thermo scientific

50 and 500 L HyPerforma DynaDrive S.U.B. User's Guide

DOC0090 • Revision B

December 2020

ThermoFisher SCIENTIFIC

Contents

Warnings, safety, and warranty information

Thank you for purchasing high-quality Thermo Scientific equipment. We have included safety information in this guide, based on our knowledge and experience. It is important, however, for you to work with your Safety Management personnel to ensure that this equipment is integrated into your safety practices. Please take some time to perform your own job safety analysis in order to identify and control each potential hazard.

WARNING: Read and understand this user's guide before operating the equipment.
The Thermo Scientific™ HyPerforma™ DynaDrive Single-Use Bioreactor (S.U.B.) is designed to be operated under traditional eukaryotic cell culture conditions. A general understanding of bioreactor systems and their operation is important prior to using the system for the first time. Read and understand this user's guide before operating; failure to do so could result in injury and potential loss of product. Only trained operators should be allowed to operate the equipment.

WARNING: Hazardous voltage inside.
The agitation motor, motor controller, and electrical control panel (E-Box) all have electrical components. There is a risk of electrical shock and injury. Disconnect power before opening electrical components. Service should be performed by certified personnel only.
Please note any electrical hazard labels on the equipment. Thermo Fisher Scientific recommends using standard lockout procedures when working on electrical components. The main breaker on the E-Box may be locked out.

WARNING: Static electricity may build up in BPCs.

- BioProcess Containers (BPCs) may act as insulators for electrostatic charge. If electrostatic charge is transferred to a BPC, the charge may be stored in the BPC and/or the product inside. This phenomena varies by product and use; therefore, it is the sole responsibility of the end user to ensure a hazard assessment is conducted and the risk of electrostatic shock is eliminated.
- Where applicable, a product contact stainless steel coupler may be grounded to the frame to dissipate electrostatic buildup from the material within a BPC. It is good practice to dissipate electrostatic buildup by grounding all BPCs prior to coming in contact with them. When working with BPCs, the use of nonconductive materials, such as nonconductive gloves, is recommended.

WARNING: Rotating parts—entanglement hazard.
Rotating and moving parts can cause injury. Keep hands away from moving parts during operation.

- Do not operate this equipment unless the supplied guarding is in place and properly functioning.
- It is the responsibility of the end user to assess this equipment and ensure that equipment and safeguards are in good working condition, and that all operators are trained and aware of entanglement hazards and associated protective devices, such as hazard signs and guarding.

WARNING: Follow lockout/tagout procedures.
To prevent injury, when servicing equipment, use your company's lockout/tagout procedures to isolate electrical, mechanical, pneumatic, hydraulic, chemical, thermal, gravitational, or any other potential energy and protect workers from the release of hazardous energy.

WARNING: Use caution with hazardous chemicals or materials.
Personnel servicing equipment need to know the hazards of any chemicals or materials that may be present on or in the equipment. Use general hazard communication techniques such as Safety Data Sheets, labels, and pictograms to communicate any hazards. Note that this machine does not produce or process any toxic, corrosive, flammable, and explosive substances, nor uses any additives, compounds of mercury, cadmium, chromium, asbestos, CFC, or HCFC for machine maintenance purposes.

WARNING: Use a properly configured and approved power cord for voltage supply in your facility.

WARNING: Burst hazard—air under pressure.
The DynaDrive S.U.B. BPC chamber is under slight pressure under normal operating conditions. Normal passive venting prevents any excess of pressure building up within the chamber. Chamber pressure and inlet line pressure should be monitored for proper settings.

- Contents under pressure
- Do not exceed 34 mbar (0.5 psi) BPC pressure
- Do not exceed 340 mbar (5 psi) inlet pressure
- Ensure vent filter is correctly positioned and working properly

WARNING: Hot surface. Do not touch.
The heating jacket is designed to heat the inner vessel wall. Normal operating conditions generate heat, and could create hot surfaces.

- Hot surface inside
- Contact with surfaces may cause burns
- Do not touch while in operation

WARNING: Pinch hazard.
To avoid pinching and injuring an operator or causing damage to the equipment or the BPC, use caution when opening and closing the door, securing the BPC to the bottom port in the tank, or during operation of the DynaDrive S.U.B.

WARNING: Tipping hazard. The vessel should only be moved by pushing using the provided handles or at the mid-point of the vessel.
If pulled or moved too quickly, the vessel can tip, potentially leading to damage to equipment or injury to personnel. To reduce the risk of tipping, the vessel should only be moved slowly over smooth, flat surfaces by at least two qualified personnel. During movement, any locking feet should be retracted, and casters should be in the unlocked position. The vessel should not be moved by pulling of any kind.

WARNING: The Thermo Scientific HyPerforma DynaDrive S.U.B. may not be installed in a potentially explosive atmosphere as set forth in the applicable EU ATEX Directive.
It is the responsibility of the end user to review and understand the potential dangers listed in the ATEX 2014/34/EU guidelines.

WARNING: Use ladders and elevated platforms with caution.
A few operations, such as loading a BPC into a 500 L DynaDrive S.U.B., may require the use of a ladder or platform. Before use, ensure the ladder has been inspected and weight-rated for its user. When using a ladder or platform, be sure it is stable, maintain three points of contact, and make sure the steps are clean.

Protective earth grounding

Protective earth grounding must be verified prior to plugging the DynaDrive S.U.B. into any electrical outlet. Ensure the receptacle is properly earth grounded.

Environmental conditions

- Operating: 17 to 27°C; 20 to 80% relative humidity, non-condensing
- Storage: –25 to 65°C
- Installation category II (over voltage) in accordance with IEC 664
- Altitude Limit: 2,000 meters (6,561.68 ft.)

Electrical connections

Power should be supplied by a non-GFCI 15 amp circuit. Ground faults occur when current is leaking somewhere; in effect, electricity is escaping to the ground. **Electrocution can occur when the human body serves as the path for the leakage to the ground.** A ground fault circuit interrupter (GFCI) senses the current flowing to the ground and switches off the power (trips the GFCI) in a fraction of a second at currents well below those that are considered dangerous. Due to the sensitivity of GFCIs to electrical leakage (a few mA), it is recommended that DynaDrive S.U.B.s are NOT plugged into a GFCI outlet.

Power outlet accessibility

For safety, the power outlet used to power the unit must be accessible at all times. In case of emergency, you must be able to immediately disconnect the main power supply to all of the equipment. Allow adequate space between the wall and the equipment so that power cords can be disconnected in case of emergency.

Water jacket vessel information

The DynaDrive S.U.B. water jacket has been designed to be operated with water as the heat transfer medium, with temperatures not exceeding 50°C (122°F) under less than 1 MPa (150 psig) operating pressure. For the utmost safety, it is recommended that the DynaDrive S.U.B. be operated at 5.17 bar (75 psig) or less.

Note: The DynaDrive S.U.B. BPC operating limits for temperature are 5°C to 40°C. The internal pressure should not exceed 30 mbar (0.5 psi). The water jacket is not required to be registered, inspected and stamped with the Code U symbol per section U-1(c)2(f) of the ASME Boiler and Pressure Vessel Code and/or European Pressure Equipment Directive (PED) 97/23/EC. Upon request, a Declaration of Conformity, PED Sound Engineering Practices can be made available.

Warranty information

Any warranties, if applicable, covering this equipment exclude: (a) normal wear and tear; (b) accident, disaster or event of force majeure; (c) your misuse, fault or negligence; (d) use of the equipment in a manner for which it was not designed; (e) causes external to the equipment such as, but not limited to, external puncturing, power failure or electrical power surges; (f) improper storage and handling of the equipment; (g) use of the equipment in combination with equipment or software that we did not supply; (h) equipment sold to you as 'used' products; (i) contact with improperly used or unapproved chemicals or samples; (j) installation, removal, use, maintenance, storage, or handling in an improper, inadequate, or unapproved manner, such as, but not limited to, failure to follow the documentation or instructions in the deliverables or related to the equipment, operation outside of stated environmental or other operational specifications, or operation with unapproved software, materials or other products; (k) manufacture in accordance with requirements you gave us; (l) installation of software or interfacing or use of the equipment in combination with software or products we have not approved; (m) use of the deliverables or any documentation to support regulatory approvals; (n) the performance, efficacy or compatibility of specified components; and (o) the performance of custom equipment or products or specified components or achievement of any results from the equipment, specified components or services within ranges desired by you even if those ranges are communicated to us and are described in specifications, a quote, or a statement of work. **ADDITIONALLY, ANY INSTALLATION, MAINTENANCE, REPAIR, SERVICE, RELOCATION OR ALTERATION TO OR OF, OR OTHER TAMPERING WITH, THE EQUIPMENT PERFORMED BY ANY PERSON OR ENTITY OTHER THAN US WITHOUT OUR PRIOR WRITTEN APPROVAL, OR ANY USE OF REPLACEMENT PARTS WE HAVE NOT SUPPLIED, WILL IMMEDIATELY VOID AND CANCEL ALL WARRANTIES WITH RESPECT TO THE AFFECTED EQUIPMENT. IF THE EQUIPMENT IS TO BE USED IN THE UNITED STATES, WE MAY VOID YOUR WARRANTY IF YOU SHIP THE EQUIPMENT OUTSIDE OF THE UNITED STATES.**

Use restrictions

You must use this equipment in accordance with our documentation and if applicable, with our other associated instructions, including without limitation, a "research use only" product label or "limited use" label license. This equipment is intended for research use or further manufacturing in bioprocessing applications and not for diagnostic use or direct administration into humans or animals, we do not submit the equipment for regulatory review by any governmental body or other organization, and we do not validate the equipment for clinical or diagnostic use, for safety and effectiveness, or for any other specific use or application.

Seismic guidance

The buyer of the equipment is responsible to ensure country specific codes and seismic values are assessed for suitability of equipment installation and safety at the designated site. In addition, it is the buyer's responsibility to assess the building structure for the designated equipment to ensure correct seismic anchoring and tethering designs for both the equipment and facility. It is highly recommended that the buyer consult with a local, licensed third party architecture and engineering firm to provide the buyer with correct engineering analysis and stamped documentation prior to equipment installation at the facility. In addition, the buyer will be responsible for rigging and anchoring of the equipment to a specified, fixed location. Thermo Fisher can assist with establishing compliant seismic anchoring and tethering designs for purchased equipment based on building and country codes upon request at an agreed-upon fee.

It is also noted that movable equipment (i.e. non-fixed or caster mount) is exempt from seismic design requirements according to ASCE 7-16, Chapter 13, section 1.4. Although these units are exempt from the seismic design requirements of ASCE 7, it should be noted that such equipment is susceptible to overturning during a seismic event. Therefore, it is the responsibility of the buyer to address seismic safety for movable equipment at the designated facility.

How to use this guide

Scope of this publication

This user's guide contains information about the standard 50 and 500 L Thermo Scientific™ HyPerforma™ DynaDrive S.U.B. systems, including hardware, components, 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

Revision	Date	Section	Change made	Author
A	09/2020	--	Initial release (50 L only)	E. Hale
B	12/2020	--	Added information for 500 L	E. Hale
B	12/2020	4.5	Corrected part numbers for foam probe holder and BPC tab holders	E. Hale

Questions about 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.

Related publications

Please contact your local sales representative for information about the related publications listed below.

Publication	Document number
HyPerforma DynaDrive S.U.B. Unpacking Guide	DOC0149
50 L HyPerforma DynaDrive S.U.B. Quick Start Guide	DOC0148
500 L HyPerforma DynaDrive S.U.B. Quick Start Guide	DOC0171
HyPerforma DynaDrive S.U.B. Validation Guide	DOC0172
BioProcess Container (BPC) Unpacking and Inspection Guide	DOC0021

Abbreviations/acronyms

Refer to the list below for definitions of the abbrieviations and acronyms used in this publication.

ASCE	American Society of Civil Engineers
ASME	American Society of Mechanical Engineers
BPC	BioProcess Container
cGMP	Current good manufacturing practices
DO	Dissolved oxygen
E-Box	Electrical control panel
ETP	Equipment Turnover Package
GFCI	Ground fault circuit interrupter
IEC	International Electrical Code
OD	Outer diameter
PED	Pressure Equipment Directive
P/V	Power input to volume
RTD	Resistance temperature detector
S.U.B.	Single-Use Bioreactor
TCU	Temperature control unit
USP	United States Pharmacopeia
VFD	Variable frequency drive

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50 and 500 L DynaDrive S.U.B. overview

Chapter contents

1.1 Introduction to the DynaDrive S.U.B.

The Thermo Scientific HyPerforma DynaDrive Single-Use Bioreactor (S.U.B.) offers a flexible new alternative to traditional stirred-tank mixing. The system uses a redesigned impeller system: a drive train is connected to both an overhead mixing motor via a sealed bearing assembly and the bottom of the tank, allowing improved mixing while maintaining the integrity of the system. In addition, the DynaDrive S.U.B. facilitates greater scalability by allowing users to begin mixing at only 10% volume in 50 L units and 5% volume in 500 L units.

Each DynaDrive S.U.B. system consists of the following main components:

- **Stainless steel outer support container** with a water jacket heating system. The outer support container is made of 304 stainless steel, and holds and supports the BioProcess Container (BPC). The square shape of the DynaDrive S.U.B. allows an optimized footprint in contrast to traditional round reactors.
- **BPC**, which is supplied gamma irradiated for ready-to-use, single-use mixing. The flex drive train is located entirely inside of the BPC, and connects to the reactor at the bottom of the tank in addition to the standard top hub, removing the need for traditional drive shafts.
- **Control system**, provided by Thermo Scientific or a third party.

The **outer support container** is a stainless steel vessel that is engineered and fabricated to fully support each BPC and allow easy access for operation. The outer support container contains the water jacketed tank on casters. Load cells are standard for all systems.

Figure 1.1. 50 and 500 L DynaDrive S.U.B. systems.

The **BPC** includes the impeller assembly, sparger, vent filter inlet/outlet ports, probe integration ports, and filling, dispensing, and sampling ports. Each BPC comes fully assembled and gamma irradiated. The materials are fully qualified for biological product contact per USP Class VI guidance. Each assembly is manufactured under current good manufacturing practices (cGMP) and is supported by qualification and validation information. The system allows for the integration of the mixing shaft, pH/dissolved oxygen (DO) probes, and the resistance temperature detector (RTD). The probe and temperature interfaces are comparable to traditional systems with the design allowing for simple aseptic connections. Integrated spargers are built into the BPC through universal ports.

The HyPerforma DynaDrive S.U.B. utilizes an open architecture design for the **control system**, allowing for integration with customer systems or with third-party controllers for feed pumps, mass flow controls, and human-machine interface (HMI) screens. Controls for agitation are integrated into the S.U.B., with pH/DO probes and controls being supplied by the user or a third-party integrator. HyPerforma DynaDrive S.U.B. systems require a temperature control unit (TCU) selected and supplied by the end user or by Thermo Fisher Scientific.

This user's guide covers the setup, operation, maintenance, and troubleshooting of 50 and 500 L DynaDrive S.U.B. systems.

1.2 Hardware characteristics

1.2.1 DynaDrive S.U.B. hardware components

Figures 1.2–1.5 below illustrate all available components of 50 and 500 L DynaDrive S.U.B. systems.

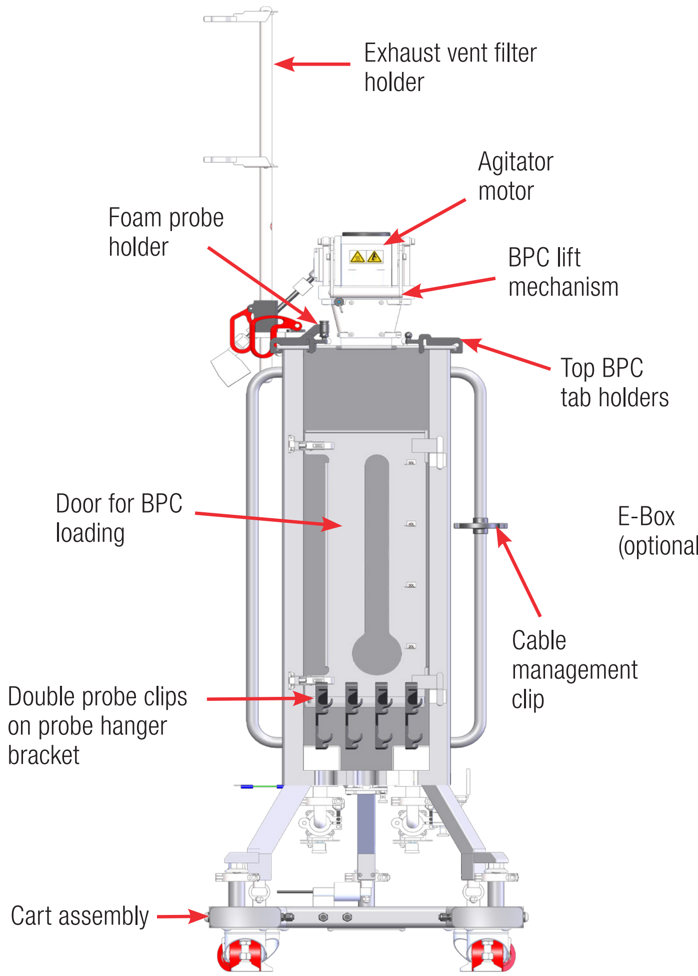


Figure 1.2. Front view of 50 L DynaDrive S.U.B. (without optional E-Box).

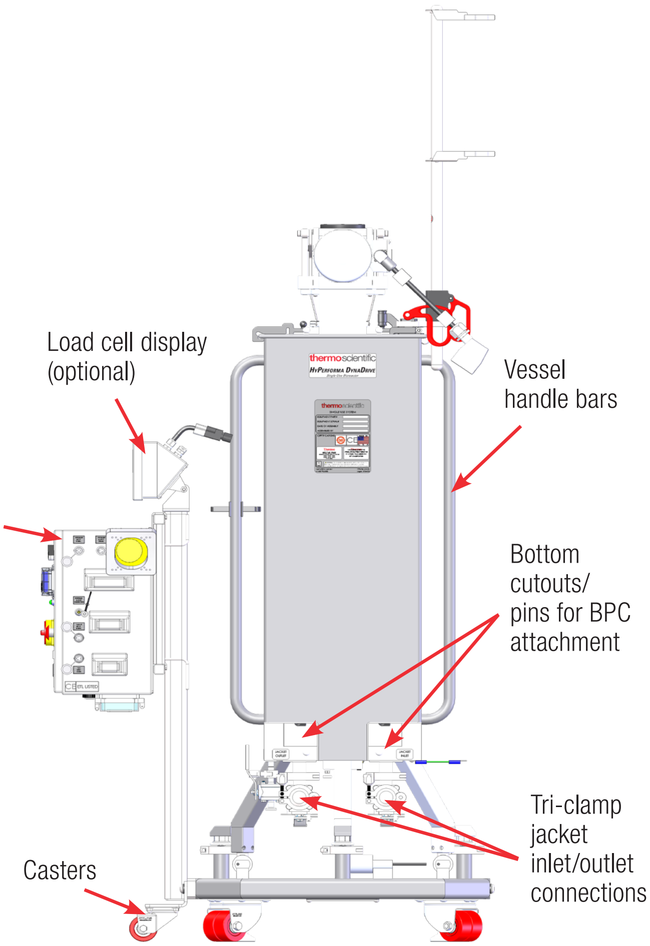


Figure 1.3. Back view of 50 L DynaDrive S.U.B. (with optional E-Box).

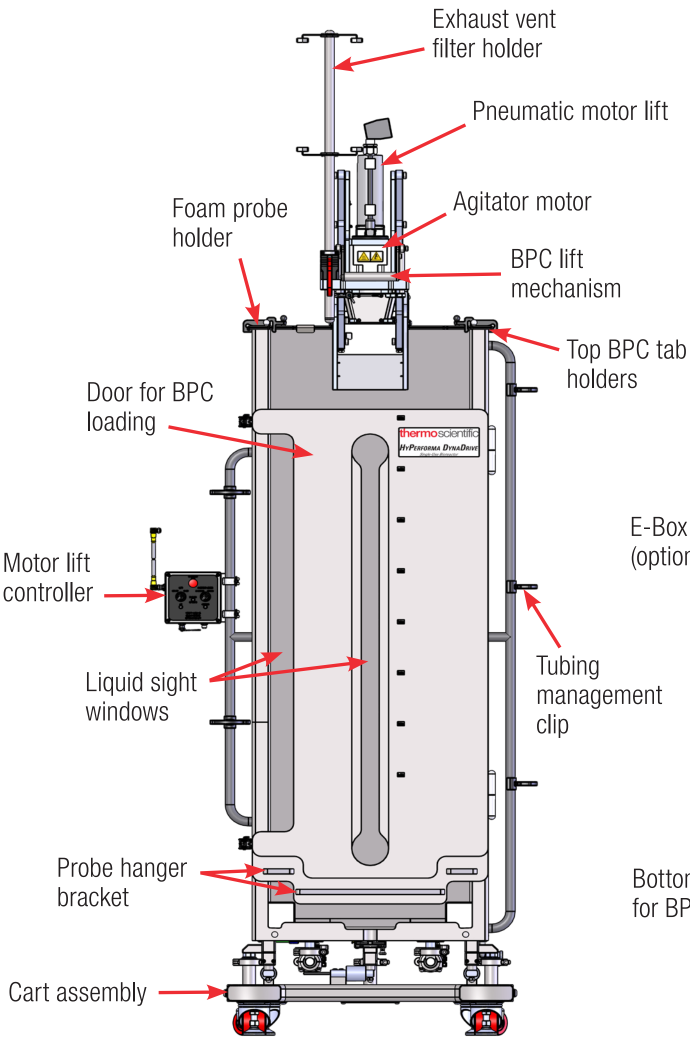


Figure 1.4. Front view of 500 L DynaDrive S.U.B. (without optional E-Box).

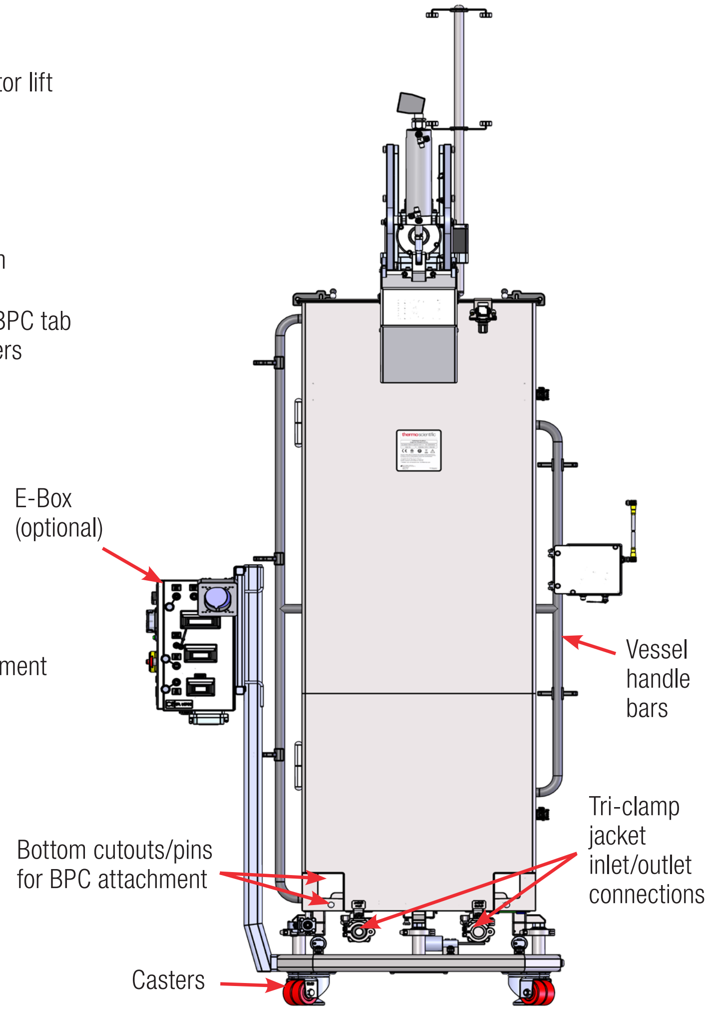


Figure 1.5. Back view of 500 L DynaDrive S.U.B. (with optional E-Box).

1.2.2 S.U.B. system features

The S.U.B. is designed for system mobility and easy integration, and utilizes a straightforward operator interface. The following sections give general descriptions of S.U.B. hardware features.

Agitation

Agitation is dependent on your system integration. If your system uses an AC motor and a Thermo Scientific electrical control panel (E-Box), the stirring speed is adjusted by using the E-Box keypad interface. The agitation control interface utilizes a digital display to indicate stirring speed in units of revolutions per minute (rpm). Power is supplied to the motor by a two-position power switch. The up and down arrows on the agitation keypad adjust the stirring speed.

Bioreactor control system

The DynaDrive S.U.B. is designed to integrate with existing bioreactor control systems in their numerous configurations, including Thermo Scientific G3 controllers using TruBio with Emerson™ DeltaV operating software. The S.U.B. control system supplied with the Thermo Scientific E-Box manages the agitation process parameters. Parameters of pH and DO, gas management, feed addition, and base addition control must be managed by an external controller supplied by the end user or a third-party integrator.

Temperature

The S.U.B. can be operated within the temperature range from ambient to 40°C. The process temperature is measured by means of a supplied RTD (pt-100) that is inserted into the thermowell of the BPC. Water jacket system temperature control is maintained through the TCU.

Heating performance

Heating times for the S.U.B. systems vary based upon operating liquid volume and temperature, ambient or heating fluid temperature, sparge rate, and mixing rate. Users should adjust process liquid staging and seeding strategies to the unique aspects of the S.U.B. Process controllers are designed to provide optimum heat transfer and to minimize heat-up times while maintaining the material integrity of the polymer film construction of the BPC. Refer to section 3.1.4 for expected heating times.

1.2.3 Additional system components

Probe integration

The optional autoclave tray (Figure 1.6) holds electrochemical probes and bellows in place during the autoclave sterilization process. Design elements include the following:

- Fabricated from stainless steel
- Features a plastic handle for easy transport right out of the autoclave
- Positions probes on 15% incline for greater probe/membrane longevity
- Will restrain probe bellows from collapsing during sterilization
- Accommodates two reusable probes

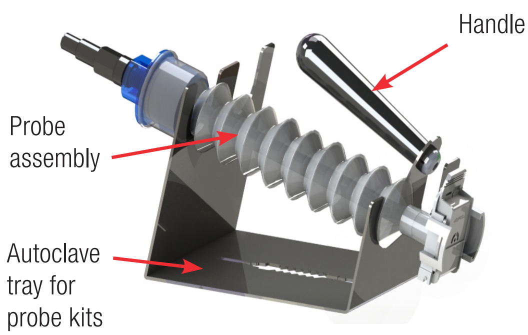


Figure 1.6. Autoclave tray and probe assembly.

The probe assembly (Figure 1.7) is an innovative design to package user-supplied pH and DO probes for sterilization, and to aseptically connect them to the BPC. The probe assembly includes an aseptic connector, molded bellows cover, and threaded probe adapter.

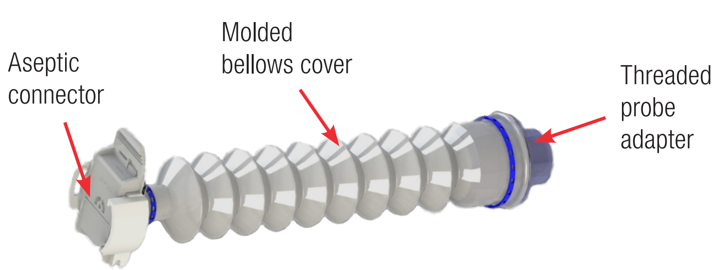


Figure 1.7. Probe assembly.

Pneumatic motor lift (500 L only)

The 500 L DynaDrive S.U.B. uses a pneumatic motor lift (Figure 1.8) to fully raise the BPC inside the outer support container. The motor lift controller mounted to a front vessel handle bar (Figure 1.9) is used to control the lift. **Note:** The pneumatic motor lift requires 80–90 psi of air pressure to operate.

Turn the lift switch to "Lower" or "Raise" to adjust the position of the pneumatic motor lift. Turn the motor lock switch to "Locked" to prevent the pneumatic motor lift from being lowered or raised. **Note:** The pneumatic motor lift will not lock if it is not fully raised. Check the indicator lights to determine if the motor lift is in the "Up" position, locked, and safe to operate. The lights will remain red if these requirements are not met (Figure 1.10).

Figure 1.8. Pneumatic motor lift.

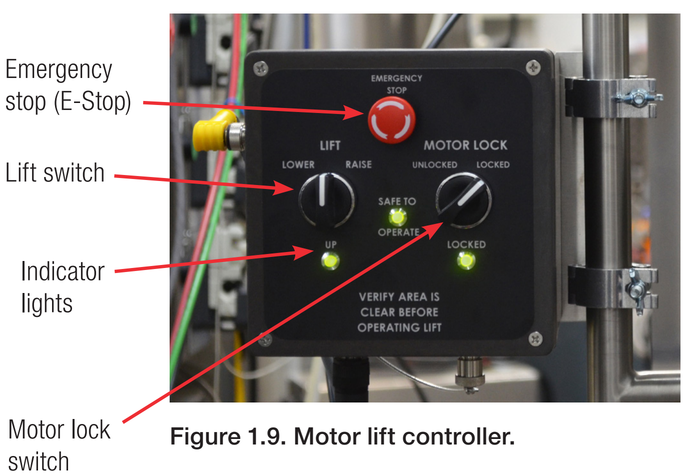


Figure 1.9. Motor lift controller.

Figure 1.10. Red lights indicating lift is not raised, locked, or safe to operate.

Options and accessories

The following additional system components may or may not be installed on your DynaDrive S.U.B. system. To order accessories for retro-fitting to your unit, contact your sales representative.

Exhaust vent filter heaters

The exhaust vent filter heater system, which includes the heater, a controller, and power cord (Figures 1.11 and 1.12), is available for increased longevity of the exhaust filter on the BPC. The heating element is fully insulated with molded silicone and secured around the filter by use of snap retainers, fully encapsulating the exhaust filters for consistent temperature regulation. Heating the filter sufficiently to eliminate the formation of condensation reduces the risk of fouling the filter membrane.

Figure 1.11. Vent filter heater for 50 L DynaDrive S.U.B.

Figure 1.12. Vent filter heater for 500 L DynaDrive S.U.B.

The heater is factory preset to operate between 40°C to 50°C, but can easily be adjusted to the demand of the application. Temperature settings above 60°C are not recommended.

Load cells

Load cells, which are used to determine the weight of the contents of a S.U.B., are optional for all standard DynaDrive S.U.B. systems. Load cells arrive uncalibrated. The load cell manufacturer or a qualified technician should calibrate these systems onsite.

The load cell kit comes with three load cells, summing block (for systems using the Thermo Scientific E-Box), wiring, and a display screen with a choice of several data interfaces (see Figure 1.13).

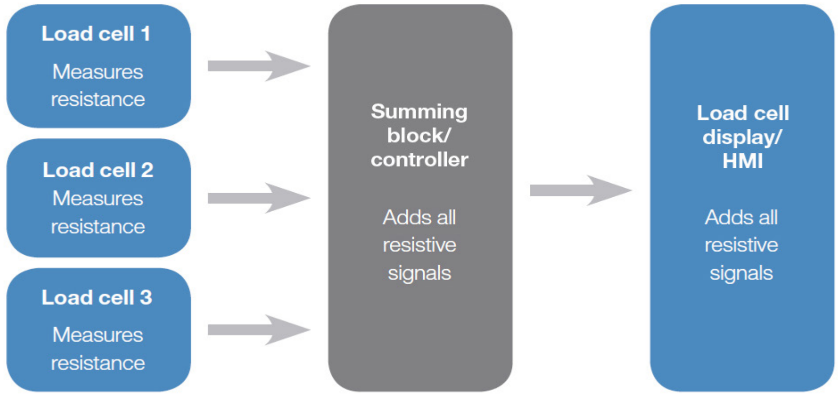


Figure 1.13. Load cell system overview.

Load cells are typically radial-mounted in sets of three. The mounting location (Figure 1.14) allows easy access to the bottom drain or sparging mechanisms and tubing.

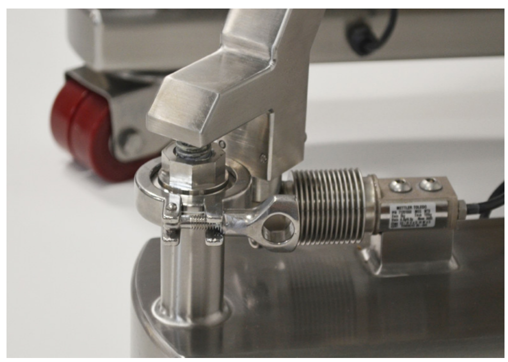


Figure 1.14. Load cell location.

AC motors

AC motors are required for all DynaDrive S.U.B. systems, and may be used with the Thermo Scientific E-Box. AC motors include a variable frequency drive, and are controlled using either the provided keypad or a controller specified by the end user. **Note:** Permanent magnet motors require a variable frequency drive (VFD) capable of this kind of control.

Miscellaneous items

The miscellaneous items listed here are ancillary components that support the operation of the HyPerforma DynaDrive S.U.B. for cell culture production, and enhance the overall performance of the complete system.

- **Sampling manifold with luer lock**
- **Temperature sample port**—For RTD calibration/validation
- **Double probe clips**—For holding probes and sensors from double rows of probe ports (Figure 1.15).

- **Heavy-duty tubing clamps (typically four or five)**—Tubing clamps (Figure 1.16) are required for pinching off line sets that are not in use in order to prevent process fluids from moving into the line sets. If no probe is going to be inserted, a tubing clamp must be placed to close off probe ports. For more information, see the BPC loading instructions in Chapter 3 of this publication.
- **Foam probe holders**—Foam probe holders secure the foam probe at the top of the BPC, and vary between sizes (Figures 17 and 18).
- **Tubing management clips**—Tubing management clips snap onto the vessel handle bars with a firm amount of pressure, and assist in organizing tubing (Figure 1.19). They can be configured in multiple ways for increased flexibility.

Figure 1.15. Double probe clip.

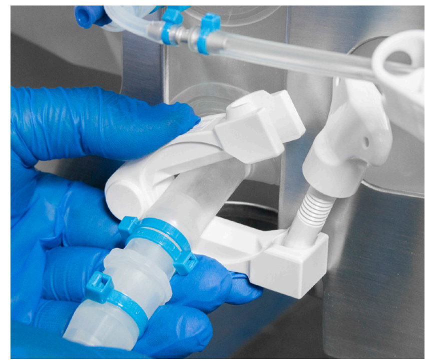


Figure 1.16. Heavy-duty tubing clamps.

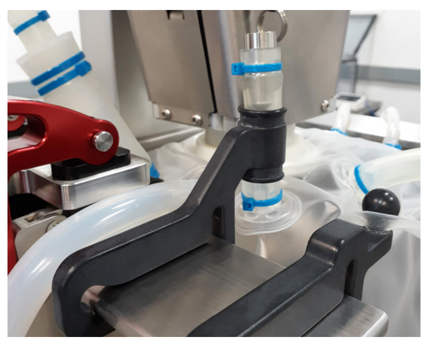


Figure 1.17. 50 L foam probe holder.

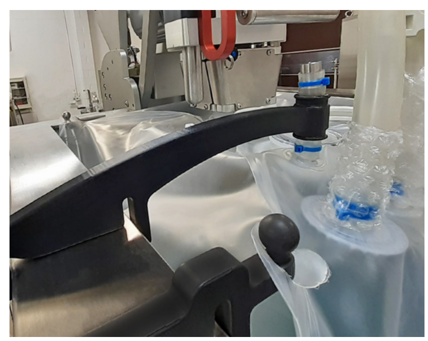


Figure 1.18. 500 L foam probe holder.

Figure 1.19. Tubing management clip.

1.3 End user and third-party supplied components

1.3.1 pH and DO probes

Table 1.1 shows the length and diameter requirements for traditional sensors (probes) that can be integrated into the S.U.B. These requirements are based on the necessary insertion depth of the probe when used with the probe ports. **Note:** The presence of a properly positioned O-ring on the probe is critical for use with the S.U.B.

Table 1.1. Manufacturers and models of compatible pH/DO probes.

Probe lengths (from O-ring to tip) must not exceed 235 mm				O-ring to probe tip	
				Print/lit.	Actual
Probe	**Part number**	**Diameter**	**Thread type**	**Length**	**Length**
AppliSens DO	Z010023525	12 mm (0.47 in.)	13.5 PG	235 mm (9.25 in.)	235 mm (9.25 in.)
AppliSens pH	Z001023551	12 mm (0.47 in.)	13.5 PG	235 mm (9.25 in.)	235 mm (9.25 in.)
Mettler Toledo DO	InPRO 6800/12/220, PN 52200966	12 mm (0.47 in.)	13.5 PG	215 mm (8.46 in.)	215 mm (8.46 in.)
Mettler Toledo pH	405-DPAS-SC-K8S/225, PN 104054481IG	12 mm (0.47 in.)	13.5 PG	195 mm (7.67 in.)	219 mm (8.62 in.)
Broadley-James DO	D140-B220-PT-D9	12 mm (0.47 in.)	13.5 PG	215 mm (8.46 in.)	214 mm (8.42 in.)
Broadley-James pH	F-635-B225-DH	12 mm (0.47 in.)	13.5 PG	225 mm (8.85 in.)	219 mm (8.62 in.)
Hamilton OxyFerm DO	F140-2109-225	12 mm (0.47 in.)	13.5 PG	225 mm (8.85 in.)	220 mm (8.66 in.)
Hamilton EasyFerm Plus pH	F140-2105-225	12 mm (0.47 in.)	13.5 PG	225 mm (8.85 in.)	220 mm (8.66 in.)

Note: Consult the probe manufacturer's website for appropriate probe cable connection and part number.

1.3.2 Controllers

Thermo Scientific products are designed with an open-architecture approach to the integration of controls. Our industry-leading S.U.B. has been integrated with most controllers on the market, allowing customers to choose the control system they want, or to reduce expense by integrating with a controller that is already onsite.

In order to facilitate integration, electrical schematics are provided in the ETP supplied with the HyPerforma DynaDrive S.U.B. Companies that offer control solutions in either current good manufacturing practices (cGMP) format or non-cGMP format for Thermo Scientific DynaDrive S.U.B. units are listed below.

- ABEC
- Bellco
- Broadley-James
- Dasgip
- Emerson
- Honeywell
- New Brunswick Scientific
- Pendotech
- Sartorius Stedim Biotech

The HyPerforma DynaDrive S.U.B is also available as a complete turnkey system through Thermo Fisher Scientific. These S.U.B. units may be provided with integrated controls, pump towers, a control monitor, and advanced features such as data logging, multiple S.U.B. connections, and optional 21CFR part 11 compliance for cGMP manufacturing. A variety of single-use sensors are available for pH, DO, and pressure control. Thermo Fisher Scientific can provide complete, integrated solutions using the manufacturers listed below.

- Allen-Bradley
- Applikon PLC eZ-controller
- Emerson Delta V
- Siemens

Contact your local sales representative for more information.

Note: The DynaDrive S.U.B. will work well with any of the various control system platforms, such as PLC, PC, DCS, or proprietary operating system based controllers.

1.4 DynaDrive S.U.B. BPC features

The cell culture itself is contained inside the BPC, which is supplied gamma irradiated. The chamber is manufactured from film, which is a co-extruded structure specifically designed for biopharmaceutical process usage. All materials are qualified for a broad range of physical, mechanical, biological, and chemical compatibility requirements. Refer to data in our BPC catalog and film validation guides; contact your sales representative for a copy.

1.4.1 Spargers

The standard DynaDrive BPC is designed with spargers (drilled hole, cross flow, and overlay) that produce very efficient mass transfer of oxygen. They typically require much less gas inflow than conventional spargers. Gas flow rates supplied as overlay or through the cross flow sparger should also be reduced as much as possible; this will minimize both liquid evaporation and demand on the exhaust filter. For more information, refer to sections 3.1 and 3.4 in this user's guide.

1.4.2 Exhaust vent filter

The exhaust vent filter used on 50 and 500 L DynaDrive S.U.B.s has hydrophobic PVDF membranes, and can be substituted for another appropriate filter. To maintain a sterile connection, the standard BPC is supplied with the filter arrow pointing toward the BPC. This ensures that the filter vents are outside of the sterile connection. For users with more demanding applications, an optional vent filter heater can be used. Up to two vent filters of variable sizes (5–10 inches) can be used on the 50 L DynaDrive S.U.B, while 500 L units only use 10 inch filters.

1.4.3 Connections

Multiple aseptic connection options exist for DynaDrive S.U.B. users. Standard BPCs include sections for use with the tubing welder, quick-connects, and CPC™ AseptiQuik™ connections. The BPC is designed with various lengths and dimensions of thermoplastic tubing for the purpose of adding to and dispensing from the BPC.

Sampling port

The S.U.B. is equipped with a small volume sample port that is adjacent to the BPC thermowell. This small-diameter silicone dip tube of 152.4 mm length (6 in.) allows low void volume samples to be taken for cell viability and density, as well as analyte analysis. This dip tube is supplied with a luer lock connector (SmartSite™) that allows for direct sampling or attachment of various sampling manifolds by use of standard luer lock connection. Alternatively, manifolds can be welded onto the C-Flex sample line using a tubing welder.

2

Hardware assembly and setup

Chapter contents

2.1 Initial installation preparation

2.1.1 Hardware shipment and setup

The DynaDrive Single-Use Bioreactor (S.U.B.) hardware will arrive crated. For detailed unpacking instructions and contents of the crate, please refer to the packaging drawings, which are included in the shipping crate, and the 50 and 500 L DynaDrive S.U.B. Unpacking Guide (DOC0149). Be sure to follow the unpacking instructions provided and retain all packaging materials.

2.1.2 Hardware uncrating

The DynaDrive S.U.B. hardware will arrive with the following items:
- Outer support container with platform, tank, exhaust vent filter holder, and optional electrical control panel (E-Box)
- Resistance temperature detector (RTD) and four probe clips
- Equipment Turnover Package (ETP), provided on a USB drive (shipped separately)

2.1.3 Site preparation

Because DynaDrive S.U.B.s use AC motors, the system cannot be used on circuits equipped with ground fault circuit interrupter (GFCI) circuit protection because of the potential for nuisance tripping.
The electrical plug on the S.U.B. is a connector that offers a secure ground. These connectors meet the electrical safety codes for portable equipment and are International Electrical Code (IEC) rated (meet IEC standard 60309). This plug provides electrical ground prior to power connection. The supplied electrical receptacle should be hardwired into the facility by a qualified electrical technician; for U.S. installations, the receptacle will require the use of an adapter mounting plate (supplied), which will fit into a two-gang box. For additional information on the adapter mounting plate, please see the ETP. Alternatively, the system can be hardwired directly into the facility. **Note:** The yellow plug and receptacle are for 120 VAC, and the blue are for 240 VAC S.U.B.s.

Outer support container preparation

Each outer support container is shipped directly from the manufacturer, and arrives with various safety mechanisms in place. Use the following guidelines to set up the DynaDrive S.U.B. upon arrival.

WARNING: Any procedure that requires the E-Box to be opened should be performed with the main electrical disconnect in the locked out position and all power sources removed from the E-Box. For operator safety, secure the location of the DynaDrive S.U.B. outer support container by disabling the swivel casters before servicing.

Electrical preparation (for systems with optional E-Box)

1. Using a flat-head screwdriver, open the E-Box and locate the breakers for the pressure sensor, continuous power outlets non E-stoppable (2), and continuous power outlets E-stoppable (2) (Figure 2.1). These breakers should be in the "on" position ("up" position or pressed in, depending on the breaker type) during operation. For electrical schematics, please refer to the ETP, which is provided on a USB drive.

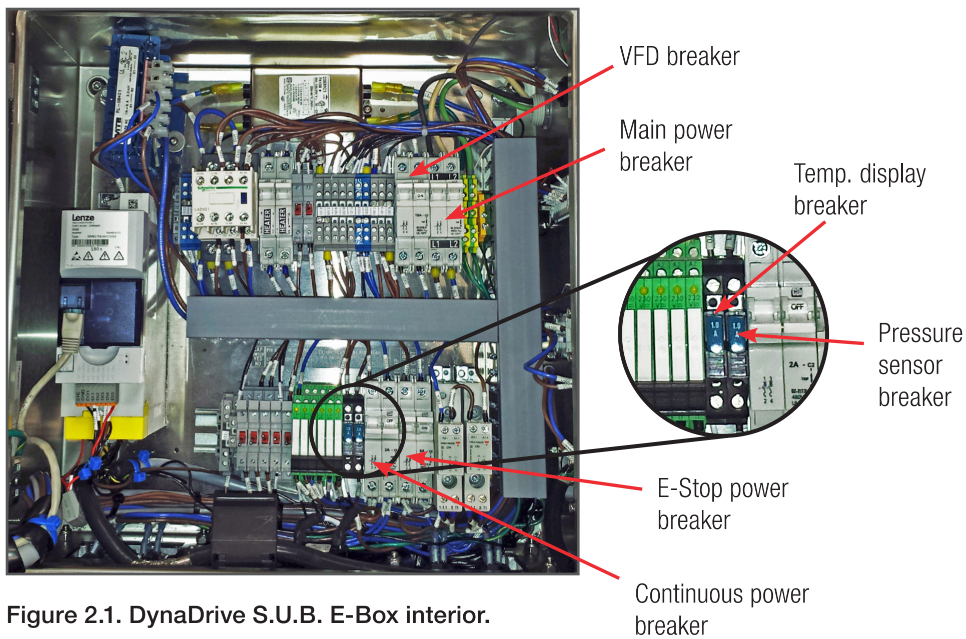


Figure 2.1. DynaDrive S.U.B. E-Box interior.

2. Close the E-Box and lock the panel using a flat-head screwdriver before continuing.

2.2 Installation and setup

2.2.1 Preparing load cells

All manual movements of mobile DynaDrive S.U.B. hardware should be over smooth surfaces, with the S.U.B. empty and disconnected from all power and gas/feed sources. All load cells must be fully locked down in order to move the DynaDrive S.U.B. **Note:** An adjustable (up to 3.175 cm (1.25 in.)) wrench (not supplied) is needed for locking and unlocking load cells.

WARNING: Tipping hazard. The vessel should only be moved by pushing using the provided handles or at the mid-point of the vessel.
If pulled or moved too quickly, the vessel can tip, potentially leading to damage to equipment or injury to personnel. To reduce the risk of tipping, the vessel should only be moved slowly over smooth, flat surfaces by at least two qualified personnel. During movement, any locking feet should be retracted, and casters should be in the unlocked position. The vessel should not be moved by pulling of any kind.

Follow the steps below to prepare load cells for use. Figure 2.2 illustrates the location and components of load cells, which will be referenced throughout the load cell preparation process.

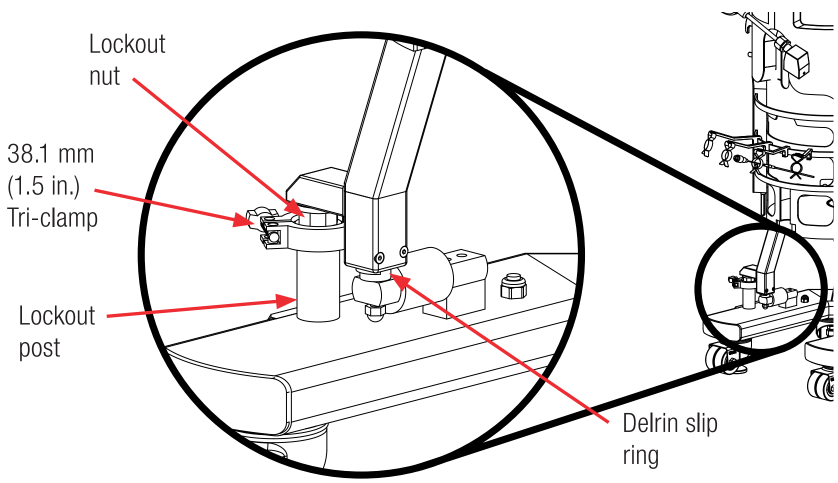


Figure 2.2. Close up view of load cells.

1. For DynaDrive S.U.B. hardware units purchased with factory-installed load cells, the load cells are shipped in the locked position (threaded up) for equipment protection.

2. To unlock the load cells, remove and discard the delrin slip ring if it is present. Remove the tri-clamp. Loosen the lockout nut, using the small end of an adjustable (up to 3.175 cm (1.25 in.)) wrench (not supplied), until the nut is tight against the base or leg of the S.U.B. Repeat this process for each load cell until all of the lockout nuts are disengaged from the lockout posts. Do not reinstall the tri-clamp.

3. At this point, the DynaDrive S.U.B. hardware is ready to be prepared for a cell culture run.

4. For systems with load cell display screens, refer to Appendix B for information about calibrating load cells.

CAUTION: Never move the unit while load cells are unlocked, as this can damage the load cells.

5. To lock load cells that have been unlocked, hand-tighten the lockout nut onto the post. Use the adjustable wrench to turn the nut an extra 1/4 turn.

CAUTION: To avoid damaging the load cells, do not over-tighten the nut. Assemble a standard stainless 38.1 mm (1.5 in.) tri-clamp around the flanges.

6. Complete this process for all load cells.

2.2.2 Leveling and connecting the system

All manual movements of mobile DynaDrive S.U.B. hardware should be over smooth surfaces, with the S.U.B. empty and disconnected from all power and gas/feed sources. All load cells must be fully locked down in order to move a S.U.B. Refer to the previous subsection of this guide for illustrations.

1. Verify that the facility electrical supplies are sufficient to support the power requirements of the DynaDrive S.U.B. and ancillary components, such as controllers or pumps.

2. Locate the outer support container in the area for the cell culture run.

3. When monitoring the batch volume, the unit may be placed on a weight scale if load cells are not part of the system. Other methods may be used to measure all incoming and outgoing liquids.

4. Level the platform by disabling the swivel casters on the bottom of the outer support container. This is accomplished by threading the leveling feet (at the center of each caster) to the floor.

5. Verify the location of the pH/DO controllers and ensure that the cable and tubing lengths are sufficient.

WARNING: Risk of electrical shock.

6. Verify that the main power is off and the emergency stop (E-Stop) is pulled out. **Note:** The E-Stop disconnects all power to the system. An alarm buzzer will sound when the E-Stop is activated.

7. Verify that the main motor power switch is in the "off" position.

8. Connect all electrical plugs to facility power. Refer to hardware/electrical labels and schematics to ensure proper electrical voltage is connected to the S.U.B. The main power switch can now be turned on.

9. Connect the inlet and outlet lines from the temperature control unit (TCU) quick-connects to the jacket (Figure 2.3). The inlet is typically on the right side if you are facing the connectors; refer to the permanent labels on the inlet and outlet lines. **Note:** Refer to the TCU manufacturer's guidelines for detailed TCU setup information.

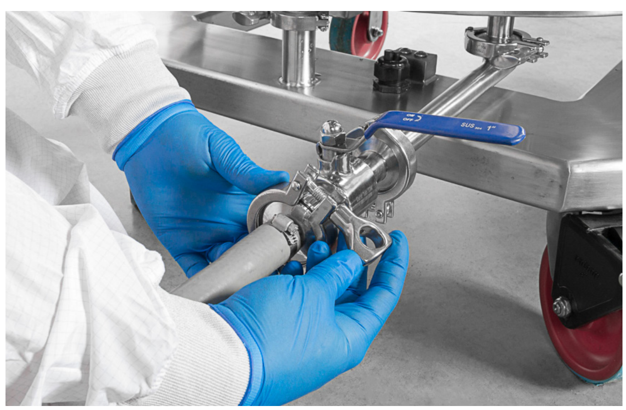


Figure 2.3. Attaching water jacket port using tri-clamp.

2.2.3 Additional items for assembly

Use the tri-clamp fitting to attach the water jacket inlet/outlet ports to the bottom of the outer support container (Figure 2.4). **Note:** Figure 2.4 shows the tri-clamp fitting and inlet/outlet ports on a standard HyPerforma S.U.B. The location and process is the same for DynaDrive S.U.B.s.

Figure 2.4. Removing the tri-clamp and attaching the fitting.

3

BPC loading and operating information

Chapter contents

3.1 General system operating information

3.1.1 BPC preparation

Each outer support container is designed for a specific BPC. Confirm that the correct volume and type of BPC is being used for the corresponding volume outer support container. Section 3.2 covers the installation and setup of BPCs. Follow these instructions in the order in which they are presented.

3.1.2 BPC handling instructions

If you are using a sharp object when opening outer polybags, take care to avoid damaging the BPC. Do not drag containers over corners or sharp objects. Do not lift the container by the corners or top seams. Carefully coil the tubing on top of the BPC to prevent puncturing the container with cable ties or clamps. Use cushioning between the tubing and the container in storage and transport.

3.1.3 BPC operating information

Working volume

Each DynaDrive S.U.B. is designed for a specific working volume range. The minimum working volume and the rated working volume are listed in the specification tables provided in Chapter 4 of this user's guide. The total volume listed includes the headspace needed for proper aeration and gas management.

Note: Actual working volumes should not exceed the indicated rated working volumes by more than 10% for 50 L units, or 5% for 500 L units. In addition, working volumes less than 10% or 5% of the rated volume in 50 and 500 L units, respectively, can result in damage to the BPC and/or the S.U.B. hardware.

Operating pressure

The BPC does not operate as a closed system; it has both inlet and exhaust filters that are utilized to maintain a sterile environment for cell growth. However, conditions can be encountered when the gas inlet flow rate may exceed the exhaust flow rate. This may be encountered in the unlikely event of a pressure regulator failure on a gas feed, or when excessive foam within the bioreactor creates a vent blockage.
Note: The BPC must be inflated prior to filling to avoid causing damage.

WARNING: The BPC is not rated as a pressure vessel. Gas pressure within the BPC headspace should not exceed 30 mbar (0.5 psi) at any time. Pressure above 30 mbar (0.5 psi) may result in BPC damage or personal injury.

- More demanding applications may warrant an optional exhaust vent heater.
- If foaming is excessive in your cell culture process, it is best to reduce the operating volume of the process to 80% of maximum rated working volume of the S.U.B. system being used to provide greater headspace volume.
- Single-use pressure transducers are available on custom S.U.B. configurations. This technology combined with high-level control systems (common with industrial applications) can regulate gas pressure within the confines of the S.U.B.

Aeration

Gas to liquid mass transfer in cell culture bioreactors is controlled by the solubility of the gas in the liquid, its distribution, and the temperature and pressure. Direct air sparging provides for the oxygen requirements of eukaryotic cell cultures. It allows optimal aeration of the culture process and effective carbon dioxide stripping. However, when compared to 2:1 mixing (50% working volume), 10:1 and 20:1 mixing can cause more carbon dioxide buildup in the extra headspace in the BPC when operating at 10% working volume in 50 L DynaDrive S.U.B.s and 5% working volume in 500 L units. This blanket of carbon dioxide may prevent proper cell respiration.

A cross flow sparging strategy disrupts the dense carbon dioxide blanket at the bottom of the BPC headspace, which lets users take advantage of low-volume mixing without compromising cell cultures. This strategy requires temporarily rerouting the overlay sparger to a cross flow port near the surface of the liquid when operating at 10% or 5% working volume. When the volume is increased above 10% or 5%, the sparge line should be returned to the standard overlay port to reduce carbon dioxide in the headspace, and a single drilled hole sparger is the main source of aeration.

Aseptic connections

The most commonly recommended process for making connections to the tubing lines is with an aseptic tubing fuser. Other connection options are available as a custom BPC assembly. By following the recommended tubing welder operating instructions, successful connections can be made for filling, supplementing, sampling, or dispensing from the BPC as needed.

Draining and harvest

The S.U.B. is equipped with a bottom drain line that allows for liquid harvest by means of peristaltic pump. Connection of the bottom drain line can be accomplished by use of a tubing welder or the fitting that is provided. The bottom drain exits the BPC at the lowest vertical position on the side of the S.U.B. This allows for easy access for the user and minimizes the accumulation of cells in the area of the drain during the cell culture run. Manipulation of the BPC as the last few liters of media drain will minimize liquid hold-up within the S.U.B.

3.1.4 Hardware operating information

Heating performance

Heating times for DynaDrive S.U.B. systems vary based on liquid volume and temperature, ambient or heating liquid temperature, sparging rate, and mixing rate. For 50 and 500 L heating times, see Table 3.1.

WARNING: Do not heat the system if the BPC is not at 10% liquid volume or greater in 50 L units, or at 5% or greater in 500 L units. Batch temperature should not exceed 40°C.

Table 3.1. Heating times for S.U.B. systems. Ambient temperature of 25°C; values assume a TCU heater size of at least 9 W/batch liter.

System	Liquid batch volume (10% / 100%)	Initial liquid	Liquid target	Time (10% / 100%)
50 L	5 L/50 L	5°C	37°C	1 hr/1.1 hr
500 L	50 L/500 L	5°C	37°C	1 hr/3 hr

Note: Conditions may vary based on your system connections and environment.

Protective earth grounding

Protective earth grounding for the DynaDrive S.U.B. hardware system and the controller is provided through the ground terminal of the power plug. Source power to the controller must provide protective earth grounding to this terminal in order to minimize the hazard of a possible shock in the occurrence of a fault condition. Please refer to Appendix A for information about electrical receptacles. A ground wire is provided underneath the S.U.B. and must be tied to the controller before operation.

Agitation control interface for units with E-Box enclosures

The agitation control interface utilizes a digital display to indicate stirring speed in units of revolutions per minute (rpm). Power is supplied to the motor by a two-position power switch that is illuminated in green when turned to the "on" position (right position). **The agitation should not be operated at volumes less than 10% for 50 L units and less than 5% for 500 L units.** Stirring speed is adjusted using the up and down arrows on the agitation keypad interface on the E-Box, or using the settings on an integrated third-party controller. Due to the auto-restart capabilities of the S.U.B., the green start button on the keypad has been disabled; however, the red stop button on the keypad is active.

If the red stop button has been used to stop the motor, the controller can be reset and agitation restarted by using the main motor toggle switch on the left side of the E-Box. For more information, see the illustrations in the E-Box detail in section 4.3.

Circuit protection

Electrical components of the S.U.B. are equipped with circuit protection. The variable frequency drive used to power the mixer motor is protected by the use of a 10 A double pull resettable breaker with a type C time delay (5-10 x LN). Other components are protected with resettable breakers.

In the case of an electrical fault condition, these safety devices are designed to protect the user from electrical shock and prevent electrical system components from being damaged. Fuses can be replaced and/or the breakers reset once the fault condition is resolved.

Electrical breaker notes:

- The normal "on" setting for these breakers is in the up position.
- A tripped breaker will be in the mid position.
- The "off" setting is in the fully down position.
- To reset a tripped breaker, it must first be moved from the mid position to the "off" setting (fully down position) before moving it to the "on" setting (fully up position).

Scales and weighing systems

Monitoring liquid volume within the DynaDrive S.U.B. during operation can be critical in cell culture applications that involve nutrient media feeds. This can also be a useful method for increasing the scalability of the S.U.B. by starting the process run at minimum operating volume. The ability to track operating volume by use of load cells or weigh scales allows the user the ability to control liquid volume and cell density as the bioreactor is increased to rated working volume during the process run.

A load cell kit for weight/volume measurement is available for all DynaDrive S.U.B. units, which can be installed at the factory or can be added later by a certified service technician. The load cell kit comes with three load cells, summing block, wiring, and display with a choice of several interfaces.

Refer to Appendix B for load cell display calibration instructions.
Ensure that load cells are locked down before any movement of the DynaDrive S.U.B. unit.

To lock the load cells before transporting any size S.U.B., follow the steps below and refer to Figures 2.2 and 2.3 in section 2.1.3.

1. Hand-tighten the load cell lockout nut onto the load cell lockout post. You may need to use an adjustable (up to 3.175 cm (1.25 in.)) wrench to loosen the load cell lockout nut from the bottom of the base.

2. After the nut is hand-tightened against the post, use an adjustable wrench (not supplied) to turn it an extra 1/4 turn.

CAUTION: To avoid damaging the load cell, do not overtighten the nut.

3. Assemble a standard stainless 28.6 mm (1.5 in.) tri-clamp around the flanges.

4. Repeat steps 1 through 3 for all load cells on the S.U.B.

3.1.5 External data logging and control

Digital display weighing scales can be sourced from manufacturers such as Mettler Toledo. Bench top scales are commonly used to measure the amount of bulk source media stored in a smaller-volume BPC as it is transferred by peristaltic pump into the DynaDrive S.U.B.

Floor scales can be used to measure the fluid content within the S.U.B. This is accomplished by rolling the S.U.B. onto the scale platform and leveling the S.U.B. skid once in position.

The S.U.B. hardware systems are designed to allow advanced users to control all aspects of the operation of the bioreactor. Contact technical support for Thermo Scientific HyPerforma products general integration guidance.

3.2 BPC loading instructions

3.2.1 50 L BPC loading instructions

Checkpoints prior to BPC loading

- ✓ The correct size DynaDrive BPC is being used for the size of your outer support container (50 L).
- ✓ The outer support container is stationary, with the casters locked in place.
- ✓ Two operators are available for BPC loading.
- ✓ The Thermo Scientific BPC Unpacking and Inspection Guide (DOC0021) has been reviewed for information on handling, transporting, and storing BPCs.

Use the following steps to install and set up the BPC.

1. Open the door on the bioreactor outer support container.

2. Use a safety cutter to slit the taped sides/ends of the cardboard box in which the BPC is shipped (Figure 3.1).

Figure 3.1. Slitting open taped sides of the BPC box.

3. Lift the lid off the top of the box, then lift the cardboard tray out of the box and set it on a flat, raised surface (Figures 3.2 and 3.3).

Figure 3.2. Lifting lid off the box.

Figure 3.3. Lifting cardboard tray out of box.

4. Use a safety cutter to cut the plastic cling wrap securing the BPC to the cardboard tray. Remove the cling wrap and undo the flaps that are folded on the underside of the tray (Figure 3.4).

Figure 3.4. Undoing flaps on bottom of tray.

5. Use a safety cutter to carefully open the outer polybag (Figure 3.5). Take care to not damage the BPC.

6. Hold the exposed end of the BPC in place and use your other hand to pull the outer polybag away from the BPC (Figure 3.6).

Figure 3.5. Opening the outer polybag.

Figure 3.6. Removing the outer polybag.

7. The BPC is also protected by an inner polybag. Use a safety cutter to open the inner polybag (Figure 3.7), taking care to not damage the BPC, and remove the polybag while holding the BPC in place.

Figure 3.7. Opening the inner polybag.

8. Ensure the DynaDrive S.U.B. door still is open. Push the blue and black button on the hub cover located at the top of the S.U.B. to unlock it (Figure 3.8). Swing the cover open (Figure 3.9).

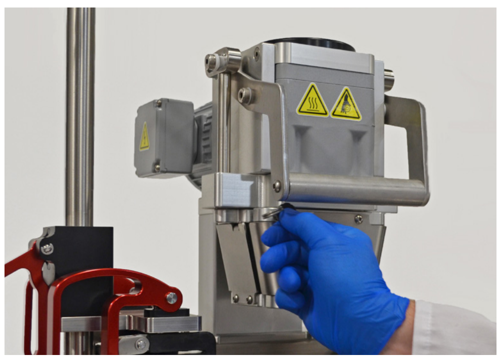


Figure 3.8. Pushing button on hub cover.

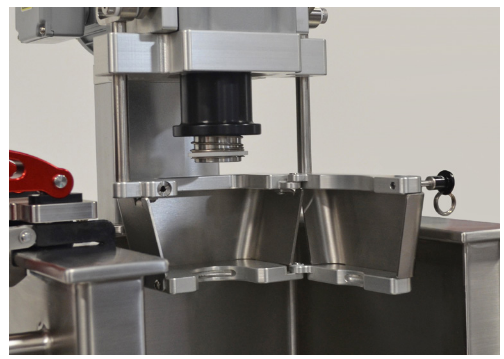


Figure 3.9. Hub cover opened.

9. Raise the BPC lift mechanism lever fully, which will simultaneously lower the bearing hub port (Figure 3.10).

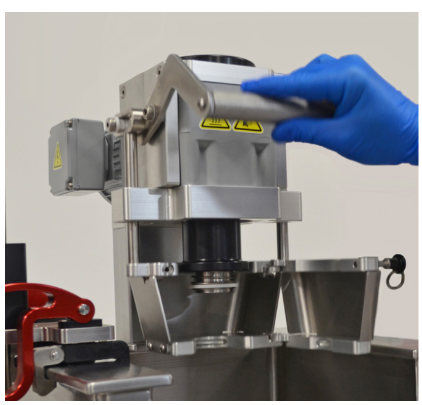


Figure 3.10. Raising BPC lift mechanism lever.

10. Do not allow the BPC or line sets to touch the floor as you carefully unfold the BPC and locate the top bearing hub and front line sets. Do not remove the polybags from the line sets at this stage, as the BPC may become difficult to manage.

11. Ensure the line sets are facing the front, and align the bearing hub with the purple bearing (Figure 3.11). Pull down on the black hub locking mechanism as you insert the top bearing hub into the bearing. Ensure that the locking mechanism fully engages; the lip at the bottom should be completely hidden from view when the locking mechanism retracts.

12. Pull down on the BPC lift mechanism lever (Figure 3.12). The lever will not move all the way down until the black hub locking mechanism is pulled down, as well. After the hub mechanism has been lowered and subsequently raised, the purple bearing hub will lock into place. **Note:** Ensure the hub and lift mechanism lever are fully engaged by attempting to push the lever back up. If the hub is not locked, the hub will fall out and the arm will raise.

Figure 3.11. Aligning bearing hub with the bearing.

Figure 3.12. Pulling down on BPC lift lever and locking mechanism.

13. Once the hub is locked into place, close and lock the hub cover. The blue and black button must be pressed again to lock the cover. The BPC should be hanging freely.

14. Begin slowly filling the BPC with air to allow the drive train to separate from the inside of the BPC. This also aids in the proper alignment of the BPC in the outer support container.
    - Attach the air supply to one of the sparging gas inlet lines after removing the bubble wrap from the line set. **Note:** Air pressure to the gas line on the DynaDrive S.U.B. BPC should not exceed 34 mbar (0.5 psi).

- Begin air inflation through one of the sparging gas lines. Times will vary based upon flow rate and inlet pressure.

WARNING: The BPC is not rated as a pressure vessel. **DO NOT EXCEED** 34 mbar (0.5 psi) within the BPC or the system could fail, causing personal injury or damage to equipment. DO NOT leave the BPC unattended while inflating. Consult your sales representative for recommended air flow rates. The operating pressures at the level of the DynaDrive S.U.B. are of primary importance, and these values must be adhered to.

15. While the BPC continues filling with air, remove all bubble wrap and polybags from the line sets. Guide any top line sets through the opening at the top of the unit.

16. Remove all bubble wrap from the exhaust vent filter. Secure the exhaust vent filter to the top-mounted holder on the rim of the tank (Figure 3.13). Use the red handles shown in Figure 3.13 to adjust the height of the exhaust vent filter holder.

Figure 3.13. Securing the exhaust vent filter to the holder.

17. Attach the two hanging tabs at the top back side of the BPC to the pins on the top back of the outer support container (Figure 3.14). Check the BPC to ensure that the foam probe is hanging freely, and is not entangled in the drive train.

18. Clamp (or slide on, from the front) the black top tab holders on both sides of the outer support container (Figure 3.15). Attach the two hanging tabs at the top front side of the BPC to the black plastic pins on the top front of the outer support container.

Note: Attaching the top tabs will help keep the BPC properly oriented inside the tank. Figure 3.16 shows the top front BPC tab attached to the tab holder.

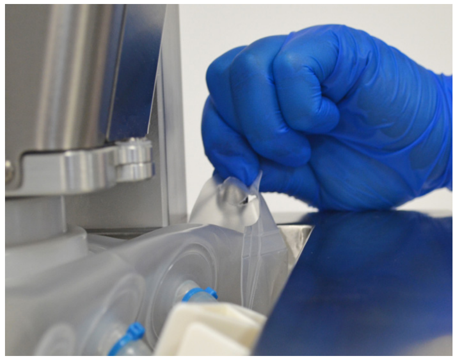


Figure 3.14. Pulling a top back hanging tab on the BPC towards the pin.

Figure 3.15. Placing the black top tab holders on the top front of tank.

Figure 3.16. Black top tab holder with BPC tab attached.

19. Gently pull at the bottom corners of the BPC (Figure 3.17) until the sides of the BPC are straight. **Note:** You may need to wait for the BPC to fill with more air before this is possible.

Figure 3.17. Pulling the bottom corners of the BPC to straighten out the sides.

20. Locate the yellow positioning loop at the bottom center of the BPC. Pull the loop toward the center cutout at the bottom front of the outer support container (Figure 3.18). Once the loop is aligned with the correct cutout, slide it toward the back of the DynaDrive S.U.B. until you feel it shift into place.

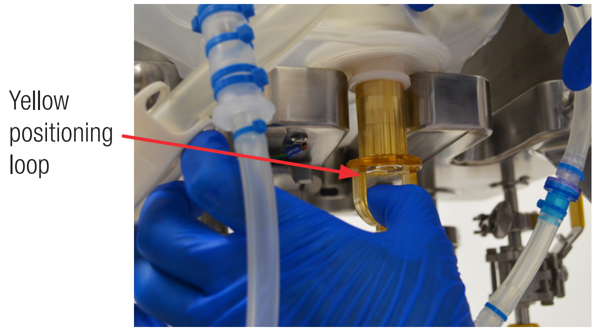


Figure 3.18. Yellow positioning loop aligned with the center cutout.

21. Use the following steps to lock the positioning loop in place:
    - Pull down the white-topped pin to open the gate (Figure 3.19).
    - Swing the gate connected to the pin forward and to the right until the pin aligns with the drilled hole on the right side of the bottom loop cutout (Figure 3.20).
    - Push the pin back up to lock the gate. Figure 3.21 shows the positioning loop locked into place.

Figure 3.19. Pulling down on the white pin.

Figure 3.20. Swinging the gate to the right.

Figure 3.21. Positioning loop locked in place.

22. Guide all line sets on the bottom front of the BPC through the bottom cutouts in the outer support container (Figure 3.22).
    Note: Verify that all line clamps are closed and located as close as possible to the body of the BPC.

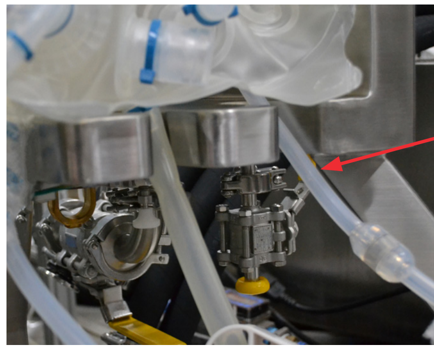


Figure 3.22. All line sets placed in proper cutouts.

23. Attach the hanging tabs on the bottom of the BPC to the pins at the bottom back of the outer support container (Figure 3.23).
    Note: Do not attach the bottom front BPC tabs.

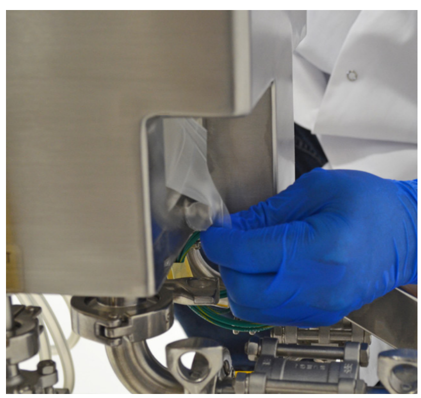


Figure 3.23. Pulling BPC bottom hanging tab toward bottom pin.

24. Carefully close the door on the front of the outer support container (Figure 3.24). Before latching the door shut, ensure that the cross flow sparger line is aligned through the left-most cutout in the door, the perfusion port (if present) is aligned in the center cutout of the door, and both rows of probe ports are aligned just below the bottom front of the door.

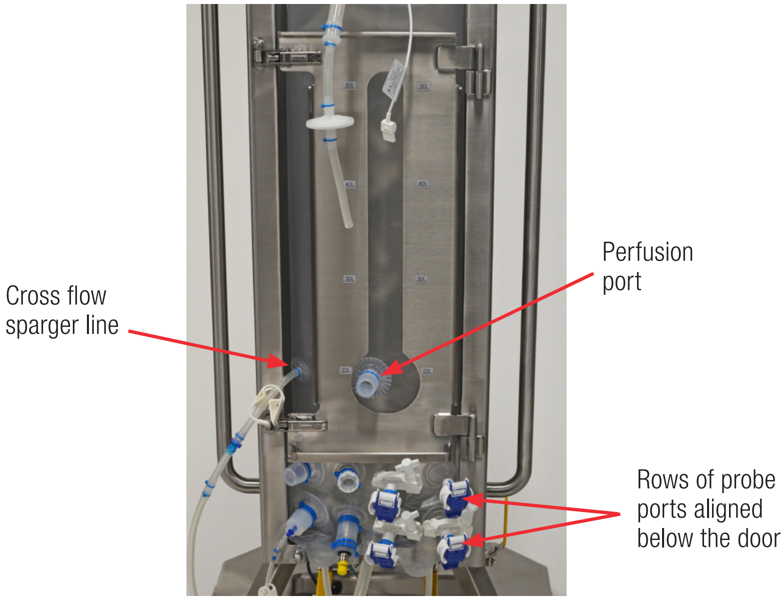


Figure 3.24. Door shut, with lines and ports aligned in cutouts.

25. Close and secure the latches at the top and bottom of the door (Figures 3.25–3.27).

Figure 3.25. Open door latch.

Figure 3.26. Closing door latch.

Figure 3.27. Door latch secured.

26. Remove the polybag from the drain line set, position the line clamp as close as possible to the BPC port, and then close the clamp. Use a cable tie around the clamp to ensure it does not open.

27. Remove the plastic insert located in the thermowell, if present.

28. Insert the resistance temperature detector (RTD) into the thermowell (Figure 3.28) using the steps below. **Note:** Due to the shorter thermowell on DynaDrive BPCs, the 15.24 cm (6 in.) RTD is the ONLY compatible size. **DO NOT** use larger RTDs, which will damage the BPC.
    - Place a small amount of glycerol (0.5 mL) in the thermowell to aid in heat transfer. The glycerol also serves as a lubricant and aids in insertion.
    - The sensor should be inserted until the base of the RTD meets the mouth of the thermowell.
    - Secure by twisting the luer lock collar, if provided.
    - Place a double probe clip on the probe support hanger and place the RTD so it is resting in the hook (Figure 3.29).

Figure 3.28. Inserting the RTD.

Figure 3.29. RTD placed in a double probe clip.

29. Clamp the black foam probe holder to the outer support container, behind the top left tab holder, if facing the front of the S.U.B. Insert the foam probe into the foam probe holder on the outer support container (Figure 3.30). See section 3.4.7 for more information on foam probe use.

    CAUTION: The foam probe must be placed into the foam probe holder to prevent the foam sensor inside the BPC from becoming entangled with the drive train.

Figure 3.30. Foam probe in foam probe holder.

30. Optional: Connect a pressure sensor to the CPC aseptic connector at the top of the BPC. Then connect the appropriate pressure transducer cable to the third-party controller.

Note: Refer to section 3.3.3 for probe insertion instructions.

3.2.2 500 L BPC loading instructions

Checkpoints prior to BPC loading

✓ The correct size DynaDrive BPC is being used for the size of your outer support container (500 L).
✓ The outer support container is stationary, with the casters locked in place.
✓ At least two operators are available for BPC loading.
✓ The Thermo Scientific BPC Unpacking and Inspection Guide (DOC0021) has been reviewed for information on handling, transporting, and storing BPCs.

Use the following steps to install and set up the BPC.

1. Release the top and bottom latches to open the door on the bioreactor outer support container.

2. Use a safety cutter to slit the taped sides/ends of the cardboard box in which the BPC is shipped (Figure 3.31). The BPC will be secured to a cardboard insert inside the box (Figure 3.32).

Figure 3.31. Slit the taped sides of the BPC box.

Figure 3.32. BPC secured to cardboard insert in box.

3. Carefully lift the BPC out of the box (Figure 3.33) and place on a raised, flat surface. Fold up the cardboard flaps to release the BPC from the cling wrap on the cardboard insert. Remove and discard the insert (Figure 3.34).

Figure 3.33. Carefully lifting out the BPC.

Figure 3.34. Folding up flaps on the insert.

4. Use a safety cutter to carefully open the outer polybag (Figure 3.35). Take care to not damage the BPC.

Figure 3.35. Opening outer polybag.

5. While another operator holds the exposed end of the BPC in place, pull the outer polybag away from the BPC (Figure 3.36). Repeat this step to remove the inner polybag once the BPC is in the clean room and ready to be loaded.

Figure 3.36. Removing the outer polybag.

6. Ensure the DynaDrive S.U.B. door is still open. Push the blue and black button on the hub cover located at the top of the S.U.B. to unlock it (Figure 3.37). Swing the cover open (Figure 3.38).

Figure 3.37. Pushing button on hub cover.

Figure 3.38. Hub cover opened.

7. Raise the BPC lift mechanism lever fully, which will simultaneously lower the bearing hub port (Figure 3.39).

Figure 3.39. Raising BPC lift mechanism lever.

8. Do not allow the BPC or line sets to touch the floor as you carefully unfold the BPC and locate the top bearing hub and front line sets. Do not remove the polybags from the line sets at this stage, as the BPC may become difficult to manage.

9. Ensure the line sets are facing the front, and align the top bearing with the purple bearing hub (Figure 3.40). Pull down on the black hub locking mechanism as you insert the top bearing hub into the bearing. Ensure that the locking mechanism fully engages; the lip at the bottom should be completely hidden from view when the locking mechanism retracts.

10. Pull down on the BPC lift mechanism lever (Figure 3.41). The lever will not move all the way down until the black hub locking mechanism is pulled down, as well. After the hub mechanism has been lowered and subsequently raised, the purple bearing hub will lock into place. **Note:** Ensure the hub and lift mechanism lever are fully engaged by attempting to push the lever back up. If the hub is not locked, the hub will fall out and the arm will raise.

Figure 3.40. Aligning bearing hub with the bearing.

Figure 3.41. Pulling down on BPC lift lever and locking mechanism.

11. Once the hub is locked into place, close and lock the hub cover. The blue and black button must be pressed again to lock the cover (Figure 3.42). The BPC should be hanging freely.

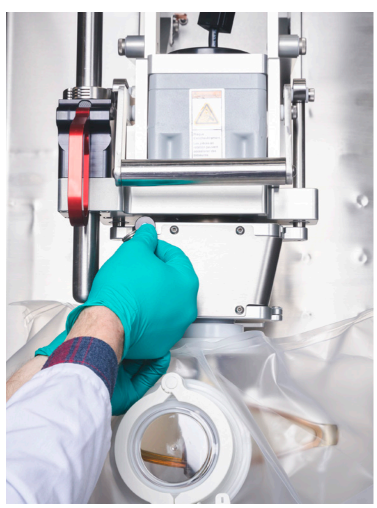


Figure 3.42. Locking hub cover.

12. Locate the bottom hub at the bottom center of the BPC. Pull the hub toward the center cutout at the bottom front of the outer support container. Once the hub is aligned with the correct cutout, slide it toward the back of the DynaDrive S.U.B. until you feel it shift into place (Figure 3.43).

Figure 3.43. Sliding the bottom hub into place in the front center cutout.

13. Use the following steps to lock the bottom hub in place:
    - Pull down the metal pin to open the gate.
    - Swing the gate connected to the pin forward and to the right (Figure 3.44) until the pin aligns with the drilled hole on the right side of the bottom hub cutout (Figure 3.45).
    - Push the pin back up to lock the gate (Figure 3.46).

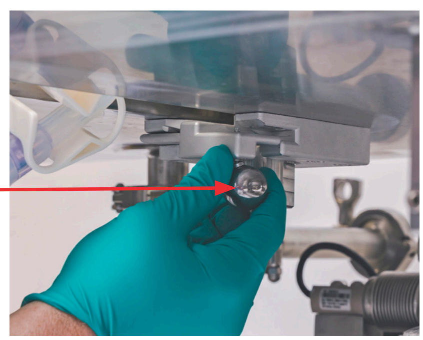


Figure 3.44. Swinging the gate to the right.

Figure 3.45. Closing the gate completely.

Figure 3.46. Pushing the metal pin up to lock the gate.

14. Place the exhaust vent filter into the holder attached to the pneumatic motor lift (Figure 3.47). **Note:** A ladder may be required to reach the exhaust vent filter holder.

Figure 3.47. Securing the exhaust vent filter to the holder.

15. After the BPC top hub is properly loaded and the hub cover is locked, with the DynaDrive S.U.B. door open, turn the lift switch to "Raise" until the pneumatic motor lift is fully raised. Observe the BPC while the lift is being raised to ensure tubing line sets do not become entangled. Turn the motor lock switch to "Locked" before continuing to load the BPC. **Note:** The pneumatic motor lift will not lock if it is not fully raised. After raising the motor lift to its highest position, turn the lock dial on the motor lift controller.

Figure 3.48. Pneumatic motor lift in lowest position.

Figure 3.49. Pneumatic motor lift fully raised.

16. Attach the top back BPC tabs to the pins on the top back of the outer support container. **Note:** A ladder is needed to reach the top back BPC tabs.

17. Guide all line sets on the bottom of the BPC through the bottom cutout in the outer support container (Figure 3.50). **Note:** Verify that all line clamps are closed and located as close as possible to the body of the BPC.

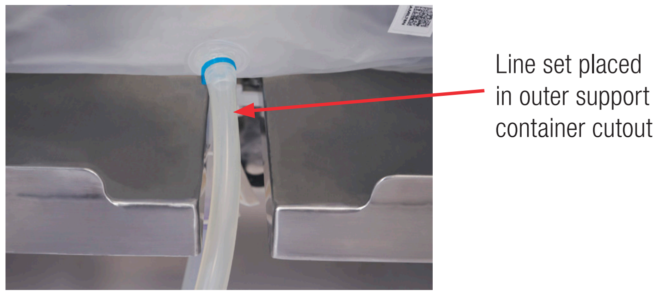


Figure 3.50. Line sets placed in bottom cutout.

18. Attach the hanging tabs on the bottom of the BPC to the pins at the bottom back of the outer support container (Figure 3.51). **Note:** Do not attach the bottom front BPC tabs.

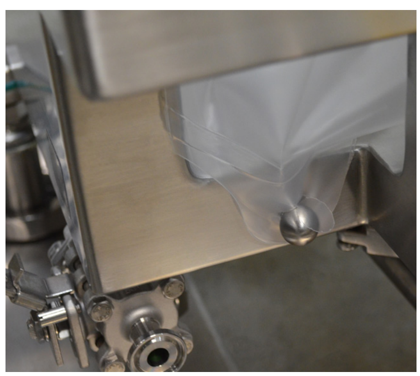


Figure 3.51. BPC bottom hanging tab attached to bottom pin.

19. Carefully close the door on the front of the outer support container. Before latching the door shut, ensure that one operator holds the front tubing line sets above the door so none of the tubing is caught as the door closes (Figure 3.52). Ensure that the row of probe ports is aligned just below the bottom front of the door (Figure 3.53).

Figure 3.52. Lifting tubing line sets above the door while closing it.

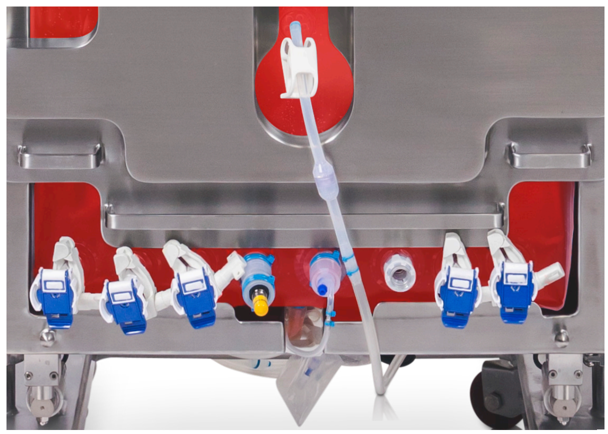


Figure 3.53. Probe port row aligned underneath the closed door (BPC shown filled).

20. Close and secure the latches at the top and bottom of the door (Figures 3.54 and 3.55).

Figure 3.54. Closing the top door latch.

Figure 3.55. Securing the top door latch.

21. Begin slowly filling the BPC with air to allow the drive train to separate from the inside of the BPC. This also aids in the proper alignment of the BPC in the outer support container.
    - Attach the air supply to one of the sparging gas inlet lines after removing the bubble wrap from the line set.
      Note: Air pressure to the gas line on the DynaDrive S.U.B. BPC should not exceed 34 mbar (0.5 psi).
    - Begin air inflation through one of the sparging gas lines. Times will vary based upon flow rate and inlet pressure.

WARNING: The BPC is not rated as a pressure vessel. **DO NOT EXCEED** 34 mbar (0.5 psi) within the BPC or the system could fail, causing personal injury or damage to equipment. DO NOT leave the BPC unattended while inflating. Consult your sales representative for recommended air flow rates. The operating pressures at the level of the DynaDrive S.U.B. are of primary importance, and these values must be adhered to.

22. Check the BPC to ensure that the foam probe is hanging freely, and is not entangled in the drive train.

23. Clamp (or slide on, from the front) the black top tab holders on both sides of the outer support container (Figure 3.56). Attach the two hanging tabs at the top front side of the BPC to the black plastic pins on the top front of the outer support container. **Note:** Attaching the top tabs will help keep the BPC properly oriented inside the tank. Figure 3.57 shows the top front BPC tab attached to the tab holder.

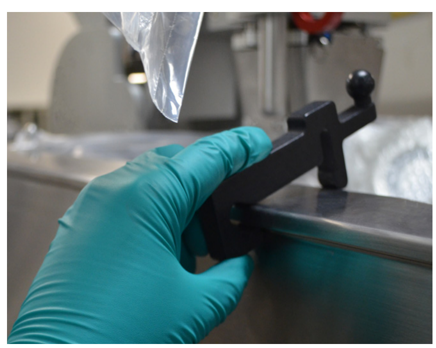


Figure 3.56. Placing the black top tab holders on the top front of tank.

Figure 3.57. Black top tab holder with BPC tab attached.

24. Gently pull at the bottom corners of the BPC until the sides of the BPC are straight. **Note:** You may need to wait for the BPC to fill with more air before this is possible.

25. While the BPC continues filling with air, remove all bubble wrap and polybags from the line sets.

26. Remove the polybag from the drain line set, position the line clamp as close as possible to the BPC port, and then close the clamp. Use a cable tie around the clamp to ensure it does not open.

27. Remove the plastic insert located in the thermowell, if present.

28. Insert the resistance temperature detector (RTD) into the thermowell (Figure 3.58) using the steps below. **Note:** Due to the shorter thermowell on DynaDrive BPCs, the 15.24 cm (6 in.) RTD is the ONLY compatible size. **DO NOT** use larger RTDs, which will damage the BPC.
    - Place a small amount of glycerol (0.5 mL) in the thermowell to aid in heat transfer. The glycerol also serves as a lubricant and aids in insertion.
    - The sensor should be inserted until the base of the RTD meets the mouth of the thermowell.
    - Secure by twisting the luer lock collar, if provided.
    - Place a probe clip on the probe support hanger and place the RTD so it is resting in the hook (Figure 3.59).

Figure 3.58. Inserting the RTD.

Figure 3.59. RTD placed in a probe clip.

29. Clamp the black foam probe holder to the outer support container, behind the top left tab holder, if facing the front of the S.U.B. Insert the foam probe into the foam probe holder on the outer support container (Figure 3.60). See section 3.4.7 for more information on foam probe use.

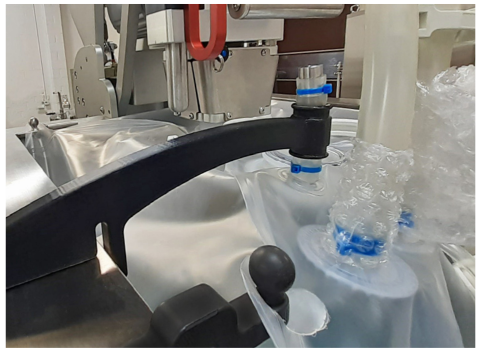


Figure 3.60. Foam probe in foam probe holder.

CAUTION:
- The foam probe must be placed into the foam probe holder to prevent the foam sensor inside the BPC from becoming entangled with the drive train.
- The 500 L foam probe holder must be removed prior to raising or lowering the motor lift to avoid damaging the BPC.

30. Optional: Connect a pressure sensor to the CPC aseptic connector at the top of the BPC. Then connect the appropriate pressure transducer cable to the third-party controller.

Note: Refer to section 3.3.3 for probe insertion instructions.

3.3 Probe preparation and insertion

3.3.1 Preparation and sterilization

1. Select the appropriate probe (see section 1.3.1). Verify the presence of a Teflon™ support ring and O-ring on the probe and visually inspect the probe for damage.

2. Perform any required probe maintenance and calibrate the pH probe (see section 3.5.4 for probe calibration information).

3. Insert the probe into the probe assembly through the threaded adapter.

4. Verify that the probe tip is not touching (more than 6.35 mm (0.25 in.) gap) the membrane of the aseptic connector before threading into the probe adapter.

5. Hand-tighten the adapter and verify that the probe tip is not touching the membrane.

6. Place the probe assembly with probe into the autoclave tray for probe kits (Figure 3.61).

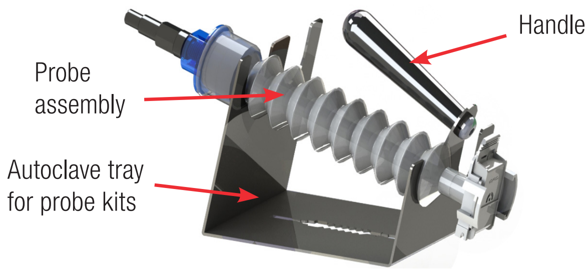


Figure 3.61. Probe assembly and autoclave tray.

7. Autoclave the probe assembly using a validated sterilization cycle (approximately 30 minutes at 122°C). A 30-minute sterilization cycle is generally sufficient. Options of wet or dry cycle parameters can be used. Slow exhaust cycles are preferred, as this minimizes stress on the probes during the temperature and pressure changes of autoclaving.

8. Allow sufficient time for the probe assembly to cool completely before connecting to the BPC for probe insertion.

9. When stored properly, autoclaved probe assemblies can be stored dry for short periods of time (less than 24 hours) without loss of sensor longevity, performance, or sterility.

3.3.2 Making CPC AseptiQuik connections

CPC AseptiQuik G genderless connector components

Figures 3.62 and 3.63 illustrate the components of CPC™ AseptiQuik™ G genderless connectors. Connectors with white protective cover pull tabs may be autoclaved. Generally, connectors with blue pull tabs are gamma irradiated, not autoclaved. Visit the Colder Products Company website for more information.

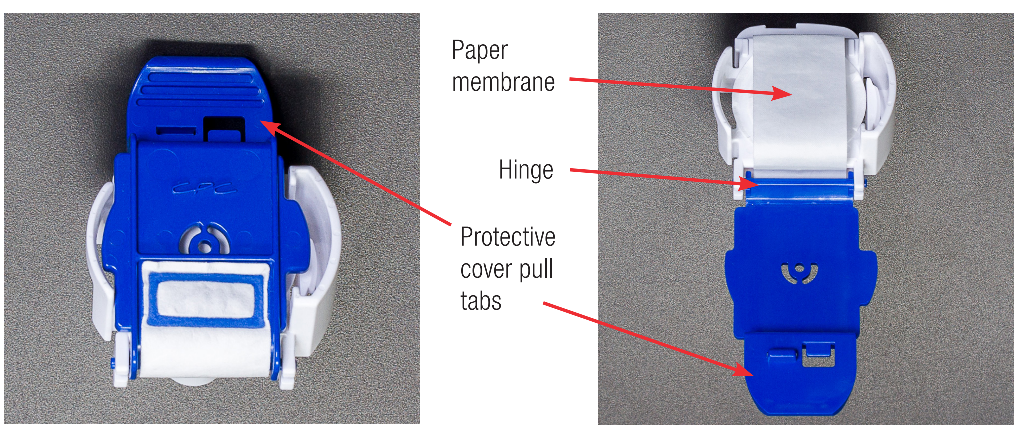


Figure 3.62. CPC AseptiQuik G connector (closed).

Figure 3.63. CPC AseptiQuik G connector (open).

For instructions on making an aseptic connection, see the following section.

CPC AseptiQuik connection instructions

The following steps outline the process of making a sterile aseptic connection using CPC AseptiQuik G genderless connectors.

1. Tear open and remove the plastic covering on the connector located on the BPC (Figures 3.64 and 3.65).

Figure 3.64. Pulling the tear strip.

Figure 3.65. Removing plastic covering from the connector.

2. Unsnap and flip open the protective cover pull tabs on both connectors (Figure 3.66).

3. Align the two connectors and push them together (Figure 3.67).

Figure 3.66. Opening the protective cover pull tab on the port.

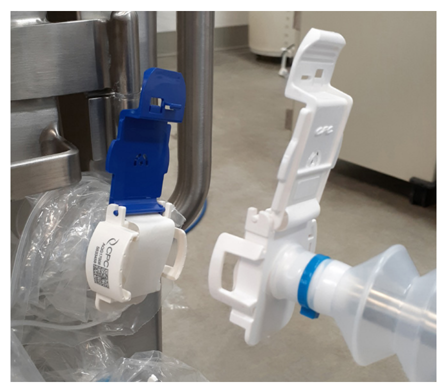


Figure 3.67. Aligning the connectors.

4. Squeeze each side of the connectors (Figure 3.68) until you hear a click.

5. Grab the joined pull tabs and pull upward to remove the paper membranes from the connectors (Figure 3.69). The pull tabs will also be removed.

Figure 3.68. Squeezing the two connectors together.

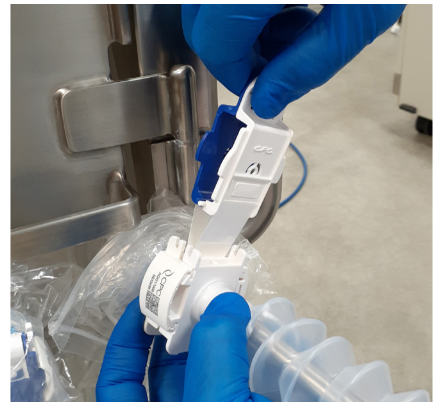


Figure 3.69. Pulling the tabs to remove the paper membranes.

3.3.3 Probe insertion

Before beginning probe insertion, please become familiar with the aseptic connector procedure outlined in section 3.3.2.

1. Attach probe clips onto the probe clip hanger on the outer support container, above the probe assembly. Plastic probe clips slide onto the probe clip hanger using a firm amount of pressure.

2. Install the pre-sterilized sensor and probe kit using the aseptic connection methods described in section 3.3.2. The aseptic connection is completed prior to the bellows being collapsed.

3. Insert the probe by collapsing the bellows (Figures 3.70 and 3.71). **Note:** If the BPC is already filled with liquid, the best practice is to squeeze the bellows to expel air prior to collapsing it. Then insert the probe fully, as described.

Figure 3.70. Probe insertion.

Figure 3.71. Collapsed bellows.

4. Position the probe clip in the desired horizontal location. Lift the probe and set it into the bellows hook of the probe clip (Figure 3.72).

Figure 3.72. Lifting the probe before setting it into the bellows hook.

5. The probe should be resting in the bellows hook (Figure 3.73). Release the probe assembly and verify that the probe remains at the proper insertion depth and angle when the bellows expand to rest freely in the probe clip.

Figure 3.73. Inserted probe resting in bellows hook.

3.3.4 Probe calibration

Probe calibration is controller-specific; however, the following general rules apply:

- If you are using a liquid batch-to-tank grounding cable with the stainless steel connector of the sample line, the sample line should be purged of air prior to probe calibration.

- pH probes must be calibrated prior to steam sterilization; the calibration of the probe can be standardized by comparison of an off-line sample once the pH probe has been connected to the S.U.B.
- Dissolved oxygen (DO) probes are generally calibrated after steam sterilization. They can be calibrated once the probe is connected to the S.U.B. and is given time to polarize (six to eight hours of continuous connection to the power supply provided by a controller or polarization module).

3.4 Cell culture operating instructions

3.4.1 Operating conditions for cell culture applications

Optimal operating parameters for cell culture vary greatly between cell lines and media formulations. Exceeding these operating limits may result in premature exhaust filter failure, excessive foaming, and excessive pressure build-up in the gas delivery line sets or the BPC.

When reducing gas flow rate limits, the following trade-offs should be expected.

- Reducing drilled hole sparger maximum operating limits will reduce system foaming but increase reliance on O_2. A suggested gas operating control strategy is to run the drilled hole sparger on air initially, and after total flow rate limits are reached, subsitute oxygen.
- Reducing overlay maximum operating limits will reduce the exhaust load (increasing filter lifespan) but will sacrifice sparger performance if reduced far enough to allow CO_2 buildup.

If cell culture density is not increasing at expected rates, this may be due to CO_2 buildup in the headspace. Increasing air flow in the headspace, reducing the agitation rate, and adding ballast gas can all increase CO_2 stripping.

3.4.2 Checkpoints prior to media fill

Verify the following before proceeding to liquid fill.

✓ The BPC has been loaded into the hardware by following the instructions provided in section 3.2.

✓ All aseptic connector port heavy-duty clamps are closed and located as close as possible to the BPC.

✓ The exhaust filter is upright and secured using the holder, with the exhaust filter heater installed.

✓ The clamp on the drain tube is closed and located as close as possible to the BPC.

- ✓ The temperature RTD is completely seated in the thermowell and secured.
- ✓ The air-filled BPC is properly oriented in the outer support container and the BPC bottom tabs are secured.
- ✓ The gas line sets are connected to the drilled hole sparger and either the cross flow sparger or overlay sparger.
- ✓ All gas filters are placed above the maximum liquid level.
- ✓ The load cell display has been tared, if applicable.
- ✓ All sensors are inserted and connected to their respective transmitters. Sensors must be properly oriented to ensure that they are below the liquid level after media fill.
- ✓ All sparge and drain lines pass through the hardware cutouts and are not obstructed by the outer support container.

3.4.3 Media fill

1. Select the desired line set from the BPC for fluid introduction.

2. Make an aseptic connection (tubing welder or aseptic connector) and begin liquid fill.

3. While the BPC is filling, continuously verify the position of the BPC in the outer support container, particularly the sparger and the drain line. Adjust positioning if necessary for proper fit.

4. Ensure that the BPC tabs are connected to the tab holders/pins to reduce wrinkles during filling. **Note:** If the BPC wrinkles are not eliminated during liquid fill, excessive film tension below the bearing port will result.

5. Fill to the desired liquid volume (10–100% of the rated volume for 50 L DynaDrive BPCs and 5–100% of the rated volume for 500 L DynaDrive BPCs is recommended).

6. Ensure that all sensors are below the liquid level after the BPC has been filled.

3.4.4 Agitation control

WARNING: Agitation must be stopped when the liquid level falls below 10% of the rated working volume for 50 L units, or below 5% for 500 L units, otherwise damage to the hardware or BPC may result.

Agitation control using the optional E-Box

1. After the media has reached the desired liquid volume, use the

motor controller power switch to start the agitation using the electrical control panel (E-Box) (Figure 3.74).

Figure 3.74. Front view of the E-Box.

2. Using the arrow keys on the motor speed control keypad, adjust the setpoint speed to the desired level. The adjustment of the stirring speed rpm is done using Hz. The display reverts back to displaying rpm after 2–3 seconds of inactivity. Adjust desired agitation rate within the recommended range provided in Chapter 4—System features and specifications.

3. Allow the speed to stabilize, then make fine adjustments if necessary.

Agitation control using a third-party controller

If you are using a third-party controller instead of the Thermo Scientific E-Box, refer to your controller manufacturer's guidelines for setup and operating instructions.

3.4.5 Temperature control

Temperature setpoints are controlled by the TCU or controller. Refer to the TCU or controller manufacturer's guidelines for setup and operating instructions.

1. Connect to an external TCU using the large couplings located on the vessel jacket. Ensure the inlet/outlet ports are connected properly; improper installation may result in poor heating/cooling performance.

2. Open the valves after connecting the TCU (Figure 3.75).

Figure 3.75. Opening valves.

Note: The water jacket should be purged of air any time the vessel jacket lines are reconnected, as any air in the jacket will result in reduced performance. To purge the water jacket, open the bleed valve located near the bottom of the S.U.B. A container may be needed to catch any glycol that is released. Close the valve as soon as glycol begins flowing.

3.4.6 Sparging strategy

Sparging strategy and gas supply setup

All standard DynaDrive BPCs are supplied with overlay, drilled hole, and cross flow spargers. 50 L BPCs also have porous frit spargers. Figure 3.76 illustrates the location of each sparger on a standard 50 L BPC, and Figure 3.77 shows 500 L BPC spargers. The cross flow sparger is used to reduce carbon dioxide buildup in the headspace near the liquid surface when the liquid volume is at or below 10%.

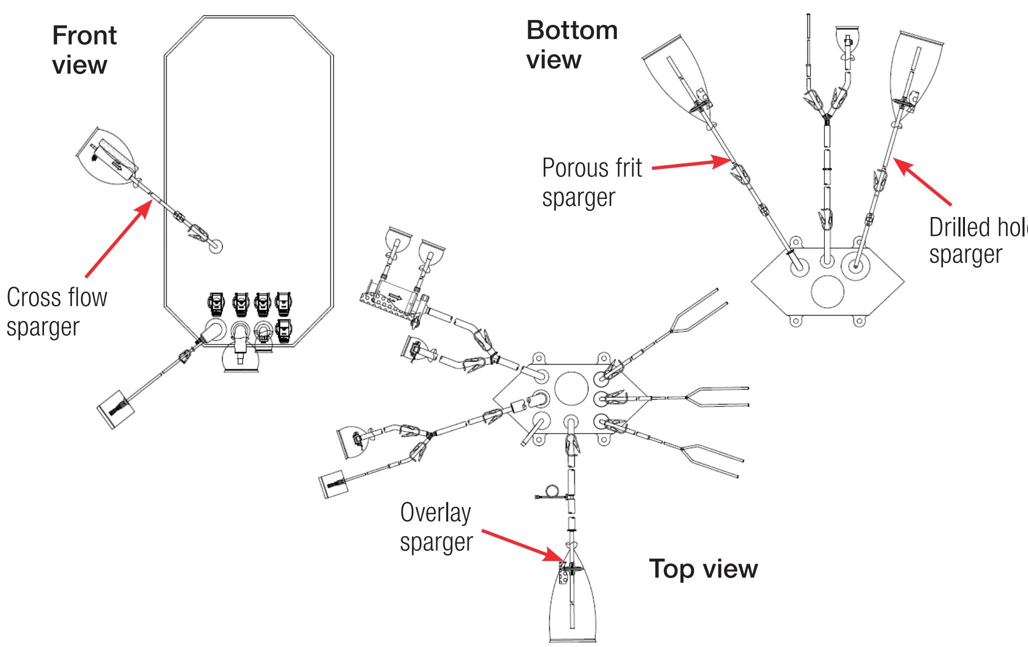


Figure 3.76. 50 L DynaDrive S.U.B. BPC spargers.

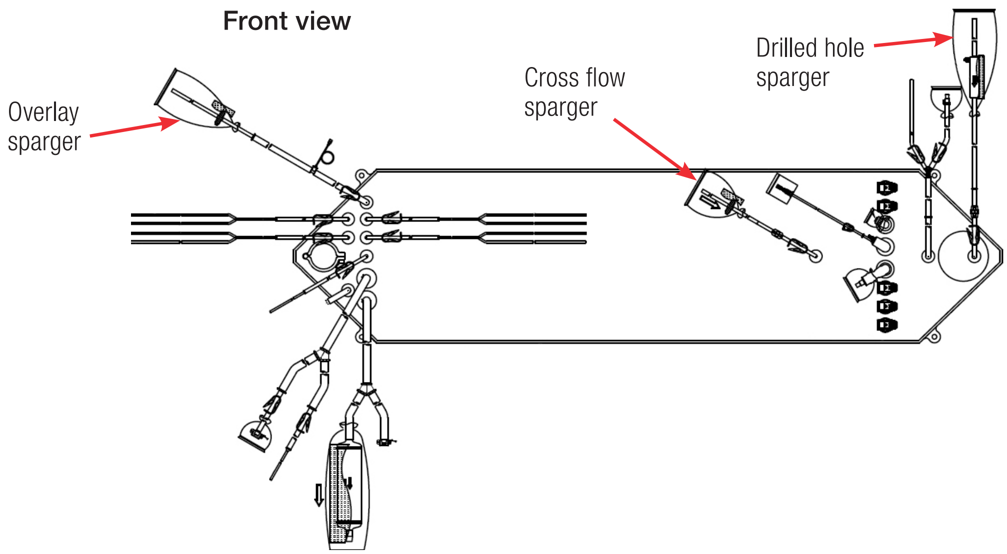
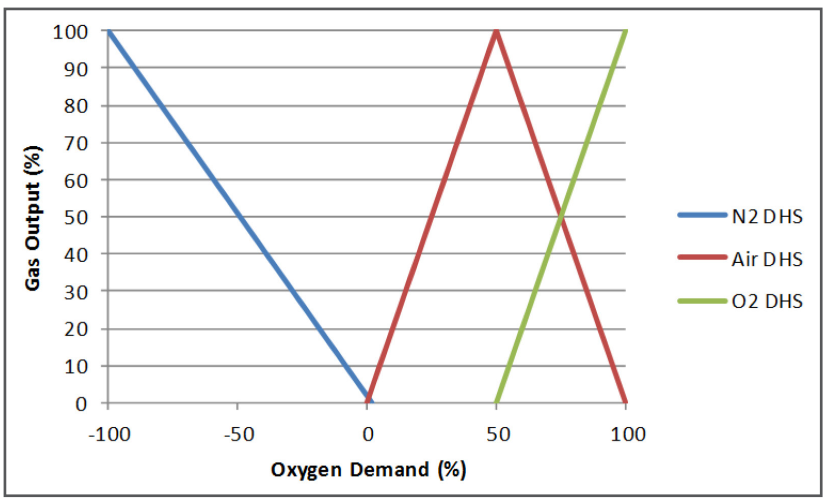


Figure 3.77. 500 L DynaDrive S.U.B. BPC spargers.

Graph 3.1 depicts an example of a dissolved oxygen (DO) management strategy. Refer to your Thermo Scientific sales representative for gas flow rate recommended maximum values. In developing a gassing strategy for a S.U.B. with a drilled hole sparger configuration, it is optional to have a crossover from nitrogen to air when progressing from negative to positive DO control. Graph 3.1 depicts a minor crossover.

Graph 3.1. Example of a drilled hole sparger DO control strategy for DynaDrive S.U.B. systems.



When progressing into higher positive DO control, the drilled hole sparger system is designed to maintain optimal oxygen delivery to carbon dioxide stripping rates. When drilled hole sparger flow rate limits are reached, supplant the sparger air flow with a steadily increasing ratio of oxygen to allow a higher degree of control.

Gas flow rates

Standard DynaDrive BPCs are supplied with drilled hole, overlay, and cross flow spargers. If foaming or exhaust filter load/lifespan is of primary concern, priority should be placed on tuning the system to operate primarily by adding oxygen through the drilled hole sparger. If carbon dioxide stripping is of primary concern, priority should be placed on running the drilled hole sparger at flow rates sufficient to reduce or eliminate the need for base addition.

In optimal conditions, without condensation or fouling, exhaust filters have a flow capacity of at least 20 and 90 slpm at 0.006 bar (0.1 psi) for the small and large standard equipped filter types. The total flow rate of gas into the system must be less than the sum flow rate capacity of active exhaust filters.

3.4.7 Foam probe use

The optional foam probe is used to monitor the level of foaming during the cell culture process. Place the foam probe into the foam probe holder (Figure 3.78), and plug the foam sensor into the port at the top of the BPC (Figure 3.79).

CAUTION: The foam probe must be placed into the foam probe holder to prevent the foam sensor inside the BPC from becoming entangled with the drive train.

Figure 3.78. 50 L Foam probe in foam probe holder.

Figure 3.79. Foam sensor plugged into 50 L foam probe port.

3.4.8 pH and DO probe calibration

Calibrate pH and DO probes according to the product manufacturer's specifications.

3.4.9 Checkpoints prior to inoculation

Before inoculation, verify that:

- ✓ BPC tabs have been connected to the S.U.B. hardware.
- ✓ The pH, DO, and other probes are properly connected and calibrated according to the manufacturer's specifications.
- ✓ The RTD is completely seated in the thermowell and secured.
- ✓ Ensure that all sensors are below the liquid level. The top row of sensors will be submerged once the 50 L unit has reached 20% working volume, and the 500 L unit has reached 10% working volume. **Note:** 500 L DynaDrive BPCs have a maximum of two ports on the top row.
- ✓ Operating parameters (temperature, agitation, pH, and DO) are at the desired setpoints.
- ✓ A method for making aseptic tubing connections is available.
- ✓ Air is connected to the cross flow sparger when operating at ≤ 20% volume.

3.4.10 Cell inoculation

Once the S.U.B. is operating at the targeted steady equilibrated state and has achieved the proper temperature, the S.U.B. is ready for inoculation. Connect the inoculum addition line set to the seed culture vessel (equipped with the proper connectors/tubing) and transfer the inoculum into the S.U.B.

Typically, this is done with the tubing connection process (aseptic connection or tube welding) and peristaltic pump. Pump the desired volume of seed cells into the S.U.B.

Note: For shear sensitive cultures, cells can be introduced by manipulating the addition port to direct the inoculum down the interior wall of the BPC and into the bulk fluid, reducing the shear on the cells.

3.4.11 Volume scale up

1. Using a sterile connection, connect media to the BPC with the media fill port.

2. Begin pumping media into the BPC at the desired flow rate. Ensure that the vessel temperature does not drop below culture limits.

3. Remove the air line from the cross flow sparger, replace onto the overlay gas port, and clamp the cross flow sparger port as close to the BPC as possible.

4. Increase the volume to the desired level.

3.4.12 In-process checkpoints

Verify the following once or twice daily during the culture run.

- ✓ Rising bubbles are visible through the access window.
- ✓ Process parameters, such as temperature and agitation, are at setpoint.
- ✓ The BPC is operating at < 30 mbar (0.5 psi).
- ✓ The temperature sensor/RTD is completely seated and secured.
- ✓ The vent filter heater is working properly.

Noise note: Noise may be emitted from the mixing assembly during operation. This noise may vary in intensity and frequency, but generally has no significant effect on performance or overall durability of the BPC during the intended life of the product.

3.4.13 BPC sampling

During operation of the S.U.B., samples may need to be taken for monitoring of various parameters established by the user. The following sections describe two techniques for sampling: aseptic sampling with a sterile syringe, and sampling with a sterile manifold.

Aseptic sampling

Using a standard luer lock on a 60 mL syringe or manifold:

1. Remove the dust cover from the SmartSite needle-free valve, which is connected to the end of the sample port (Figure 3.80).

Figure 3.80. Removing dust cover from the SmartSite.

2. Clean the SmartSite with a sanitary wipe.

3. Connect the sanitary luer lock type syringe (Figure 3.81).

Figure 3.81. Connecting the syringe.

4. To purge the sample line, apply a small amount of vacuum pressure by pulling out the syringe plunger slightly.

5. Open the pinch clamp and pull sample (approximately 20 mL), using care not to allow any back flow.

6. Close the pinch clamp and remove the syringe. This will be a purge sample.

7. Clean the SmartSite with a sanitary wipe.

8. Connect the sanitary luer lock type syringe.

9. Pull the sample by applying a small amount of vacuum pressure using the syringe.

10. Open the pinch clamp and pull the desired sample volume (approximately 10–20 mL), taking care not to allow any back flow.

11. Close the pinch clamp and remove the syringe. This will be a representative sample.

12. Clean the SmartSite with a sanitary wipe and replace the dust cap.

Sampling with a sterile manifold

Use the steps below to attach a sample manifold (if purchased):

1. Remove the manifold from its protective polybag package.

2. Close all of the clamps on the manifold lines.

3. Use a sterile tubing welder to connect the manifold to the sample line (Figure 3.82).

Figure 3.82. Tubing welder.

4. Inspect the welds and open flow path by pinching the welds.

5. Open two clamps at the inlet and the clamp at the purge container (100 mL container).

6. Purge the sample line by filling the purge container (30–60 mL is recommended).

7. Close the clamp nearest to the purge container.

8. Open the clamp to the sample container (50 mL container) (Figure 3.83).

Figure 3.83. 50 mL manifold.

9. Allow the container to fill with liquid by the force of gravity (10–20 mL is recommended).

10. Close the clamps at the sample manifold inlet.

11. Close the clamps nearest the sample container.

12. Remove the filled manifold from the S.U.B. by welding a new manifold onto the sample line, which will be used for taking the next sample.

3.4.14 Dispense and harvest

1. Connect the bottom drain tubing set to the intended transfer line.
2. Open the clamp positioned at the bottom drain port.
3. Begin to drain, using a peristaltic pump.
4. Stop the impeller motor when volume reaches 10% maximum volume in 50 L units and 5% maximum volume in 500 L units.
5. Disable the temperature control to ensure that the S.U.B. does not overheat.
6. Manipulate the BPC to maximize drainage.

3.4.15 BPC disposal

After the BPC has been drained, it can be removed from the outer support container. Filters can be removed and integrity tested as needed according to the user’s standard procedures. All product contact materials related to the DynaDrive S.U.B. can be disposed of in an appropriate waste container or incinerator.

3.4.16 S.U.B. shutdown

1. After the run is complete, verify that the motor agitation is off, and turn off the power to the outer support container by switching off the main power disconnect.
2. If the S.U.B. hardware has come in contact with caustic materials during the course of a run, rinse the affected areas with a light water rinse, followed by normal routine cleaning (see the following section).
3. Loose items, such as the tools and RTD probes, should be returned to their storage locations to prevent accidental damage.

3.4.17 Preparation for the next run

Between runs, the S.U.B. hardware (outer support container, probe shelf, mixer drive, etc.) can be wiped down with a sanitary wipe. The outer support container can be cleaned with standard stainless steel cleaner.

The S.U.B. hardware system can be cleaned to the extent of standard laboratory cleaning procedures. Care should be taken to ensure electrical connections have been disconnected and electrical enclosures are closed tightly. A wipe-down with normal disinfectant solutions is sufficient. Avoid using excessive amounts of liquid. The unit must be allowed to fully dry prior to being brought back into operation.

3.5 Verification procedures

3.5.1 Mixing speed verification

To verify the mixing speed, use a calibrated tachometer. Expect accuracy of ± 1.5 rpm or 1% of the setpoint, whichever is greater. Speed scaling can be modified if the calibration needs to be adjusted.

3.5.2 Temperature controller verification

To verify the temperature controller/RTD, use a S.U.B. silicone thermowell, the existing 3.175 mm (1/8 in.) outer diameter (OD) RTD and a user-supplied calibrated temperature bath.

3.5.3 Pressure monitor verification (when present)

To verify the calibration of the pressure monitor, use a calibrated pressure standard. Pressures can be verified by clamping the BPC inlet line and supplying gas through the overlay gas filter. Expect accuracy of ± 0.1 psi. The monitor can be calibrated manually by referencing the monitor operator's manual supplied in the Equipment Turnover Package (ETP).

3.5.4 Load cell verification

It is recommended that the load cell manufacturer or a qualified technician verify the load cells onsite. Expect an accuracy of ± 0.5 kg. Basic load cell default parameters are listed in the electrical schematic included with the ETP.

4

System features and specifications

Chapter contents

4.1 Hardware features

4.1.1 50 L DynaDrive S.U.B. hardware features

Figures 4.1 and 4.2 (below) illustrate the hardware features of 50 L DynaDrive S.U.B. systems. Electrical control panel (E-Box) features are illustrated in section 4.3.

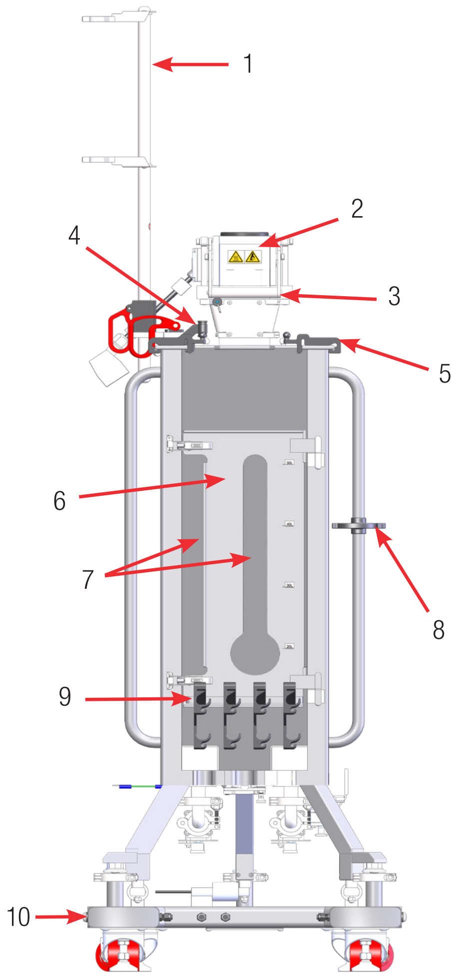


Figure 4.1. Front view of 50 L DynaDrive S.U.B. (without optional E-Box).

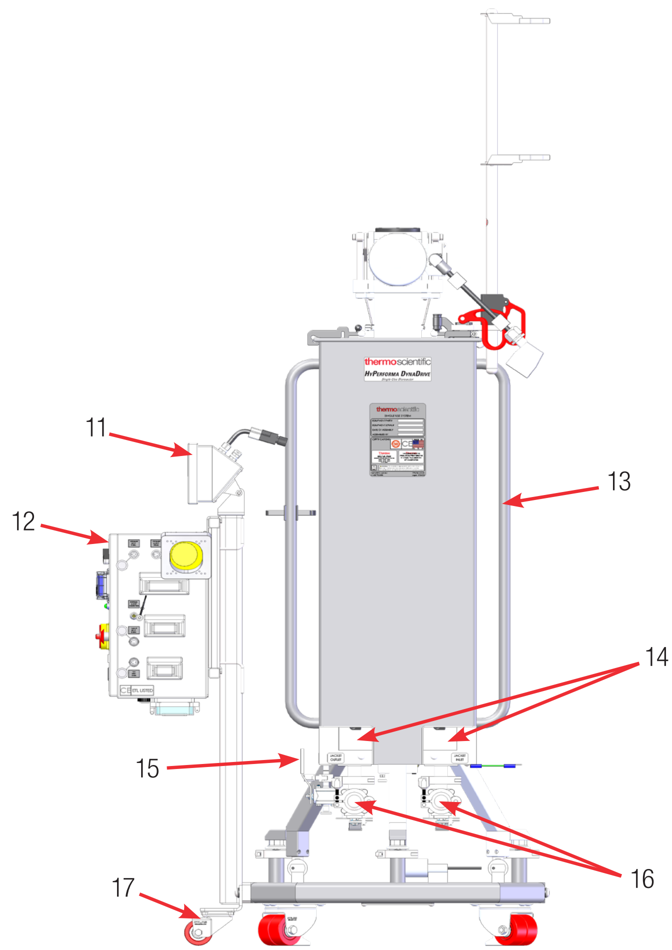


Figure 4.2. Back view of 50 L DynaDrive S.U.B. (with optional E-Box).

1. Exhaust vent filter holder
2. Agitator motor
3. BPC lift mechanism
4. Foam probe holder
5. Top BPC tab holders
6. Door for BPC loading
7. Liquid sight windows
8. Cable management clip
9. Probe hanger bracket with four (4) double probe clips
10. Cart assembly
11. Load cell display, optional
12. Electrical control panel (E-Box), optional
13. Vessel handle bars
14. Bottom cutouts/pins for BPC attachment/alignment
15. Bleed jacket valve
16. Tri-clamp jacket inlet/outlet connections
17. Casters

4.1.2 500 L DynaDrive S.U.B. hardware features

Figures 4.3 and 4.4 (below) illustrate the hardware features of 500 L DynaDrive S.U.B. systems. Electrical control panel (E-Box) features are illustrated in section 4.3.

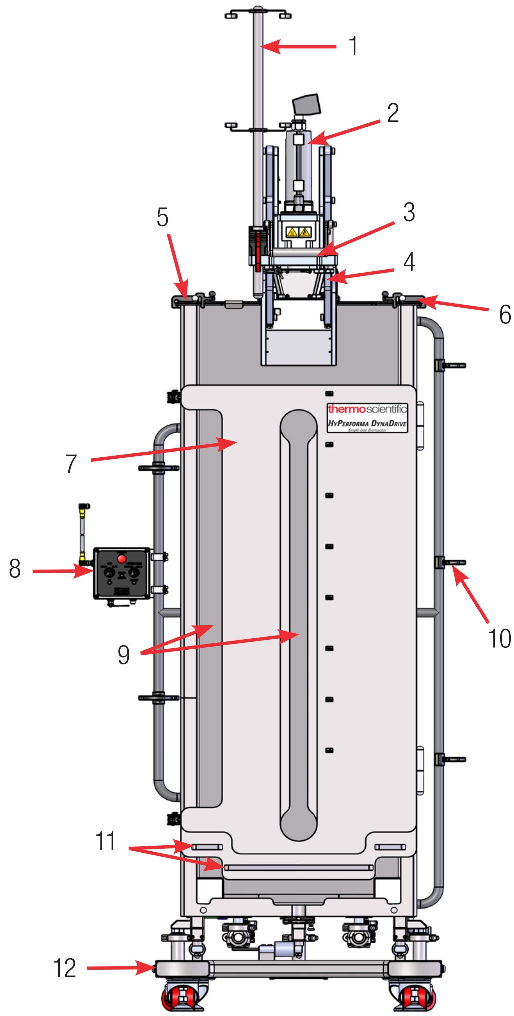


Figure 4.3. Front view of 500 L DynaDrive S.U.B. (without optional E-Box).

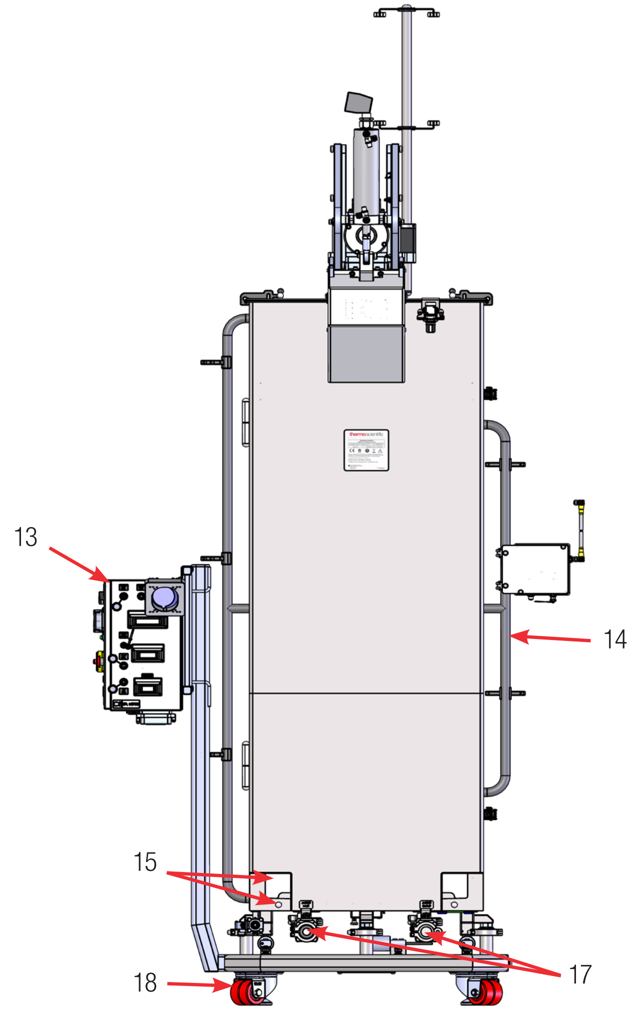


Figure 4.4. Back view of 500 L DynaDrive S.U.B. (with optional E-Box).

1. Exhaust vent filter holder
2. Pneumatic motor lift
3. Agitator motor
4. BPC lift mechanism
5. Foam probe holder
6. Top BPC tab holders
7. Door for BPC loading
8. Motor lift control box
9. Liquid sight windows
10. Cable management clip
11. Probe hanger brackets
12. Cart assembly
13. Electrical control panel (E-Box), optional
14. Vessel handle bars
15. Bottom cutouts/pins for BPC attachment/alignment
16. Bleed jacket valve
17. Tri-clamp jacket inlet/outlet connections
18. Casters

4.2 Hardware specifications

The following tables and figures provide specifications for 50 and 500 L DynaDrive S.U.B.s.

Table 4.1. 50 L DynaDrive S.U.B. specifications.

		Specification
Bioreactor geometry	Rated liquid working volume	50 L
	Minimum liquid working volume	5 L
	Total reactor volume (liquid & gas)	65.5 L
	BPC chamber diameter	29.4 cm (11.59 in.)
	BPC chamber shoulder height	102.23 cm (40.25 in.)
	Liquid height at rated working volume	74 cm (29.13 in.)
	Fluid geometry at working volume (height/diameter) ratio	2.5:1
	Overall reactor geometry (height/diameter ratio)	3.5:1
Impeller	Impeller (quantity x blade count)	3 x 2 modified pitch blade, 1 x 2 sweep impeller
	Impeller scaling (impeller diameter/tank diameter)	0.37
	Impeller diameter	10.85 cm (4.275 in.)
Agitation	Agitation speed range of VFD	30–250 rpm ± 1.5 rpm or 1% of setpoint, whichever is greater
	Recommended minimum during cell culture agitation (at all volumes)	> 120 rpm
	Nominal tip speed	68 cm/s (26.77 ft./min.)
Motor	Agitation motor drive (type, voltage, phase)	Induction, 208 VAC, 3
	AC motor power rating	186.4 W (0.25 hp)
	Motor torque rating	9.5 Nm (82 in-lb.)
	Gear reduction	10:1
	Programmable VFD, remote panel interface, power fault auto restart	Standard
	Motor communication methods (for external controller)	0-10 V, 4-20 mA, Modbus
Temperature control	Jacket area: full/10% volume	0.51 m^2 (5.5 $ft.^2$)/0.06 m^2 (0.65 $ft.^2$)
	Jacket volume	3 L
	Jacket flow rate at 3.4 bar (50 psi)	136 L/min.
	Process connection	1.5 in. Sanitary tri-clamp
	Nominal heating/cooling load (W)	500 W
	Approximate liquid heat-up time (5°C to 37°C)—10% volume, with ThermoFlex 2500 TCU	2 hr
	Approximate liquid heat-up time (5°C to 37°C)—100% volume, with ThermoFlex 2500 TCU	2 hr
	RTD or thermocouple, 3.18 mm (1/8 in.) OD	RTD: Pt-100 (standard)

Table 4.2. 50 L DynaDrive S.U.B. specifications (continued).

		Specification
Support container	Overall width	102.80 cm (40.5 in.) with optional E-Box 68.58 cm (27 in.) without E-Box
	Overall length	76.55 cm (30.1 in.)
	Overall height	177.55 cm (69.9 in.)
	Dry skid weight (mass)	236 kg (519 lb) with optional E-Box 195 kg (430 lb.) without E-Box
	Wet skid weight—rated working volume (mass)	286 kg (631 lb.) with optional E-Box 245 kg (542 lb.) without E-Box
General	Electrical power supply requirement (voltage, phase, amp)	120/240 VAC, single, 20/10 A
	pH & DO probe—autoclavable and single-use options available (single-use are integrated into the BPC)	12 mm diameter x 215–235 mm insertion length x 13.5 PG (pipe) thread
	Noise level	< 70 dB at 1.5 m
Recommended operating parameters	Operating temperature range	Ambient to 40°C ± 0.5°C (104°F ± 0.9°F)
	Motor speed	90–200 rpm
	Volume range	5–50 L
	Maximum bag pressure	34 mbar (0.5 psi)

Figures 4.5 and 4.6 show the dimensions of the 50 L DynaDrive S.U.B. hardware.

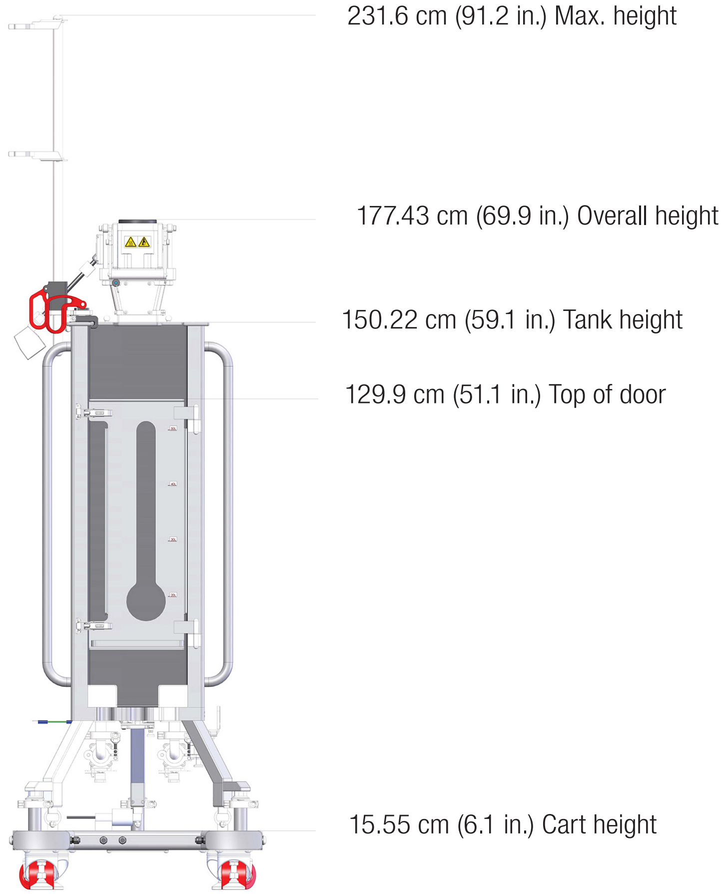


Figure 4.5. Dimensions of 50 L DynaDrive S.U.B. without optional E-Box (front view).

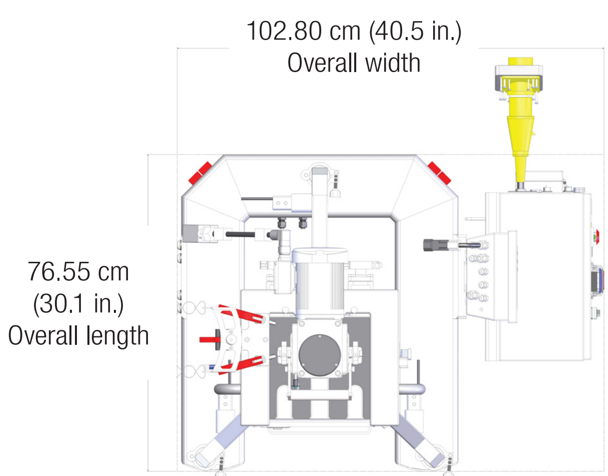


Figure 4.6. Dimensions of 50 L DynaDrive S.U.B. with optional E-Box (top view).

Table 4.3. 500 L DynaDrive S.U.B. specifications.

		Specification
Bioreactor geometry	Rated liquid working volume	500 L
	Minimum liquid working volume	25 L
	Total reactor volume (liquid & gas)	586 L
	BPC chamber diameter	63.4 cm (24.9 in.)
	BPC chamber shoulder height	186.69 cm (73.5 in.)
	Liquid height inside tank at rated working volume	158.75 cm (62.5 in.)
	Fluid geometry at working volume (height/diameter) ratio	2.5:1
	Overall reactor geometry (height/diameter ratio)	2.5:1
Impeller	Impeller (quantity x blade count)	3 x 2 modified pitch blade, 1 x 2 sweep impeller
	Impeller scaling (impeller diameter/tank diameter)	0.37
	Impeller diameter	22.9 cm (9.03 in.)
Agitation	Agitation speed range of VFD	35–120 rpm ± 1.5 rpm or 1% of setpoint, whichever is greater
	Recommended minimum during cell culture agitation (at all volumes)	> 50 rpm
	Nominal tip speed	60 cm/s (118 ft./min.)
Motor	Agitation motor drive (type, voltage, phase), AC motor only	Induction, 208 VAC, 3
	AC motor power rating	400 W (0.5 hp)
	Motor torque rating	5.6 Nm (76 in-lb.)
	Gear reduction	20:1
	Programmable VFD, remote panel interface, power fault auto restart	Standard
	Motor communication methods (for external controller)	0-10 V, 4-20 mA
	Motor lift power supply requirements	24 VDC, 90 psi of air
Temperature control	Jacket area: full/10% volume	0.51 m^2 (5.5 $ft.^2$)/0.06 m^2 (0.65 $ft.^2$)
	Jacket volume	13.6 L
	Jacket flow rate at 3.4 bar (50 psi)	71 L/min.
	Process connection	1.5 in. Sanitary tri-clamp
	Recommended heating/cooling load (W)	5000 W
	Approximate liquid heat-up time (5°C–37°C)—10% volume, with ThermoFlex 10,000 TCU	1 hr
	Approximate liquid heat-up time (5°C–37°C)—100% volume, with ThermoFlex 10,000 TCU	3 hr
	RTD or thermocouple, 3.18 mm (1/8 in.) OD	RTD: Pt-100 (standard)

Table 4.4. 500 L DynaDrive S.U.B. specifications (continued).

		Specification
Support container	Overall width	141.0 cm (55.5 in.) with optional E-Box 103.2 cm (40.6 in.) without E-Box
	Overall length	111.8 cm (44 in.)
	Overall height	310.8 cm (122.4 in.)
	Dry skid weight (mass)	479.9 kg (1,058 lb) with optional E-Box 446.78 kg (985 lb.) without E-Box
	Wet skid weight—rated working volume (mass)	978.85 kg (2,158 lb.) with optional E-Box 945.74 kg (2,085 lb.) without E-Box
General	Electrical power supply requirement (voltage, phase, amp)	120/240 VAC, single, 20/10 A
	pH & DO probe—autoclavable and single-use options available (single-use are integrated into the BPC)	12 mm diameter x 215–235 mm insertion length x 13.5 PG (pipe) thread
	Noise level	< 70 dB at 1.5 m
Recommended operating parameters	Operating temperature range	Ambient to 40°C ± 0.5°C (104°F ± 0.9°F)
	Motor speed	35–120 rpm
	Volume range	25–500 L
	Maximum bag pressure	34 mbar (0.5 psi)

Figures 4.7 and 4.8 show the dimensions of the 500 L DynaDrive S.U.B. hardware.

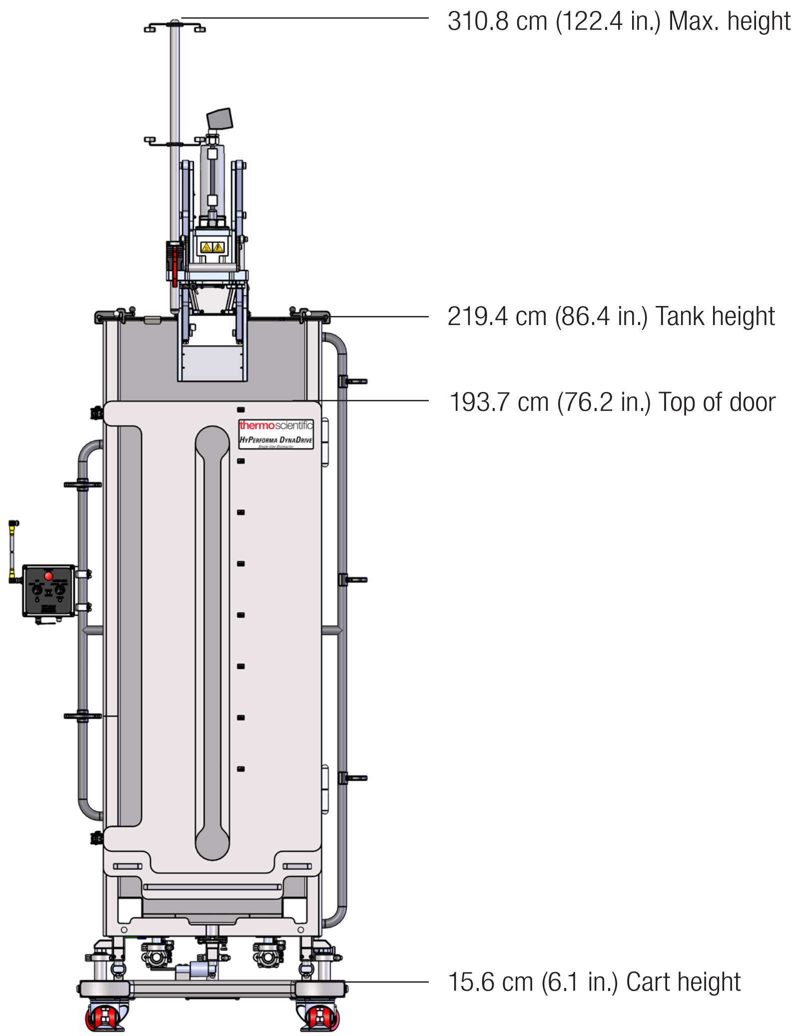


Figure 4.7. Dimensions of 500 L DynaDrive S.U.B. without optional E-Box (front view).

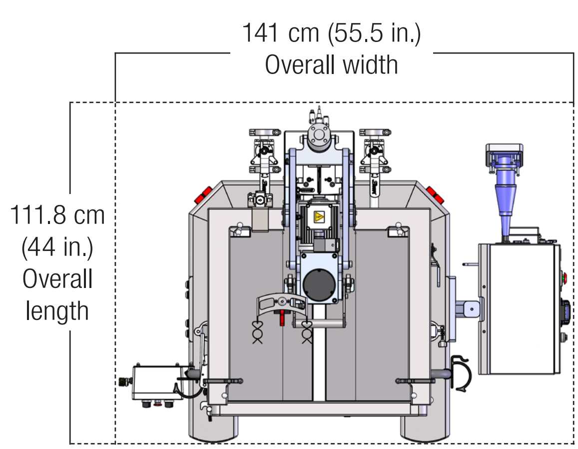


Figure 4.8. Dimensions of 500 L DynaDrive S.U.B. with optional E-Box (top view).

4.3 Features of optional E-Box

Figure 4.9 illustrates the features of the optional Thermo Scientific E-Box available for 50 and 500 L DynaDrive S.U.B. units. Figure 4.10 illustrates the bottom view of the E-Box.

Figure 4.9. Front view of the E-Box for 50 and 500 L DynaDrive S.U.B.s.

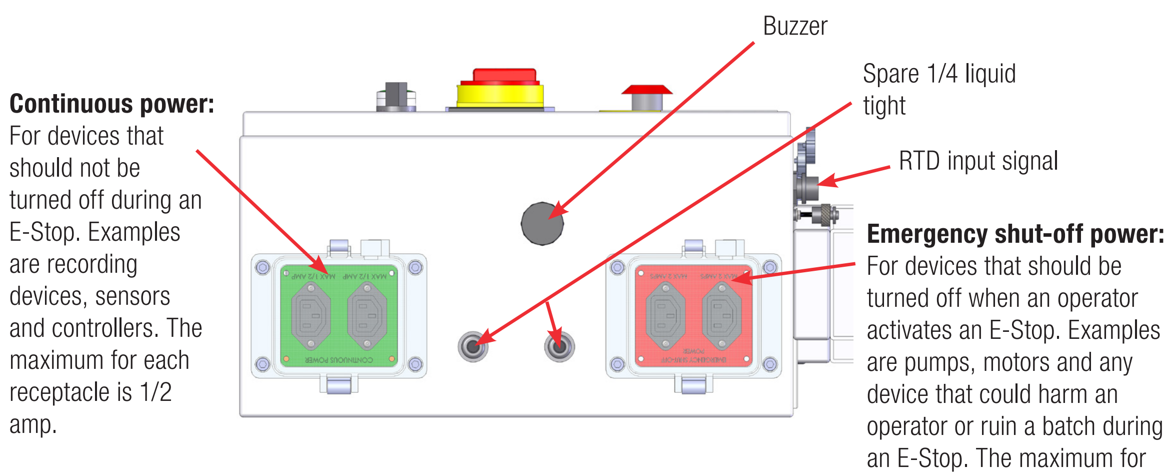


Figure 4.10. Bottom view of E-Box.

4.4 BPC specifications

The following figures and tables provide specification information for the two standard 50 L DynaDrive S.U.B. BPCs, with or without an alternating tangential flow (ATF) port, and the standard 500 L BPC.

4.4.1 50 L BPC specifications

Standard 50 L DynaDrive S.U.B. BPC with ATF

Specification information for the labeled items in Figure 4.11 is located in Table 4.5 on the following page.

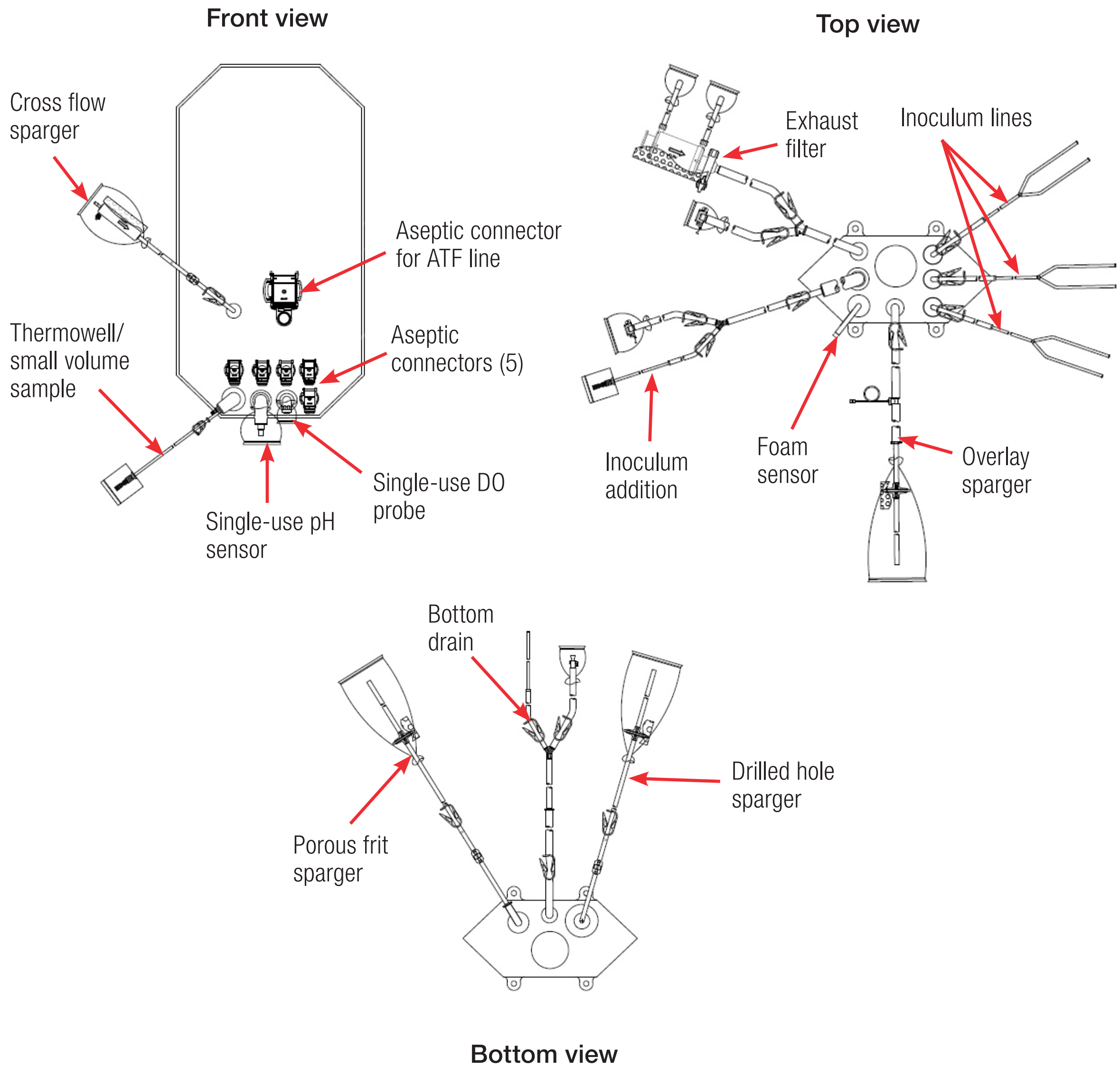


Figure 4.11. Front, top, and bottom views of 50 L DynaDrive S.U.B. BPC with ATF.

Table 4.5. 50 L DynaDrive S.U.B. BPC with ATF specification information.

Description	Tubing set (ID x OD x length)	End treatment
Inoculum lines	2 x 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 152 cm (60 in.) connected to "Y" connector x 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 8 cm (3 in.) and 6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) OD x 15 cm (6 in.)	Plugged
Overlay gas sparger	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 15 cm (6 in.) connected to filter x 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 10.16 cm (4 in.) reduced to 12.7 mm (1/2 in.) ID x 19.1 mm (3/4 in.) OD C-Flex tubing x 20 cm (8 in.)	Hydrophobic vent filter with Emflon II, connected to 15 cm (6 in.) C-Flex tubing; Pendotech pressure sensor connected to 15 cm (6 in.) C-Flex tubing
Cross flow sparger	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 8 cm (3 in.) connected to check valve and 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 183 cm (72 in.)	Meissner Steridyne 50 mm (1.97 in.) filter
Aseptic connectors (5)	Oetiker stepless ear clamp, 20.63 mm (13/16 in.) OD tube	CPC AseptiQuik G aseptic connectors
Bottom drain	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 152 cm (60 in.) reduced to 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.) splits to 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 30 cm (12 in.) reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.) and 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.)	Plugged and 9.5 mm (3/8 in.) MPC insert
Thermowell/small volume sample	Thermowell adapter for 3.2 mm (1/8 in.) diameter RTD and 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 46 cm (18 in.)	Luer lock and SterilEnz pouch with injection site assembly
Single-use pH sensor	N/A	Hamilton OneFerm sensor and adapter and molded silicone tube for adapter
Single-use DO probe	N/A	Hamilton VisiFerm DO single-use probe
Pressure sensor port	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 8 cm (3 in.)	CPC AseptiQuik aseptic connector
Inoculum addition	9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 152 cm (60 in.) splits to 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 30 cm (12 in.) reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.) and 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.)	SteriEnz pouch with injection site assembly and 9.5 mm (3/8 in.) MPC body
Exhaust filter	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 20 cm (8 in.) connected to 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 15 cm (6 in.) and 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 25 cm (10 in.)	CPC AseptiQuik aseptic connector— Pall Kleenpak 0.2 micron exhaust vent filter
Drilled hole sparger 8.9 cm (3.5 in.) disk with 360 x 0.178 mm (0.007 in.) holes	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 8 cm (3 in.) connected to check valve and 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 97 cm (38 in.)	Meissner Steridyne 0.2 micron hydrophobic filter connected to 15 cm (6 in.) C-Flex
Aseptic connector for ATF line	2.54 cm (1 in.) ID x 3.49 cm (1 3/8 in.) OD x 0.47 cm (3/16 in.) wall C-Flex tubing	CPC AseptiQuik L connector

Standard 50 L DynaDrive S.U.B. BPC without ATF

Specification information for the labeled items in Figure 4.12 is located in Table 4.6 on the following page.

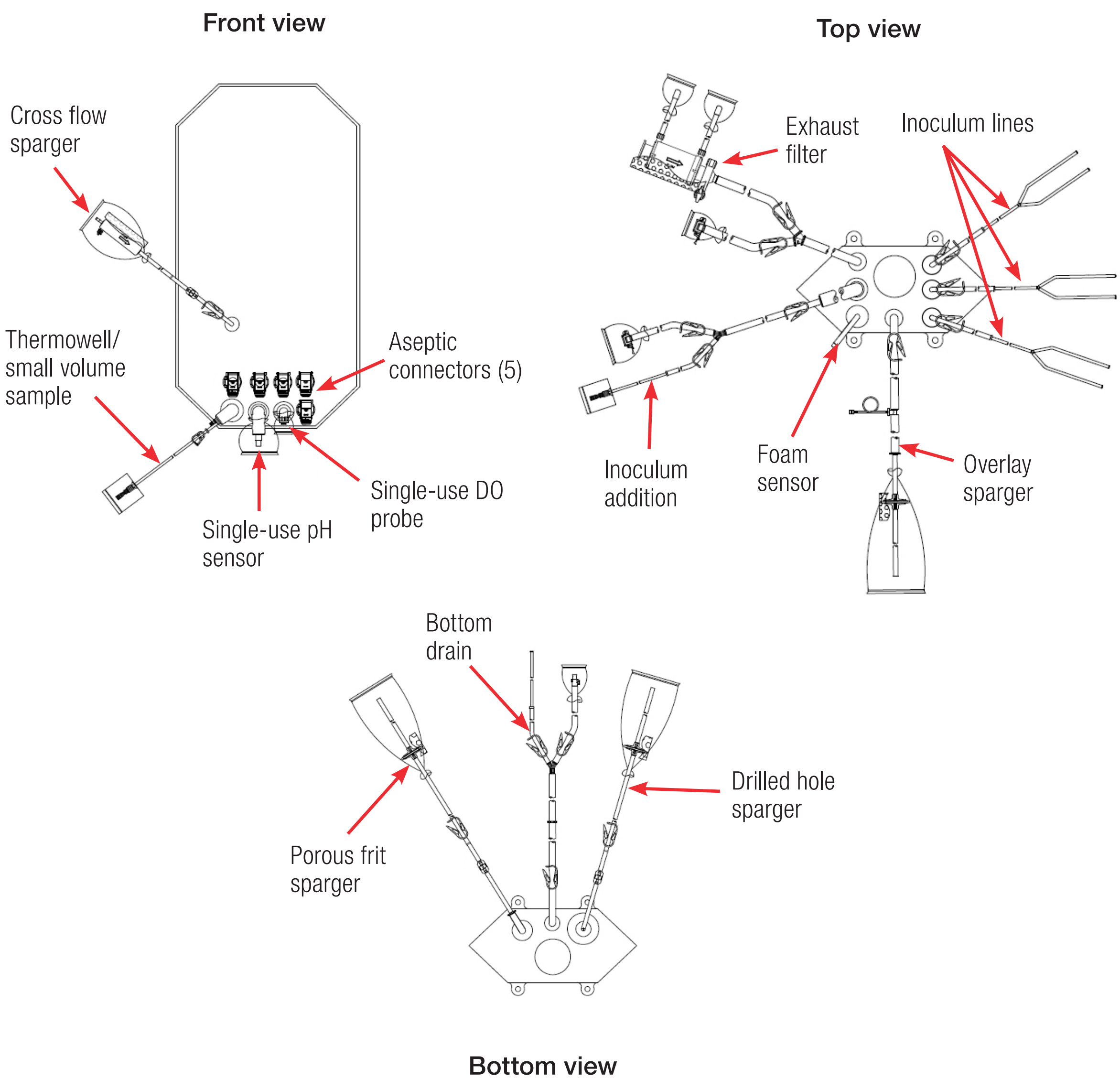


Figure 4.12. Front, top, and bottom views of 50 L DynaDrive S.U.B. BPC without ATF.

Table 4.6. 50 L DynaDrive S.U.B. BPC without ATF specification information.

Description	Tubing set (ID x OD x length)	End treatment
Inoculum lines	2 x 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 152 cm (60 in.) connected to "Y" connector x 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 8 cm (3 in.) and 6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) OD x 15 cm (6 in.)	Plugged
Overlay gas sparger	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 15 cm (6 in.) connected to filter x 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 10.16 cm (4 in.) reduced to 12.7 mm (1/2 in.) ID x 19.1 mm (3/4 in.) OD C-Flex tubing x 20 cm (8 in.)	Hydrophobic vent filter with Emflon II, connected to 15 cm (6 in.) C-Flex tubing; Pendotech pressure sensor connected to 15 cm (6 in.) C-Flex tubing
Cross flow sparger	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 8 cm (3 in.) connected to check valve and 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 183 cm (72 in.)	Meissner Steridyne 50 mm (1.97 in.) filter
Aseptic connectors (5)	Oetiker stepless ear clamp, 20.63 mm (13/16 in.) OD tube	CPC AseptiQuik G aseptic connectors
Bottom drain	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 152 cm (60 in.) reduced to 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.) splits to 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 30 cm (12 in.) reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.) and 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.)	Plugged and 9.5 mm (3/8 in.) MPC insert
Thermowell/small volume sample	Thermowell adapter for 3.2 mm (1/8 in.) diameter RTD and 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 46 cm (18 in.)	Luer lock and SterilEnz pouch with injection site assembly
Single-use pH sensor	N/A	Hamilton OneFerm sensor and adapter and molded silicone tube for adapter
Single-use DO probe	N/A	Hamilton VisiFerm DO single-use sensor
Pressure sensor port	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 8 cm (3 in.)	CPC AseptiQuik aseptic connector
Inoculum addition	9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 152 cm (60 in.) splits to 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 30 cm (12 in.) reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.) and 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.)	SteriEnz pouch with injection site assembly and 9.5 mm (3/8 in.) MPC body
Exhaust filter	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 20 cm (8 in.) connected to 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 15 cm (6 in.) and 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 25 cm (10 in.)	CPC AseptiQuik aseptic connector— Pall Kleenpak 0.2 micron exhaust vent filter
Drilled hole sparger 8.9 cm (3.5 in.) disk with 360 x 0.178 mm (0.007 in.) holes	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 8 cm (3 in.) connected to check valve and 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 97 cm (38 in.)	Meissner Steridyne 0.2 micron hydrophobic filter connected to 15 cm (6 in.) C-Flex

4.4.2 500 L BPC specifications

Standard 500 L DynaDrive S.U.B. BPC

Specification information for the labeled items in Figure 4.13 is located in Table 4.7 on the following page.

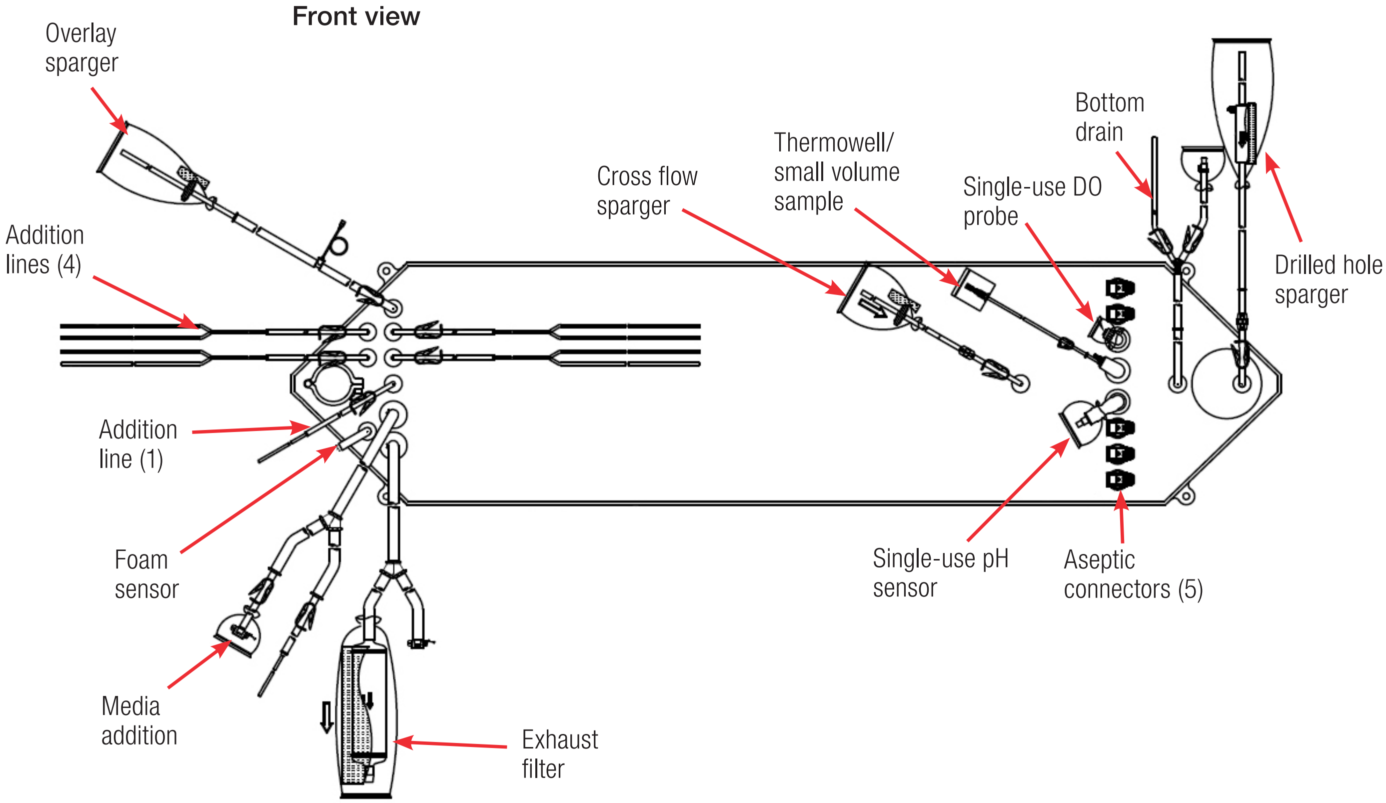


Figure 4.13. Front, top, and bottom views of 500 L DynaDrive S.U.B. BPC.

Table 4.7. 500 L DynaDrive S.U.B. BPC specification information.

Description	Tubing set (ID x OD x length)	End treatment
Addition line (1)	6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) OD C-Flex tubing x 218 cm (86 in.) connected to 3.2 mm (1/8 in.) ID x 6.3 mm (1/4 in.) OD C-Flex tubing x 61 cm (24 in.)	Plugged
Addition lines (4)	4x 6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) OD C-Flex tubing x 15 cm (6 in.) splits to 2x 3.2 mm (1/8 in.) ID x 11.1 mm (1/4 in.) OD C-Flex tubing x 213 cm (84 in.)	Plugged
Overlay gas sparger	12.7 mm (1/2 in.) ID x 19.1 mm (3/4 in.) OD C-Flex tubing x 15 cm (6 in.) connected to pressure sensor connected to 12.7 mm (1/2 in.) ID x 19.1 mm (3/4 in.) OD C-Flex tubing x 48 cm (19 in.) connected to 6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) OD C-Flex tubing x 10 cm (4 in.) connected to vent filter connected to 6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) OD C-Flex tubing x 15 cm (6 in.)	Meissner Steridyne 50 mm (1.97 in.) filter connected to 15 cm (6 in.) C-Flex tubing; Pendotech pressure sensor connected to 15 cm (6 in.) C-Flex tubing
Cross flow sparger	6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) OD C-Flex tubing x 15 cm (6 in.) connected to check valve and 6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) OD C-Flex tubing x 8 cm (3 in.) connected to 6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) OD C-Flex tubing x 183 cm (72 in.) connected to vent filter connected to 6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) OD C-Flex tubing x 15 cm (6 in.)	Meissner Steridyne 50 mm (1.97 in.) filter
Aseptic connectors (5)	Oetiker stepless ear clamp, 20.63 mm (13/16 in.) OD tube	CPC AseptiQuik G aseptic connectors
Bottom drain	12.7 mm (1/2 in.) ID x 19.1 mm (3/4 in.) OD C-Flex tubing x 60 cm (24 in.) connected to 9.5 mm (3/8 in.) ID x 15.9 mm (5/8 in.) OD C-Flex tubing x 30 cm (12 in.) splits to 6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) OD C-Flex tubing x 30 cm (12 in.) connected to 3.2 mm (1/8 in.) ID x 6.4 mm (1/4 in.) OD C-Flex tubing x 30 cm (12 in.) and 9.5 mm (3/8 in.) ID x 15.9 mm (5/8 in.) OD C-Flex tubing x 30 cm (12 in.)	Plugged and 9.5 mm (3/8 in.) MPC insert
Thermowell/small volume sample	Thermowell adapter for 2.54 cm (1 in.) port connected to 6.4 mm (1/4 in.) ID x 3.2 mm (1/8 in.) OD x C-Flex tubing x 61 cm (24 in.)	Luer lock and SterilEnz pouch with 3.2 mm (1/8 in.) SmartSite assembly
Single-use pH sensor	N/A	Hamilton OneFerm sensor and adapter and molded silicone tube for adapter
Single-use DO probe	N/A	Hamilton VisiFerm DO single-use sensor
Media addition	19.1 mm (3/4 in.) x 25.4 mm (1 in.) C-Flex tubing x 213 cm (84 in.) splits to 19.1 mm (3/4 in.) x 25.4 mm (1 in.) C-Flex tubing x 10 cm (4 in.) connected to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 61 cm (24 in.) and 19.1 mm (3/4 in.) x 25.4 mm (1 in.) C-Flex tubing x 10 cm (4 in.) connected to 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) x 61 cm (24 in.)	CPC AseptiQuik G aseptic connector
Exhaust filter	19.1 mm (3/4 in.) ID x 25.4 mm (1 in.) OD C-Flex tubing x 41 cm (16 in.) splits to 19.1 mm (3/4 in.) ID x 25.4 mm (1 in.) OD C-Flex tubing x 15 cm (6 in.) and 19.1 mm (3/4 in.) ID x 25.4 mm (1 in.) OD C-Flex tubing x 15 cm (6 in.)	CPC AseptiQuik aseptic connector—Meissner UltraCap 0.2 micron exhaust vent filter
Foam sensor	12.7 mm (1/2 in.) ID x 19.1 mm (3/4 in.) OD C-Flex tubing x 8 cm (3 in.)	Foam sensor anode; 1.3 cm (1/2 in.) port, 20.9 cm (8.25 in.) wire
Drilled hole sparger 17.14 cm (6.75 in.) disk with 980 x 0.368 0.177 mm (0.007 in.) holes	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 8 cm (3 in.) connected to check valve and 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 97 cm (38 in.)	Meissner Steridyne 0.2 micron hydrophobic filter connected to 15 cm (6 in.) C-Flex

BPC packing information

Standard DynaDrive S.U.B. BPC packaging is listed in Table 4.8.

Table 4.8. Standard DynaDrive S.U.B. BPC packaging.

Outer packaging	Supplied "flat-packed"; two polyethylene outer layers
Label	Description, product code, lot number, expiry date on outer packaging and shipping container
Sterilization	Irradiation (25 kGy to 40 kGy) inside outer packaging
Shipping container	Durable cardboard carton
Documentation	Certificate of Analysis provided with each lot for delivery

4.5 Additional system component part numbers

The following tables list part numbers for additional DynaDrive S.U.B. system components, such as load cell kits and accessories.

Table 4.9. Harsh mount load cell display part numbers for 50 and 500 L systems using the Thermo Scientific E-Box.

Description	Cat. no.
Mettler Toledo IND331 display, harsh mount style with analog interface (STD), 120 VAC US line cord/plug	SV50177.306
Mettler Toledo IND331 display, harsh mount style with Allen-Bradley RIO interface, 120 VAC US line cord/plug	SV50177.307
Mettler Toledo IND331 display, harsh mount style with Device Net interface, 120 VAC US line cord/plug	SV50177.308
Mettler Toledo IND331 display, harsh mount style with Ethernet/IP and Modbus TCP interface, 120 VAC US line cord/plug	SV50177.309
Mettler Toledo IND331 display, harsh mount style with Profibus interface, 120 VAC US line cord/plug	SV50177.310

Table 4.10. 50 L DynaDrive vent filter heater kit part numbers for use with Pall KA3 vent filters. Includes vent filter heater, controller with water-tight closure, quick-connects, and installation power cord.

Description	Cat. no.
120 VAC, 23.8 W, Pall Kleenpak KA3 series 46 vent filter heater, integrated, M12–4 pin connector (used when integrated with controller)	SV50191.45
240 VAC, 30.3 W, Pall Kleenpak KA3 series 46 vent filter heater, integrated, M12–4 pin connector (used when integrated with controller)	SV50191.46

Table 4.11. 500 L DynaDrive vent filter heater kit part numbers for use with Meissner 10 in. series 46 vent filters. Includes vent filter heater, controller with water-tight closure, quick-connects, and installation power cord.

Description	Cat. no.
120 VAC, 99.6 W, Meissner 10 in. series 46 vent filter heater, integrated, M12–4 pin connector (used when integrated with controller)	SV50191.47
240 VAC, 99.6 W, Meissner 10 in. series 46 vent filter heater, integrated, M12–4 pin connector (used when integrated with controller)	SV50191.48

Table 4.12. Miscellaneous and accessory part numbers.

Component	Cat. no.
Probe assembly with CPC AseptiQuik connector (non-sterile, for use in autoclave)	SH30720.02
Probe assembly with Pall Kleenpak connector (non-sterile, for use in autoclave)	SH30720.01
Heavy-duty tubing clamp—single	SV20664.01
Heavy-duty tubing clamp—pack of 10	SV20664.04
Stainless steel autoclave tray, for autoclaving probe assemblies	SV50177.01
Double probe clips	SV51256.01
Sterile sampling manifold with luer lock—single	SH30845.01
Sterile sampling manifold with luer lock—pack of 10	SH30845.02
Adjustable filter bracket	SV50177.313
Foam probe holder (50 L units only)	SV51253.01
Foam probe holder (500 L units only)	SV51253.02
BPC top tab holders	SV51254.01
Cable management clips	SV51255.01

5

Maintenance and troubleshooting

Chapter contents

5.1 Maintenance

5.1.1 Routine maintenance

Environmental conditions, operating parameters, and adhering to standard operating procedures as outlined in this user's guide have significant impact upon the useful life of your DynaDrive S.U.B. hardware system. The following guidelines are based upon the standard operating conditions outlined in this user's guide.

High-wear items such as bearings, seals, O-rings, and sterilization valves common to conventional bioreactor systems have been purposefully considered in the design of the construction of the DynaDrive S.U.B. The S.U.B. system is inherently robust and requires low levels of routine maintenance. Taking time between bioreactor runs to clean the exterior of the hardware will improve the appearance and overall longevity of the system.

5.1.2 Preventive maintenance

Replacement of the mixing motor is recommended every five years, or as needed.

5.2 Troubleshooting and frequently asked questions

5.2.1 Hardware operation issues

Issue: **The DynaDrive S.U.B. will not operate.**

Solution: **Check the power supply.**

- Verify the position of the main electrical plug connection at the wall outlet, the main power disconnect, and the emergency stop switch.
- Verify the condition of the main electrical circuit breaker at your facility. If the protection breaker has been tripped, determine the fault condition. The condition may exist where other electrical systems are requiring current loads beyond those allowed by the breaker. The DynaDrive S.U.B. system should be placed on its own electrical circuit.
- Disconnect the main power cord. Inspect the electrical circuit breakers and fuses inside the electrical box of the S.U.B. controller. Determine the fault condition by visual inspection. If the fault condition cannot be determined by visual inspection, contact the manufacturer.

Issue: **The DynaDrive S.U.B. temperature is below target or slow to respond.**

Solution: **Check the temperature controller and sensor.**

- Verify that the temperature probe (RTD) is not loose, and has been fully inserted into the BPC thermowell.
- Verify that the thermowell has been filled with sufficient glycerol to aid in heat transfer.
- Verify that the temperature control unit (TCU) is operating, and all of the ball valves are open.
- Verify that the system is filled with a sufficient volume of fluid. There must be enough media (minimum volume) in the BPC to provide contact with the container. Add more media if the BPC is not touching the heater area.

Issue: **Noise is being emitted from the mixer assembly.**

Solution: **No action is required.**
The bearing port assembly supplied with the DynaDrive S.U.B. is an important component in maintaining a sterile environment during cell growth. The special seals used in the DynaDrive S.U.B. may generate some noise during operation, particularly after the first day of operation. This noise may vary in intensity and frequency, but generally has no significant effect on performance or overall durability of the BPC during the intended life of the product.

Issue: **The mixer controller does not respond to user inputs.**

Solution: **Allow the speed to stabilize before using the keypad interface.**

- Adjusting the speed control too rapidly may require several seconds for speed stabilization.
- Wait ten seconds, then attempt to adjust the speed at the keypad interface.
- Verify the position of the input select switch of the variable frequency drive (VFD). If the toggle switch is not in the middle position, the controller will not be able to receive control inputs from the control keypad on the front panel.

Issue: **I typically use level sensors to control the volume and feed rate or supplement during a bioreactor run; how would I do this with the DynaDrive S.U.B.?**

Solution: **Use load cells or a scale to control volumes based upon weight.**
The DynaDrive S.U.B. is not equipped with level sensors. However, the S.U.B. can be set up to allow supplement feeds and volumes to be managed by weight.

5.2.2 Cell culture operation issues

Issue: **Dissolved oxygen readings are low or slow to respond.**

Solution: **Check the physical condition of the dissolved oxygen (DO) probe, the calibration of the probe, and gas flow rate into the DynaDrive S.U.B.**

- DO probes require routine maintenance; replace the damaged probe or membrane when necessary.
- Verify the DO probe calibration relative to setpoints of zero and span.
- Inspect the line sets connected to direct spargers for restriction (closed tubing clamp, pinched line, low supply pressure).

Issue: **Dissolved oxygen readings are erratic or unstable.**

Solution: **Adjust the bioreactor controller to suit the volume of your DynaDrive S.U.B. system.**

- Many different parameters can affect the ability of a bioreactor controller to maintain a target setpoint during process control. Modern controllers utilize computer algorithms to adjust targeted parameters. The most common technique is that of a tunable controller that uses proportional, integral, and derivative (PID) variables. Tuning these PID values to the specific characteristics of the system dynamics will, in most cases, stabilize process parameters to an acceptable level. We recommend that you consult the user guide of the particular bioreactor controller you are using.
- A grounding reference to the media can be created by using a grounding lead between the tank and the body of the stainless steel DO probe or to the stainless steel connector (if present) on the sample line of the BPC.

Issue: **pH levels are questionable or out of range.**

Solution: **Verify the calibration of the probe and utilize either media or gas buffers.**

- pH levels can be managed in a similar manner to conventional bioreactors once calibration of the probe is verified by use of an off-line sample. Carbon dioxide gas sparged through the media or headspace, biocarbonate levels in the media and the addition of liquid titrant solutions all serve to manage the pH balance of the bioreactor environment. See section 3.5.4 for more information on probe calibration.
- A grounding reference to the media can be created by using a grounding lead between the tank and the body of the stainless steel DO probe or to the stainless steel connector (if present) on the sample line of the BPC.

Issue: **We are not achieving the cell growth we expected in the DynaDrive S.U.B. while running under our normal bioreactor agitation and sparging rates. What should we do?**

Solution: **Reduce agitation and sparging rates.**

- Often low cell viability and cell growth can be attributed to excessive sparging or agitation. We recommend that you reduce the sparge rate compared to what you might use in a conventional bioreactor. Gas flow rates supplied as overlay should also be reduced as much as possible. Too much gas creates excess foam and higher shear conditions. Provide only the level of agitation needed (low viability and lysed cells), reduce agitation speed (cell aggregation and settling), and increase agitation.
- Media formulation can also have a significant effect on cell culture growth in the DynaDrive S.U.B. Surfactants such as Pluronic decrease shear and increase k_La, but at a cost of increased foaming. Thermo Scientific can offer custom media especially for the S.U.B. and your specific cell line(s).

5.2.3 Sparging issues

Issue: **There is excessive foam in the bioreactor headspace.**

Solution: **Alter the liquid surface tension related to the culture media and/or sparge gas.**

- A media supplement of antifoam can be used in the DynaDrive S.U.B. These serve to lower the surface tension of the media and will reduce the presence of foam.
- High sparge rates of air can result in the presence of excessive foam. Testing has shown that sparging with oxygen will typically result in a dramatic reduction of foam in the headspace.

Issue: **The sparger does not seem to be working although gas is present.**

Solution: **Allow the sparger membrane to purge.**

- If the DynaDrive S.U.B. is filled with liquid and allowed to sit idle for extended periods of time without gas being supplied to the sparger, liquid can accumulate between the membrane and check valve. Various media additives may restrict the membrane temporarily. Several minutes of gas pressure being supplied to the sparger should purge the membrane, allowing it to function properly.
- Certain operating conditions can create situations when the sparger membrane may become restricted due to insufficient line pressure from the bioreactor controller gas feed line. Increasing the flow rate to one liter per minute, or momentarily raising the pressure

regulator outlet pressure to 340 mbar (5 psi) may alleviate the problem. Alternatively, several seconds at this higher pressure will allow the membrane to purge pores that may be blocked due to the presence of accumulated liquid.

5.2.4 Probe and connector issues

Issue: **We forgot to introduce the pH and DO probes prior to media fill; can we still make a sterile connection under these conditions?**

Solution: **Yes, as long as the clamps were closed on the aseptic connector probe ports before liquid fill.**

- The aseptic connectors must be dry to make the connection of the probe assemblies. When media is already present in the DynaDrive S.U.B., follow the probe insertion procedures as outlined in section 3.5.3.
- Some fluid may enter the bellows when the probe is inserted into a BPC already filled with media. This is normal and will not affect the sterility of the system.

5.2.5 Other issues

Issue: **The BPC seems overly tight.**

Solution: **Verify that the container is venting and inspect it for the cause of overpressure.**

- Reduce the inlet gas flow rate of overlay and direct sparger.
- Inspect the exhaust filter for restriction or blockage.
- Excessive foaming should be avoided for several reasons. If foam levels are allowed to reach the exhaust filter, the filter will become restricted, resulting in excessive internal pressure within the confines of the DynaDrive S.U.B. This may cause product failure and bursting of the BPC.

6

General ordering information

Chapter contents

6.1 Ordering instructions

BPCs and hardware components for the DynaDrive S.U.B. can be ordered directly from Thermo Fisher Scientific. These items include all components that have part numbers beginning with the following digits:

- SH
- SV
- SUB

6.2 Ordering/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 (1) 670 734 093
Fax: +44 (1) 670 732 537
Email: customerservice.bioprocessing@thermofisher.com

6.3 Technical support

Technical support for the DynaDrive S.U.B. 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 Scientific sales representative for general product pricing, availability, delivery, order information and product complaints.

Call +1 435 792 8500 (United States) or +44 (1) 670 734 093 (Europe, U.K.) for direct and immediate response to overall product questions, and product technical information (Technical Support). You can also contact Technical 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 each S.U.B. system. If you require assistance in setting up and operating your S.U.B. system, please inquire at the time of purchase.

Training

Training can be provided for startup and operation of the S.U.B. Contact your Thermo Scientific sales representative.

Appendix A—Installation of female electrical receptacle

1. In order to complete the installation for units with AC motors, the facility must be equipped with an electrical housing of sufficient size.
   - Typically in the U.S. the plug will require a two-gang box when using the adapter plate (supplied).
   - For installations outside the U.S. (where an adapter plate is not supplied), we recommend that an electrical control panel (E-Box) be modified to accommodate the cutout dimensions as shown in Figure A.1 below.

2. Verify that electrical power has been disconnected and locked out for safety.

3. Verify that the holes for mounting the receptacle housing are positioned properly. Center to center measurement of respective mounting holes is 85 mm (3.35 in.) tall and 77 mm (3 in.) wide.

4. Verify the condition of the three exposed wire leads and strip back to expose new wire if needed.

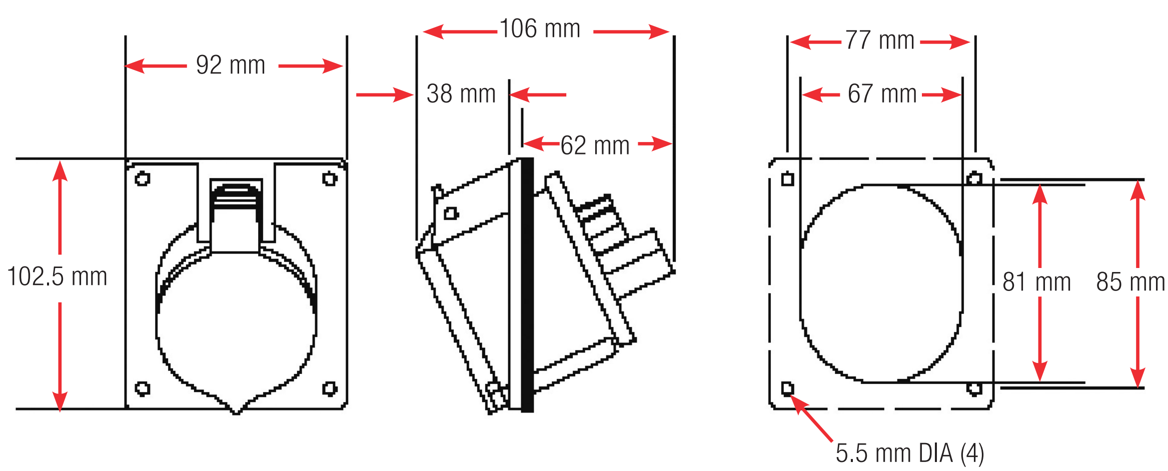


Figure A.1. Panel cutout.

5. Connect the wire leads on the receptacle (shown in Figure A.2 below) using the screw terminals, paying strict attention to obtain the correct wiring position as it is labeled on the receptacle.
   - Green (ground)
   - White (common)
   - Black in the U.S., Blue in the E.U. (hot)

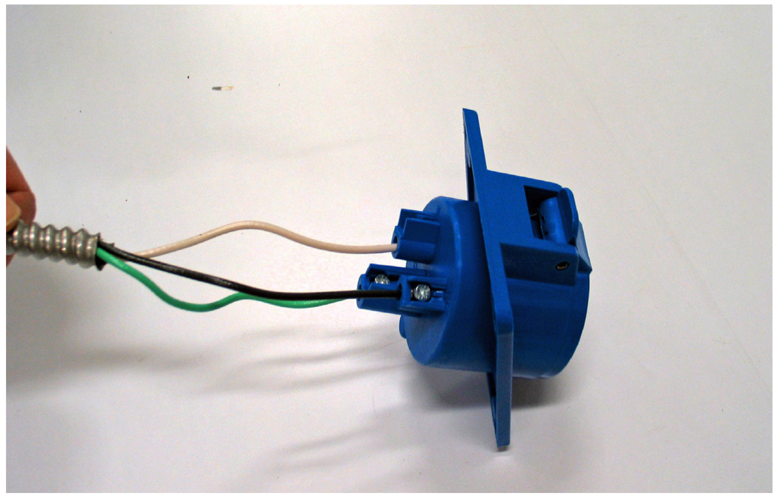


Figure A.2. Female receptacle (blue for 240 VAC, yellow for 110 VAC).

6. If you are using the adapter mounting plate, secure it to the selected facility electrical housing as per drawing (Figure A.3 on the following page), otherwise proceed to Step 7.

7. Secure the electrical receptacle using the four supplied screw fasteners.

8. Connect power back to the electrical circuit.

9. Test the circuit with a multimeter prior to making any connections to the electrical receptacle.

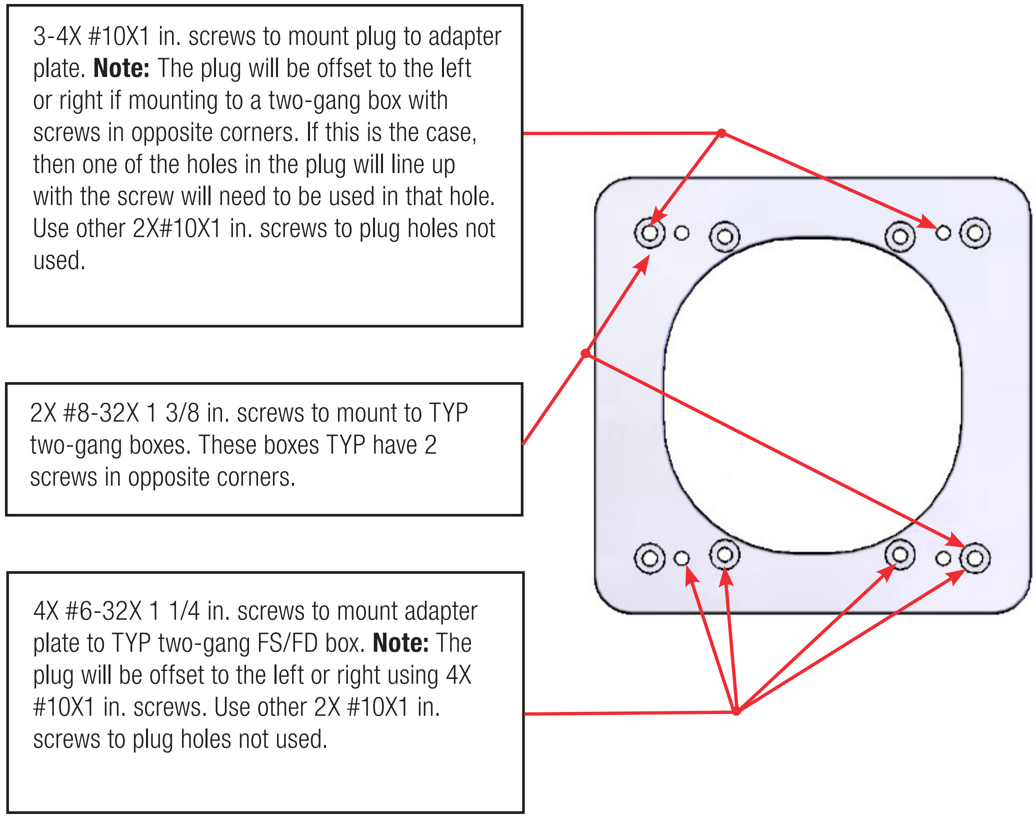


Figure A.3. Adapter mounting plate

Appendix B—Mettler Toledo IND331 display load cell calibration instructions

Please refer to the instructions and reference material found in the Mettler Toledo IND Terminal Technical Manual for specific procedures and troubleshooting methods.

Verify the following before beginning load cell calibration:

- The Mettler Toledo IND display, load cell summing block, and load cell transducers have been specified, installed, and configured properly.
- The load cell transducers do not have the transport lockout nuts in place (load cells must be ready for use prior to calibration).

The calibration accuracy achieved cannot exceed the precision of the reference used for calibration.

- Field calibration is most often performed using calibrated reference weights or flow meters for volumetric mass reference.
- Factory-trained technicians have the experience and tools necessary to provide the best system performance and reliability. **If in doubt, contact your factory service representative.**

Introduction

- Setup mode is accessed by pressing and holding the "Print" key for approximately three seconds. See the Mettler Toledo IND Terminal Technical Manual for further detail.
- Pressing "Print" is equivalent to pressing "Enter." Use this key to proceed through the sub-block numbers until you find your desired choice.
- Press "Select" to toggle the values of the selected sub-block.
- The S.U.B. electrical schematic contains a table showing the sub-blocks that have changed from the default settings.

Span calibration

The scale's span calibration can be determined with or without a linearity adjustment. With linearity disabled, a single reference point is used to calibrate the scale. This is the normal method of span calibration. If linearity is enabled, an additional mid-range weight reference point is added to the adjustment procedure. Linearity can be enabled or disabled in the setup mode.

For further information, refer to the Mettler Toledo IND331 manual at: http://mt.com

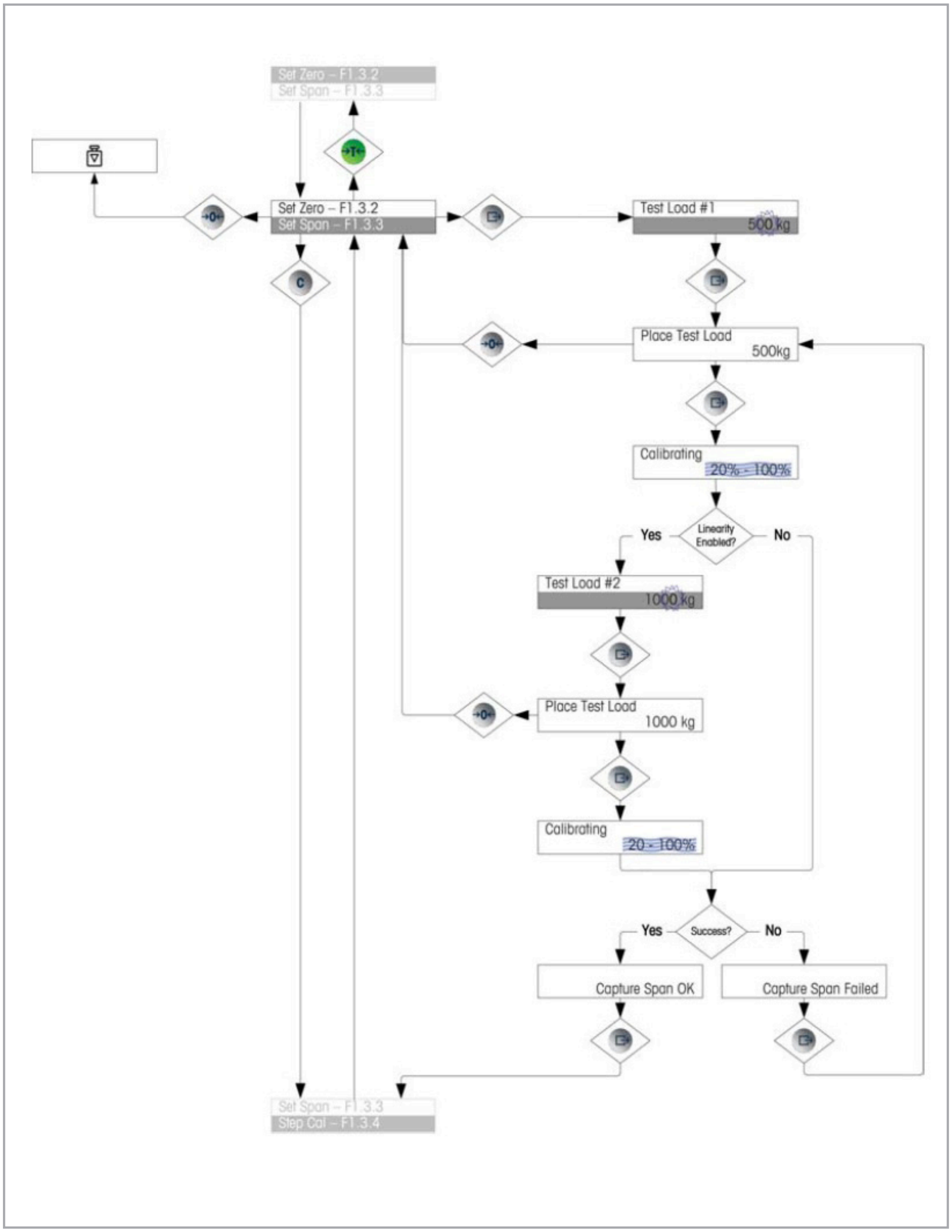


Figure B.1. Span calibration.

Find out more at **thermofisher.com/dynadrive**

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