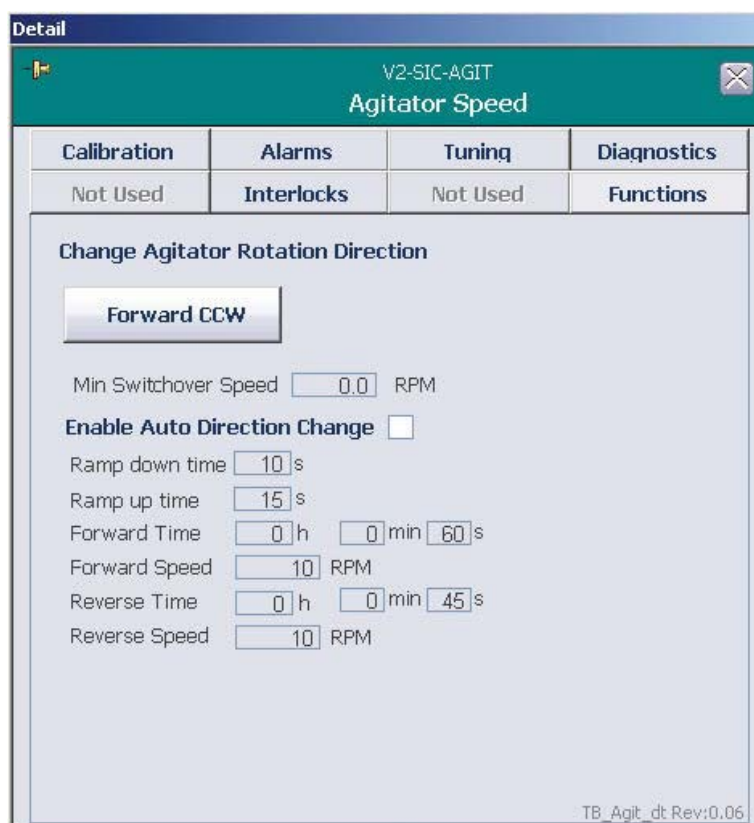


Figure 4.25. Agitator detail window.

2. Set the Minimum Switchover Speed, Ramp Down Time, and Ramp Up Time.
3. Click **Forward CCW**, located under “Change Agitator Rotation Direction.” If the agitator speed has not yet reached the set Minimum Switchover Speed, the following error message appears (Figure 4.26).

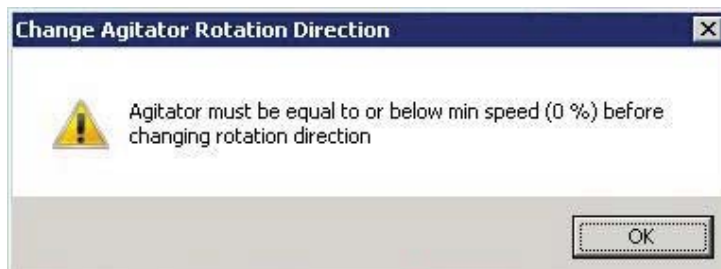


Figure 4.26. Error message appears if speed has not yet reached minimum switchover speed.

4. Allow the agitator to reach the minimum speed and then click the button again. A confirmation pop-up window will appear.
5. Click **OK** to change the agitator rotation direction. This procedure can be performed as often as desired.

Using the function at specific intervals

To set the agitator to reverse direction at specific intervals, use the following steps:

1. Set the agitator to “Auto” mode on the faceplate.
2. In the “Functions” tab of the Detail screen, click **Enable Auto Direction Change**.
3. Enter values for all of the parameters, then click **Change Rotation Direction**. Another confirmation pop-up window will appear.
4. Click **Yes** to run the agitator for the specified durations at the user-defined speeds.

Note: Agitator reverse direction functionality is only available for the ATMI and Xcellerex™ S.U.B. types when used in conjunction with a G3Pro Universal controller.

4.4 Pump setup—pre-programmed pump functions

The pumps can be set up to deliver media, glucose, or other materials to the bioprocessor/fermentor. The pumps can be controlled by the following methods:

- From the pump faceplate, by setpoint control
- With pre-programmed Pump functions, by selecting “Function” from the faceplate’s Detail icon
- With user-defined Dose functions from the Dose control box at the bottom of the faceplate (the “Total Flow Dosing Strategy”)
- By configuring multiple feed pumps to act together, from the “Multi-feed” control box on the Main screen (the “Pump MultiFeed Strategy”)

The pump faceplate method is a basic faceplate operation, which involves a setpoint and setting the controller mode to “Auto.”

For the pre-programmed Pump Functions method, the setup is flexible and offers several options: ramp, continuous, and dose. This method can be performed with or without a scale.

If a scale is used, accuracy is based on scale feedback. If you do not use a scale, dose accuracy relies on a pump counter, which is set by the pump calibration.

To select a scale, open the Configuration page and then open the pump configuration box. Select the correct scale from the “Scale Selection” drop-down menu. Run a pump calibration using the selected scale prior to dosing.

Note: Thermo Fisher Scientific strongly recommends that a scale be used to ensure the greatest accuracy.

To set up pump dosing, use the following steps.

1. Open the faceplate, followed by the Detail screen.
2. Click on the “Functions” tab. Then click **Dose** (Figure 4.27).

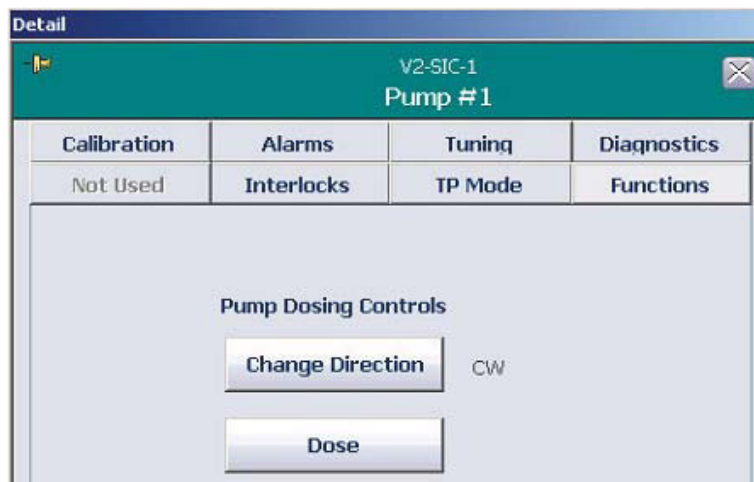


Figure 4.27. Select “Dose” on Pump Dosing Controls screen.

- From the Pump Function drop-down menu, choose the desired function: Ramp, Continuous, or Dose (Figure 4.28). Each function is described in the following sections.

Note: In the following examples, no scale is selected for weight feedback.

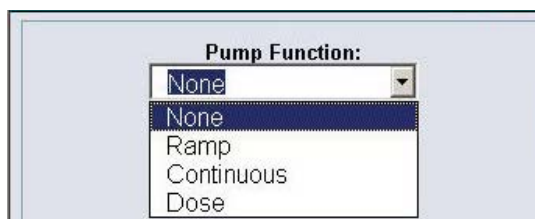


Figure 4.28. Drop-down menu for pump functions.

Ramp function

Use the “Ramp” function (Figure 4.29) to raise the pump rate over a defined period of time, and then run continuously at the final speed.

Faceplate FB

V2-SIC-1
Pump #1

Pump Function:
Ramp

Scale Selected:
None

Start Rate: 0.00 RPM
End Rate: 0.00 RPM
Start Delay: 0.00 Minutes
Ramp Time: 0.00 Minutes

Max Rate: 175.00 RPM

NOTE: Pump will remain off for Start Delay Time

Start

Time Units: Minutes
 Hours

Speed/Flow: RPM
 g/Min

Figure 4.29. Ramp pump function.

Enter the appropriate values and select the “Time Units” and “Speed/Flow” preference. Either the Start Rate and/or Start Delay may be zero, if preferred.

The diagram in Figure 4.30 shows the Start Rate (a short period), the Ramp Time as set by the user, and the End Rate. If a Start Delay is used, the Pump Rate will be zero during the delay, then will run at the Start Rate before beginning the ramp.

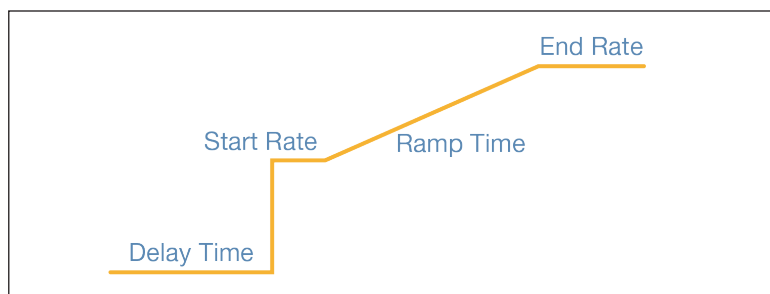
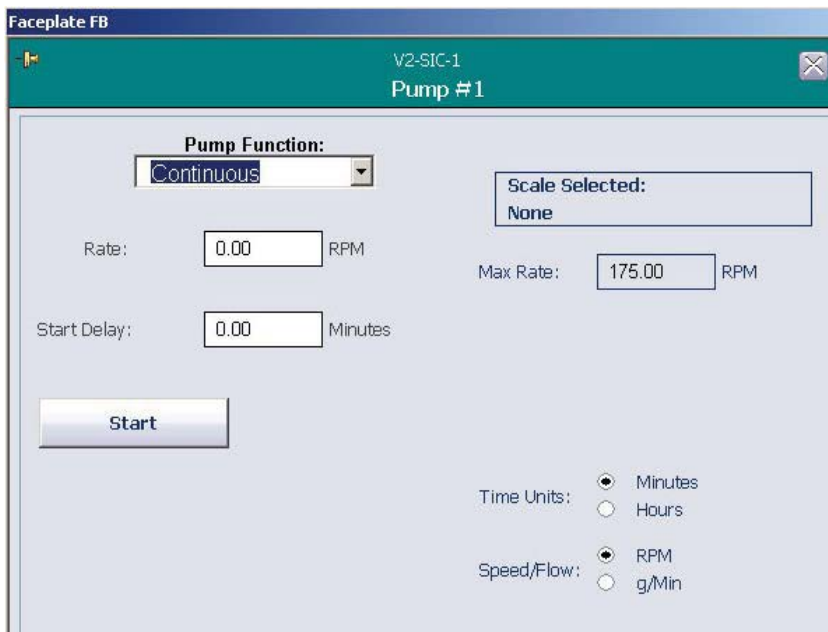


Figure 4.30. Representation of the ramp function with a Start Delay.

Continuous function

Use the Continuous function (Figure 4.31) to run the pump at the selected rate after the Start Delay represented by the diagram in Figure 4.32.



Faceplate FB

V2-SIC-1
Pump #1

Pump Function:
Continuous

Rate: 0.00 RPM

Start Delay: 0.00 Minutes

Scale Selected:
None

Max Rate: 175.00 RPM

Start

Time Units:
 Minutes
 Hours

Speed/Flow:
 RPM
 g/Min

Figure 4.31. Continuous pump function.

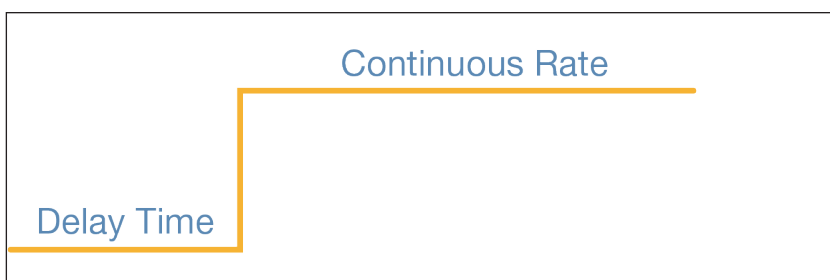


Figure 4.32. Representation of the continuous function with a Start Delay.

Dose function

The “Dose” function can also be referred to as the “bolus” function. The pump delivers the selected number of doses with a set period of time (the Settle Time) between doses (Figure 4.33).

The screenshot shows the 'Faceplate FB' software window for 'V2-SIC-1 Pump #1'. The 'Pump Function' is set to 'Dose'. The configuration includes:

- Add Amount:** 0.00 g
- Dose Duration:** 0.00 Minutes
- Delay Time:** 0.00 Minutes
- Number of Cycles:** 1
- Scale Selected:** None
- Max Flow:** 111.36 g/Min
- NOTE:** Dose Cycle Time = Delay Time + Dose Duration
- Cycles Completed:** 0
- Amount Added:** 0.00 g
- Remaining:** 0.00 g
- Time Units:** Minutes (selected), Hours
- Speed/Flow:** RPM (selected), g/Min
- Start** button
- Dose Mode:** Continuous (Run Pump for Dose Duration) (selected), Dump (Run at 'Pump Speed' until amount added)

Version: TB_PUMP_Dose_fp2 Rev:0.03

Figure 4.33. Dose pump function.

Note that the “Add Amount” is user-specified rather than a set volume. This means that the user must calculate the appropriate pump speed and run time, based on the concentration of the solution being added. For example, assume that 100 g of glucose is added in each five minute cycle and the concentration of the supply solution is 10 g/dL. In this case, for each dose, 1 L must be added.

If a Series 313 pump is in use, the calculation is similar. Using tubing of 8.0 mm ID, the flow rate at the maximum speed of 300 rpm is 808.1 mL/min. The required dose is 24.75% of the maximum flow, or 74.25 rpm for 200 mL/min. Again, for ease of setting pump speeds, a rate of 75 rpm may be used for four minutes and 57 seconds or 80 rpm for four minutes and 38 seconds.

Note: These calculations are examples only, and not intended to be used for actual processes. User calculations will be based on the actual pumps and tubing being used on-site and the pump calibration data.

The Settle Time is the time between cycles where no dosing occurs; in other words, a waiting period. It is designed to allow a scale to settle before the weight is recorded. The diagram in Figure 4.34 illustrates the Dose function.

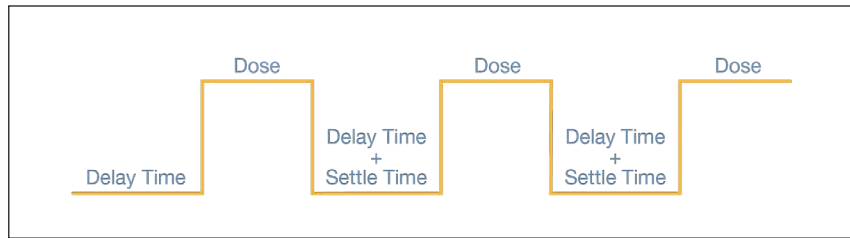


Figure 4.34. Representation of the Dose function with a Start Delay.

Thermo Fisher Scientific recommends that the pump not be run at the maximum rate at any time. This could lead to over-delivery of material if the pump shuts down abruptly when running at maximum rate. When all parameters are set up, click “Start” to initiate the function.

4.5 Pump total flow dosing strategy

A feature introduced in TruBio version 4.7 allows the user to set up a pump strategy that is designed to feed a specific quantity at user-defined flow rates into the vessel. The Total Flow Dosing strategy uses the loss in weight from a scale to determine the cycle. Therefore, a scale must be selected to use this option.

Use the following steps to set up total flow dosing.

1. Open the Configuration screen and click the pump to be used to open the pump configuration screen (Figure 4.35).

Figure 4.35. Setting up total flow dosing for Pump #1.

2. Set the Control Mode to “Dose” and the Speed/Flow mode to “Flow Control.” The Remote Setpoint will be disabled.
3. Use the drop-down menu to select the Dose Total Flow Setpoint. Then click **Apply Values**.
4. In the Main screen, open the faceplate for the same pump. The faceplate will have a slightly different appearance (Figure 4.36).

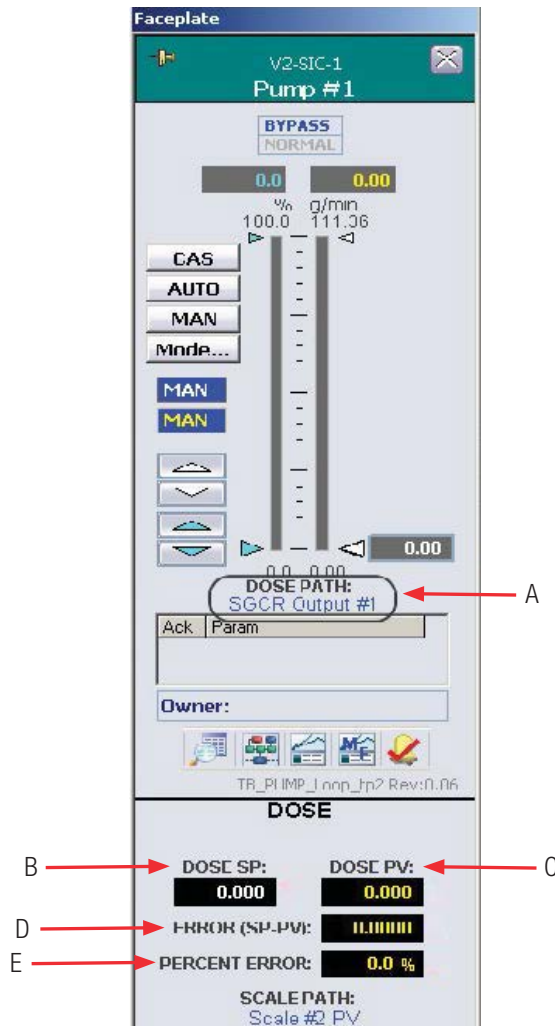


Figure 4.36. Dose path Pump #1 faceplate.

The following features are identified on Figure 4.36:

- A. **DOSE PATH**—Cascade setpoint path
- B. **DOSE SP**—Cascade setpoint from the calculation
- C. **DOSE PV**—Total current dose
- D. **ERROR (SP-PV)**—Difference between setpoint and total dose
- E. **PERCENT ERROR**—Difference expressed in percentage

In the Detail screen, the “Alarms” tab has an additional alarm function for the dosing feature. The units are set by the user and may differ from those in the following example (Figure 4.37).

Calibration	Alarms	Tuning	Diagnostics
Not Used	Interlocks	TP Mode	Functions

Alarm Settings

Alarm	Priority	Enab	Supp	Limits
Hi Hi	UNIT_CRIT	<input type="checkbox"/>	<input type="checkbox"/>	90.00 g/min
Hi	UNIT_WARN	<input type="checkbox"/>	<input type="checkbox"/>	90.00 g/min
Dev Hi	UNIT_ADVIS	<input type="checkbox"/>	<input type="checkbox"/>	0.00 g/min
Dev Lo	UNIT_ADVIS	<input type="checkbox"/>	<input type="checkbox"/>	0.00 g/min
Lo	UNIT_WARN	<input type="checkbox"/>	<input type="checkbox"/>	0.00 g/min
Lo Lo	UNIT_CRIT	<input type="checkbox"/>	<input type="checkbox"/>	0.00 g/min
Tripped	UNIT_CRIT	<input type="checkbox"/>	<input type="checkbox"/>	
Interlock	UNIT_ADVIS	<input type="checkbox"/>	<input type="checkbox"/>	
PV Bad	UNIT_CRIT	<input type="checkbox"/>	<input type="checkbox"/>	

Dose ALM UNIT_CRIT Hi Lim: 1 Lo Limit: -10 g

Priority Adj: 0

Conditional Alarming

Alarm	Delay On(s)	Delay Off(s)	Enab Delay(s)	Hys (%)	Enabled
Hi Hi	0.0	0.0	0.0	0.5	
Hi	0.0	0.0	0.0	0.5	
Lo	0.0	0.0	0.0	0.5	
Lo Lo	0.0	0.0	0.0	0.5	
Dv Hi	0.0	0.0	0.0	0.5	
Dv Lo	0.0	0.0	0.0	0.5	

TB_PUMP_dt2 Rev:0.07

Figure 4.37. Dosing alarm enabled.

- After the limits and alarms are entered, set up the dosing strategy.
- On the Configuration screen, open a blank Characterizing Curve form. As shown in Figure 4.38, the dose adds 1.6 kg over 13 minutes (0.22 hr).

	Input (X)	Output (Y)
1	0	0
2	0.1	0.1
3	0.12	0.1
4	0.13	0.6
5	0.17	0.6
6	0.22	1.6
7	0	0
8	0	0
9	0	0
10	0	0
11	0	0
12	0	0
13	0	0
14	0	0
15	0	0
16	0	0
17	0	0
18	0	0
19	0	0
20	0	0
21	0	0

Figure 4.38. Characterizing Curve form.

When setting up the dosing strategy the following guidelines must be observed:

- Values for X and Y in Line 1 should always be zero (0). Otherwise, the pump will begin to operate as soon as the pump is set to “Cascade” mode and not when the timer is started.
- Each X value must be larger than the preceding one.
- The input (X) is usually the batch timer, expressed in hours.
- The output (Y) is the flow value, in units matching that of the pump.
- The Control Mode must be set to “Dose” to enable the Dose Total Flow Setpoint.

Figure 4.39 shows another example.

	Input (X)	Output (Y)
1	0	0
2	0.1	0.1
3	0.12	0.1
4	0.13	2
5	0.2	2
6	0.4	6
7	0	0
8	0	0
9	0	0
10	0	0
11	0	0
12	0	0

Figure 4.39. Second example of Characterizing Curve form.

- From 0 to 0.1 hours, add a total of 0.1 kg (lines 1 to 2)
 - Wait 0.02 hours (lines 2 to 3)
 - Over 0.01 hours, add 1.9 kg. This is a bolus addition (flow demand > pump capacity; lines 3 to 4)
 - Wait until the elapsed time is 0.2 hours (lines 4 to 5)
 - Over 0.2 hours, add 4 kg (lines 5 to 6)
 - Stop Dose (X and Y set to 0)
 - Overall total flow setpoint is 6 kg
8. When the curve is configured, go back to the pump configuration and set the total flow setpoint to the Characterizing Curve used (Figure 4.40). Then click **Apply Values**.

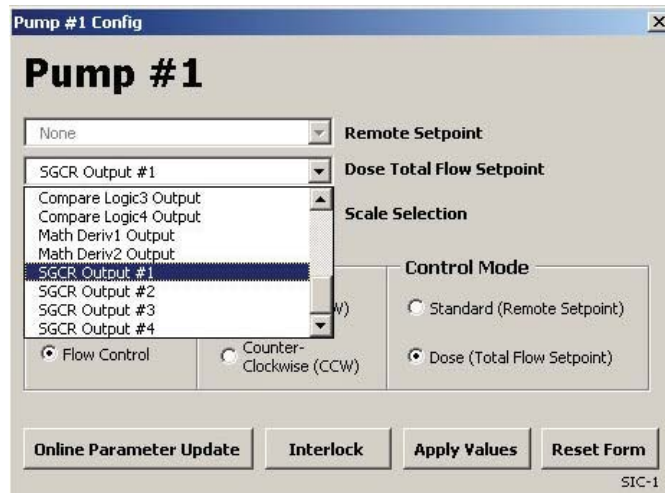


Figure 4.40. Setting total flow setpoint to Characterizing Curve used.

9. Select the appropriate timer display from the Main screen and ensure that the timer is set to zero.
10. Open the pump faceplate and set the pump into “Cascade” mode. The “Start” button appears on the timer faceplate. After the dosing process begins, the “Start” button changes to “Pause” (Figure 4.41).

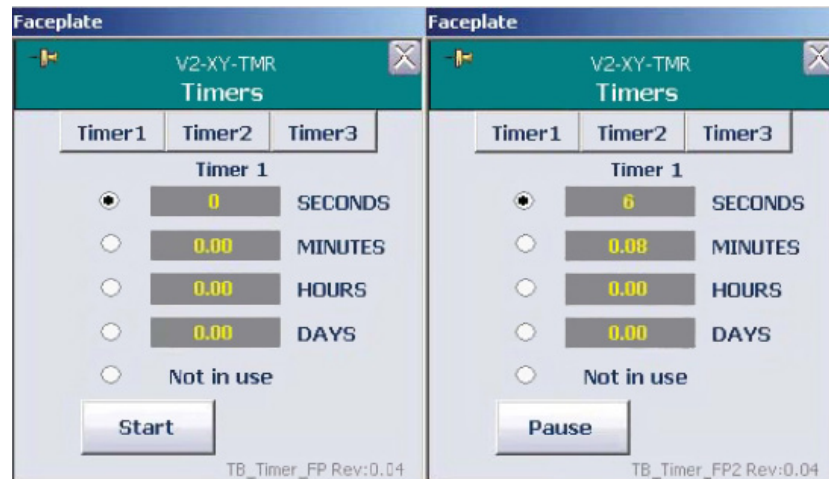


Figure 4.41. “Start” and “Pause” buttons on faceplate after setting into Cascade mode.

If the timer is Paused, the display will offer the option to Restart or Reset (Figure 4.42).

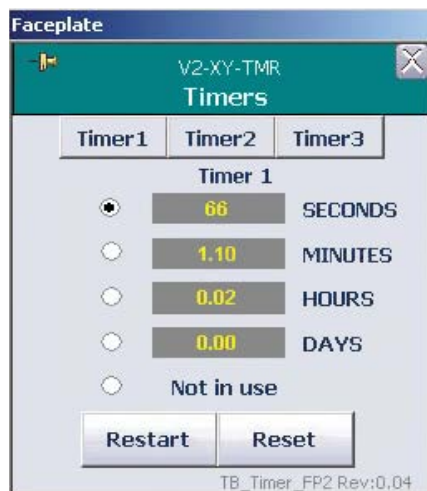


Figure 4.42. “Restart” and “Reset” buttons on faceplate when paused.

Note: If the scale is tared or zeroed after the dose has started, the dose will abort. If the pump total is reset from the totalizer box while the pump is in Cascade mode and the timer is not equal to zero, the total flow setpoint will automatically reset.

11. To pause the dose, stop the timer on the Main screen.

Historian collection

The following Total Flow Dose parameters are included in the process history collection:

- Add_Actual: Current total dose reading
- Error: Current value for the difference between the setpoint and the process value
- Input 1: Profile setpoint

These values may be displayed in either tabular or graphic format.

4.6 Pump MultiFeed strategy

Another feature in TruBio Software, version 5.0 is the ability to feed the bioreactor/fermentor vessel using up to four pumps, either on the same weigh scale or up to four weigh scales. Note: This feature is not available in TruBio Discovery systems.

1. To activate the MultiFeed capability, go to the Configuration page and click **Online Parameter Update**.
2. Verify that the correct vessel is displayed and click **Default** in the “Category” column (Figure 4.43).

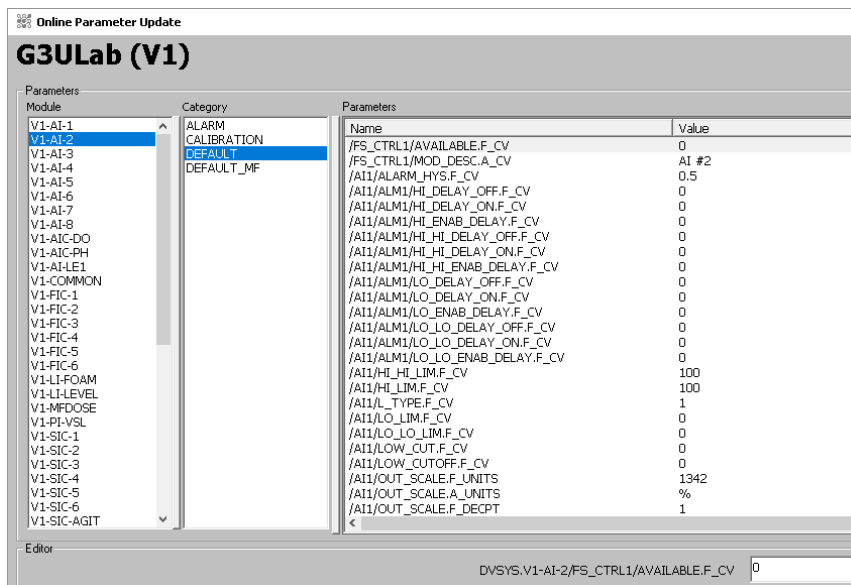


Figure 4.43. “Default” selected in “Category” column.

3. In the “Module” column, locate and click the string reading **Vx-MFDOSE** with x being the vessel number in use. Then click **DEFAULT_MF** in the “Category” column again.
4. In the “Parameters” column, locate the Name string **/FS_CTRL1/AVAILABLE.F_CV**. Click the string to highlight it (Figure 4.44).

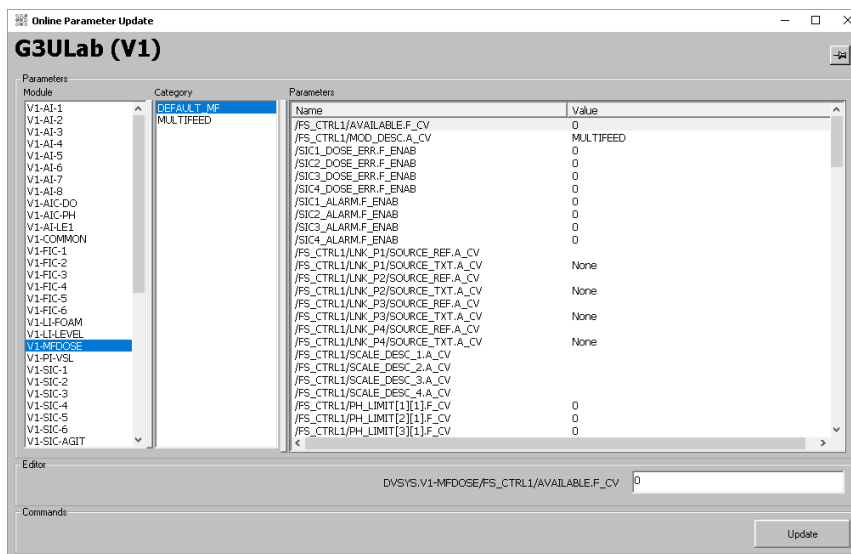


Figure 4.44. Dosing alarm enabled.

Available Values for this Name are “0” and “1.” If the MultiFeed function is enabled, the value will be “1.” Otherwise, the value will be “0.”

5. To activate the function, enter “1” in the field in the lower right of the screen and click **Update**.
6. Ensure that the scale is available by verifying that the Value for the Name **/FS_CTRL1/AVAILABLE.F_CV** is set to “1.”
7. To set up pumps on the scale, click the **MultiFeed** box on the Configuration page. This opens the “MultiFeed Config” box (Figure 4.45).

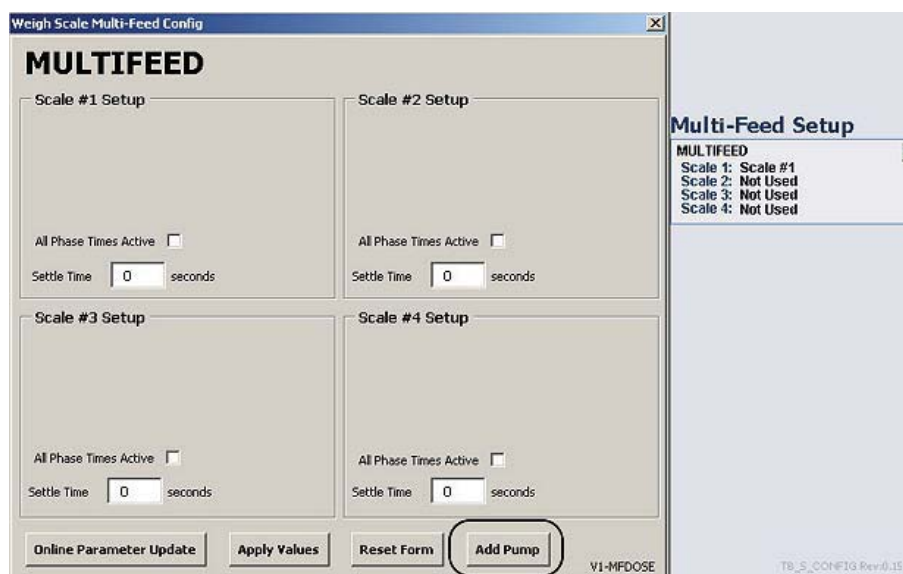


Figure 4.45. MultiFeed Config box.

8. Click **Add Pump** at the bottom right of the pop-up box. Then select the pump to be added and click **OK**.
9. Click **Apply Values** to save the change.

Deleting a pump

To delete a pump:

1. Open the MultiFeed menu from the Configuration page (Figure 4.46).

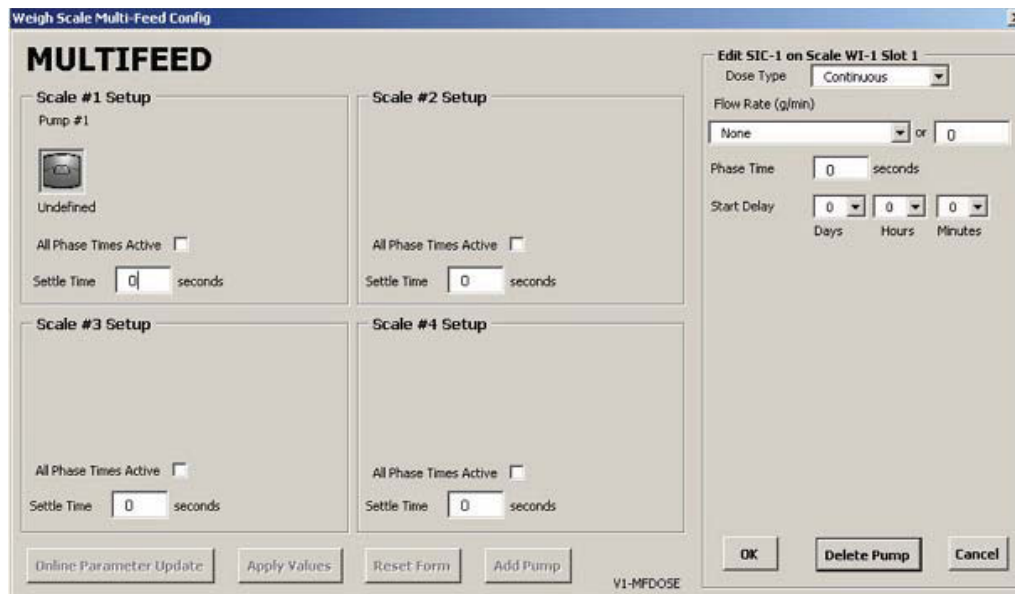


Figure 4.46. MultiFeed menu from Configuration page.

2. Click the icon for the pump to be removed. Then click **Delete Pump**.
3. Click **Apply Values** to save the change.

Pump setup

The pumps are set to operate in the left-to-right sequence shown in Figure 4.47. Pump #1 starts, operates, and stops, followed by Pump #3, Pump #2, and lastly, Pump #4. The sequence then repeats.

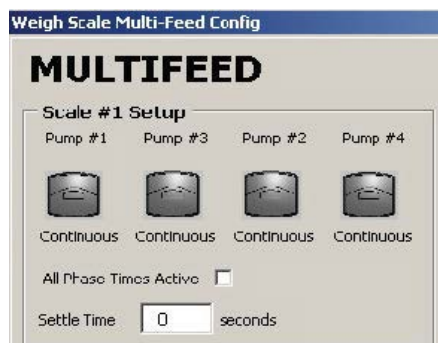


Figure 4.47. Sequence of Pumps #1–4.

1. To access the MultiFeed control faceplate (Figure 4.48) from the Main screen, click the **MultiFeed** control box, located immediately above the pump control boxes.

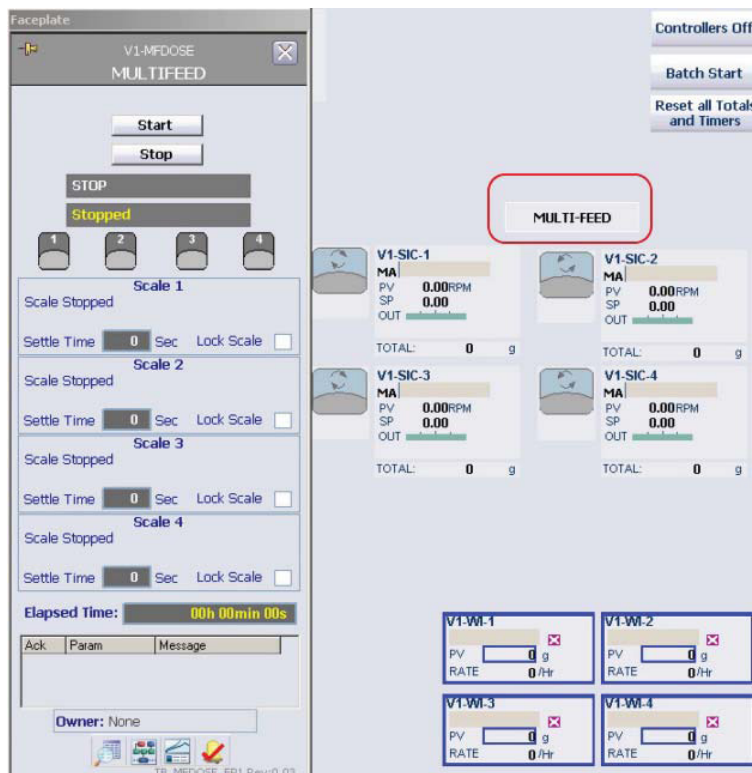


Figure 4.48. MultiFeed control faceplate.

2. On the faceplate, click **Detail** to open the MultiFeed menu (Figure 4.49). Dose limits, alarms, and status checking can be done from this menu.

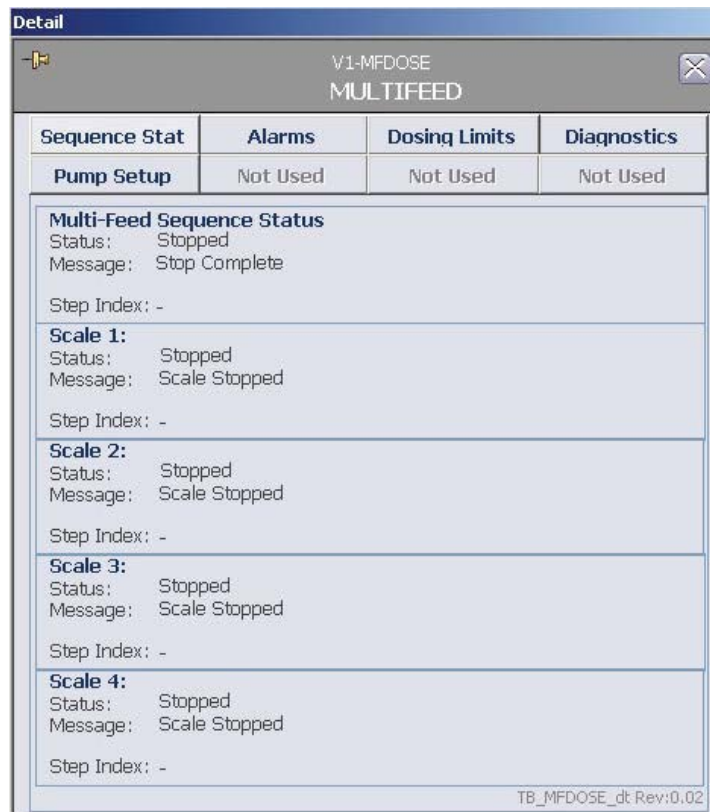


Figure 4.49. MultiFeed menu.

The “Sequence Status” indicates which pumps are in use and which pump will be activated next.

The Pump Setup screen (Figure 4.50) shows limits for the dose alarms and auto-calibration settings. Pumps can have different limits and each pump must be set up separately.

Detail			
V1-MFDOSE MULTIFEED			
Sequence Stat	Alarms	Dosing Limits	Diagnostics
Pump Setup	Not Used	Not Used	Not Used
V1-SIC-1	V1-SIC-2	V1-SIC-3	V1-SIC-4
Pump #1 Large Increase/Decrease in Scale Weight Check Limit Value <input type="text" value="100.000"/> g Scan Time <input type="text" value="40"/> s No Decrease in Scale Weight Check Limit Value <input type="text" value="50.0000"/> g Scan Time <input type="text" value="60"/> s Dosing Errors Error Limit <input type="text" value="10.0"/> % Minimum Doses Before Check <input type="text" value="5"/> Auto Calibration Settings Number of Doses per Calibration <input type="text" value="3"/> Number of Calibrations <input type="text" value="0"/> Maximum Calibration Change <input type="text" value="10.0"/> %			
TB_MFDOSE_dt Rev:0.02			

Figure 4.50. Pump Setup on MultiFeed menu.

The “Large Increase/Decrease in Scale Weight Check” settings will trigger an alarm if the load on the scale increases or decreases rapidly. This can be caused by such issues as an accidental load on the scale (increase), or a leaky or broken controller (decrease). In Figure 4.50, a 100 gram load change in less than 40 seconds will trigger an alarm.

The “No Decrease in Scale Weight Check” will trigger an alarm if the weight does not decrease as the pumps run. This will alert the user to issues, such as empty containers or clogged tubing. In Figure 4.50, if there is no change in weight for 60 seconds, an alarm will be triggered.

For both of the Scale Weight Checks, the Scan Time must be less than the Phase Time (to be set below).

Dosing Errors will trigger an alarm if the weight change differs from the expected value by the percentage set here. For small dose amounts, the initial error percentage could be very large, even though the absolute error in grams is very small. The Dosing Error should be set to avoid this initial high-percent error.

In Figure 4.50, an alarm would not be triggered for an error greater than 10% until five doses had been completed.

The Auto Calibration Settings automatically adjust the calibrated range of the pump, based on the pump error. The previous figure shows that the calibrated maximum pump rate should be adjusted by the average of the last three dose errors. Auto calibration will occur only after three dosings have been performed; it would then occur after each of three doses for a total of three calibrations. The maximum change from the initial calibration would be limited to 10%.

Auto calibration can be used to check the accuracy of the initial calibration for the actual dose rate. This can occur if the initial calibration was based on a wide range of pump rates and the set dose is a very small percentage of the maximum pump rate.

The alarms are enabled or suppressed on the Alarms tab shown in Figure 4.51. The Priority Adjust feature enables the user to set the alarm levels from “Critical” to “Advisory.”

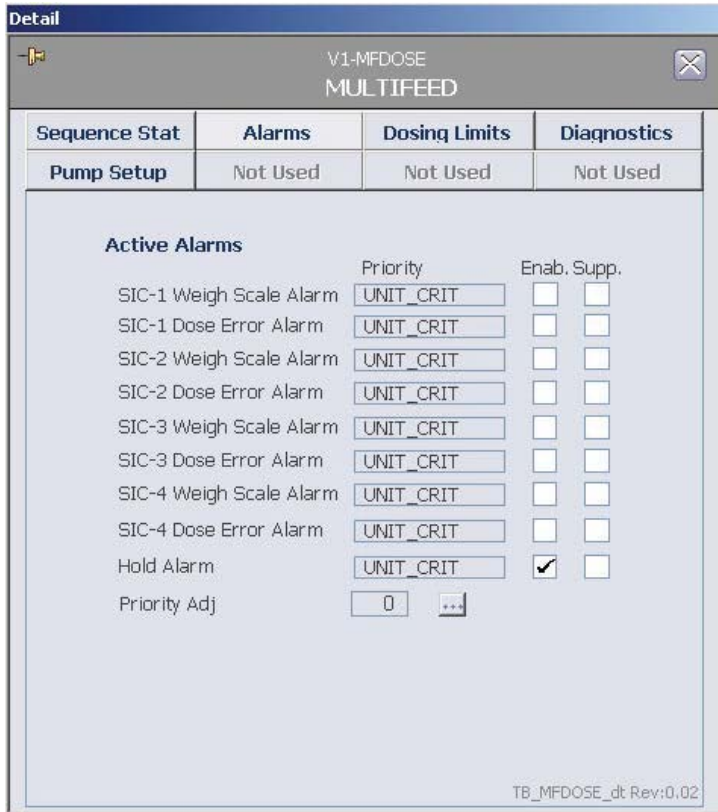


Figure 4.51. Alarms on MultiFeed menu.

The Dosing Limits tab sets limits for restricting the number of doses per hour (1 and 2), based on the dose rate. The user inputs these limits as a percentage of the maximum flow (Figure 4.52). “Max Flow” is the calibrated maximum flow rate for each pump that is shown on the pump faceplate.

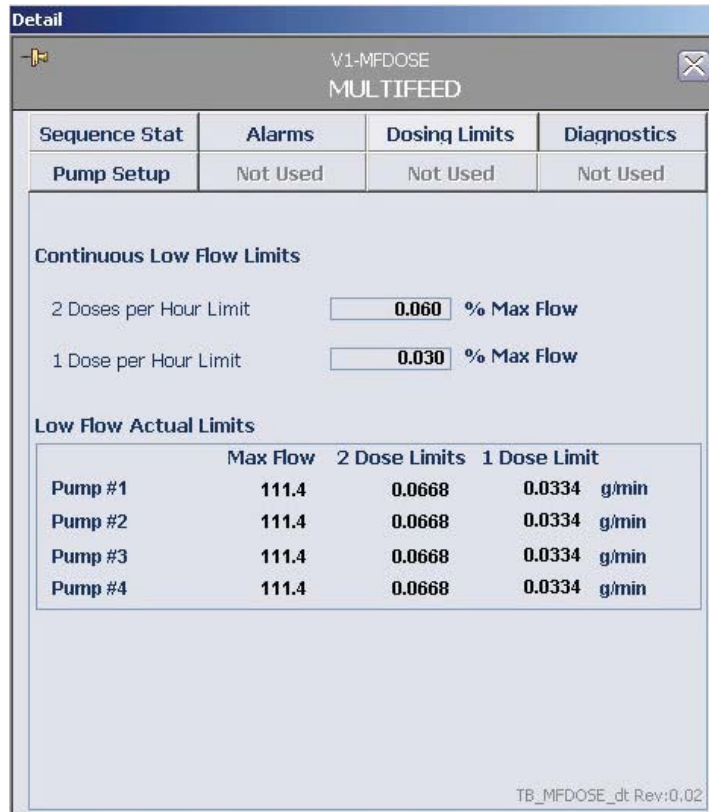


Figure 4.52. Dosing Limits tab flow limits.

In Figure 4.52, if the maximum flow rate of Pump #1 is 1258.3 g/hr, then the “1 Dose per Hour Limit,” shown above, would be $1258.3 \times 0.03\%$ or 0.378 g/hr. Therefore, if the selected dose rate is less than 0.378 g/hr, then only one dose per hour will be generated. If the rate is between 0.378 and 0.755 g/hr, two doses per hour will be generated. If the rate is above 0.755 g/hr, the number of doses would be based on the number of pump phases per hour.

When setting the “2 Doses per Hour Limit,” the value must be greater than the “1 Dose per Hour Limit,” but need not be twice the 1-Dose limit.

The Diagnostics tab (Figure 4.53) enables the user to check the functioning of the module. In the case of an alarm situation, a description of the malfunction that prompted the alarm displays.



Figure 4.53. Diagnostics on MultiFeed menu.

The Diagnostics tab enables the user to check the functioning of the module. In the case of an alarm situation, a description of the malfunction that prompted the alarm displays.

4.7 Locking and unlocking pumps

It is possible to lock a pump in the MultiFeed strategy. This can be done if the user does not want to add the substance that the pump is feeding for a period of time, or to do maintenance on a pump or container. To lock a pump:

1. Open the faceplate from the Main screen.
2. Click the icon of the pump to be locked. A confirmation pop-up screen displays (Figure 4.54).

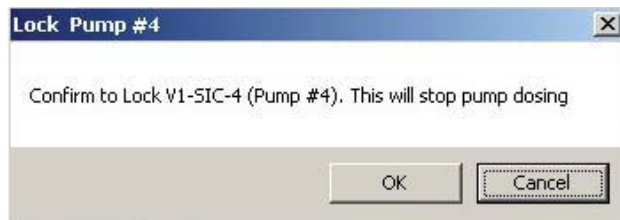


Figure 4.54. Lock Pump confirmation pop-up.

3. Click **OK** and a lock symbol will appear on the pump icon (Figure 4.55) and on the MultiFeed box on the Main screen.



Figure 4.55. Lock symbol next to pump icon.

4. The lock function is a toggle. Click the icon again to unlock the pump. Another confirmation pop-up screen will display (Figure 4.56).

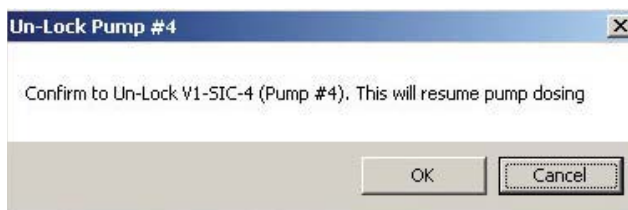


Figure 4.56. Unlock Pump confirmation pop-up.

5. Click **OK** to resume pump operation and remove the lock symbol.

4.8 Setting up MultiFeed dosing

Dosing is set up from the MultiFeed box on the Configuration screen. It is possible to have four pumps per scale, including a virtual pump, which is used only if needed as a placeholder in the sequence. Pumps are added to each scale as described above.

Note: When adding a pump, be certain to click **Apply Values**.

1. After a pump is added, click the pump icon to open the screen to allow definition of the dose type.
2. Click the dose type to open the drop-down menu.
3. Choose one of the four dose types: Continuous, Bolus, pH base, or pH acid (Figure 4.57). Click **OK**.

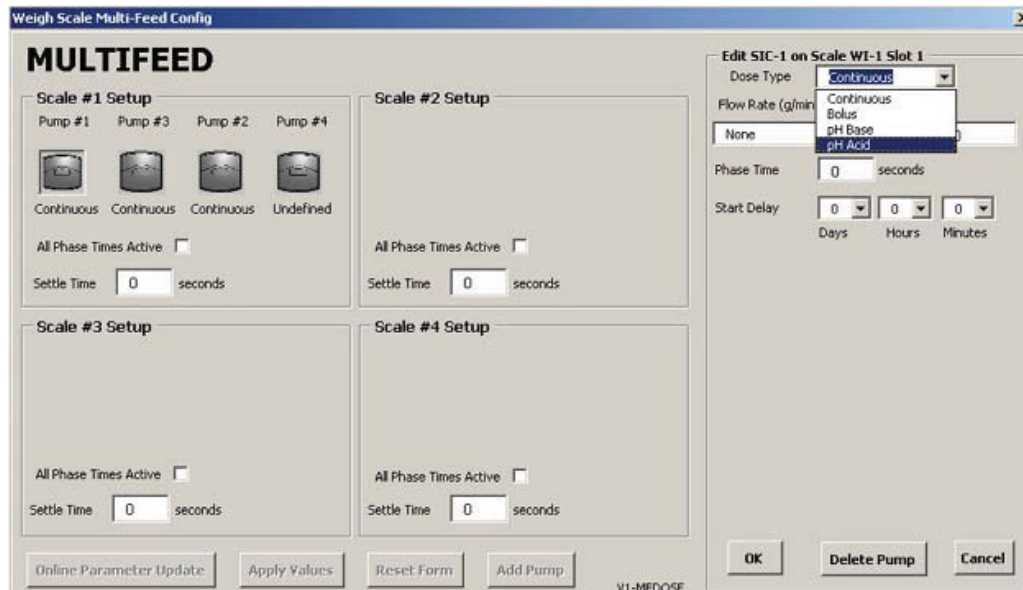


Figure 4.57. Selecting dose type.

4.8.1 Continuous feed

The “continuous feed” can be set to deliver either a specific dose rate, according to the pump setup, or can be linked to other outputs, such as calculations or comparisons.

1. Select the dose flow rate either from the drop-down menu or by typing in a value.
 - The “Phase Time” is the maximum length of time the pump can operate; the pump may run for a shorter time.
 - The “Start Delay” is the initial time delay before the first activation of the pump and is not repeated for subsequent pump activations.
2. After the dose parameters are entered, click **OK** to close the edit screen. Click **Apply Values**.

Note: Changes are not saved until **Apply Values** is clicked.

4.8.2 Bolus feed

The “bolus feed” (Figure 4.58) is similar to the “continuous feed,” except that the dose is by delivered weight instead of rate, and the weight addition may be repeated at a specified repeat time.

The screenshot shows a dialog box titled "Edit SIC-1 on Scale WI-1 Slot 1". It contains the following fields and controls:

- Dose Type:** A dropdown menu set to "Bolus".
- Amount to add (g):** A dropdown menu set to "None" followed by "or" and a text input field containing "0".
- Phase Time:** A text input field containing "0" followed by the label "seconds".
- Start Delay:** Three dropdown menus for "Days", "Hours", and "Minutes", all set to "0".
- Dump Mode:** A dropdown menu set to "Continuous".
- Dose Duration:** A text input field containing "0" followed by the label "seconds".
- Repeat Time:** Three dropdown menus for "Days", "Hours", and "Minutes", all set to "0".
- Number of Doses:** A text input field containing "1".
- Buttons:** "OK", "Delete Pump", and "Cancel" buttons at the bottom.

Figure 4.58. Bolus feed dose type.

As with the continuous feed, the user can select either a weight to add, or link the addition to calculations or logic by making a selection from the drop-down menu.

The “Phase Time” and “Start Delay” are the same as for the Continuous Feed mode. The Bolus Feed dosing is illustrated in Figure 4.59, and contains the following elements:

- **Repeat Time** is the interval between each bolus.
- **Number of Doses** is the number of times the pump will be activated per cycle.
- **Dose Duration** is the time the user calculates will be needed for the selected amount to be delivered.

This value should be shorter than the phase time so that if additional dose time is needed, it will not overrun the phase time. Any dosing that is in progress when the phase time expires will be stopped.

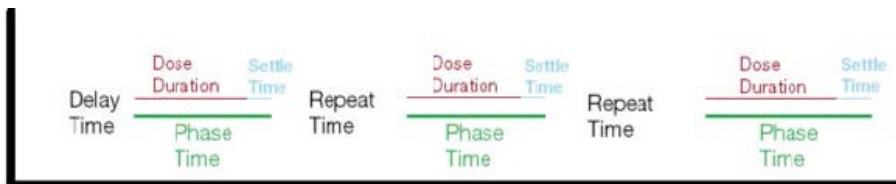


Figure 4.59. Bolus Feed diagram.

There are two options for the Dump Mode: “Continuous” and “Dump” (“Dump” is shown in Figure 4.60).

Figure 4.60. “Dump” selected as Dump Mode.

The “Continuous” mode uses the pump calibration to calculate the speed needed to deliver the selected dose within the Dose Duration time. If the dose has not been delivered, the pump will continue to run.

When “Dump” is selected for the dump mode, the user must specify the pump “Run Speed,” after calculating what pump speed will be needed to deliver the required dose within the Dose Duration time. The Dose Duration is an estimate. If the dose is completed prior to the time limit, it will stop. If the dose is not completed, the pump will continue to run past the time limit.

The Low Flow Time at End of Dose allows the pump to run slowly for a specified period, which reduces the possibility of over-delivery.

4.8.3 pH base and pH acid

The pH base and pH acid feeds operate in two modes. In the first mode, acid and base feeds are continuously added until the pH controller error (measured as PV minus SP) is minimized, or until the phase time is reached. These feeds will be sequenced with the other pump phases. The pH controller must be in AUTO mode for this mode.

In the second mode, the pH base or pH acid feeds will interrupt the sequence of pump operations to add acid/base using the pH controller until the measured pH reaches the “Interrupt Cascade SP.” The pH controller action is as discussed previously. The “Interrupt Cascade SP” is measured as a percent of the pH base or pH acid feed pump range.

For example, assume the “Interrupt Cascade SP” is set at 5% and the base feed range is 1800 g/hr. If the setpoint, as remotely set by the pH controller, is > 90 g/hr, then the base pump will operate. The pH controller output range is typically -100 to +100. If the 0 to +100% output is translated to a smaller base pump range of 0 to 1000 g/hr, then a pH controller output of +9% will activate the base pump.

4.8.4 Pump sequence

Whatever the dose type or dump mode selected, the pump will shut down at the end of the phase time, even if the programmed dose has not been delivered.

When more than one pump is associated with a scale, the system will cycle each pump once, then repeat.

The user must consider the total time for the entire sequence. The total time consists of the dose duration phase time plus the settle time for each pump. The settle time allows the scale weight to equilibrate before being read. The first cycle for each pump may be delayed if a delay time has been programmed. Figure 4.61 shows two cycles of a representative MultiFeed strategy.

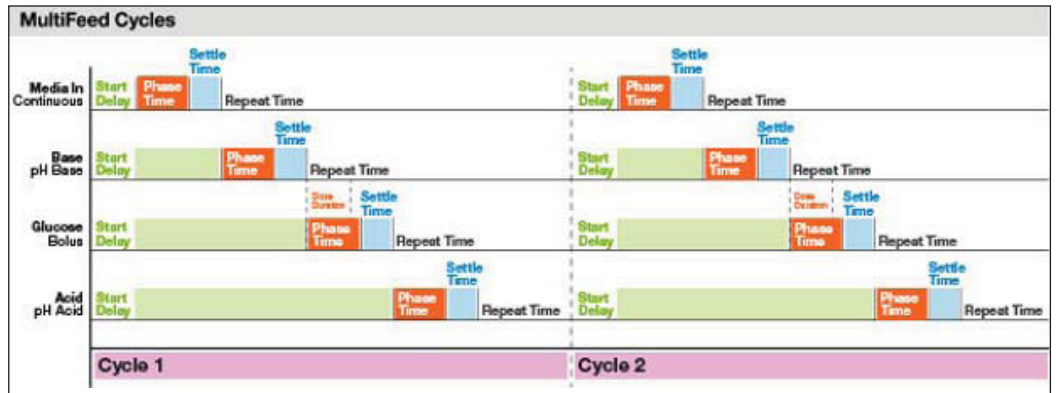


Figure 4.61. MultiFeed cycles.

For Bolus pumps, the subsequent pump starts are restricted by the “Repeat Time.” For example, assume that Pumps 1–3 deliver continuous dose and Pump 4 delivers a bolus dose. The total first cycle time for Pumps 1–5 is 45 minutes. If Pump 4 has a repeat time of one hour, it will not start on the second cycle but will wait for the third cycle to run.

The pH acid and pH base pumps will start in the cycle sequence as shown in Figure 4.61. At the end of each pump phase, the pH is checked to verify that the “Interrupt Cascade SP” has not been exceeded. If the SP has been exceeded, then either the acid or base pump as required to balance the pH will start. The acid and base pumps will not interrupt the current cycle, nor will they be the first pump cycle. The pH monitoring will begin at the end of the first phase of the first cycle. This is shown in Figure 4.62, where an acid pump interrupt occurs in the first and third cycles. A base pump interrupt occurs in the third cycle.

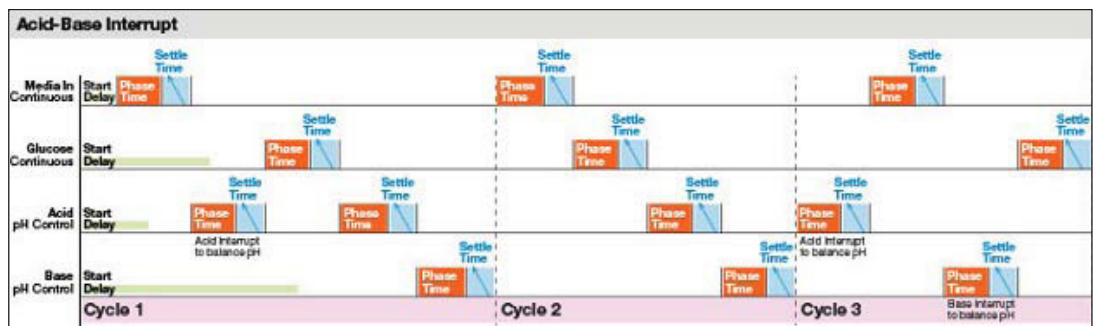


Figure 4.62. Acid-base interrupt.

4.8.5 Pump totals

Totals and other information are available from the totals section of the pump control boxes on the Main screen.

Clicking the “Totals” section at the lower edge of the box will open the Faceplate box (Figure 4.63).

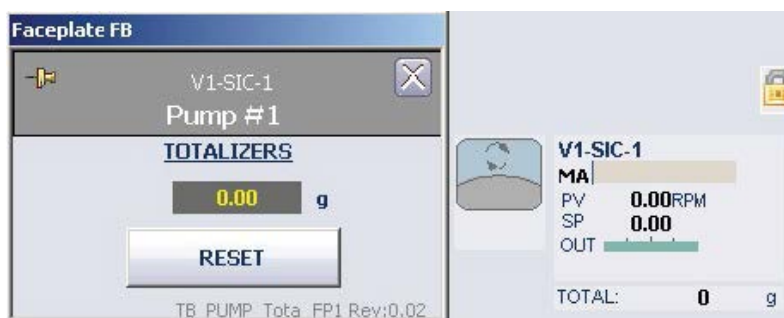


Figure 4.63. Faceplate box.

When feeding very small doses, pumps may be required to run at speeds below their minimum continuous feed. If so, Pulse Width Modulation (PWM) of the pump can be used with the Time Proportioning Settings.

4.8.6 Starting MultiFeed pumps

1. On the Main screen, click the MultiFeed box above the pump boxes to open the faceplate (Figure 4.64).



Figure 4.64. MultiFeed faceplate.

- After all the pumps are set up and their limits are established, click **Start** at the top of the faceplate to activate the MultiFeed module. Click **Stop** when the run is finished, or the MultiFeed function is no longer needed. After **Start** is clicked, the button will change to “Hold” (Figure 4.65).



Figure 4.65. “Hold” button appears after clicking “Start.”

The “Hold” function will immediately stop the entire process and trigger an alarm, which is shown as a red bar in the Alarm section at the bottom of the faceplate. When **Hold** is clicked, the button changes to “Resume” (Figure 4.66).



Figure 4.66. “Hold” button changed to “Resume.”

3. After resolving the situation that prompted the Hold, click **Resume** to start the process again, wherever it was halted. Clicking **Resume** inactivates the alarm.
4. To remove the alarm, click **Acknowledge Alarm**. In addition, when **Resume** is clicked, the button changes again to “Hold,” and the interface indicates that the process has started (Figure 4.67).

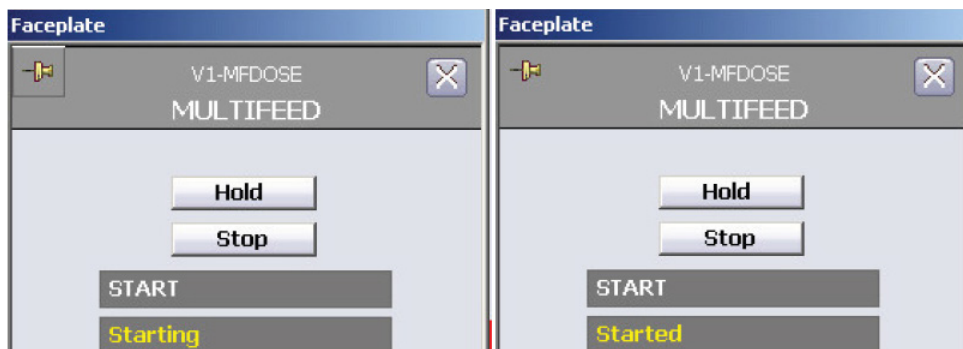


Figure 4.67. “Starting” and “Started” statuses shown.

When **Hold** is clicked, the timer continues, so the “Elapsed Time” will continue to increase. The timer can be stopped, but doing this can cause undesired consequences.

Because “Hold” stops the system immediately, any phases that are running at the time will resume when **Resume** is clicked, regardless of whether the timer runs or not. However, any future processes might be affected.

If the timer is stopped when **Hold** is activated, the user can become unaware of how much time elapses during the hold.

Consider the options and ramifications carefully, and possibly discuss the matter with your Thermo Scientific representative before deciding whether to stop the timer during a hold.

5. To change the setting, open the Configuration screen and select the “Online Parameter Update.”
6. Verify that the correct vessel is displayed. Figure 4.68 shows “Vessel 2” selected.
7. Under the “Module” column (first from the left), locate and click the string “**Vx-MFDOSE,**” with x being the vessel number (Figure 4.68).
8. Under the “Category” column, click “**DEFAULT_MF**” (Figure 4.68).
9. Under the “Parameters” column, listed in the “Name” column (third from the left), locate the string “**/FS_CTRL1/TMR_RUN_IN_HOLD.F_CV**” (Figure 4.68).

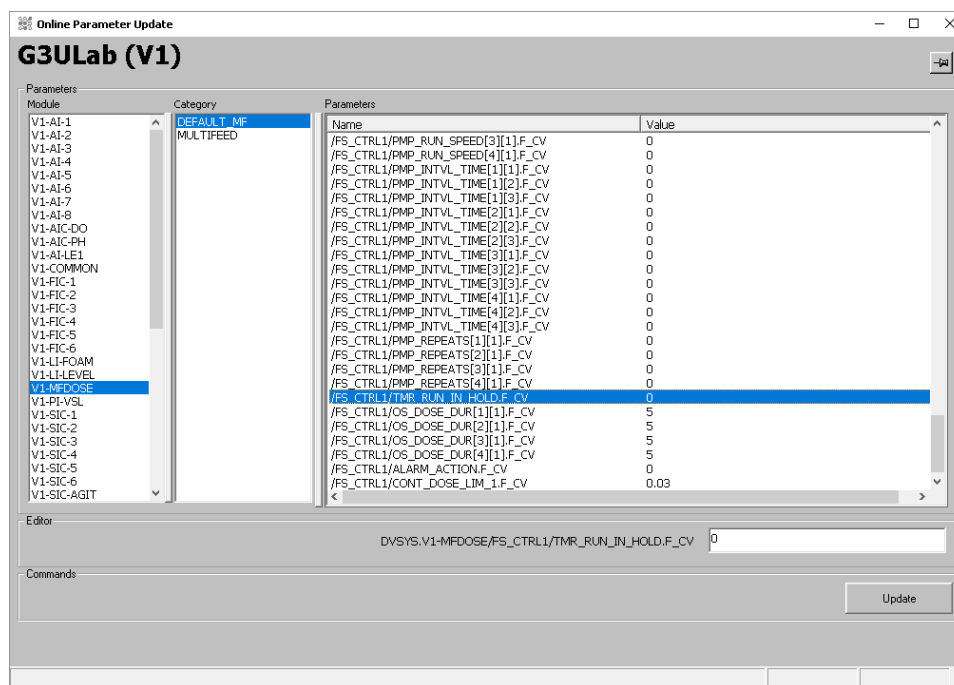


Figure 4.68. Vessel 2 options selected: Module, Category, and Name.

The following values are available for this name:

- 0 (zero): Stops the timer when “Hold” is activated
- 1 (one): Allows the timer to continue running

10. Enter the selected value and click **Update**.

4.9 Weight control setup (S.U.B. vessels only)

The weight control in larger vessels provides the same function in large systems as the level control in smaller systems. The system should be calibrated on installation; professional calibration services are recommended. If calibrations are performed manually, they are done from the faceplate in the same way as any other parameter in the system.

On the Scale Controls tab, select either **Gross** or **Net** readings (Figure 4.69).

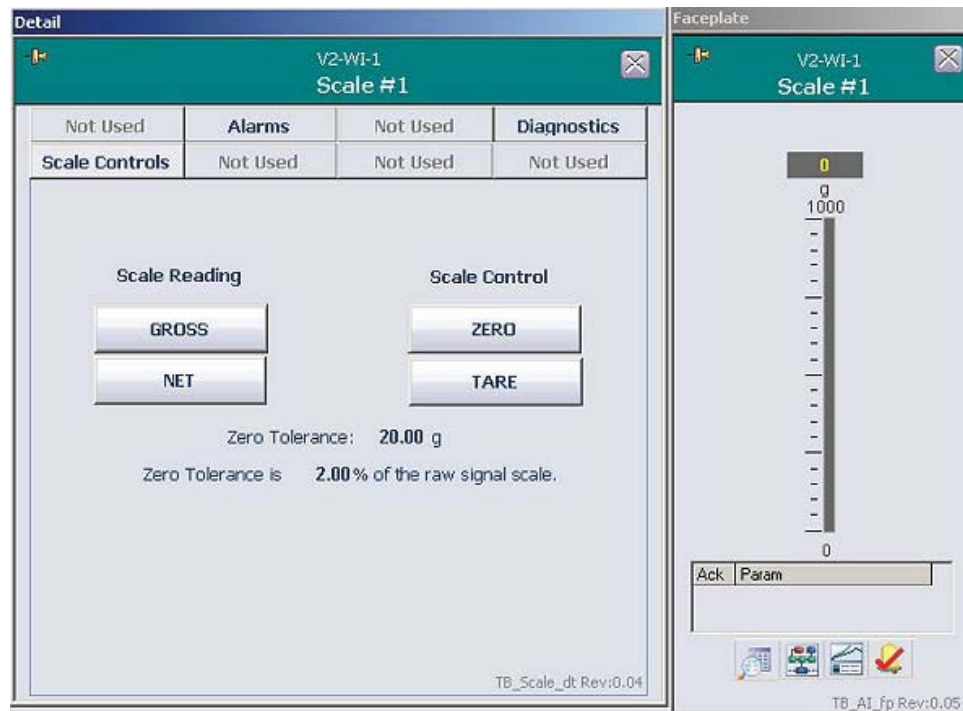


Figure 4.69. Gross and Net reading options shown for Scale #1.

Note: Allow at least 15 seconds after selecting a function to perform another action. This applies only to the vessel weight functions. Set the limits, alarms, and interlock, as for any other parameter.

4.10 Foam/level control setup

The foam/level control prevents the liquid in the vessel from overflowing, or foam in the vessel from rising high enough to block inlets/outlets. When the sensor detects foam or liquid, it waits a set period of time (called a splash delay) and then either sounds an alarm or triggers the foam control loop.

Clicking on either of the boxes opens the faceplate. In this case, the faceplate allows the user to view and acknowledge alarms, review the sensor diagnostics, and open the Control Studio and the Process History View.

To set up foam and level controls, click the appropriate box on the Configuration screen (Figure 4.70).

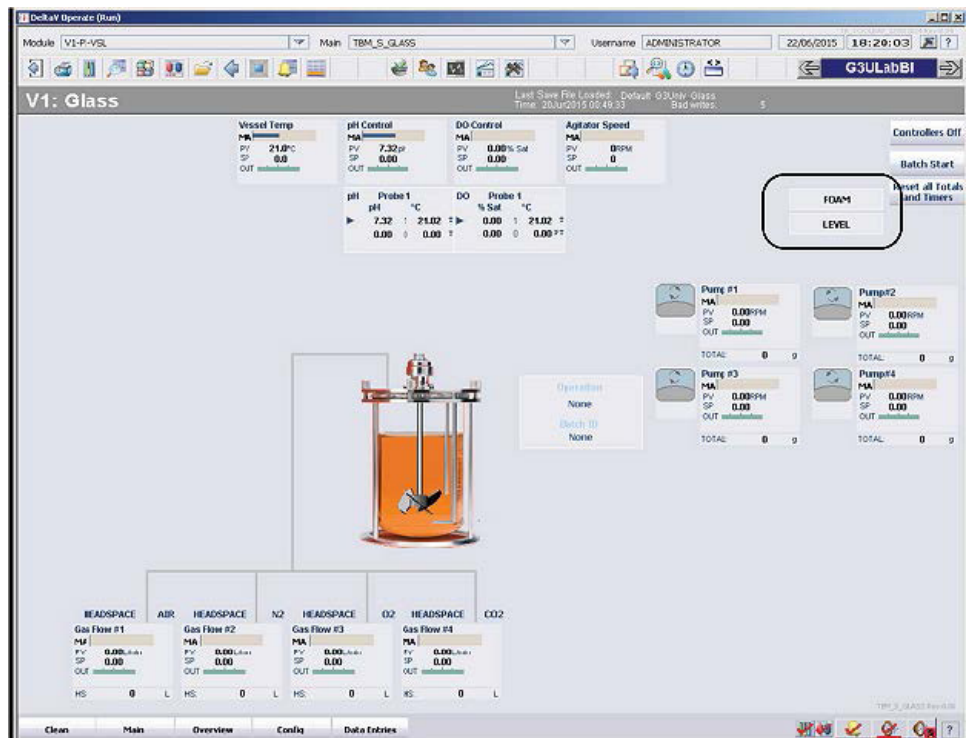


Figure 4.70. Foam and level buttons shown on Configuration screen.

Clicking either box will open the configuration form for the parameter (Figure 4.71). Figure 4.72 shows the “Foam” form, and Figure 4.73 shows the “Level” form.

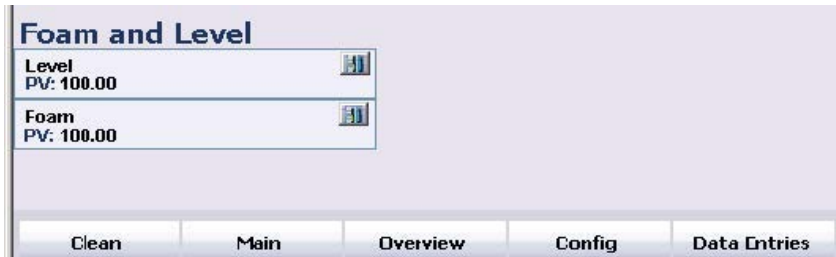


Figure 4.71. Foam and level detail.

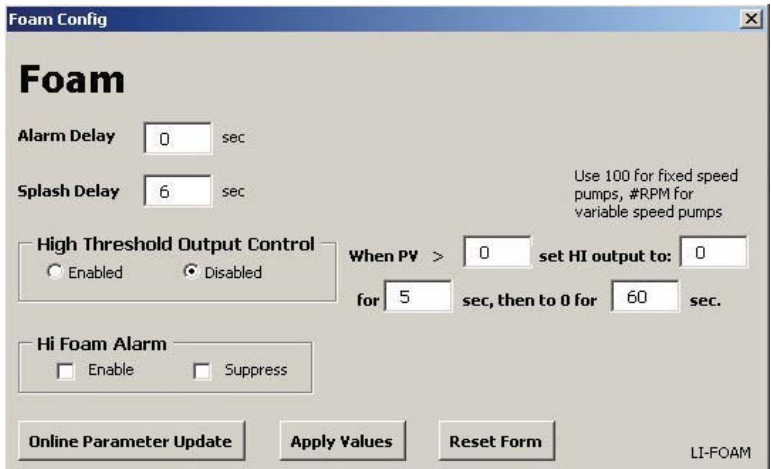


Figure 4.72. Foam configuration form.

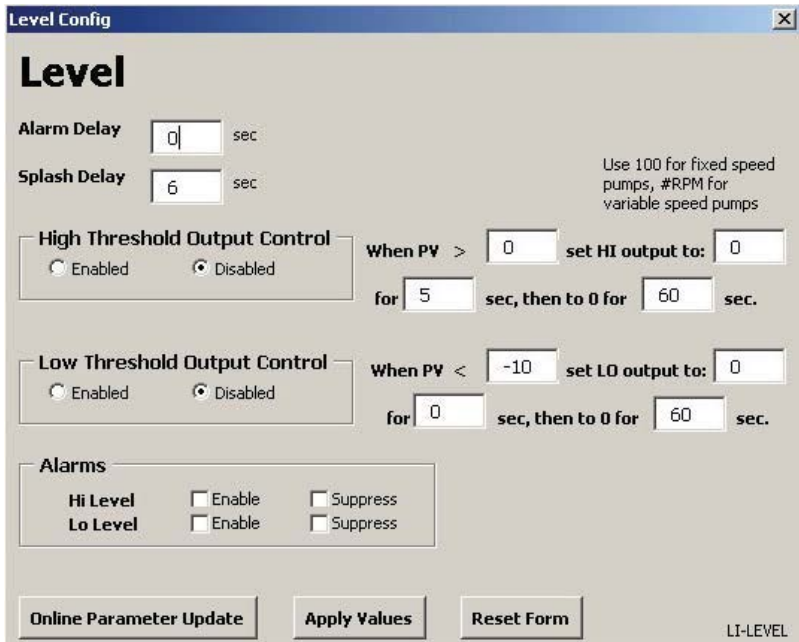


Figure 4.73. Level configuration form.

Both configuration forms allow the user to set the following:

- **Alarm delay**—sets the time (in seconds) before an alarm is activated (if the alarm is enabled).
- **Splash delay**—sets the time (in seconds) during which the alarm is prevented from being triggered, which allows a temporary contact with liquid.
- **Threshold control**—allows the selection of an action when the process value (PV) exceeds the selected range. The controller output can be set to a specified time, with a specified interval for mixing before the controller is activated again.
- **Alarms**—can be enabled or suppressed as the user prefers.

Click **Apply Values** to save the settings. The PV will be displayed on the configuration page, as shown in Figure 4.73.

4.11 Key parameter setup

This user-defined function makes essential values available on the Overview screen so they can be easily monitored (Figure 4.74).



Figure 4.74. Overview screen.

1. On the Configuration screen, click **Key Parameter Setup** (Figure 4.75) to select parameters to be displayed using the drop-down menus.

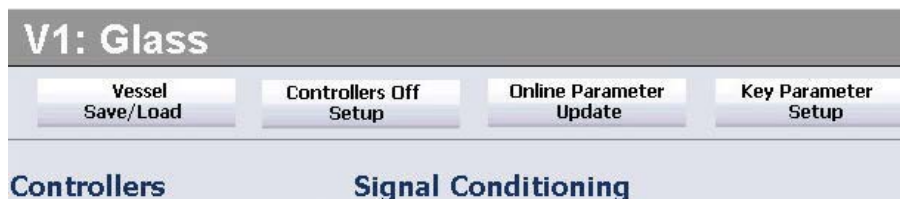


Figure 4.75. Foam and level detail.

2. If fewer than eight parameters are required for display, leave the default setting at “None” (Figure 4.76).
3. Click **Apply Values** to save the setting (Figure 4.76).

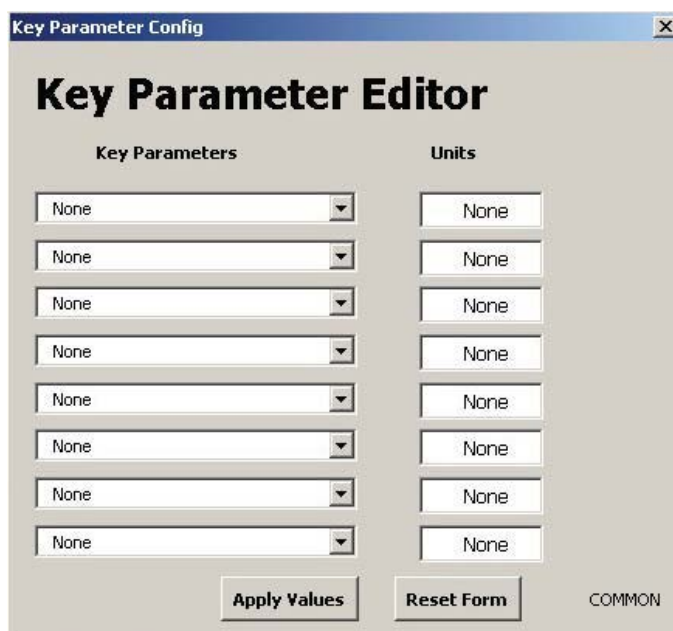


Figure 4.76. Key parameter editor screen.

4.12 Saving the file

Activating the control loops starts the system, so it should now be running, but none of the parameters have been saved. Saving the files is important for the safety of the system, and for future use.

1. From the Configuration screen, select **Vessel Save** and then **Load**.
2. Click **Vessel Save** and then select **Setup** from the drop-down menu. Select a name according to facility protocol and then click **Save** (Figure 4.77).

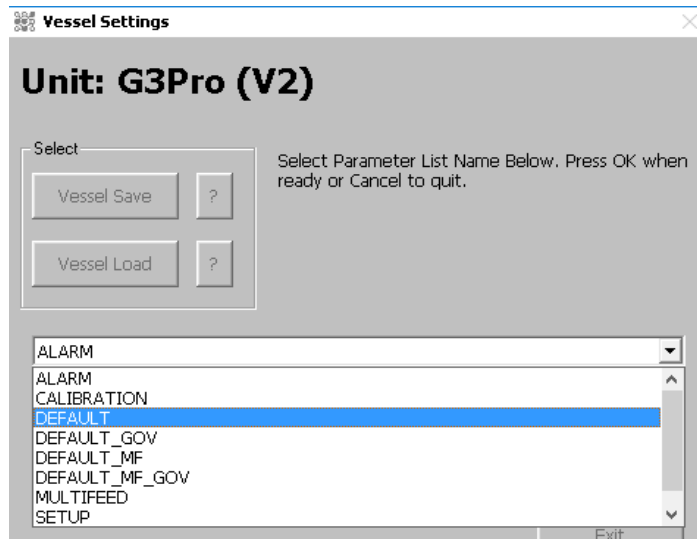


Figure 4.77. Choose “Setup” from menu after clicking “Vessel Save.”

Note: Saving a Default file will not save the calibrations, modes, or setpoints, although it will save all of the other parameters discussed previously. Saving a Default_MF file will save MultiFeed parameters, as well as those saved by the Default file. Calibration records are saved in separate records, and will be saved regardless of whether they are saved here, but the user may wish to save calibration files here, as well.

3. Click **Vessel Save** again, select the “Default_MF” file (Figure 4.78). Select a name according to facility protocol and save the default file.

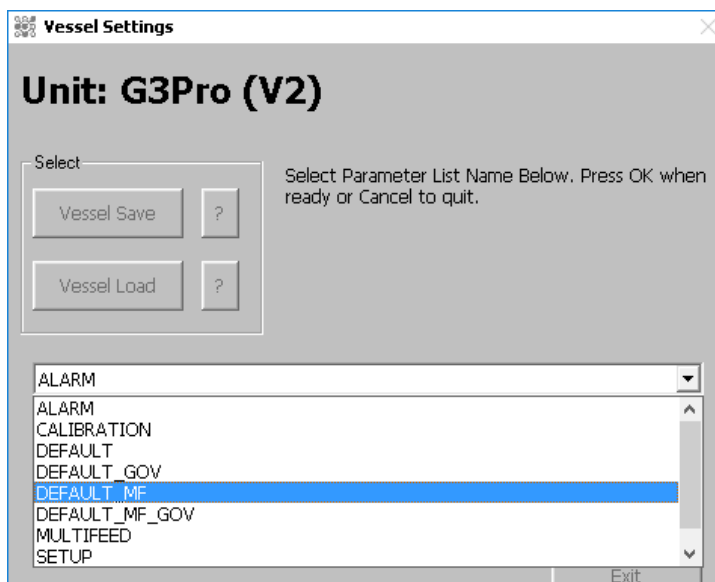


Figure 4.78. Default_MF file selected from drop-down menu.

Note: If the facility has no protocol for naming files, we strongly recommend using a unique identifier, such as the date and/or a lab notebook reference. This makes it possible to easily track files for future reference. The system does not allow duplicate names for the same vessel.

A good example for a name would be “‘Product name’-V1-2015-5-15-Model-Default.” A wise practice is to include the name of the base file (“Default,” in this case) to identify the file that the named file was created from.

There is no limit to the length of the name string.

4.13 Starting the run

The system starts when all control loops are set up and each of the associated faceplates is set to AUTO.

We recommend that the system be allowed to run for a period of time to ensure that all control loops are functioning properly before inoculation. The length of time will depend on the volume of the bioreactor and the complexity of the control loops.

If the “Batch Start” button is in use, it can be started when the system is inoculated. Note that the “Batch Start” button only starts the timer; it doesn’t start the run, itself.

5

Maintenance

Chapter contents

- 5.1 Backup and recovery
- 5.2 Computer cleanup
- 5.3 Power loss

5.1 Backup and recovery

Archiving, backup, and disaster recovery procedures should be performed by Automation/IT department personnel, in accordance with their SOPs for the system. The following files should be backed up:

- Exported configuration database (FHX text files)
- Native configuration database (objectivity database)
- VCAT SQL database
- DeltaV admin database backups
- Custom DeltaV operation displays, faceplates, and detail displays
- System-supplied DeltaV operation displays and templates
- Historical configuration (charts)
- Historical data archives
- TruBio folder (in the DeltaV/DVData folder)

The system can be designed to automatically and regularly back up data that is stored on the server or on local PCs, without shutting down the system.

If data backups are not automated, they should be performed at specified time intervals.

When data is archived, the system has the ability to quickly restore data with a minimal recovery time. If a method is in place to completely restore the main system in the event of a catastrophic failure, successive restores other processes (i.e. the operating system, application, configuration, and data) should not be required.

In addition, the system has archival capability to move data from primary storage to long term or permanent storage. The archived information can be easily retrieved from primary storage for data analysis if desired.

The system includes diagnostic functions that are used to ascertain the overall status of the system.

5.2 Computer cleanup

Routine computer maintenance is generally the responsibility of the local Automation/IT department. However, if the computer system is slow, the user may consider the following suggestions.

- Check the computer disk space. To access this information, click the “Start” button on the lower left of the monitor screen, then click “Computer.”
- Perform a disk cleanup. Click the button below the pie chart showing available disk space.
- If the free disk space is *greater than 20%*, do the following, depending on the computer in question:
 - **On the ProPlus workstation:** access the DeltaV Database Administration menu and run a DeltaV Database clean.
 - **On the App station:** ensure that routine database backups are being performed.
- If the free disk space is *less than 20%*, do the following:
 - **On the ProPlus workstation:** remove all old files, defragment the hard drive, and run a DeltaV Database clean.
 - **On the App station:** remove old files by exporting old datasets to another location. If the system is idle, defragment the hard drive.

If the previous steps do not solve the problem, or if you are uncertain about performing such maintenance, consult your IT personnel or your service representative.

5.3 Power loss

Response to power loss depends on the part of the system that suffers the loss. The Thermo Scientific TruLogic control unit incorporates an uninterrupted power supply (UPS) to protect the system in case of brief power interruptions.

If power is lost to the DeltaV controller, perform a Vessel Load and manually restore the vessel to the appropriate settings.

If power is lost to the bioreactor/fermentor I/O tower, all equipment (pumps, MFCs, agitator) stops, and must be manually restarted after power is restored.

In case of a general power loss that extends beyond the UPS capability, the computers must be rebooted, the TruBio and TruLogic systems restarted, and all systems must be reset. In such a case, consultation with your service representative is strongly recommended.

In the event of a brief interruption of power, the Main screen might display a warning about pump mapping. This results from the pumps resetting after power restoration and the message disappears after a few seconds. Do not attempt to modify pump settings during this time. If the message persists for more than five minutes, contact your service representative.

6

Data storage

Data storage is part of the 21 CFR Part 11 (cGMP) requirement. TruBio Software, version 5.0 data storage is based on the DeltaV Continuous Historian and satisfies the cGMP requirements.

Click **Data History** for any parameter at the bottom of the faceplate to open a display of the parameter history. Options are available to select the length of time covered by the record. The data can be printed, or copied and pasted into Microsoft™ Word or Excel™ files, to create hard copy documentation.

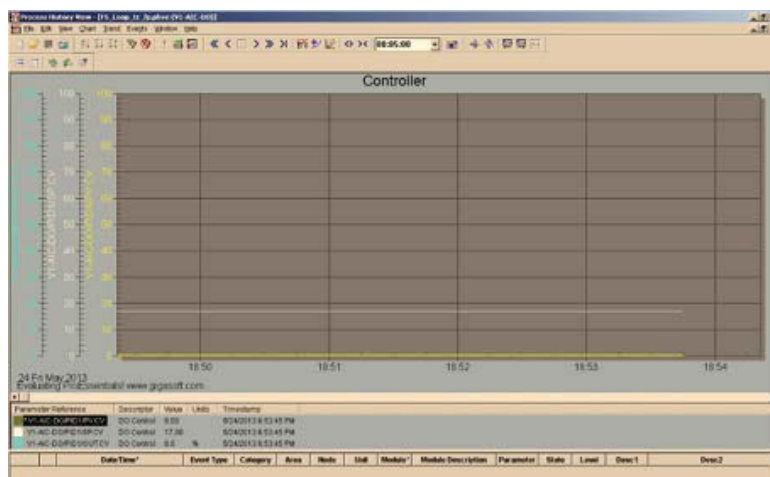


Figure 6.1. Display of parameter history.

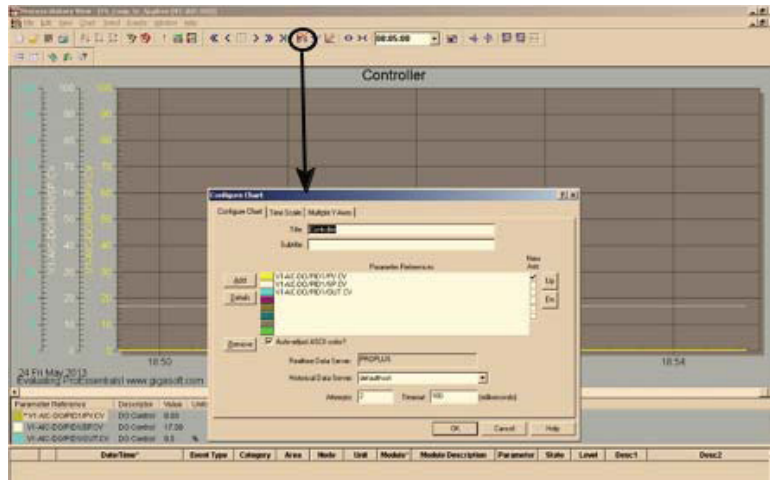


Figure 6.2. Display of parameter history detail.

The DeltaV Continuous Historian subsystem is used for the continuous collection and storage of process data. It is included with TruBio Software, version 5.0 and can be configured to perform the following:

- Create a single historical database
- Open an unlimited number of trend screens with up to eight user-definable values per screen
- Display trends either horizontally or vertically
- Display either process trends, alone, or a combination of process trends and the associated event log
- Display trends in seconds, minutes, hours, days, or weeks

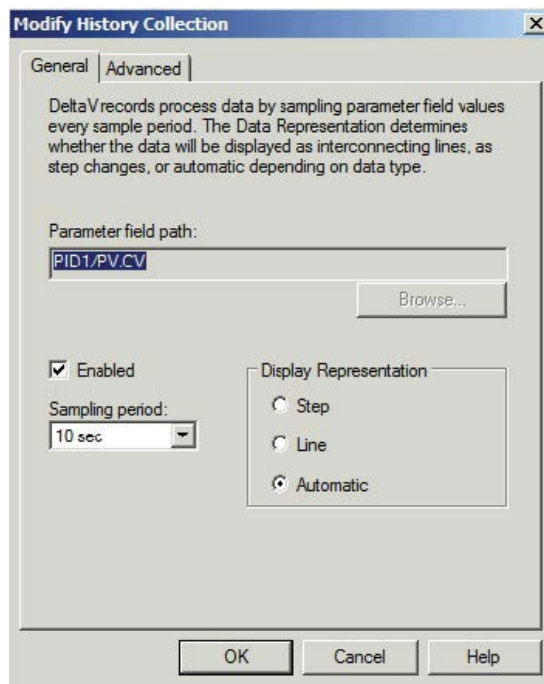


Figure 6.3. General settings for modifying history collection.

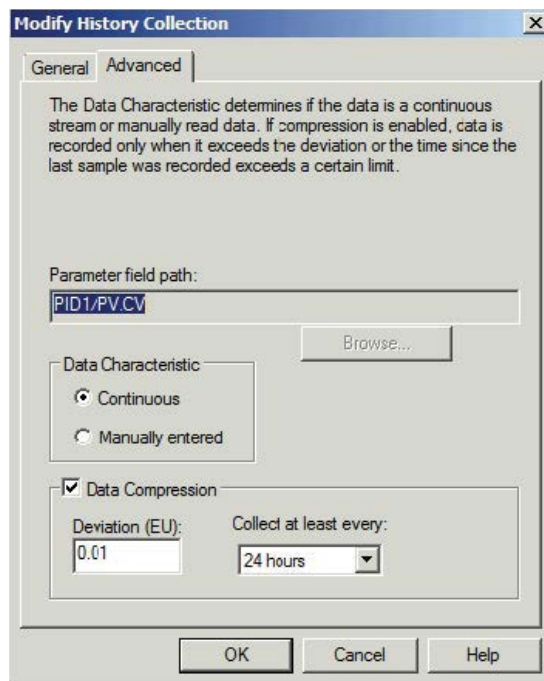


Figure 6.4. Advanced settings for modifying history collection.

Table 6.1 shows history collection properties for parameters in the DeltaV system.

Table 6.1. History collection properties for DeltaV parameters.

General settings	Description
Parameter field path	The path of the module parameter whose history is being collected.
Enable	Activates collection of field values specified in the parameter field path.
Display representation	<ul style="list-style-type: none"> • Step: Displays the values as step changes on the trend chart. Step representation is typically used for discrete values. • Line: Displays the data collected with point-to-point connection. • Automatic: Determines the representation based on data type.
Sampling period	Available sampling frequencies are 1, 2, 5, 10, 30, and 60 seconds, and 5 minutes.
Advanced settings	Description
Data characteristic	<ul style="list-style-type: none"> • Continuous: Continuously-collected data, represented with interconnecting lines • Manually entered: Values entered by a user, displayed as markClics on the trend, with no interconnecting lines.
Enable (data compression)	Enables data compression.
Collect at least every (data compression)	Controls the maximum time between stored values, even if values change very little. Options are 15 minutes, and 1, 4, 8, 24, and 72 hours.

To exit the historian view, click **X** in the upper right corner twice. This will not close the TruBio program.

7

General ordering information

Chapter contents

- 7.1 Ordering and support contact information
- 7.2 Technical support

7.1 Ordering and support contact information

In the Americas and Asia

1726 Hyclone Drive
Logan, Utah 84321
United States
Tel: +1 435 792 8500
Email: customerservice.bioprocessing@thermofisher.com

In Europe

Unit 9 Atley Way
Cramlington, NE 23 1WA
Great Britain
Tel: +44 (0) 670 734 093
Fax: +44 (0) 670 732 537
Email: customerservice.bioprocessing@thermofisher.com

7.2 Technical support

Technical support for the TruBio Software, version 5.0 platform is available in a variety of formats. Some or all of the following may be appropriate, depending on individual experience and circumstances.

Technical service hotline and email

Contact your Thermo Fisher Scientific sales representative for general product pricing, availability, delivery, order information, and product complaints.

Call +1 435 792 8500 (United States) or +44 (0) 670 734 093 (Europe, U.K.) for direct and immediate response to overall product questions, and product technical information (Technical Support). You can also contact Tech Support by emailing:
techsupport.bioprocessing@thermofisher.com

Initial setup and operation

Appropriate technical support is available to assist in the initial setup and operation of the system. If you require assistance in setting up and operating your TruBio software system, please inquire at the time of purchase.

Training

Training can be provided for start-up and operation of the TruBio software system. Contact your Thermo Fisher Scientific sales representative for more information.

Appendices

Appendix contents

Appendix A	Faceplate detail
Appendix B	Details of the Configuration screen
Appendix C	Smart Device information
Appendix D	Time proportioning of pumps
Appendix E	Electrical connections and Controllers Off function
Appendix F	Perfusion
Appendix G	Alarms
Appendix H	Chart Builder feature
Appendix I	5:1 Turndown add-on
Appendix J	Agitator speed governor add-on
Appendix K	Bag integrity add-on
Appendix L	TruBio Discovery

Appendix A—Faceplate detail

Figure A.1 below details the components of the faceplate.

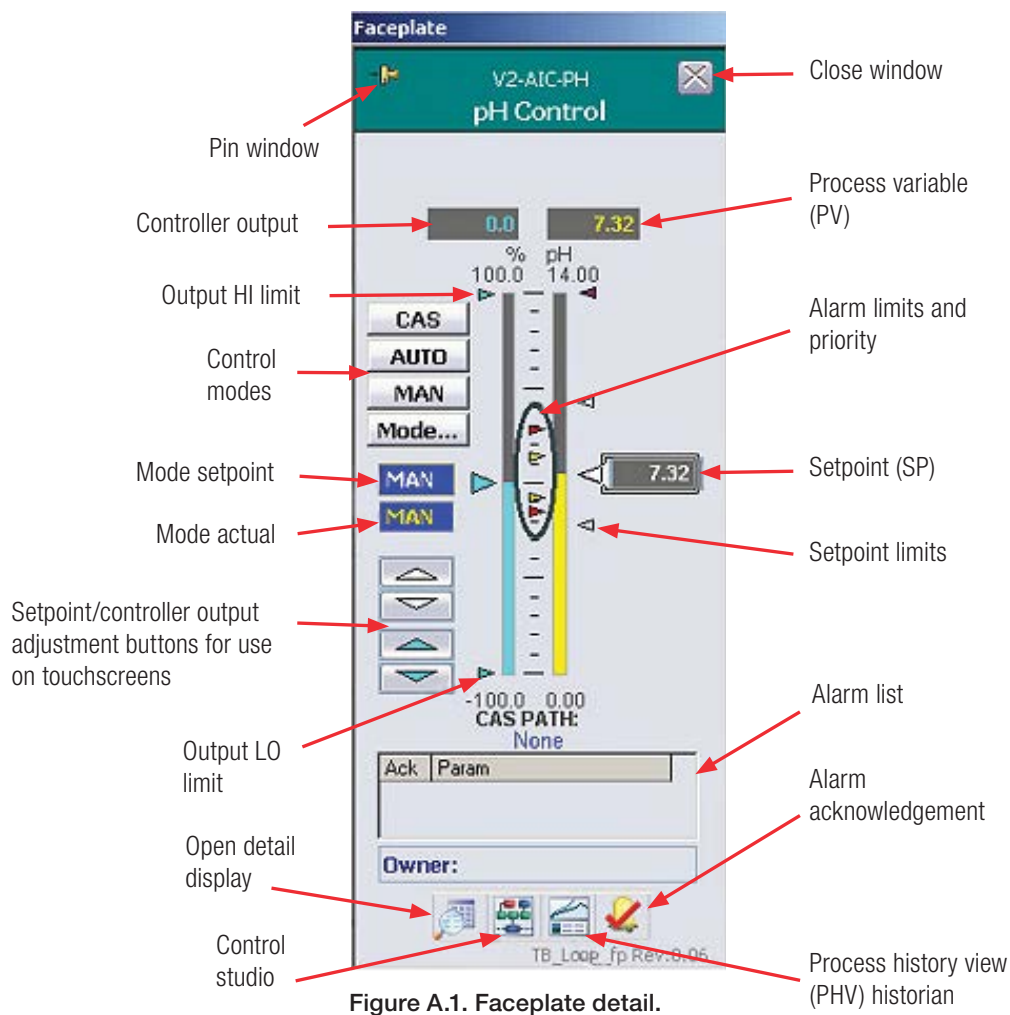


Figure A.1. Faceplate detail.

The **faceplate** is opened when the user clicks a control box on the Main screen. A faceplate includes the following features:

- The **pin window button** allows the user to open multiple faceplates at once. If a faceplate is no longer needed, it can be closed with the “Close Window” icon.
- The **process variable** or **process value (PV)** is the value of the parameter in real time.
- The **setpoint** is the user-defined target value for the parameter.

- The **setpoint limits** define the range within which the setpoint is established. This prevents the setpoint from being inadvertently changed to a non-survivable value. The usual limits are the range outside of which the cells in the bioreactor will not survive.
- The **alarm limits** are set within the setpoint limits and define when an alarm will be triggered. There are four alarm levels: Hi-Hi, Hi, Lo, and Lo-Lo, and are set in the Detail screen, discussed below.
- The **alarm list** details any alarms that are active for the parameter that is referenced by the faceplate. If an alarm has been triggered, it is acknowledged by clicking the “Alarm Acknowledgement” icon. If the system includes an audible alarm, that is silenced by clicking the button in the lower right corner of the screen.
- The **controller output** shows the activity of the control loop maintenance functions in percentage of the maximum. For example, if the faceplate for DO is open and the controller output shows 20%, it may mean that the MFC that is controlling the air flow is running at 20% of its maximum output.
- The **output HI** and **output LO** limits specify the percentage of the permitted maximum output. Maximum output is defined as the limit of the agitator or pump. For example, if the maximum output of a pump is 200 rpm, the output HI limit may be set for any value up to 200. We recommend that an output controller not be run at either the minimum or maximum value unless necessary, and only for brief durations.
- The white and blue **up/down arrows** are one method for adjusting the setpoint and the controller output values.
- The **control mode** is used to select whether a mode is under manual control, automated control, or part of a cascade. In manual mode, the user must maintain control of the parameter. In auto or cascade mode, the system controls the parameter.
- The **open detail display button** opens the detail screens for calibration, alarm limits, and probe selection. These are discussed in more detail below.
- The **Control Studio icon** provides access to DeltaV tools. More information on DeltaV tools is available through DeltaV Books Online.

- The **Process History View icon** is similar to parameter trending, but can show more than one parameter at a time. For example, a user may wish to examine both pH and temperature together.

The following screens are opened from the “Detail” icon.

The **Calibration** tab (Figure A.2) enables the user to calibrate the sensors for the parameter that is associated with the faceplate. Electrochemical calibration is the normal procedure. If a virtual transmitter is part of the pH or DO control loop, the user will have the option to run the calibration through the virtual transmitter.



Figure A.2. Calibration tab details.

The “Alarms” tab (Figure A.3), in Trubio Software, version 5.0, combines the parameters of what were the “Alarms and Limits” tabs in previous TruBio Software versions. In this tab, the user can set and enable the alarms.

The “Probe Dev” limit is used when there are multiple probes in use, and will trigger an alarm when the probe readings differ by the value set here. The “SP Limits” have been moved from the Alarms tab to the Tuning tab, which is discussed later in this section.

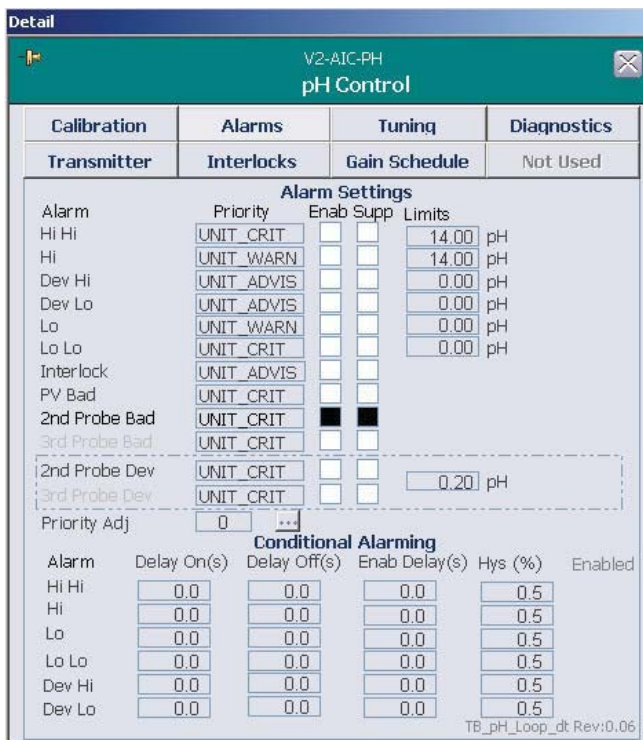


Figure A.3. Alarms tab details.

The **Tuning** tab (Figure A.4) allows the user to view and change the tuning parameters of the control loop. For modules that support deadband local override, the user can also enable or disable the deadband local override function and enter upper and lower deadband limits, as desired.

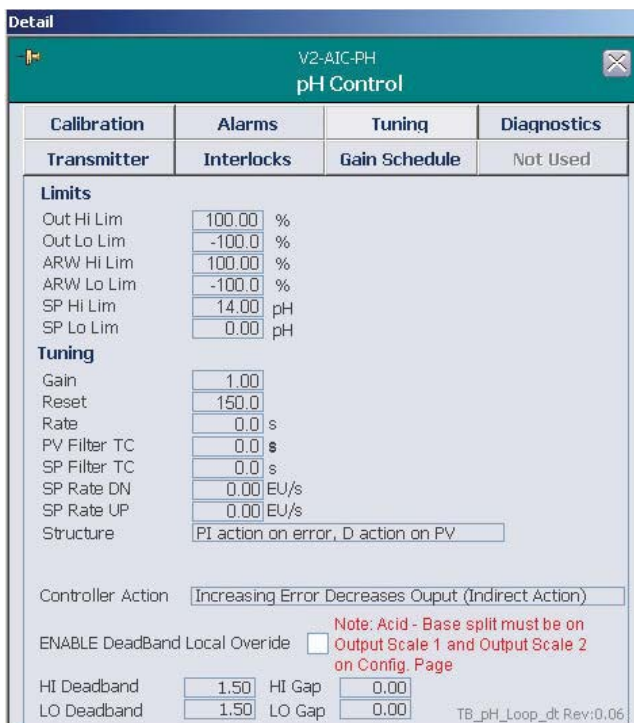


Figure A.4. Tuning tab details.

The Tuning tab includes the following parameters:

- **Out Hi/Lo Lim:** Limits the output of the controller.
- **ARW Hi/Lo Lim:** Designed to prevent an over-correction if the setpoint is changed.
- **SP Hi Lim and SP Lo Lim:** Limits outside of which the contents of the S.U.B. would be irrevocably compromised. Setting these limits prevents the SP being accidentally reset to a value that threatens the process.
- **Gain:** Gain setting of the PID loop.
- **Reset/Rate:** Time constants of the PID loop. Reset corresponds to the Integral; Rate corresponds to the Derivative. [Integral feedback is $K1 * E1$ where $E1$ is a time integral of error (therefore, a multiple of time). “Reset” constant $K1$ should be inverse seconds (1/s).]
- **PV Filter TC:** Time constant (in seconds) of a first-order PV filter. Applies in Auto and Cascade modes.
- **SP Filter TC:** Time constant (in seconds) of a first-order SP filter. Applies in Auto and Cascade modes.
- **SP Rate DN:** Ramp rate at which downward setpoint changes are acted on in Auto mode, in PV units per second. If the rate is set to 0.0, the setpoint is used immediately. For control blocks, rate limiting applies only in Auto mode.
- **SP Rate UP:** Ramp rate at which upward setpoint changes are acted on in Auto mode, in PV units per second. If the rate is set to 0.0, the setpoint is used immediately. For control blocks, rate limiting applies only in Auto mode.
- **Structure:** Defines how the software responds to errors.
- **Controller Action:** Default is indirect action. This is changed if a continuous feed or perfusion process is being used.
- **Enable Deadband Local Override:** Control parameter option that sets controller output to mid-range when the process value (PV) is within the defined range (HI_Deadband, LO_Deadband) from the setpoint (SP). This is typically used for pH control.
- **Hi/Lo Deadband:** Range above and below the setpoint in which a control loop is not activated. Applies to pH and DO loops only.

- **Hi/Lo Gap:** Larger than the deadband, this range allows for equilibration after a control loop has been activated.

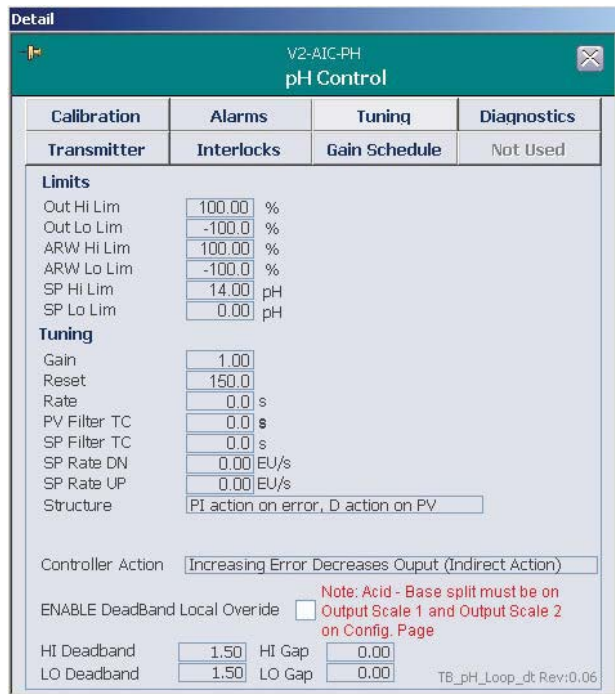


Figure A.5. Hi/Lo Deadbands and Gaps.

In the **Diagnostics** tab, the user can check errors and status of the module referenced by the faceplate.

The **Transmitter** tab (Figure A.6) allows the operator to select the probe for the control loop module.

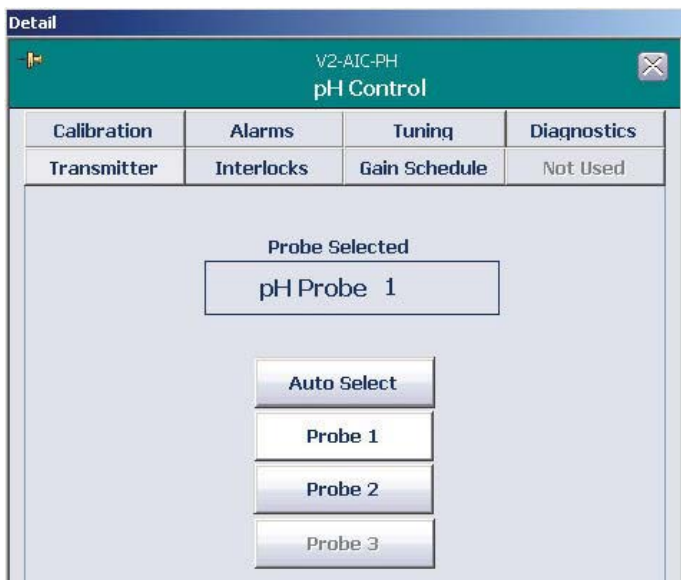


Figure A.6. Transmitter tab details.

The **Interlocks** tab (Figure A.7) is used only in parameters whose control loops involve gases or liquids. If the pressure in the bioreactor/ fermentor rises to the Hi-Hi alarm level, the Interlock will disable any further addition until the pressure drops.

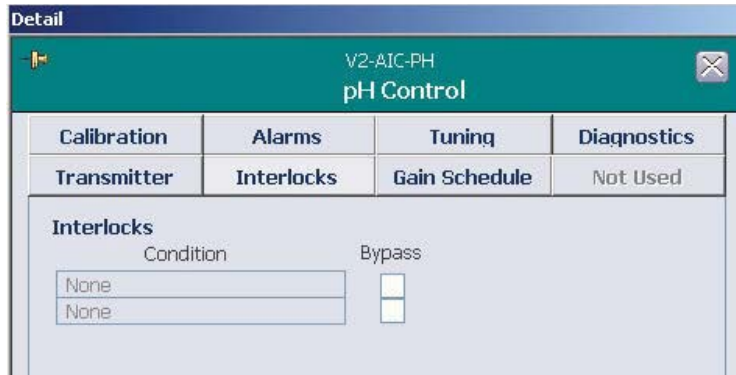


Figure A.7. Interlocks tab details.

The **Gain Schedule** tab (Figure A.8) allows the user to monitor and change three sets of tuning parameters, the gain scheduling reference parameter, the gain scheduling regions, and enable/disable the gain scheduling function.

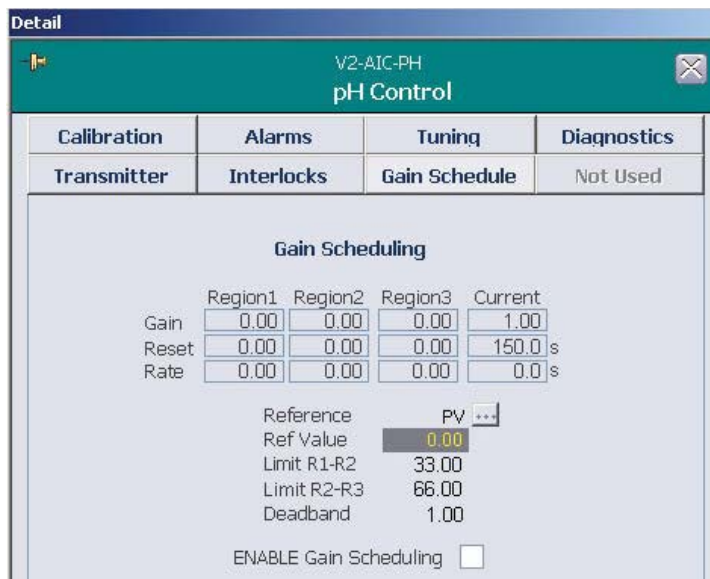


Figure A.8. Gain Schedule tab details.

The reference variable can be selected from the process variable, the controller output, and an auxiliary.

- **Region 1/2/3** shows the PID parameter settings for the three different regions.
- **Current** settings are the actual PID parameters being used in the control loop at that particular time.
- **Reference** shows which of the three parameters has been selected.
- **Ref Value** shows the actual value in the process at that particular time. The three regions are defined as intervals delimited by two values of the reference variable, **Limit R1-R2** and **Limit R2-R3**.
- The **Deadband** prevents tuning parameter change when transitioning from one region to the next until the deadband limit is exceeded.

At the bottom of the faceplate are three more icons (Figure A.9):

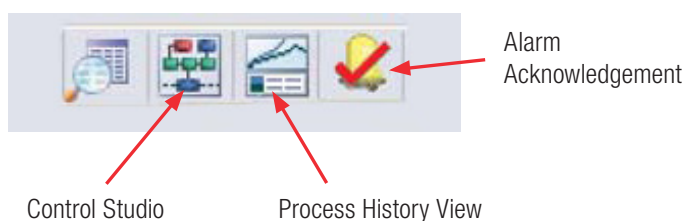


Figure A.9. Icons at the bottom of the faceplate.

- The **Control Studio** button provides access to DeltaV operations. For more information on this option, refer to the DeltaV Books Online.
- The **Process History View** is similar to the Parameter Trending function, but allows for more options. Other parameters can be included in the graph, and the time covered by the graph can be modified from minutes to weeks.
- The **Alarm Acknowledgement** button is used to acknowledge an alarm, so that the cause of the alarm can be investigated. If an audible alarm is part of the system, the sound is silenced with the Silence Alarm button in the lower right corner of the Main screen. See the Enabling and Suppressing Alarms section for more information.

Appendix B—Details of the Configuration screen

The Configuration screen (Figure B.1) allows the user to set up required parameters and control loops. The screens accessed by clicking on the various control boxes will vary according to the parameter, but the following examples will be representative.

Controllers were discussed earlier as part of the control loop setup. The illustrations shown are representative.

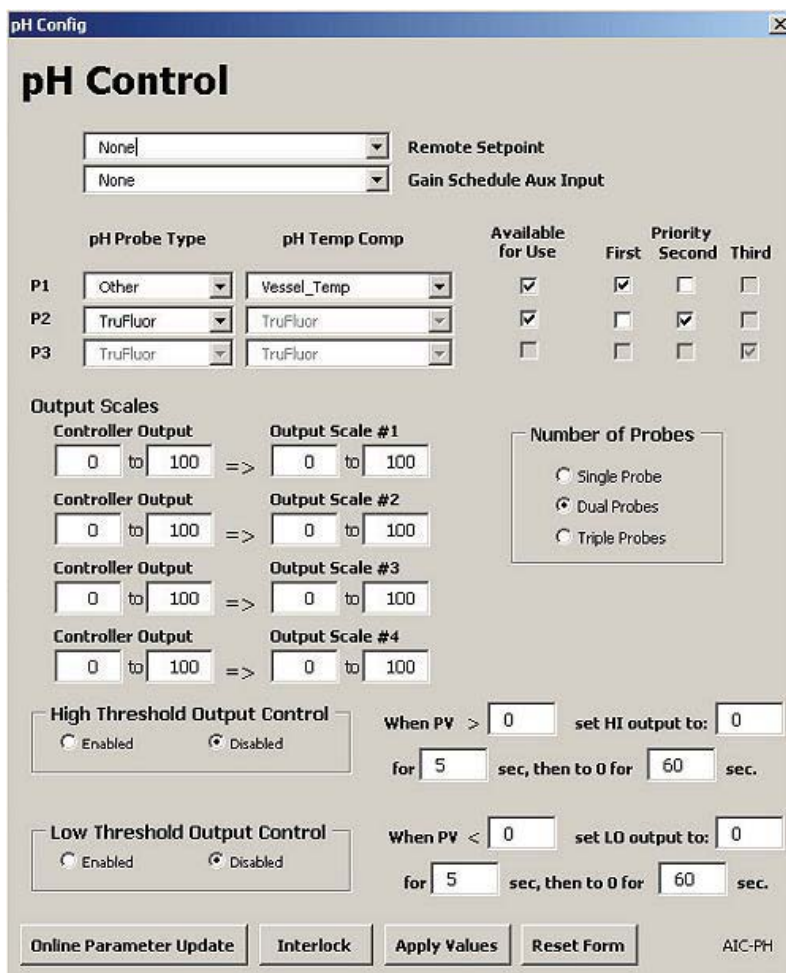


Figure B.1. Configuration screen detail.

- The **Remote Setpoint** is used only when the setpoint is dependent upon another parameter and is not set from the faceplate. This was done when setting the temperature control loop.

- The **Gain Schedule Auxiliary Input** should only be used under the direction of qualified Thermo Scientific personnel.
- The **Probe** information is seen only on pH and DO controllers. It is essential as it will become part of the batch record. If a probe has been used previously, it can be selected using the drop-down menu. Identify all probes used and assign the priorities according to facility procedures.
- The **Controller Output** of the **Output Scales** is expressed as a percentage of maximum output, e.g. a percentage of the maximum 250 rpm of a pump. The Output Scale is expressed in the engineering units of the device being controlled. The numbers in the Output Scales may add up to 100% when a control loop is set up, but it is not necessary that they do so.
- The **High and Low Threshold Output Controls** are a way of controlling a parameter if the cells are tolerant of moderate variations in the parameter. For example, the cells in culture will tolerate a range of pH 6–8, then the user could set the base pump to run for a specified time (pre-set at five seconds) if the pH dropped below 7, and to run the MFC delivering CO₂ if the pH went above 7. However, this method is not optimal, as it can produce wide swings in the parameter PV.
- When entering data into the control screens, the user must always click **Apply Values** to save the settings.
- If the values entered are not correct, the entire form can be returned to factory-set values by clicking **Reset Form**.
- The **Interlock** is used to halt gas/liquid delivery if the pressure in the vessel rises above the levels set in the Limits section.
- **Online Parameter Update** is a link to DeltaV settings.
- The **Characterizing Curve** (Figure B.2) is used to configure more closely the output from the parameter control above. It should be used only by an experienced operator under direction of Thermo Scientific service personnel.

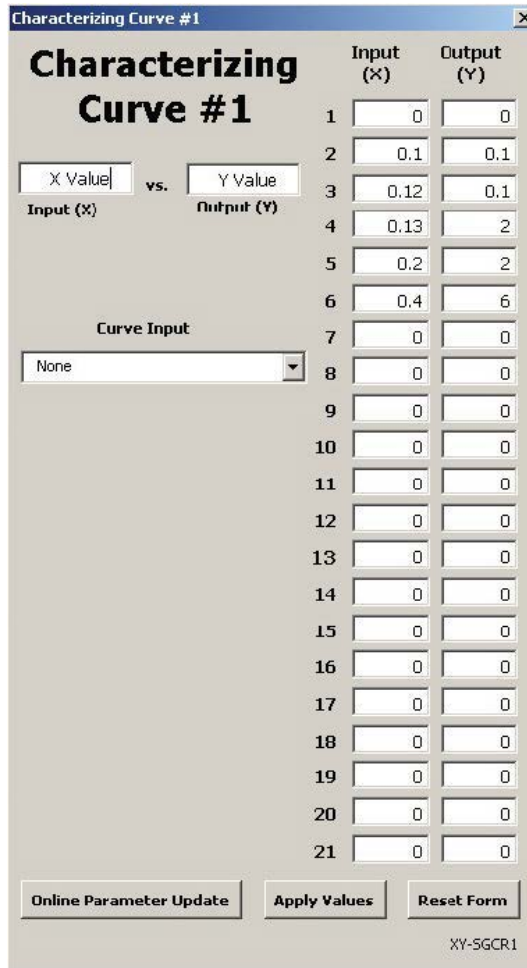


Figure B.2. Characterizing Curve screen.

The **Logic and Comparison** screen (Figure B.3) is another tool for use in setting up control loops. If used in conjunction with the Control screen, it can reduce the variations in parameter control.

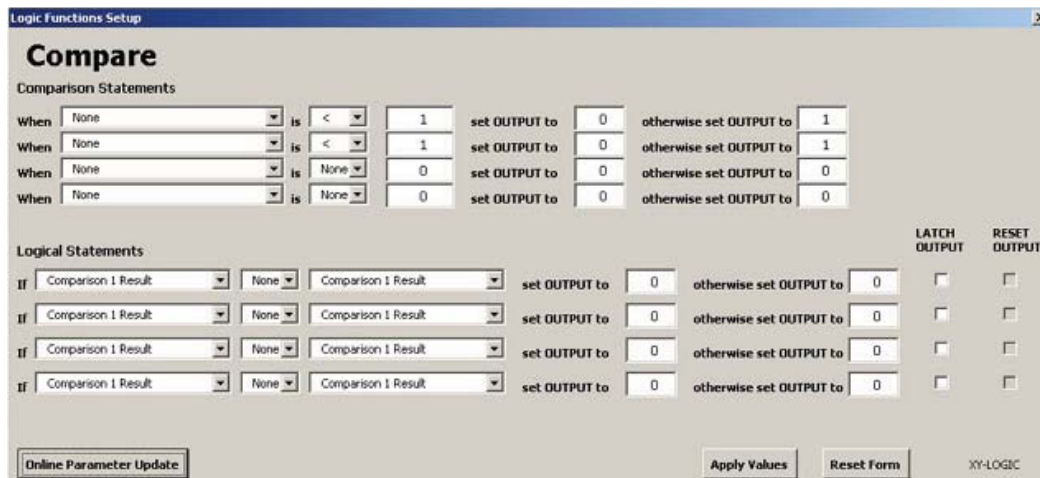


Figure B.3. Logic and Comparison screen.

After making changes in this screen, select **Apply Values** to save the entries. You can return to factory-preset values by clicking **Reset Form**.

The **Math Function** (Figure B.4) contains two independent derivative calculations that can be used by the calculation function or by other TruBio Software functions. The derivative function calculates the rate of change of the input variable, based upon a configured time base units in minutes or hours. If a filter is required, we recommend the use of an input filter. The output filter applies a DeltaV filter function block onto the calculated rate of change value.

The screenshot shows a window titled "Math Functions Config" with a close button in the top right corner. The main heading is "Math". Below it, there are two sections for derivative settings:

- Derivative #1 Settings:**
 - A dropdown menu set to "None" with the label "Input" to its right.
 - An input field containing "300" with the label "Input Filter Time (sec)".
 - An input field containing "0" with the label "Output Filter Time (sec)".
 - A section titled "Derivative Time Base" with two radio buttons: "Units / Minute" (unselected) and "Units / Hour" (selected).
- Derivative #2 Settings:**
 - A dropdown menu set to "None" with the label "Input" to its right.
 - An input field containing "300" with the label "Input Filter Time (sec)".
 - An input field containing "0" with the label "Output Filter Time (sec)".
 - A section titled "Derivative Time Base" with two radio buttons: "Units / Minute" (unselected) and "Units / Hour" (selected).

At the bottom of the window, there are three buttons: "Online Parameter Update", "Apply Values", and "Reset Form". In the bottom right corner, the text "XY-MATH" is displayed.

Figure B.4. Math Functions config screen.

The **Calculation Form** (Figure B.5) was used as part of the DO control loop setup. It is used to set up relationships between functions for maximum control. The formula can contain up to 10 separate functions.

Free Form Equation #1 Config

Calc #1

Formula = Calculation Steps Remaining: 9

Constants

C1	<input type="text" value="1"/>	C6	<input type="text" value="0"/>
C2	<input type="text" value="2"/>	C7	<input type="text" value="0"/>
C3	<input type="text" value="0"/>	C8	<input type="text" value="0"/>
C4	<input type="text" value="0"/>	C9	<input type="text" value="0"/>
C5	<input type="text" value="0"/>	C10	<input type="text" value="0"/>

Operators

+	exp(^)	sin	()
-	sqr	cos	Delete
*	log	tan	Clear
/	ln	e	

Enter formula using buttons. Press Apply when complete

Variables

Note: Trig functions are in degrees, not radians

V1	<input type="text" value="None"/>	V6	<input type="text" value="None"/>
V2	<input type="text" value="None"/>	V7	<input type="text" value="None"/>
V3	<input type="text" value="None"/>	V8	<input type="text" value="None"/>
V4	<input type="text" value="None"/>	V9	<input type="text" value="None"/>
V5	<input type="text" value="None"/>	V10	<input type="text" value="None"/>

XY-FUNC1

Figure B.5. Calculation form.

When setting up a formula, enter values by clicking the appropriate button. The fields do not accept direct entry of values or symbols.

After all values are entered, click **Apply Values** to save the settings. If necessary, click **Reset Form** to return the entire form to factory-set values; in the case of the Calculation form, the fields will be blank.

The **Mass Flow Controllers (MFCs)**, contained in the TruFlow gas manifold, are used to deliver gases to the bioreactor/fermentor vessel and are generally set up as part of a control loop. See Figure B.6 for the Mass Flow Controller Config screen. The gases are introduced into the vessel either at the top of the media (headspace) or bubbled in from below (spargers), depending on the process requirement.

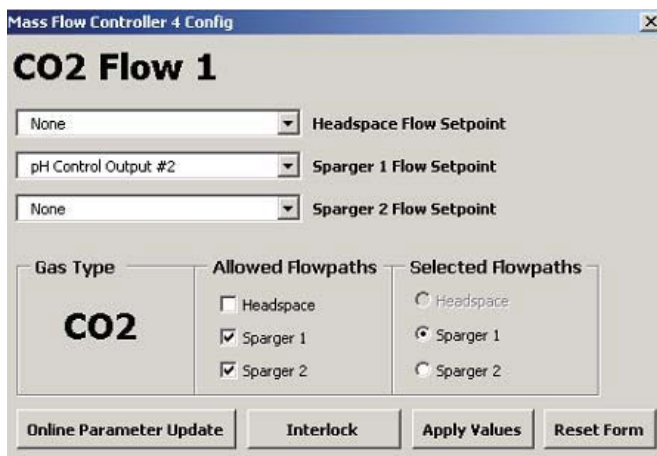


Figure B.6. MFC config screen.

The user must take care that the gas supplies are connected to the correct output and that the lines are not in danger of being kinked or occluded.

Care must also be taken that the sparger output agrees with the selected flowpath. If, as shown in Figure B.6, CO₂ is programmed for Sparger 1 Flow Setpoint, but the box for Sparger 2 is clicked in the Selected Flowpath the control loop will not function correctly. Save changes by clicking **Apply Values**.

The Interlock is used to shut off the flow of gas if the pressure in the vessel rises above a predetermined point, as set in the Alarms tab.

The pumps (Figure B.7) are used to deliver liquids, such as base for pH control, or nutrients for cells. For that reason, they are usually set up as part of a control loop with a remote setpoint, although they can also be controlled directly through the appropriate faceplate.

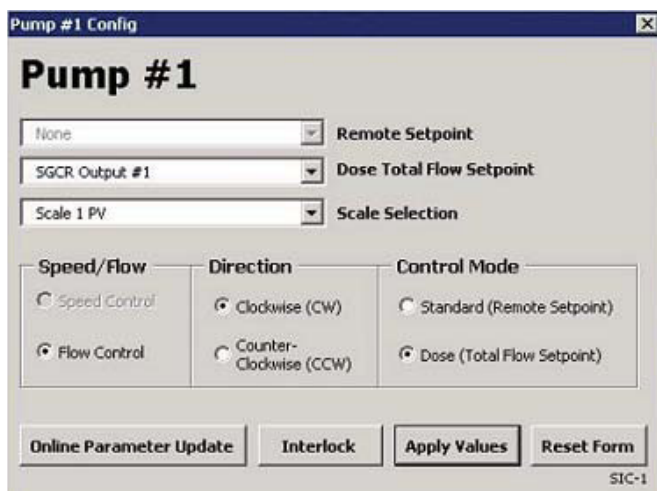


Figure B.6. MFC config screen.

As with MFCs, the user must take care that pump tubing is protected from kinking or occlusion.

In addition to the Remote Setpoint, pumps can be configured to deliver a set weight. This can be done by linking in a scale, but the scale must be configured into the system by Thermo Scientific service personnel. In this case, the user would select one of the scales in Scale Selection and click the “Flow Control” radio button.

The usual Speed/Flow setting is Speed Control, with the output speed set below pump maximum speed. Clockwise rotation delivers fluid TO the vessel, counterclockwise rotation removes fluid FROM the vessel. Click **Apply Values** to save the pump settings.

The Interlock function halts fluid delivery if the pressure in the bioreactor/fermentor rises above the limits set in the Alarms tab.

Appendix C—Smart Device information

In the TruBio Software, the Smart Device information is now located on the Configuration page (Figure C.1).



Figure C.1. Location of Smart Device Info button.

Clicking on this box opens a pop-up screen with information on the pumps and mass flow controllers used in the Controller (Figure C.2).

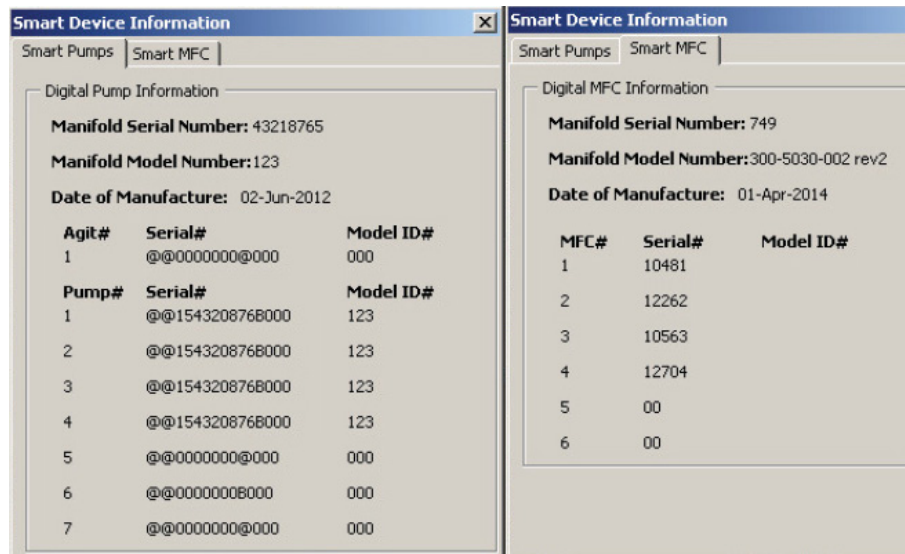


Figure C.2. Smart Device Information screens.

Appendix D—Time proportioning of pumps

On some occasions, it could be necessary to run a pump at a lower rate than the operating range.

Note: For information about Thermo Scientific SmartPump specifications and other product information, contact your sales representative.

If the pump flow rate drops to a level below the operating range, it will begin what is called time proportioning, which is indicated by “TP” on the appropriate icon on the Main screen. Rather than running continuously at a low rate, the pump will run for a portion of the time relative to the minimum operating range.

It should be noted that the pumps should not be run at such low rates for an extended period of time, as the accuracy of delivery is not always reliable. If such low rates are required, the pump should be exchanged for one with a lower operating range.

An alternative to replacing the pump head is to use tubing with a smaller inner diameter (ID). The decrease in tubing ID decreases the flow rate. Any tubing change will, of course, require that the pumps be recalibrated.

If a user usually runs pumps in the normal operating range, but must run at low rates on occasion, custom calibration can be performed to ensure accuracy at low rates. Consult your Thermo Scientific service representative for further information.

Using this feature requires that time proportioning be enabled.

To enable time proportioning, open the pump faceplate and then the Detail screen (Figure D.1). Then click the TP Mode tab.

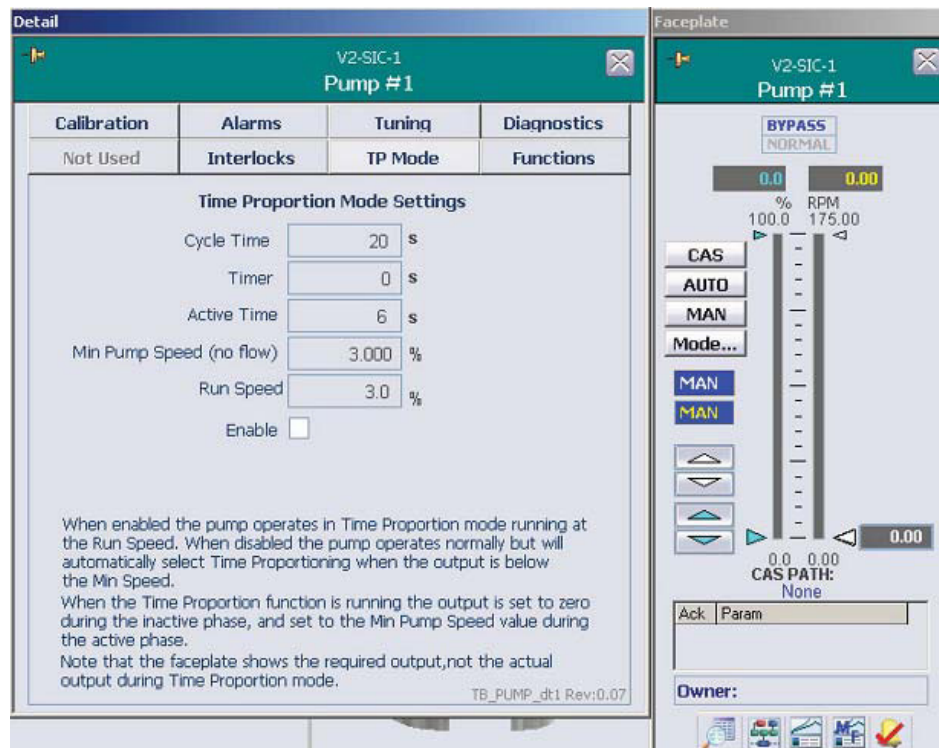


Figure D.1. Pump faceplate and detail screens.

The “Enable” check box in this screen should only be checked if Time Proportioning is to be used at all pump speeds. The pump will run at the Run Speed for the portion of the Cycle Time that is determined by the Pump Output value.

Leaving “Enable” unchecked will only operate Time Proportioning below the Minimum Speed. “Enable” is usually left unchecked.

Cycle time is the duration of the Time Proportion, from the start of one pulse to the start of the next. The time (in seconds) should not exceed the MultiFeed Phase Time for that pump.

Min Speed is the Time Proportion enable speed (in percent of the maximum pump rpm). Typically, this is set at the lower continuous pump operating range. For Watson Marlow™ 313 and 520 series pump heads, this is 0.34 (1 rpm/300 rpm x 100%). For Watson Marlow 114 series pump heads, this is 2.85 (5 rpm/175 rpm x 100%).

Run Speed is the estimated pump run speed in percent of the maximum pump rpm. It cannot be lower than the Min Speed at 5%.

When Time Proportioning is enabled, a clock symbol appears in the appropriate pump box on the Main screen (Figure D.2).

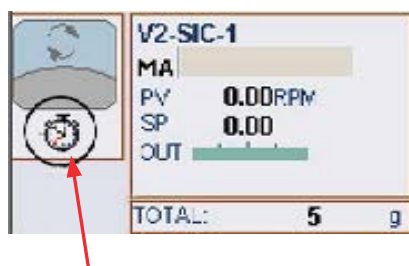


Figure D.2. Clock symbol appears in pump box.

Please contact your service representative for detailed information about TP setup.

Appendix E—Electrical connections and Controllers Off function

Electrical connections

To protect against electrical interference from current leakage, all equipment must be grounded (earthed) to a true earth ground, such as a metallic structure in the facility.

Thermo Scientific controllers have grounding studs on the exterior of the cabinet. Commercial bioreactor containers also have grounding points. Refer to the appropriate user's guide for more information.

Controllers Off function

If an emergency occurs that requires the immediate halt to all functions associated with the bioreactor/fermentor, the user can press the “Stop” button on the I/O tower or click “Controllers Off” on the Main screen. The Controllers Off configuration is set up in the Configuration screen.

Settings on the Controllers Off configuration screen will determine the mode that the controllers will be set to if “Controllers Off” is clicked. As displayed in Figure E.1, the default is Manual (MAN) mode with 0% output.



Figure E.1. Controllers Off config screen.

When **Controllers Off** is clicked, the display changes to “Reset.” After the system is restarted, a “Vessel Save” must be run to return the system to the original state.

Appendix F—Perfusion

Perfusion, sometimes known as continuous-feed technology, is the process of feeding fresh media into an actively growing culture while simultaneously removing waste and/or product. Properly done, this process provides much higher yields in mammalian-cell cultures by maximizing culture time and productivity per cell.

The perfusion process requires at least two scales or load cells, and two pumps, depending on the filtration process used. The BPC is placed on one scale and the container of fresh media placed on a second scale. The process is driven by the weight removed from the BPC through the filter. This weight is replaced by fresh media.

One peristaltic pump moves liquid from the bioreactor vessel through the filtering system to a collection vessel for downstream processing. This is referred to as the “Filtrate Out” pump. The controller of this pump is set to maintain the bioreactor vessel at a constant weight.

The specific filtration system dictates whether a third pump is required to feed the filtration process.

The Thermo Scientific MultiFeed system is used to feed fresh media at a constant flow rate into the BPC. This pump, referred to as the “Media In” pump, is controlled by the MultiFeed system, which adjusts the flow rate, based on the loss of weight from the container of fresh media.

The “Filtrate Out” side of the process requires that the Vx-WIC-VSL be configured as a “Direct” acting loop, where x indicates the number of the vessel in use. The standard is for all loops configured as “Reverse” acting loops when the system is shipped.

Change loop to direct action

To change the loop to “Direct” action, do the following:

1. On the ProPlus workstation, access “Exploring DeltaV” from the task bar (Figure F.1).



Figure F.1. Exploring DeltaV button on task bar.

- Open the Equipment mode. Then locate the module “Vx-WIC-VSL” in the left column (Figure F.2).

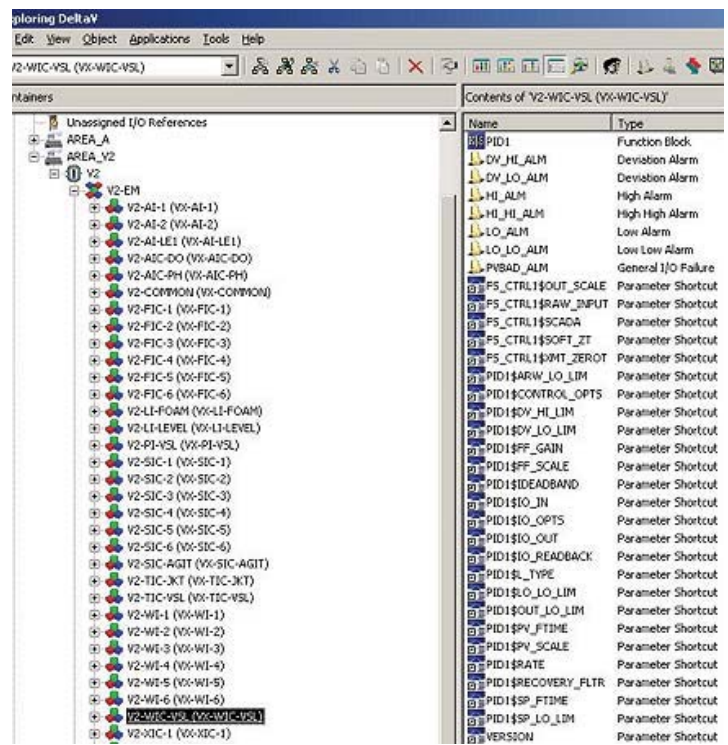


Figure F.2. Module name in the left column.

- Double-click **PID1\$CONTROL_OPS** in the right column (Figure F.3).

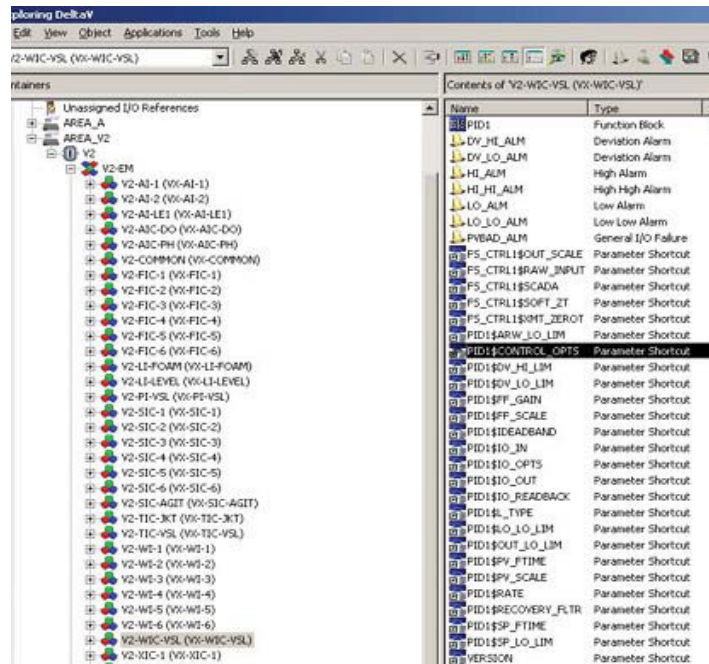


Figure F.3. Module name in the right column.

- When the control box opens, click to deselect the check box “Use default value from library object” and select “Direct Acting” under “Properties” (Figure F.4).

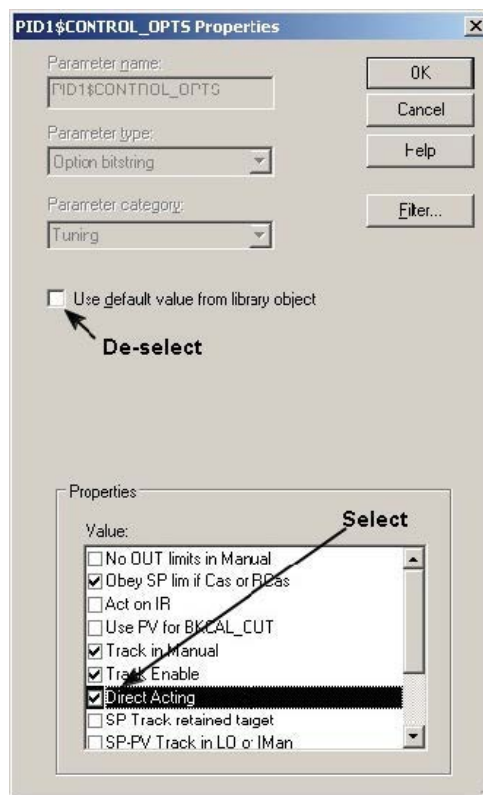


Figure F.4. Options to select and deselect.

- Click **OK** in the upper right corner of the box to save the selections. A blue triangle appears next to **Vs-WIC-VSL**, indicating a download is required (Figure F.5).

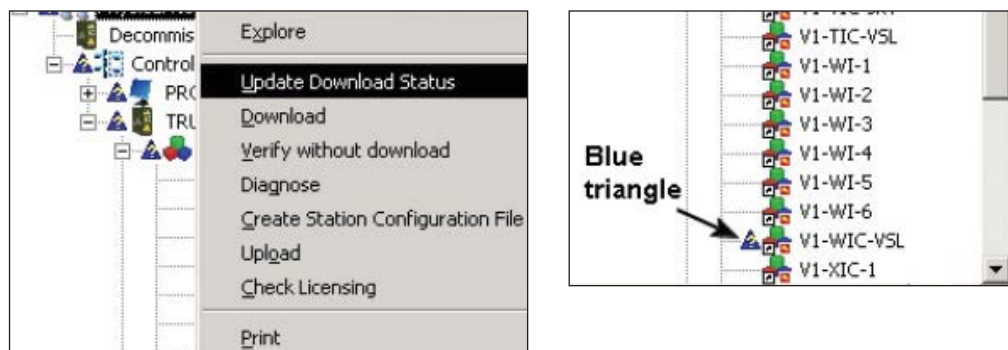


Figure F.5. “Update Download Status” and blue triangle detail.

- Right-click the module. In the menu that appears, click **Download** and then, **Control Module** (Figure F.6).

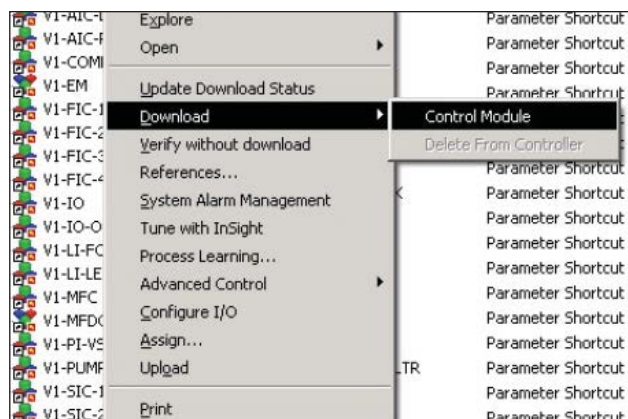


Figure F.6. Right-click module, select “Download,” then “Control Module.”

- After the control module has downloaded, minimize “Exploring DeltaV.”
- To restore the alarm files and other settings, open “Vessel Settings Management” in the Online Parameter Update screen. Then reload the “Default” file.

The output of the loop can now be linked to the remote setpoint of the “Filtrate out” pump (Pump #2).

9. Click the selected pump on the Configuration screen. Set the Remote Setpoint to “Vessel Weight Output.”

Set up “Media In” pump

Use the following steps to set up the “Media In” pump.

1. Configure the pump and scale according to the MultiFeed procedure previously outlined.
 - The scale/load cell associated with the fresh media is called **Vx-W1-1** in this example; the scale/load cell associated with the BPC and the filtration device is called **Vx-WIC-VSL**, where *x* is the number of the vessel, as identified in the TruBio software.
2. Place **Vx-WIC-VSL** into “Auto” mode, with the desired vessel weight as the setpoint.
 - The output of the **Vx-WIC-VSL** loop becomes the setpoint for the “Filtrate Out” pump (Pump #2).
3. Place Pump #2 into Cascade (CAS) mode.
 - Interlocks can be set such that, if the weight of the bioreactor vessel is outside of limits, the “Media In” pump (Pump #1) can be stopped and/or the “Filtrate Out” pump (Pump #2) can be stopped.

If the filter needs to be changed during processing or the media supply replenished, the “Filtrate Out” loop should be placed into Manual (MAN) mode and set to 0%, which will stop Pump #2.

The MultiFeed control for the “Media In” pump (Pump #1) can be paused (scale-locked) by clicking the Pump #1 symbol on the MultiFeed faceplate. The user will be prompted to confirm the pump lock request. When the request is confirmed, a padlock will display on the MultiFeed faceplate.

To restart/resume the perfusion process, use the Pump #2 faceplate to reset the mode to CAS. To restart Pump #1, click the padlock button on the MultiFeed faceplate and confirm the pump unlock request.

After the Perfusion process is set up, at least one scale will track media volume (weight), in addition to one pump that delivers media to the vessel. Another scale tracks the total vessel weight, which feeds back to a pump that removes media from the vessel.

Because the MultiFeed process requires a Phase Time to be set, there will be short interruptions to the action of Pump #1 when one phase ends and the next begins. The effect on the weight of the BPC vessel is minimal, as shown in Figure F.7.

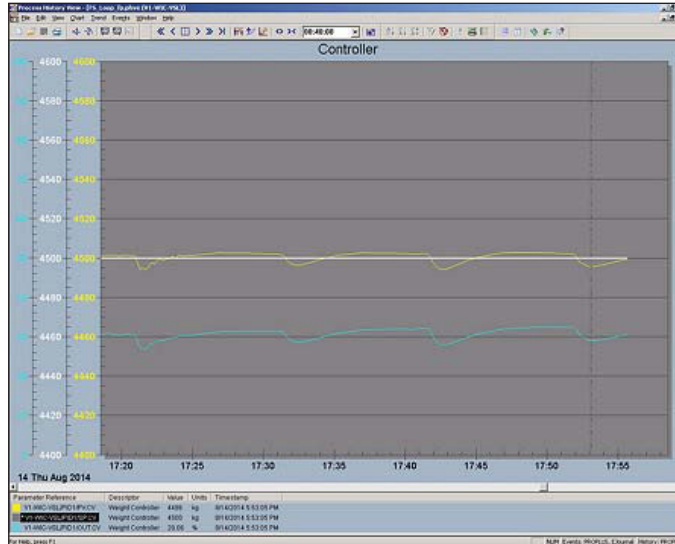


Figure F.7. Graph showing minimal effect of weight on BPC vessel.

Based on our testing, the preferred tuning parameters for **Vx-WIC-VSL** are:

- Gain = 150
- Reset = 500
- Rate = 0

Appendix G—Alarms

When an alarm is triggered, the outline of the control box on the Main screen flashes, and the alarm bar at the bottom of the Main screen displays the vessel number in a red or yellow box.

The user can acknowledge the alarm at the faceplate of the parameter that triggered the alarm. Doing so immediately makes available any information necessary to correct the condition that triggered the alarm.

Click **Alarm Page** to view a full description of all alarms on the system on the Alarms page.

The Alarms table shows the following information:

- Date and time of the alarm
- Whether or not the alarm was acknowledged
- The unit (vessel number) on which the alarm occurred
- The module that was involved and a description of the module
- A brief description of the problem
- The alarm priority

The levels of alarm are Critical (Unit_Crit), Warning (Unit_Warn), and Advisory (Unit_Advis). Because alarm table information can appear complex, the abbreviations are described in Table G.1. The notation “VX” indicates the vessel number; in an alarm condition, the X will be replaced by a number.

Table G.1. Alarm abbreviations.

TruBio control mode	Name
Analog input control module	VX-AI-1 through 8
Lab entry control module	VX-AI-LE1
DO control module	VX-AIC-DO
pH control module	VX-AIC-PH
Common unit control module	VX-COMMON
MFC module	VX-FIC-1 through 6
Foam control module	VX-LI-FOAM
Level control module	VX-LI-LEVEL
Pressure control module	VX-PI-VSL
Auxiliary control module	VX-SIC-AGIT
	VX-XIC-1 through 4
Pump control module	VX-SIC-1 through 6
Temperature control module	VX-TIC-JKT
	VX-TIC-VSL
Scale control mode	VX-WI-1 through 6
Weight control mode	VX-WIC-VSL
Freeform equation control module	VX-XY-FUNC1 through 6
Logic control module	VX-XY-LOGIC
Math control module	VX-XY-MATH
Signal characterizer control module	VX-XY-SGCR
Timer control module	VX-XY-TMR
Input and output control module	VX-IO
	VX-IO-OUT
	VX-IO-WAVE
	VX-IO-OUT-WAVE
TruFluor virtual transmitter	VX-TF-DO2
	VX-TF-DO3
	VX-TF-PH2
	VX-TF-PH3
Digital MFC control module	VX-MFC
Digital pump control module	VX-PUMP
MultiFeed control module	VX-MFDOSE

Appendix H—Chart Builder feature

The Chart Builder feature allows you to easily create and configure charts that track historical data for the following component parameters:

- Setpoint
- Output
- Process value

Up to six trends can be tracked on a single chart. You can also include events in a chart.

To use Chart Builder, follow these steps:

1. On the Main screen, right click any dynamo, such as the example in Figure H.1. The context menu opens, displaying several parameters you can add to Chart Builder.

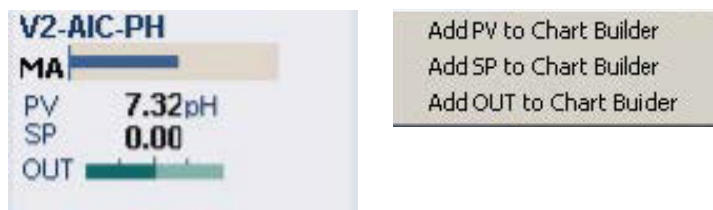


Figure H.1. Dynamo example and parameters that can be added to Chart Builder.

2. Click one of the menu options. The parameter you chose is added to Chart Builder as Trend 1 (Figure H.2).



Figure H.2. Chosen parameter added as Trend 1.

3. Repeat Steps 1–2 to add up to five more trends to the chart, using any other dynamos in the Main screen.
4. To select a different time span from the default (four hours), click a button in the “Span” section. **Note:** Regardless of the timespan you choose to create a chart, you can easily increase and decrease the span after you build the chart.
5. (Optional) To include events in your chart, click the “Include Events” checkbox.
6. After you add and configure the elements to your liking, click **Build Chart**. The Process History View window appears, showing the chart with your selected parameters. The chart contains the following features:
 - The main (gray) area of the chart shows the parameter trends, charted over the time span (shown on the X-axis).
 - To the left of the main area is a group of vertical (Y-axis) scale readings, with each parameter in a different color.
 - Below the chart is a legend, showing the color-coded parameter list. Each item in the list details the color, parameter reference, descriptor, value, unit of measure, and timestamp.

For information on modifying charts in the Process History View, refer to DeltaV Books Online.

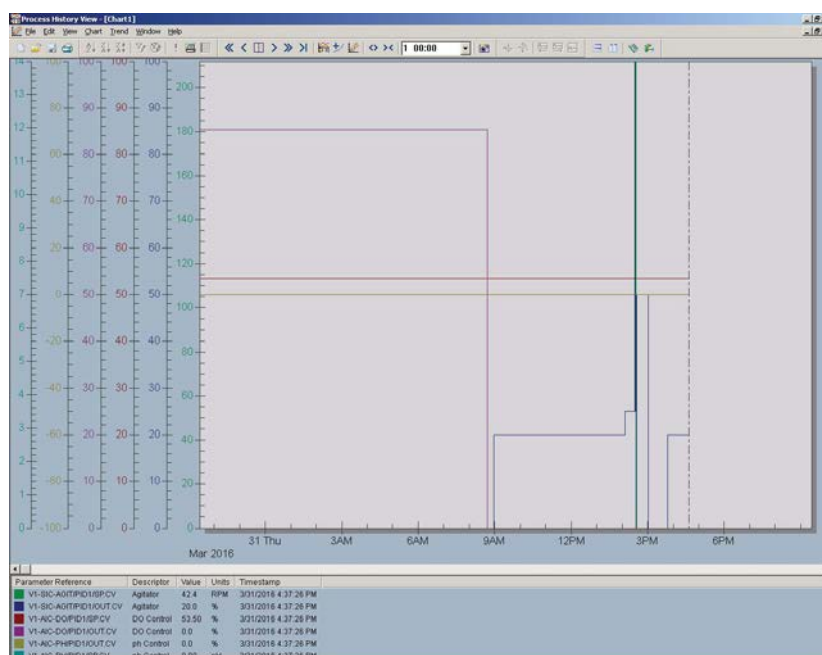


Figure H.3. Chart builder example.

Appendix I—5:1 Turndown add-on

Overview

The 5:1 turndown mechanism is a Thermo Fisher Scientific product used to move the agitator motor up and down. The turndown mechanism is operated by a handheld controller, which directly commands the pneumatically-actuated turndown motion. There will be no control function from TruBio, but a number of signals will be fed into TruBio for interlocks to inhibit agitator rotation.

This software add-on is compatible with the Speed Governor add-on, which is used to control the maximum speed of the agitator. This protects the agitator shaft from warping. Typically, the Speed Governor add-on is used for 2,000 L vessels, but can be set up for smaller vessels, as well.

Operational description

The 5:1 turndown mechanism is intended to be used only to move the agitator motor from the standard position to a lower “5 to 1” ratio position. During the operation of the 5:1 turndown, the agitator rotation will be interlocked to allow the operator to safely move the agitator assembly to the desired position, and carry out the procedure for loading and filling the BPC inside the S.U.B.

If the Speed Governor is disabled or not installed, and the 5:1 turndown is in the “Down” position, the maximum speed of the agitator will be limited to 55% of range. This value can be changed in the offline database. If changed, a module download is required. If the Speed Governor is enabled, the maximum speed limitation will be controlled by the Speed Governor software.

System setup

Ensure that the handheld controller is available and connected to the TruBio system. The TruBio software system and graphics should be set up per the relevant add-on installation instructions. There are no parameter lists or SaveFiles supplied as standard for this add-on package.

Handheld controller operation

The handheld controller (Figure I.1) allows the operator to move the agitator motor up using the “Raise” turn dial, and move it down using the “Lower” turn dial.



Figure I.1. Handheld controller.

There are LED indicators on the handheld controller to indicate the following:

- **Up** position: The agitator motor is rotating up from the current relative position.
- The motor safety cap is either **Locked** into position or **Unlocked**.
- **Down** position: The agitator motor is rotating down from the current relative position.
- **Intermediate** position: Any position other than “Up” or “Down” is considered to be in an “Intermediate” position. This is an interlocked position by TruBio software. The motor will be inhibited from turning in this position. The indication is only visible on the controller, as the TruBio display will not indicate this position on the operator graphic.
- **Enabled**: The device is enabled for operation.
- **Power**: The device power is enabled.
- **Emergency Stop**: Pressing the emergency stop (E-Stop) push button releases all pneumatic air from the device. To reset the E-Stop, twist the push button to return to the normal state.

User interaction

There is no software control action required by the user during this add-on operation. The statuses received from the handheld controller are indicated on the TruBio operator display in “Run” mode. Refer to the following sections for more detailed information about each mode.

User interface

The user interface for this add-on consists of a dynamo display object that enables the user to view the status of the 5:1 turndown. This display object can be placed onto the desired vessel graphic per user requirements.

Operator display

Figure I.2 shows the 5:1 turndown display in “Run” mode. Each of the five indicators (Up, Down, Locked, MSA, and E-Stop) will animate depending on the status indication received from the turndown hardware.



Figure I.2. Five indicators on operator display.

Table I.1. Modes of operation for 5:1 turndown.

Device state	Display status	Operation
UP		<ul style="list-style-type: none"> • Turndown in “Up” position. • Locking pin is locked. • Motor safety cap pin is in position.
DOWN		<ul style="list-style-type: none"> • Turndown in “Down” position. • Locking pin is locked. • Motor safety cap pin is in position.
MOVING/ INTERMEDIATE POSITION		<ul style="list-style-type: none"> • The motor safety cap pin will be out. • The locking pin will be unlocked. • “Intermediate Position” due to the motor not being in either the “Up” or “Down” positions. • The agitator will be interlocked.
E-STOP		<ul style="list-style-type: none"> • E-Stop activated by a button on the handheld device. • The agitator will be interlocked. • When depressed, the motor will stop, the system will release all pneumatic air, and will behave as follows in the 3 positions: 1) In “Down” position, motor will remain in “Down” position; 2) In “Up” position, motor will remain in “Up” position; 3) In “Intermediate” position, motor will be supported/pushed up by the BPC if pressure is sufficient, or slowly drift to the “Down” position.

Alarms

An Emergency Shutdown (ESD) alarm is generated and indicated on the TruBio Alarm List graphic and alarm banner when the E-Stop button is pressed on the 5:1 handheld controller. Together with this ESD alarm, an I/O failure alarm is generated for the E-Stop I/O. Figure I.3 shows the list of alarms generated for this add-on.

Alarm List								Unack: 1	Suppressed: 4
								Total: 1	
Ack	Time In	Unit	Module/Param	Description	Alarm	Help	Message	Priority	
	12/02/2018 17:01:43	V2	V2-TURNDOWN/ESD	5:1 Agglator Turndown Control Mod Alarm			5:1 Turndown E-Stop	UNIT_CRIT	

Figure I.3. 5:1 Add-on alarm list.

Data historian

The following modes are historized by default for any turndown add-on:

- DOWN
- ESTOP
- LOCKED
- MSA
- UP

Event journal and process history

There are no events recorded in the alarms and event journal as standard for this add-on package.

Appendix J—Agitator speed governor add-on

This add-on will restrict the existing agitator's speed depending on the volume contained within the vessel. No additional hardware is required to perform this function.

Operational description

Thermo Fisher vessels are supplied with an agitator that is mounted at the top of the vessel. A mixing shaft is attached to the agitator motor in order to mix the contents of the vessel. There is a power input to volume (P/V) specification on agitation that reduces the strain on the shaft. The agitator speed governor will restrict the existing agitator's maximum speed via its controller limits (SP limits and OUT limits) depending on the volume of fluid in the vessel in order to meet this specification.

Note that the maximum allowable speed is calculated using the equations and assumptions contained within the Thermo Fisher Scientific document "Agitation Operating Guidelines for 2,000 L S.U.B. Scale-Up" by Jones, N., Balekai, S., and Goodwin, M. This document contains the following assumptions regarding the equation used to calculate the maximum allowable speed: "These values assume an impeller power number of 2.1, viscosity similar to water, and a constant density of 993 kg/m³." See your local Thermo Fisher representative for a copy of this document.

Operational requirements

The following list provides the requirements necessary for the correct functioning of the speed governor:

- The vessel's weight is measured in kg, and this process value (PV) will be that of Vx-WIC-VSL.
- During the normal operation of the process, it is assumed that the user will perform a "zero" of the vessel's weight only once during normal operation, when the vessel is ready for media transfer with its BPC, filters, and all accessories attached.
- The vessel's weigh scale should be left in "Gross" mode. Taring the vessel's weight after this initial zeroing is not allowed if the speed governor is in use for the vessel. Taring the vessel's weight will give the speed governor an inaccurate weight reading for the vessel's contents that will result in incorrect limits being written to the agitator's control module.
- When the speed governor is enabled, the PV value of Vx-WIC-VSL is the weight of the contents of the vessel.

- The PV scale for the agitator is in rpm.
- The OUT scale for the agitator is in %.

Note: If any of the prior conditions are not met, the agitator speed governor will not function as intended.

System setup

There is no requirement of additional hardware for this add-on scope. The TruBio Software, version 5.0 and its graphics should be set up per the relevant add-on installation instructions.

A parameter list named “AGIT_SPD_GOV” is supplied as standard for this add-on package, but there are no TruBio SaveFiles supplied as standard.

User interaction

- The user is expected to manually fill non-zero values in the configuration form on the config graphic, change values via online parameter update (OPU) configuration tool, or load in a SaveFile.
- The speed governor indication on the main graphic is activated when the “Enabled” button is applied via the configuration form or the “Enable” parameter is set to 1 in OPU. This indicates that the speed governor is now active.
- The speed governor functionality can be disabled by applying the “Disable” button on the configuration form. The indication on the main graphic will be deactivated.
- When enabled, the speed governor limits the agitator output limit and setpoint limit. These can both be viewed on the agitator detail faceplate.

User interface

The user interface for this add-on consists of the following components:

- Agitator speed governor user configuration form
- Agitator speed governor interlock form
- Agitator speed governor faceplate
- Agitator speed governor dynamo

Agitator speed governor configuration form

Figure J.1 shows the agitator speed governor form display in “Run” mode after initialization. Table J.1 provides details about the labeled items in the image of the form display.

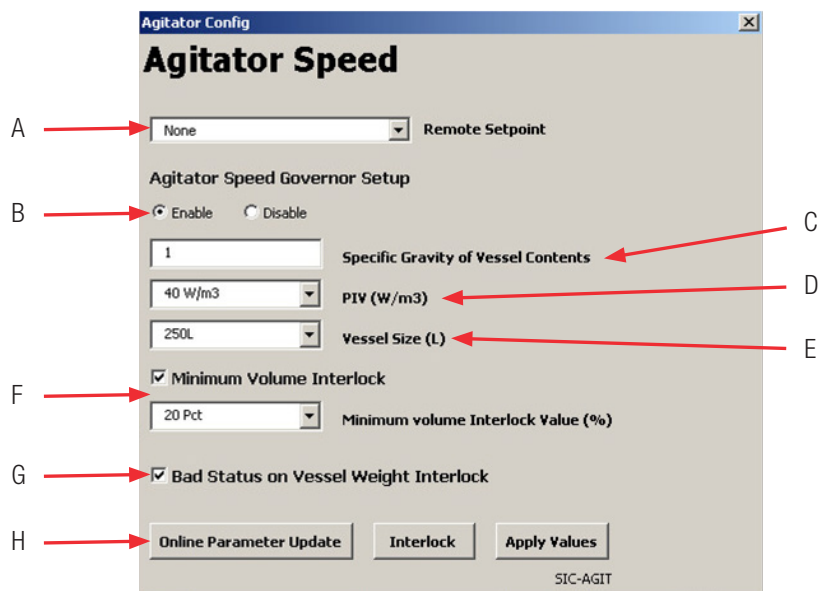


Figure J.1. Agitator speed governor form display.

Table J.1. Agitator speed governor form display details shown in Figure J.1.

Label	Parameter	Available values	Default values
A	Remote setpoint for agitator	N/A	None
B	Enable or disable agitator max. speed limitation	Enable/Disable	Disable
C	Specific gravity of vessel contents	User-defined	1
D	P/V value selection (in W/m ³)	10 W/m ³ , 20 W/m ³ , and 40 W/m ³	20 W/m ³
E	Vessel size selection (in liters)	50 L, 100 L, 250 L, 500 L, 1,000 L, and 2,000 L	2,000 L
F	Enable or disable minimum volume interlock and set the minimum volume interlock value (in percent)	Enable / Disable, 20% / 50%	Enable, 50%
G	Enable or disable the bad status on vessel weight interlock	Enable/Disable	Enable
H	Open Online Parameter Update (OPU), open the speed governor interlock form, and apply Speed Governor/Agitator settings	N/A	N/A

Users can perform the following from the speed governor configuration form:

- Enable or Disable the agitator speed governor functionality.
- Enter specific gravity of the vessel contents as required (value to be defined by the user).
- Select from three preset P/V values: 10 W/m³, 20 W/m³, and 40 W/m³.
- Select from five pre-defined vessel sizes (in liters): 50, 100, 250, 500, 1,000, and 2,000 L.
- Enable or Disable minimum volume interlocking based on one of two pre-defined vessel volume limits (specified as a percentage): 20% and 50%. This interlock will stop the agitator when the vessel volume is below the minimum volume value chosen.
- If the vessel is equipped with 5:1 turndown capability, the recommended setting for the interlock value is 20%. This selection, however, depends on the end user's requirements.
- Enable or Disable "Bad" status on vessel weight interlock.
- Open Online Parameter Update (OPU).
- Load agitator speed governor interlock settings form.
- Apply agitator speed governor settings.

Agitator speed governor interlock form

Figure J.2 shows the agitator speed governor interlock form. The objects outlined in red have been disabled for the agitator when the speed governor add-on is installed. "Interlock 2" is reserved for the minimum volume and "Bad" vessel weight interlocks, and cannot be configured by an end user. "Interlock 1" remains configurable, however, the interlock value source cannot be changed, as this setting is shared by both "Interlock 1" and "Interlock 2," with "Interlock 2" settings given priority.

The screenshot shows the 'Agitator Speed Interlock Configuration' window. It features a title bar with the text 'Agitator ConfigInterlock Configuration'. The main title is 'Agitator Speed Interlock'. Below the title, there is a 'Condition' section with 'Interlock 1' set to 'None' and 'Interlock 2' set to 'Min Vol / Bad Vsl Weight'. The 'Interlock 2' row is highlighted with a red box. To the right of the dropdowns are 'Invert' and 'Bypass' checkboxes. Below this is the 'Interlock Value Source' section, also highlighted with a red box, containing two radio buttons: 'Hold Last Output Value' (unselected) and 'Internal Value' (selected). Next to the 'Internal Value' radio button is a text box with the value '0'. At the bottom of the window are 'Apply Values' and 'Reset Form' buttons, and the text 'SIC-AGIT'.

Figure J.2. Agitator speed governor interlock form.

Note that depending on whether both interlocks are selected, just one is selected, or none are selected, the text description for the interlock will change to one of four values: Min Vol/Bad Vsl Weight (both interlocks enabled), Min Vsl Vol (minimum volume interlock enabled only), Bad Vsl Weight (bad status on vessel weight interlock enabled only), or None (no interlocks selected). If no interlocks are enabled, the user will still not be allowed to configure Interlock 2.

Agitator speed governor faceplate

The agitator speed governor faceplate is shown in Figure J.3 (this is distinct from the agitator’s controller faceplate). It can be accessed from the Main process graphic of the vessel by clicking on the speed governor dynamo. See the following numbered list for descriptions of the various operation fields of the faceplate.

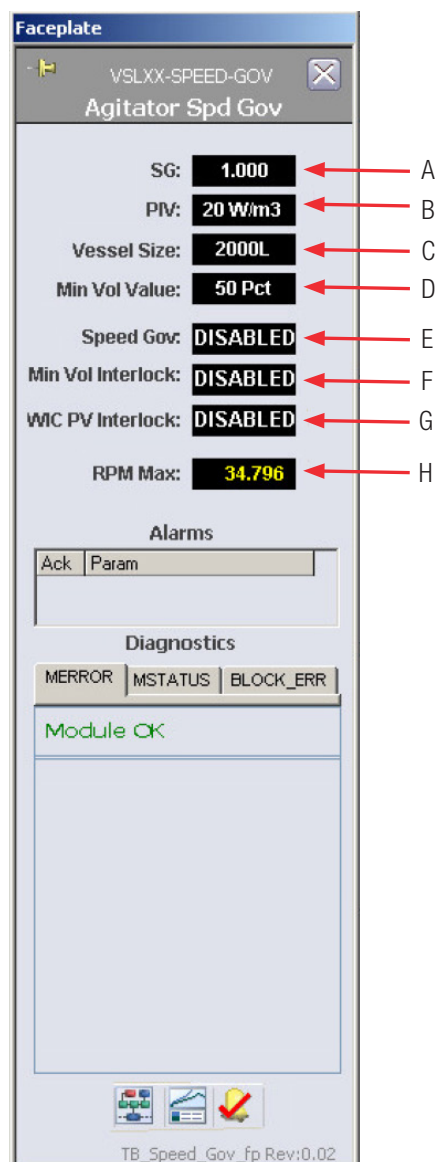


Figure J.3. Agitator speed governor faceplate.





- A. **SG:** The Specific Gravity chosen by user in the configuration form.
- B. **P/V:** The P/V value chosen by user in the configuration form.
- C. **Vessel Size:** The vessel size chosen by the user in the configuration form.
- D. **Min Vol Value:** The current minimum interlock value (in %) chosen by the user in the configuration form.
- E. **Speed Gov:** This displays whether the speed governor has been enabled or disabled by the user in the configuration form.
- F. **Min Vol Interlock:** This displays whether the minimum volume interlock has been enabled or disabled by the user in the configuration form.
- G. **WIC PV Interlock:** This displays whether the bad status on vessel weight interlock has been enabled or disabled by the user in the configuration form.
- H. **RPM Max:** This displays the maximum speed in rpm calculated by the speed governor.

Note: To view the interlock status of the minimum volume or bad vessel weight interlocks (i.e. whether they are active or inactive), go to the Detail display of the Agitator module itself, Vx-SIC-AGIT.

Agitator speed governor dynamo

The agitator speed governor dynamo is located on the Main process graphic for the vessel. Table J.2 displays the different states of the dynamo and what they indicate.

Table J.2. Speed governor dynamo operations.

	Display status	Operation
Speed governor graphic dynamo		<ul style="list-style-type: none"> Agitator speed governor control is not enabled AGIT_SPEED_ALM and/or INTEG_ALM alarms are not active
		<ul style="list-style-type: none"> Agitator speed governor control is not enabled AGIT_SPEED_ALM or INTEG_ALM alarm is active (the border blinks between red and white when the alarm is active but not acknowledged and solid red when active but acknowledged)
		<ul style="list-style-type: none"> Agitator speed governor control is enabled AGIT_SPEED_ALM and INTEG_ALM alarms are not active
		<ul style="list-style-type: none"> Agitator speed governor control is enabled AGIT_SPEED_ALM and/or INTEG_ALM alarm is active

Alarms

The AGIT_SPEED_ALM alarm will be generated when the agitator’s current speed is greater than the maximum rpm value (calculated).

Note: This alarm is generated regardless of whether the logic is configured to restrict the agitator speed or not.

The INTEG_ALM is generated when there is “Bad” status on the PV from the Vx-WIC-VSL vessel weight control module.

Figure J.4 shows the list of alarms generated for this add-on, and how they appear in the Alarm List view. Note that these alarms cannot be disabled via OPU.

Ack	Time In	Unit	Module/Param	Description	Alarm	Help	Message	Priority
	09/05/2018 10:39:57	VSLXX	VSLXX:SPEED-GOV/INTEG_ALM	Agitator Speed Governor Add On Version1.0.0	IOF		General I/O Failure	UNIT_CRIT
	09/05/2018 10:39:18	VSLXX	VSLXX:SPEED-GOV/AGIT_SPEED_ALM	Agitator Speed Governor Add On Version1.0.0	HIGH		High Alarm Value 41 Limit 34.7958	UNIT_CRIT

Figure J.4. Agitator speed governor alarm list.

Event journal

Event logs are recorded in the event journal each time the settings on the speed governor form is modified and applied (Figure J.5).

Date/Time*	Event Type	Category*	Area	Node	Unit	Module*	Module Description	Parameter	State	Level	Desc1	Desc2
13/02/2018 13:43:08.587	CHANGE	USER	AREA_V2	PROPLU V2	V2-SPEED-GOV	Agitator Speed Governor	FS_CTRL1/MIN_VOL_ENAB.CV				ADMINISTR	NEW VALUE = 1
13/02/2018 13:43:08.587	CHANGE	USER	AREA_V2	PROPLU V2	V2-SPEED-GOV	Agitator Speed Governor	FS_CTRL1/MIN_VOL_VAL_PER.CV				ADMINISTR	NEW VALUE = 50
13/02/2018 13:43:08.587	CHANGE	USER	AREA_V2	PROPLU V2	V2-SPEED-GOV	Agitator Speed Governor	FS_CTRL1/SPECIFIC_GRAVITY.CV				ADMINISTR	NEW VALUE = 5
13/02/2018 13:43:08.571	CHANGE	USER	AREA_V2	[PROPLU] V2	V2-SPEED-GOV	Agitator Speed Governor	FS_CTRL1/VESSEL_SIZE.CV				ADMINISTR	NEW VALUE = 2000L
13/02/2018 13:43:08.571	CHANGE	USER	AREA_V2	PROPLU V2	V2-SPEED-GOV	Agitator Speed Governor	FS_CTRL1/PIV_VALUE.CV				ADMINISTR	NEW VALUE = 40 W/m3
13/02/2018 13:43:08.571	CHANGE	USER	AREA_V2	PROPLU V2	V2-SPEED-GOV	Agitator Speed Governor	ENABLE.CV				ADMINISTR	NEW VALUE = 1

Figure J.5. Agitator speed governor event journal.

Process history

A chart named TB_Speed_Gov_fp.phve is supplied as standard as a part of the add-on package. The chart can be loaded using the “Process History View” button on the speed governor faceplate. The following parameters are displayed on the chart as standard:

- ENAB_SPD_GOV
- RPM_MAX_VAL
- PIV

Setting up the speed governor

Users can set up the speed governor in one of three ways:

1. By using the Agitator/Speed Governor configuration form on the associated “Config” graphic
2. Changing values via the OPU configuration utility
3. Loading a speed governor SaveFile

IMPORTANT: To set up and configure the speed governor, the DeltaV user is expected to have the RESTRICTED CONTROL key assigned to them. Without this key, the user will be unable to write the settings to the speed governor control module.

Agitator speed governor configuration form (recommended)

The agitation speed governor configuration form can be accessed from the “Config” graphic of the relevant vessel. The user can select and enter settings that match their requirements. The “Apply Values” button must then be clicked in order to apply the settings. These settings can be confirmed by opening the speed governor faceplate for the relevant vessel and confirming the values displayed there.

Via the OPU utility

The agitation speed governor can also be set up via the OPU utility. Open the OPU utility from the relevant vessel’s “Config” graphic. Select the speed governor module. The parameters shown in Figure J.6 should be displayed. Values can be changed here as for other standard TruBio modules. However, this is not the recommended method of setting up the speed governor.

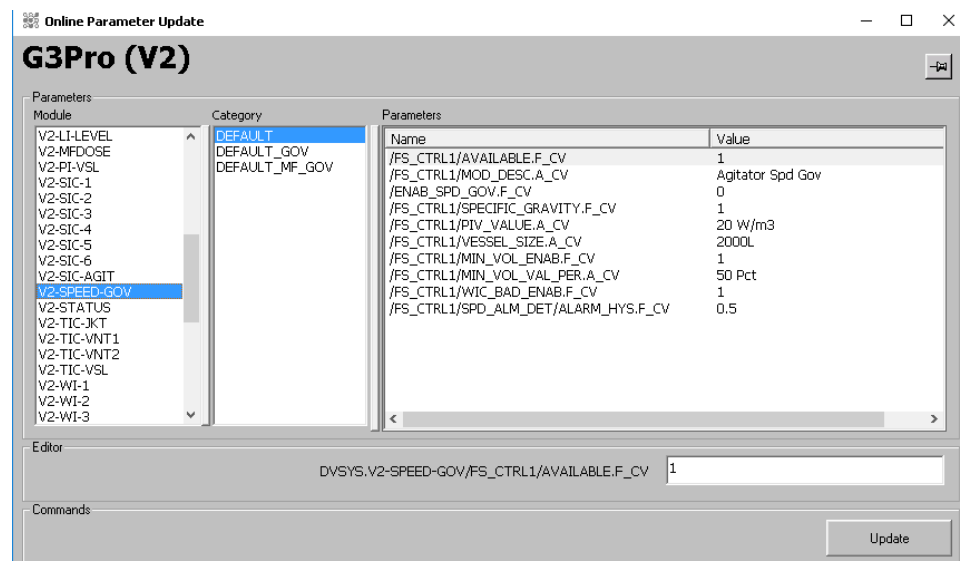


Figure J.6. OPU utility parameters for agitation speed governor.

Loading a speed governor SaveFile

After the speed governor has been set up according to the site's requirements, the user (with the correct security privileges) can create a SaveFile that contains these settings using the Vessel Settings utility.

1. Open the "Vessel Settings" utility from the vessel's "Config" graphic.
2. Select **Vessel Save** from the pop-up window.
3. Ensure that "AGIT_SP_GOV" is selected in the drop-down box. Then select **OK**.
4. Enter a name for the new SaveFile. Then select **OK**.
5. Ensure that there were no errors when creating the SaveFile. Then select **Exit**.

This SaveFile can then be loaded whenever the user requires the speed governor functionality. Always verify the speed governor settings using the speed governor faceplate.

Appendix K—Bag integrity add-on

Overview

The TruBio bag integrity add-on is used to check for leaks in the BioProcess Container (BPC), referred to here as the “bag,” to ensure its integrity before it is used for production.

Operational description

The TruBio bag integrity add-on provides a method of verifying bag integrity. Using the MFCs, the add-on will automatically inflate the bag to a desired pressure. The add-on will also measure the pressure drop for a configurable amount of time.

System setup

Ensure that the bag to be inflated and MFCs are available and connected to the TruBio system.

The TruBio Software, version 5.0 and its graphics should be set up per the relevant add-on installation instructions. A parameter list named BAG_INTEG and a SaveFile named Default_Bag_Integ are supplied as standard for this add-on package. This SaveFile must be loaded separately from the Default SaveFile.

Bag inflation procedure

The user should ensure the following before starting the bag integrity check:

- The bag is inflated per normal site procedure.
- The MFC being used for the test has tubing connected to the bag.

The bag integrity software can now be used to test for leaks.

User interaction

- The user is expected to manually add non-zero values to the configuration form, or load in preconfigured values using the SaveFile supplied prior to the start of the bag integrity check. The “Start” button will only be visible when the configuration form is populated.
- During the “Run” mode of the sequence, the user is not expected to perform control actions.
- The user has the choice of aborting the test as and when required during the bag integrity check.
- Any alarms generated will be visible to the user on the TruBio display. Refer to the sections below for detailed information about each mode.

User interface

The user interface for this add-on consists of the dynamo display object and accompanying faceplate that enables the user to:

- View the status of the bag integrity sequence
- Start the bag integrity check
- Abort the bag integrity check
- Enter the desired test parameter values for the bag integrity check
- View “leak detected” and “pressure timeout” alarm indications.

Operator display

Figures K.1 and K.2 show the bag integrity display in “Run” mode after initialization, and the bag integrity check faceplate (labeled in Table K.1).



Figure K.1. Bag integrity display.

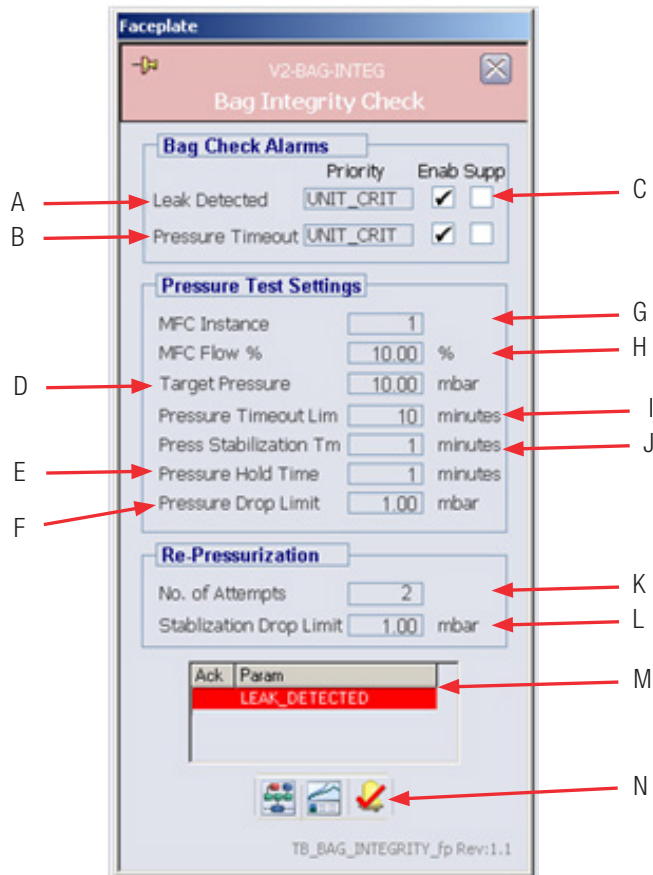


Figure K.2. Bag integrity check faceplate.

Table K.1. Bag integrity check display details shown in Figure K.2.

Label	Parameter	Available values	Default values
A	Leak detected alarm enable/disable	Enable/Disable	Enable
B	Pressure timeout alarm enable/disable	Enable/Disable	Enable
C	Alarm suppression setting enable/disable	Enable/Disable	Disable
D	Pressure target value	1–999	10 (<i>Dynamic units</i>)
E	Pressure hold time under test	0–180 min.	1 min.
F	Allowable differential pressure	0–50	1 (<i>Dynamic units</i>)
G	Instance of MFC	1–6	1
H	MFC flow setting	0–100%	10%
I	Timeout value for pressure	0–999 min.	10 min.
J	Pressure stabilization time	0–999 min.	1 min.
K	No. of re-pressurization attempts	0–25	2
L	Stabilization drop limit	0–999 min.	1 (<i>Dynamic units</i>)
M	Alarm summary box	N/A	N/A
N	Control Studio online, PHV charts, alarm acknowledge buttons (<i>standard DeltaV function</i>)	N/A	N/A

Modes of operation

The diagram below shows an overview of the modes for the bag integrity sequence. These modes are further detailed and explained in the following diagrams and tables.

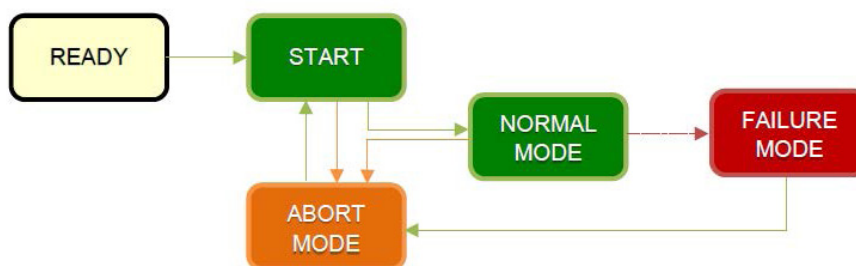


Figure K.3. Overview of modes for the integrity sequence.

Bag Integrity Check - Operation Flow Chart

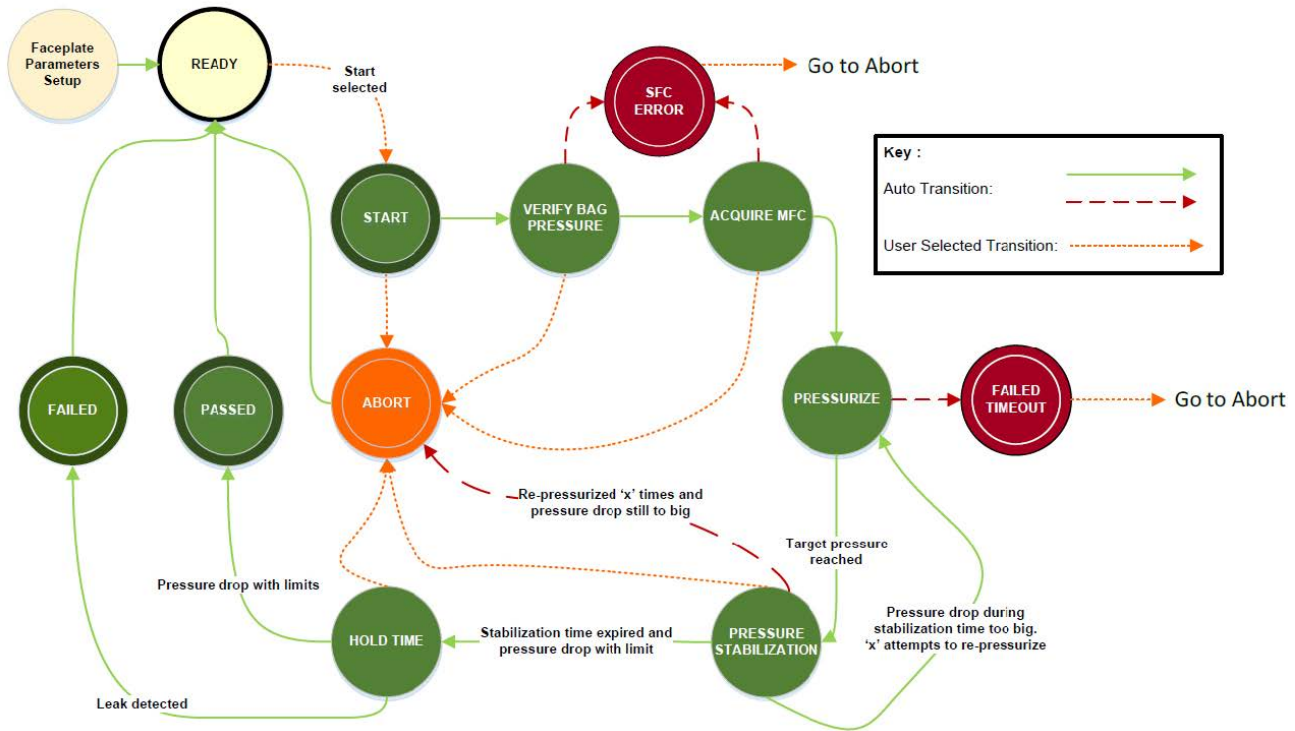


Table K.2. Bag integrity operation in normal mode.




Mode	Display status	Operation
FACEPLATE PARAMETER SETUP		<ul style="list-style-type: none"> Initial mode of bag integrity check. The user must enter the desired test parameters in the faceplate display. <p>Note: Faceplate to be opened by clicking the “Config” button.</p>
		<p>Next normal mode: READY</p> <p>Failure mode: N/A</p>
READY		<ul style="list-style-type: none"> The “Start” button will appear once the configuration form (available from “Config” button) has been correctly filled. The configuration settings can be filled in automatically by loading in the Bag Integrity SaveFile. Clicking on the “Start” button will open the confirmation message. Bag integrity check functionality enabled and awaiting user to start the check process.
		<p>Next normal mode: START</p> <p>Failure mode: N/A</p>
START		<ul style="list-style-type: none"> Bag integrity check functionality started. Selecting the “Abort” button will skip the below steps and proceed to SEQUENCE ABORTED in the “Abort Mode” table. <p>Note: The user will be presented with a confirmation box to when the “Abort” button is clicked.</p>
		<p>Next normal mode: VERIFY BAG PRESSURE* ACQUIRE MFC</p> <p>Failure mode: N/A</p>

Table K.3. Bag integrity operation in normal mode (continued).



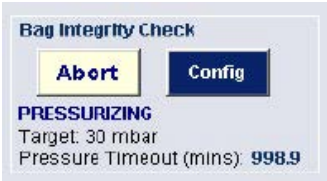

Mode	Display status	Operation	
VERIFY BAG PRESSURE*		<ul style="list-style-type: none"> Difference in the current vessel pressure and target pressure (D) entered by the user is evaluated. If the current bag pressure is greater than the target pressure (D), the sequence will enter a failure mode and request the user to abort the sequence. <p>Note: This step will only be visible to the user if the current bag pressure is greater than or equal to the target pressure. If this condition is not true, the sequence will automatically skip next normal mode.</p>	
		<p>Next normal mode: ACQUIRE MFC</p>	<p>Failure mode: SFC ERROR</p>
ACQUIRE MFC		<ul style="list-style-type: none"> Sequence automatically sets the user-entered MFC instance (G) into service. The MFC setpoint value (H) will be fixed by the sequence. Selecting the “Abort” button will skip the below steps and proceed to SEQUENCE ABORTED in the “Abort Mode” table. 	
		<p>Next normal mode: PRESSURIZE</p>	<p>Failure mode: N/A</p>
PRESSURIZE		<ul style="list-style-type: none"> Sequence will automatically pressurize the bag up to the target pressure (D). This pressurization will take place for up to the pressure timeout value (I) entered by the user. Sequence will automatically transition to FAILED step in the “Abort Mode” table if pressurization time exceeds (I), i.e. the bag doesn’t pressurize in the given amount of time. 	
		<p>Next normal mode: PRESSURE STABILIZATION</p>	<p>Failure mode: FAILED TIMEOUT</p>
PRESSURE STABILIZATION		<ul style="list-style-type: none"> Sequence waits for the current bag pressure value to stabilize for the given pressure stabilization time (J). MFC will close once the target pressure is met. Selecting the “Abort” button will skip the below steps and proceed to SEQUENCE ABORTED in the “Abort Mode” table. <p>Note: If the stabilization time expires and the pressure drop is with the configured limit then the sequence will move to the PRESSURE HOLD TIME step. If the pressure drop is greater than the limit, the sequence will enter the Pressurize step, if the user has set up the sequence to re-pressurize. If not, the sequence will go into the Failure Mode.</p> <p>If the user has entered a number of attempts (K), then the sequence will automatically loop to pressurize the bag again to the set value in (D). After completing the maximum number of attempts, if the pressure is still less than the allowable stabilization drop limit (L), the sequence will fail to failure mode SFC ERROR. However, if at any point during this operation, the pressure is within the allowable stabilization drop limit, the sequence will proceed to next normal mode.</p>	
		<p>Next normal mode: PRESSURE HOLD TIME</p>	<p>Failure mode: N/A</p>

Table K.4. Bag integrity operation in normal mode (continued).



Mode	Display status	Operation
PRESSURE HOLD TIME		<ul style="list-style-type: none"> Sequence will verify that the bag pressure is still within the allowable pressure drop limit (F). Sequence will wait for the pressure hold time (E) to ensure there is no leakage in the bag. If the pressure drops below the drop limit before the time expires, the sequence will go to the Failure Mode. Selecting the “Abort” button will skip the below steps and proceed to SEQUENCE ABORTED in the “Abort Mode” table.
		<p>Next normal mode: TEST PASSED</p> <p>Failure mode: FAILED</p>
PASSED		Sequence completes successfully, confirming no leakage in the bag.

Table K.5. Bag integrity operation in failure mode.

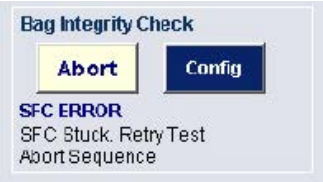
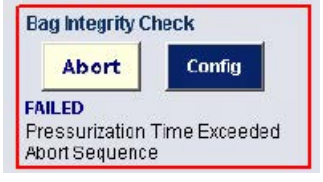
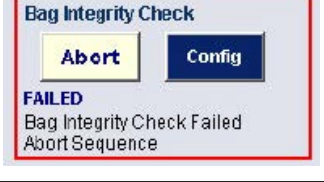
Mode	Display status	Operation
SFC ERROR		<ul style="list-style-type: none"> Sequence in error state and will not proceed to next stage without user action. Occurs if the number of repressurization has exceeded and the current pressure is not within the allowable stabilization drop limit. The user is requested to select the “Abort” button and restart the sequence.
FAILED TIMEOUT		<ul style="list-style-type: none"> Sequence failed due to pressurization not completing within the user-entered pressurization timeout limit. PRESS_TIMEOUT alarm is visible to the user. The user is requested to select the “Abort” button and restart the sequence.
FAILED		<ul style="list-style-type: none"> Sequence failed due to leakage detected within the bag. LEAK_DETECTED alarm is visible to the user. The user is requested to select the “Abort” button and restart the sequence.

Table K.6. Bag integrity operation in abort mode.


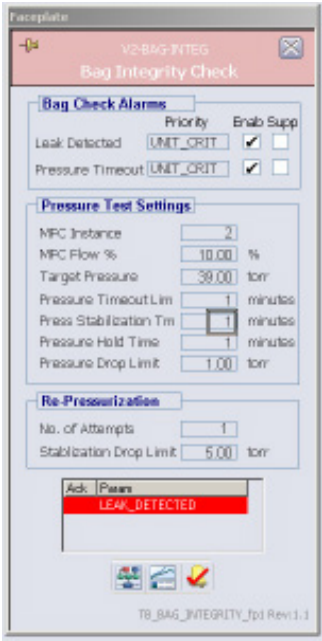
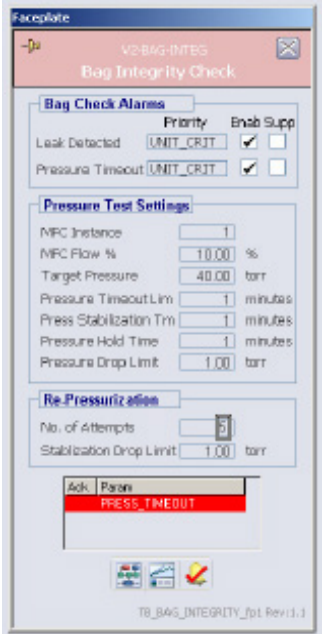
Mode	Display status	Operation
SEQUENCE ABORTED		<ul style="list-style-type: none"> Sequence aborted by user. The “Start” button is visible once the sequence is automatically reset and ready for next transition.

Table K.7. Bag integrity alarms.

Mode	Display status	Operation
<p>LEAK_ DETECTED</p>		<ul style="list-style-type: none"> • Alarm is displayed once the bag integrity check sequence fails due to pressure difference between the target pressure (D) set by the user, and the current pressure is greater than the allowable pressure drop limit (F). • Alarm is visible if the “Enabled” checkbox is selected per (A). • If the “Alarm Suppress” checkbox is selected per (C), the alarm will be active but suppressed from operator display.
<p>PRESS_ TIMEOUT</p>		<ul style="list-style-type: none"> • Alarm is displayed when the bag integrity check fails to pressurize the bag within a given amount of time set by the user (I). • Alarm is visible if the “Enabled” checkbox is selected per (B). • If the “Alarm Suppress” checkbox is selected per (C), the alarm will be active but suppressed from operator display.

Data historian

The following values are recorded in the historian by default for the bag integrity add-on:

- Pressure Hold Time
- Pressure Drop Time
- Pressure Timeout Limit
- Pressure Stabilization Time
- Target Pressure
- Current Step (Mode)

Event journal

An event log is recorded in the event journal each time the bag integrity check is performed. The log message will display the status of whether the bag integrity check TEST PASSED or SEQUENCE ABORTED. See Figure K.4.

Date/Time*	Event type	Category	Area	Node	Unit	Module	Module Description	Parameter	State	Level	Desc1	Desc2
20/09/2017 15:04:47.260	EVENT	PROCESS	AREA_V2_PROPLU_V2		V2-BAG-1	Control Module				PROCES		Bag Integrity Check TEST PASSED
20/09/2017 15:04:47.260	ALARM	PROCESS	AREA_V2_PROPLU_V2		V2-BAG-1	Control Module		LEAK_DETECTED	INACTIU	14-UNIT_Alarm		Bag Integrity Check
21/08/2017 11:11:36.195	EVENT	PROCESS	AREA_V2_PROPLU_V2		V2-BAG-1	Control Module				PROCES		Bag Integrity Check SEQUENCE ABORTED
21/08/2017 11:11:36.195	ALARM	PROCESS	AREA_V2_PROPLU_V2		V2-BAG-1	Control Module		PRESS_TIMEOUT	INACTIU	14-UNIT_Alarm		Bag Integrity Check

Figure K.4. Event journal example.

Process history

A chart named TB_BAG_INTEGRITY_fp.phve is supplied as standard as part of the add-on package. The chart can be loaded using the “Process History View” button on the bag integrity check faceplate. The following parameters are displayed on the chart as standard:

- Pressure Hold Time
- Pressure Drop Limit
- Pressure Timeout Limit
- Pressure Stabilization Time
- Target Pressure
- Current Step (Mode)

Security

Table K.8 defines which actions can or cannot be made by different users of the Bag Integrity add-on.

Table K.8. Available user actions for Bag Integrity add-on.

Function	Administrator	Supervisor	Operator	Maintenance
Change setup parameters	Yes	Yes	No	No
Start/Abort bag integrity test	Yes	Yes	Yes	No
Enable/Disable alarms	Yes	Yes	Yes	No

Appendix L—TruBio Discovery

Overview

TruBio Discovery Software is the name given to the offering of TruBio Software, powered by the DeltaV™ Discovery Distributed Control Platform from Emerson.

Architecture

The following diagram shows the architecture of a typical 4 vessel TruBio Discovery system.

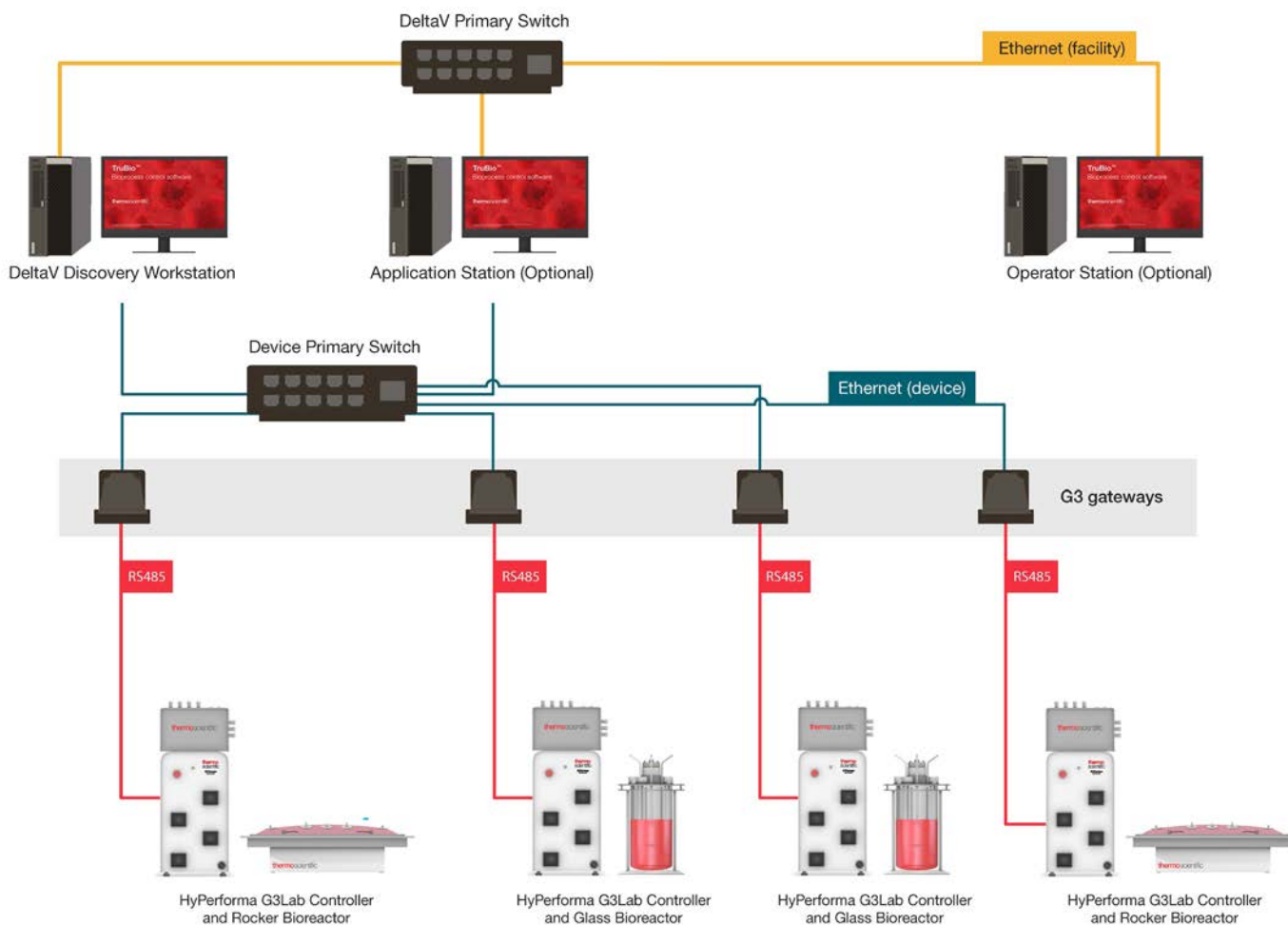


Figure L.1. Architecture of a typical 4 vessel TruBio Discovery system.

The table below describes the main architectural components:

Table L.1. Main architectural components.

Architectural Component	Description
Discovery Workstation Application Station	<p>A workstation-based controller to execute control strategies and performance calculations. Control modules, which are normally assigned to a physical controller, are assigned to the Workstations or Application Stations, reducing footprint and the need for physical controllers.</p> <p>See Emerson DeltaV Books Online for further information and licensing.</p>
Operator Station	Optional. Additional TruBio terminal station.
VEIOC	DeltaV Discovery supports Ethernet-based I/O which can further reduce footprint by eliminating the need for I/O cards and physical controllers. Ethernet-based I/O includes standard OPC communications as well as direct Modbus TCP and Ethernet/IP communications using Emerson's Virtual Ethernet I/O Card (VEIOC), which runs in the workstation.
DeltaV Primary Network (including the network switch)	DeltaV communications network used for process information and other DeltaV specific traffic. In this architecture, the DeltaV networks is simplex, i.e. there is no redundancy in the form of a DeltaV secondary network.
G3 Gateway	This device converts the RS-485 Modbus RTU packets from the G3Lab communications port to Modbus over TCP/IP (and vice versa).
G3Lab Controller	The Thermo Scientific HyPerforma G3Lab Controller can control most brands of single-use or autoclavable bioreactors or fermentors that are ≤ 50 L, including stirred-tank and rocking models. The controller operates using TruBio software, which provides easy process scale-up or scale-down and the configurability to modify your control strategy along with your process. The enclosure contains state-of-the-art transmitters along with power supplies, pumps, input/output (I/O) modules, and the hardware required to connect to the control network, providing maximum control capability.

These tables show the difference and limitations between a TruBio Discovery system and a TruBio system based on a standard DeltaV system with TruLogic Controllers.

Table L.2. Software comparison

Features	TruBio Discovery Software (powered by DeltaV Discovery platform)	TruBio Software (powered by DeltaV platform)
Standard TruBio Software interface	✓	✓
Control key process parameters	✓	✓
Integrate process parameters	✓	✓
Process Alarms	✓	✓
Building alarms*		✓
Event historian	✓	✓
Save/load files for tech transfer	✓	✓
Batch control and event history collection	✓	✓
GMP compliance*		✓
Profibus scales*		✓
Multifeed dosing function*		✓
G3Lab I/O signals	✓	✓
External signals*		✓
Redundant control*		✓
TruBio Discovery Software cannot be used with TruLogic Controllers		

*Typical functionalities that are important in Commercial Manufacturing facilities

Table L.3. Software comparison Matrix

Feature	TruBio Discovery Software	TruBio Software with conventional DeltaV
Communication limitations: # of vessels per workstation	4 units (vessels) per DeltaV Application station	Up to 8 units (vessels) per TruLogic module
Supported vessel size	Up to 50 L	No set vessel size limit
Typical users	<ul style="list-style-type: none"> Non-GMP Research and PD facilities who may be transferring processes to GMP commercial facilities 	<ul style="list-style-type: none"> GMP and 21 CFR Part 11 applications CMOs
Applications	<ul style="list-style-type: none"> Cell culture PD-scale cell expansion Early drug lifecycle phase 	<ul style="list-style-type: none"> Cell expansion Clinical Pilot launch Commercial mftg (applicable for both GMP and non-GMP environment)
Communication protocol	Supports connections with devices using OPC-DA, Modbus TCP/IP, or Ethernet/IP	Can connect with devices supported by DeltaV
Architecture	Workstation based control using Modbus TCP/IP to connect to G3Lab via G3 Gateways	TruLogic controller (hosting DeltaV MX or MQ controller) using Serial MODBUS to connect to G3Lab via Emerson DeltaV Serial cards.

TruBio Discovery and Conventional TruBio DeltaV employ different DeltaV licensing from Emerson. Emerson does not support the installation of DeltaV Discovery on a DeltaV PAS system.

Find out more at thermofisher.com/sut

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