Thermo Fisher
S C I E N T I F I C

Bioprocess control software

TruBio Bioprocess Control Software Version 5.0 User's Guide

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thermo scientific

Contents

Contents

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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

A summary of the changes that have been made to this document are listed below.

Revision	Date	Section	Description	Author
A	01/2020	--	Initial release	E. Hale, T. Golightly
B	08/2021	--	Reformatted to align with current style guide	C. Jones
B	08/2021	--	Updated images throughout to reflect the current interface	C. Jones
B	08/2021	--	Added information for TruBio with GXCore	C. Jones
B	08/2021	--	Extensive reformatting to enhance the user experience	C. Jones
B	08/2021	3.5	Added guidelines for vent heater filter settings	C. Jones
B	08/2021	5.3	Expanded steps for setting up control loops	C. Jones
C	03/2022	--	Reformatted in new style	C. Jones
C	04/2022	3.4	Added section detailing how to enable Bypass mode	C. Jones
C	03/2022	3.1	Corrected user rights in table 3.1.	C. Jones
D	03/2022	3.5.1	Updated sensor calibration instructions	C. Jones
D	03/2022	3.5.1, 3.5.2, 3.5.3	Updated instructions for calibration	C. Jones
D	03/2022	Appendix G	Added appendix for sensor specific calibration instructions	C. Jones
D	04/2022	1.3	Updated Table 1.3 with the amount of controllers per workstation	C. Jones

Feedback on this publication

If you have any questions or concerns about the content of this publication, please contact **technicaldocumentation@thermofisher.com** and your Thermo Fisher Scientific sales team.

Abbreviations

The list below provides definitions of abbreviations and acronyms used in this publication.

AI/AO	Analog Input/Analog Output
ARW	Anti-Reset Windup
BPC	BioProcess Container
cGMP	Current Good Manufacturing Practice
GAMP5	Good Automated Manufacturing Practice version 5
DO	Dissolved Oxygen
DV	DeltaV
ETP	Electronic Turnover Package
FRS	Functional Requirement Specification
KBA	Knowledge-Based Article
MFC	Mass Flow Controller
MSA	Motor Safety Alarm
OPU	Online Parameter Update
PHV	Process History View
PID	Proportional Integral Derivative
PV	Process Value (or Process Variable)
P/V	Power Input to Volume
PWM	Pulse Width Modulation
QC	Quality Control
RTU	Remote Terminal Unit
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

1

TruBio Software overview

Chapter contents

1.1 Introduction

The Thermo Scientific TruBio 5.0 Bioprocess Control Software powered by DeltaV™ distributed control system from Emerson™. This configurable software solution is designed to provide a flexible system for the control of bioprocesses. TruBio Software has been developed according to the Good Automated Manufacturing Practice version 5 (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 is designed for use with a wide range of bioreactor/fermentor or mixing vessels, from small tabletop development systems to high-volume manufacturing vessels. It also allows you to:

- Use different bioprocess equipment in the same network with no change in the operator interface

- Quickly view total pump and gas delivery volume on the Main Screen

- Integrate data from offline equipment, such as chemistry analyzers

- Display the full record of the last vessel load performed

- 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.

We recommend you to become familiar with the other guides included on the electronic turnover package (ETP) to obtain maximum performance from the system.

Thermo Scientific offers additional software training as needed. Please contact your Thermo Fisher Scientific sales representative for further information.

1.2 Usage information

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.

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1.2.1 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.) or Single-Use Fermentor (S.U.F.), 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 (HS)**—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 made 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.

- **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.

1.3 Architecture and installation

This section describes physical network, software, hardware, and provides installation information.

1.3.1 Physical network

The physical network consists of controllers and workstations within the DeltaV system and can be used on GMP or non-GMP systems. The Control Network is dedicated to the DeltaV system. A separate Ethernet interface is provided via a DeltaV ProfessionalPLUS station or Professional station to connect the DeltaV system to a plant-wide LAN.

The primary way to connect the DeltaV system to the plant LAN or to run non-DeltaV applications, is through a DeltaV Application Station.The Control Network can be designed to be redundant for improved reliability. The secondary network is routed through a separate Ethernet network. The Ethernet network system can use TCP/IP communication to all network resident devices with a minimum bandwidth of 100 Mbit/sec.

1.3.2 Hardware overview

TruBio Software is installed on a ProfessionalPLUS PC/Server and requires a DeltaV dongle. The TruLogic cabinet houses the DeltaV Controller, an 8-wide carrier, and requires DeltaV serial cards for connecting G3- or GX-series controllers.

The ProPlus, TruLogic, and G3 series of Controller (G3Lab, G3Lite, and G3Pro) or GXCore Bioprocessing Controller, form a control network with the 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 Controller.

Figure 1.1 shows a typical network architecture.

Note: TruBio Discovery Software does not require a TruLogic cabinet. See section 1.3.3 for further details.
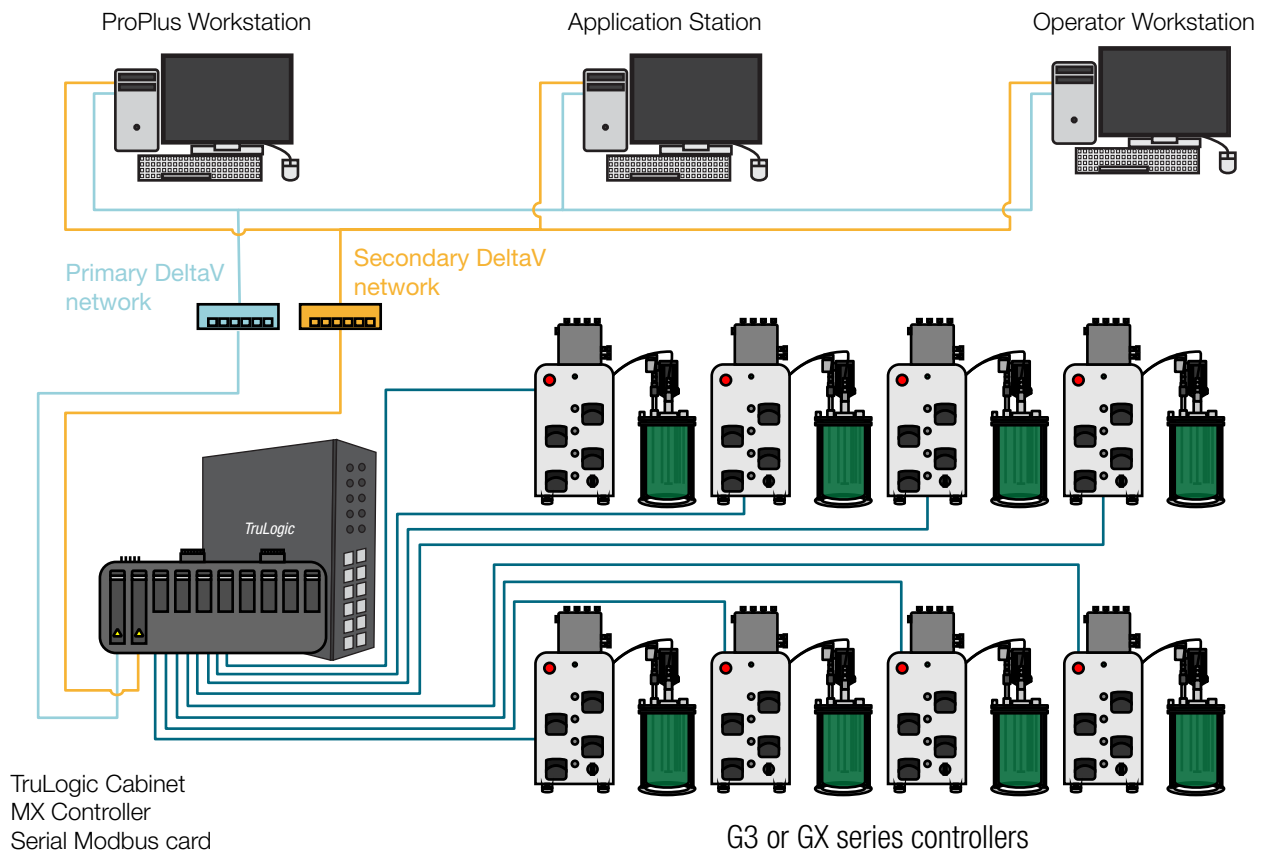

Figure 1.1. DeltaV physical network with ProPlus station and workstations.

TruBio Software must be installed on all DeltaV workstations that are used to control and view bioreactor operations. Refer to Emerson Process Management for a list of PCs/ Servers currently recommended and supported.

The TruLogic cabinet (Figure 1.2) requires a DeltaV Controller with an associated 2-Wide Power Supply, 8-Wide Carrier, and Serial Card. Optional interface cards include Classic I/O, HART, DeviceNet, Profibus DP, and Foundation Fieldbus.

Figure 1.2. TruLogic cabinet.

1.3.3 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

Figure 1.3 shows the architecture of a typical four vessel TruBio Discovery system.
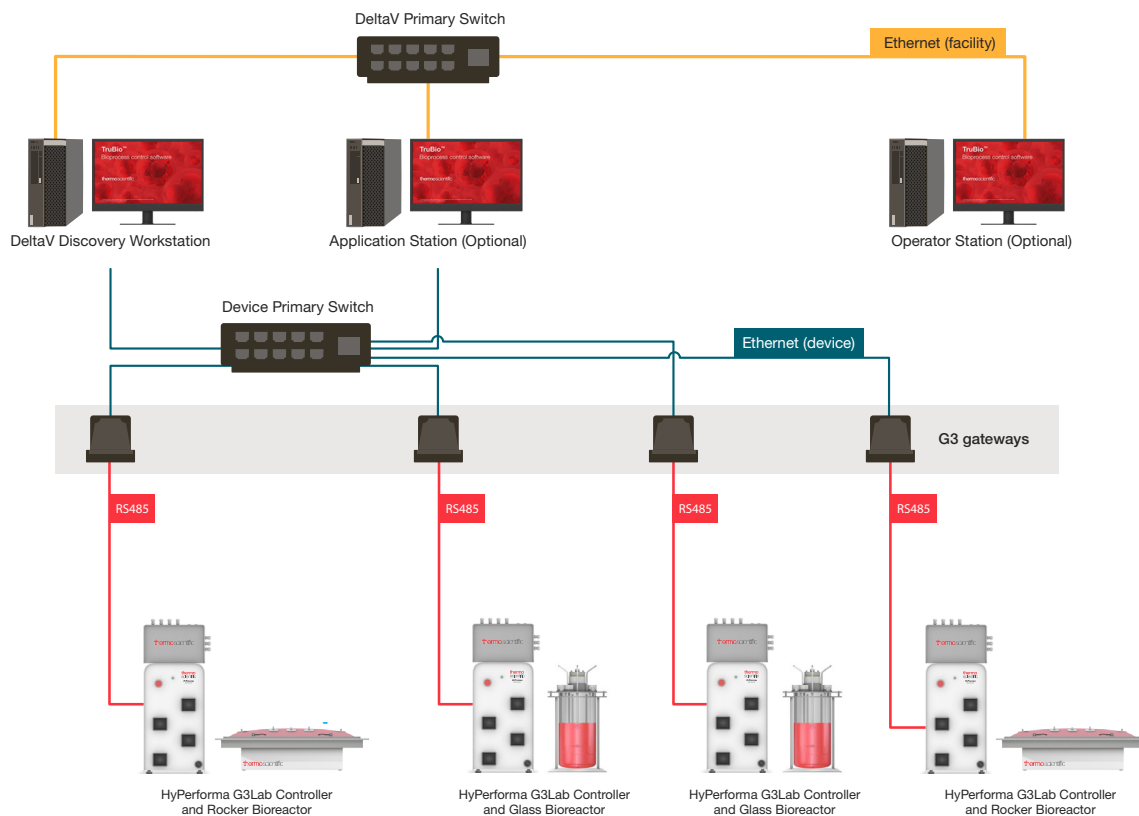
Figure 1.3. Architecture of a typical 4 vessel TruBio Discovery system.

Note: The Architecture with a GXCore Controller looks the same, but does not require the G3 gateway. The GXCore Controller connects directly to the DeltaV Discovery Workstation.

Table 1.1 describes the main architectural components:

Table 1.1. Main architectural components.

Architectural component	Description
Discovery Workstation Application Station	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 Worksations or Application Stations, reducing footprint and the need for physical controllers. See Emerson DeltaV Books Online for further information and licensing.
Operator Station	Optional. Additional TruBio terminal station.
Emerson's Virtual Ethernet I/O Card (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 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 Remote Terminal Unit (RTU) packets form the G3Lab communications port to Modbus over TCP/IP (and vice versa).
G3- or GX-series controller	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.

*The GXCore controller does not require or use the G3 gateway.

Tables 1.2 and 1.3 show the difference and limitations between a TruBio Discovery system and a TruBio system based on a standard DeltaV system with TruLogic Controllers.

Table 1.2. Software comparison.

Feature	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*	✕	✓
Multi-Feed dosing function*	✕	✓
GXCore	✓	✓
G3Pro	✕	✓
G3Lite	✕	✓
G3Lab	✓	✓
External devices**	✕	✓
Redundant control*	✕	✓
TruBio Discovery Software cannot be used with TruLogic Controllers		

*Important in Commercial Manufacturing facilities.

**Devices that do not connect to the controller, but connect directly to the DeltaV serial card or Profibus card. Important in Commercial Manufacturing facilities.

Table 1.3. Software comparison matrix.

Feature	TruBio Discovery Software	TruBio Software with conventional DeltaV Controller
Maximum number of controllers per workstation	4 units (vessels) per DeltaV 14 Application station	• Up to 8 HyPerforma GXCore Controllers • Up to 6 HyPerforma G3Lab Controllers • Up to 5 HyPerforma G3Pro Controllers • Up to 6 HyPerforma G3Lite Controllers
	4 units (vessels) per DeltaV 12 and 13 Application station	• Up to 8 HyPerforma GXCore Controllers • Up to 8 HyPerforma G3Lab Controllers • Up to 8 HyPerforma G3Pro Controllers • Up to 8 HyPerforma G3Lite Controllers
Supported vessel size	Up to 50 L	No set vessel size limit
Typical users	• Non-GMP Research and PD facilities who may be transferring processes to GMP commercial facilities	• GMP and 21 CFR Part 11 applications
Applications	• Cell culture • Process Development-scale cell expansion • Early drug life cycle phase • CTGT	• Cell expansion • Clinical • Pilot launch • Commercial mfg (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	TruLogic controller (hosting DeltaV MX or MQ controller) using Serial MODBUS

Note: TruBio Discovery Softwareand conventional TruBio Software powered by DeltaV employ different DeltaV licensing from Emerson. Emerson does not support the installation of DeltaV Discovery on a DeltaV PAS system.

1.4 Field instrumentation

The field instrumentation per 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 vessel control. The TruBio software configuration can include the following instruments per vessel under control:

Table 1.4. Main architectural components.

Instrument type	Process values
ph	Millivolts
DO	Nanoamps or optical
Temperature	°C or °F
Jacket temperature	°C or °F
Agitation	Rate (rpm)
Foam/Level	microSiemens; Threshold
Pumps	Rate (rpm); flow rate (Mass/Unit time)
Gas Flow	Rate (SLPM); Volume
Weight	kg (net, gross); kg (zero/tare)
Pressure	psi (a), psi (g), Bar, and mmHg
Auxiliary input	Configurable
Auxiliary control loop	Configurable

1.5 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 are required by Emerson Process Management.

1.5.1 Locating TruBio Software license information

Use the following steps to locate license information.

1. From the ProPlus station, select **TruBio** from the Windows™ taskbar (Figure 1.4).

Figure 1.4. TruBio button shown on Main Screen.

2. This displays the TruBio Engineering window. Select **License Info** (Figure 1.5) to display the current licensing information for the system (Figure 1.6).
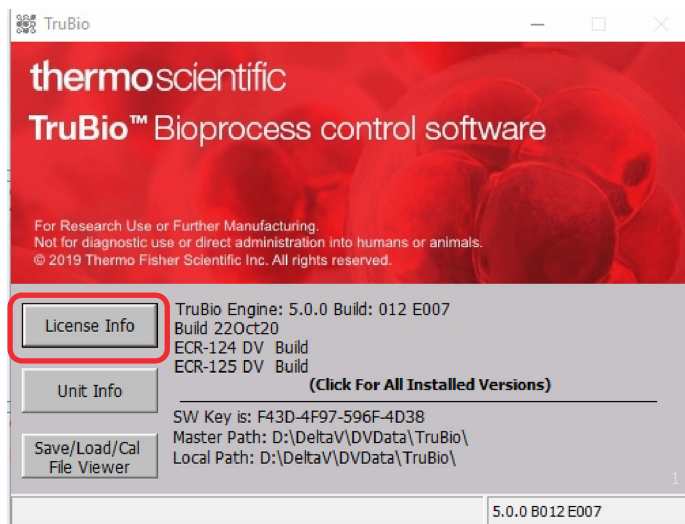
Figure 1.5. TruBio Engineering window on the ProPlus station.
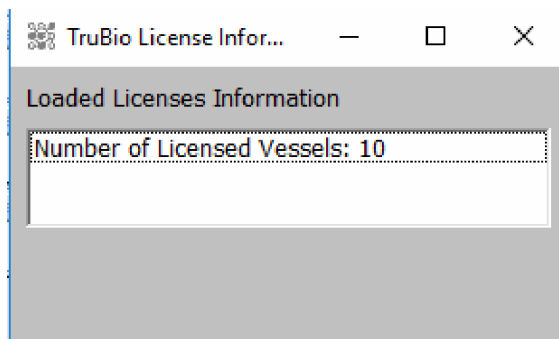
Figure 1.6. TruBio License Information window.

1.5.2 Locating the DeltaV license information

1. Use the following steps to locate license information.

2. From the ProPlus station select **DeltaV Utilities** from the top toolbar, and then select **Exploring DeltaV** from the **DeltaV Utilities** window (Figure 1.7).

   Note: You can also select **Exploring DeltaV** from the Windows Taskbar.
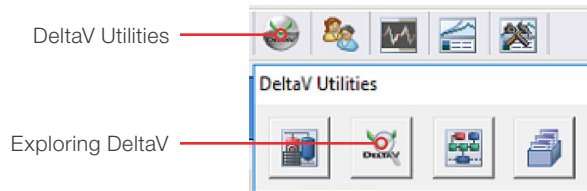
Figure 1.7. Exploring DeltaV button.

3. Open the **File** menu in the **Exploring DeltaV** window, select **Licensing**, then **Licensing Report** (Figure 1.8).
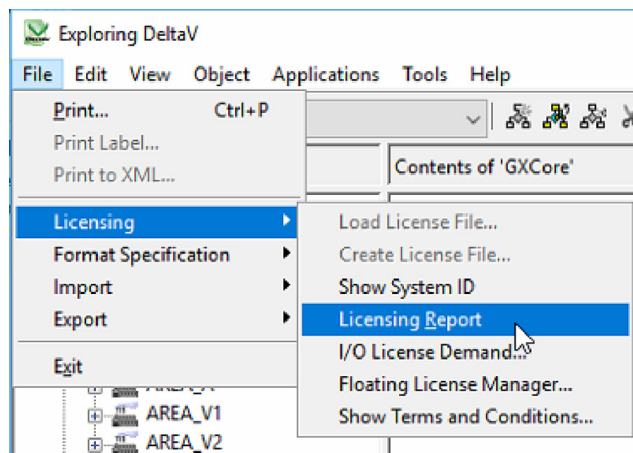
Figure 1.8. Location of Licensing Report in the File menu.

Figure 1.9 shows a sample Licensing Report. Licensing information can be printed, or a screenshot can be copied into another program.
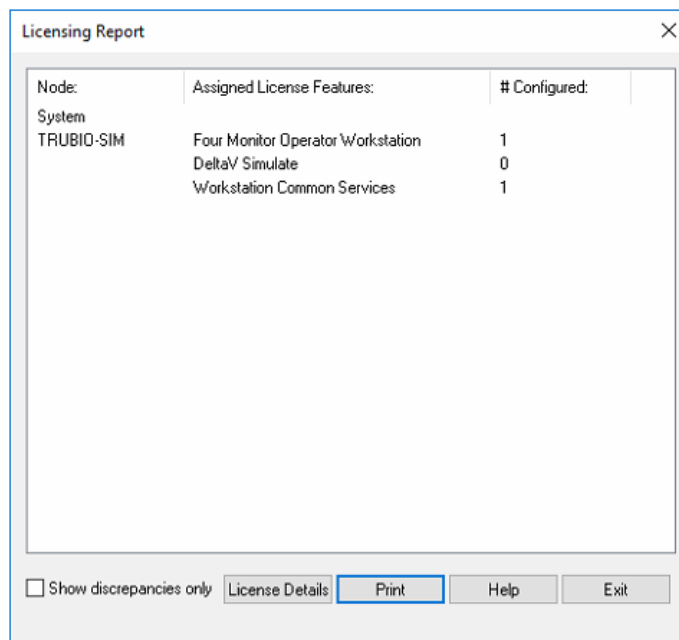
Figure 1.9. Sample licensing report.

1.6 DeltaV Books Online

DeltaV Books Online is a help desk for information regarding the DeltaV platform. It is accessed from the **DeltaV Utilities** toolbar (Figure 1.10)
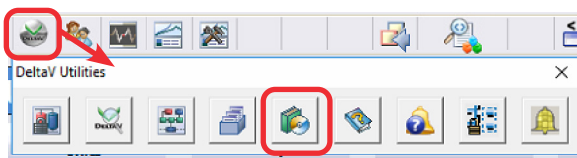
Figure 1.10. DeltaV Books Online on the DeltaV Utilities toolbar.

2

User interface

Chapter contents

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

- Splash screen (opening screen)

- Overview screen

- Main bioreactor or fermentor screen

- Configuration screen

- Online Parameter Update screen

- Individual parameter faceplates

- Data Entry screen (for offline information)

- Cleaning screen

2.1 Splash screen

The **Splash** screen (Figure 2.1) appears when the software is launched. It contains the alarm banner and toolbar. Click anywhere in the red TruBio graphic to enter the program.
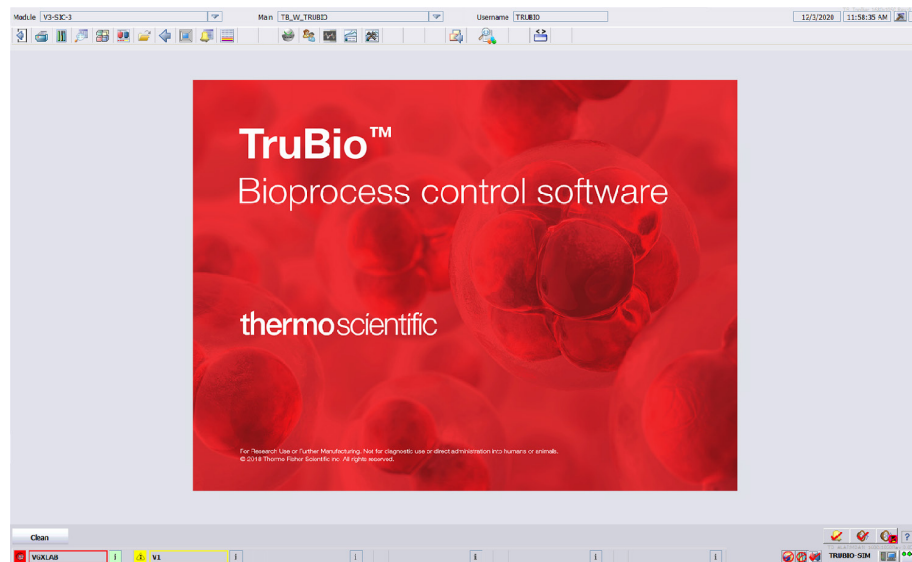
Figure 2.1. Splash screen.

2.2 Overview screen

The **Overview** screen appears after you click the **Splash** screen graphic.

The buttons on this screen (shown in Figure 2.2) represent individual bioreactor or fermentor vessels. Each vessel button displays the configured **Key Parameters** (if any) for the associated vessel (See section 2.6.2).

Vessel buttons

Key Parameters
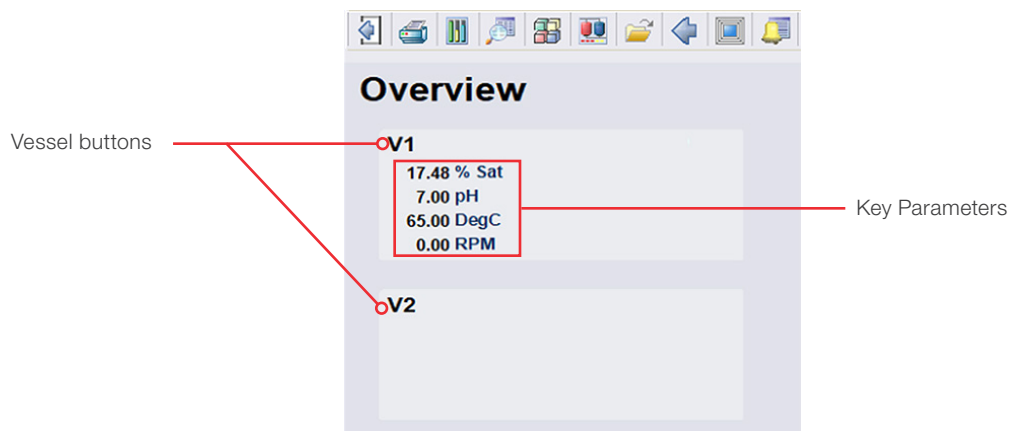
Figure 2.2. Vessel buttons on the Overview screen.

Select a vessel button to open the **Main** screen for the associated vessel.

2.3 Main screen

This screen displays buttons and control modules for control loop and measurement values (Figure 2.3).

Note: TruBio with GXCore features an optional unique user interface (UI) that is discussed in section 2.4.
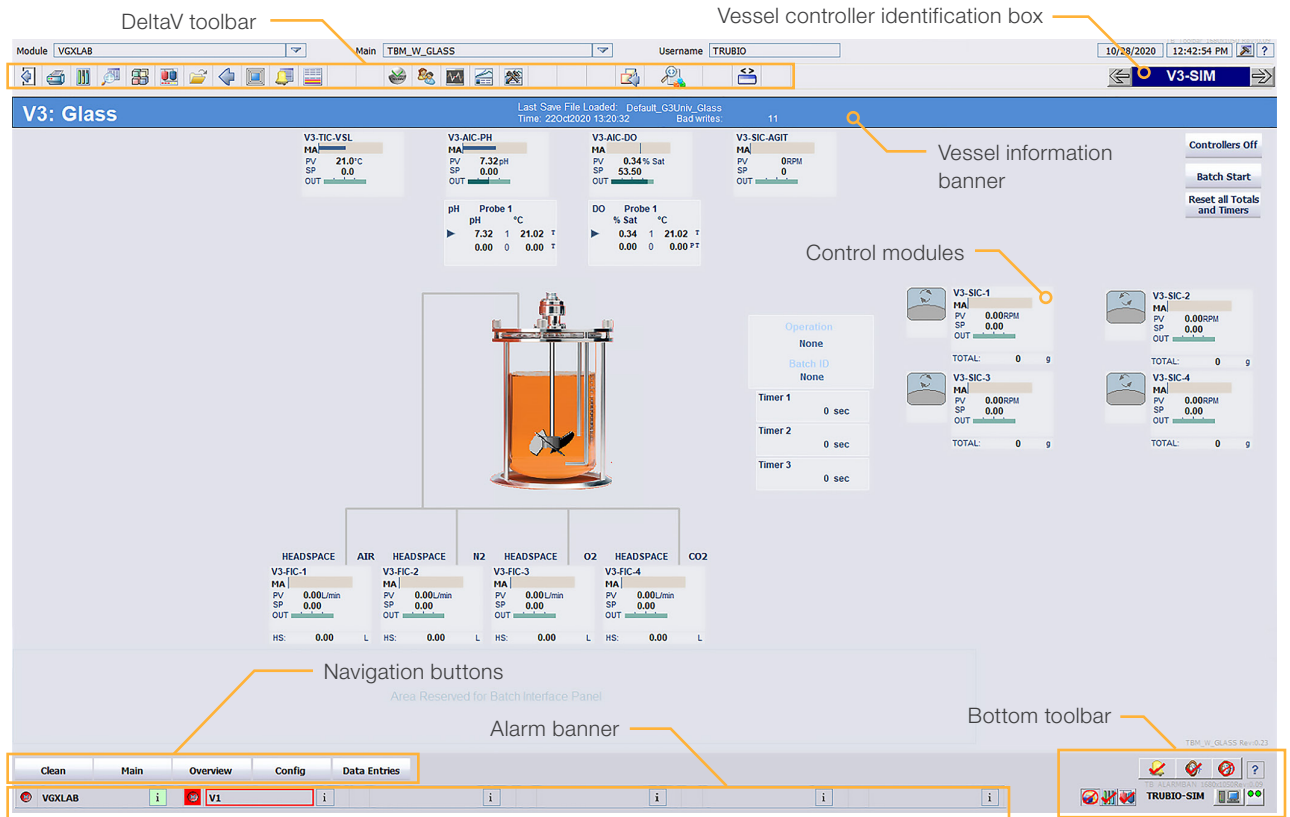
Figure 2.3. Main screen example.

2.3.1 DeltaV toolbar

Provides quick access to features such as the alarm list, diagnostics, and Process History View. Table 2.1 provides a description for each button.

Table 2.1. DeltaV toolbar button icons and functionality descriptions.

| Icon	Description
	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 module.
	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.
	Allows you to select a graphic screen from the graphics root directory. Limited access as errors may crash the Operator Interface.
	Returns you to the previous Main screen.
	Opens the Overview screen, with links to each tower and vessel graphic. An easy way to navigate quickly between vessels.
	Opens the Alarm Summary screen, showing all active and unacknowledged alarms.
	Opens the Alarm Filter screen, excluding alarms from inactive vessels and showing only alarms from active vessels.
	Opens DeltaV Utilities; provides access to Emerson Process Management functions.
	Opens the DeltaV logon; logs user into DeltaV workstation.
	Opens the DeltaV System Diagnostics screen to facilitate troubleshooting.
	Opens the Process History View.
	Opens the Chart Builder
	Toggles the applications running in the background to the foreground.
	Starts the Tag Search Utility.
	Toggles which tag is displayed for control modules. Choose between Module Tag, Description, Friendly Name, and No Display (see section 2.3.2.)

2.3.2 Tag Display settings

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—Displays labels with the name string found in the Online Parameter Update (OPU) lists (e.g. V3-TIC-VSL)

Description—Displays labels with a preconfigured common name (e.g. Vsl Temperature)

Friendly Name—Displays labels with a preconfigured "friendly name" (e.g. Vessel Temp)

No Display—Displays no labels

2.3.3 Vessel Controller identification box

The Vessel Controller identification box (Figure 2.4) identifies which controller is in use. Click the **forward** or **back** arrows to cycle the graphic display.

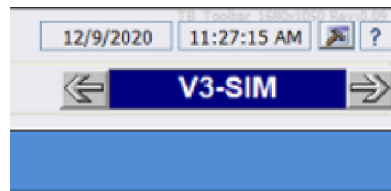**Figure 2.4. Vessel Controller Identification box.**

2.3.4 Vessel information banner

The vessel type and number are displayed in this banner. This banner indicates which type of vessel is in use. The color of the banner matches the color assigned to the vessel (Figure 2.5).

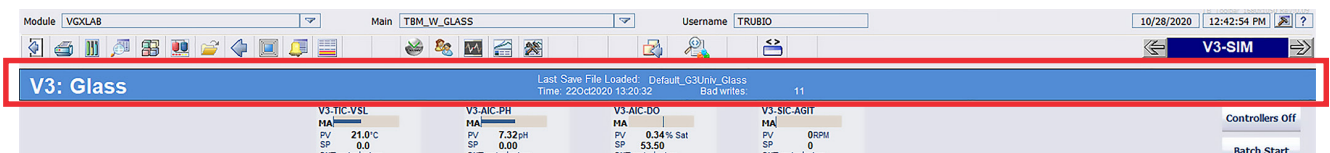When a SaveFile has been loaded the type of file and the date loaded are also displayed.

Figure 2.5. Vessel information banner.

2.3.5 Alarm banner

The alarm banner (Figure 2.6) displays the status of active alarms. You can click an active alarm to open a faceplate where the alarm can be viewed in detail and acknowledged. If the alarm is triggered when the PV exceeds, the Hi or Lo limit without exceeding the Hi-Hi or Lo-Lo, 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.
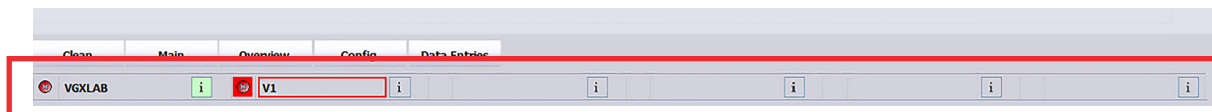
Figure 2.6. Alarm banner with active alarms.

2.3.6 Navigation buttons

Navigation buttons (Figure 2.7) provide quick access to the different graphic screens of the selected vessel.
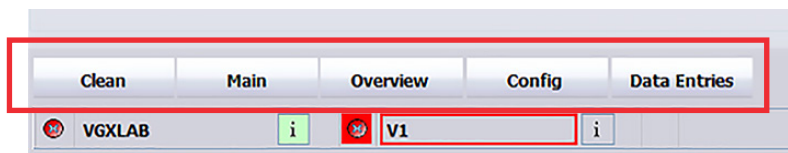
Figure 2.7. Navigation buttons.

2.3.7 TruBio control mode descriptions

Tables 2.2 and 2.3 provide a description of the TruBio control modes.

Table 2.2. Control module name strings.

TruBio control module	Module tag*
Analog input	V*x*-AI-1 through 8
Lab entry	V*x*-AI-LE1
DO	V*x*-AIC-DO
pH control	V*x*-AIC-PH
Common unit	V*x*-COMMON
MFC	V*x*-FIC-1 through 6
Foam	V*x*-LI-FOAM
Analog input	V*x*-AI-1 through 8
Lab entry	V*x*-AI-LE1
Foam	V*x*-LI-FOAM
Level	V*x*-LI-LEVEL

* '*x*' represents the vessel number.

Table 2.3. Control mode name strings (continued).

TruBio control module	Module tag*
Pressure	V*x*-PI-VSL
Auxiliary	V*x*-SIC-AGIT
	V*x*-XIC-1 through 4
Pump	V*x*-SIC-1 through 6
Temperature	V*x*-TIC-JKT
	V*x*-TIC-VSL
Scale	V*x*-WI-1 through 6
Weight	V*x*-WIC-VSL
Freeform equation	V*x*-XY-FUNC1 through 6
Logic	V*x*-XY-LOGIC
Math	V*x*-XY-MATH
Signal characterizer	V*x*-XY-SGCR
Timer	V*x*-XY-TMR
Input and output	V*x*-IO
	V*x*-IO-OUT
	V*x*-IO-WAVE
	V*x*-IO-OUT-WAVE
TruFluor virtual transmitter	V*x*-TF-DO2
	V*x*-TF-DO3
	V*x*-TF-PH2
	V*x*-TF-PH3
Digital MFC	V*x*-MFC
Digital pump	V*x*-PUMP
Multi-Feed	V*x*-MFDOSE

* '*x*' represents the vessel number.

2.3.8 Control modules

Control modules (sometimes called dynamos) represent vessel instrumentation. The **Main** screen contains control modules for all instruments associated with the vessel.

Click a control module to bring up its faceplate. Faceplates contain options for controlling ancillary components such as pumps, sensors, and mass flow controllers (MFCs).

Note: The control modules for each smart device (MFCs and pumps) will only appear when the device is connected to the controller.

pH and DO control modules

The upper control module displays (Figure 2.8) 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 image).

The lower control module (Figure 2.8) displays the raw probe data (up to three probes), with the blue arrow indicating the probe from which the controller is reading the PV.
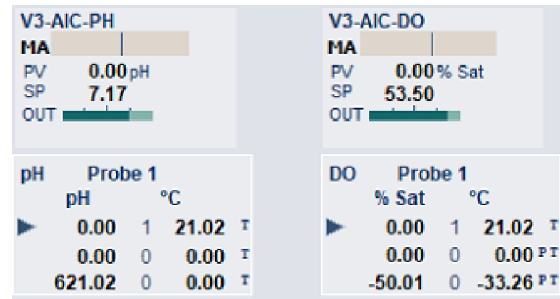

Figure 2.8. pH and DO control modules.

MFC control modules

The lines connecting the control modules to the vessel represent the gas flow path. In Figure 2.10, Air and O_2 reach the vessel through the headspace flow path. There are up to three possible flow paths.

The total gas added by each MFC is shown in the lower part of the display box for the selected gas.

The control module also displays the selected remote setpoint at the bottom of the control module. Figure 2.9 shows an example of the gas flow path to the vessel.
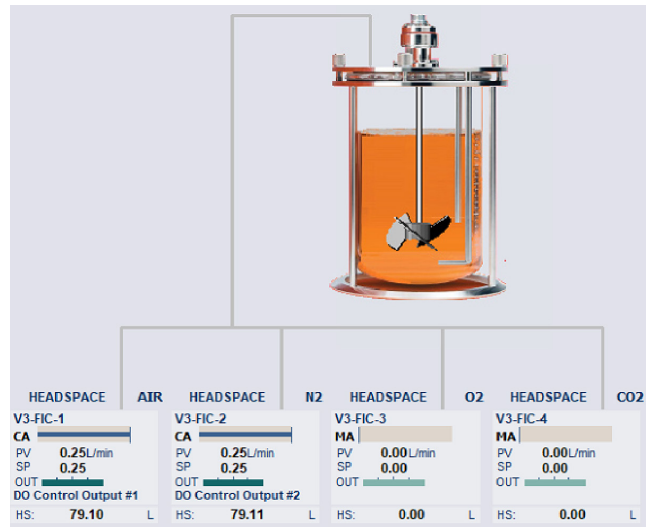
Figure 2.9. Flow path of gases to the vessel.

The lower portion of the control module for gases and pumps is a totalizer box (Figure 2.10). Click it to open the Totalizer faceplate. Click **Reset** when you want to reset the totals to zero (0).
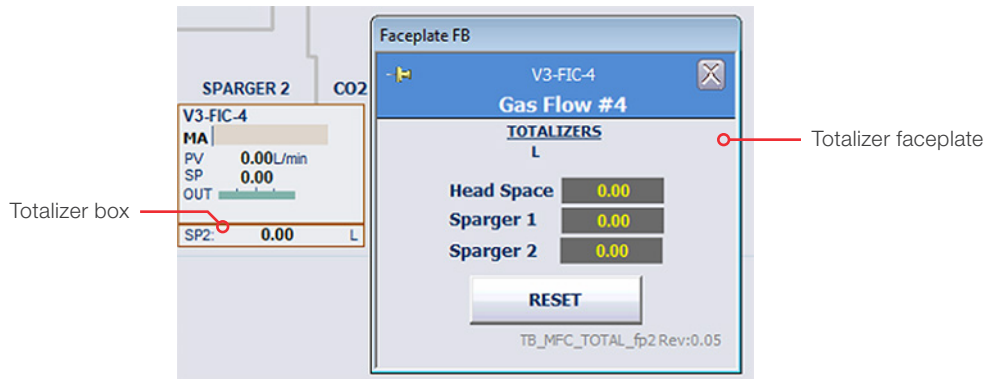

Figure 2.10. Totalizer faceplate for Gas Flow #4.

2.3.9 Faceplates

Click a control module to open its faceplate. Figure 2.11 details the components of the faceplate.
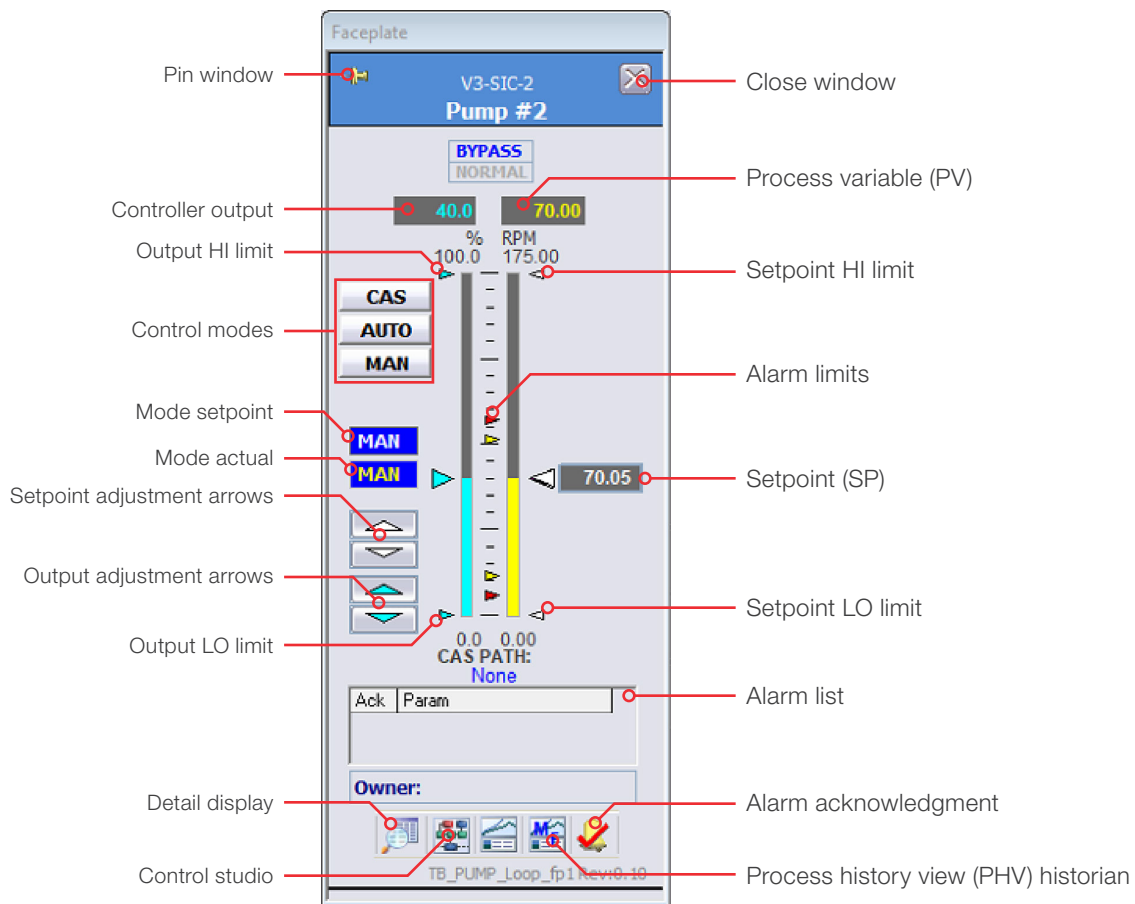

Figure 2.11. Faceplate detail.

Note: TruBio with GXCore features a mini-faceplate. Click the faceplate button to access the full faceplate (see section 2.4.2).

- **Pin window**—Allows you to open multiple faceplates at once.

- **Close window**—Closes the faceplate.

- **Controller output**—Shows the activity of the control loop maintenance functions in percentage of the maximum, e.g. if the faceplate for a pump is open and the controller output shows 20%, it may mean that the pump is running at 20% of its maximum speed.

- **Process value (PV) or process variable**—displays the value of the parameter in real time.

- **Setpoint**—Displays the user-defined target value for the parameter.

- **Setpoint HI and LO limits**—Defines 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.

- **Output HI and LO limits**—Defines the percentage of the permitted maximum output. Maximum output is defined as the limit of the agitator or pump. E.g. 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.

  Note: With TruBio for GXCore, SP: and Out: allow you to control the setpoint and output without opening the full faceplate. Click one to open the Data Entry window, enter a value in the New Value field, and click OK.

- **Alarm limits**—Shows limits on the PV bar display and defines when an alarm will be triggered. There are four alarm levels: Hi-Hi, Hi, Lo, and Lo-Lo. Alarm limits are set in the Detail screen.

- **Alarm list**—Details any active alarms for the parameter that is referenced by the faceplate.

- **Alarm Acknowledgment**—Acknowledges all triggered alarms in the faceplate. Audible alarms can be silenced by clicking **Silence Alarms** in the alarm toolbar at lower right corner of the screen.

- **Setpoint adjustment arrows**—Increase (up arrow) or decrease (down arrow) the setpoint by a single digit.

- **Output adjustment arrows**—Increase (up arrow) or decrease (down arrow) the output control by a single digit.

- **Control mode**—Sets the control mode between **Manual** (MAN), **Automatic** (AUTO), or **Cascade** (CAS) mode. A description of each mode is provided below.

- **Detail**—Opens the detail window for calibration, alarm limits, and probe selection. Refer to section 2.3.10 for more information.

- **Control Studio icon**—Provides access to DeltaV tools. More information on DeltaV tools is available through DeltaV Books Online.

- **Process History View icon**—Similar to parameter trending, but can show more than one parameter at a time.

Control modes

Manual (MAN)

In **Manual** mode, the operator manually sets the controller output (CO). The control system does not perform any control calculation based on set point (SP) and it is up to the operator to monitor the process variable (PV) and make any required changes to the output to maintain control.

Automatic (AUTO)

In **Automatic** mode, the operator manually sets the set point and the control module automatically calculates the control output based on the tuning parameters and the relationship between the process variable and the set point. Once the set point is set, the control module should hold the process variable near the set point (assuming the tuning parameters are set correctly).

Cascade (CAS)

Cascade mode is similar to AUTO except that instead of the set point being set by the operator it is set by another control element via a link. This link is shown on the faceplate below the "CAS PATH:" text under the PV and OUT indications. The control module in the CAS mode is the cascade slave and the control module that is linked to is the cascade master. The operating set point of the slave is determined by whatever logic the master is linked to the slave. This link can be set in the Configuration screen. If the link is set to none then the control module will not be able to shift to cascade mode.

Local Override (LO)

Local Override is not a selectable option, but instead appears in the Mode actual display when the internal block output is overridden due to output tracking being enabled. This usually indicates an active interlock being triggered. Output cannot be changed when internal block is in LO until the interlock is remedied.

2.3.10 Detail Display

Each control module has a Detail display that provides access to most tuning parameters and diagnostic information. It allows you to monitor and/or control various configurable parameters i.e. limits, tuning, alarms, gain scheduling, diagnostic simulation, input types, interlocks and calibration functions.

Calibration

The Calibration tab (Figure 2.12) enables calibration of the sensors for the parameter associated with the faceplate. Electrochemical calibration is the normal procedure. If a virtual transmitter is part of the pH or DO control loop, you have the option to run the calibration through the virtual transmitter. See section 3.5 for calibration instructions.

Figure 2.12. Calibration tab details.

Alarms

In TruBio Software, version 5.0, the **Alarms** tab (Figure 2.13), combines the parameters of what were the separate **Alarms** and **Limits** tabs in previous TruBio Software versions. In this tab, you can set and enable the alarms. See Chapter 4 for detailed instructions.
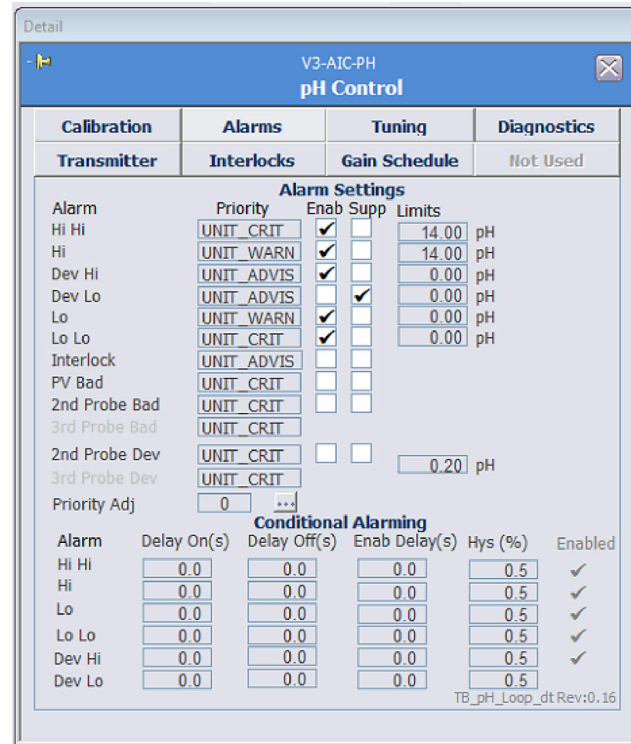

Figure 2.13. Alarms tab details.

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.

Note: The **SP Limits** have been moved from the **Alarms** tab to the **Tuning** tab, which is discussed in the next section.

Tuning

The **Tuning** tab (Figure 2.14) allows you to view and change the tuning parameters of the control loop. For modules that support deadband local override, can also enable or disable the deadband local override function and enter upper and lower deadband limits, as desired.

Figure 2.14. Tuning tab details.

The **Tuning** tab includes the following parameters:

- **Out Hi/Lo Lim**—Limits the output of the controller.

- **Anti-Reset Windup (ARW) Hi/Lo Lim**—Prevents an over-correction if the setpoint is changed which improves process recovery from saturated conditions.

- **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**—Adjusts the gain setting of the Proportional Integral Derivative (PID) loop.

- **Reset**—Resets time constants of the PID loop. Reset corresponds to the Integral. Integral feedback is K1 x E1 where E1 is a time integral of error (therefore, a multiple of time). Reset constant K1 should be inverse seconds (1/s).

- **Rate**—Rate corresponds to the derivative.

- **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.

Interlocks

The **Interlocks** tab (Figure 2.15) is mostly used in control loops that involve gases or liquids with some exceptions. Interlocks are user-configurable and set defined system features to interlock when alarm limits are breached.
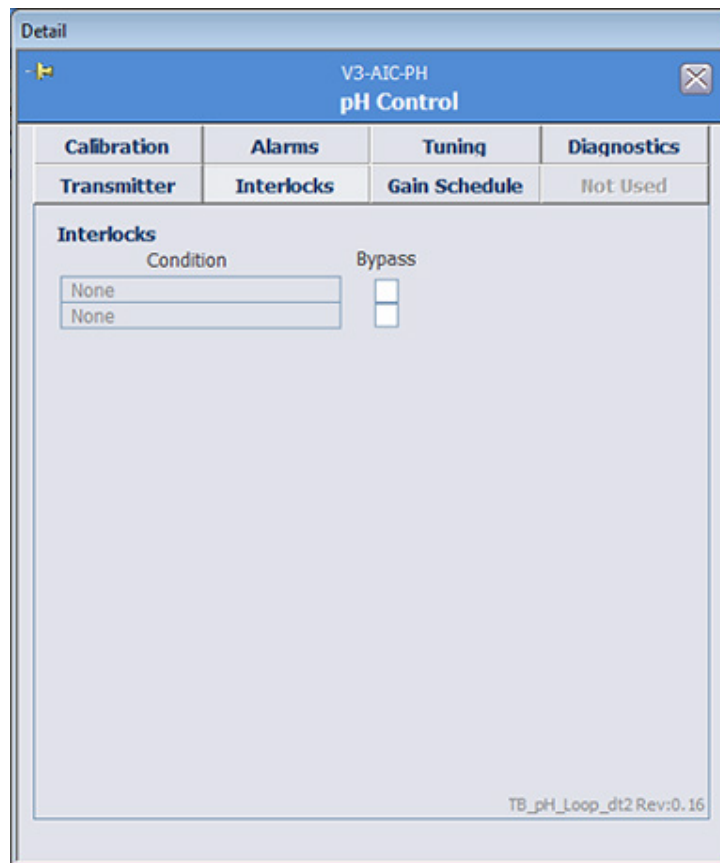

Figure 2.15. Interlocks tab details.

Gain Schedule

The **Gain Schedule** tab (Figure 2.16) allows you 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 2.16. Gain Schedule tab details.

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

- **Region 1/2/3**—Shows the PID parameter settings for the three different regions.

- **Current**—Sets 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.

- **Deadband**—Prevents tuning parameter change when transitioning from one region to the next until the deadband limit is exceeded.

Time Proportion mode

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

Time Proportion (TP) mode (Figure 2.17) is specific to the pump **Detail** windows. When enabled, the pump operates in **TP** mode at the Run Speed. When disabled, the pump operates normally, but automatically selects the **TP** mode when the output is below the Minimum Speed.
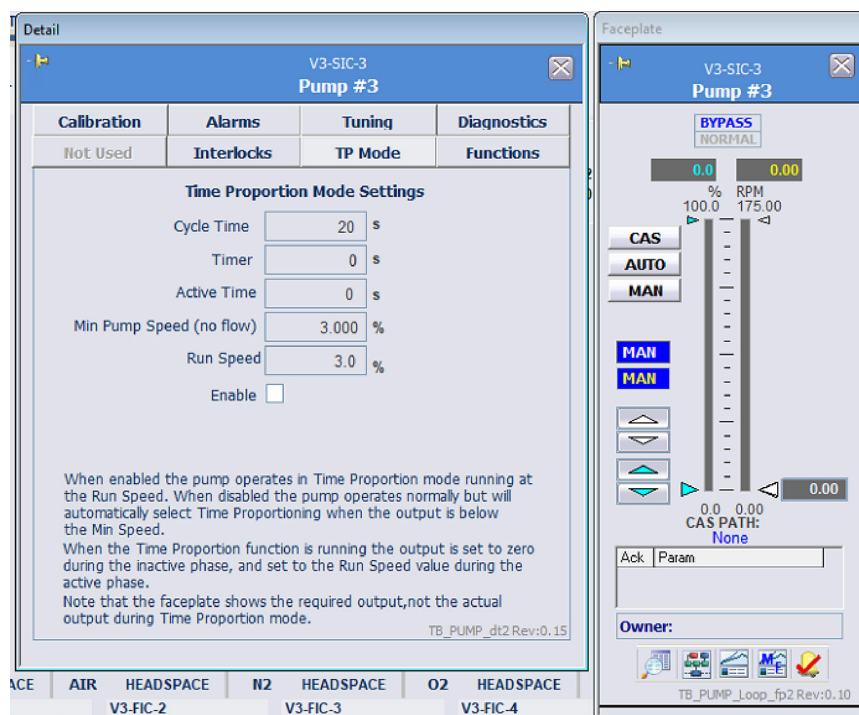

Figure 2.17. TP Mode tab details.

When **TP** mode is enabled, the output is set to zero during the inactive phase, and set to the Run Speed value during the active phase.

Notes:

• The faceplate shows the required output, not the actual output during **TP** mode.

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

It is not recommended to run pumps 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. However, changing tubing requires that the pumps be recalibrated.

If you usually run 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. Using this feature requires **TP** mode to be enabled. Consult your Thermo Scientific service representative for further information.

Refer to Figure 2.17 for the following steps. To enable time proportioning:

1. Open the **Pump** faceplate and then the **Detail** screen. Then click the **TP Mode** tab.

2. Enter the **TP Mode** settings:

   – **Cycle Time** is the duration of the TP, from the start of one pulse to the start of the next. The time (in seconds) should not exceed the Multi-Feed phase time for that pump.

   – **Min Pump Speed** is the TP enable speed (in percent of the maximum pump rpm). This is typically 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%.

3. Click the **Enable** check box. The pump will run at the **Run Speed** for the portion of the **Cycle Time** that is determined by the **Pump Output** value.

When **TP Mode** is enabled, a clock symbol appears in the appropriate pump box on the Main screen (Figure 2.18).

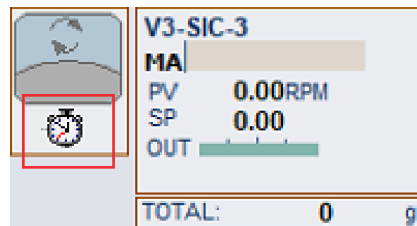Please contact your service representative for detailed information about TP setup.

Figure 2.18. Clock symbol appears in pump box.

Diagnostics

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

Transmitter

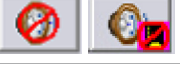The **Transmitter** tab (Figure 2.19) allows the operator to select the probe for the control loop module.
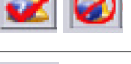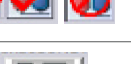

Figure 2.19. Transmitter tab details.

2.3.11 Bottom toolbar

Buttons in this toolbar provide control over alarms (see Chapter 3) and provide communication status information. Table 2.4 provides a description of each button in the bottom toolbar.

Table 2.4. DeltaV toolbar button icons and functionality descriptions.

Icon	Description
	Acknowledges all alarms.
	Silences the horn audible alarms.
	Enables or disables the horn for audible alarms.
	Opens the Alarm Banner Help window.
	Enables or disables alarm direct access to the Alarm Help.
	Enables or disables alarm direct access to the faceplate display.
	Enables or disables alarm direct access to the Primary Control display.
	Opens the DeltaV Node status window.
	Displays the Communication Integrity Status. Green—good, red—bad, and blank—not configured.

2.3.12 Reset all Totals and Timers

Reset all Totals and Timers (Figures 2.20 and 2.21) allows you to reset all timers and totals to zero (0).
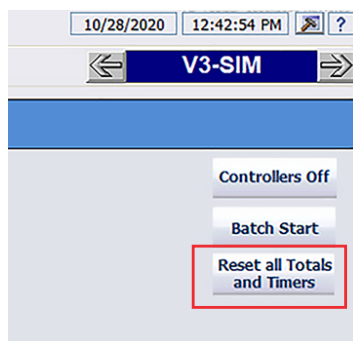

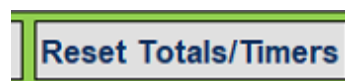Figure 2.20. Reset all Totals and Timers button in standard TruBio.

Figure 2.21. Reset Totals and Timers button on the Quick Access toolbar in TruBio for GXCore.

2.3.13 Batch Start

Batch Start (Figures 2.22 and 2.23) creates a flag that is recorded in the **Event Chronicle**. Please note that this will NOT start the batch and is required if using XLReporter™ or DreamReporter™.
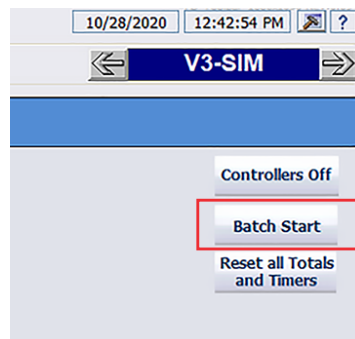

Figure 2.22. Batch Start button in standard TruBio.

Figure 2.23. Batch Start button on the Quick Access toolbar in TruBio for GXCore.

Adding Batch Start to the Main screen

To make this button visible on the screen, use the following protocol.

1. From the **Main** screen, select **Config** at the bottom left of the screen.

2. Click **Online Parameter Update** from the **Configuration** screen toolbar to open the Online Parameter Update window (Figure 2.24).
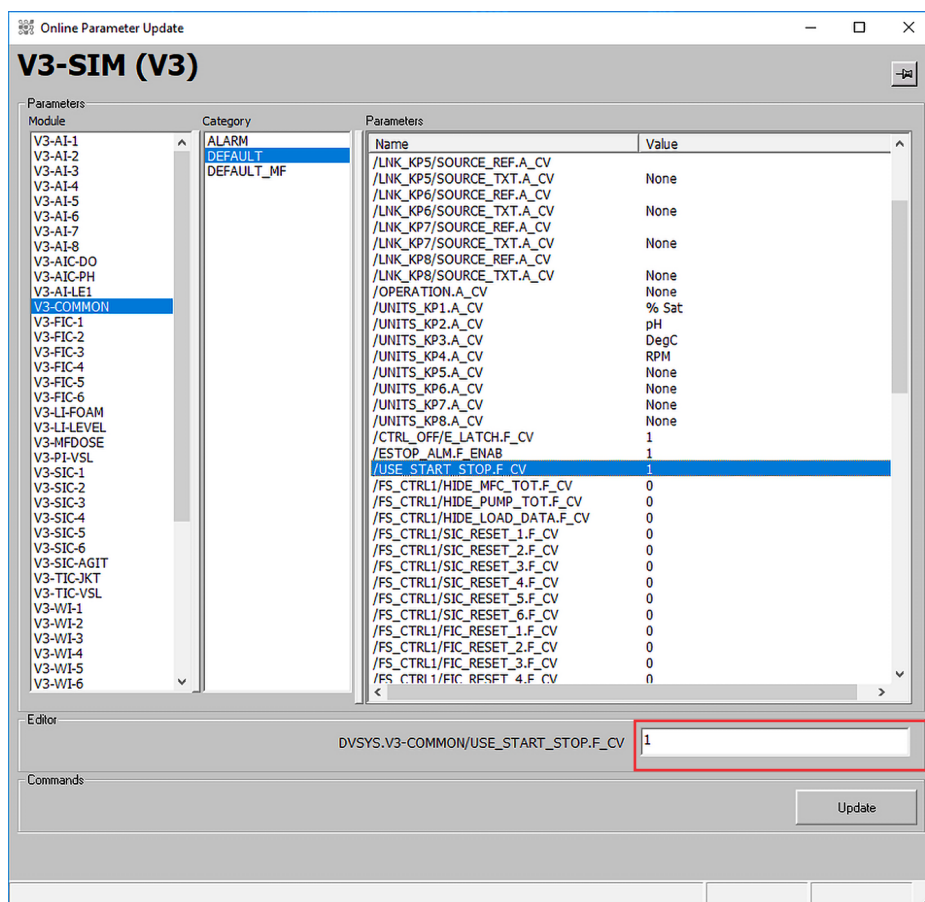
Figure 2.24. Batch Start option selected.

3. Verify that the correct vessel is displayed at the top of the pop-up screen.

   Note: For TruBio with GXCore, **Online Parameter Update** is found in the **Vessel Setup** drop-down on the **Quick Access toolbar**.

4. In the first column (Module), click on **V*x*-COMMON**, where *x* indicates the vessel number (Vessel 3 shown in example).

5. In the second column (Category) click **Default**.

6. In the third column (Parameters) locate and click on the string **/USE_START_STOP.F_CV**.

7. The value for this string can be either 0 (disabled) or 1 (enabled). Set the value to 1 and click **Update** to save the change.

The **Batch Start** button appears in the upper right corner of the **Main** screen.

2.3.14 Operation and Batch ID

Operation and **Batch ID** (Figure 2.25) on the **Main** screen allow you to enter the batch ID and operation comments (up to 16 characters) which are recorded as part of the event log in the historian.

To change either, click on the respective field to bring up the respective form. Enter the desired value and click OK or Enter (Figures 2.26 and 2.27).
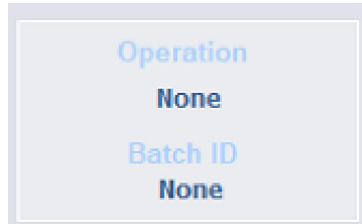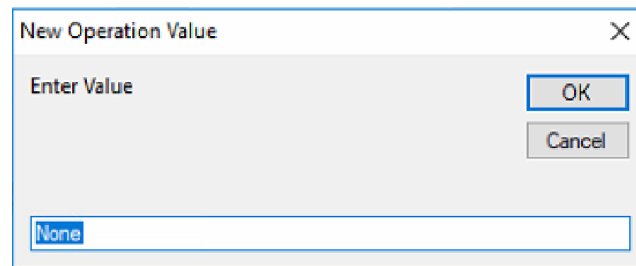
Figure 2.25. Operation and Batch ID fields

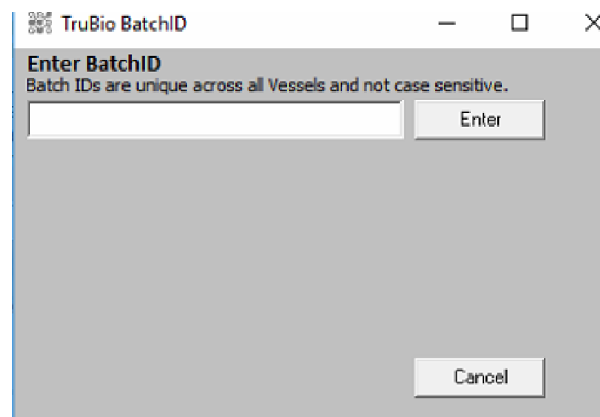**Figure 2.26. New Operation Value form.**

Figure 2.27. New Batch ID Value form.

2.4 TruBio with HyPerforma GXCore Bioprocessing Controller

TruBio for GXCore features an optional unique UI built for ease of use and intuitive control. This UI is only available for GXCore Controller users and is not backward compatible with the G3Lab Controller.

2.4.1 TruBio with GXCore Main screen

Figure 2.28 provides an example of the TruBio with GXCore Main screen.
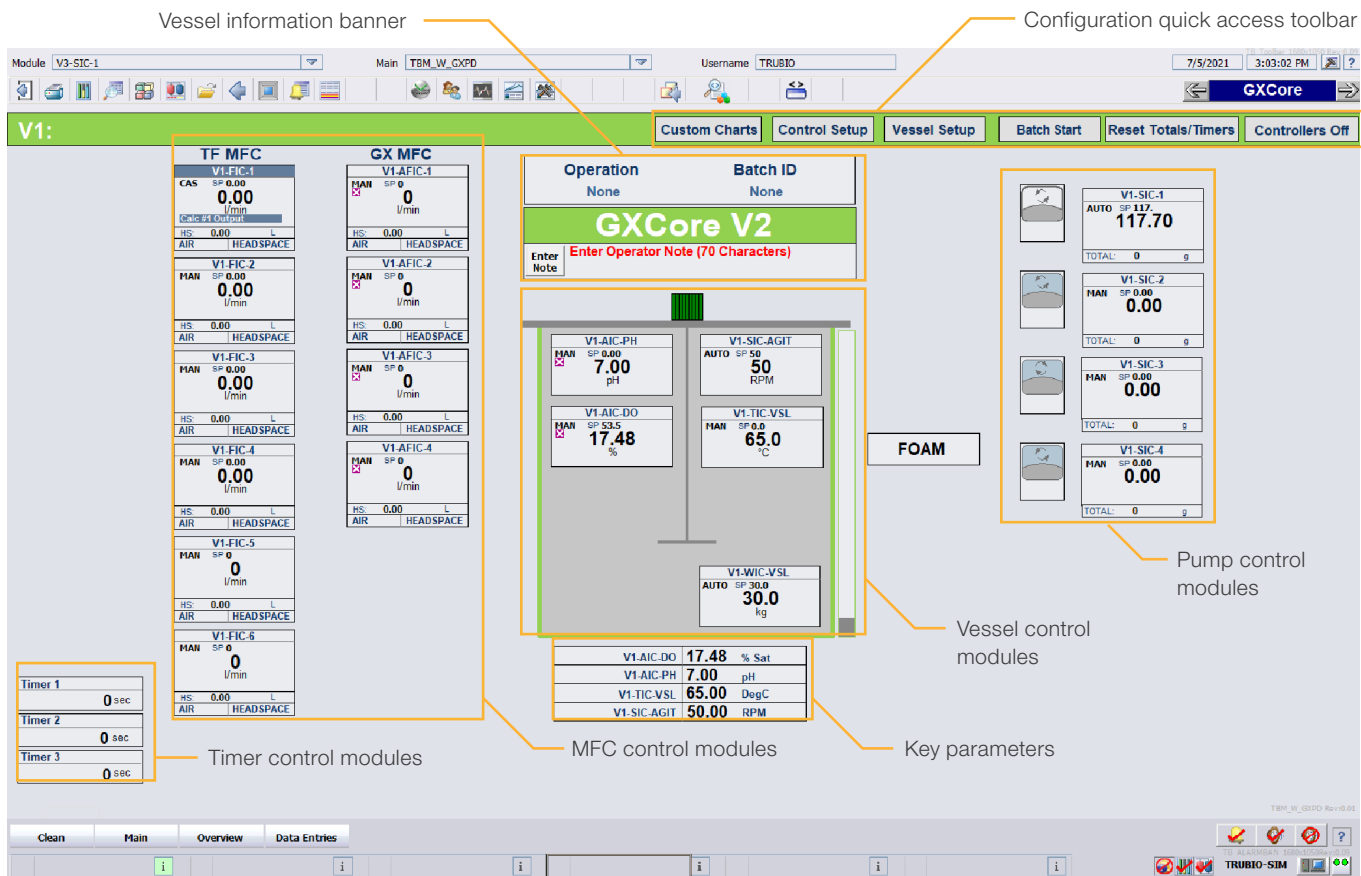

Figure 2.28. TruBio with GXCore Main Screen.

Note: The control modules for each smart device (MFCs and pumps) will only appear when the MFC is connected to the GXCore Controller. Control modules for both are shown in Figure 2.28 for display purposes only.

2.4.2 TruBio with GXCore Control modules

Control modules with GXCore provide a new way to view information and make it easier to access controls. Control modules contain up to four sections described in Figure 2.29.
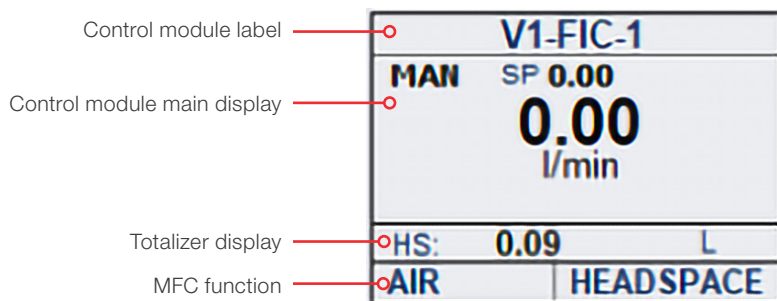
Control module label ——

Control module main display ——

Totalizer display ——

MFC function ——

Figure 2.29. Description of a TruBio with GXCore MFC control module.

- **Control module label**—displays the designated label of the control module.

- **Control module information display**—displays the mode, setpoint, and output of the associated component.

- **Totalizer display**—(specific to MFC and pump control modules) displays the total gas or fluid supplied through the selected flowpath. Click anywhere in this section to open the **Totalizer** faceplate for this control.

- **MFC function**—(specific to MFC control modules) displays the gas type for the MFC and selected flowpath. See Configure MFC for CO_2 on page 133.

Mini-faceplate

The **mini-faceplate** (Figure 2.30) appears when you click inside the control module. It provides quick access to most of the functions of the smart device.
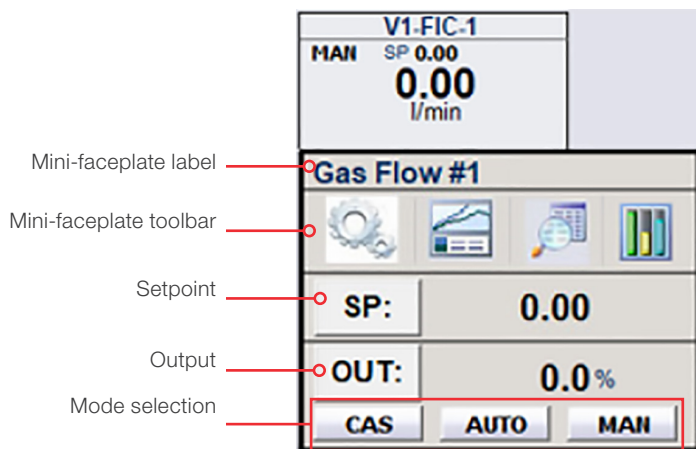
Mini-faceplate label ——

Mini-faceplate toolbar ——

Setpoint ——

Output ——

Mode selection ——

Figure 2.30. Description of a TruBio with GXCore control module.

- **Mini-faceplate label**—Designated name of the mini-faceplate.

- **Mini-faceplate toolbar**—Quick access to functions related to the control module. From left to right: **Configuration**, **Chart Builder**, **Detail**, and **faceplate**.

- **Setpoint**—Click **SP:** to change the setpoint if operating in **Auto** mode. The window that appears will display the current setpoint and a field to enter a new setpoint. The current setpoint is displayed to the right.

- **Output**—Click **OUT**: to change the output if operating in **Manual** mode. The window that appears will display the current output and a field to enter a new output as a percentage. The current output percentage is displayed to the right.

- **Mode selection**—Click a button to change to that mode. From left to right: **CAS** (Cascade), **AUTO** (Automatic), and **MAN** (Manual).

2.4.3 Vessel information banner

The vessel information banner (Figure 2.31) allows you to enter information about the run.
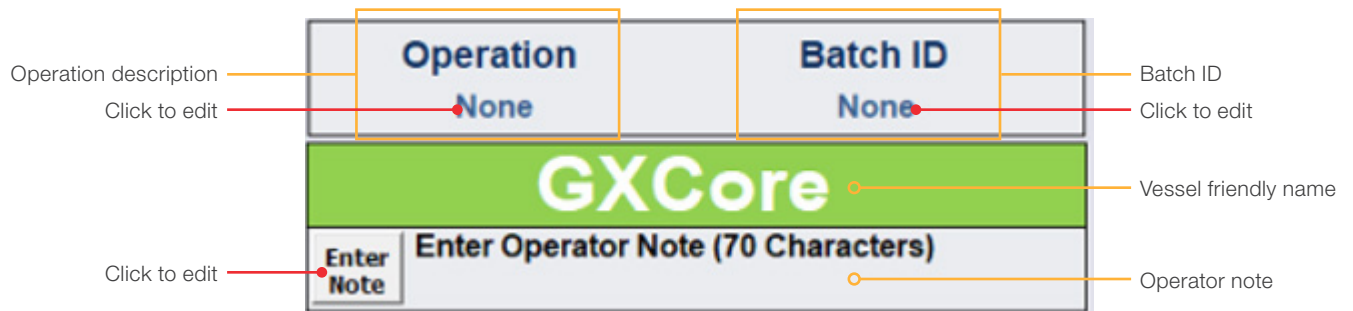

Figure 2.31. TruBio with GXCore vessel information banner.

From here you can:

- Click the text under **Operation** to enter a description. There is no character limit, but only 16 characters can be displayed in the banner.

- Click the text under **Batch ID** to enter a unique Batch ID. There is no character limit, but only 16 characters can be displayed in the banner.

- Click **Enter Note** to change the vessel friendly name or Enter an operator note. The vessel friendly name is limited to 15 characters while an operator note can have up to 70 characters.

2.4.4 Vessel interface

The **vessel interface** appears in the center of the screen (Figure 2.32) and is a representation of the vessel.

Inside the graphic are the control modules for **pH**, **DO**, **Agitator**, **Temperature**, and **Weight**. The **agitation indicator** appears green when agitation is active. The bar to the right is a visual representation of how full the vessel is if the vessel weight scale is connected to the controller. Below the graphic are **key parameters** where the bottom four parameters of the key parameter configuration form are shown (see section 2.6.2 for setup instructions).
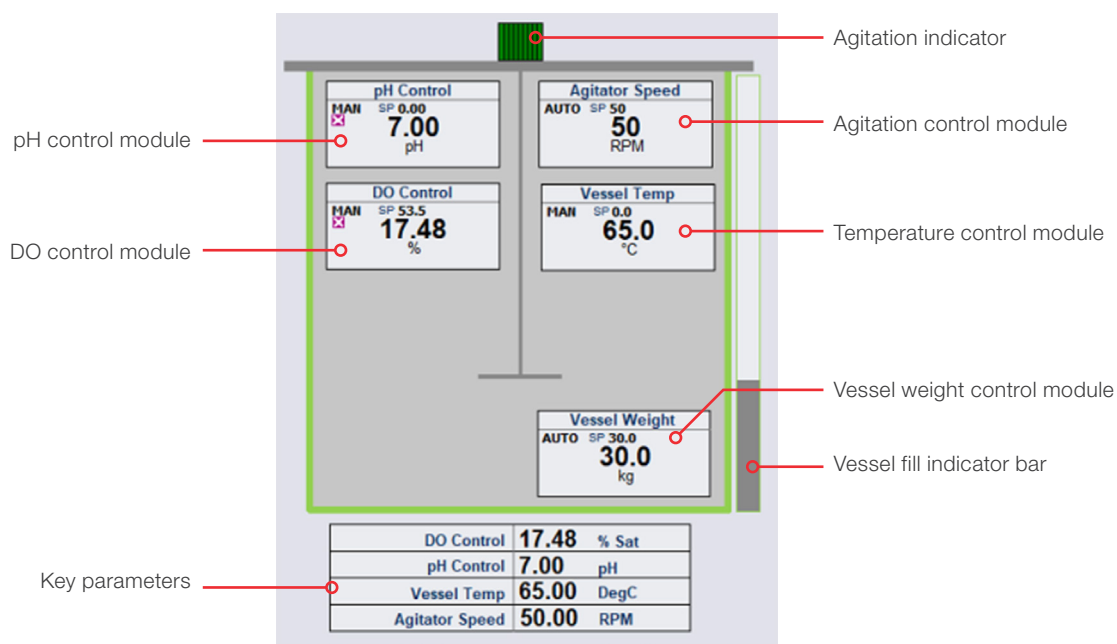

Figure 2.32. TruBio with GXCore vessel interface.

2.4.5 Configuration Quick Access toolbar

A major difference in TruBio for GXCore is that the functions that are found in the Configuration screen on other vessels have been localized into a single toolbar (Figure 2.33). This toolbar provides quick access to these functions without leaving the **Main** screen.
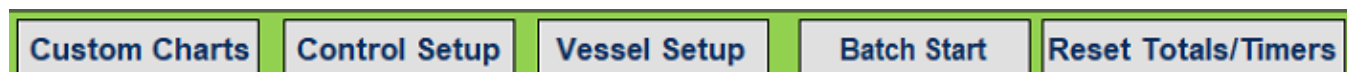

Figure 2.33. Configuration toolbar on TruBio with GXCore interface.

Click a button to open a drop-down to view the available features. The structure of the toolbar is outlined in the following sections.

Custom Charts

Up to 3 custom charts can be configured and saved where the charts can be opened from this control. For information on modifying charts in the **Process History View**, refer to DeltaV Books Online.

Control Setup

The following options are found under Control Setup:

- Characterizing Curves

- Compare and Math

- Freeform Calculations

- Vessel info

See the respective header in section 2.6.1 for more details.

Vessel Setup

The following options are found under Vessel Setup:

- Vessel Save/Load

- Online Parameter Update

- Engineering Units

- Key Parameter Setup

- Smart Device Info

- Controllers Off Setup

See section 2.6 for a description of each option.

Batch Start

See section 2.3.13 for details.

Reset Totals and Timers

See section 2.3.12 for details.

2.5 Main screen with HyPerforma Rocker Bioreactor

The HyPerforma™ Rocker Bioreactor **Main** screen is the same as other vessel screens (except GXCore), with the addition of the agitation control located immediately above the image of the rocker. The rocker settings also include **Rock Angle, Rock Speed,** and options to control the rocker enclosed in Figure 2.34.
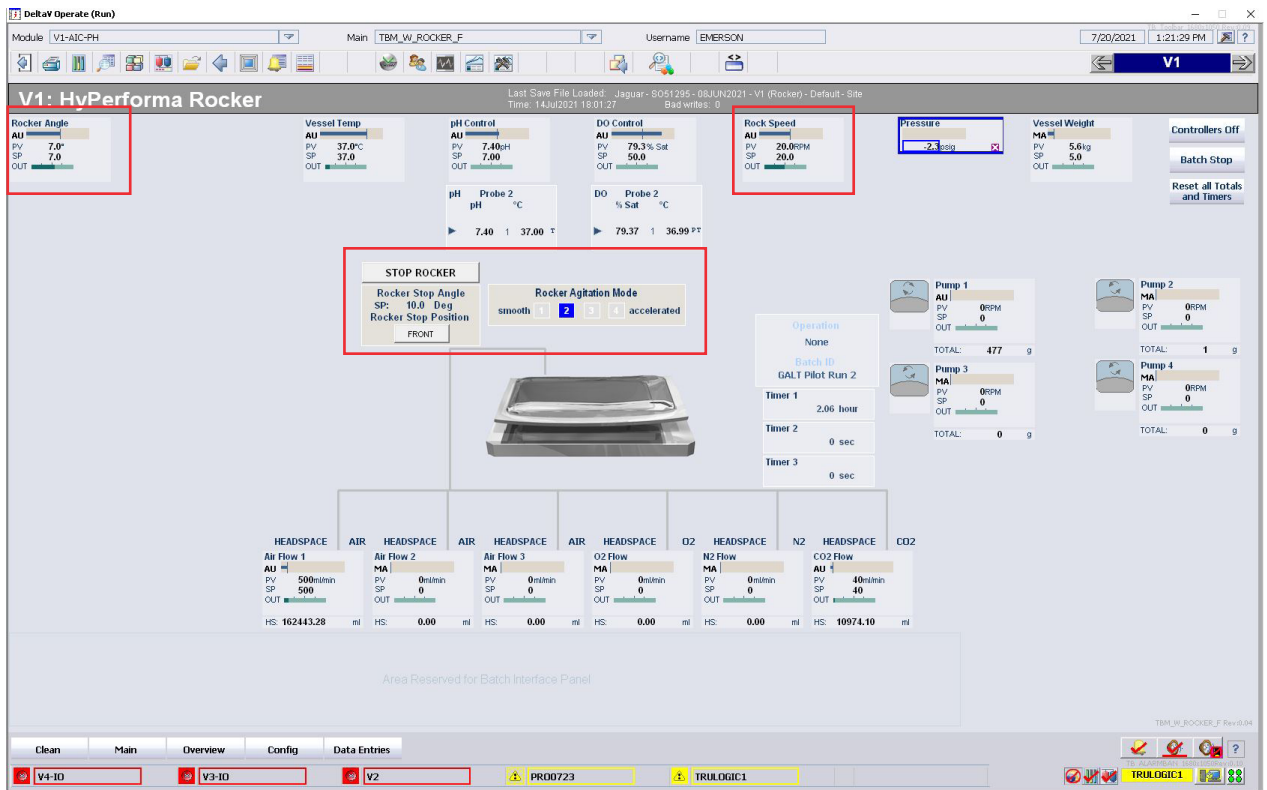

Figure 2.34. Rocker Main screen.

2.6 Configuration screen

Click **Config** from the **Navigation** bar to open the **Configuration** screen (Figure 2.35). This screen allows you to configure control loops, signal conditioning, vessel type selection, define measurement parameters, and set up control loop strategies.

Note: TruBio for GXCore does not have a Configuration screen. See section 2.4.5.
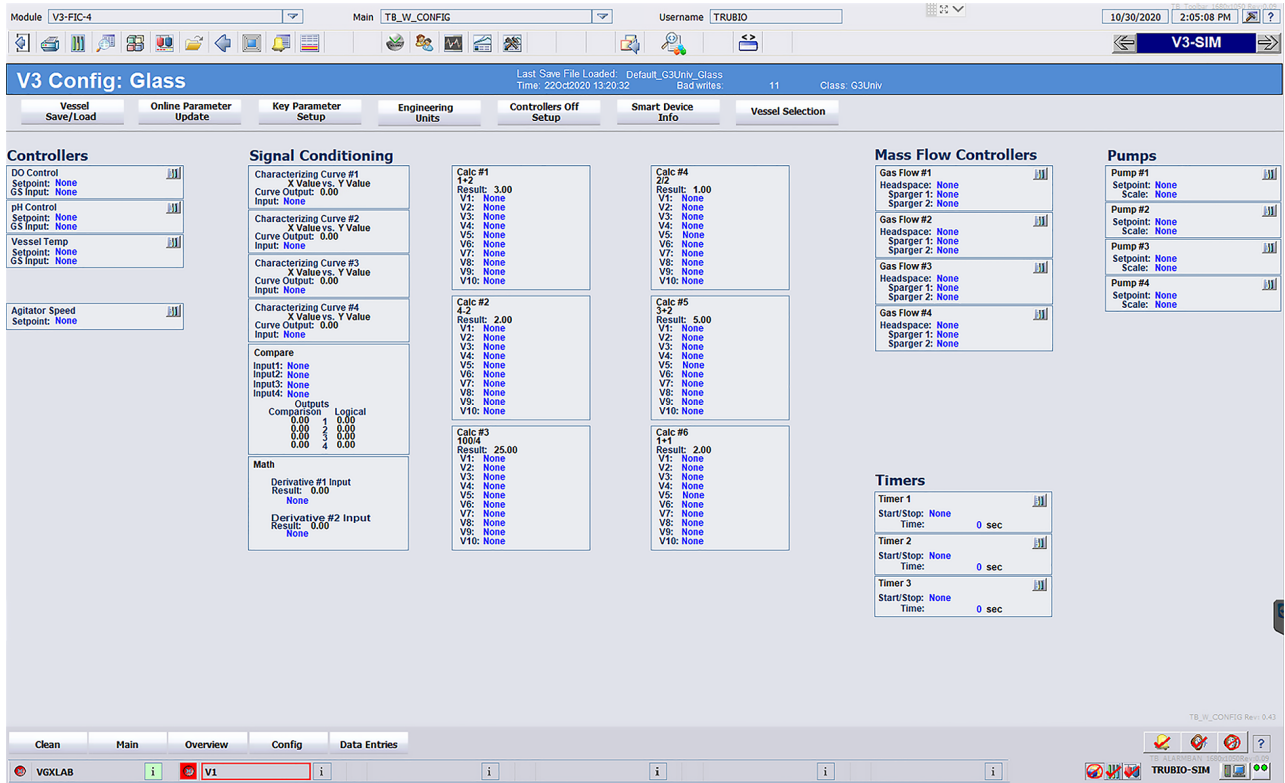

Figure 2.35. Configuration screen.

The body of this screen is divided as follows:

- Controllers

- Signal Conditioning

- Mass Flow Controllers (MFCs)

- Pumps

- Timers

The configuration toolbar provides quick access to the following functions:

- **Vessel Save/Load**—Allows you to load or save the configuration input on this screen.

- **Controllers Off setup**—Allows you 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**—Defines parameters to be displayed on the **Overview** screen vessel box.

- **Smart Device Information**—Provides model and serial numbers for connected SmartMFC gas controllers and SmartPumps.

- **Vessel Selection**—Allows you to define the vessel type being controlled.

- **Engineering Units**—A list of the units available in the software, such as g/hr or rpm.

2.6.1 User forms and Configuration screens

User forms are used to perform event-based tasks, such as calibration or control strategy setup. Most user forms are accessed from the **Configuration** screen and are used to configure a bioprocess for a desired control strategy.

Control strategy configuration

Figure 2.36 shows an example of a control configuration form. Common elements are described below.

Figure 2.36. pH Control Configuration window.

- **Remote Setpoint**—is used only when the setpoint is dependent upon another parameter and is not set from the faceplate.

- **Gain Schedule Auxiliary Input**—should only be used under the direction of qualified Thermo Scientific personnel.

- **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.

- **Output Scales**—Output Scales is broken into two sections, **Controller Output** and **Output Scale**.

  - **Controller Output** is expressed as a percentage of maximum output, e.g. a percentage of the maximum 250 rpm of a pump.

  - **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.

- **High and Low Threshold Output Controls**—A way of controlling a parameter if the cells are tolerant of moderate variations in the parameter. For example, if the cells in culture will tolerate a range of pH 6–8, then you could set the base pump to run for a specified time (pre-set at five seconds) if the pH drops below 7, and to run the MFC delivering CO_2 if the pH went above 7. However, this method is not optimal, as it can produce wide swings in the parameter PV.

- **Apply Values**—click to save data entered in the control screens.

- **Reset Form**—click to return the entire form to factory-set values.

- **Interlock**—can be 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 Online Parameter Update.

Characterizing Curve

The Characterizing Curve (Figure 2.37) is used to configure more closely the output from the parameter control above. It should be used only by an experienced operator.

Figure 2.37. Characterizing Curve 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**.

Math Functions configuration

The **Math Function** (Figure 2.38) 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.

Figure 2.38. Math Functions Config screen.

Calculation Configuration

The **Calculation** form (Figure 2.39) is used to create a calculation which can contain up to 10 separate functions. The result of the calculation can be used as part of a control strategy by linking the result to a remote setpoint.

Figure 2.39. 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 clear all fields.

Mass Flow Controller Configuration

The Mass Flow Controllers (MFCs), contained in the TruFlow gas manifold or GXCore MFC, are used to deliver gases to the bioreactor/fermentor vessel and are generally set up as part of a control loop. See Figure 2.40 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 2.40. MFC config screen.

Ensure that the gas supplies are connected to the correct output and that the lines are not in danger of being kinked or occluded.

The sparger output must agree with the selected flowpath. If sparger output 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**.

Interlock can be 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.

Pump Configuration

The pumps (Figure 2.41) 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 2.41. Pump Config screen.

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, 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, **Counter-Clockwise** 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.

Pressure Configuration

TruBio Software enables you to program up to 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. The **MFC High Pressure** interlock can be set to lock all MFCs if the Hi or Hi Hi pressure limit is reached (Figure 2.42).
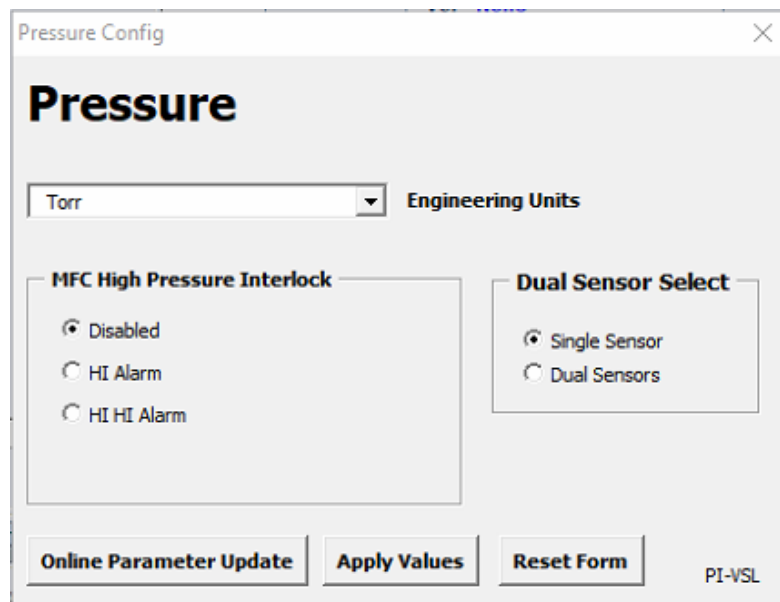
Figure 2.42. Selecting preferred units for pressure configuration.

Click **Apply Values** to save any changes.

Online Parameter Update

The **Online Parameter Update** (OPU) function (Figure 2.43) allows control module parameters to be changed from the user interface without having to open the control module in DeltaV Control Studio. The OPU screen displays the online parameter values for all control modules.
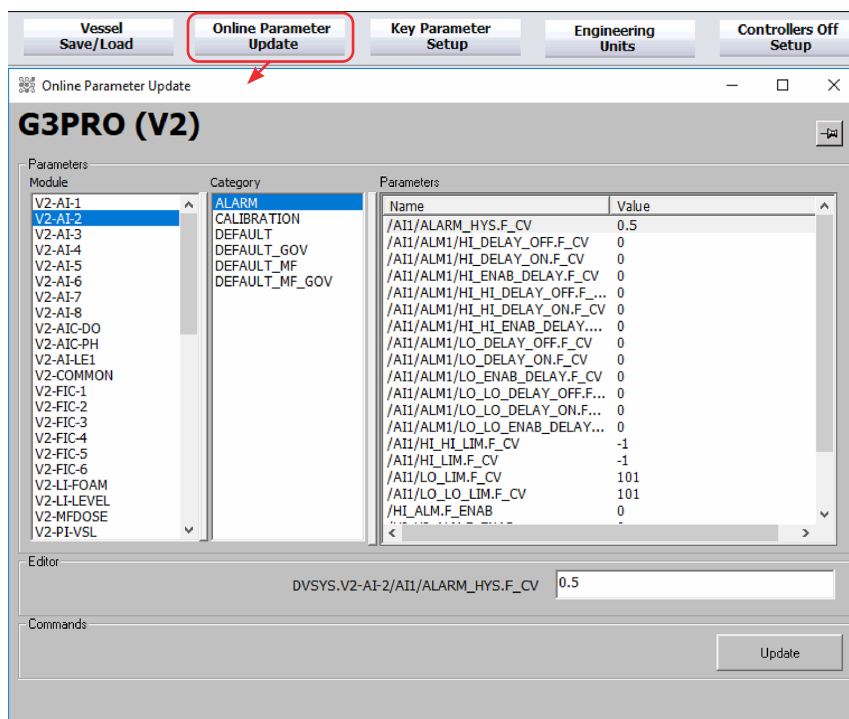
Figure 2.43. Online Parameter Update screen.

You can view the current value of a selected parameter and enter a new value, as desired. A new value can only be written if you have 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 (see section 3.2).

2.6.2 Key parameter setup

This user-defined function makes essential values available on the **Overview** screen so they can be easily monitored (Figure 2.44).

Figure 2.44. Key parameters on the Overview screen.

1. On the **Configuration** screen, click **Key Parameter Setup** to select parameters to be displayed using the drop-down menus (Figure 2.45).

   Note: For TruBio with GXCore, select **Key Parameter Setup** from the **Vessel Setup** drop-down in the **Configuration Quick Access** toolbar.

   – If fewer than eight parameters are required for display, leave the default setting at **None**.
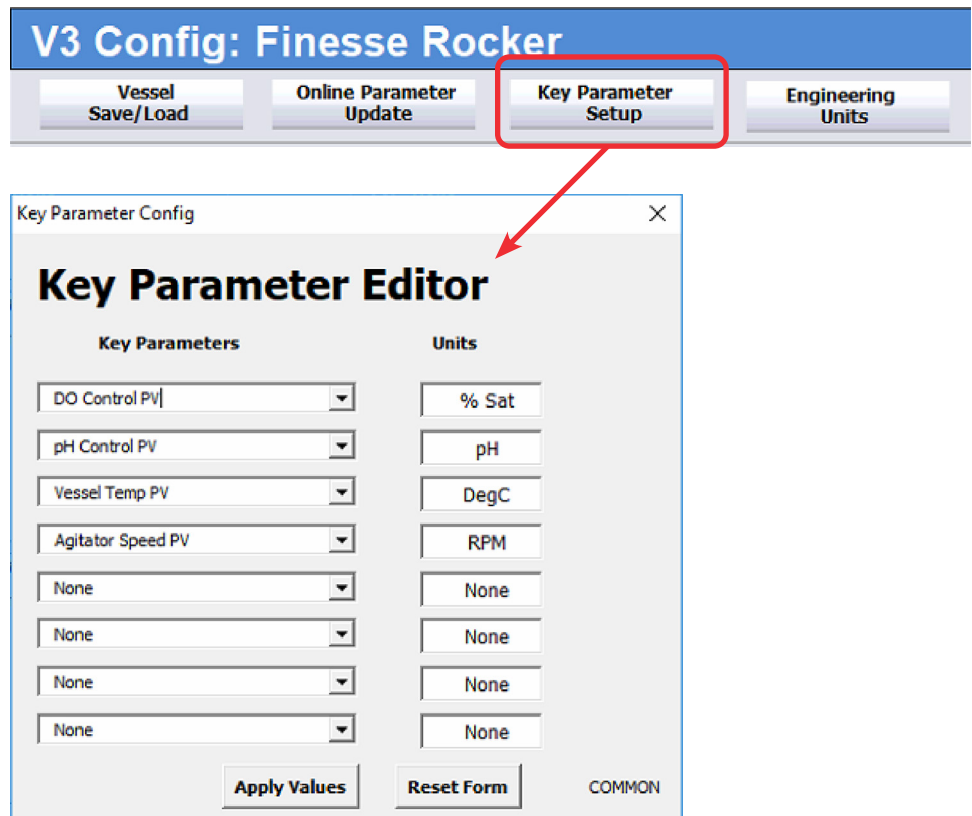
Figure 2.45. Key Parameter Editor screen.

2. Click **Apply Values** to save the setting.

2.6.3 Smart Device information

In the TruBio Software, the **Smart Device Info** is located on the **Configuration** screen (Figure 2.46).

Note: For TruBio with GXCore, select **Smart Device Info** under the **Vessel Setup** menu in the **Configuration Quick Access** toolbar.

Figure 2.46. Location of Smart Device Info button.

Click **Smart Device Info** to open a pop-up screen with information on the pumps and mass flow controllers used in the controller (Figure 2.47).

Figure 2.47. Smart Device Information screens, Smart Pumps (Left) and Smart MFC (Right).

GXCore Smart Device Information screen

GXCore has additional tabs on the **Smart Device Information** screen (Figure 2.48).

Figure 2.48. Additional tabs on the Trubio with GXCore Smart Device Information screen.

These tabs are from left to right:

- Smart pumps

- TF (TruFlow) MFC

- GX MFC

- Smart TX

- Scale

- LA

2.7 Data Entry screen

Click **Data Entries** from the bottom toolbar (Figure 2.49) to open the **Offline Analyzer Data Entry** screen (Figure 2.50).

This screen is a single graphic screen that illustrates both manual and automated process data collection for a bioreactor vessel. The displayed data is configurable (standard is 15 values).
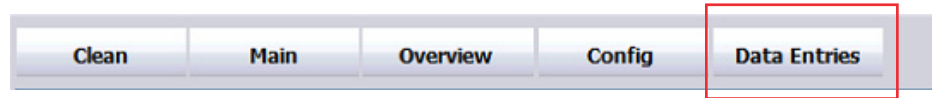
Figure 2.49. Data Entries button located under main graphic.
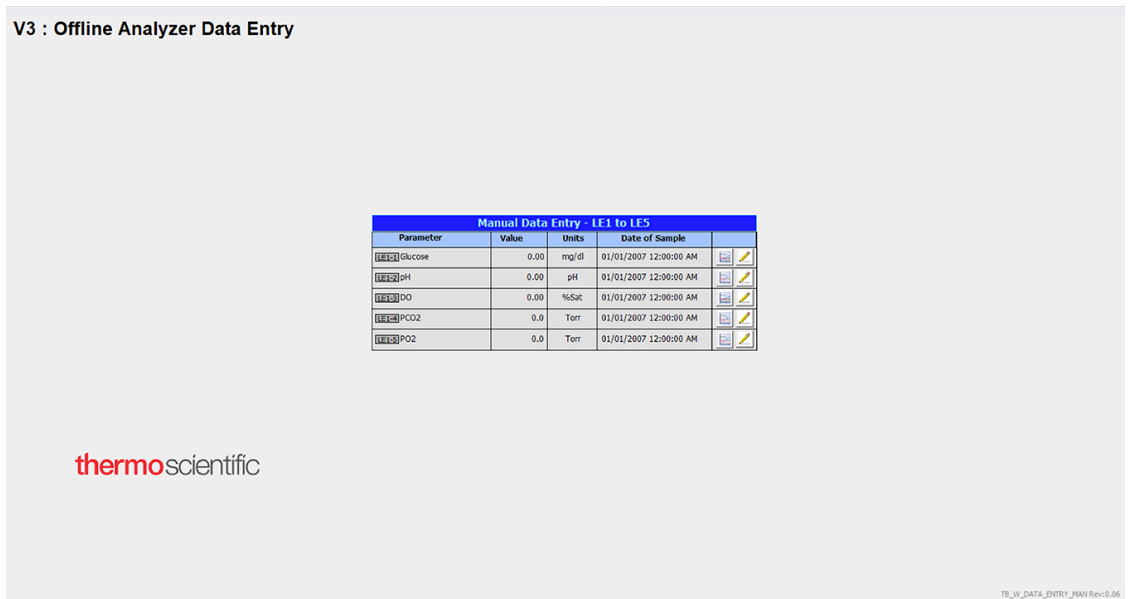
Figure 2.50. Offline analyzer data entry screen.

Data Entry

Click **Data Entry** (pencil icon) to bring up a form where you can enter manual data (Figure 2.51). The time stamp can be manually set at time of entry. To preserve batch integrity, once data has been entered, it cannot be deleted.
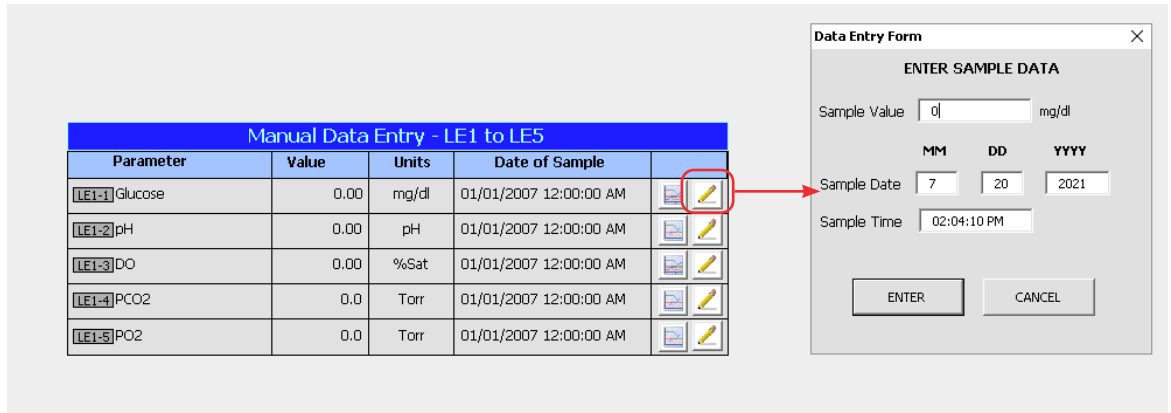
Figure 2.51. Offline analyzer Data Entry Form.

Parameter faceplate

Data Entry Setup records the sample value and the sample time and checks for the validity of the sample. This includes **High** and **Low Sample Value Limits** and **Maximum** and **Minimum Sample Delay Time Limits**.
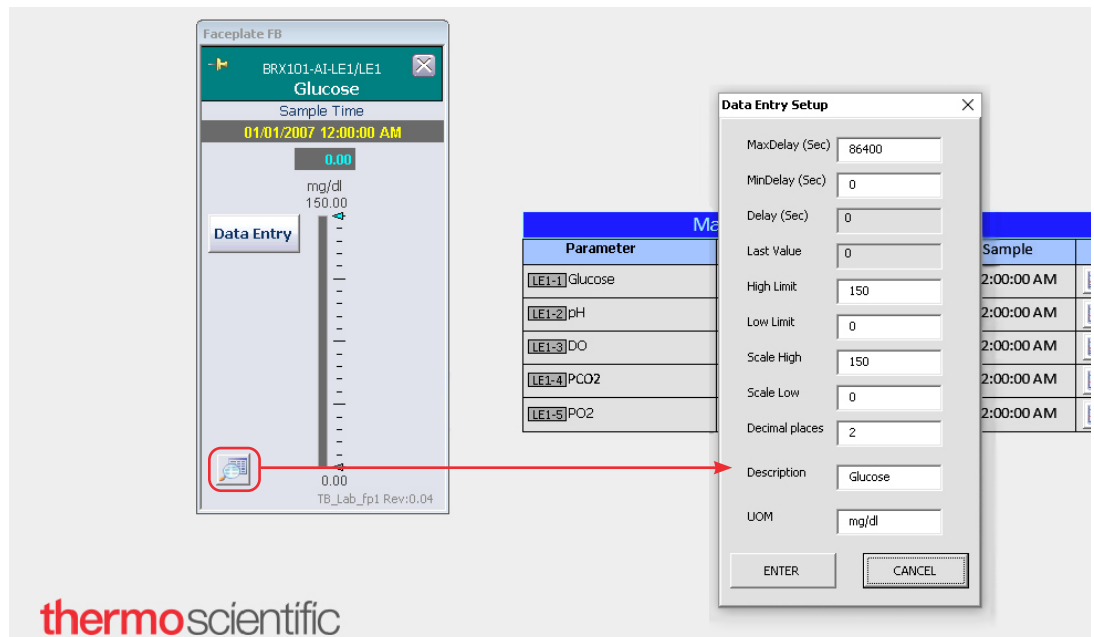
Figure 2.52. Offline analyzer Data Entry Setup.

Trend

Click **Trend** (graph icon) to bring up a chart that displays the manually entered data (Figure 2.53).

- Sample value—recorded as the function output in user-defined units.
- Sample time—date and time stamp.
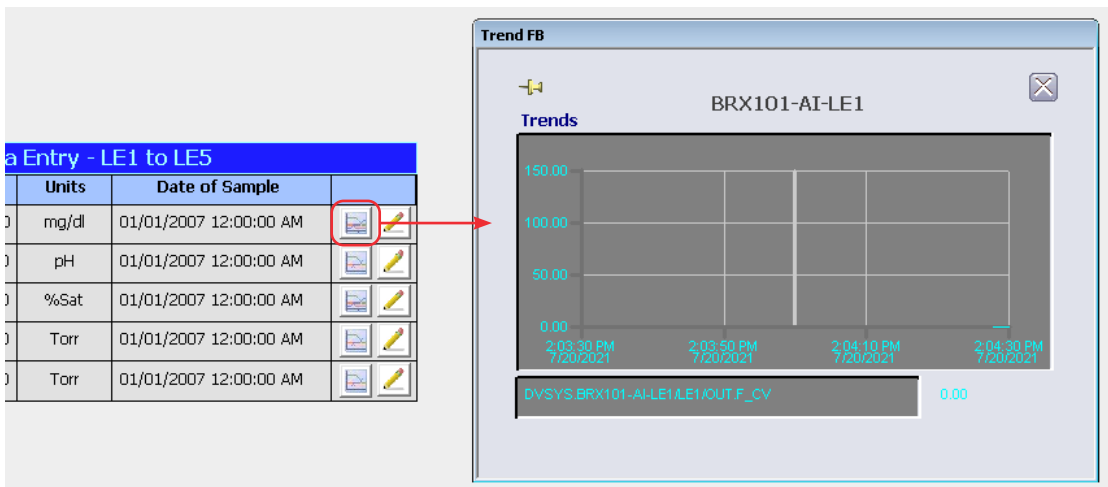
Figure 2.53. Offline analyzer Trend chart.

2.8 Cleaning screen

Click **Clean** from the **Navigation** bar to open the **Cleaning** screen (Figure 2.54). This screen remains active for 21 seconds so you can clean a touchscreen while preventing the accidental entry of erroneous data or interference with an ongoing process.

Double-click **HERE** three times to close the screen before the countdown ends
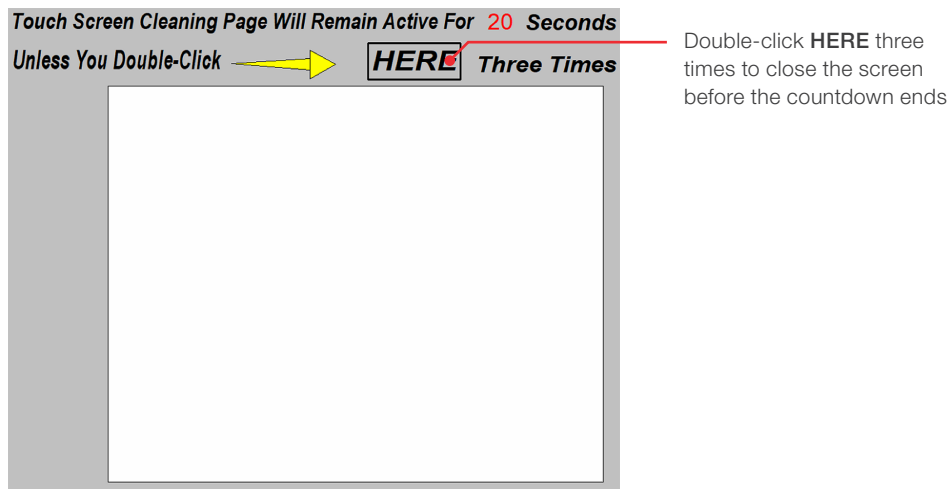
Figure 2.54. Cleaning screen.

3

General system operation

3.1 User login

Click the **User Login** icon on the toolbar (Figure 3.1). 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.

The list of users and available actions is given in Tables 3.1–3.2 below. Contact your Thermo Scientific sales representative for a list of default passwords.
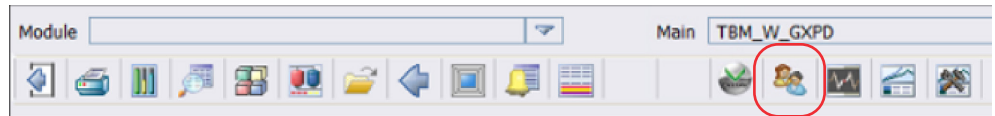
Figure 3.1.   User login icon on toolbar.

Table 3.1. Available actions for each user level.

Action	Operator	Maintainer	Supervisor	Administrator
Access Windows desktop	✕	✕	✕	✓
Exit DeltaV Operate	✕	✕	✕	✓
Access Overview screen	✓	✓	✓	✓
Access Configuration screen	✓	✓	✓	✓
View Smart Device info	✓	✓	✓	✓
Vessel Select	✕	✕	✕	✓
Vessel Save/Load	✓	✓	✓	✓
OPU access	✕	✕	✕	✓
Access control module configuration forms	✕	✕	✕	✓
Key parameter setup	✕	✕	✕	✓
Controllers off setup	✕	✕	✕	✓

Table 3.2. Available actions for each user level (continued).

Action	Operator	Maintainer	Supervisor	Administrator
Controllers off access	✗	✗	✓	✓
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	✓	✗	✓	✓

* Access for all non-Administrator users is restricted to view only.

To add, change, or delete a user or group, click the **Exploring DeltaV** icon 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.

3.2 Loading and saving a vessel file

You must be logged into both the DeltaV and TruBio systems in order to load and save vessels. See section 3.1 for more information.

Loading a vessel file

1. From the **Configuration** screen, open **Vessel Settings Management**. Then click **Vessel Load** (Figure 3.2).

   Note: For TruBio with GXCore, select **Vessel Save/Load** from the **Vessel Setup** drop-down in the **Configuration Quick Access** toolbar.
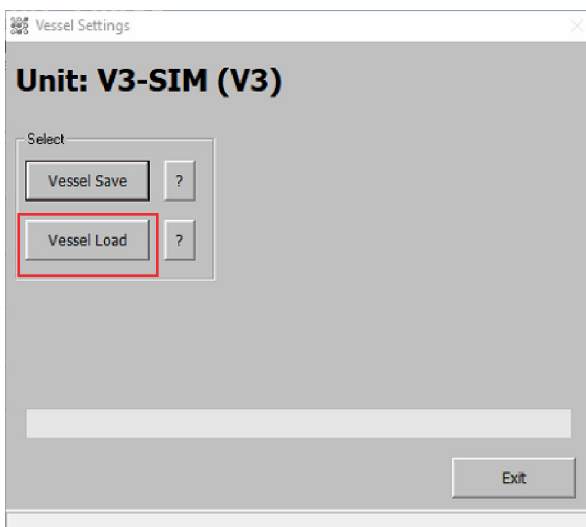
Figure 3.2. Vessel Settings.

2. 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. Select the appropriate file from the drop-down menu (Figure 3.3).

   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 you choose must have been used to load the Thermo Scientific S.U.B. Otherwise, parameters designed for a 500 L vessel may be applied to a 10 L vessel with potential damage to the system.
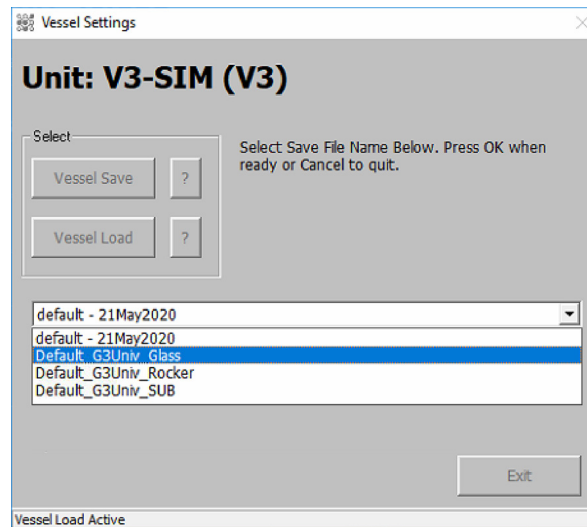
Figure 3.4. Selecting default file.

3. Type a new name according to your facility standards, or open the drop-down menu to select from a list of recently saved files and click OK.

Loading the file requires a few seconds, during which the activity displays in the message bar (Figure 3.4).

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. You may receive bad writes under normal operation; however, if you experience unexpected behavior, reach out to your local sales representative.
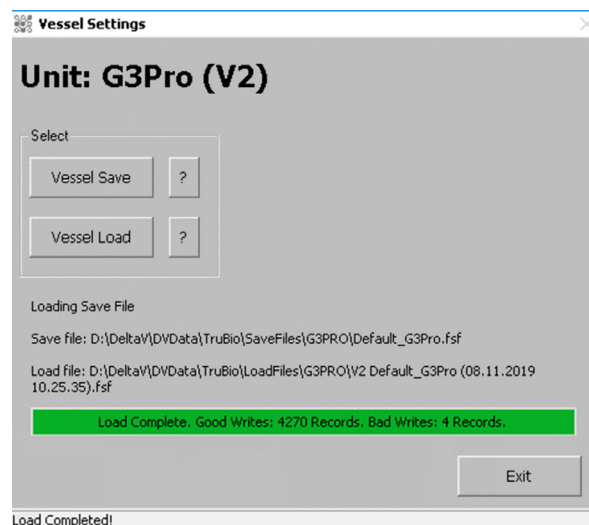
Figure 3.3. Loading progress shown in green bar.

Saving a vessel file

1. From the **Configuration** screen, open **Vessel Settings Management**. Then click **Vessel Save**.

2. Select the category to be used for the save file (Figure 3.5). The **DEFAULT** category may be used.

    Note: Saving a **Default** file will not save the calibrations, modes, or setpoints. It will save all of the other parameters discussed previously. Saving a **Default_MF** file will save Multi-Feed parameters, as well as those saved by the **Default** file.
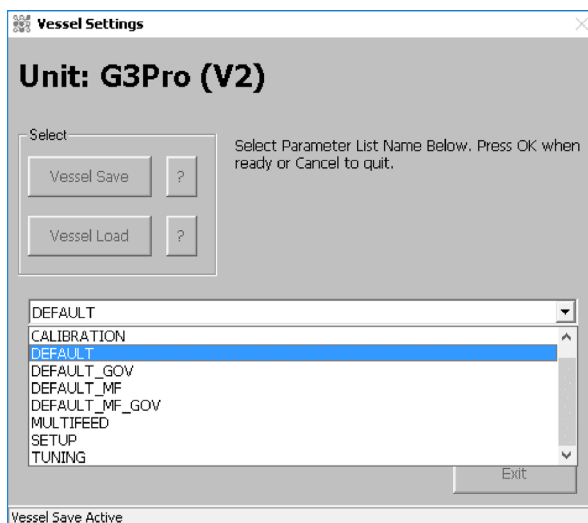
Figure 3.5. Selecting a category to use as save file.

Note: Calibration records are saved in separate records, and are saved regardless of whether they are saved here, but can be saved here if desired.

3. After selecting the category, specify a new save file name according to facility protocol. Click **OK** to save the file. There is no limit to the length of the name string and the system does not allow duplicate names for the same vessel.

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, e.g. **[Product name]-V1-2015-5-15-Model-Default**. We recommend including the name of the base file ("Default," in this case) to identify the file that the named file was created from.

4. After the vessel save completes, click **Exit**.

Notes:

- Save files can be transferred from one facility to another. The save file can be loaded at a second facility, provided that the G3 or GX series controller and the vessel hardware are identical. Consult your customer service representative for more information.

- If the vessel save process produces bad reads at approximately 30% or greater, check to ensure you are logged into the DeltaV system. If bad reads continue, contact your service representative.

Save file categories

The following table provides a description of each vessel file selection.

Table 3.3. Save file categories.

Save file	Description
CALIBRATION	Load/Save the current calibration configuration
DEFAULT	Load/Save the default parameters*
DEFAULT_GOV	Load/Save the default parameters for systems with Speed Governor enabled*
DEFAULT_MF	Load/Save the default parameters for systems with Multifeed enabled*
DEFAULT_MF_GOV	Load/Save the default paramters for systems with both Multifeed and Speed Governor enabled*
MULTIFEED	Load/Save the Multifeed configuration only
SETUP	Load/Save the control loop setup only (e.g. Setpoint, Control Mode, and Control Output settings)
ALARM	Load/Save alarm paramters only
TUNING	Load/Save control loop tuning parameters only

*Default save files include alarms and tuning parameters.

3.3 Setup information

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

Pump setup

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

How to display missing control modules

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

1. From the **Configuration** screen, click **Online Parameter Update**. This opens the display shown in Figure 3.6. Refer to the figure for the following steps.

   Note: With TruBio for GXCore, select **Online Parameter Update** from the **Vessel Setup** drop-down in the **Configuration Quick Access** toolbar.

2. Click the string that reads **Vy-SIC-x**, with *Vy* being the vessel name and *x* being the pump number to be set up (V1-SIC-1 in the example) in the **Module** column (first column in the figure).

3. Click **Default** in the **Category** column (second column in the figure).

4. Click to highlight the **Name** string, **/FS_CTRL1/AVAILABLE.F_CV** in the **Parameters** column (third column in the figure).

The available values for this **Parameter** tag are 0 for inactive and 1 for active. Smart pumps are automatically activated when installed and working correctly.
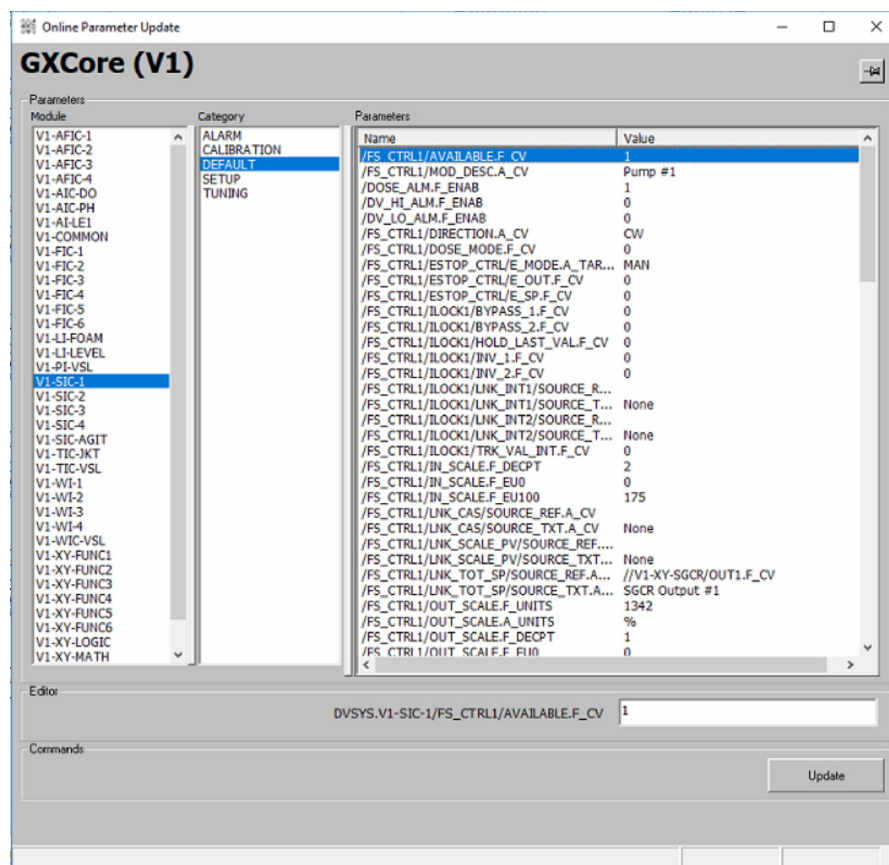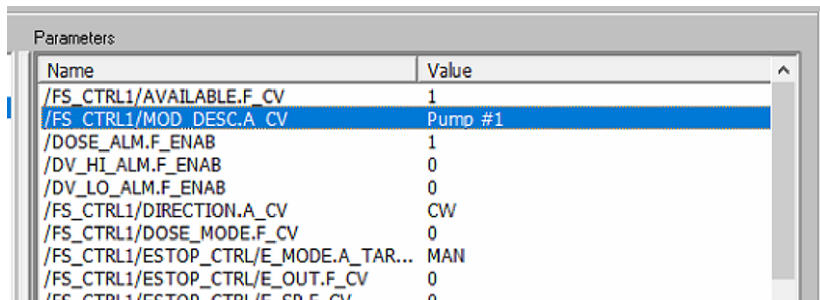
Figure 3.6. Online Parameter Update screen for pumps.

How to rename a control module

In addition, you 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,

1. Click to highlight the name string, **/FS_CTRL1/MOD_DESC.A_CV** (Figure 3.7).

Figure 3.7. Description string highlighted in the Parameters field.

2. Enter the desired name (Value), up to 28 characters.

3. Press **Enter** or click **Update**.

3.4 Bypass mode

Some operations require you to set a specific faceplate into **Bypass** mode. Typically this operation pertains to the **Pump**, **MFC**, or **Agitator** faceplate.

To set a faceplate into **Bypass** mode:

1. Set the respective faceplate to **Manual** mode.

2. Open the **Online Parameter Update** window from the **Configuration** screen.

3. Select the appropriate module from the Module column.

   – For pumps: **V*x*-SIC-*y*** (where x is the vessel number and y is the pump number).

   – For MFCs: **V*x*-MFC** (where x is the vessel number).

   – For the Agitator: **Vx-SIC-AGIT** (where x is the vessel number).

4. Select **Default** from the **Category** column.

5. Highlight the string, **/PID1/BYPASS.F_CV,** from the **Parameters** column.

6. Enter "2" in the value field at the lower right corner of the screen and click **Update** or press **Enter**.

Note: To return to normal operation enter "1" in the value field and click **Update** or press **Enter**.

7. Close the **OPU** window.

3.5 Calibration

After the save file is loaded, the individual parameters can be adjusted for the particular run. For more information, see section 3.2.

Electrochemical sensors, if used, must be calibrated prior to insertion into the sterile bag.

Note: 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, you need 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.

3.5.1 Traditional pH calibration

This section details calibration steps for traditional polarographic pH sensors. This can be performed as a one-point calibration or a two-point calibration using NIST buffers prior to autoclaving.

To access the pH calibration, open the Calibration tab on the pH Detail window (Figure 3.8).

Note: For TruBio with GXCore, you can select **Detail** from the mini-faceplate or the full faceplate.
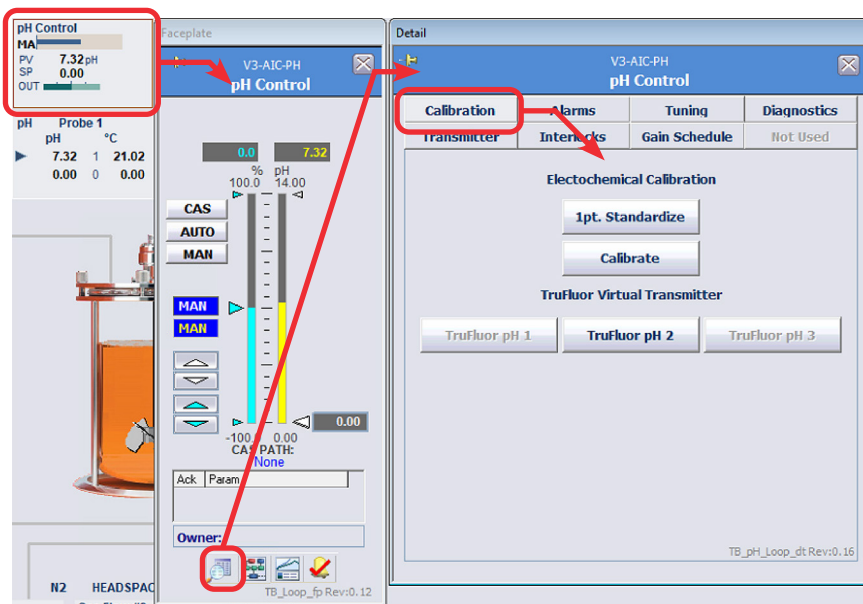
Figure 3.8.   Opening the pH control module Calibration tab.

There are two options for calibration: **1pt. Standardize** or **Calibrate** The process for each is described in the following sections.

Note: See Appendix C for more information on Calibrating TruFluor devices.

Single-point standardization

For single-point standardization, you will need:

• pH Sensor

• Calibrated pH meter with NIST-traceable standards.

1. Use a sterile procedure, as defined by your facility, to remove an aliquot of media from the bioreactor/fermentor.

2. Using a standard pH meter that has been calibrated with NIST-traceable standards, determine the pH of the media.

3. Click the **1pt. Standardization box** in the **Calibration** tab of the **Detail** window, which opens the following screen (Figure 3.9).
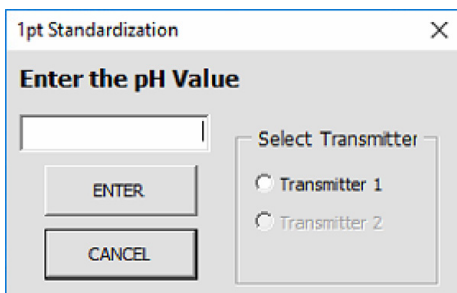
Figure 3.9. 1pt Standardization box.

4. Select the appropriate transmitter by clicking the radio button.

5. Enter the pH value obtained by testing the aliquot.

6. Click **Enter**. The pH curve will be updated.

Two-point calibration

For two-point calibration, you will need:

* pH sensor

* Lower calibration NIST pH buffer

* Upper calibration NIST pH buffer

Note: A Supervisor or Administrator username and password are required to save the calibration.

1. From the **Calibration** tab of the **Detail** window, click **Calibrate**. This opens a series of screens that will walk you through the process (Figure 3.10).

   Note: TruBio Software allows multiple probes to be calibrated concurrently.

User entry forms

Vessel information
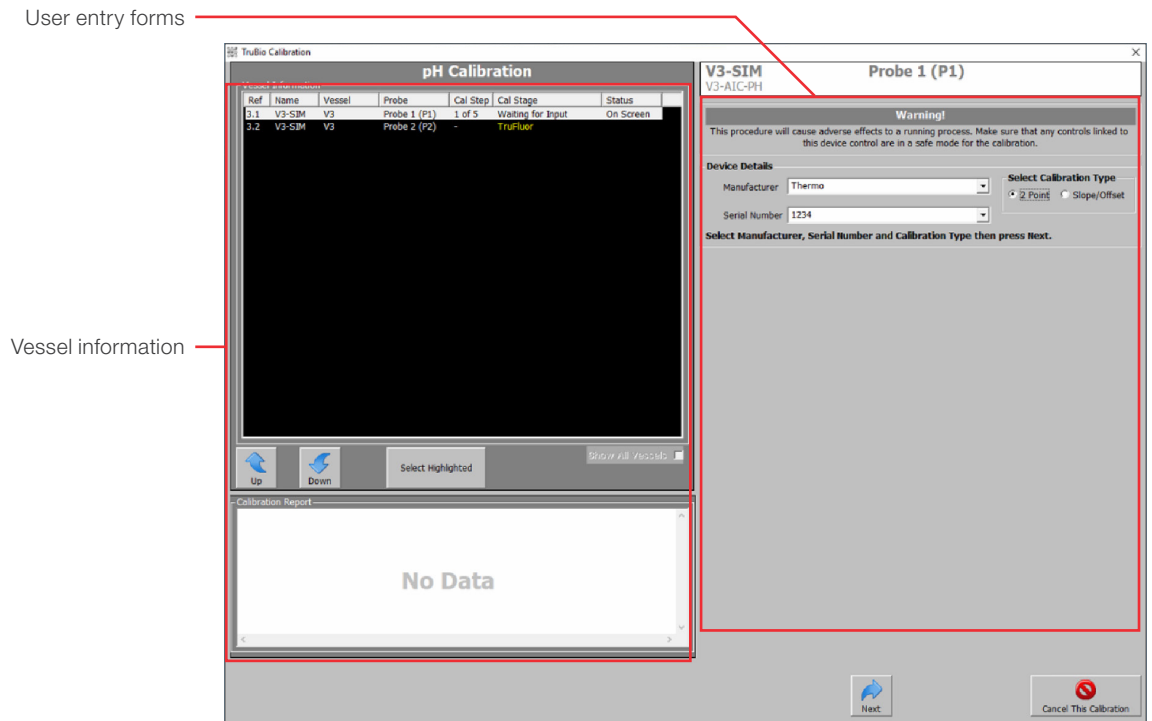
Figure 3.10. ph Calibration window.

2. Enter the manufacturer and the serial number of the probe to be calibrated under **Device Details**. If the probe has previously been calibrated, you can select the serial number from the Serial Number drop-down menu (see Figure 3.10).

3. Select the **2 Point** radio button under **Select Calibration Type** (Figure 3.11).
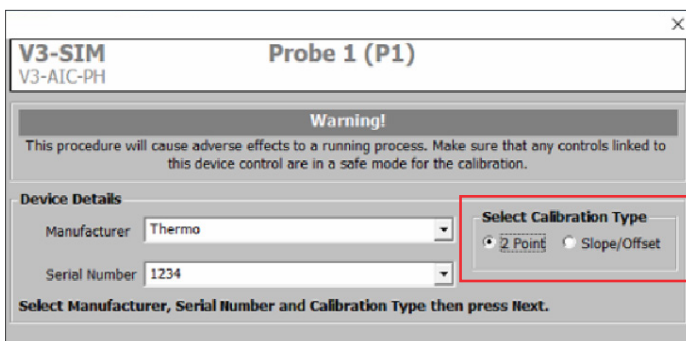
Figure 3.11. Device Details entered; 2 Point Calibration Type selected.

4. Click **Next** at the bottom of the screen.

5. The display advances to the **Zero/Low Calibration** screen. Place the probe in the lower pH 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 3.12).

   – The display can be either numeric or graphic. Click a view button at the bottom right (Figure 3.12) to change the display. Both display options are labeled in Figure 3.14.
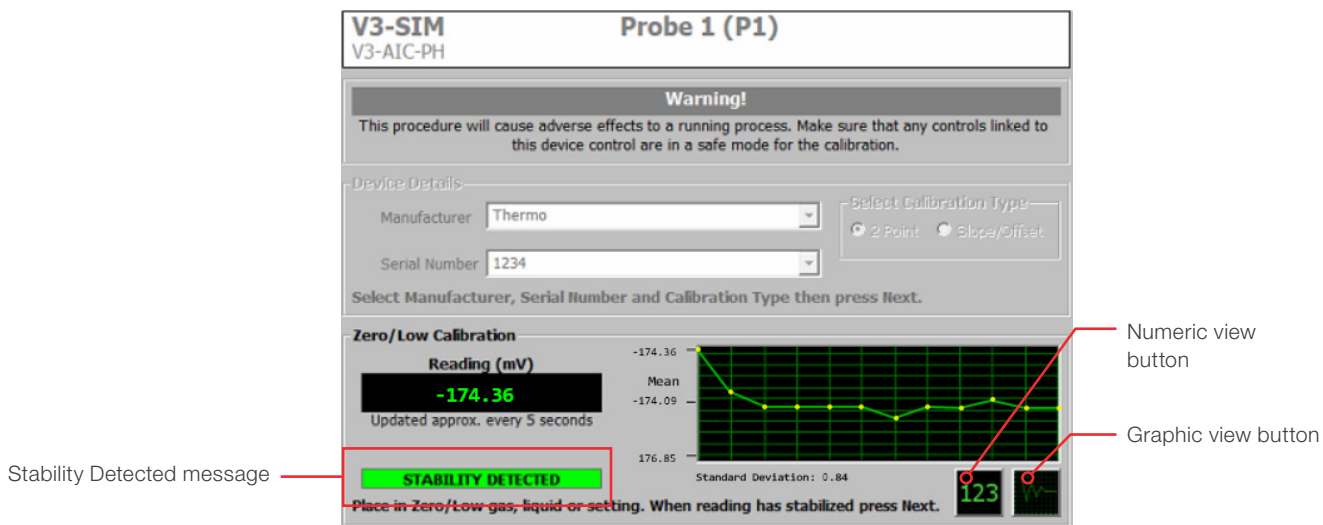
Figure 3.12.   Stability Detected message for first calibration point.

6. Click **Next** to lock in the first buffer value. The display will advance to the **Span/High Calibration** screen.

    –   Place the probe in the upper calibration pH buffer and observe the screen. When the standard deviation of the displayed points is less than 1%, the **Stability Detected** message appears.

    –   The graphic display auto adjusts to the pH range of the buffer being read.

    –   If you are using a probe that incorporates temperature measurement or a separate temperature probe/sensor, click the Use the **Temperature Compensation Value** check box (Figure 3.13). 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.
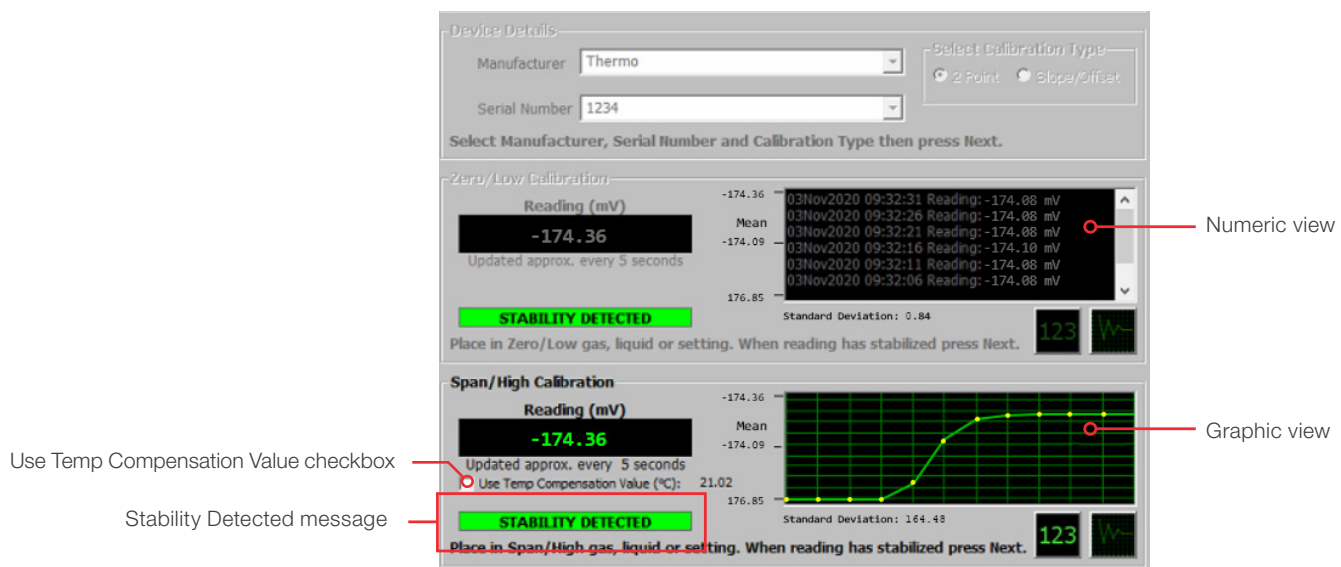
Figure 3.13.   Stability Detected message for second calibration point.

7. After the second reading stabilizes, click **Next** and the display will request the **Calibration Details** (Figure 3.14).

8. Under **Calibration Details**, enter the pH values for the buffer solutions used in the **LOW** and **HIGH Scale** fields (Figure 3.14).

9. If you are not using Temperature Compensation, enter the temperature from an external temperature device in the **Temperature Compensation** field.

Figure 3.14. Calibration Details.

10. Click **Next**. The entire calibration record (Figure 3.15) will display for review. Comments may also be entered on this screen.

11. Enter in a Supervisor or Admin level username and password in the respective fields.

Figure 3.15. Temperature compensation—calibration record.

12. 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.

1. Click the vessel and probe number to bring up the first calibration screen.

2. Enter the probe information.

3. Click **Next**.

   – The **Calibration Report** window will display the detailed calibration history for the probe (Figure 3.16). Once written into the file, records cannot be modified or deleted.

Figure 3.16. Calibration saved confirmation window.

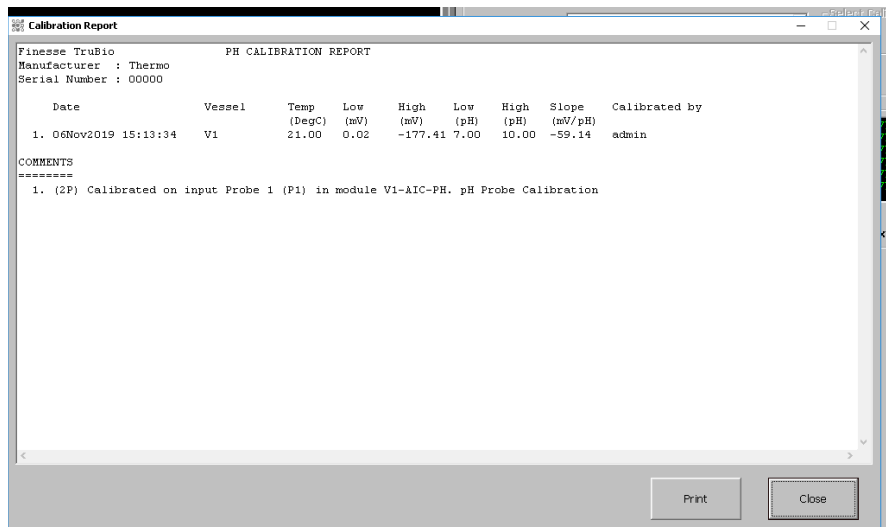4. When the calibration process or review is completed, click the **X** in the upper right corner of the screen to close the calibration screen.

3.5.2 Single-use pH Sensor calibration process

This section details calibration steps for sensors pre-calibrated from the manufacturer, but do require a **Slope/Offset** calibration. These sensors are shipped with certification sheets or labels that detail the slope offset.

To access the pH calibration, open the Calibration tab on the pH Detail window (Figure 3.17).

Note: For TruBio with GXCore, you can select **Detail** from the mini-faceplate or the full faceplate.

For a **Slope/Offset** calibration, you will need the pH sensor along with the manufacturer provided calibration label.
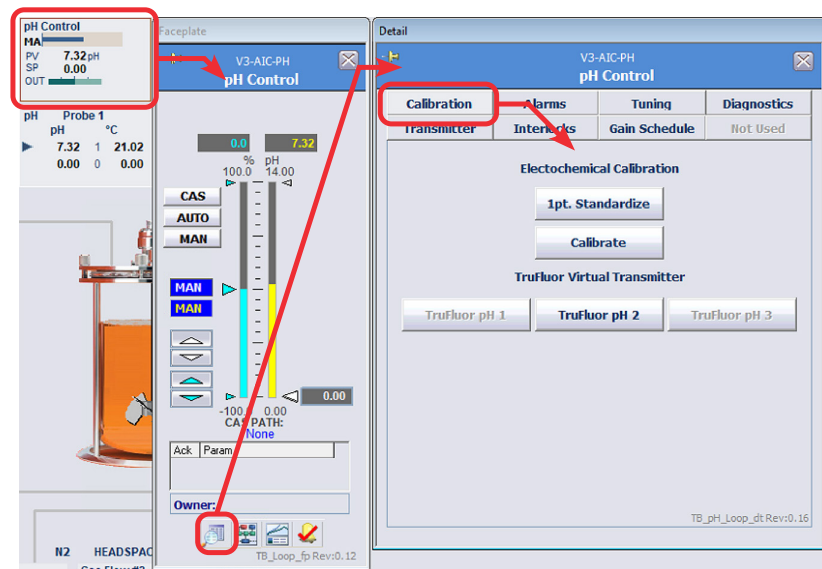
Figure 3.17. Opening the pH Control Calibration tab.

Note: A Supervisor or Administrator username and password are required to save the calibration.

1. From the **Calibration** tab of the **Detail** window, click **Calibrate**. This opens a series of screens that will walk you through the process (Figure 3.18).

   Note: TruBio Software allows multiple probes to be calibrated concurrently.

   – Enter the manufacturer and the serial number of the probe to be calibrated under **Device Details**. If the probe has previously been calibrated, you can select the serial number from the Serial Number drop-down menu (see Figure 3.18).

User entry forms

Vessel information
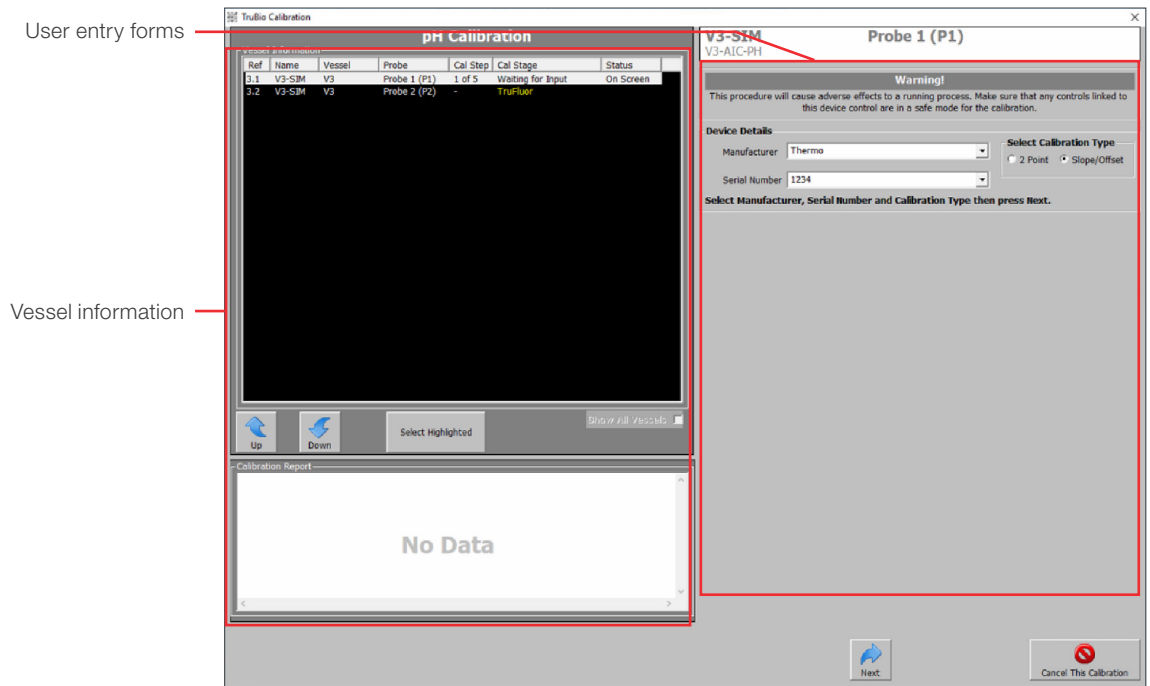
Figure 3.18. ph Calibration window.

2. Select the **Slope/Offset** radio button under **Select Calibration Type** (Figure 3.19).
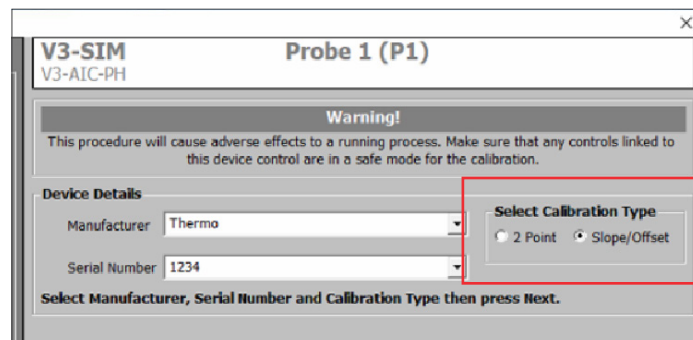
Figure 3.19. Slope/Offset selected as Calibration Type.

3. Click **Next** at the bottom of the screen.

4. The display advances to the **Calibration Details** screen. Enter the slope and offset found on the calibration label on the probe (Figure 3.20).

    – **Note:** The label on Hamilton SU sensors uses different terminology. For slope, enter the Sensitivity value, and for offset, enter the Zero-Point value.

Figure 3.20. pH calibration details.

5. Click **Next**. A confirmation screen will appear.

6. Enter your Supervisor or Administrator username and password.

7. 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:

1. Click the vessel and probe number to bring up the first calibration screen.

2. Enter the probe information.

3. Click **Next**.

    – The **Calibration Report** window will display the detailed calibration history for the probe (Figure 3.21). Once written into the file, records cannot be modified or deleted.
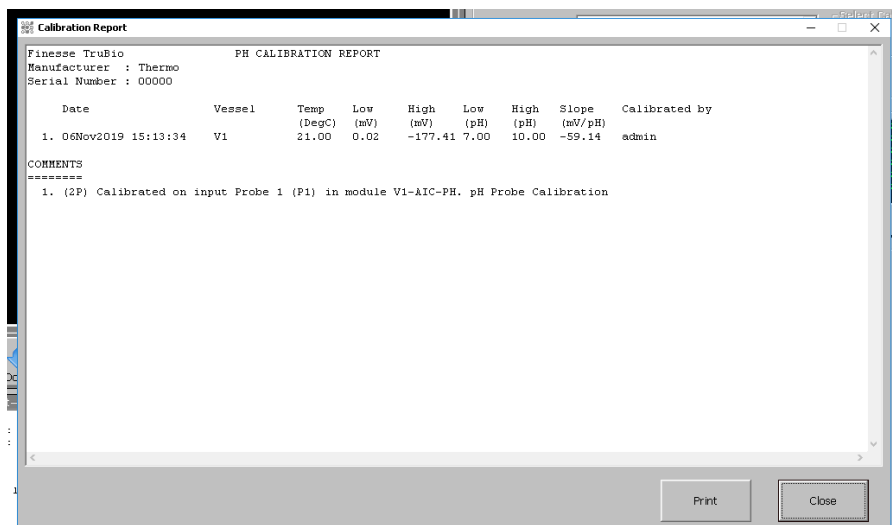
Figure 3.21. Calibration saved confirmation window.

4. When the calibration process or review is completed, click the **X** in the upper right corner of the screen to close the calibration screen.

3.5.3 DO calibration

It is important to note that polarographic DO probes should be connected and polarized for four to six hours prior to calibration, while optical DO probes do not need to be polariazed prior to calibration.

Optical DO sensors have slightly different instructions and are covered in detail in Appendix G.

Single-point verification

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

Two-point calibration

Two-point calibration is usually performed in the bioreactor at the target temperature (for offline calibration, see section G.1.1). For two-point calibration, you will need:

• DO sensor

• Air and nitrogen set up in your mass flow controller (MFC)

1. From the **Calibration** tab of the **Detail** window, click **Calibrate**. This opens a series of screens that walk you through the process.

    Note: TruBio Software allows multiple probes to be calibrated concurrently.

2. Enter the manufacturer and the serial number of the probe to be calibrated under **Device Details**. If the probe has previously been calibrated, you can select the serial number from the Serial Number drop-down menu (see Figure 3.22).

User entry forms

Vessel information
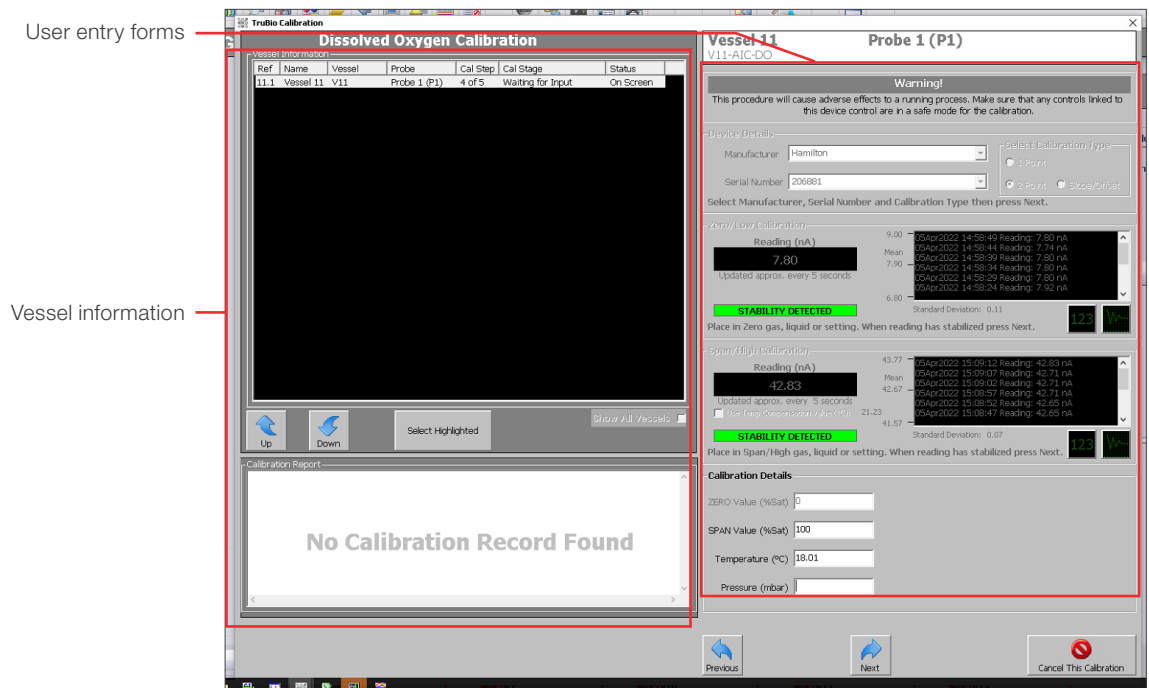
Figure 3.22. DO Calibration window.

3. Select the **2 Point** radio button under **Select Calibration Type** (Figure 3.23).
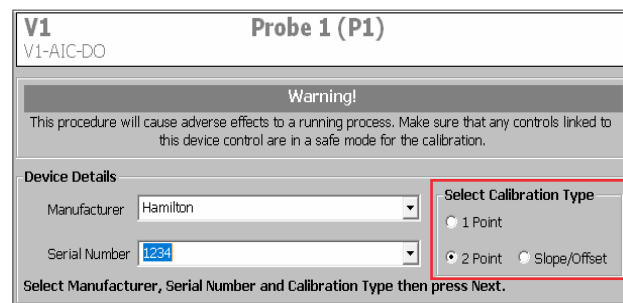
Figure 3.23. DO Calibration window.

4. Click **Next** at the bottom of the screen.

5. The display advances to the **Zero/Low Calibration** screen. The zero/low calibrator for DO is usually a flow of nitrogen. Sparge nitrogen into the bioreactor solution sufficiently long to obtain a 0% solution.

   – The display can be either numeric or graphic. Click a view button at the bottom right (See Figure 3.13) to change the display.

6. Once the **Zero/Low** reading is stable (Figure 3.24), click **Next**.

Stability Detected message —
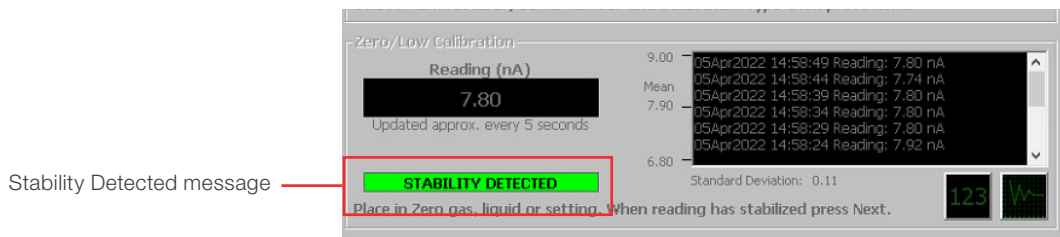
Figure 3.24.   Stability Detected message for first calibration point.

7. Stop nitrogen gas flow and initiate air gas flow. The span/high reading (100% saturation) is generally taken with air.

   – If you are using a probe that incorporates temperature measurement or a separate temperature probe/sensor, click the Use the **Temperature Compensation Value** check box (Figure 3.25). Place the temperature probe (if separate) in the buffer along with the DO probe, and the system will integrate the temperature reading from the probe.

Use Temp Compensation Value checkbox —

Stability Detected message —
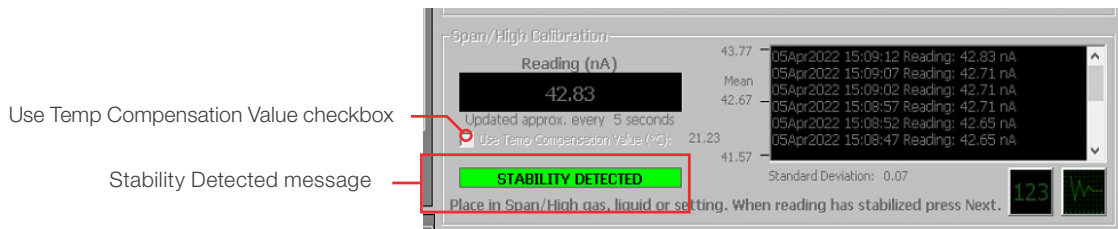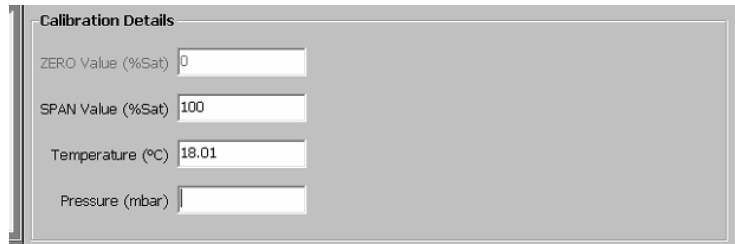
Figure 3.25.   Stability Detected message for second calibration point.

8. Once the **Span/High** reading is stable, click **Next**.

9. Under **Calibration Details**, enter the actual DO values in the **LOW** and **HIGH Scale** fields.

10. If you are not using Temperature Compensation, enter the temperature from an external temperature device in the **Temperature Compensation** field (Figure 3.26).

11. Enter the actual pressure reading in mbar in the **Pressure** field (Figure 3.26).

Calibration Details

ZERO Value (%Sat)	0
SPAN Value (%Sat)	100
Temperature (°C)	18.01
Pressure (mbar)	

Figure 3.26. DO Calibration Details.

12. Click **Next**.

13. Add any required comments, enter the supervisor or administrator user name and password, and click **Write Calibration Data**.

3.5.4 Temperature calibration

Refer to the images in section 3.5.1 for reference of the different calibration fields.

The calibration standards for **Zero/Low** and **Span High** are water baths that are set to a known temperature and then verified by calibrated thermometers. We recommend temperatures between 10°C and 40°C.

1. Open the **Temperature Calibration** window.

2. Enter the **Device Information** and select **2 Point** for the **Calibration Type**.

3. Allow the **Zero/Low** reading to stabilize and click **Next**.

4. Allow the **Span/High** reading to stabilize and click **Next**.

5. Under **Calibration Details**, enter the actual temperatures from the calibrated thermometers in **LOW** and **HIGH Scale** fields.

6. Click **Next**.

7. Add any required comments, enter the supervisor or administrator user name and password, and click **Write Calibration Data**.

3.5.5 Jacket temperature

The temperature 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. See section 3.5.4.

3.5.6 Agitator calibration

Refer to the images in section 3.5.1 for reference of the different calibration fields.

1. When calibrating the agitator, be sure to set the mode to **Manual** from the faceplate.

2. Open the **Calibration** tab from the **Agitator Detail** window.

3. Click **Calibrate** to open the **Agitator Speed Calibration** window.

4. Move the windows so that the **Agitator Speed** faceplate is visible.

5. Enter the **Device Details** and select **2 point** for the **Calibration Type**.

6. Click **Next**.

7. Use the **Agitator Speed** faceplate to set the agitator output to 0% or a number lower than the intended run speed. For example, if the maximum agitator speed is 250 rpm and the desired value is 75 rpm (30% of 250), set the output to 30.

   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.

8. Wait for the PV (right side column) on the faceplate to come to the value set above and the **Stability Detected** message to appear in the **Zero/Low Calibration** section of the **Calibration** window, and then click **Next**.Set the agitator output on the faceplate to a higher value.

9. Wait for the PV (right side column) on the faceplate to come to the value set above and the **Stability Detected** message to appear in the **Span/High Calibration** section of the **Calibration** window, and then click **Next**.

10. Turn the agitator off by setting the output value to zero on the faceplate.

11. Under **Calibration Details**, enter the actual rpm values from a calibrated tachometer in the **LOW** and **HIGH Scale** fields.

12. Click **Next**.

13. Add any required comments, enter the supervisor or administrator user name and password, and click **Write Calibration Data**.

3.5.7 Analog inputs

Analog inputs can be calibrated in the same way as other modules with calibration in the system. Refer to the steps and images in section 3.5.1.

3.5.8 Vent filter heaters

Refer to the images in section 3.5.1 for reference of the different calibration fields.

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. Place a calibrated thermo probe into the vent filter heater (Figure 3.27). Be careful to not place it at the hinge point.

Calibrated thermo probe

Figure 3.27. Thermo probe placed in the vent filter heater.

2. Open the **Vent Heater** faceplate and the **Vent Heater Detail** screen.

3. Select the **Calibration** tab.

4. Select either the **1-point Standardization** for single-point calibration or **Calibrate** for two-point calibration.

Single-point calibration

1. Set the **Vent Heater** faceplate to **Auto** mode.

2. Set the setpoint to a desired value.

3. Allow the temperature to equilibrate, and read the value from the thermometer.

4. Type the value from the thermometer in the text field and click **Enter**.

Two-point calibration

1. Enter the **Device Details** information and select **2 Point** for the **Calibration Type**.

2. Move the screen to one side so the **Vent Heater** faceplate can be seen on the side of the calibration screen.

3. Enter **Device Details**.

4. Click **Next** on the **Calibration** window.

5. Set the vent heater faceplate to **Auto**.

6. Change the setpoint of the temperature to the lower point of the desired range on the **Vent Heater** faceplate. Click the box and type in the value, and then select **OK**. Room temperature is recommended. Allow the temperature to equilibrate. At least 40 minutes is recommended

7. After equilibration and the **Stability Detected** message appears, take note of the thermometer temperature (used for Low Scale later) and click **Next**.

8. On the **Vent Heater** faceplate, change the setpoint of the temperature to the higher value. Allow the temperature to equilibrate. At least 40 minutes is recommended.

9. After equilibration and the **Stability Detected** message appears, take note of the thermometer temperature (used for High Scale later) and click **Next**.

10. Under **Calibration Details**, enter the actual temperatures from the calibrated thermo probe in **LOW** and **HIGH Scale** fields.

11. Click **Next**.

12. Add any required comments, enter the supervisor or administrator user name and password, and click **Write Calibration Data**.

13. Create a **Calibration** save file to save your changes (see section 3.2).

14. After calibration is complete, turn off the vent filter heater.

3.5.9 Pressure calibration

TruTorr II pressure sensor

Pressure sensors are factory calibrated and requires no further verification by the user. If desired, you can perform a one point (zero) calibration with no pressure on the sensor:

1. Open **1pt. Calibration** from the **Pressure Detail** window.

2. Enter the pressure value from the pressure sensor in the field and click **Enter** (Figure 3.28).
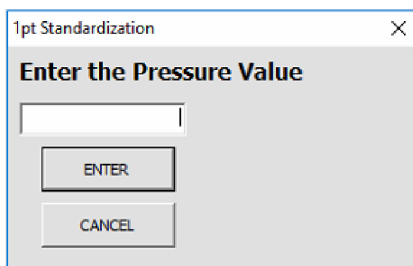
Figure 3.28. 1pt Standardization window.

PendoTECH pressure sensor taring

The PendoTECH™ pressure sensor can be tared as needed.

1. Open the **Function** tab from the **Pressure Detail** window.

2. Click **Tare** (Figure 3.29) with no pressure inside the BPC.

   Note: The sensor must be connected for the tare function to work properly.

Figure 3.29. Tare button on the Functions tab of the Pressure Detail window.

The **Pressure** control module will display zero psig after taring (Figure 3.30).

Figure 3.30. Pressure shown before (left) and after (right) taring on the Pressure control module.

3.5.10 Vessel weight

Refer to the images in section 3.5.1 for reference of the different calibration fields.

1. In the **Scale Control** tab, select **Gross** and tare the scale.

2. Open the **Vessel Weight Calibration** window from the **Detail** window.
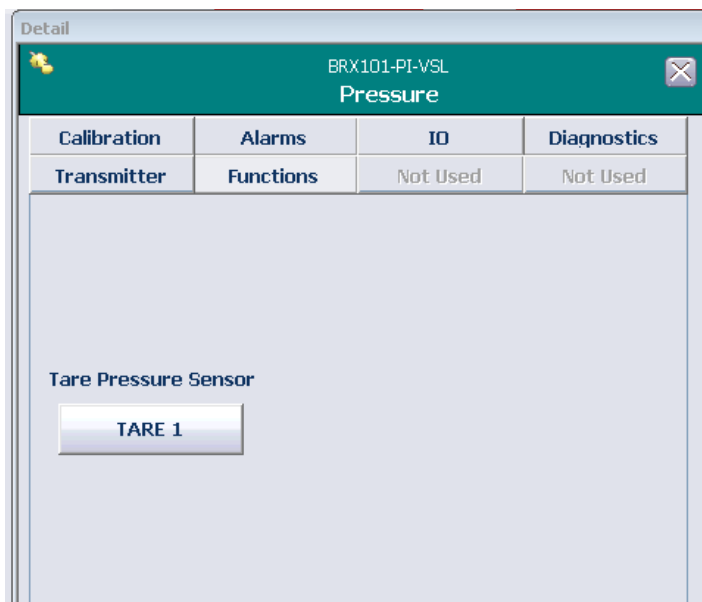
3. Enter the **Device Details** and select **2 point** for the **Calibration Type**.

   Note: It is recommended to enter the serial number as the vessel number and WIC-VSL.

4. Because the Zero/Low calibration point is always zero (0), record the weight with the vessel empty.

5. 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.

6. Under **Calibration Details**, enter the actual weights in **LOW** and **HIGH Scale** fields.

7. Click **Next**.

8. Add any required comments, enter the supervisor or administrator user name and password, and click **Write Calibration Data**.

3.5.11 Pump calibration

Updated pump features in 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 to be used in the process. Using different tubing will result in inaccurate pump delivery.

Manual calibration

Prior to calibration ensure that the pumps are set up.

1. Click the appropriate **Pump** control module to open the faceplate.

2. Click **Detail** to open the **Detail** window.

3. Click the **Calibration** tab if it is not already open.

   Note: For TruBio with GXCore, you can select **Detail** from the mini-faceplate or the full faceplate.

4. Click **Calibrate**, which opens the screen shown in Figure 3.31. The screen displays the default settings for the calibration.

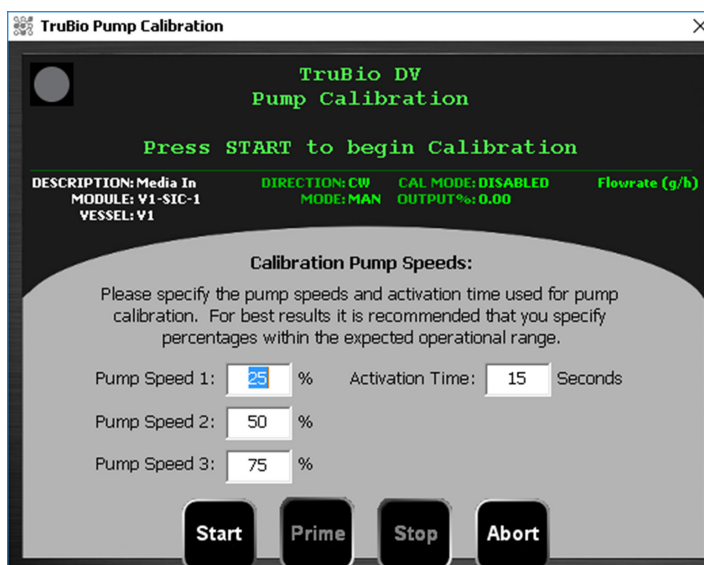Figure 3.31. Calibration pump speeds screen.

5. Modify the settings as desired. Then click **Start**.

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

6. At the warning screen (Figure 3.32), ensure that the device is in a safe mode and click **Start** again.

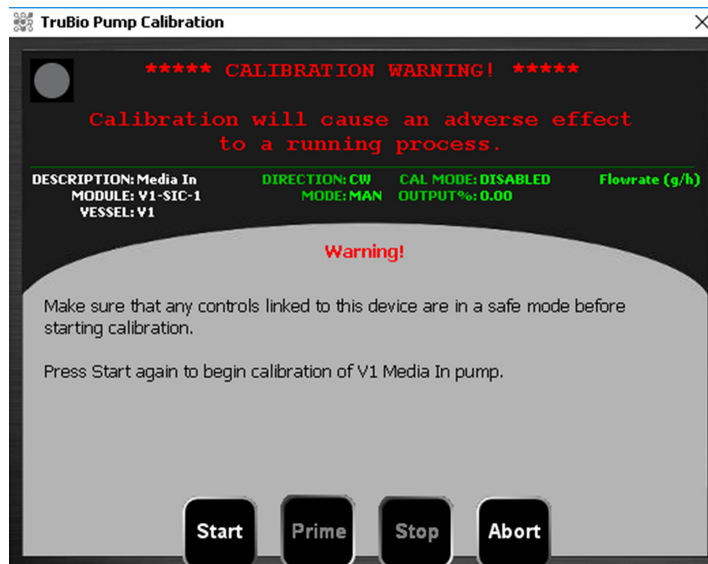Figure 3.32. Calibration warning screen.

Note: If the pump calibration is performed below the minimum speed set in the TP Mode on the pump **Detail** screen, the calibration time must be a multiple of the cycle time.

7. Select the method (**Manual** or **Automatic**) and the pump direction (Figure 3.33). Then, click Start.
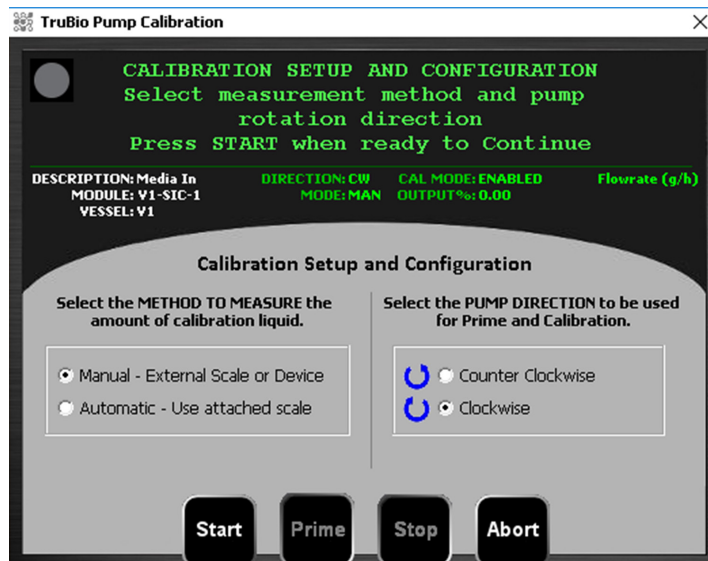
Figure 3.33. Selecting method and pump direction for calibration.

8. Follow the instructions on the **Calibration Step 1/3** screen to complete the calibration (Figure 3.34).

Figure 3.34. Calibration step 1 of 3: Setup to prime the pump.

9. At the end of the pump activations, a prompt appears to enter the weight recorded on the scale (Figure 3.35). **DO NOT** tare or zero the scale between measurements. **DO NOT** empty the receiver container between measurements.
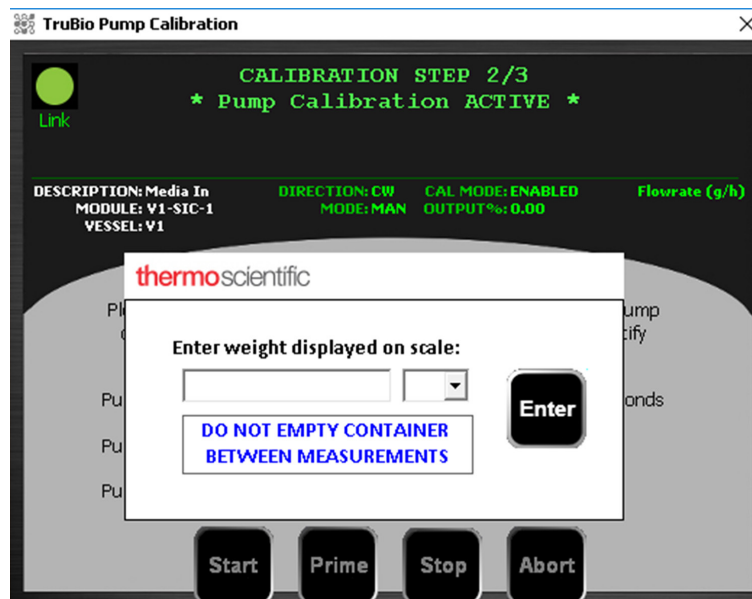
Figure 3.35. Screen for entering weight displayed on scale.

10. At the end of the three runs, a prompt appears for a username and password (Figure 3.36). You can also add comments. To write the calibration to the record, click **Apply**.
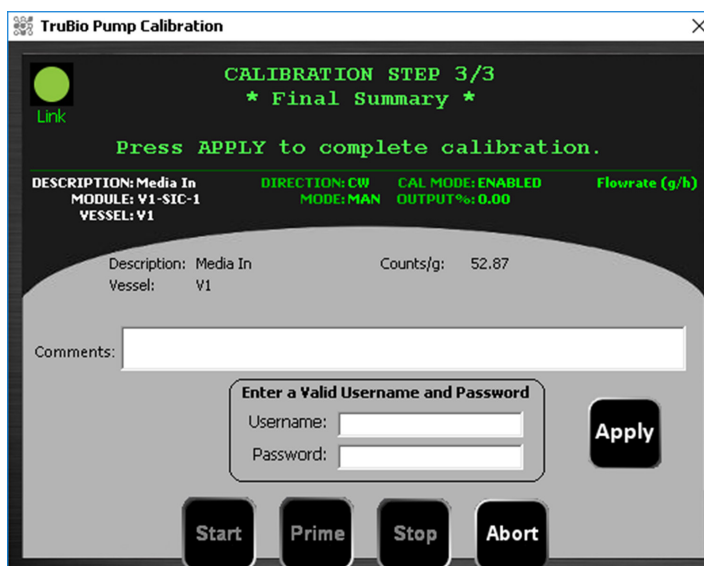
Figure 3.36. Prompt for username and password.
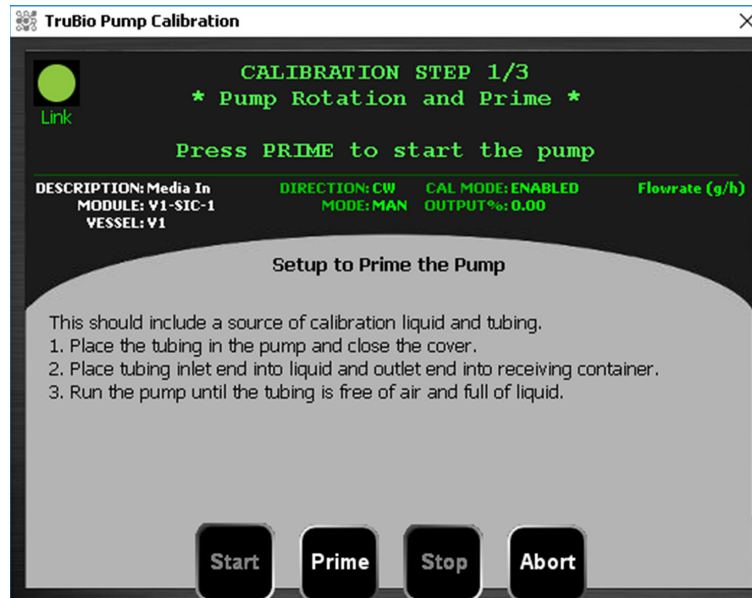
11. Repeat these steps for any other pumps to be used.

Automated pump calibration

An automated pump calibration may be run if a scale has been assigned to the pump. The pump is calibrated in units of weight/time. Therefore, the pump operating mode must be set to **Flow Control**.

1. Verify that the correct vessel number is displayed and open the **Configuration** screen. Then click the pump to open the **Pump Configuration** window (Figure 3.37).

   Note: For TruBio with GXCore, select **Configuration** from the pump's mini-faceplate.
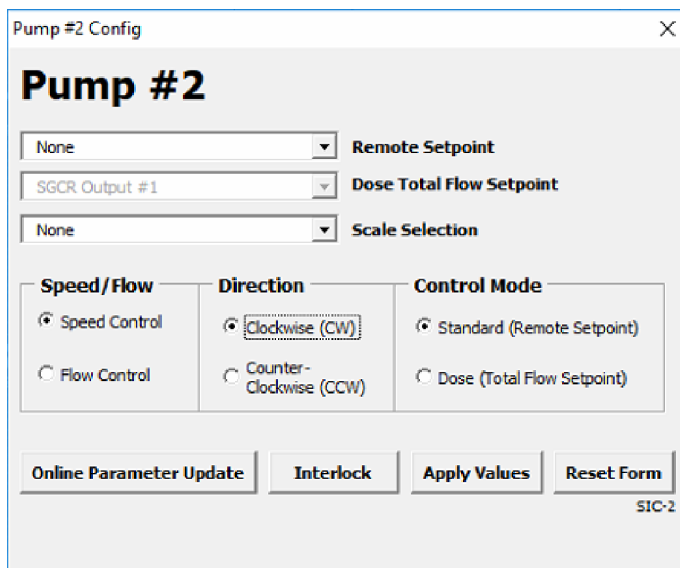
Figure 3.37. Pump Configuration form.

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 (see Figure 3.33 on page 105), select **Automatic**.

5. Choose either **Pump liquid ONTO the scale** or **Pump liquid FROM the scale** (Figure 3.38).

6. Select **Start** (Figure 3.38).

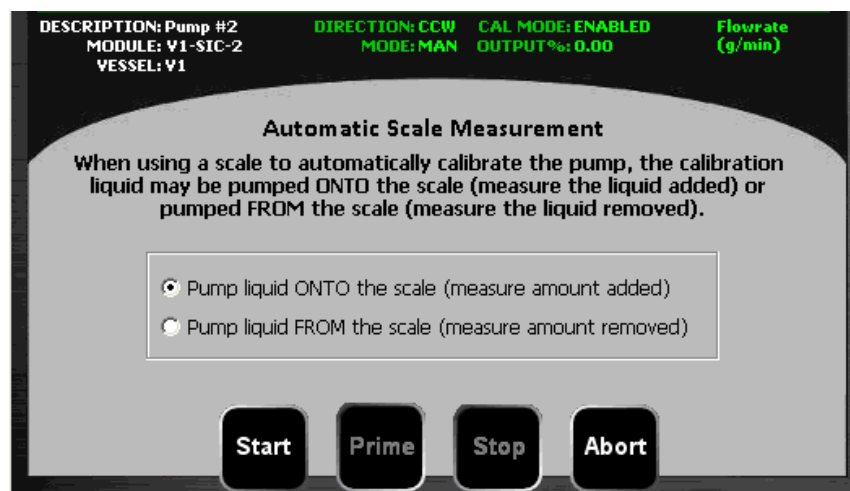Figure 3.38. Pump Automatic Scale Measurement window.

7. 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.

3.6 Vessel selection

TruBio software allows you 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 you want to change to a Thermo Scientific HyPerforma S.U.B.

Note: Vessel Selection is only available on the G3Lab and G3Pro Universal Controllers and should only be used to change the assigned vessel type.

Although one controller controls only one vessel at any given time, up to seven vessel types may be programmed into the software for ease of switching between vessels.

The number of available vessels depends on the controller. The HyPerforma G3Lab and GXCore controllers only control benchtop vessels, while the G3Lite, and G3Pro control larger vessels.

Open the **Configuration** screen and click **Vessel Selection** to view the the **Vessel Select** form.

The menu available depends on the size of the controller. Figure 3.39 shows the form for smaller controller, while Figure 3.40 shows the form for a larger controller.

Select the type of vessel to be added (substituted) and click **Apply Values**. A confirmation window will appear warning that values will be reset (Figure 3.32). Click **Yes** to continue or **No** to cancel.

Figure 3.39. Vessel Selection pop-up window for small vessels.

Figure 3.40. Vessel Selection pop-up window for large vessels.
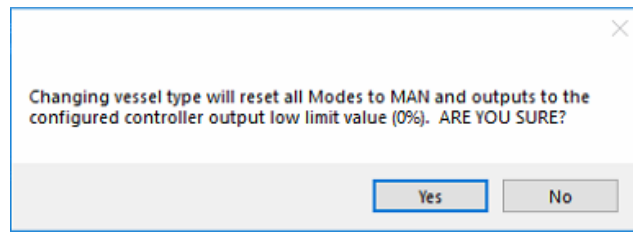
Figure 3.41. Vessel Selection confirmation pop-up window.

3.7 Vent filter heater operating guidelines

There is potential for damage to the vent filter heater if operated outside of specified parameters. The following steps can help alleviate this risk.

Before you begin

1. Prior to setting alarms, ensure that the correct power voltage is applied for each vent filter heater in use and the vent filter heaters have been calibrated properly (see section 3.5.8).

2. If operating with a G3Lite or G3Pro controller, open the cabinet and set the rotary switches on the OMRON temperature monitoring relay is set to 70°C (158°F (Figure 3.42)).

Figure 3.42. Rotary switches set to 70°C.

Vent heater filter Detail settings

1. Open the **Vent Heater Filter** faceplate and click the **Details** button.

2. Click the **Alarms** tab.

3. In the Limits fields, set the **Hi Alarm** to 60°C and the **Hi Hi Alarm** to 65°C. Then click the **Enab** (enable) checkbox to enable both the **Hi** and **Hi Hi** alarms (Figure 3.36).

   Note: You must press Enter on your keyboard in the **Limits** fields to save your changes. Pressing Tab will not save changes.
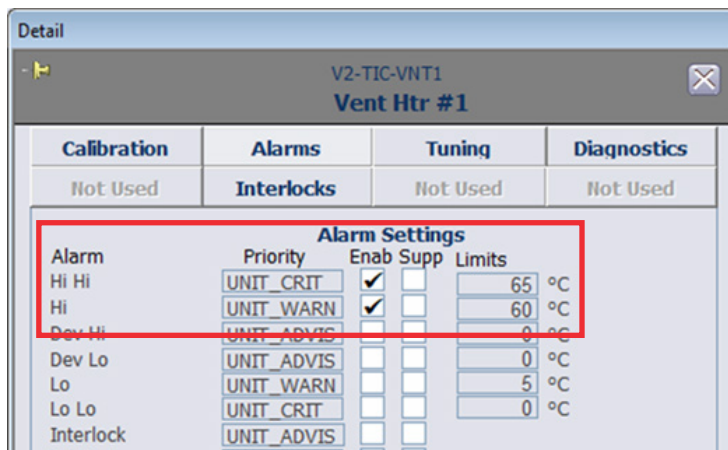

Figure 3.43. Vent filter heater alarms set and enabled.

4. Click the **Tuning** tab.

5. Enter the values as they appear in Figure 3.44 and Table 3.4.

   Note: You must press Enter on your keyboard in the **Limits** and **Tuning** fields to save your changes. Pressing Tab will not save changes.

Figure 3.44. Vent filter heater tuning settings set.
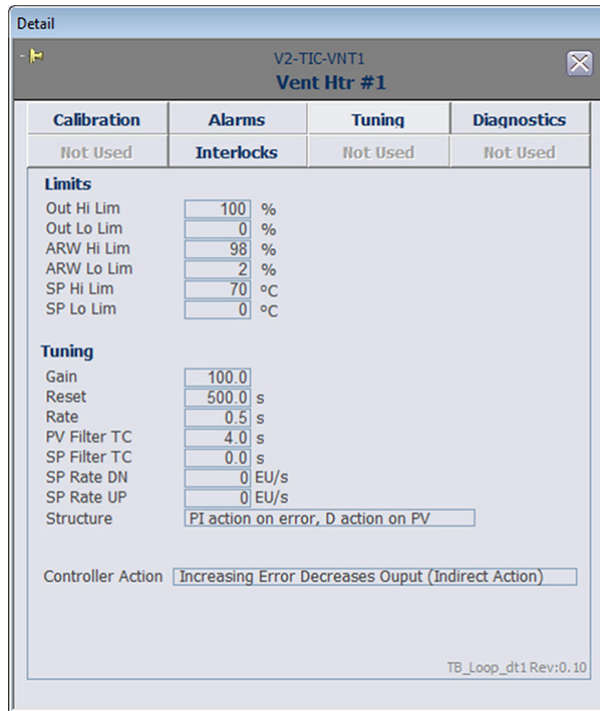
Table 3.4. Vent filter heater tuning settings.

Interlock	Value
Out Hi Lim	100%
Out Lo Lim	0.0%
ARW Hi Lim	98.0 %
ARW Lo Lim	2.0 %
SP Hi Lim	70.0 °C
SP Lo Lim	0.0 °C
Gain	10.00
Reset	500.0 s
Rate	0.5 s
PV Filter TC	4.0 s
SP Filter TC	0.0 s
SP Rate DN	0.0 EU/s
SP Rate UP	0.0 EU/s

6. Close the **Detail** window and vent filter heater faceplate.

7. Repeat for all vent filter heaters in all of the vessels.

Vent heater interlocks

Refer to (Figure 3.45) for the following steps.

1. Open the vent filter heater Interlocks **Configuration** window from the **Configuration** screen.

2. Click Interlock to open the **Interlock Configuration** form.

3. Select **Vent Htr #1 HI HI Trp** from the **Interlock 1** dropdown.

   Note: When setting interlock for the second vent heater filter, select **Vent Htr #2 HI HI Trp** from the **Interlock 1** dropdown instead.

4. Leave **Interlock 2** set to **None**.

5. Select **Internal Value** and leave the value at zero.

6. Select **Apply Values**.

7. Close the **Configuration** window.

8. Repeat for all vent filter heaters in all of the vessels.
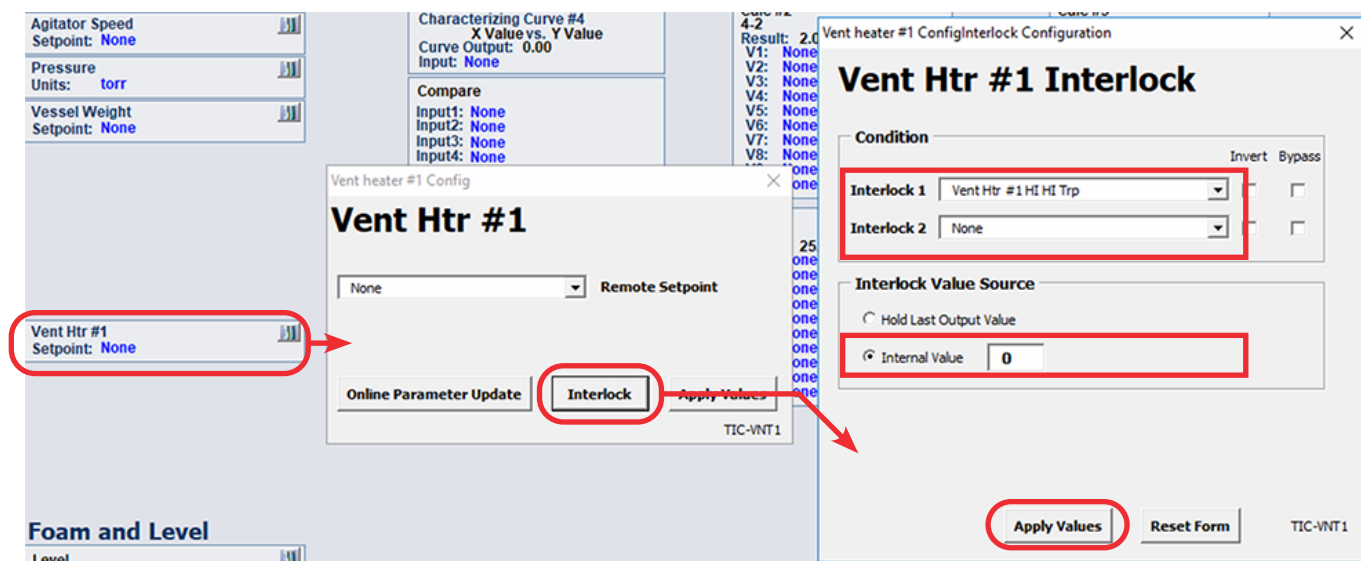
Figure 3.45. Vent filter heater interlock settings.

Vent heater Online Parameter Update settings

Refer to Figure 3.46 for the following steps.

1. Open the **OPU** window from the configuration screen.

2. Locate the **/FS_CTRL1/IN_SCALE.F_EU100** parameter and set it to 70.

    Note: This decreases the maximum output available on the vent filter heater faceplate.

3. Ensure the **/FS_CTRL1/IN_SCALE.F_EU0** parameter is set to zero. This is the default value.

Figure 3.46. Vent filter heater OPU settings.

3.8 Chart Builder

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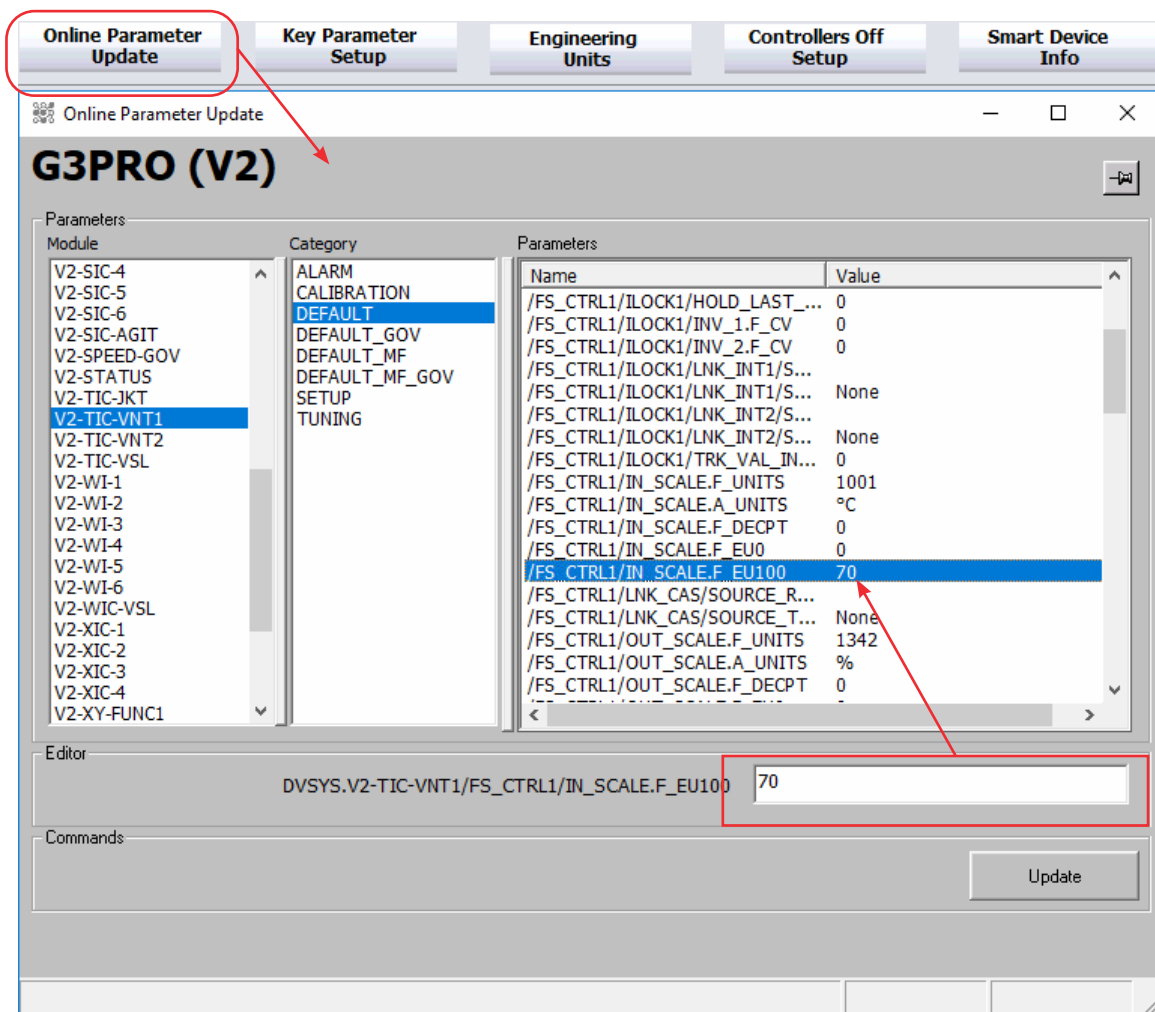
- Setpoint

- Output

- Process value

Up to six trends can be tracked on a single chart. Events can also be included in the chart.

To use **Chart Builder**, follow these steps:

1. On the **Main** screen, right-click a control module. The context menu opens, displaying several parameters you can add to **Chart Builder** (Figure 3.47).
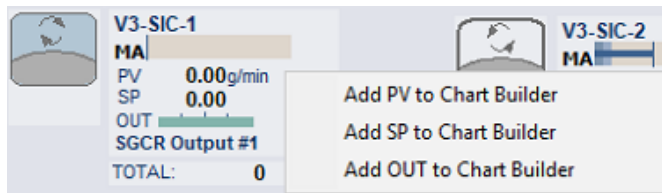

Figure 3.47. Control module example and parameters that can be added to Chart Builder.

2. Click one of the menu options. The parameter you chose is added to **Chart Builder** (Figure 3.48).
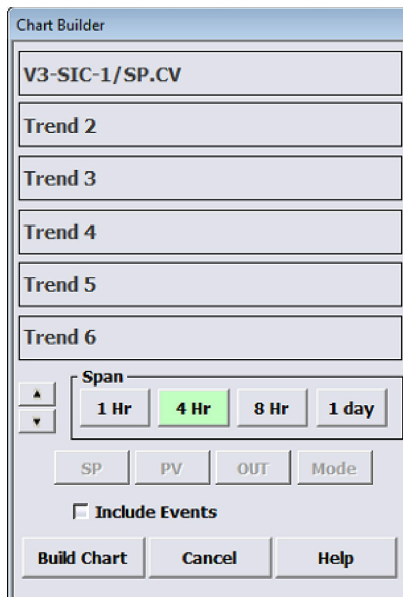

Figure 3.48. Chosen parameter added as Trend 1.

3. Repeat Steps 1–2 to add up to five more trends to the chart, you can add from any control modules in the **Main** screen.

4. To select a different time span, click a button in the **Span** section.

   Note: Timespan can be changed at anytime without affecting the data.

5. (Optional) To include events in your chart, click the **Include Events** check-box.

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 (Figure 3.49) 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. The color on the left coordinates with the Y-axis scale and the trend line shown in the main area.

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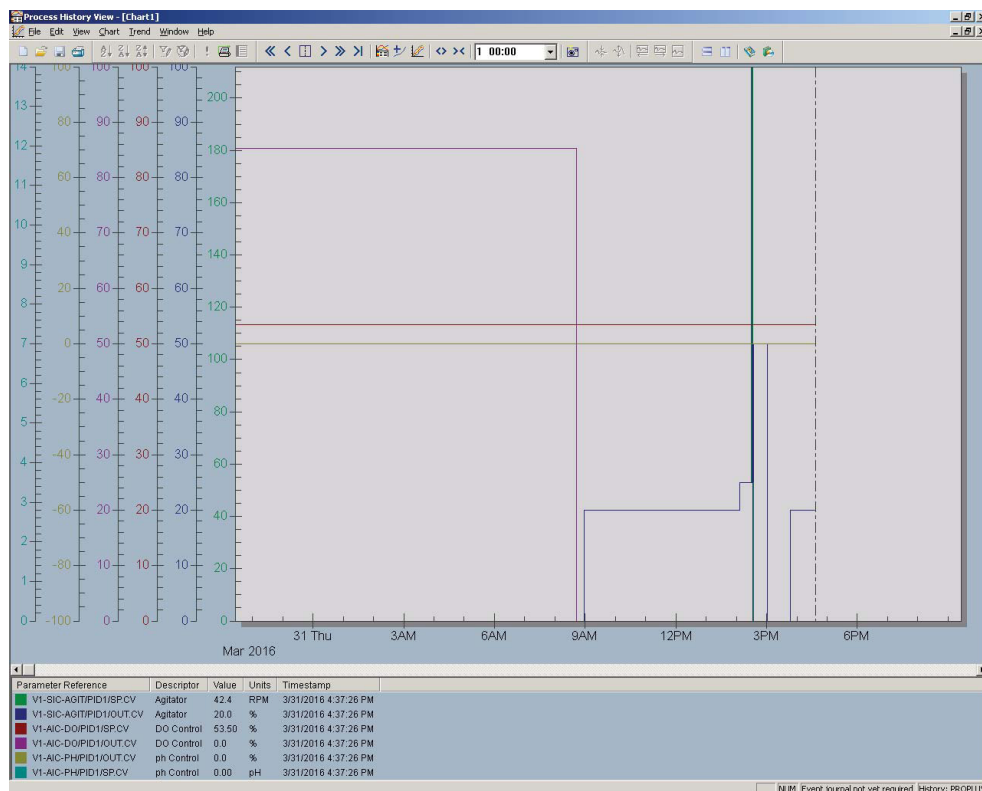

Figure 3.49. Chart builder example.

4

Alarms and limits

Chapter contents

4.1 Explanation of alarms and limits

A general scheme for alarms and limits in relation to the setpoint is shown in Figure 4.15 below.

Figure 4.1. 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 to trigger 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 can 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.

4.1.1 How to set alarms

1. To set control limits and alarms for any parameter, open the faceplate for that parameter, click **Detail**, and then select the **Alarms** tab. Figure 4.2 shows the alarm settings for pH control, as an example.

   – If **Enable** is checked and the alarm condition met, an alarm box will appear in the alarm banner, and an audible alarm will sound if provided in the hardware. The control module 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. See section 4.2.

Note: It is recommended that alarms not be enabled until the system has stabilized, with all parameters within limits. Otherwise, the alarms will trigger until it reaches the target level.
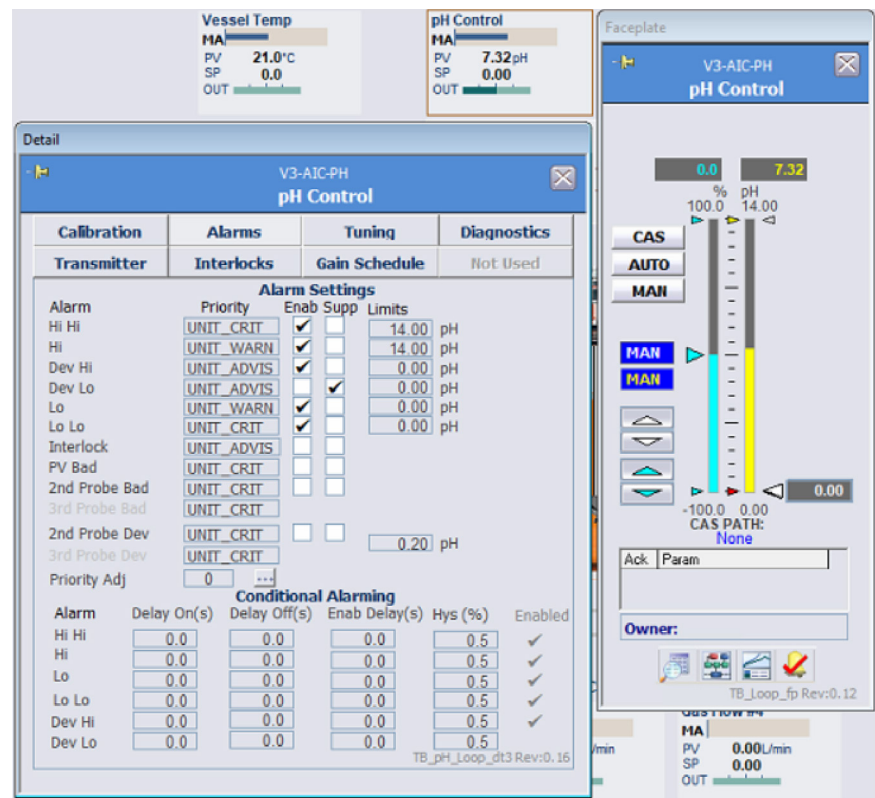

Figure 4.2. Alarm settings screen for pH control.

2. Click the **Tuning** tab and set the limits by typing in the values (Figure 4.3), then confirm the entry by pressing Enter on the keyboard.

   Note: You must press Enter on your keyboard in the **Limits** and **Tuning** fields to save your changes. Pressing Tab will not save changes.

Figure 4.3. SP Hi and Lo limits for pH control.

Additional alarm settings

Additional alarm settings are found on the **Alarms** tab.

- **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 is displayed on the faceplate.

- **Priority Adj**—This function lowers the priority of alarms (e.g. from Hi-Hi to Hi) and should not be used unless under direction of your service representative.

TruBio Software allows you to disable the TruFluor alarms if a transmitter is configured, but the system will reset the alarm. In TruBio Software, version 5.0, the alarm can be permanently disabled, if desired. Consult your customer service representative for more information.

Note: New in the TruBio Software, version 5.0, the conditional alarm settings are now on the Main screen. The alarm delays can be set to your preference.

Hysteresis

The last block of settings on the **Alarms** tab is marked **Hys** (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, if the pH SP 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.

4.2 Alarm management

Enabling and suppressing alarms

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. Note that prior to an alarm being triggered, there is only a thin brown border around the control module (Figure 4.4) and no alarm message in the faceplate.
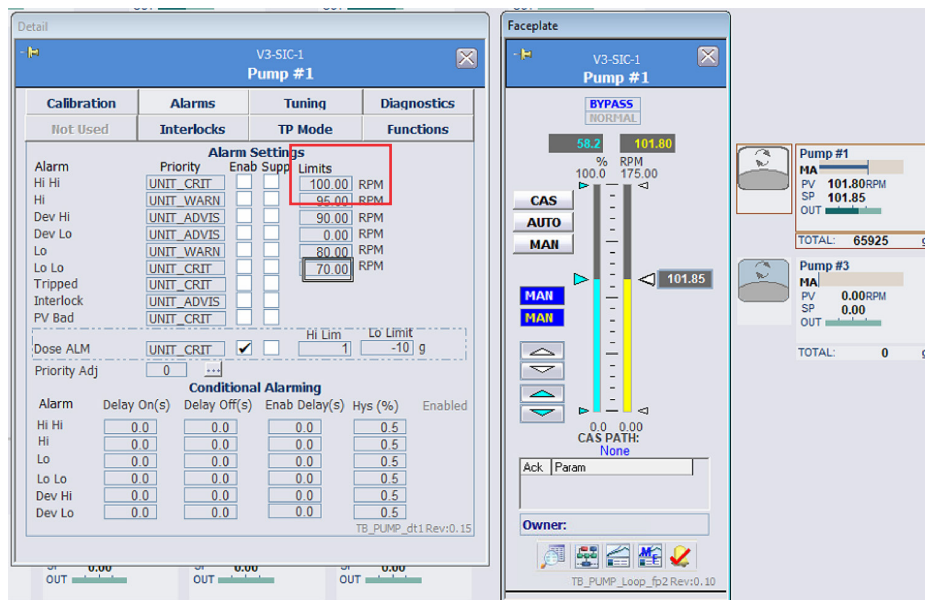
Figure 4.4. Alarm settings screen for Pump #1.

When **Enable** is checked for **Hi** or **Low** alarms, the limits display on the faceplate. When triggered a yellow border flashes on the control module, and the alarm appears on the faceplate (Figure 4.5).
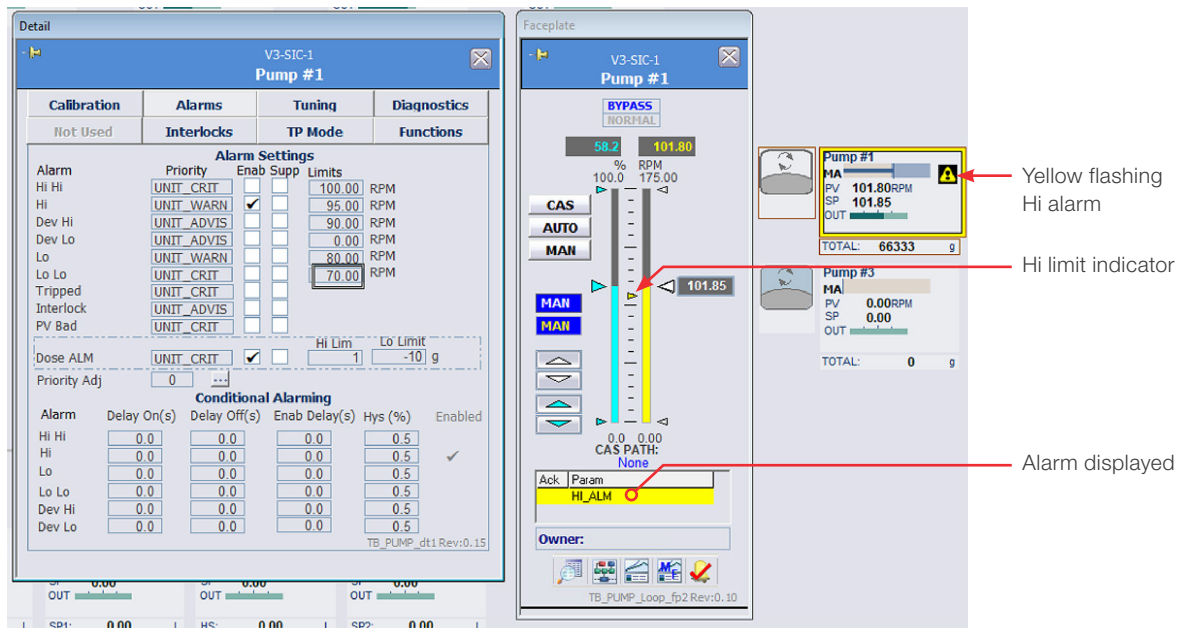
Figure 4.5. Alarm settings screen for Pump #1.

The **Hi-Hi** alarm looks the same, except the alarm bar and the border of the control module will be red (Figure 4.6).
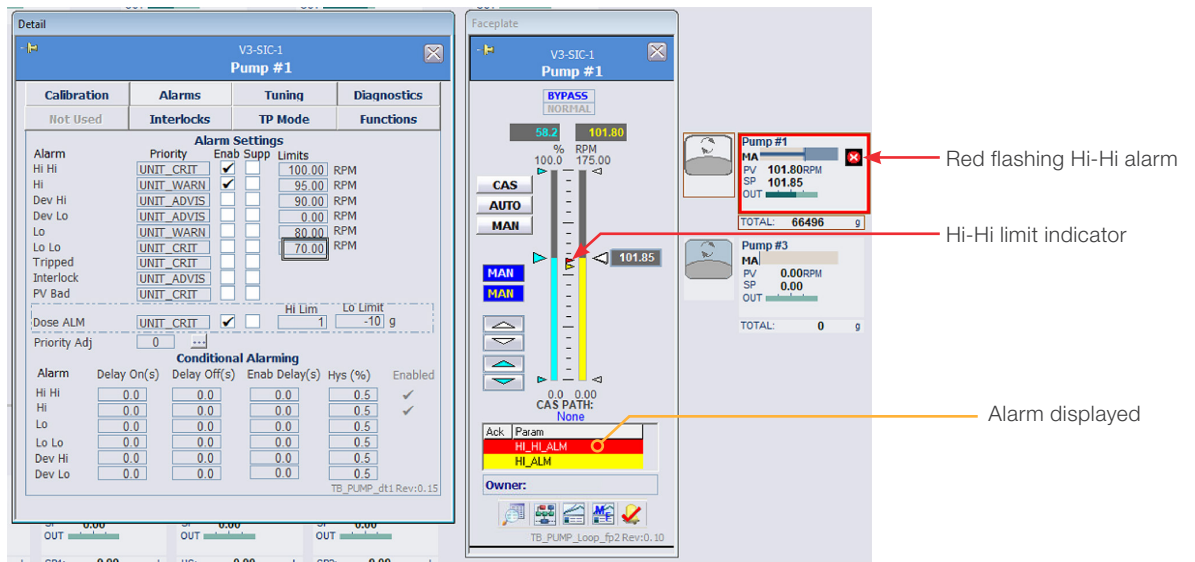
Figure 4.6. Hi-Hi alarm (red) for Pump #1.

If both **Enable** and **Suppress** are checked when the alarm is triggered, the limits will be shown on the faceplate and the border of the control module will turn blue (Figure 4.7), but there will not be an visible or audible alarm notification.
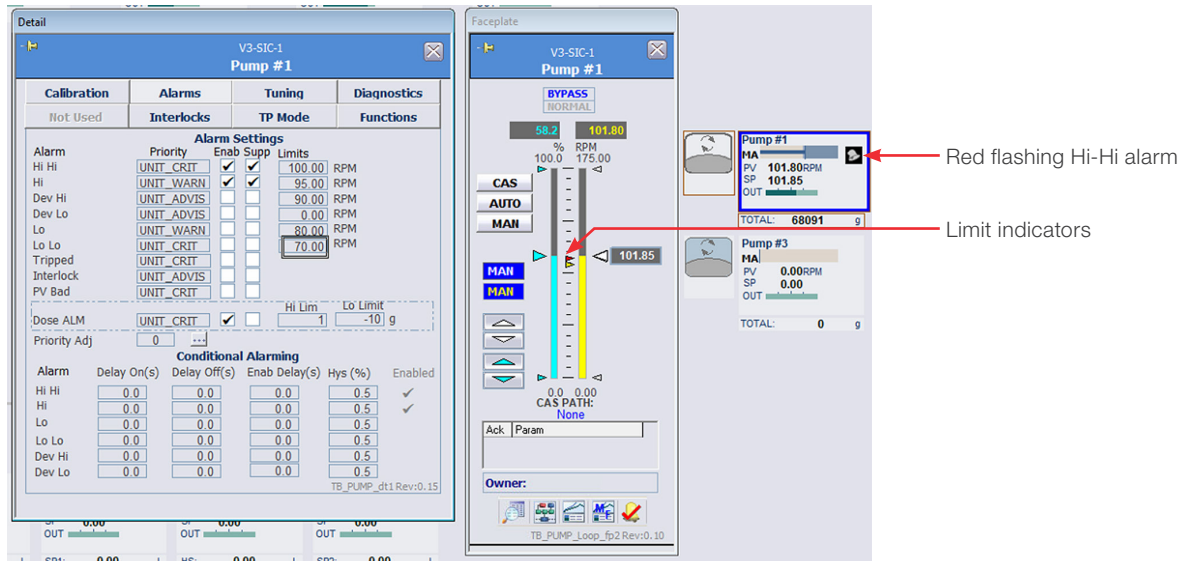
Figure 4.7. Alarms both enabled and suppressed.

Alarms can be suppressed from the **Alarm** screen. To do so, use the following instructions.

1. Click the **Alarm List** button in the toolbar, to open the list of alarms (Figure 4.8).
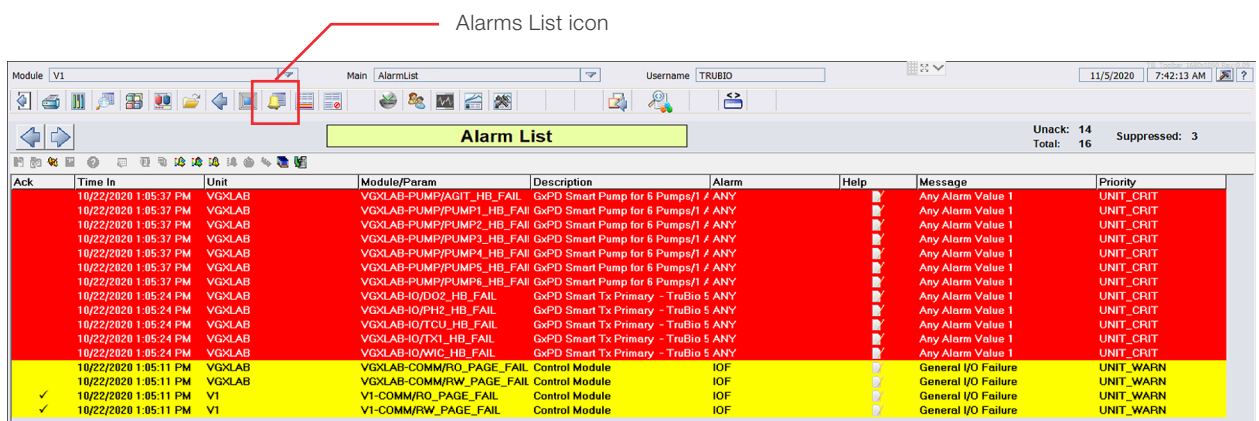
Figure 4.8. Alarm list.

2. Right-click an alarm.

3. From the menu, select **Shelve Alarm** (Figure 4.9).
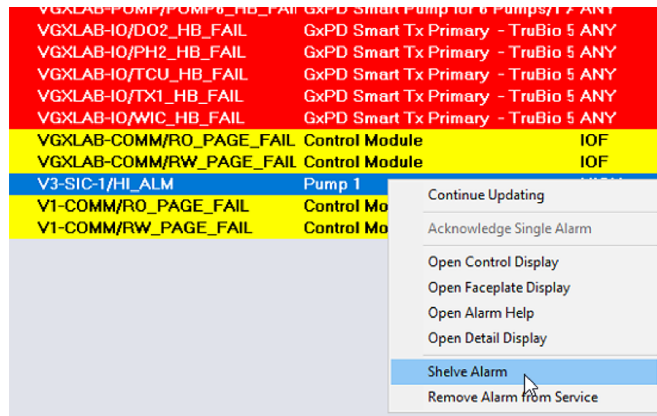
Figure 4.9. Shelve Alarm option in menu.

Suppressed alarms appear on the **Suppressed List**. You can see if there are any suppressed alarms at the top right of the screen (Figure 4.10).
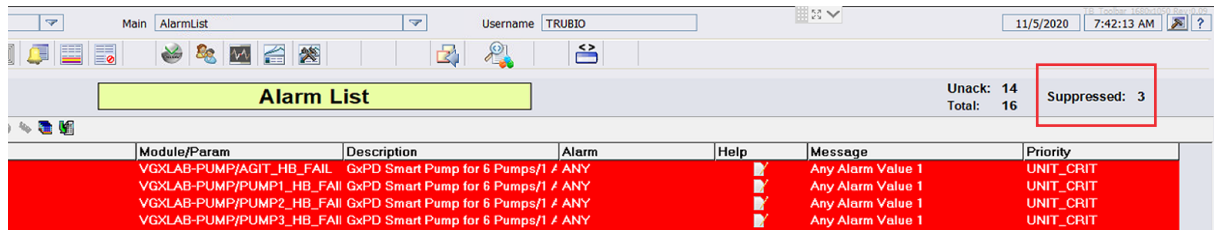
Figure 4.10. Status display noting suppressed alarm.

When **Alarm Suppress** is clicked, the list of suppressed alarms displays. Right-click the selected alarm to display the menu and click **Unshelve Alarm** (Figure 4.11).

Note: You can also disable suppressed alarms from the **Detail** window.

Alarm Suppress
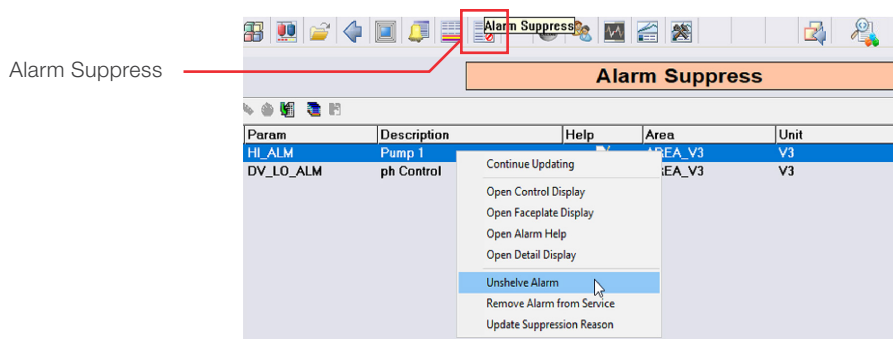
Figure 4.11. Unshelve Alarm option in menu.

Acknowledging and silencing alarms

At the bottom of all screens (except the **Cleaning** screen) is the alarm banner.

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 **Silence Audible Alarm** on the lower right corner of the screen (Figure 4.12).

Acknowledge all Alarms

Silence Audible Alarm

Enable/Disable Alarm Horn
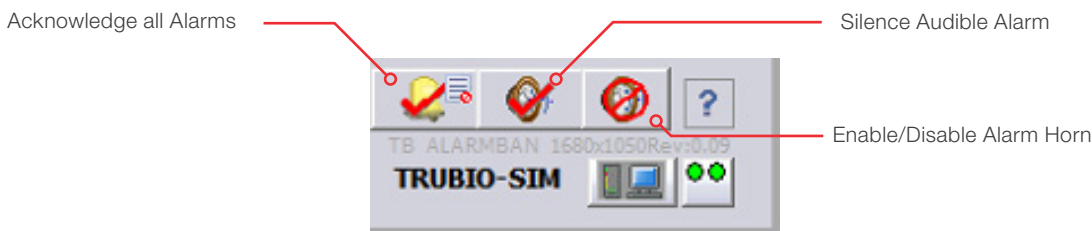
Figure 4.12. Icons for controlling alarms.

If there is an active, unacknowledged alarm, the banner displays a flashing box, as seen on Vessel 2 (V2) in Figure 4.13. If the alarm is active, but has been acknowledged, the box will not flash.

Figure 4.13. Active unacknowledged alarm in banner.

Click the box in the alarm banner to open the alarm faceplate for the relevant vessel. An active alarm flashes and displays an **Acknowledgment** button to the left. An acknowledged alarm does not flash and has no button (each state can be seen in Figure 4.14).
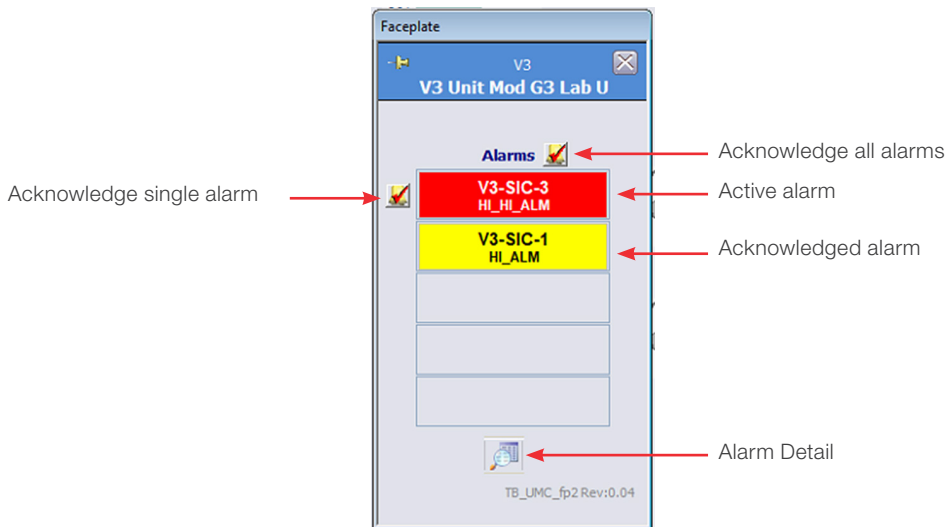
Figure 4.14. Alarm faceplate showing active and acknowledged alarms.

If there are more than five alarms, they can be viewed in the **Alarm Detail** screen (Figure 4.15).
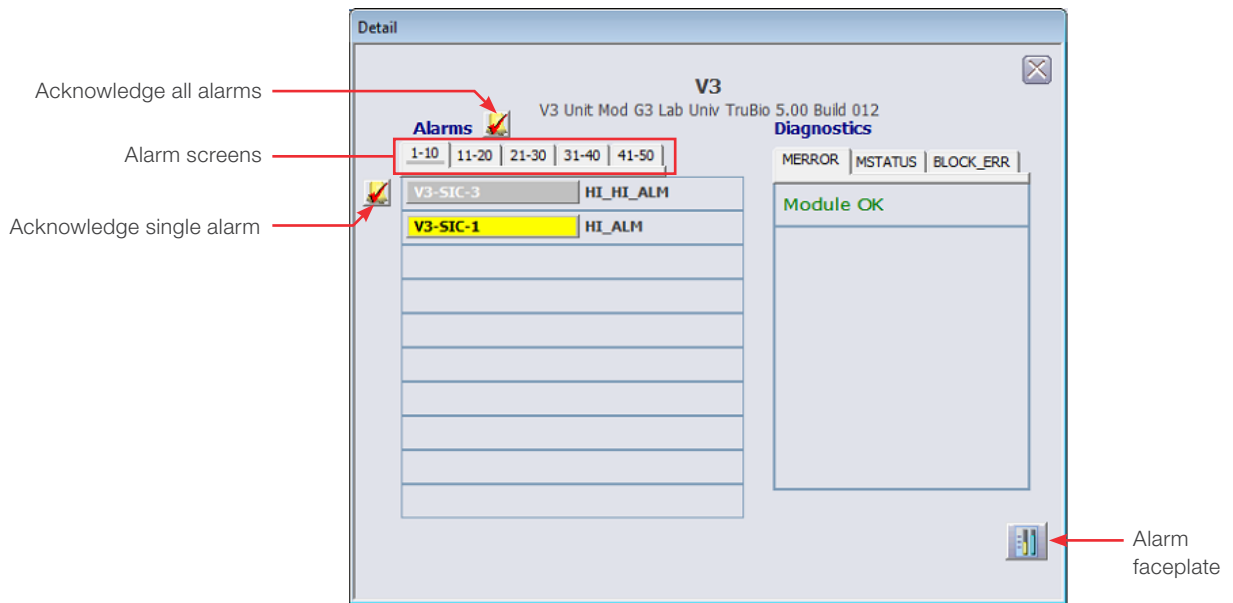
Figure 4.15. Alarm faceplate showing active and acknowledged alarms.

Use the **Alarm** screen tabs to swap between views if there are more than 10 alarms in the list.

You can acknowledge alarms from this screen as well using the **Acknowledgment** buttons indicated in Figure 4.15.

4.3 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.

5

Setting up a run

Chapter contents

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

5.1 Hardware checkpoints

Prior to setting up a run, ensure the following checkpoints are complete:

- ✓ The vessel and BPC (if applicable) are set up according to their respective user's guides.

- ✓ If using steralizable probes, the probe has been inserted into the vessel according to factory specified procedure and the cables are attached.

- ✓ All other devices are properly connected. Refer to the associated hardware user's guide or third party manual.

- ✓ 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.

- ✓ When setting up pump connections, ensure that the tubing is not kinked and is protected from occlusion by chairs, other equipment, etc.

5.2 Load a vessel file

From the Configuration screen, open Vessel Settings Management. Then click Vessel Load. Refer to section 3.2 for detailed instructions.

Note: For TruBio with GXCore, select **Vessel Save/Load** from the **Vessel Setup** dropdown in the **Configuration Quick Access** toolbar.

5.3 Set up control loops

5.3.1 Gas manifold

The gas supplies that are connected to the TruFlow mass flow controller (MFCs) or GXCore MFC 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 TruFlow should be regulated at 2–2.4 bar (30–35 psi), while pressure for each GXCore MFC 2.07–2.76 bar (30–40 psi)

CAUTION: Supply of gases should not exceed 2.4 bar (35 psi) for the TruFlow or 2.76 bar (40psi) for the GXCore MFC. Excess pressure will damage the internal components.

5.3.2 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 CO_2 (via sparging).

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

Configure the pH setpoint

1. Click the **pH** control module to open the **pH Control** faceplate.

2. Select **Auto** mode.

3. Use the sliding box on the right-hand side of the faceplate or click the box and type in the value in the pop-up window to set the desired pH setpoint.

4. Allow the system to equilibrate prior to setting alarms to prevent unnecessary alarm triggers while the process ramps up.

Configure pH control alarms

1. On the **pH Control** faceplate, click **Detail** to open the **pH Detail** window.

2. Click the **Alarms** tab. Set the Hi-Hi limit, Hi limit, Lo limit, and Lo-Lo limit. The ranges for alarms should be narrow enough to provide optimum growth conditions, yet wide enough to prevent excessive alarms.

    Note: When setting the alarm values, press Enter on the keyboard to set up the value. If Tab is pressed, the values will NOT be saved.

3. You may wish to set optional limits on the **Tuning** tab:

    a. Set the **SP Hi** and **SP Lo** limit.

    – These represent the range of the setpoint, to prevent accidental altering of the setpoint. As the values are set, small triangles appear around the setpoint arrow. The SP limit is indicated by small white arrows on the right side of the column, and the alarm limits by red and yellow arrows on the left side of the column.

    b. The **Out limits** are to limit the output of the controller, and the ARW is generally set to a smaller range.

    – Set a deadband at the bottom of the **Tuning** tab.

       • 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.

    – Set a gap above and below the deadband.

       • This allows extra time for equilibration if the control loop has been activated. Figure 5.1 illustrates the operation of a control loop, with the deadband and the gap shown.
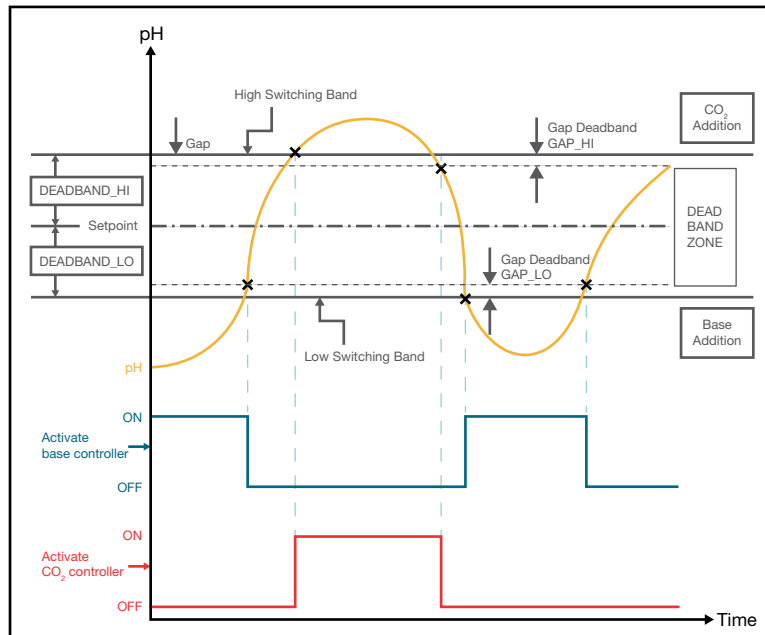
Figure 5.1. Operation of control loop with deadband and gap.

4. 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.

Configure pH control settings

The following example will be set up to maintain 7 pH in the vessel.

1. On the **Configuration** screen, click the **pH Configuration** control module on the left-hand side of the screen to open the **pH Configuration** window (Figure 5.2).

   Note: For TruBio with GXCore, select **pH Configuration** from the pH mini-faceplate.

   – The remote setpoint is used only if setup and the pH controller is in **Cascade** mode.

2. Enter the probe types being used and select the priority of reading.

Figure 5.2. pH Control Configuration form.

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 dropdown menu.

4. Set the **Number of Probes** by selecting the corresponding radio button. If more than one probe is being used, set the **Priority** for each probe.

   Note: The priority you set determines the order the system tries to read data from when **Auto Select** is selected from the **Transmitter** tab of the **pH Detail** window.

5. Set **Output Scales** for CO_2 control. The first row will be used in this example.

   a. The **Controller Output** for pH ranges from –100 to 100%. Set these values to 1 to 100%.

   b. **Output Scale #1** is based on the units of measurement used by the control module. In this case, the MFC for CO_2 is L/min. Set these values to 0 to 7 L/min.

6. Set the **Output Scales** for base addition. The second row will be used in

this example.

   a. Set the **Controller Output** values to –1 to –100%.

   b. **Output Scale #2** is based on the units of measurement used by the control module. In this case, the pump for the base is rpm. Set these values to 0 to 66 rpm.

Note: The maximum ranges are displayed over the setpoint on each faceplate (Figure 5.3). 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 CO_2 (or acid) and/or base can kill cells in the area of the sparger or pump port before adequate mixing can take place.

– The pH controller output range is –100 to +100, with the –100 to 0 range being acid (pH of 0 to 7) and the 0 to +100 range being base (pH of 7 to 14). The remainder of the form will not be used here.
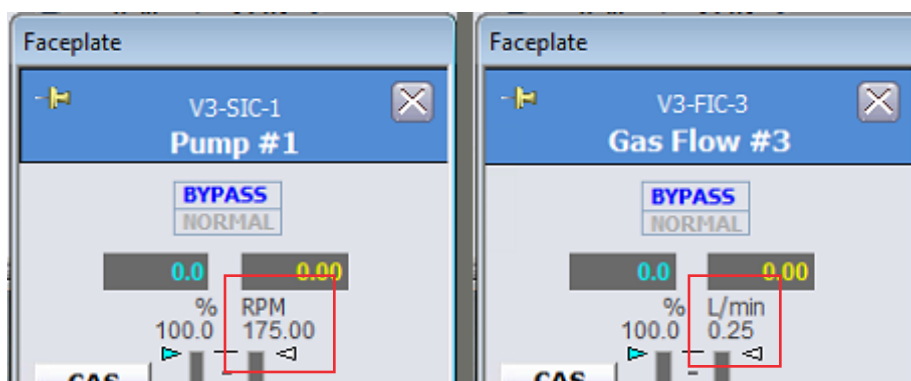
Figure 5.3. Faceplates for base pump (Pump #1) and CO2 MFC (Gas Flow #4).

7. Click **Apply Values** to save the settings and close the window.

Configure MFC for CO_2

1. Click the **MFC Configuration** control module that is assigned for CO_2 output (Figure 5.4). In the examples below **Gas Flow #4** is selected.

   Note: For TruBio with GXCore, select **Configuration** from the MFC mini-faceplate.

2. Set the **Allowed Flowpaths** and **Selected Flowpaths** radio buttons to the same output.

3. Set the appropriate flow setpoint to pH Control Output #2. (Figure 5.4). In this example **Sparger 1** will be used for CO_2 addition.

4. Click **Apply Values** to save the settings and then close the window.

Figure 5.4. MFC Configuration form for Control Output #4.

Configure pump for base addition

1. Click the pump configuration box for base addition. In this example **Pump #2** is used.

    Note: For TruBio with GXCore, select **Configuration** from the Pump mini-faceplate.

2. Set the **Remote Setpoint** to **pH Control Output #2** in the dropdown menu.

3. Select the **Speed Control** radio button and set the correct pump direction to flow into the vessel (usually **Clockwise (CW)**) (Figure 5.58).

4. Click **Apply Values** to save the settings and close the window.

Figure 5.5. Pump #2 Configuration form with Speed/Flow, Direction, and Control Mode options.

Configure faceplates for base and CO$_2$

The faceplates for the base pump and CO$_2$ MFC are configured in the same way. Follow the steps below for each faceplate.

1. Open the respective faceplate.

   Note: This can be done on the **Main** screen or by clicking the faceplate button on the control module on the **Configuration** screen.

2. At the top of the **MFC** faceplate, ensure **Bypass** (see section 3.4) is active to have TruBio bypass the CO$_2$ controller and apply the setpoint as the controller output. **Bypass** is the default setting.

   – **IMPORTANT:** If the MFC is not set to **Bypass**, it will prevent TruBio from managing the delivery.

3. On the left side of the faceplate, click **Cascade** (CAS). The **Cascade Path** (CAS PATH) will update with the respective setpoint.

4. Close the faceplate.

Configure the faceplate for pH

1. Click the **pH** control module to open the faceplate.

2. On the left side of the faceplate, confirm that the **pH Setpoint** is accurate. Then click **Auto** to enable automatic control.

   Note: The control loop will not operate unless the system is set to **Auto** mode on the faceplate.

3. Close the faceplate.

5.3.3 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 grow 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.

Adjusting DO control settings

1. On the **Configuration** screen, click the **DO Configuration** control module on the left side of the screen. 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**.

   Note: For TruBio for GXCore, select **Configuration** from the DO mini-faceplate.

2. Set up the DO probes by entering the manufacturer name from the dropdown menus.

   – Temperature compensation input may be from the pH probe, DO probe, or 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.

3. Set the **Number of Probes** by selecting the corresponding radio button. If more than one probe is being used, select the **Priority** for each probe. Click the appropriate check box for the number of probes in use.

   Note: The priority you set determines the order the system tries to read data from when **Auto Select** is selected from the **Transmitter** tab of the **DO Detail** window.

In this example (Figure 5.6), the Controller Outputs will be set up as follows:

- Output #1 will be air

- Output #2 will be oxygen

- Output #3 will be the agitator, with the maintenance speed assumed to be 75 rpm

- Output #4 will be nitrogen

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.

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.
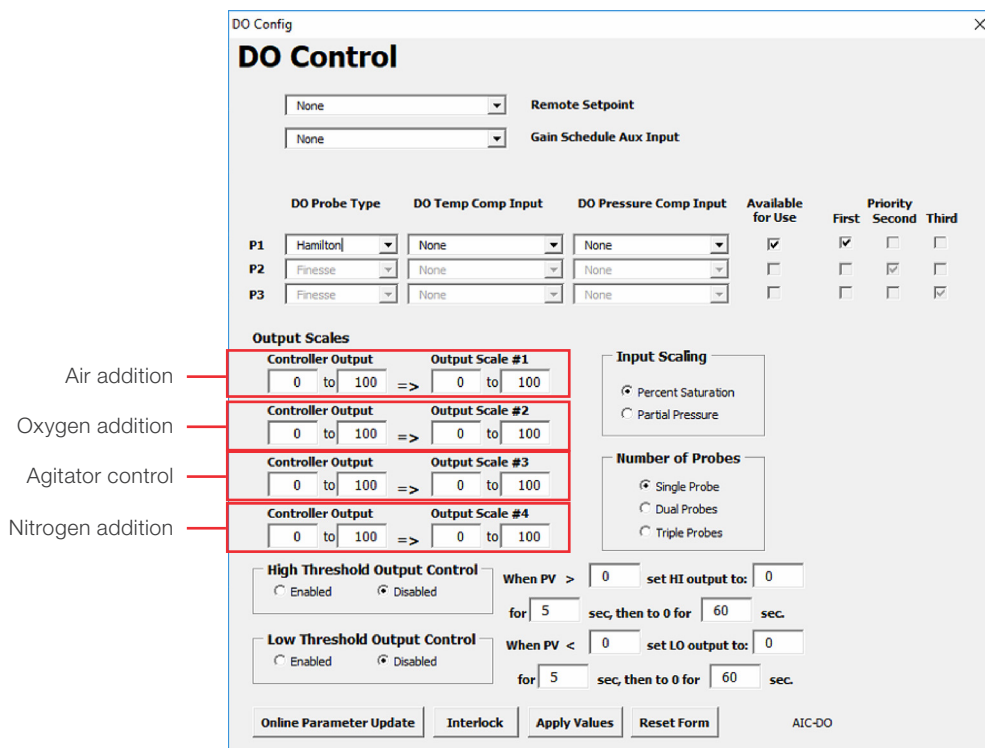

Figure 5.6. DO Control screen.

Configure a Calculation

1. On the **Configuration** screen, open an unused **Calculation** control module (Figure 5.7). **Calculation #1** is used as an example.

   Note: For TruBio with GXCore, Select **Freeform Calculations** from the **Control Setup** dropdown to open the **Freeform Calculations Configuration** faceplate. Then select an unused **Calculation** control module from the faceplate.

   – For this calculation (**Calc #1** in Figure 5.8), only **Variables** will be needed.
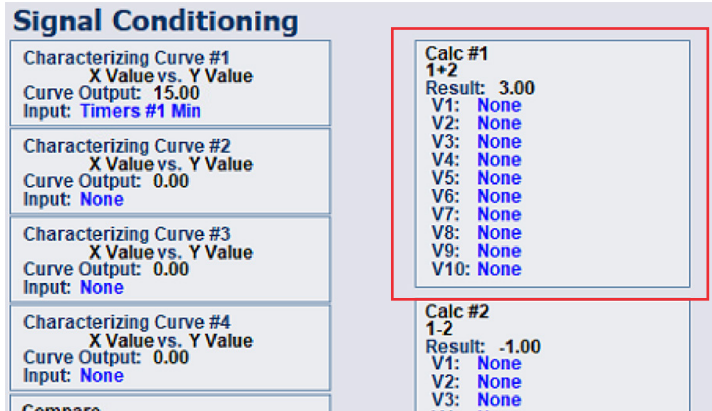

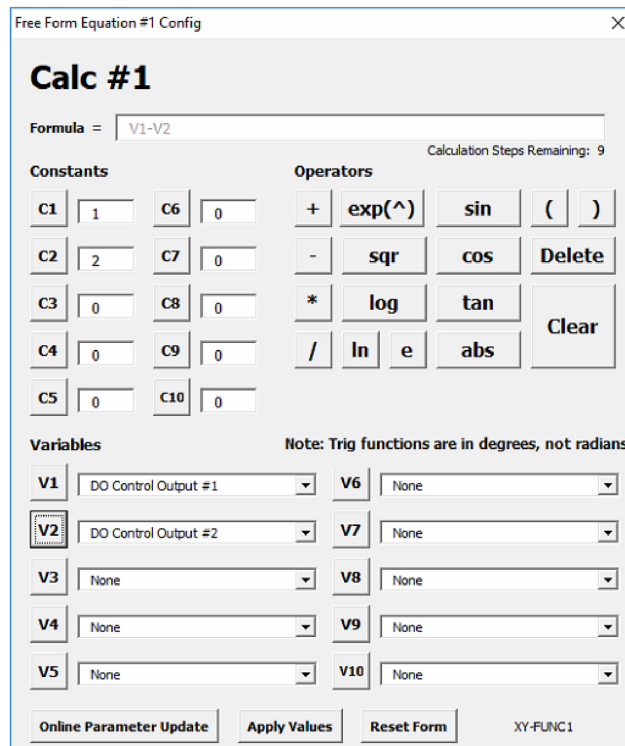Figure 5.7. Calculation #1 on the Configuration screen.

Figure 5.8. Calc #1 configuration.

2. Use the dropdown menus to set **V1** to **DO Control Output #1** and **V2** to **DO Control Output #2**.

3. To set up the formula, click the appropriate **Operator** buttons. Click **V1**, then **–** (minus symbol), and **V2**.

   Note: If there is already an equation in the field, you must select **Clear** prior to entering a new equation.

4. Click **Apply Values** to save the calculation. Then close the **Calculation** window.

Configure MFC for air

1. Click the **MFC Configuration** control module for the air supply (Figure 5.9). **Gas Flow #1** is used for example here.

   Note: For TruBio with GXCore, select **Configuration** from the MFC mini-faceplate.

Figure 5.9. 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 #1 Output** (Figure 5.10).
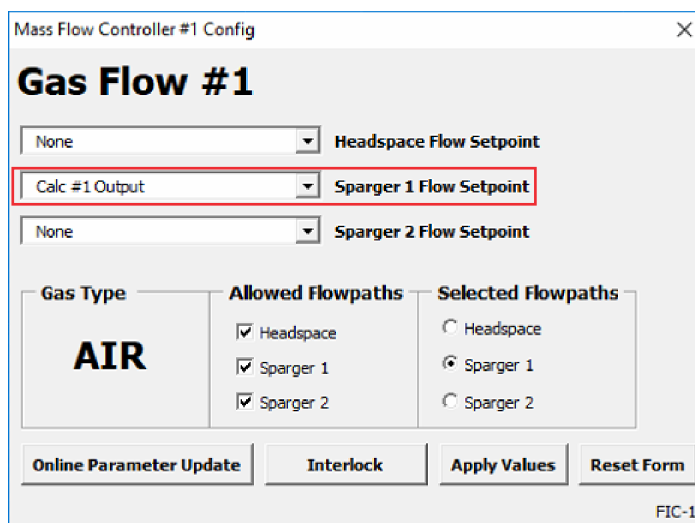

Figure 5.10. Selecting Calc #1 Output from the Sparger 1 Flow Setpoint dropdown list.

3. Ensure that the radio buttons for **Allowed** and **Selected Flowpaths** are set for the sparger being used.

4. Click **Apply Values** to save the settings and then close the window.

Configure MFC for oxygen and nitrogen

1. Click the respective **MFC Configuration** control module for the oxygen and nitrogen supply.

2. Set the appropriate sparger to **DO Control Output #2** for oxygen and **DO Control Output #4** for nitrogen (Figure 5.11) and verify that the appropriate sparger is selected.
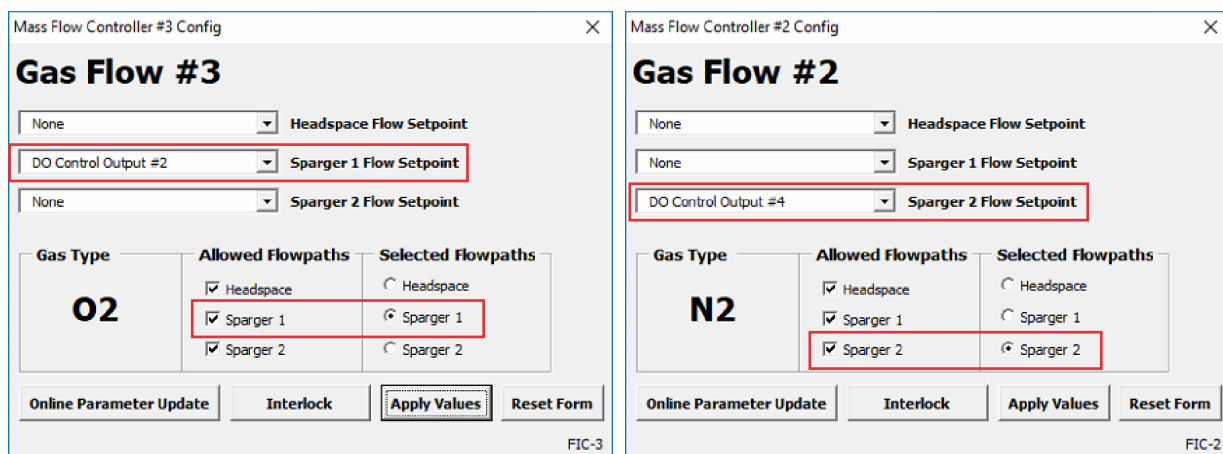

Figure 5.11. Selecting DO Control Outputs from the Sparger Flow Setpoint dropdown lists.

3. Click **Apply Values** to save the settings and then close the window.

Configure the agitator

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

1. Open the **Agitator** control module. 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** (Figure 5.12).
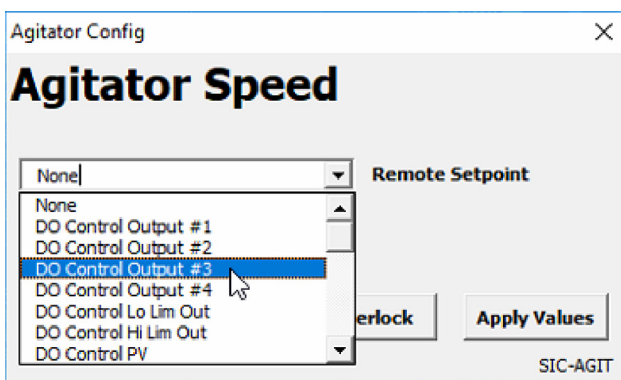
Figure 5.12. Agitator Configuration pop-up screen.

2. Return to the **Main** screen and open the **MFC** faceplate for oxygen. Ensure that **Bypass** (If not, see section 3.4) is highlighted. Click **Cascade** (CAS) to set the cascade mode and put oxygen into the DO control loop. Close the faceplate.

Configure MFC faceplates

The faceplates for air, oxygen, and nitrogen are configured in the same way. Follow the process below for each.

1. Open the respective **MFC** faceplate.

2. Ensure that **Bypass** is highlighted at the top of the screen.

3. Set each control to **Cascade** (CAS) mode. The **Cascade Path** (CAS PATH) will update to the respective setpoint.

4. Close the faceplate.

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

5.3.4 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 BPC. 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.

Configure Vessel Temperature faceplate and set alarms

1. On the **Main** screen, open the **Vessel Temperature** faceplate.

2. Set the mode to **Auto** and set the desired temperature setpoint.

3. Open the **Vessel Temperature Detail** window, click the **Alarms** tab, and set the **Hi-Hi**, **Hi**, **Lo**, and **Lo-Lo** limits. Set the setpoint limits appropriate to the process.

   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 **Vessel Temperature Detail** window and faceplate.

Configure Jacket Temperature control settings (if present)

1. On the **Configuration** screen, click **Jacket Temperature** control on the left side of the screen.

2. Set the **Remote Setpoint** to **Vessel Temp Heat Out**. Leave **Gain Schedule** set to **None**.

3. Set the **Control Modes** and **Available Outputs** to Heat Only, and click the radio button for the correct number of probes. **Discrete Output Settings** are not used (Figure 5.13).

Figure 5.13. Jacket Temperature Configuration screen.

4. Click **Apply Values** to save the settings and close the screen.

5. Return to the **Main** screen and open the **Jacket Temperature** faceplate.

6. Click **CAS** to set control to cascade mode, and link the jacket and vessel controls. The **Cascade Path** will read **Vessel Temp Heat Out**. Close the faceplate.

Configure Vessel Temperature if no jacket is present

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**.

1. From the **Configuration** screen, click the **Vessel Temperature** control module.

2. Set the **Remote Setpoint** and **Gain Schedule** to **None** and set **Temperature Control**.

3. Set **Available Outputs** to **Heat Only** and **Heat**, respectively. **Discrete Output Settings** are not used.

4. Click the radio button for the appropriate number of probes and click **Apply Values**, then close the screen.

Configure the Temperature faceplate

5. Click the **Temperature** control module to open the **Temperature** faceplate.

6. Click **AUTO** to set the temperature control to automatic control mode.

Remote start and stop for TCU units

An additional feature in the TruBio Software has been designed for TCUs that are located remotely from the S.U.B. vessel, and that require remote start and stop control (Figure 5.14). For information on this feature, contact your customer service representative.
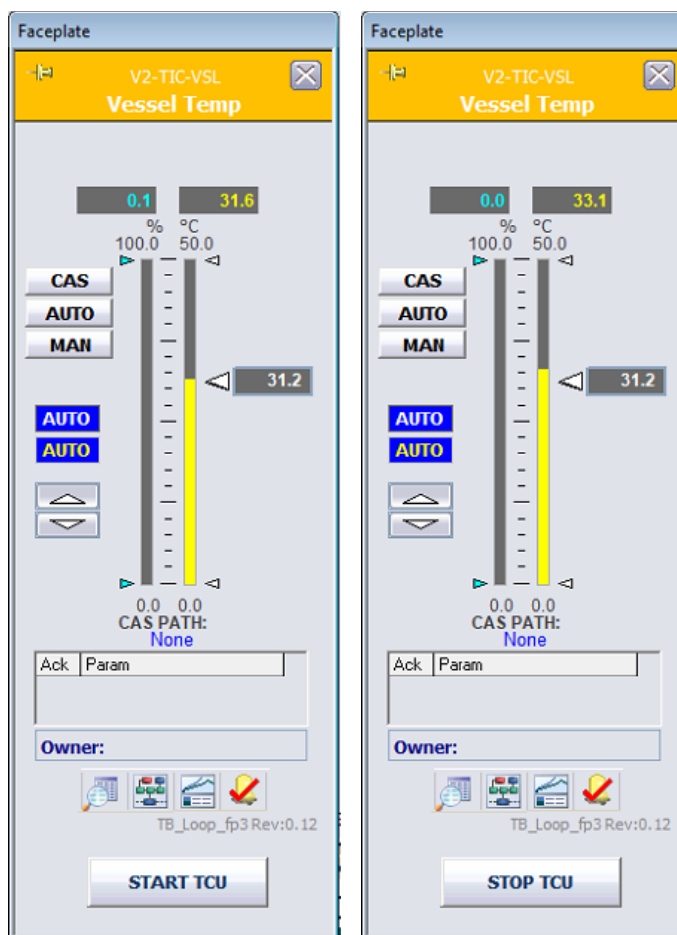

Figure 5.14. Start TCU and Stop TCU on the Vessel Temperature faceplate.

5.3.5 Agitator control

The agitator runs continuously and is remotely controlled only in the DO loop. Use the following steps to set agitator control.

1. On the Main screen, click the **Agitator** control module.

   Note: For TruBio with GXCore, you can control the setpoint and output percentage from the **Agitator** mini-faceplate, or you can open the full faceplate from the mini-faceplate.

2. 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.

3. Configure the setpoint by dragging the arrow on the right, or click in the box and enter a value.

5.3.6 Agitator reverse function

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.

This feature allows you 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 5.15).
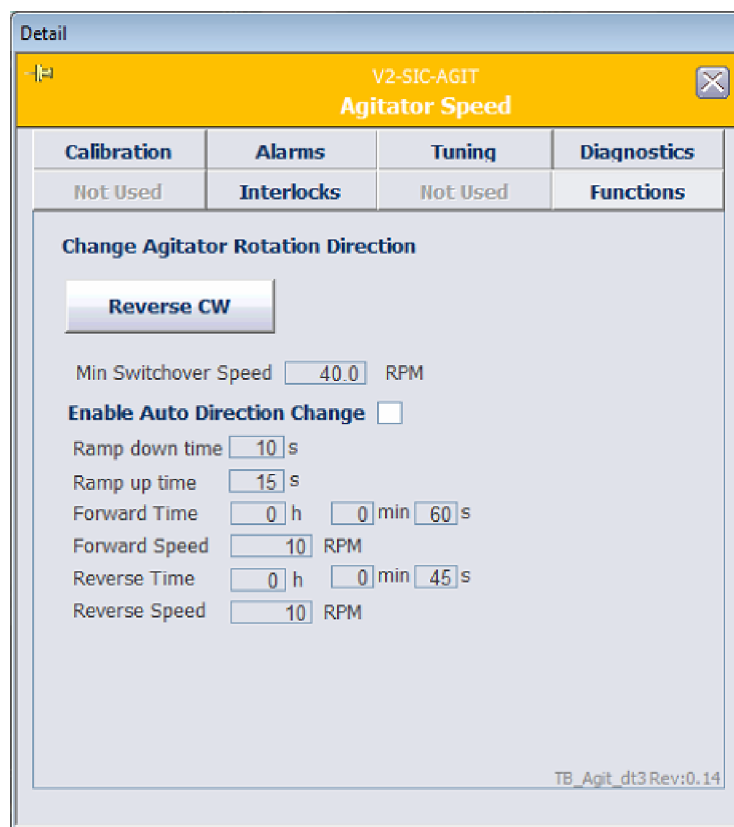
Figure 5.15. Agitator detail window.

2. Set the **Minimum Switchover Speed**.

3. Click **Forward CCW**, located under **Change Agitator Rotation Direction**.

    – Allow the agitator to reach the minimum speed and then click the button again. A confirmation pop-up window will appear. If the agitator speed has not yet reached the set minimum switchover speed, an error message will appear.

4. Click **OK** to change the agitator rotation direction. This procedure can be performed as often as desired.

Using the function at specific intervals

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

2. Set the agitator to **AUTO** mode on the **Agitator** faceplate.

3. In the **Functions** tab of the **Detail** window, click **Enable Auto Direction Change**.

4. Enter values for all of the parameters, then click **Change Rotation Direction**. Another confirmation pop-up window will appear.

5. Click **Yes** to run the agitator for the specified durations at the user-defined speeds.

5.4 Pump setup

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 using the setpoint control (see section 5.4.1).

- With pre-programmed **Pump** functions on the **Dose** faceplate (see section 5.4.2).

- With user-defined **Dose** functions from the **Dose** control box at the bottom of the faceplate (see section 5.4.3).

- By configuring multiple feed pumps to act together, from the **Multi-Feed** control module (see section 5.4.4)

5.4.1 Setup using the pump faceplate

The **Pump** faceplate method is a basic operation. Set the controller mode to **AUTO** and set a setpoint using the slider or manually entering one.

Setup using the pre-programmed **Pump** functions

Pre-programmed **Pump** functions 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 pump configuration control module from the **Configuration** screen. Select the correct scale from the **Scale Selection** dropdown menu. Perform 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 select a pump function, use the following steps:

1. Open the **Pump Detail** window from the **Pump** faceplate.

   Note: For TruBio with GXCore, select **Detail** from the **Pump** mini-faceplate or full faceplate.

2. Click the **Functions** tab. Then click **Dose** (Figure 5.16).
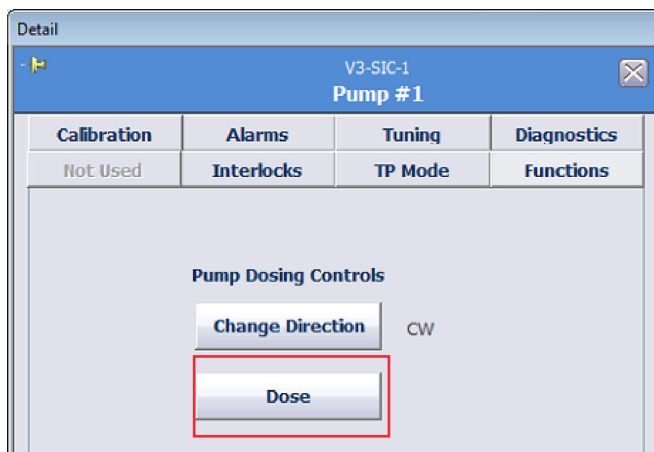
Figure 5.16. Dose on Pump Dosing Controls screen.

3. From the **Pump Function** dropdown menu, choose the desired function: **Ramp**, **Continuous**, or **Dose** (Figure 5.17). Each function is described in the following sections.

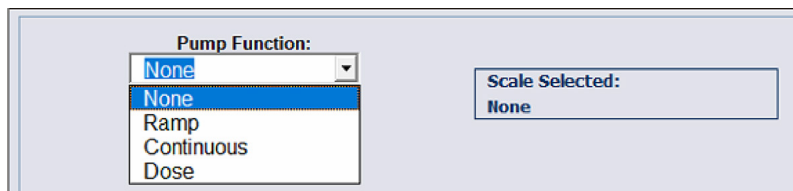   **Note:** In the following examples, no scale is selected for weight feedback.

Figure 5.17. Dropdown menu for pump functions.

Ramp function

Use the **Ramp** function (Figure 5.18) to raise the pump rate over a defined period of time, and then run continuously at the final speed.
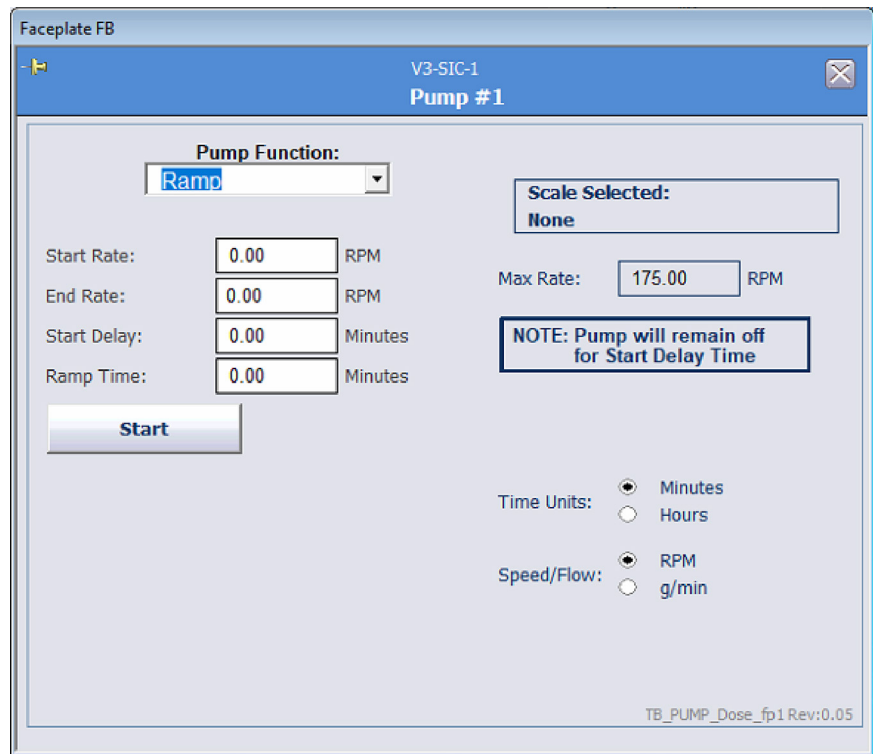
Figure 5.18. Ramp pump function.

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

The diagram in Figure 5.19 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.
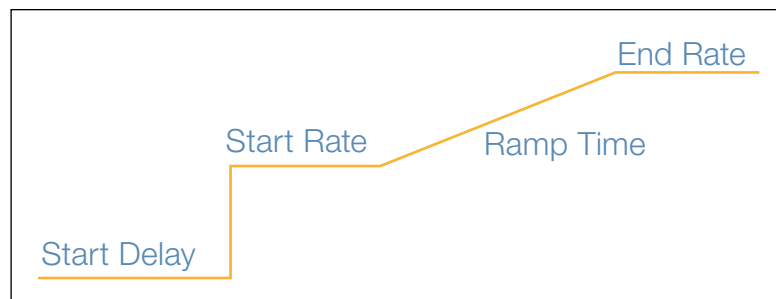

Figure 5.19. Representation of the ramp function with a Start Delay.

Continuous function

Use the **Continuous** function (Figure 5.20) to run the pump at the selected rate after the **Start Delay** represented by the diagram in Figure 5.21.
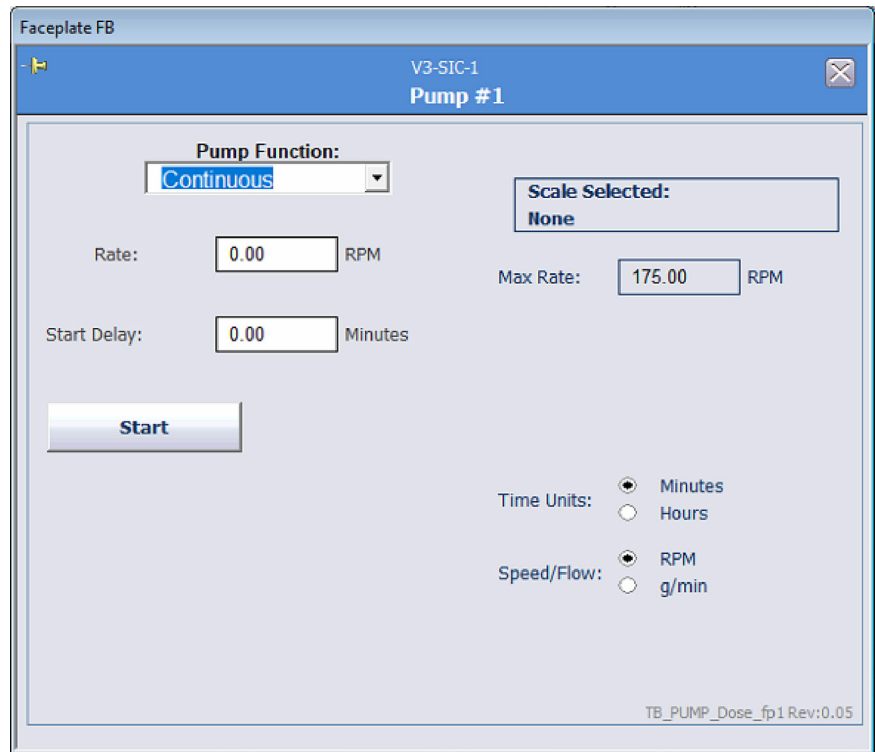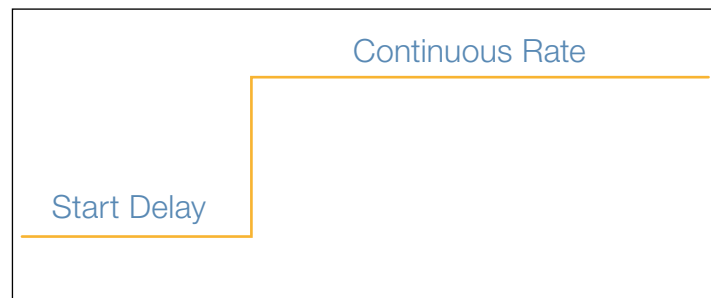

Figure 5.20. Continuous pump function.

Figure 5.21. Representation of the continuous function with a Start Delay.

Dose function

Use the **Dose** function, sometimes referred to as the "bolus function", to run the pump to deliver a select number of doses with a set period of time (the **Settle Time**) between doses (Figure 5.22).

Figure 5.22. Dose pump function.

Note that the **Amount Added** is user-specified rather than a set volume. This means that you 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 with 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 4 minutes and 57 seconds or 80 rpm for 4 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 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 5.23 illustrates the **Dose** function.
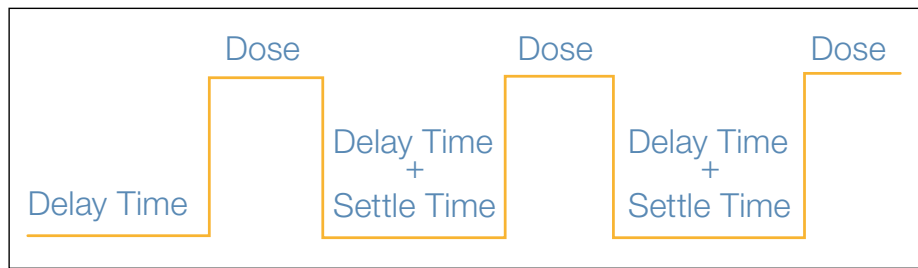
Figure 5.23. Representation of the Dose function with a Delay Time.

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.

5.4.2 Setup using pump total flow dosing strategy

Total Flow Dosing allows you to set up a pump strategy that is designed to feed a specific quantity at user-defined flow rates into the vessel. A scale is required, as **Total Flow Dosing** uses the loss in weight to determine the cycle.

Use the following steps to set up total flow dosing.

Configure a Characterizing Curve

On the **Configuration** screen, open a blank **Characterizing Curve** form. As shown in Figure 5.24, the dose adds 1.6 kg over 13 minutes (0.22 hr).

Note: For TruBio with GXCore, select a **Characterizing Curve** from the **Control Setup** dropdown.

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 5.24. Characterizing Curve form.

Figure 5.25 shows another example.

- 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)

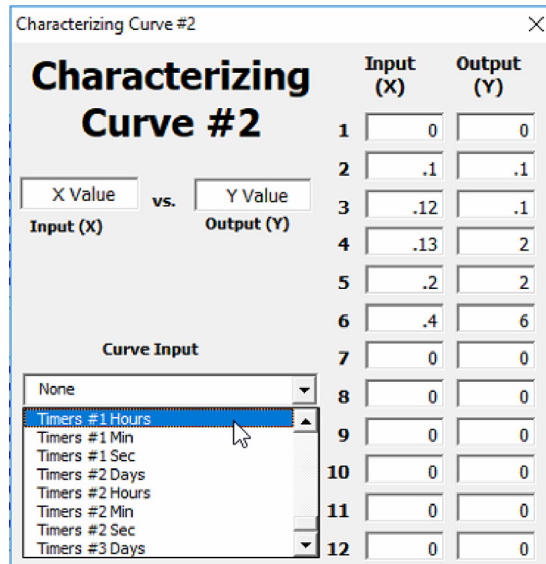- Overall total flow setpoint is 6 kg.

Figure 5.25. Second example of Characterizing
Curve form.

Configure the pump for dosing

1. Open the **Pump Configuration** form from the **Configuration** screen.

   Note: For TruBio with GXCore, select **Configuration** from the **Pump** mini-faceplate.

2. Set the **Control Mode** to **Dose** and the **Speed/Flow** mode to **Flow Control**. The **Remote Setpoint** is disabled.

3. Use the dropdown menu to set the total flow setpoint to the **Characterizing Curve** used (**SCGR Output #1** in the example in Figure 5.26).
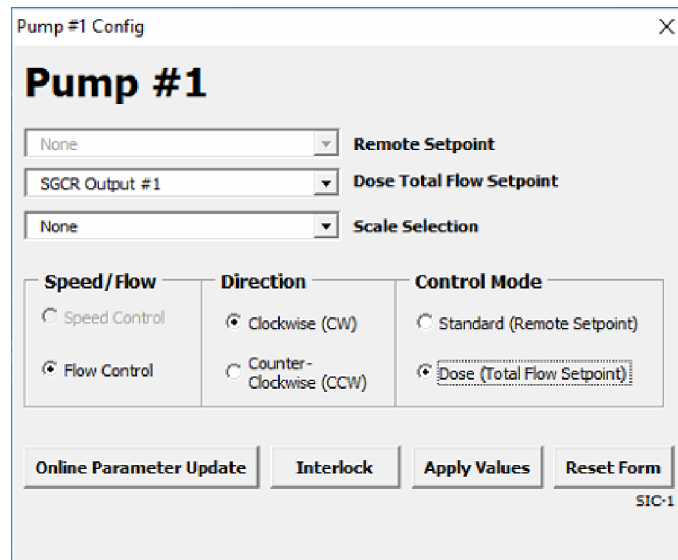

Figure 5.26. Setting up total flow dosing for Pump #1.

4. Click **Apply Values** to save changes

5. From the **Main** screen, open the faceplate for the same pump.

   Note: The faceplate will have additional features (Figure 5.27).

   – The following features are identified on Figure 5.27:

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.
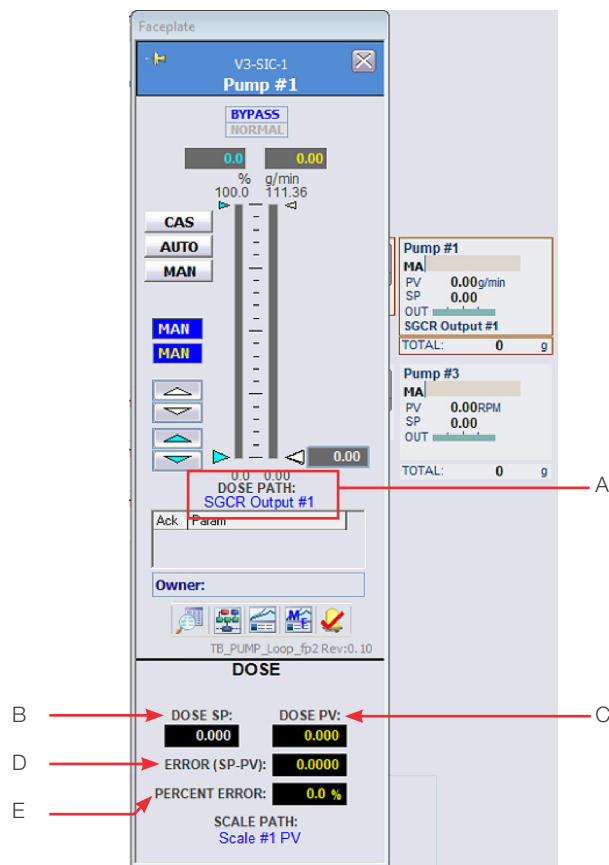

Figure 5.27. Dose path Pump #1 faceplate.

6. Open the **Alarms** tab on **Detail** window. The **Dose** alarm will appear. Click **Enable** to activate the alarm settings (Figure 5.28).

   Note: The units are based on your settings and may differ from those in Figure 5.28.
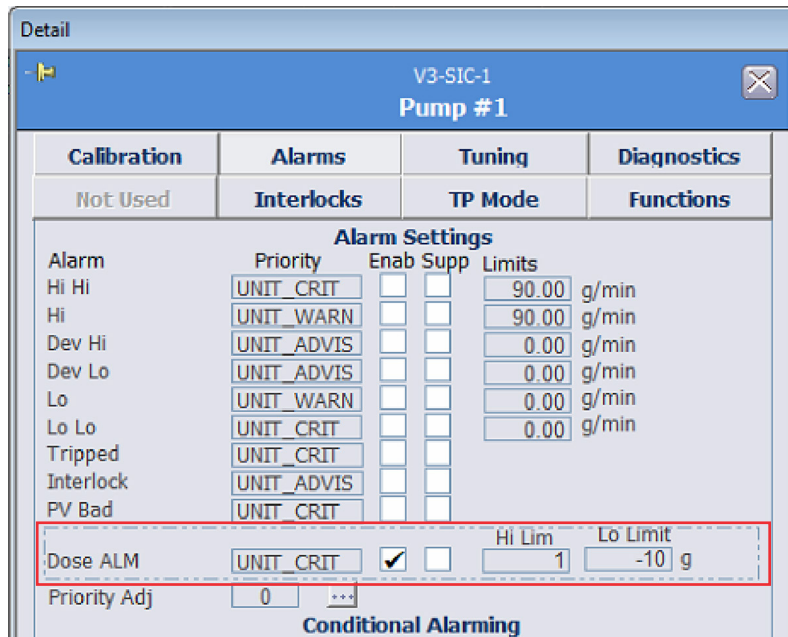
Figure 5.28. Dosing alarm enabled.

7. Close the **Detail** window.

8. Select the appropriate timer display from the **Main** screen and ensure that the timer is set to zero.

9. 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 5.29).

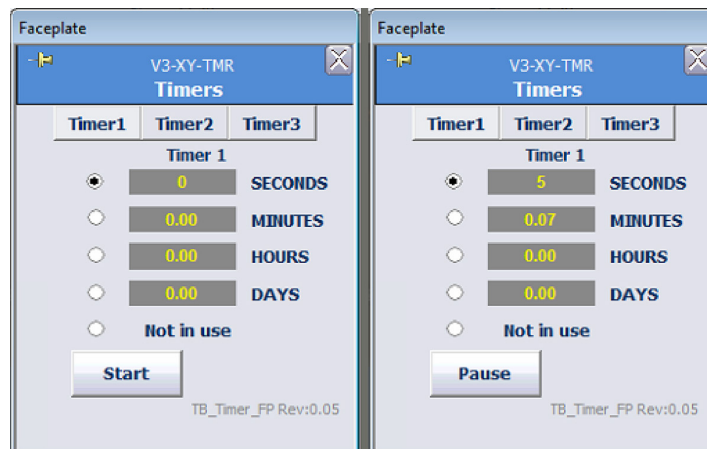   **Note:** If the timer is paused, the faceplate will offer the option to Restart or Reset (Figure 5.30).

Figure 5.29. Start and Pause buttons on faceplate after setting into Cascade mode.
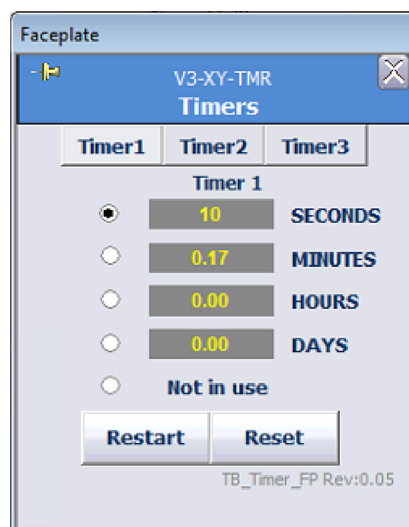
Figure 5.30. Restart and Reset buttons on faceplate when paused.

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.

10. 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.

5.4.3 Setup using a Multi-Feed strategy
TruBio Software version 5.0 provides 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.

Online Parameter Update
1. If **Multi-Feed** is not available, go to the **Configuration** screen and click **Online Parameter Update**.

2. Verify that the correct vessel is displayed.

3. In the **Module** column, locate and click the string reading **V*x*-MFDOSE** with *x* being the vessel number in use (V3-MFDOSE shown in the example below).

4. Click **DEFAULT_MF** in the **Category** column.

5. In the **Parameters** column, locate the **Name** string **/FS_CTRL1/AVAILABLE.F_CV**. Click the string to highlight it (Figure 5.31).
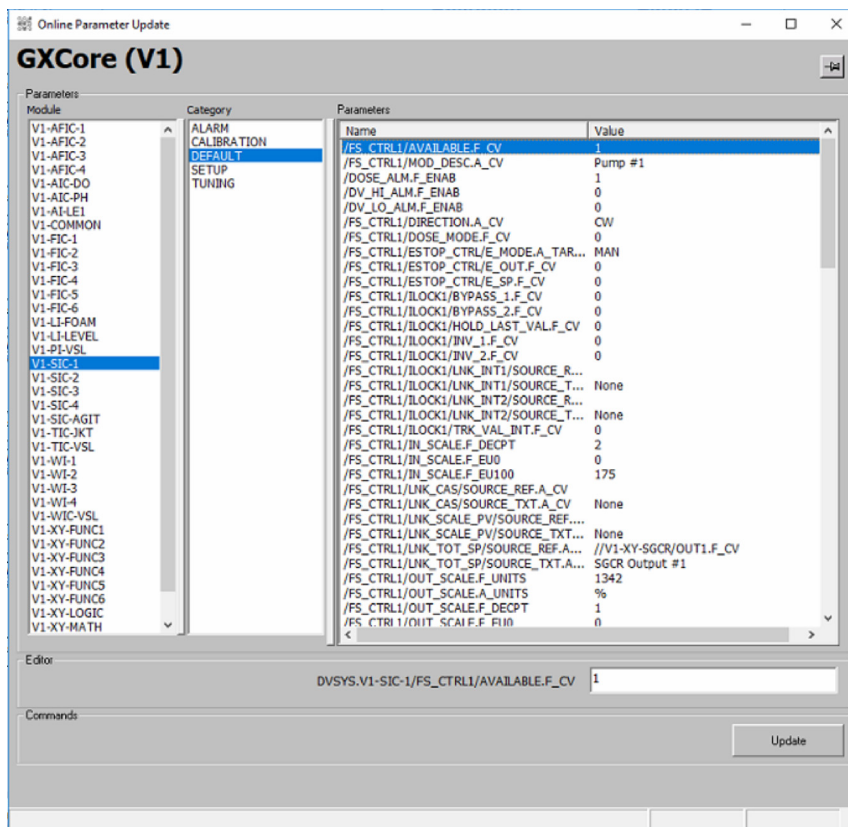

Figure 5.31. Multi-feed pumps enabled on the OPU.

6. Type "1" in the field in the lower right of the OPU window and click **Update**. Verify the value updated in the **Value** column.

Adding pumps

To set up pumps on the scale:

1. Click the **MultiFeed** box on the **Configuration** page.
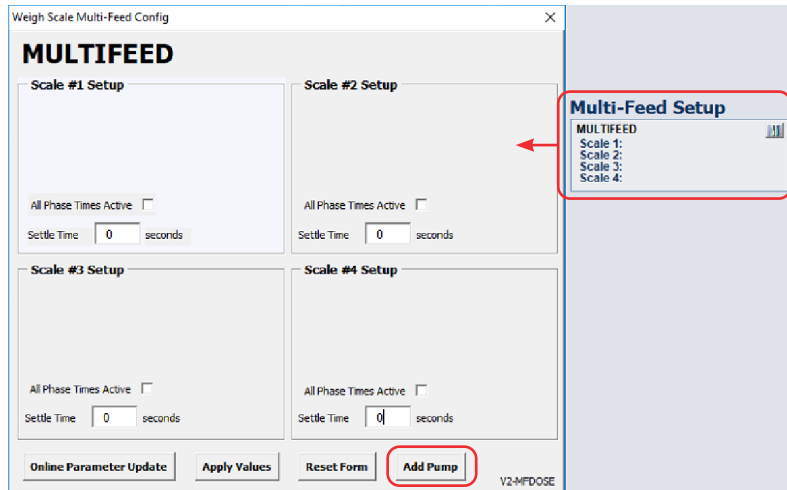
2. Click **Add Pump** (Figure 5.32).

Figure 5.32. Selecting Add Pump from the Multi-Feed Configuration window.

3. Additional options will appear (Figure 5.33). Select the pump to be added from the **Available Pumps** dropdown, and click **OK**.
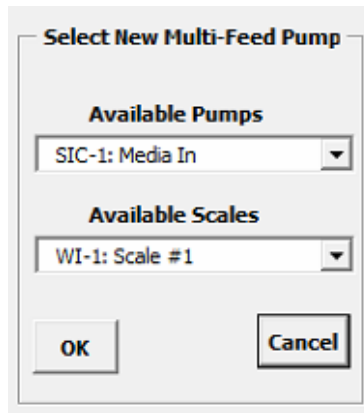

Figure 5.33. Select New Multi-Feed
Pump options.

4. Repeat for any additional pumps.

5. Click **Apply Values** to save the change.

Deleting a pump

To delete a pump:

1. Open the **Multi-Feed Config** window from the **Configuration** screen.

2. Click the icon for the pump to be removed. Then click **Delete Pump** (Figure 5.34).
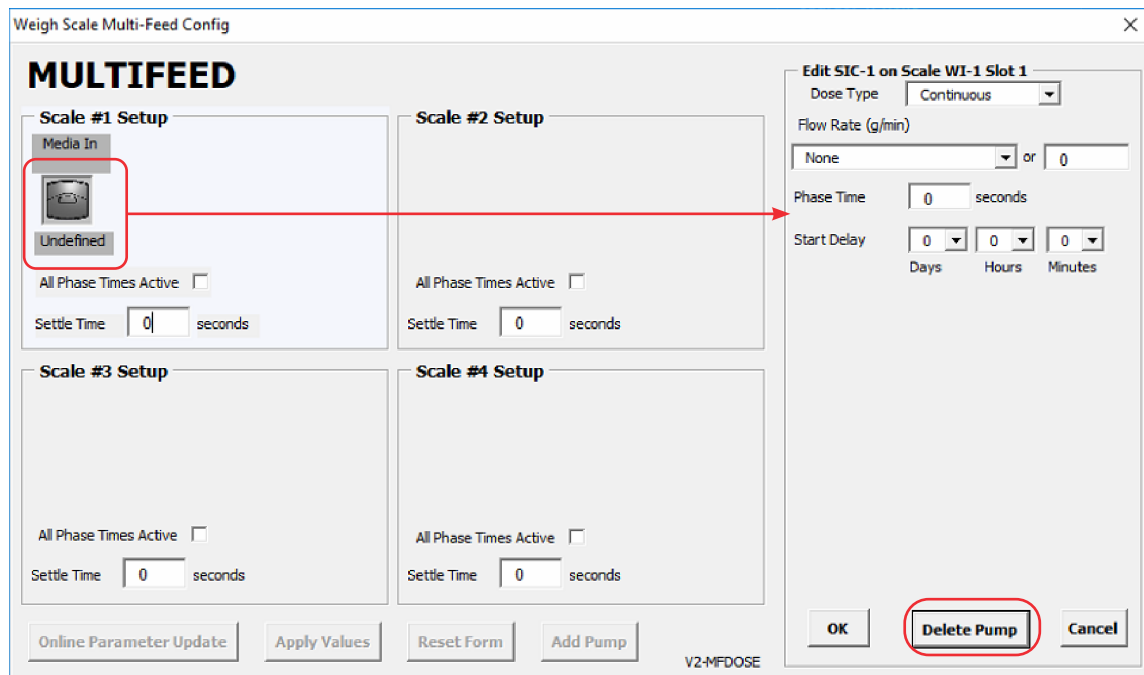

Figure 5.34. Delete Pump shown for Pump #1 on the Multi-Feed Configuration window.

3. Click **Apply Values** to save the change.

Pump configuration

The pumps are set to operate in the left-to-right sequence shown in Figure 5.35. Pump #1 starts, operates, and stops, followed by Pump #3, Pump #2, and lastly, Pump #4. The sequence then repeats.
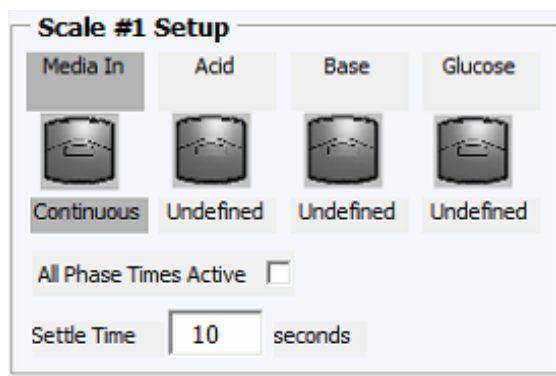
Figure 5.35. Sequence of pumps #1–4.

1. To access the **Multi-Feed** faceplate, select the faceplate button on the **Multi-Feed Configuration** control module (Figure 5.36).

   Note: You can also open the faceplate by selecting the **Multi-Feed** control module on the **Main** screen.
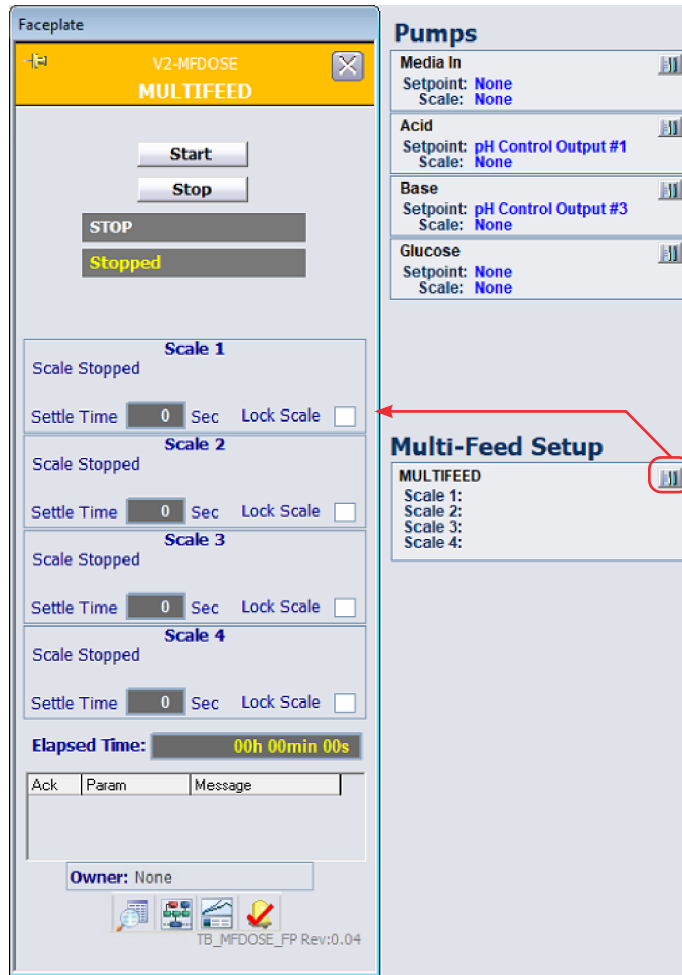
Figure 5.36. Multi-Feed control faceplate.

2. On the faceplate, click **Detail** to open the **Multi-Feed Detail** window (Figure 5.37). **Dose** limits, alarms, and status checking can be done from this menu.

   – The **Multi-Feed Sequence Status** indicates the pumps in use and which pump will be activated next.
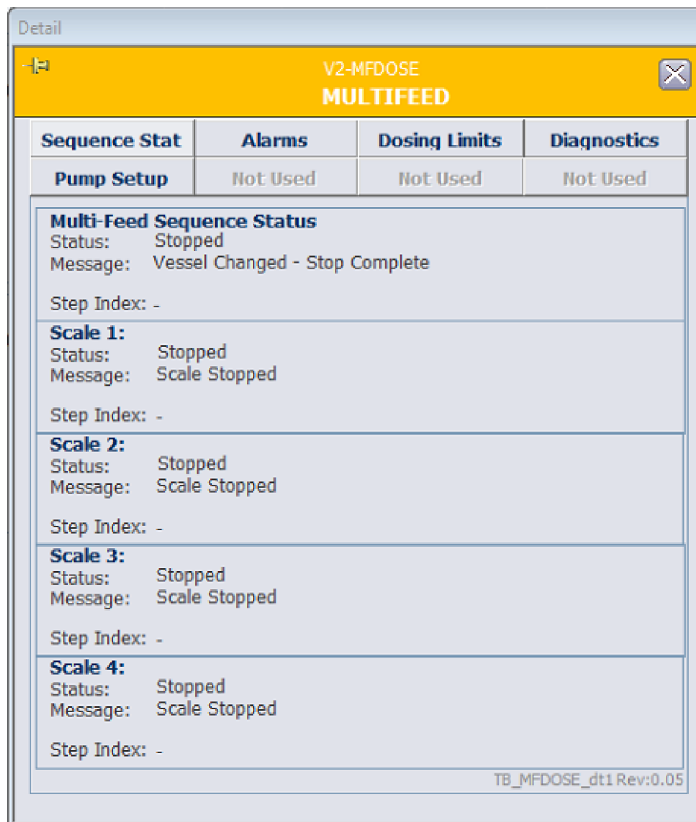
Figure 5.37. Multi-Feed Detail window.

3. The **Pump Setup** tab (Figure 5.38) shows limits for the dose alarms and auto-calibration settings. Pumps can have different limits and each pump must be set up separately.

    – 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 5.38, 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 you to issues, such as empty containers or clogged tubing. In Figure 5.38, if there is no change in weight for 60 seconds, an alarm will be triggered.

    Note: 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 5.38, 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.

- Figure 5.38 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.

Figure 5.38. Pump Setup on Multi-Feed menu.

4. The alarms are enabled or suppressed on the **Alarms** tab shown in Figure 5.39. The **Priority Adjust** feature enables you to set the alarm levels from **Critical** to **Advisory**.
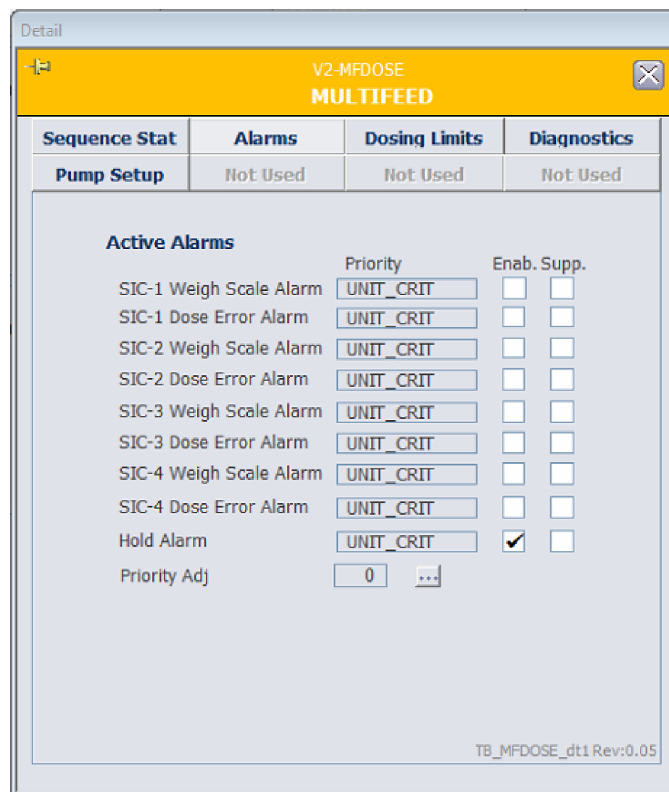
Figure 5.39. Alarms on Multi-Feed menu.

5. The **Dosing Limits** tab sets limits for restricting the number of doses per hour (1 and 2), based on the dose rate. Input these limits as a percentage of the maximum flow (Figure 5.40). **Max Flow** is the calibrated maximum flow rate for each pump that is shown on the **Pump** faceplate.

6. In Figure 5.40, if the maximum flow rate of **Pump #1** is 1258.3 g/hr, then the **1 Dose per Hour Limit**, would be 1258.3 x 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, but no greater, than twice the **1 Dose per Hour Limit**.
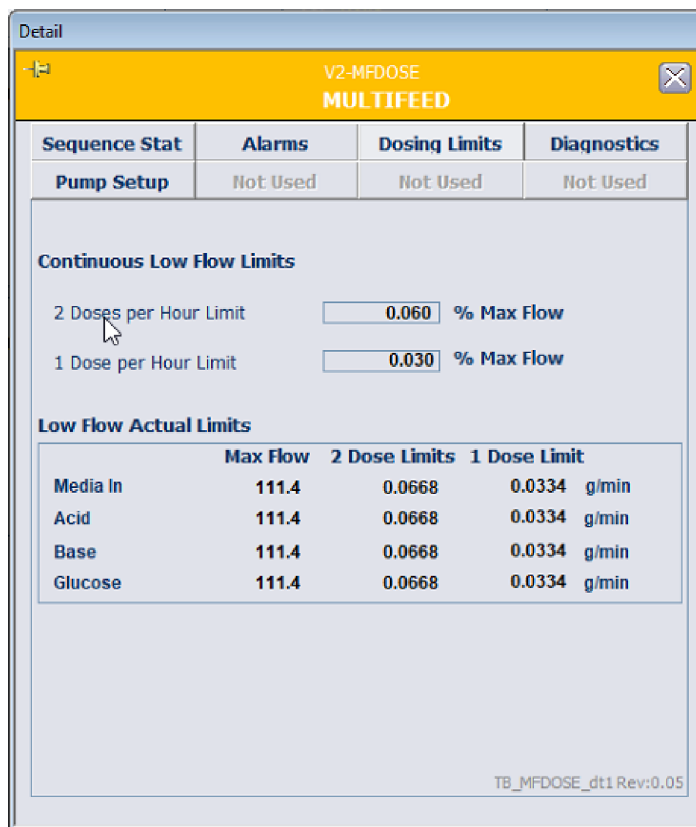
Figure 5.40. Dosing Limits tab flow limits.

Note: The **Diagnostics** tab (Figure 5.41) enables you to check the functioning of the module. In the case of an alarm situation, a description of the malfunction that prompted the alarm displays.
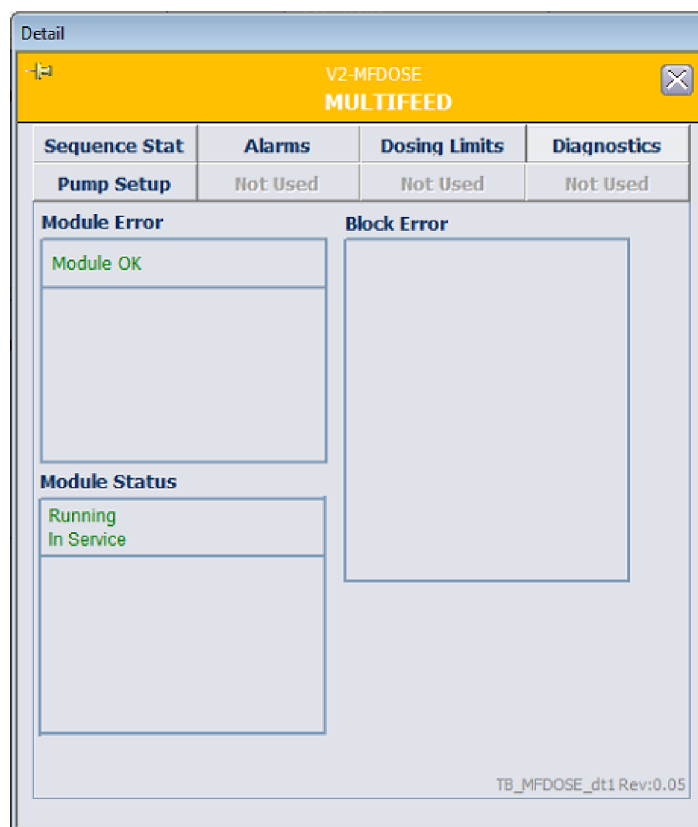
Figure 5.41. Diagnostics on Multi-Feed menu.

Locking and unlocking pumps

You can lock a pump in the multi-feed strategy. This can be done if you do 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 **Multi-Feed** faceplate from either the **Main** screen or the **Configuration** screen.

2. Click the icon of the pump to be locked. A confirmation pop-up screen displays (Figure 5.42).

3. Click **OK** and a lock symbol will appear on the pump icon (Figure 5.43) and on the **Multi-Feed** control module on the **Main** screen.

Figure 5.42. Lock Pump confirmation pop-up.

Figure 5.43. Lock symbol on Multi-Feed button (left) and on the pump icon on the Multi-Feed faceplate (right).

To unlock the pump

4. Click the icon again to unlock the pump. Another confirmation pop-up screen will display.
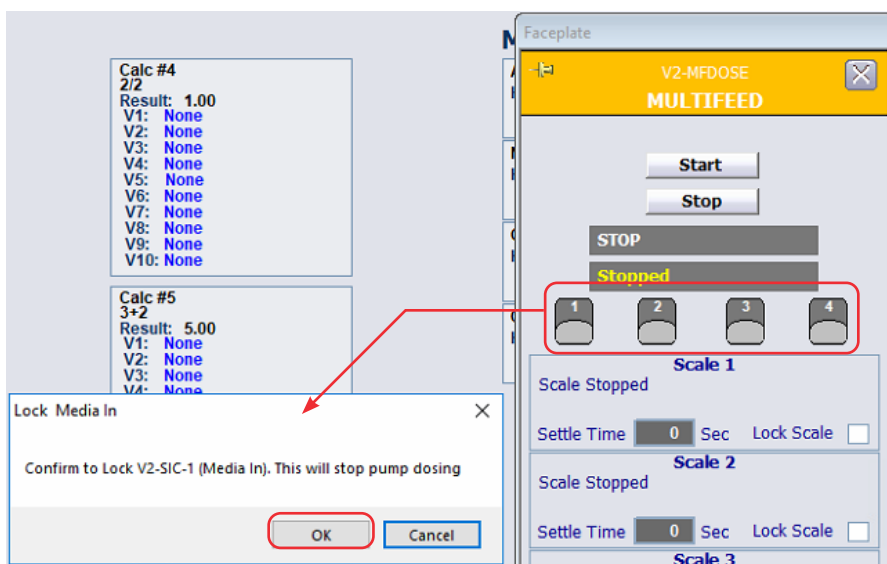
5. Click **OK** to resume pump operation and remove the lock symbol.

5.4.4 Setting up Multi-Feed dosing

Dosing is set up from the **Multi-Feed Configuration** control module 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 in "Adding pumps" on page 157.

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 **Dose Type** to open the dropdown menu.

3. Choose a dose type from the dropdown: **Continuous**, **Bolus**, **pH base**, or **pH acid** (Figure 5.44). Click **OK**.
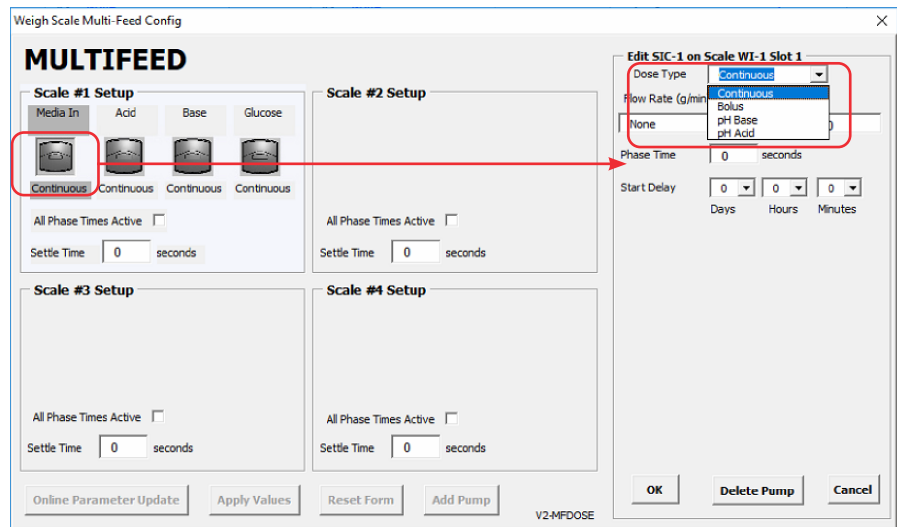
Figure 5.44. Selecting dose type.

Continuous feed

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 (Figure 5.45).
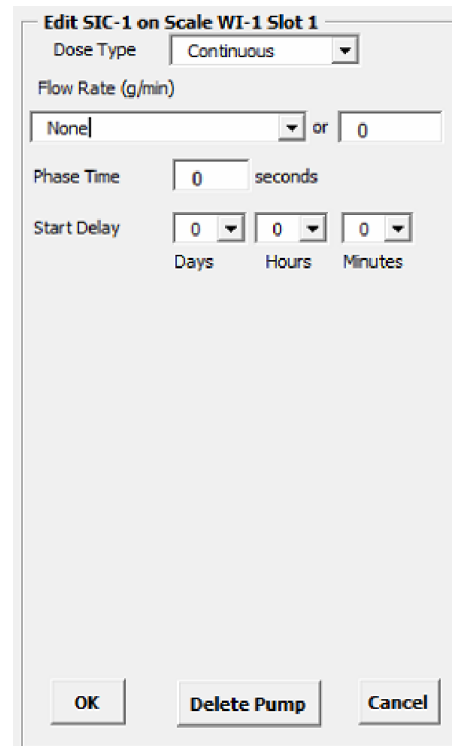

Figure 5.45. Options for Continuous feed.

1. Select the dose flow rate either from the **Flow Rate** dropdown menu or by typing a value in the entry field to the right.

2. Set the **Phase Time** and **Start Delay**.

    –   **Phase Time** is the maximum length of time the pump can operate; the pump may run for a shorter time.

    –   **Start Delay** is the initial time delay before the first activation of the pump and is not repeated for subsequent pump activations.

3. After the dose parameters are entered, click **OK** to close the edit screen.

4. Click **Apply Values** to save your changes.

Bolus feed

Bolus feed is similar to **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 Bolus Feed dosing is illustrated in Figure 5.46, and contains the following elements:

*   **Start Delay** is the period of time to wait prior to start the phase.

*   **Number of Doses** is the number of times the pump will be activated per cycle.

*   **Dose Duration** is the time that you calculate 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.
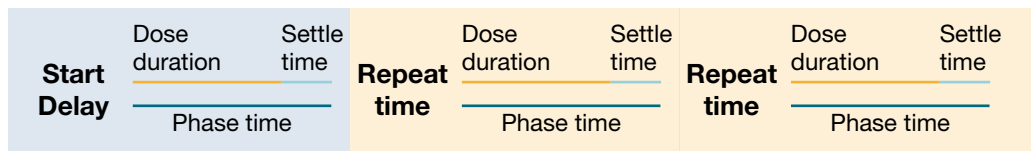
*   **Repeat Time** is the interval between each bolus.

Figure 5.46. Bolus feed diagram.

Refer to Figure 5.47 for the following instructions.

Figure 5.47. Bolus feed dose type.

1. Select the dose flow rate either from the **Flow Rat**e dropdown menu or by typing a value in the entry field to the right.

2. Enter the **Phase Time** and **Start Delay**.

3. Set the **Dump Mode** and enter the **Dose Duration**. There are two options for the **Dump Mode**: **Continuous** and **Dump**.

   – **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, specific options appear (Figure 5.48). Enter values for each field.

     • Enter **Run Speed**, after calculating what pump speed will be needed to deliver the required dose within the **Dose Duration** time.

     • Enter an estimated **Dose Duration**. If the dose is completed prior to the time limit, it will stop. If it has not completed, the pump will continue to run past the time limit.

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

Figure 5.48. Dump Mode set to Dump.

4. Enter the **Number of Doses**.

5. Select **Apply Values** to save your changes.

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 feeds will interrupt the sequence of pump operations to add acid or base using the pH controller until the measured pH reaches the **Interrupt Cascade SP**. 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.

5.4.5 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.

You 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 5.49 shows two cycles of a representative multi-feed strategy.
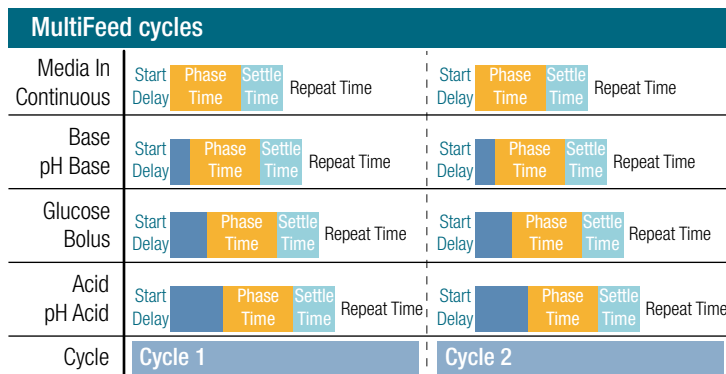

Figure 5.49. MultiFeed cycles.

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 5.50. 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 5.50, where an acid pump interrupt occurs in the first and third cycles. A base pump interrupt occurs in the third cycle.
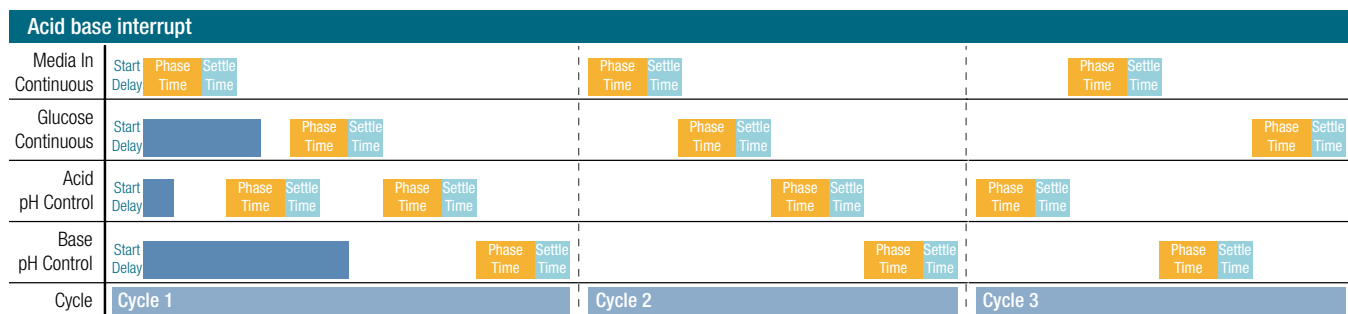

Figure 5.50. Acid-base interrupt.

5.4.6 Operating Multi-Feed pumps

Start Multi-Feed operation

1. On the **Main** screen, click the **Multi-Feed** button above the pump control modules to open the **Multi-Feed** faceplate.

2. After all the pumps are set up and their limits are established, click **Start** at the top of the faceplate to activate the **Multi-Feed** module.

   – When **Start** is clicked, the button will change to **Hold**, the current state will update to **Start**, and the status of the current state will cycle from **Starting** to **Started** (Figure 5.51).
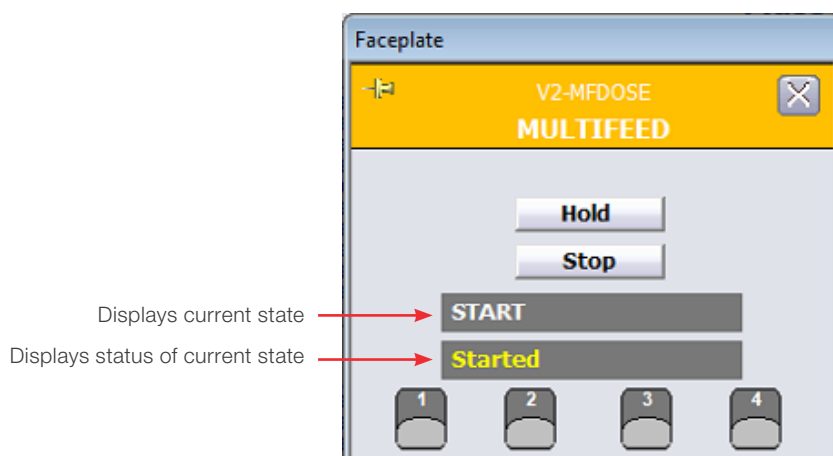

Figure 5.51. Hold button appears after clicking Start.

Hold Multi-Feed operation

The **Hold** function immediately stops the entire process and triggers an alarm, which is shown as a red bar in the **Alarm** section at the bottom of the faceplate.

When **Hold** is selected, the button changes to **Resume**, the current state will update to **Hold**, and the status of the current state will cycle from **Holding** to **Held** (Figure 5.52).
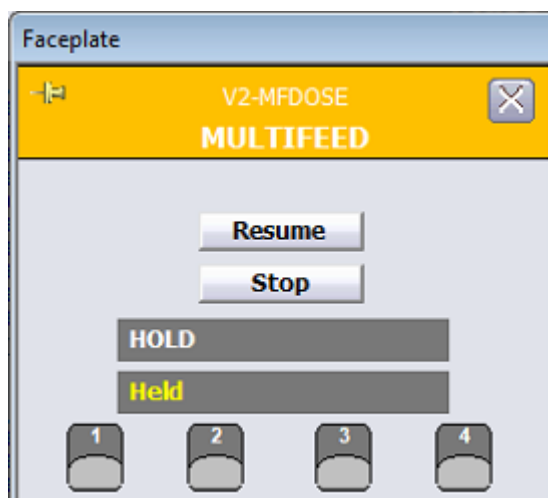
Figure 5.52. Hold button changed to Resume.

After resolving the situation that prompted the **Hold**, click **Resume** to start the process where it was halted.

To remove the alarm, click **Acknowledge Alarm**.

Stop timer on Hold

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

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, you can become unaware of how much time elapses during the hold.

Refer to Figure 5.53 for the following steps. To change the setting:

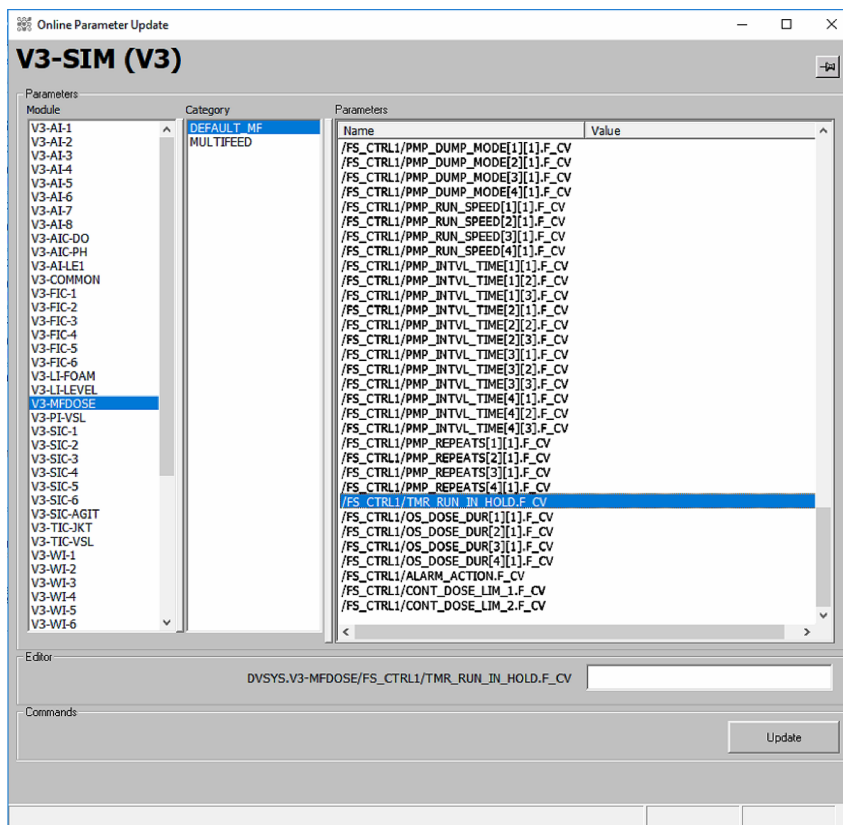1. Select **Online Parameter Update** from the **Configuration** screen.

Figure 5.53. Timer Run in Hold parameter selected in the Online Parameter Update window.

2. Verify that the correct vessel is displayed.

3. Under the **Module** column (first from the left), locate and click the string **V*x*-MFDOSE**, with *x* being the vessel number.

4. Under the **Category** column (second from the left), click **DEFAULT_MF**.

5. Under the Parameters column (third from the left), locate the string **/FS_CTRL1/ TMR_RUN_IN_HOLD.F_CV** listed in the **Name** column.

    – 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

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

Stopping Multi-Feed operation

Click **Stop** when the run is finished or the **Multi-Feed** function is no longer needed. The the current state will update to **Stop**, and the status of the current state will cycle from **Stopping** to **Stopped**. Once the operation has stopped, the **Hold** button will revert to the **Start** button.

5.5 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 5.54).

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.
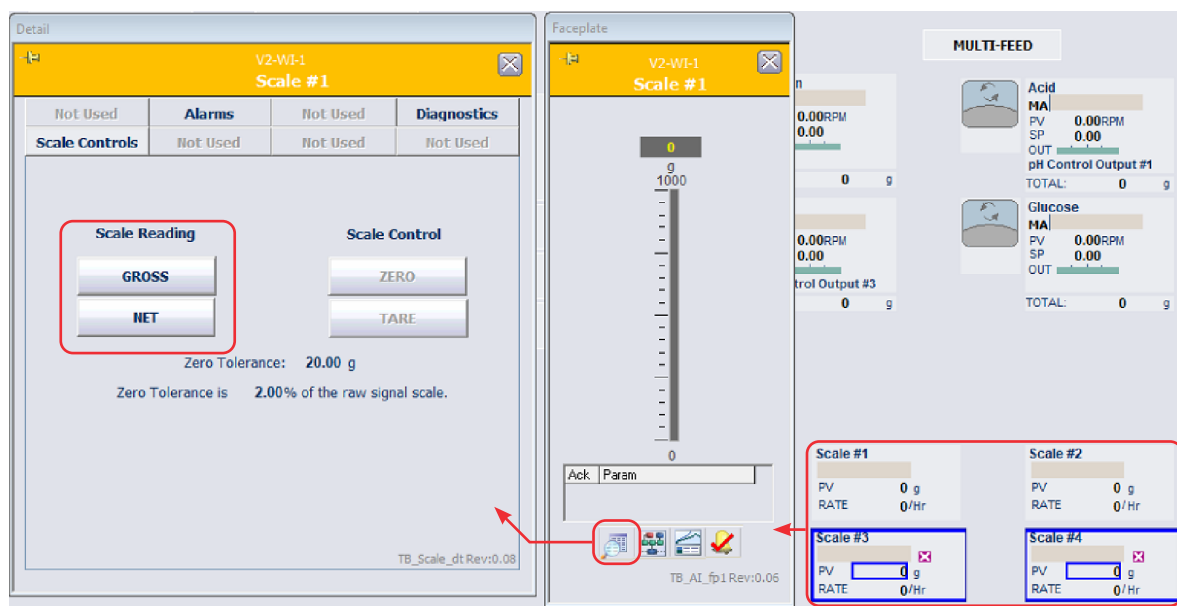

Figure 5.54. Gross and Net reading options shown for Scale #1.

5.6 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.

Click either **Foam** or **Level** control module to open the faceplate. The faceplate allows you 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:

1. Click the desired control module on the **Configuration** screen (Figure 5.55) to open the configuration form for the parameter. Figure 5.56 shows the **Level** form, and Figure 5.57 shows the **Foam** form.
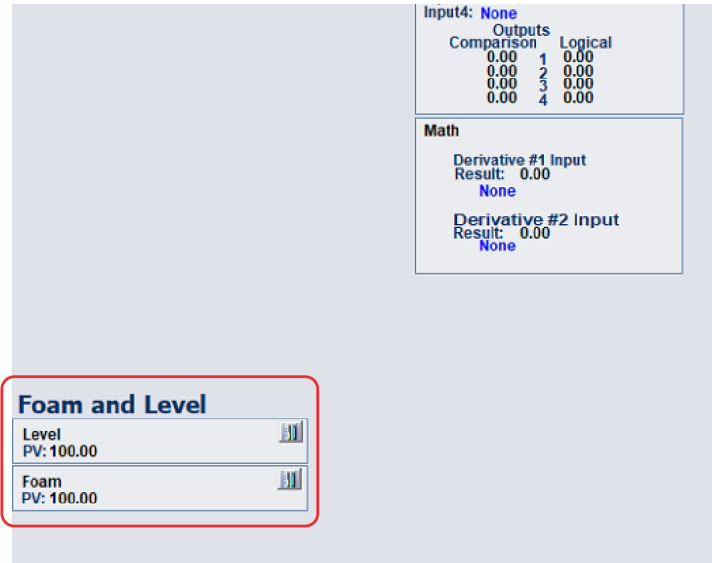

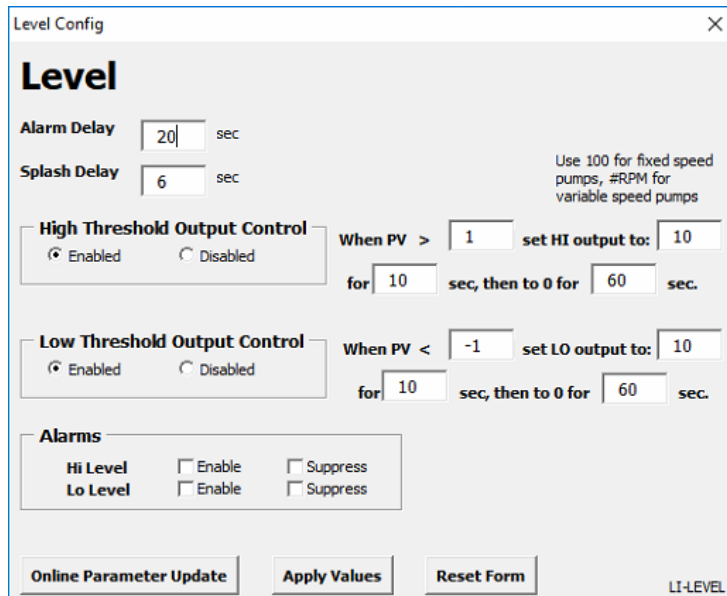Figure 5.55. Foam and level buttons shown on Configuration screen.

Figure 5.56. Level configuration form.

Figure 5.57. Foam configuration form.

2. Set the parameters on the form. Both configuration forms allow you to set:

   – **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. This must be enabled for **Hi** or **Low Threashold Output Control** to function.

   Note: The **Hi Level** alarm takes priority over the **Hi Foam** alarm if both are enabled.

3. Click **Apply Values** to save the settings. The PV is displayed on the **Configuration** screen, as shown in Figure 5.55`.

   Note: The PV readings displayed are based on media/solution resistance values interpreted by TruBio and are not a percentage indication.

5.7 Pump totals

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

Clicking the **Totals** section at the lower edge of the box will open the faceplate (Figure 5.58).
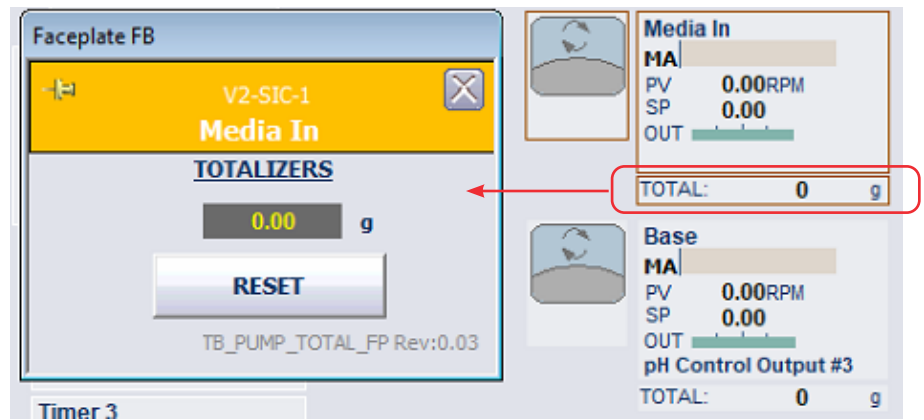
Figure 5.58. Totalaizers faceplate.

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.

5.8 Saving the run setup

Activating the control loops starts the system, but none of the parameters have been saved. Saving the run setup configuration is important for future use. Steps for saving a file is covered in section 3.2.

5.9 Activate batch start

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. The **Batch Start** button creates a flag that is recorded in the **Event Chronicle**. Note this will NOT start the batch and is required if using XL Report or DreamReport.

6

Maintenance

Chapter contents

6.1 Backup and recovery

Archiving, backup, and disaster recovery procedures should be performed by Automation or IT department personnel, in accordance with their standard operating procedures (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.

6.2 Computer cleanup

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

- Check the computer disk space. To access this information, click the Windows **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 Application 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 Application 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.

6.3 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, a controller download may be required after power is restored. After all modules (if any) have downloaded, 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 on the TruLogic, 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 TruBio Software **Main** screen will 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.

7

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 **Process History View** for any parameter at the bottom of the faceplate to open a display of the parameter history (Figure 7.1). 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 Microsoft™ Excel™ files, to create hard copy documentation.
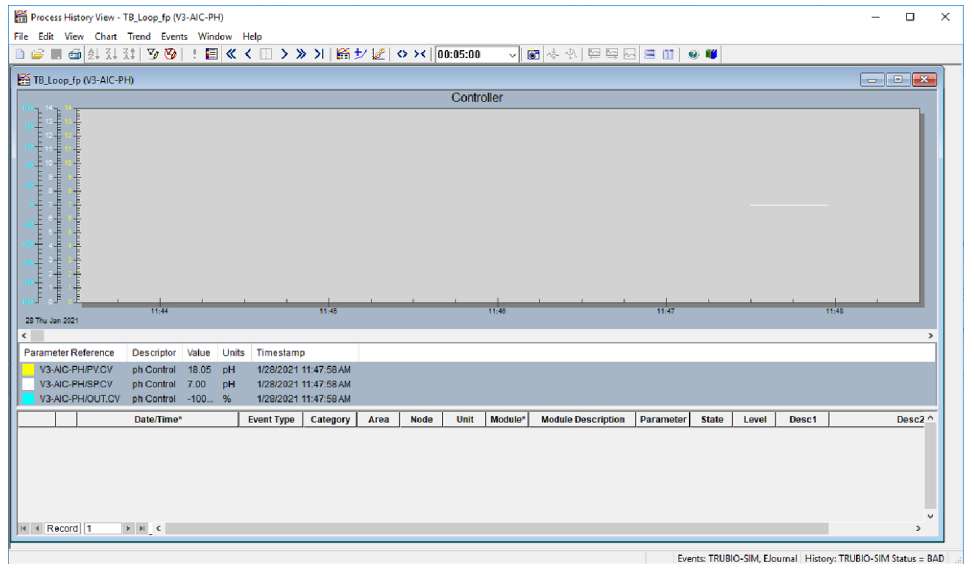

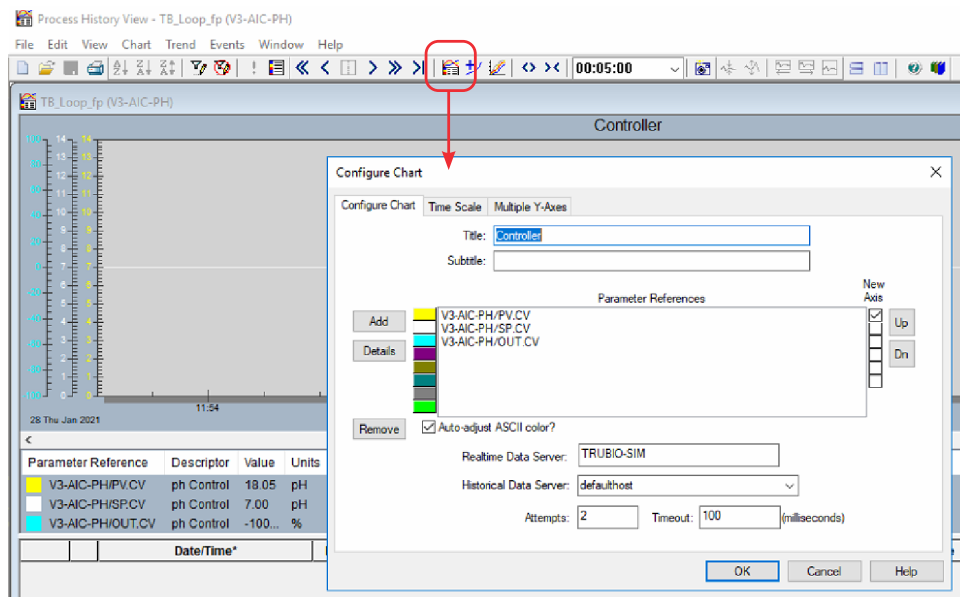
Figure 7.1. Display of parameter history.

Figure 7.2. 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

To access the **History Collection** in Read only mode:

1. Open **Exploring DeltaV** from the Windows taskbar.

2. Expand **System Configuration** > **Physical Network** > **Control Network**.

3. Expand the appropriate workstation and right-click **Continuous Historian**.

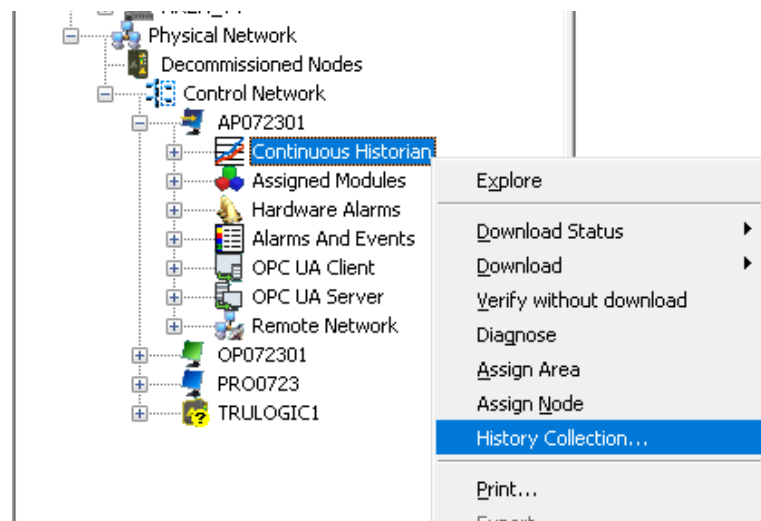4. Click **History Collection** from the list (Figure 7.3).

Figure 7.3. Selecting History collection for the Continuous Historian.

Figure 7.4. History Collection (Read-Only) window.

Note: Viewing the history collection in this method shows historian points from all of the areas assigned to the historian database for the selected application station.

To access the **History Collection** in Edit mode:

1. Open **Exploring DeltaV** from the Windows taskbar.

2. Expand **System Configuration** and click **Control Strategies**.

3. In the pane on the right, right-click the appropriate **AREA_VX** and click **History Collection** (Figure 7.5).
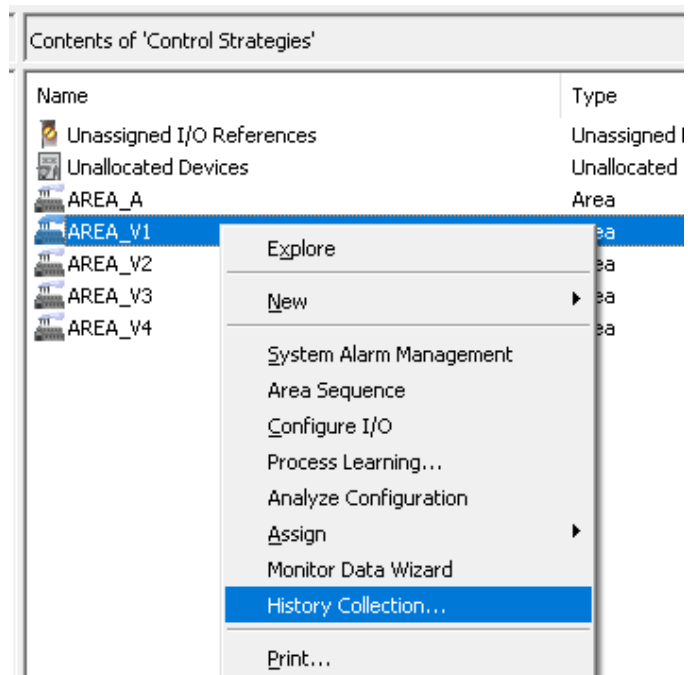
Figure 7.5. History Collection for AREA_V1.

Figure 7.6 shows the **History Collection** window.
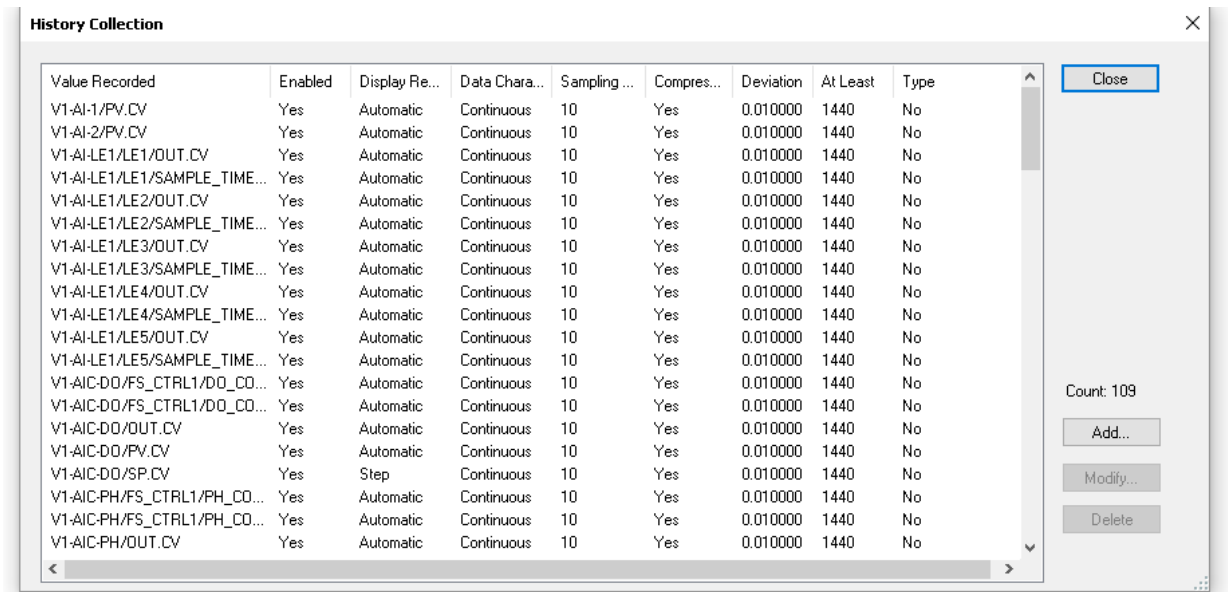
Figure 7.6. History Collection window.

Note: Viewing the history collection in this method shows historian points from only the selected **Area** assigned to the historian database for the selected application station.

From the **History Collection** window, you can add a new parameter to the trend by selecting add or select a string and click **Modify...** to modify the parameter. Both options use the same windows for customization (Figures 7.7–7.8).

Click **Help** or Refer to DeltaV Books Online for additional information on these settings.

Figure 7.7. General settings for modifying history collection.

Figure 7.8. Advanced settings for modifying history collection.

Table 7.1 shows history collection properties for parameters in the DeltaV system.

Table 7.1. History collection properties for DeltaV parameters.

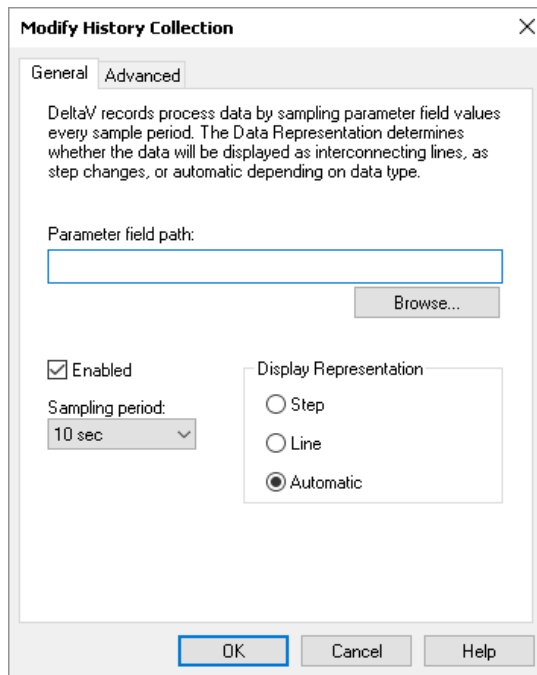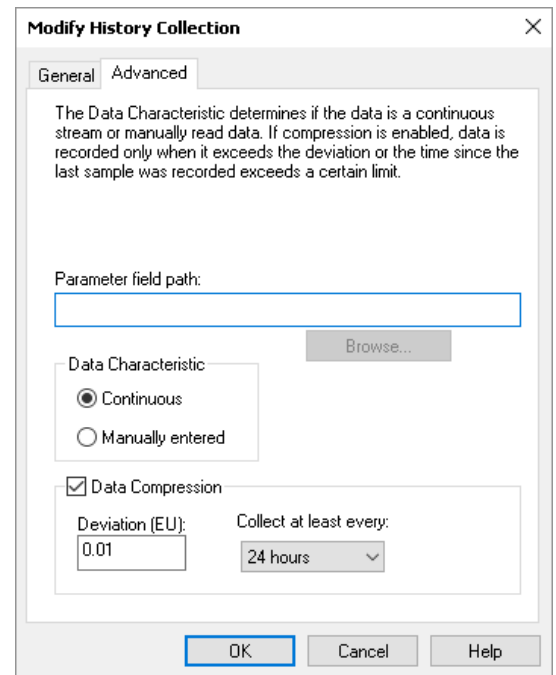| Settings	Description
General	
Parameter field path	The path of the module parameter whose history is being collected.
Enable	Activates collection of field values specified in the parameter field path.
Display representation	• **Step:** Displays the values as step changes on the trend chart. Step representation 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	
Data characteristic	• **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 of the **Historian** window. This does not close the TruBio program.

8

General ordering information

Chapter contents

8.1 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) 1670 734093

Fax: +44 (0) 1670 732537

Email: customerservice.bioprocessing@thermofisher.com

8.2 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) 1670 734093 (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—Electrical connections and Controllers Off function

A.1 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.

A.2 Controllers Off function

If an emergency occurs that requires the immediate halt to all functions associated with the bioreactor/fermentor, the user can press Stop 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** form determine the mode that the controllers will be set to if **Controllers Off** is clicked. As displayed in Figure A.1, the default is **Manual** (MAN) mode with 0% output.

Figure A.1. Controllers Off config screen.

When **Controllers Off** is selected, 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 B—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.

B.1 Change loop to direct action

To change the loop to Direct action:

1. On the ProPlus workstation, access **Exploring DeltaV** from the task bar (Figure B.1).

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

2. Open the **Equipment** mode. Then locate the module **Vx-WIC-VSL** in the left column (Figure B.2). Follow the path: **Area_Vx** > **Vx** > **Vx EM** > **Vx-WIC-VSL** where x is the vessel number.

3. Double-click **PID1$CONTROL_OPTS** in the right column (Figure B.2).
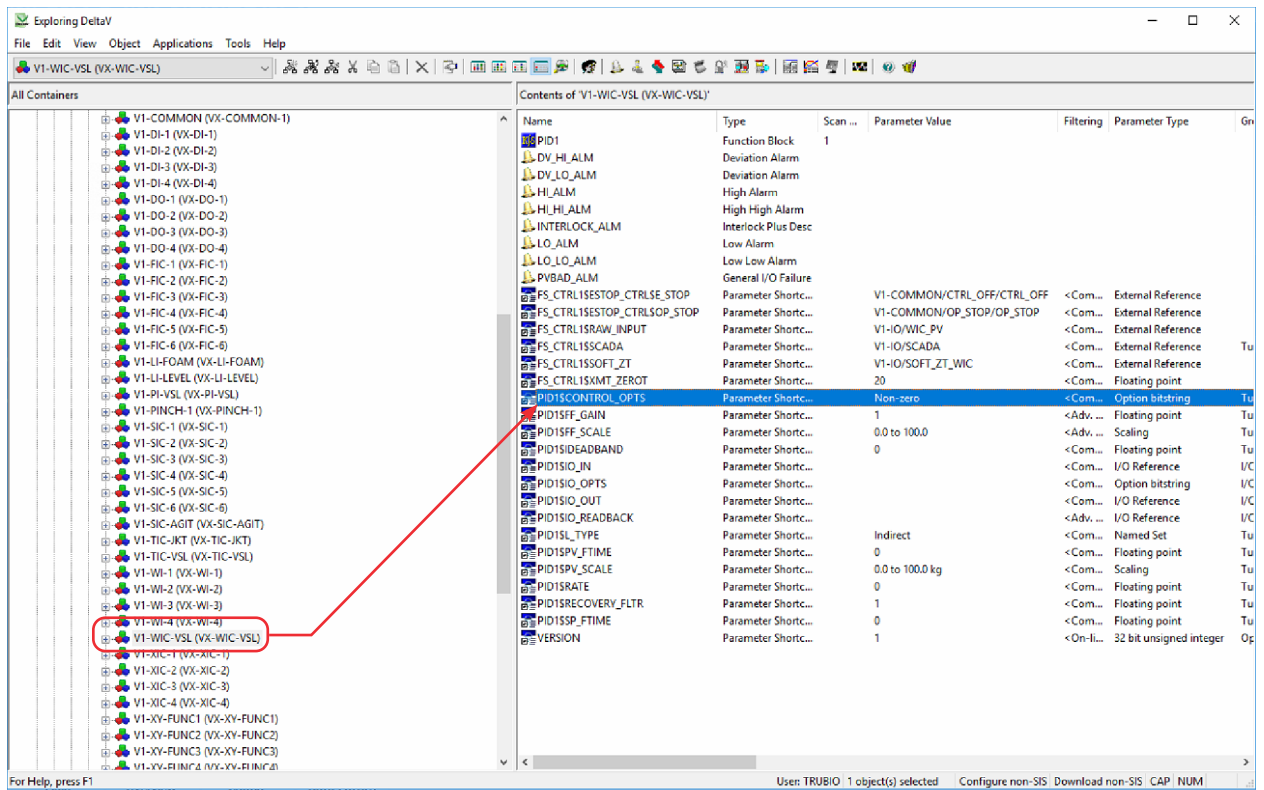
Figure B.2. File path for PID1$CONTROL_OPTS string.

4. When the form opens, click to deselect the **Use default value from library object** check box and select **Direct Acting** under **Properties** (Figure B.3).

Deselect

Select

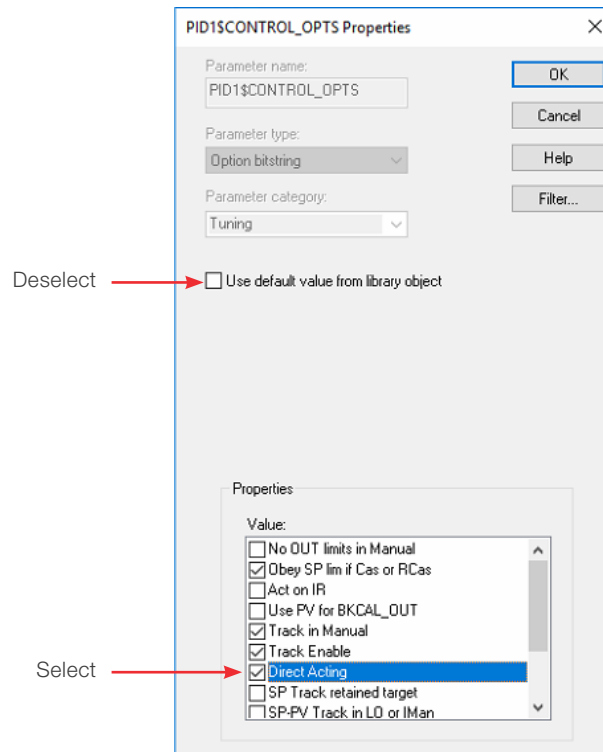Figure B.3. Options to select and deselect.

5. Click **OK** in the upper right corner of the box to save the selections. A blue triangle appears next to **Vx-WIC-VSL**, indicating a download is required (Figure B.4).
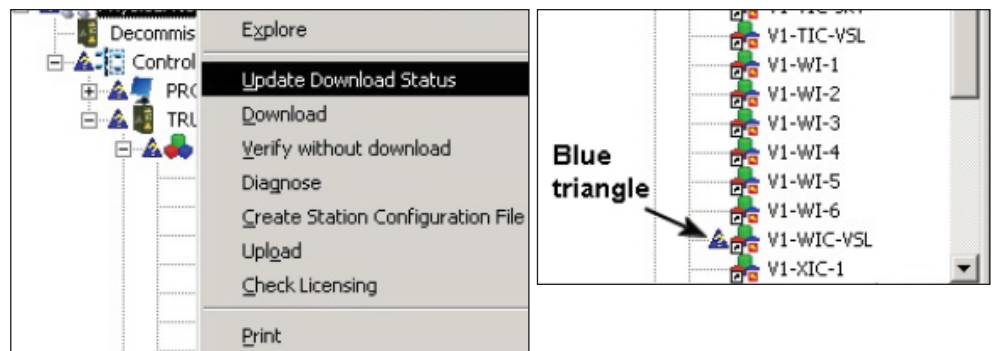

Figure B.4. Update Download Status and blue triangle detail.

6. Right-click the module. In the menu that appears, click **Download** and then, **Control Module** (Figure B.5).
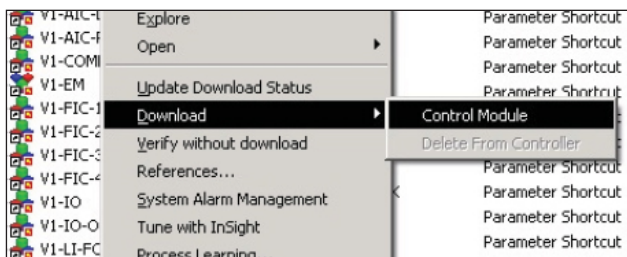
Figure B.5. Right-click module, select "Download," then
"Control Module."

7. After the control module has downloaded, minimize **Exploring DeltaV**.

8. To restore the alarm files and other settings, open **Vessel Settings Management** in the **Online Parameter Update** window. 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**.

B.2 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 outlined in section 5.4.4.

   – 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** mode.

   – Interlocks can be set where, 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.

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

The multi-feed control for the Media In pump (Pump #1) can be paused (scale-locked) by clicking the Pump #1 symbol on the **MultiFeed** faceplate. You 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 **Cascade**. 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 multi-feed 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 B.6.

Based on our testing, the preferred tuning parameters for Vx-WIC-VSL are:
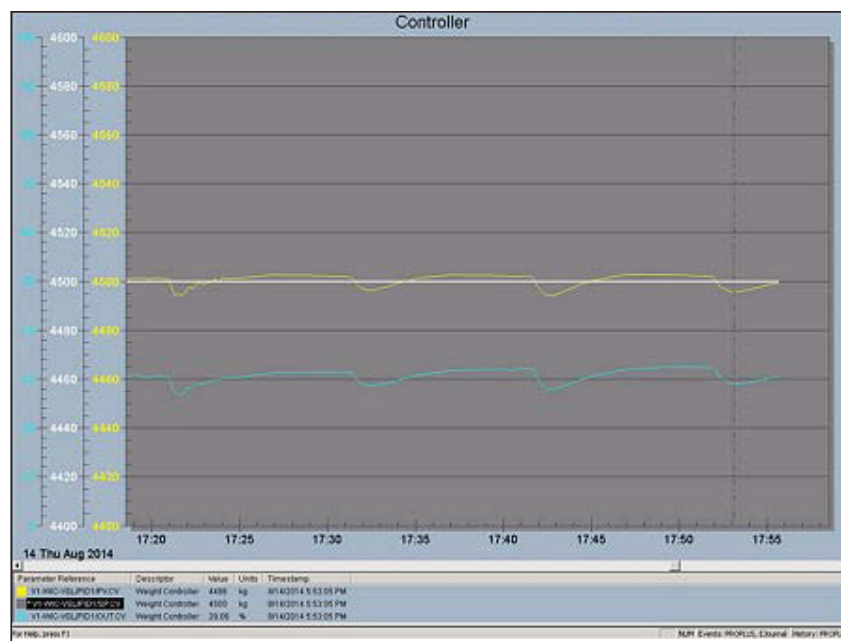
- Gain = 150

- Reset = 500

- Rate = 0

Figure B.6. Graph showing minimal effect of weight on BPC vessel.

Appendix C—TruFluor sensor calibration

C.1 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 for pH or DO control and click on the Calibration tab. Then click the appropriate TruFluor button for the TruFluor sensor being used: 1, 2, or 3 (Figure C.1).
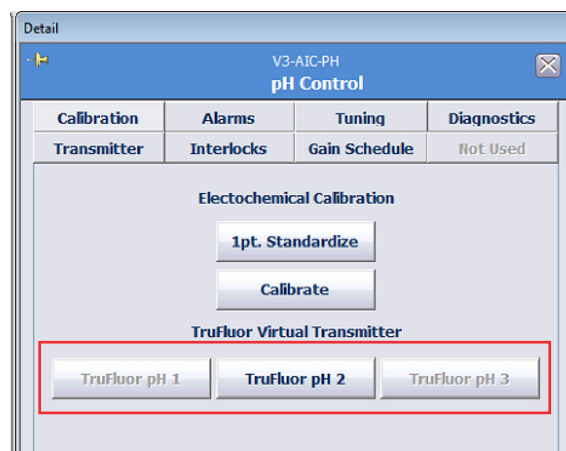

Figure C.1. TruFluor pH sensor buttons on the Calibration tab.

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

One-point calibration for TruFluor sensors

Use the following steps to complete TruFluor sensor calibration.

Note: The process is shown for TruFluor pH sensors, but the process is the same for TruFluor DO sensors.

1. In the **TruFluor pH** window, click **Menu** (Figure C.2).

Figure C.2. TruFluor pH window.

2. Navigate to **Calibrate** (Figure C.3), and click **Enter**.

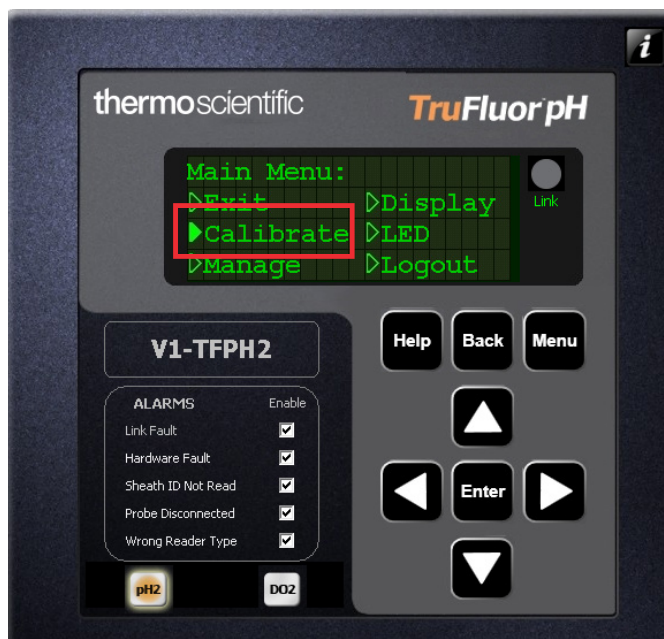3. Navigate to **pH** (Figure C.4), and click **Enter**.

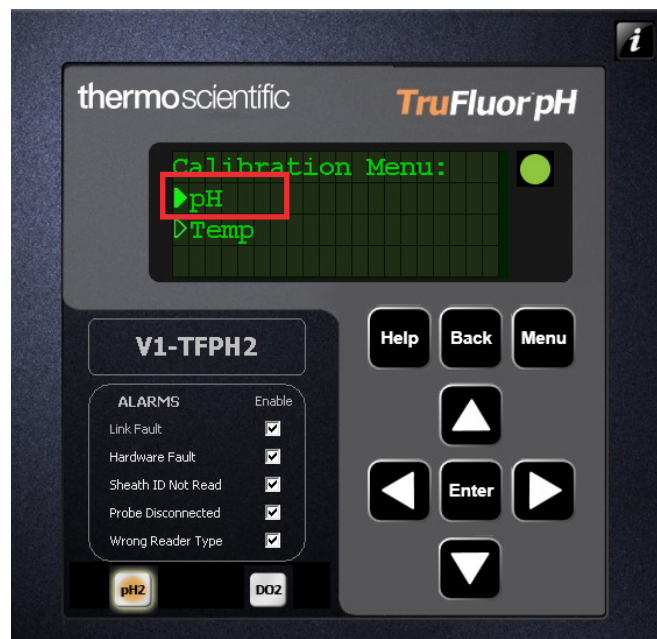Figure C.3. Selecting "Calibrate" from Main menu.

Figure C.4. Selecting "pH" from Calibration Menu.

4. In the **pH Cal Type** menu, navigate to **One Point** (Figure C.5), and then click **Enter**.

Figure C.5. Selecting "One Point" from pH Cal Type menu.

5. Remove an aliquot of media from the bioreactor/fermentor BPC according to your facility-specific aseptic processes.

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 C.6). Click **Enter** when you have finished.

8. At the **Please authenticate** prompt, click **Enter** to accept the calibration (Figure C.6).

Figure C.6. Adjusting Buffer1 pH setting.

Figure C.7. "Please authenticate" screen.

9. At the **Calibration Summary** screen, enter any notes in the **Comment** field, if desired. Then, enter a valid username and password, and click **Apply** (Figure C.8).
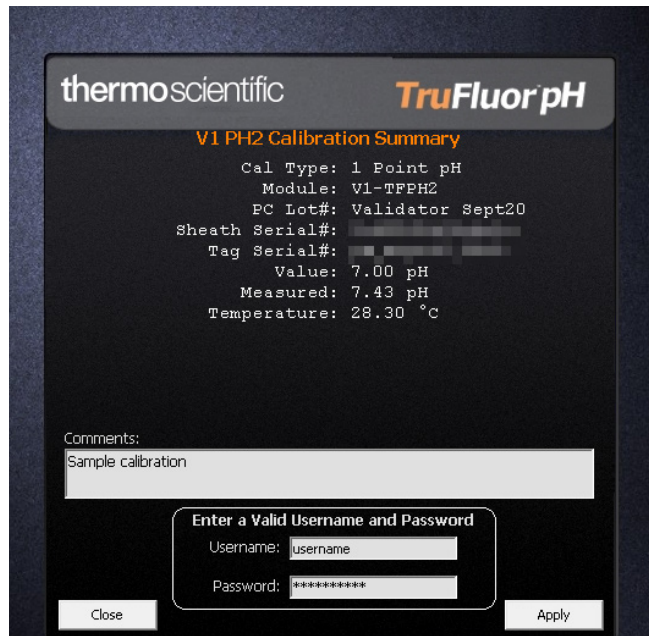

Figure C.8. Calibration summary screen.

10. 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 (Figure C.9) to indicate a non-factory calibration is in use.

Figure C.9. Asterisk next to parameter name, indicating non-factory calibration in use.

Two-point calibration of TruFluor sensors

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.

1. **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.

2. Aseptically remove a small aliquot of media from the BPC. Verify the pH using a pH meter calibrated with NIST-traceable standards.

3. 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.

4. Add CO_2 (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.

5. Remove another aliquot and verify the pH as above.

6. 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, click the **TruBio** icon from the Windows taskbar at the bottom of the screen (Figure C.10).
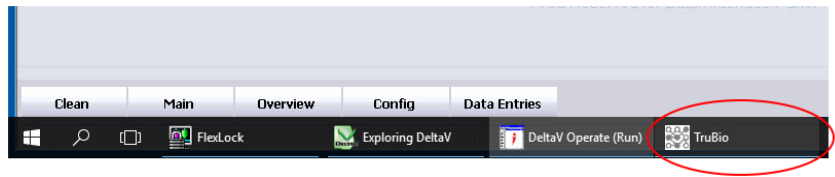
Figure C.10. TruBio icon on Windows taskbar.

2. When the TruBio screen appears, click **Save/Load/Cal File Viewer** on the lower left (Figure C.11).
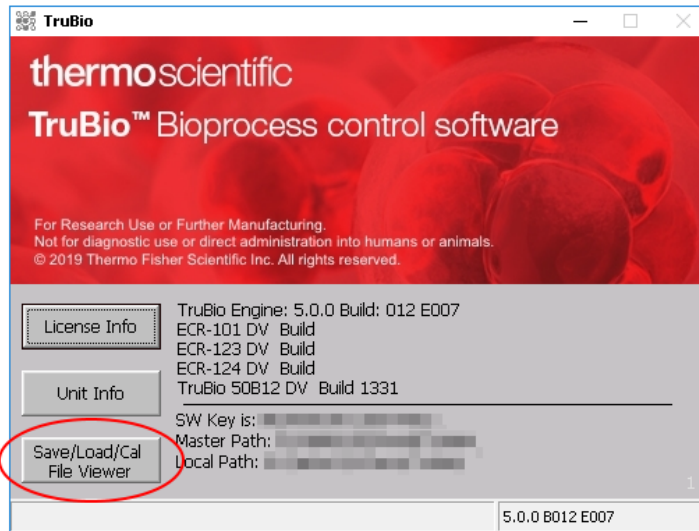

Figure C.11. "Save/Load/Cal File Viewer" button.

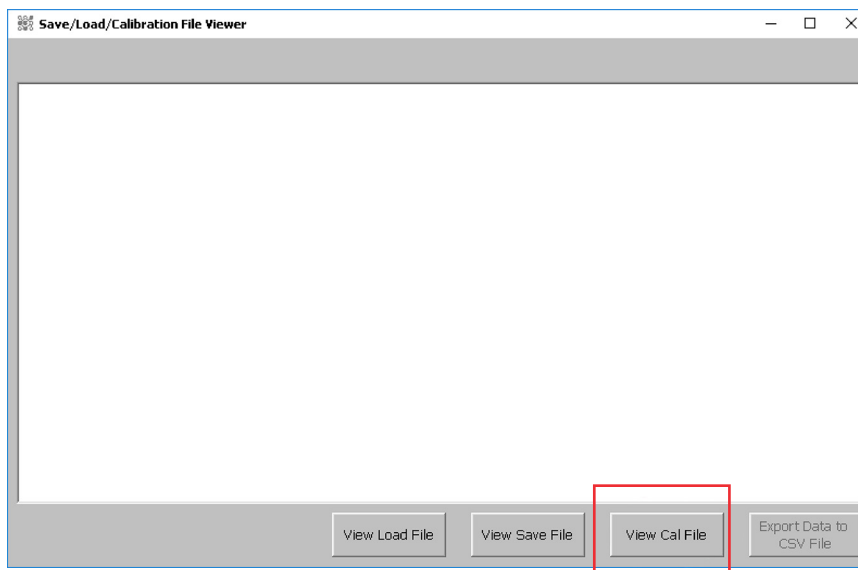3. Click **View Cal File** (Figure C.12).

Figure C.12. View Cal File button on the Save/Load/Calibration File Viewer.

4. Select either **pH** or **DO** (Figure C.13), and then select the TruFluor option.
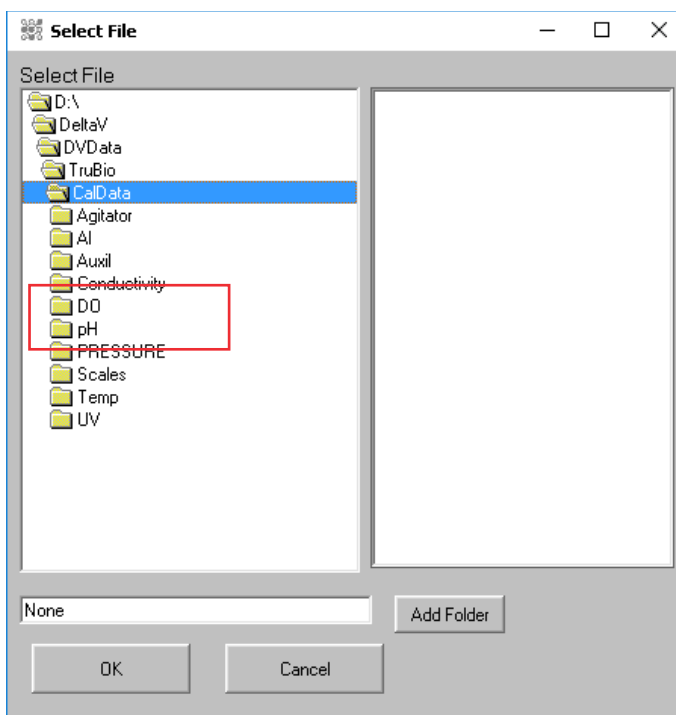

Figure C.13. Calibration files under probe heading.

5. Select the desired file from the drop-down menu (Figure C.14) to view the calibration data (Figure C.15).
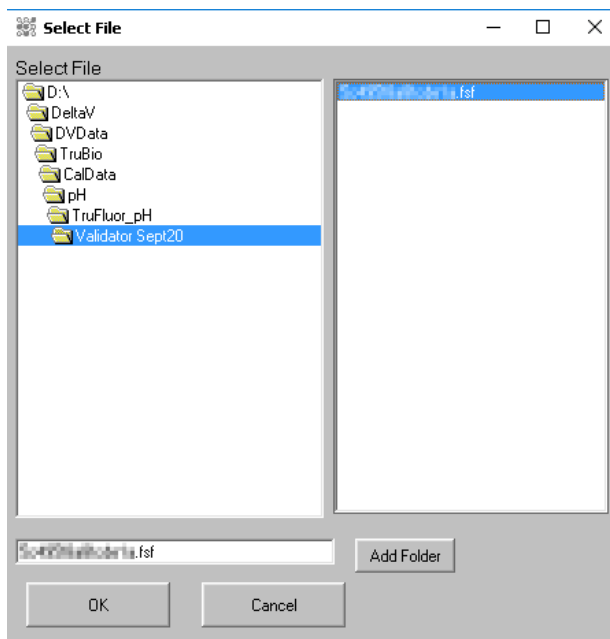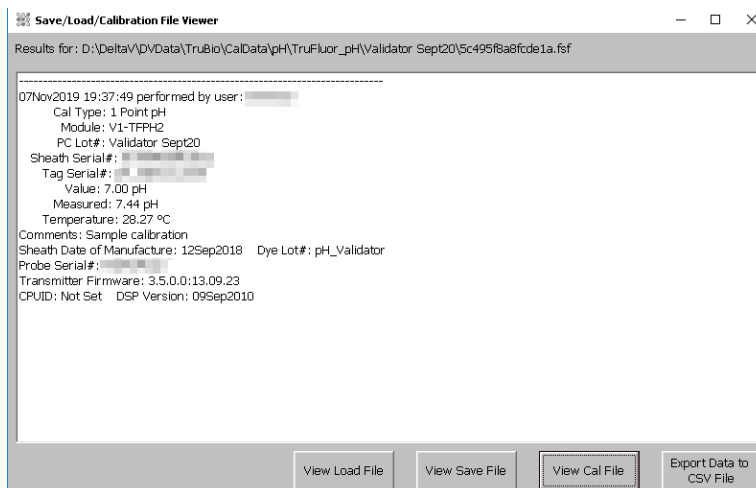

Figure C.14. Selecting desired sensor file.

Figure C.15. Save Load file results.

Appendix D—5:1 Turndown add-on

D.1 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.

D.2 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.

D.3 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.

D.4 Handheld controller operation

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

Figure D.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.

- **Lock indicators:** 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 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.

- **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.

D.5 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.

D.6 User interface

The user interface for this add-on consists of a control module display object that enables you to view the status of the 5:1 turndown. This display object can be placed onto the desired vessel graphic per user requirements.
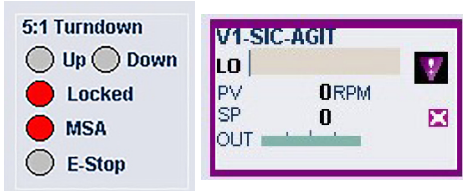
D.6.1 Operator display

Figure D.2 shows the 5:1 turndown display in Run mode. The indicators (Up, Down, Locked, MSA, and E-Stop) animate depending on the status indication received from the turndown hardware.
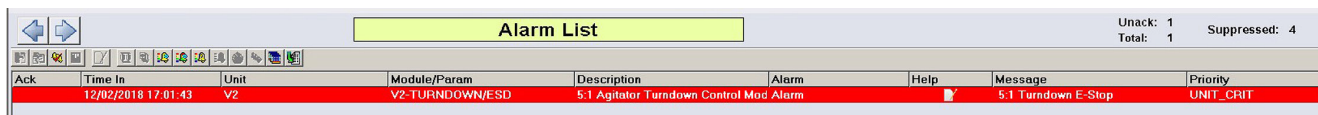

Figure D.2. Indicators in the TruBio Software.

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

Device state	Display status	Operation
Up		• Turndown in Up position. • Locking pin is locked. • Motor safety cap pin is in position.
Down		• Turndown in Down position. • Locking pin is locked. • Motor safety cap pin is in position.
Moving/ Intermediate Position		• 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 position. • The agitator will be interlocked.
E-Stop		• 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.

D.7 Alarms

An Emergency Shutdown (ESD) alarm is generated and indicated on the TruBio **Alarm List** screen 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 D.3 shows the list of alarms generated for this add-on.

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

D.8 Data historian

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

- DOWN
- ESTOP
- LOCKED
- MSA
- UP

D.9 Event journal and process history

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

Appendix E—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.

E.1 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" (DOC0104). 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/m^3." See your local Thermo Fisher representative for a copy of this document.

E.2 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.

E.3 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.

E.4 User interaction

- You are expected to manually fill non-zero values in the configuration form on the Congifuration screen, 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 **Enabled** 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** 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.

E.5 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 control module

E.6 Agitator speed governor configuration form

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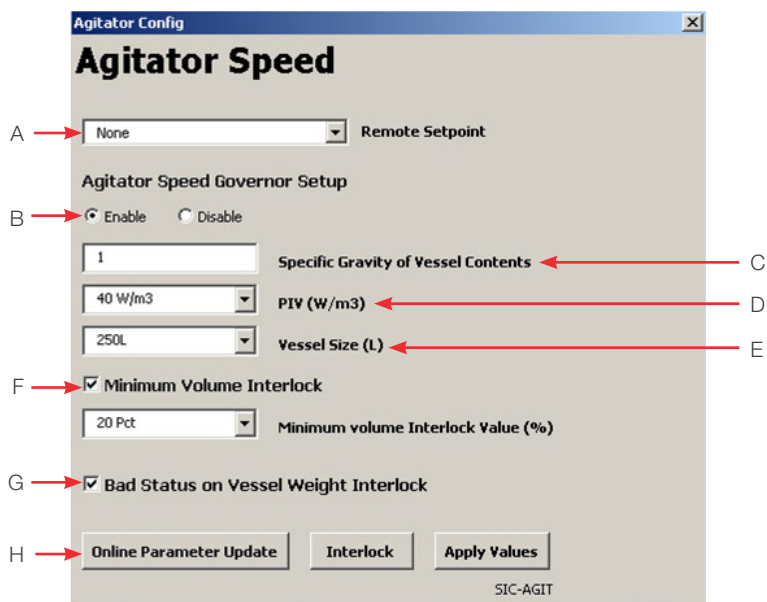
Figure E.1. Agitator speed governor form display.

Table E.1. Agitator speed governor form display details shown in Figure E.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/m³)	10 W/m³, 20 W/m³, and 40 W/m³	20 W/m³
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/m^3, 20 W/m^3, and 40 W/m^3.

- 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.

E.7 Agitator speed governor interlock form

Figure E.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.

Figure E.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.

E.8 Agitator speed governor faceplate

The agitator speed governor faceplate is shown in Figure E.3 (this is distinct from the agitator's controller faceplate). It can be accessed from the **Main** screen of the vessel by clicking on the speed governor control module. See the following numbered list for descriptions of the various operation fields of the faceplate.
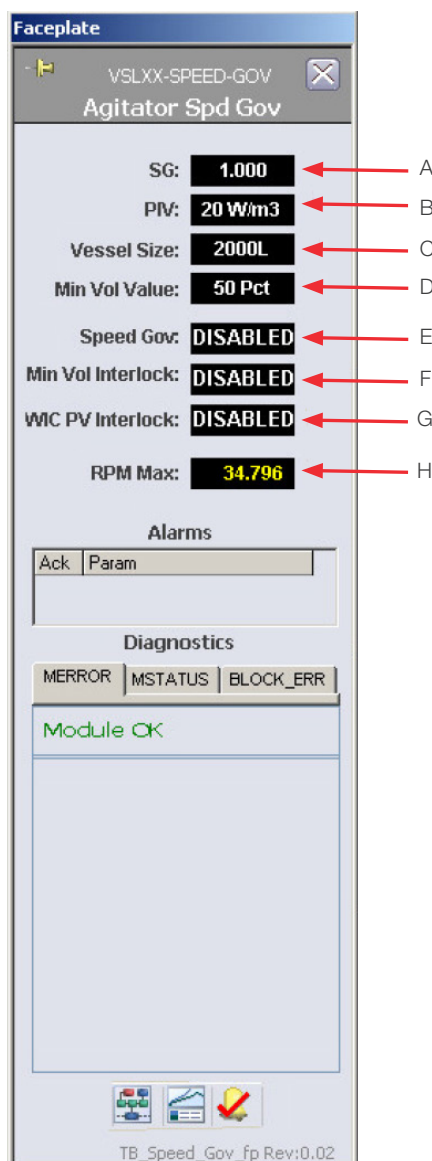
Figure E.3. Agitator speed governor faceplate.

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**.

E.9 Agitator speed governor control module

The agitator speed governor control module is located on the **Main** screen for the vessel. Table E.2 displays the different states of the control module and what they indicate.

Table E.2. Speed governor control module operations.

	Display status	Operation
Speed governor graphic control module	SPD GOV [D]	• Agitator speed governor control is not enabled • AGIT_SPEED_ALM and/or INTEG_ALM alarms are not active
	SPD GOV [D]	• 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)
	SPD GOV	• Agitator speed governor control is enabled • AGIT_SPEED_ALM and INTEG_ALM alarms are not active
	SPD GOV	• Agitator speed governor control is enabled • AGIT_SPEED_ALM and/or INTEG_ALM alarm is active

E.10 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 E.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.

Figure E.4. Agitator speed governor alarm list.

E.11 Event journal

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

Figure E.5. Agitator speed governor event journal.

E.12 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

E.13 Setting up the speed governor

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

- By using the Agitator/Speed Governor configuration form on the associated Configuration graphic

- Changing values via the OPU configuration utility

- Loading a speed governor SaveFile

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

E.13.1 Agitator Speed Governor configuration form (recommended)

The **Agitation Speed Governor** configuration form can be accessed from the **Configuration** screen of the relevant vessel. You can select and enter settings that match their requirements. Ensure that you click **Apply Values** 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.

E.13.2 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 Configuration screen. Select the speed governor module. The parameters shown in Figure E.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.
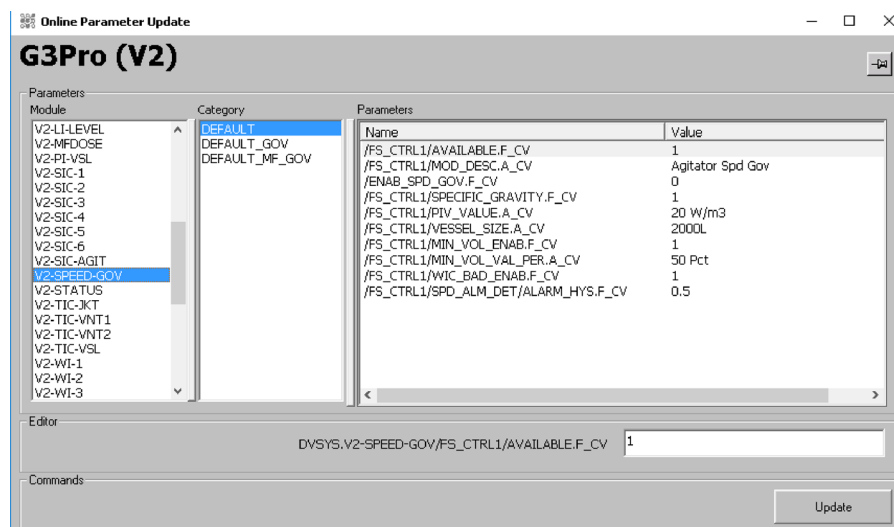

Figure E.6. OPU utility parameters for agitation speed governor.

E.13.3 Loading a speed governor SaveFile

After the speed governor has been set up according to the site's requirements, users (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 **Configuration** screen.

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 speed governor functionality is required. Always verify the speed governor settings using the **Speed Governor** faceplate.

Appendix F—Bag Integrity add-on

F.1 Overview

The TruBio Bag Integrity add-on is used to check for leaks in the BPC to ensure its integrity before it is used for production.

F.2 Operational description

The TruBio Bag Integrity add-on provides a method of verifying BPC integrity. Using the MFCs, the add-on automatically inflates the BPC to a desired pressure. The add-on also measures the pressure drop for a configurable amount of time.

F.3 System setup

Ensure that the BPC 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.

F.4 BPC inflation procedure

You should ensure the following before starting the BPC integrity check:

- The BPC is inflated per normal site procedure.

- The MFC being used for the test has tubing connected to the BPC.

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

F.5 User interaction

- You are 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 BPC integrity check. The **Start** button will only be visible when the configuration form is populated.

- During the **Run** mode of the sequence, you are not expected to perform control actions.

- You have the choice of aborting the test as and when required during the BPC integrity check.

- Any alarms generated will be visible on the TruBio display. Refer to the sections below for detailed information about each mode.

F.6 User interface

The user interface for this add-on consists of the control module display object and accompanying faceplate that enables you 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.

F.7 Operator display

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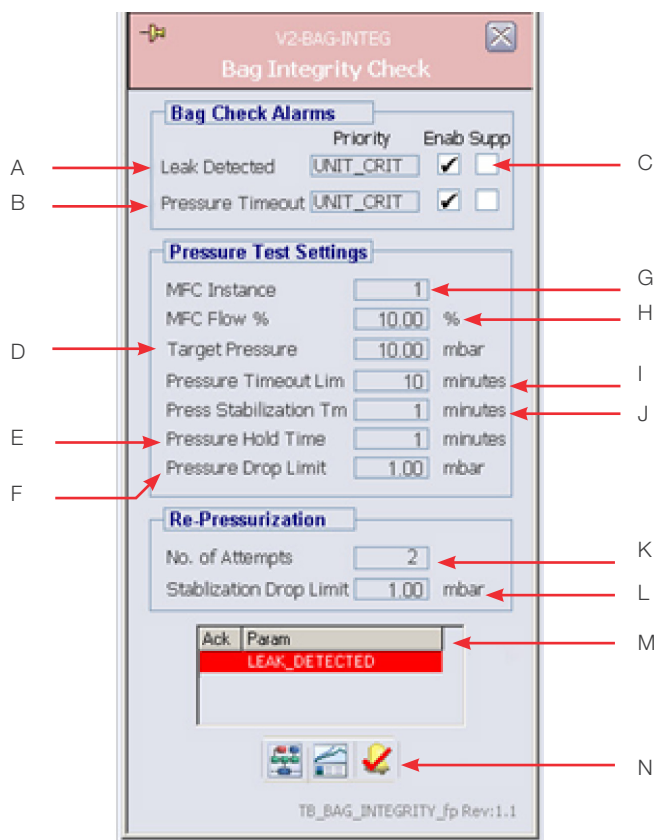

Figure F.1. Bag integrity display.

Figure F.2. Bag integrity check
faceplate.

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

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 (Dynamic units)
E	Pressure hold time under test	0–180 min.	1 min.
F	Allowable differential pressure	0–50	1 (Dynamic units)
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.

Table F.2. Agitator speed governor form display details shown in
Figure E.1. (continued).

Label	Parameter	Available values	Default values
K	No. of re-pressurization attempts	0–25	2
L	Stabilization drop limit	0–999 min.	1 (Dynamic units)
M	Alarm summary box	N/A	N/A
N	Control Studio online, PHV charts, alarm acknowledge buttons (standard DeltaV function)	N/A	N/A

F.7.1 Modes of operation

The diagram below shows an overview of the modes for the bag integrity sequence.

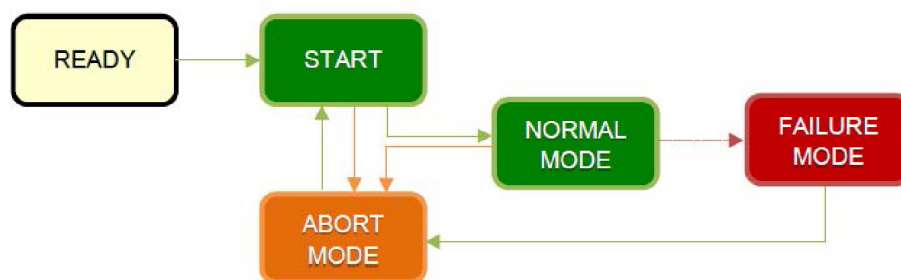These modes are further detailed and explained in the following diagrams and tables.

Figure F.3. Overview of modes for the integrity sequence.
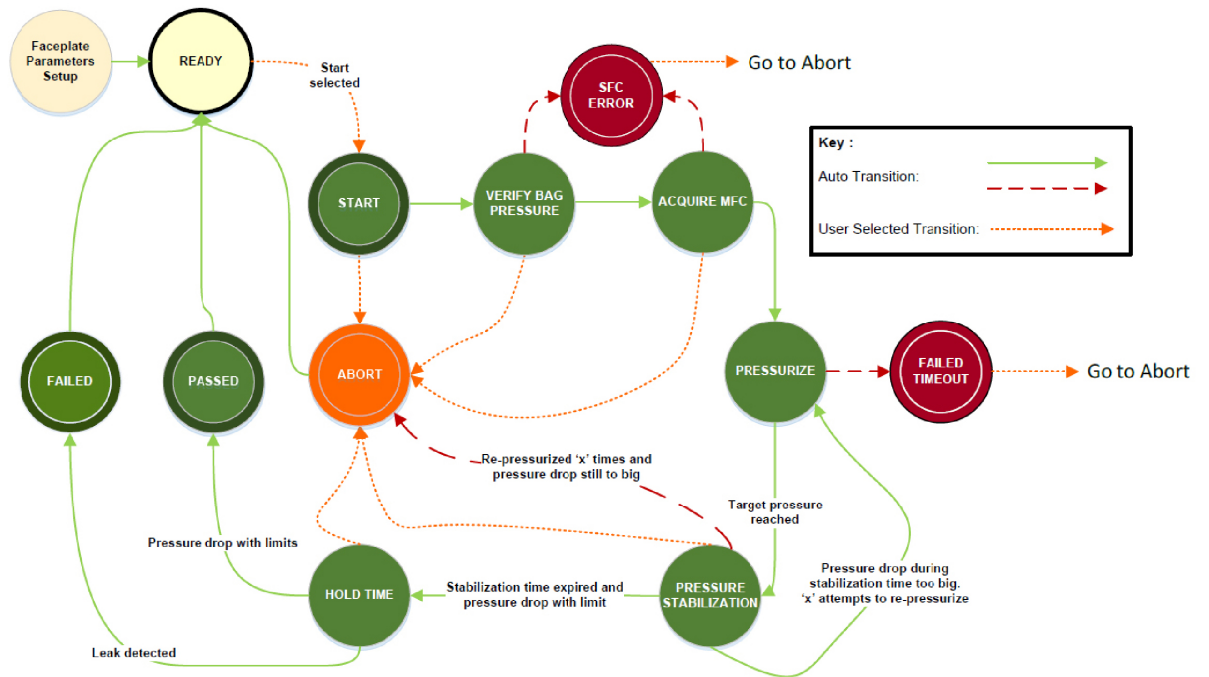
Figure F.4. Bag Integrity Check Operation Flow Chart

Table F.3. Bag integrity operation in normal mode.

Mode	Display status	Operation	
FACEPLATE PARAMETER SETUP	Bag Integrity Check — Config — STEP	• Initial mode of bag integrity check. • The user must enter the desired test parameters in the faceplate display. **Note:** Click **Config** to open the **Configuration** form.	
		Next normal mode: READY	**Failure mode:** N/A
READY	Bag Integrity Check — Start — Config — STEP Start Bag Integrity Check. ARE YOU SURE? Yes No	• The **Start** button appears once the configuration form has been correctly filled. The configuration settings can be filled in automatically by loading in the **Bag Integrity SaveFile**. • Click **Start** to open the confirmation message. • Bag integrity check functionality enabled and awaiting user to start the check process.	
		Next normal mode: START	**Failure mode:** N/A

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

Mode	Display status	Operation
START	**Bag Integrity Check** [Abort] [Config] START Starting Bag Integrity Check	• Bag integrity check functionality started. • Selecting **Abort** will skip the below steps and proceed to SEQUENCE ABORTED in the Abort Mode table. **Note:** A confirmation message appears when **Abort** is clicked. **Next normal mode:** VERIFY BAG PRESSURE* ACQUIRE MFC / **Failure mode:** N/A
VERIFY BAG PRESSURE	**Bag Integrity Check** [Abort] [Config] CURRENT PRESSURE > TARGET Target: 25 mbar Current: 106 mbar	• 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. **Note:** This step will only be visible 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. **Next normal mode:** ACQUIRE MFC / **Failure mode:** SFC ERROR
ACQUIRE MFC	**Bag Integrity Check** [Abort] [Config] ACQUIRING MFC Setting Air MFC	• Sequence automatically sets the user-entered MFC instance (G) into service. • The MFC setpoint value (H) will be fixed by the sequence. • Selecting **Abort** will skip the below steps and proceed to SEQUENCE ABORTED in the Abort Mode table. **Next normal mode:** PRESSURIZE / **Failure mode:** N/A
PRESSURIZE	**Bag Integrity Check** [Abort] [Config] PRESSURIZING Target: 30 mbar Pressure Timeout (mins): 998.9	• 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. **Next normal mode:** PRESSURE STABILIZATION / **Failure mode:** FAILED TIMEOUT

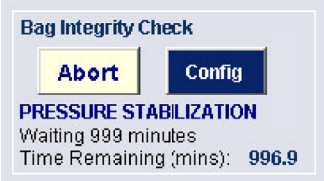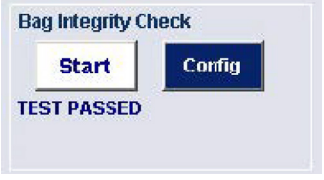Table F.5. Bag integrity operation in normal mode (continued).

Mode	Display status	Operation
PRESSURE STABILIZATION	**Bag Integrity Check** [Abort] [Config] PRESSURE STABILIZATION Waiting 999 minutes Time Remaining (mins): 996.9	• 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 **Abort** will skip the below steps and proceed to SEQUENCE ABORTED in the Abort Mode table. **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. 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.
		Next normal mode: PRESSURE HOLD TIME / **Failure mode:** N/A
PRESSURE HOLD TIME	**Bag Integrity Check** [Abort] [Config] PRESSURE HOLD TIME Change (torr): 0 Limit: 1 Time Remaining (mins): 0.4669	• 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 **Abort** will skip the below steps and proceed to SEQUENCE ABORTED in the Abort Mode table.
		Next normal mode: PRESSURE HOLD TIME / **Failure mode:** N/A
PASSED	**Bag Integrity Check** [Start] [Config] TEST PASSED	Sequence completes successfully, confirming no leakage in the bag.
		Next normal mode: PRESSURE HOLD TIME / **Failure mode:** N/A

Table F.6. Bag integrity operation in failure mode.
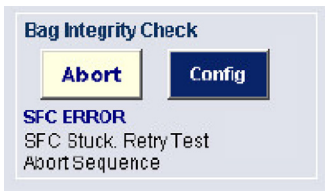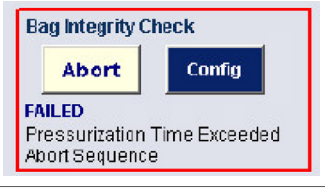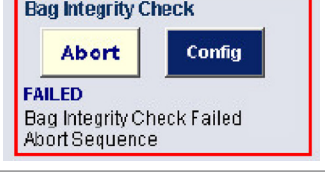
Mode	Display status	Operation
SFC ERROR		• Sequence in error state and will not proceed to next stage without user action. • Occurs if the number of repressurization has exceeded and the current pressure is not within the allowable stabilization drop limit. • The user is requested to select **Abort** and restart the sequence.
FAILED TIMEOUT		• 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 **Abort** and restart the sequence.
FAILED		• Sequence failed due to leakage detected within the bag. • **LEAK_DETECTED** alarm is visible to the user. • The user is requested to select **Abort** and restart the sequence.

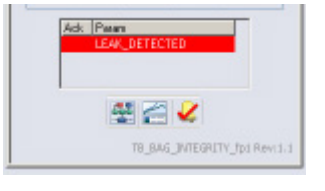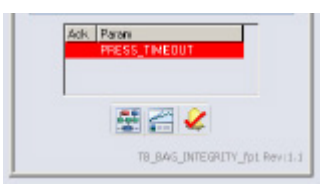Table F.7. Bag integrity operation in abort mode.

Mode	Display status	Operation
SEQUENCE ABORTED		• Sequence aborted by user. • **Start** is visible once the sequence is automatically reset and ready for next transition.

Table F.8. Bag integrity operation in abort mode.

Mode	Display status	Operation
LEAK_DETECTED		• 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.
PRESS_TIMEOUT		• 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.

F.8 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)

F.9 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 F.5.

	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-I	Control Module			PROCES		Bag Integrity Check TEST PASSED
	20/09/2017 15:04:47.260	ALARM	PROCESS	AREA_V2	PROPLU	V2	V2-BAG-I	Control Module	LEAK_DETECTED	INACTIV	14-UNIT_	Alarm	Bag Integrity Check
	21/09/2017 11:11:36.195	EVENT	PROCESS	AREA_V2	PROPLU	V2	V2-BAG-I	Control Module			PROCES		Bag Integrity Check SEQUENCE ABORTED
	21/09/2017 11:11:36.195	ALARM	PROCESS	AREA_V2	PROPLU	V2	V2-BAG-I	Control Module	PRESS_TIMEOUT	INACTIV	14-UNIT_	Alarm	Bag Integrity Check

Figure F.5. Event journal example.

F.10 Process history

A chart named **TB_BAG_INTEGRITY_fp.phve** is supplied as standard as part of the add-on package. Click **Process History View** on the bag integrity check faceplate to load the chart. 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)

F.11 Security

Table F.1010 defines which actions can or cannot be made by different users of the 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 G—Specific sensor calibration instructions

G.1 Optical DO sensor alternative calibration options

Optical DO sensors can be calibrated either by two-point calibration or one point calibration. Examples of optical DO sensors include Hamilton™ Visiferm™ and Hamilton™ Visiferm™ SU probes with S0 or S3 caps, or Mettler Toledo™ InSUS™ head and Mettler Toledo™ InSUS™ 607 cap. In order to use one-point calibration, a two-point calibration must initially be performed. A two-point calibration can be performed either online or offline. For online calibration, please refer to section 3.5.3 while noting the initial steps outlined below.

G.1.1 Offline two-point DO calibration

Initial steps

Follow these instructions to perform an offline two-point calibration for the optical DO probe (refer to the figures in section 3.5.3 DO calibration on page 95 for help):

1. From the **Calibration** tab of the **Detail** window, click **Calibrate**. This opens a series of screens that walk you through the process.

    Note: TruBio Software allows multiple probes to be calibrated concurrently.

2. Enter the manufacturer and the serial number of the probe to be calibrated under **Device Details**. Ensure that you enter an identifier for the specific probe, such as the probe serial number. Do not enter the serial number of the associated single-use cap.

3. Select the **2 Point** radio button under **Select Calibration Type** (Figure 3.23).

4. Click **Next** at the bottom of the screen. The display advances to the **Zero/Low Calibration** screen.

Zero/Low calibration point

The offline method uses alternative methods to gain the calibration point.

Offline calibration point

1. Connect the probe to a separate disposable cap, such as an S0/S3 or InSUS 607 cap. Ensure that the cap is irradiated at approximately the same dose as integrated with the BPC.

2. There are multiple options to gain a zero/low calibration point.

    – Immerse the probe in a flow of nitrogen or CO_2.

    – Immerse the probe in an Na_2SO_3 or a zero point gel.

    – Use an electrical zero by disconnecting the probe from the cap (using an electrical zero can degrade the accuracy to ±5%).

3. Allow the zero/low calibration to stabilize.

4. Once the **Zero/Low** reading is stable (Figure 3.24), click **Next**.

Span/High calibration point

Offline calibration point

1. Remove the probe from the nitrogen flow and allow 2–3 minutes for the nitrogen to dissipate. The span/high reading (100% saturation) is generally taken with the probe exposed to ambient air.

   – Click the Use the **Temperature Compensation value** check box (Figure 3.25). Place the temperature probe (if separate) in the buffer or air along with the DO probe, and the system will integrate the temperature reading from the probe.

2. Once the **Span/High** reading is stable, click **Next**.

Calibration Details

1. Under **Calibration Details**, enter the actual DO values in the **LOW** and **HIGH Scale** fields.

2. If you are not using Temperature Compensation, enter the temperature from an external temperature device in the **Temperature Compensation** field (Figure 3.26).

3. Enter the actual pressure reading in mbar in the **Pressure** field (Figure 3.26).

4. Click **Next**.

5. Add any required comments, enter the supervisor or administrator user name and password, and click **Write Calibration Data**.

G.1.2 One-point DO Calibration

A one-point calibration requires a probe that has been previously calibrated using a two-point calibration. It is important that the serial number of the probe was selected instead of the serial number of the cap.

1. From the **Calibration** tab of the **Detail** window, click **Calibrate**. This opens a series of screens that walk you through the process.

   Note: TruBio Software allows multiple probes to be calibrated concurrently.

2. Enter the manufacturer of the probe to be calibrated under **Device Details**. Select the serial number of the previously calibrated probe from the Serial Number drop-down menu (see Figure 3.22).

3. Select the **1 Point** radio button under **Select Calibration Type** (Figure 3.23).

4. Click **Next** at the bottom of the screen. The display advances to the **Zero/Low Calibration** screen pre-loaded with the calibrated zero/low value of the probe.

5. The span/high reading (100% saturation) is generally taken with the probe exposed to either ambient air or an air saturated solution in situ (such as cell culture medium or water).

   – Click the Use the **Temperature Compensation Value** check box (Figure 3.25). Place the temperature probe (if separate) in the buffer along with the DO probe, and the system will integrate the temperature reading from the probe.

6. Once the **Span/High** reading is stable, click **Next**.

7. Under **Calibration Details**, enter the actual DO values in the **LOW** and **HIGH Scale** fields.

8. If you are not using Temperature Compensation, enter the temperature from an external temperature device in the **Temperature Compensation** field (Figure 3.26).

9. Enter the actual pressure reading in mbar in the **Pressure** field (Figure 3.26).

10. Click **Next**.

11. Add any required comments, enter the supervisor or administrator user name and password, and click **Write Calibration Data**.

Table G.1 shows the accuracy of the several optical probes and caps after initial calibration.

Table G.1. Lot-to-lot accuracy of several probe and cap combinations after initial two-point calibration.

Probe	Vendor part number	Cap	Accuracy at:		
			20% saturation	100% saturation	200% saturation
Visiferm SU ECS	Hamilton 10116427	S0 or S3	± 2.5%	± 1.0%	± 5.0%
Visiferm ECS	Hamilton 243666-211	S0 or S3	± 5.0%*	± 1.0%	NA
Mettler Toledo InSUS head	Mettler Toledo 30015171	InSUS 607	NA	± 2.5%	NA

* Using an electrical zero method.