



HyPerforma Single-Use Fermentor (S.U.F.) User's Guide

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Waarschuwingen, veiligheid en garantie-informatie

Hartelijk dank voor het aanschaffen van de Thermo Scientific™ HyPerforma™ fermentor voor eenmalig gebruik (S.U.F.). We hebben de veiligheidsinformatie toegevoegd aan deze handleiding, die gebaseerd is op onze kennis en ervaring. Het is echter belangrijk dat u samenwerkt met uw afdeling Safety Management om te zorgen dat deze apparatuur in uw veiligheidspraktijken wordt geïntegreerd. Neem de tijd om uw eigen taakveiligheidsanalyse uit te voeren om alle potentiële gevaren te identificeren en beheren.



WAARSCHUWING: Zorg dat u deze gebruikershandleiding begrijpt voordat u deze apparatuur in gebruik neemt.

De Thermo Scientific HyPerforma-fermentor voor eenmalig gebruik (S.U.F.) is ontwikkeld om gebruikt te worden onder traditionele omstandigheden met microbiële celculturen. Een algemeen begrip van fermentorsystemen en hun werking is van belang voordat het systeem de eerste keer gebruikt wordt. Zorg dat u de gebruikershandleiding voorafgaand aan het gebruik hebt gelezen en begrepen. Indien u dit niet doet, kan dit leiden tot letsel. **De juiste procedures voor het afvoeren van BioProcess-containers voor eenmalig gebruik (BPC's) moeten worden opgevolgd, afhankelijk van de gebruikte cultuur.** Zie het bijbehorende hoofdstuk in deze handleiding.



WAARSCHUWING: Gevaarlijke interne spanning.

Elektrische componenten zijn vereist om de S.U.F. goed te laten functioneren. De motor van de mixer, motorregelaar en het bedieningspaneel beschikken allemaal over elektrische componenten. **Er bestaat een risico op elektrische schokken en letsel. Koppel de voeding los voordat u elektrische componenten opent. Onderhoud mag uitsluitend worden uitgevoerd door opgeleid personeel. Thermo Fisher Scientific raadt het gebruik van standaard lock-out-procedures aan wanneer onderhoud aan elektrische componenten wordt uitgevoerd. De hoofdonderbreker van het elektrische bedieningspaneel kan vergrendeld worden.**



WAARSCHUWING: Er kan statische elektriciteit worden opgebouwd in BPC's.

- BPC's kunnen als isolatie voor elektrostatische lading optreden. Indien elektrostatische lading wordt overgebracht naar een BPC kan de lading worden opgeslagen in de BPC en/of het interne product. Dit fenomeen verschilt per product en gebruikstoepassing. De eindgebruiker heeft daarom de exclusieve verantwoordelijkheid om te garanderen dat een risicobeoordeling wordt uitgevoerd en het risico op elektrostatische schokken wordt weggenomen.
- Waar van toepassing kan een roestvrijstalen koppeling van een productcontact geaard worden aan het frame om elektrostatische opbouw vanuit het materiaal in een BPC af te voeren. De juiste praktijk is om elektrostatische opbouw af te voeren door alle BPC's te aarden voordat ze worden aangeraakt. Wanneer met BPC's wordt gewerkt, is het gebruik van niet-geleidende materialen, zoals niet-geleidende handschoenen, aanbevolen.



WAARSCHUWING: Draaiende onderdelen—risico op verstrikking.

Draaiende en bewegende delen kunnen verwondingen veroorzaken. Houd uw handen uit de buurt van bewegende onderdelen.

- Gebruik deze apparatuur niet tenzij de meegeleverde afscherming is aangebracht en naar behoren werkt.
- Het is de verantwoordelijkheid van de eindgebruiker om deze apparatuur te controleren en te bevestigen dat de apparatuur en veiligheidsvoorzieningen in goede staat zijn, en dat alle gebruikers getraind en zich bewust zijn van verstrikkingsgevaaren en bijbehorende beschermende voorzieningen, zoals waarschuwborden en afschermingen.



WAARSCHUWING: Wees voorzichtig bij het gebruik van ladders en verhoogde platformen.

Voor sommige gebruikstoepassingen, zoals het bevestigen van de motor op de 300 L S.U.F. tijdens het opstellen, kan het gebruik van een ladder of platform vereist zijn. U dient voor gebruik te bevestigen dat de ladder gecontroleerd is en dat deze het gewicht van de gebruiker kan dragen. Wanneer u een ladder of platform gebruikt, dient u te zorgen dat deze stabiel staat, dat u drie contactpunten aanhoudt en dat de treden schoon zijn.

WAARSCHUWING: Volg de procedures voor lock-out/tag-out.

Om letsel te voorkomen, dient u de procedures voor lock-out/tag-out van uw bedrijf te gebruiken wanneer u onderhoud aan apparatuur uitvoert, om zo elektrische, mechanische, pneumatische, hydraulische, chemische, thermische, zwaartekracht-gerelateerde en overige potentiële energie te isoleren en daardoor medewerkers te beschermen tegen het vrijkomen van gevaarlijke energie.

WAARSCHUWING: Wees voorzichtig met gevaarlijke chemische stoffen of materialen.

Personeelsleden die onderhoud uitvoeren aan apparatuur, moeten bekend zijn met de risico's van chemische stoffen of materialen die aanwezig zijn op of in de apparatuur. Maak gebruik van algemene communicatietechnieken voor risico's, zoals veiligheidsdatabladen, labels en pictogrammen om eventuele gevaren aan te geven.



WAARSCHUWING: Heet oppervlak—niet aanraken.

De verwarmingsmantel is bedoeld om de binnenwand van het vat te verwarmen. Normale gebruiksomstandigheden genereren warmte en kunnen deze hete oppervlakken creëren.

- Heet intern oppervlak
- Contact met oppervlakken kan brandwonden veroorzaken
- Niet aanraken tijdens gebruik



WAARSCHUWING: De Thermo Scientific HyPerforma S.U.F. mag niet worden geïnstalleerd in een potentieel explosieve omgeving, zoals vastgelegd in de toepasselijke EU ATEX-richtlijn.



WAARSCHUWING: Gevaar op openbarsten.

De BPC-kamer van de S.U.F. staat lichtelijk onder druk tijdens normale gebruiksomstandigheden. Normale, passieve ventilatie voorkomt dat de druk te hoog wordt in de kamer. Er moet gecontroleerd worden of de druk in de kamer en de druk in de toevoerleiding op de juiste manier zijn ingesteld.

- Overschrijd een druk van 0,03 bar (0,5 psi) in de BPC niet
- Overschrijd een druk van 0,34 bar (5 psi) in het gedeelte van de BPC tussen het inlaatfilter en de BPC niet
- Zorg dat het ventilatiefilter goed is geplaatst en naar behoren werkt
- Houd een minimale gasstroom van 0,1 vvm of 0,01 psi aan in de BPC terwijl de mengschroef draait

Randaarde

Randaarde moet worden geverifieerd voordat de S.U.F. in een stopcontact wordt gestoken. Zorg dat het stopcontact goed geaard is.

Omgeving

- In bedrijf: 17°C tot 27°C, 20 tot 80% relatieve luchtvochtigheid, zonder condensvorming
- Opslag: -25°C tot 65°C
- Installatiecategorie II (overspanning) volgens IEC 664
- Hoogtelimiet: 2000 meter

Informatie over de watermantel van het vat

Het S.U.F.-hardwaresysteem met watermantel is ontwikkeld om gebruikt te worden met water als hulpmiddel voor warmteoverdracht. De temperatuur mag 50°C (122°F) niet overschrijden bij een bedrijfsdruk van 150 psig (1 MPa). Om de veiligheid te garanderen, raden we u aan om de S.U.F. met watermantel te gebruiken bij 75 psig of minder.

Let op: De BPC-bedrijfslimieten van de S.U.F. zijn 5°C tot 40°C wat betreft temperatuur. De interne druk mag de 0,03 bar (0,5 psi) niet overschrijden. De watermantel hoeft niet geregistreerd, geïnspecteerd en van het Code U-symbool voorzien te worden volgens artikel U-1(c)2(f) van de ASME Boiler and Pressure Vessel Code en/of de Europese richtlijn 97/23/EG betreffende drukapparatuur (PED). Op aanvraag kan een conformiteitsverklaring voor goede technische PED-praktijken beschikbaar worden gesteld.

Elektrische aansluitingen

De apparatuur moet worden gevoed door een stroomkring van 15 A zonder aardlekschakelaar. Aardingsstoringen doen zich voor wanneer stroom ergens lekt en elektriciteit dus naar de grond ontsnapt. **Wanneer het menselijk lichaam optreedt als het pad voor lekkage naar de grond, kan dit leiden tot elektrocutie.**

Een aardlekschakelaar (GFCI) controleert de stroom die naar de grond loopt en schakelt de voeding uit (activeert de GFCI) in een fractie van een seconde voor stroomspanning die veel lager is dan als gevaarlijk wordt beschouwd. Vanwege de gevoeligheid van aardlekschakelaars bij een elektrische lekkage (van een paar mA), raden we u aan de S.U.F. niet in een stopcontact met GFCI te steken.

Garantie-informatie

Eventuele garantie voor deze apparatuur is niet van toepassing op:

- (a) normale slijtage; (b) ongelukken, rampen of overmacht; (c) verkeerd gebruik, fouten of nalatigheid door uw toedoen; (d) het gebruik van de apparatuur op een manier waarvoor het niet ontworpen is; (e) externe aantasting van de apparatuur, zoals, maar niet beperkt tot, externe doorboring, stroomuitval of elektrische piekspanningen; (f) onjuiste opslag en onjuist gebruik van de apparatuur; (g) het gebruik van de apparatuur in combinatie met apparatuur of software die niet door ons is geleverd; (h) apparatuur die aan u verkocht is als 'gebruikte' producten; (i) contact met verkeerd gebruikte of niet-goedgekeurde chemische stoffen of materialen; (j) installatie, verwijdering, gebruik, onderhoud, opslag of hantering op een ongepaste, onjuiste of niet-goedgekeurde manier, zoals, maar niet beperkt tot, het niet volgen van de meegeleverde documentatie of instructies of die gerelateerd zijn aan de apparatuur, het gebruik buiten de omgevings- of andere toepassingspecificaties, of het gebruik in combinatie met niet-goedgekeurde software, materialen of overige producten; (k) productie in overeenstemming met de vereisten die u hebt opgegeven; (l) installatie van de software, interface of producten die niet door ons zijn goedgekeurd; (m) het gebruik van meegeleverde instructies of documentatie om wettelijke goedkeuringen te ondersteunen; (n) de prestaties, efficiëntie of compatibiliteit van vermelde componenten; en (o) de prestaties van aangepaste apparatuur, producten of vermelde componenten, of het verkrijgen van resultaten via de apparatuur, vermelde componenten of services binnen het bereik dat u had gewenst, zelfs als die bereiken aan ons zijn gecommuniceerd en beschreven in specificaties, een offerte of een arbeidsverklaring. **BOVENDIEN ZULLEN BIJ ELK(E) INSTALLATIE, ONDERHOUD, REPARATIE, SERVICE, VERPLAATSING, AANPASSING OF ENIGE ANDERE VORM VAN MANIPULATIE VAN DE APPARATUUR DOOR EEN NATUURLIJKE PERSOON OF RECHTSPERSOON ANDERS DAN WIJZELF ZONDER**

ONZE VOORAFGAANDE SCHRIFTELIJKE GOEDKEURING, EN BIJ ELK GEBRUIK VAN VERVANGENDE ONDERDELEN DIE NIET DOOR ONS ZIJN GELEVERD, ALLE GARANTIES OP DE BETREFFENDE APPARATUUR DIRECT VERVALLEN EN WORDEN INGETROKKEN. INDIEN DE APPARATUUR IN DE VERENIGDE STATEN WORDT GEBRUIKT, KUNNEN WE UW GARANTIE INTREKKEN INDIEN U DE APPARATUUR BUITEN DE VERENIGDE STATEN VERZENDT.

Gebruiksbeperkingen

U moet deze apparatuur in overeenstemming met onze documentatie gebruiken, en, indien van toepassing, in combinatie met onze andere bijbehorende instructies, inclusief, zonder beperking, een product-label voor 'alleen voor onderzoeksdoeleinden' of een labellicentie voor 'beperkt gebruik'. Deze apparatuur is bedoeld voor onderzoeksdoeleinden of verdere productie van bioverwerkingstoepassingen en niet voor diagnostisch gebruik of directe toediening in mensen of dieren. We leggen de apparatuur niet voor regelmatige controle voor aan een overheidsinstantie of andere organisatie en we valideren de apparatuur niet voor klinisch of diagnostisch gebruik, voor veiligheid en effectiviteit, of voor overig specifiek gebruik of toepassing.

Richtlijnen voor seismische activiteit

De koper van de apparatuur is er verantwoordelijk voor om aan de landspecifieke wetten te voldoen en voor de evaluatie van seismische waarden om te controleren of de installatie en veiligheid van de apparatuur geschikt zijn voor de betreffende locatie. De koper draagt tevens de verantwoordelijkheid voor het evalueren van de structuur van het gebouw voor de betreffende apparatuur, om te verzekeren dat de verankering en de bevestiging van de apparatuur en het gebouw bestand zijn tegen seismische activiteit. We raden de koper ten eerste aan om een plaatselijk, bevoegd, extern architecten- en ingenieursbureau om een correcte technische analyse en gecertificeerde documentatie te vragen voorafgaand aan de installatie van de apparatuur in het gebouw. De koper is bovendien verantwoordelijk voor het vastzetten en verankeren van de apparatuur op een aangegeven, vaste locatie. Thermo Fisher Scientific kan op aanvraag en tegen overeengekomen kosten ondersteuning bieden bij de seismische verankering en bevestiging voor aangeschafte apparatuur, op basis van de bouw- en landspecifieke wetten.

Verplaatsbare apparatuur (d.w.z. niet-vaste apparatuur of op een bevestiging met zwenkwielen) komt niet in aanmerking voor seismische ontwerpvereisten in overeenstemming met ASCE 7-16, hoofdstuk 13, artikel 1.4. Hoewel deze apparaten niet in aanmerking komen voor de seismische ontwerpvereisten van ASCE 7, dient u er rekening mee te houden dat dergelijke apparatuur kan omkiepen bij seismische activiteit. Het is daarom de verantwoordelijkheid van de klant om de seismische veiligheid voor verplaatsbare apparatuur in acht te nemen op de betreffende locatie.

How to use this guide

Scope of this publication

This user's guide contains information about the standard Thermo Scientific S.U.F. 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.

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B	05/2020	How to use this guide	Revised the Document change information table	C. Jones

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 documents

If you are missing any of the related publications listed below, please contact your local sales representative.

Document	Document number
Thermo Scientific HyPerforma S.U.F. Validation Guide	DOC0032
Thermo Scientific HyPerforma S.U.F. Packing and Unpacking Instructions	DOC0052

Abbreviations/acronyms

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

BPC	BioProcess Container
DO	Dissolved oxygen
ETP	Equipment Turnover Package
GFCI	Ground fault circuit interrupter
ID	Inner diameter
IEC	International Electrical Code
OD	Outer diameter
PED	Pressure Equipment Directive
PID	Proportional integral derivative
P/V	Power input to volume
rpm	Revolutions per minute
RTD	Resistance temperature detector
slpm	Standard liters per minute
STR	Stirred tank reactor
S.U.F.	Single-Use Fermentor
TCU	Temperature control unit
VFD	Variable frequency drive



Single-Use Fermentor (S.U.F.) overview

Chapter contents

- 1.1 Introduction
- 1.2 Hardware characteristics
- 1.3 End user and third-party supplied components
- 1.4 BioProcess Container characteristics
- 1.5 Additional system components

1.1. Introduction

The Thermo Scientific Single-Use Fermentor (S.U.F.) has been designed to be a single-use alternative to conventional stirred tank aerobic fermentors currently utilized in microbial cell culture applications. Based on years of accepted stirred tank reactor (STR) design, the S.U.F. emulates STR scalability and operating parameters, yet it has the unique advantage of being a single-use device. Ease of setup with respect to system operation and integration into existing facilities makes the S.U.F. an attractive alternative to its stainless steel counterpart. Critical design parameters such as height to diameter ratios, mixer design and location, and typical control system interfaces are consistent with traditional fermentation platforms. S.U.F. BioProcess Containers (BPCs) are supplied sterilized by irradiation and therefore do not require any facility hook-ups for sterilization or cleaning. A key element in the single-use design is the plastic (polyethylene) impeller with a bearing/seal assembly linking to an external mixer drive. Quick setup and changeover allows for faster turnover in microbial cell culture runs over traditional reusable systems.

S.U.F. systems consist of the following primary components:

- **Outer support container** with standard water jacket heating system
- **S.U.F. BioProcess Container (BPC)**
- **Electrical control panel (E-Box)** for agitation
- **Direct drive agitation mixing assembly** with an AC motor, drive shaft, and impeller



Figure 1.1. 300 L S.U.F. with electrical control panel, condenser, cable management system, and bottle management system.

The Thermo Scientific S.U.F. 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 HMI (human-machine interface) screens. Controls for agitation are integrated into the S.U.F., with temperature, pH/DO probes and controls being supplied by the user or a third-party integrator. Water jacketed systems require a temperature control unit (TCU) selected and supplied by the end user or by Thermo Scientific.

The stainless steel **outer support container** is engineered and fabricated to fully support each S.U.F. BPC and allow easy access for operation. The outer support container is mounted to a portable cart base and includes the mixing drive, water jacket for heating and cooling, and optional controllers for mixing. The drive shaft is detachable and reusable and is inserted into the BPC through the motor assembly and into the bearing port. Load cells are offered as an option.

The **BPC** includes the impeller assembly, sparger, vent filter inlet/outlet ports, probe integration ports and filling, dispensing, and sampling ports. The materials are fully qualified for biological product contact per USP Class VI plastics. Each assembly is manufactured under cGMP and is supported by qualification and validation information. No reuse cleaning or sterilization validations are required as the BPC is provided gamma irradiated. Innovative, proprietary technology allows for the integration of the mixing shaft, pH and 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 S.U.F. BPC through universal ports.

This user's guide covers the setup, operation, maintenance, and troubleshooting of 30 and 300 L S.U.F. systems.

1.2. Hardware characteristics

1.2.1. System features

The S.U.F. is designed for system mobility and easy integration while utilizing a straightforward operator interface. Hardware drawings and specification tables specific to volume can be found in Chapter 4 of this guide. The following topics include general descriptions of the hardware components of the S.U.F.

1.2.2. Agitation

If your system uses a Thermo Scientific electrical control panel (E-Box), the stirring speed is adjusted by using the keypad interface on the control panel. The agitation control interface utilizes a digital display to indicate stirring speed in units of revolution 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. Your system may also be integrated and managed by a third-party controller.

1.2.3. Control system

The S.U.F. is designed to integrate with existing control systems in their many configurations. The S.U.F. control system supplied with the Thermo Scientific E-Box enclosure manages the agitation process and monitors the pressure inside the BPC. 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.

1.2.4. Exhaust management system

A condenser system is recommended and is available as optional hardware. It cools exhaust gases and re-circulates the condensate into the fermentor.

1.2.5. Exhaust vent filter heater

An optional exhaust vent filter heater is available for increased longevity of the exhaust filter on the S.U.F. BPC. Heating the filter sufficiently to eliminate the formation of condensation is an effective means of reducing the risk of fouling of the filter membrane. The heater is factory preset to operate between 40°C–55°C, +/- 3 degrees. Temperature settings above 60°C are not recommended.

1.2.6. Temperature

The S.U.F. can be operated within the temperature range from 5°C to 55°C. The process temperature is measured by means of a supplied RTD (pt-100) that is inserted into the thermowell of the S.U.F. BPC. Water jacketed system temperature control is maintained through the TCU or a third-party controller.

1.2.7. Heating performance

Heating times for S.U.F. systems vary based on 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.F. 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 S.U.F. BPC. Refer to section 3.1.4 for expected heating times.

1.2.8. External control

Users can choose to bypass the mixing speed control and display pressure systems provided with the S.U.F. and utilize existing controllers. Refer to section 3.6 for more details.

1.2.9. Load cells

Load cells, used to determine the weight of the contents of a S.U.F., are optional. Load cell kits 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 data interfaces.

Load cells arrive uncalibrated. It is recommended that the load cell manufacturer or a qualified technician calibrate these systems on site.

1.3. End user and third-party supplied components

1.3.1. pH and DO probes

The following table shows the length and diameter requirements for traditional sensors (probes) that can be integrated into the S.U.F. 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.F.

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

Probe lengths (from O-ring to tip) must not exceed 235 mm (9.25 in.)				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.)
Finesse DO	DOS-OFF-VP-225	12 mm (0.47 in.)	13.5 PG	225 mm (8.85 in.)	220 mm (8.66 in.)
Finesse pH	PHS-EFP-K8-225	12 mm (0.47 in.)	13.5 PG	225 mm (8.85 in.)	220 mm (8.66 in.)
NOTE: Consult probe manufacturer's website for appropriate probe cable connection and part number.					

1.3.2. Single-use probes

Mettler Toledo single-use pH and DO sensors are supported, and BPCs may be ordered with single-use sensors as fully integrated components.

1.3.3. Controllers

Thermo Scientific operates with an open architecture approach to the integration of controls. Our industry-leading S.U.F. can be 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 Equipment Turnover Package (ETP) supplied with the Thermo Scientific S.U.F.

S.U.F. units may be provided with integrated controls, pump towers, a control monitor, and advanced features, such as data logging, multiple S.U.F. 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 Scientific can provide complete, integrated solutions with the Thermo Scientific OEM Controller, or using the manufacturers listed below.

- Applikon SUB-Controller
- Finesse PC Controller
- Emerson Delta V
- Allen-Bradley
- Siemens

Contact your local sales representative for more information.

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

1.4. BPC characteristics

1.4.1. S.U.F. BPC features

The microbial culture itself is contained inside the S.U.F. BPC (Figures 1.2 and 1.3). The chamber is manufactured from single-web, multi-layer 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, which is available from your sales representative). The BPC is presterilized using validated gamma irradiation processes.

1.4.2. Operating pressure

The S.U.F. BPC does not operate as a closed system, as it has both inlet and exhaust filters that are utilized to maintain an environment for cells to grow without concern for contamination. However, conditions can be encountered when gas inlet flow rate may exceed exhaust flow rate. This may be encountered in the unlikely event of a pressure regulator failure on a gas feed, or when excessive foaming creates conditions of vent blockage. The S.U.F. BPC is not rated as a pressure vessel [gas pressure should not exceed 0.03 bar (0.5 psi) within the BPC]. Custom BPCs can be ordered with an optional single-use pressure transducer for monitoring the pressure within the S.U.F.

1.4.3. Working volume

Each S.U.F. is designed for a working volume range. The minimum working volume and the rated working volume are listed in the specification tables provided in Chapter 4 of this guide. The total volume listed includes the head space needed for proper aeration and gas management. Actual working volumes should not exceed the indicated rated working volumes. In addition, working volumes less than the minimums listed can result in damage to the BPC and S.U.F. hardware malfunction.

1.4.4. Draining and harvest

The S.U.F. is equipped with a bottom drain line that allows for liquid harvest, typically with a peristaltic pump. Connection of the bottom drain line can be accomplished by use of a tubing welder or the aseptic connection of quick connect or fitting that is provided. Manipulation of the BPC as the last few liters of media are removed can minimize liquid hold-up within the S.U.F.

1.4.5. Aeration

Gas to liquid mass transfer in microbial culture fermentors is controlled by the solubility of the gas in the liquid, its distribution, and the temperature and pressure. Direct air sparging is a way of providing for the oxygen requirements of cell cultures. The standard S.U.F. BPC incorporates a unique rind-like film sparger design that allows for optimal aeration of the culture process.

1.4.6. Aseptic connections

Multiple aseptic connection options exist for S.U.F. users. The standard BPCs include tubing welder sections, quick connects, CPC™ AseptiQuik,™ or Pall™ Kleenpak™ aseptic connections. The S.U.F. BPC is designed with various lengths and dimensions of thermoplastic tubing for the purpose of addition to and dispensing from the S.U.F. BPC. Refer to ordering information in Chapter 4 for custom end treatment options.

1.4.7. Sampling

The S.U.F. 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 an aseptic 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 by tubing welder.

Detailed BPC drawings and standard configuration tables specific to volume can be found in Chapter 4 of this guide.

1.4.8. BPC features

Figures 1.2 and 1.3 illustrate the components of standard 30 L and 300 L S.U.F. BPCs. See Table 1.2 on the following page for more information.

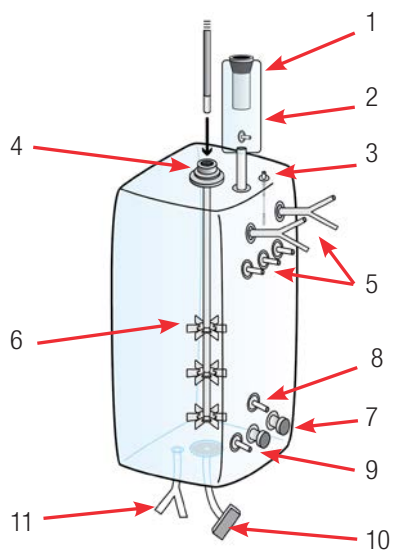


Figure 1.2. 30 L S.U.F. BPC.

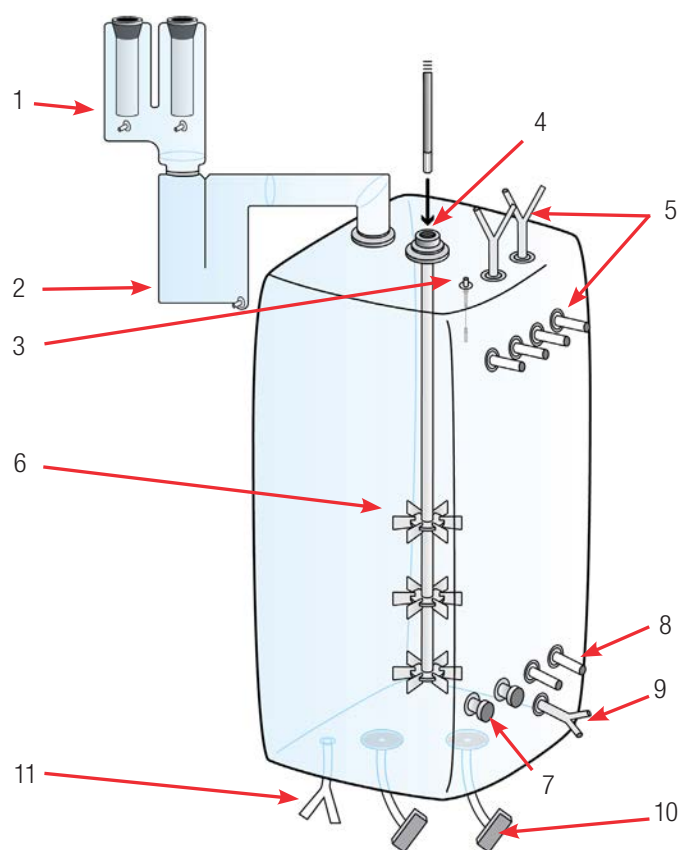


Figure 1.3. 300 L S.U.F. BPC.

Table 1.2. BPC information for Figures 1.2 and 1.3.

Component	Description
1. Exhaust vent filter	Single-use capsule filter for exhaust gas exchange (two types available)
2. Condenser bag (optional)	Optional single-use condenser bag
3. Foam sensor (optional)	Built-in single-use sensor may be used with a controller to automatically trigger addition of an anti-foaming agent when excessive foam is present
4. Seal/bearing assembly	Links with mixer motor and allows impeller to turn while retaining integrity of the S.U.F. BPC
5. Feed ports	Feed port for addition of media and other liquids
6. Impeller	Injection molded plastic; linked to seal/bearing assembly by C-Flex tubing contact material of the shaft
7. Ports with single-use sensors or standard Pall Kleenpak* connectors	Ports with single-use sensors or standard Pall Kleenpak* connectors
8. Spare sterile connect port	Spare port
9. Temperature RTD/ small volume sampling port	For integration of temperature probe while retaining integrity of the S.U.F. BPC, and for needleless sampling or connection to sampling manifold
10. Gas sparge line(s)	Drilled hole sparger integrated into the chamber and protected by gas filters and a check valve (check valve is provided on 30 L units only)
11. Drain port	Used when draining the S.U.F.

*CPC AseptiQuik aseptic connectors are also available on S.U.F. BPCs.

1.5. Additional system components

1.5.1. Probe integration

The probe assembly is an innovative design to package user-supplied pH and DO probes for sterilization and to aseptically connect them to the S.U.F. BPC. The probe assembly (Figure 1.4) includes the following components:

1. Molded bellows cover
2. Threaded probe adapter
3. Pall Kleenpak connector (KPCHT series—high temperature)
4. Cable ties

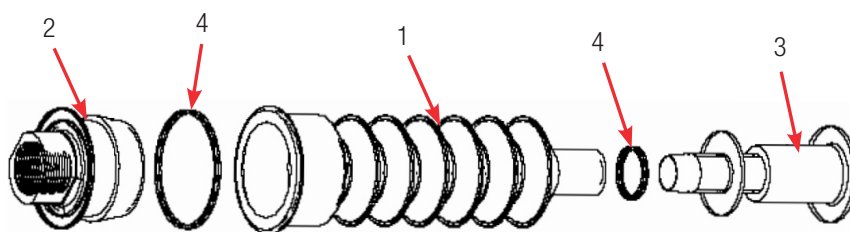


Figure 1.4. Probe assembly.

Note: Figure 1.4 shows a Pall Kleenpak connector. CPC AseptiQuik connectors are also available for S.U.F. systems.

1.5.2. Accessories

To assist in the operation of the S.U.F., additional accessories are available (see accessories below).

Required

- Heavy-duty tubing clamps

Recommended

- Exhaust management system with condenser and vent filters.

Optional

- E-Box
- Sampling manifold with luer lock
- Temperature sample port (for RTD calibration/validation)
- Vent filter heater system—for users who require additional protection for the exhaust vent filter on the standard S.U.F. BPC; includes filter heater, controller, and power cord.

- Load cells—Load cell packages include three load cells, summing block, wiring, and an optional display screen with your choice of several data interfaces
- Cable management system
- Bottle management system
- Feed bag management hook

See Chapter 4 of this guide for accessory ordering information.

2

Installation and setup

Chapter contents

- 2.1 Initial installation preparation
- 2.2 Installation

2.1. Initial installation preparation

The Single-Use Fermentor (S.U.F.) hardware will arrive crated. For unpacking instructions and detailed contents of the crate, please refer to the S.U.F. Packing and Unpacking Guide.

There will be detailed instructions for crating, uncrating, and assembly of 30 L and 300 L S.U.F. units. Be sure to follow the instructions provided and retain all packaging materials. After uncrating, contact your sales representative immediately if you find that any damage has occurred in shipping.

2.1.1. Hardware shipment and setup

The S.U.F. hardware will arrive with the following items:

- Outer support container (platform, tank, and control panel)
- Drive shaft, resistance temperature detector (RTD), four probe brackets, and standard tool set (spanner wrench and torque wrench)
- Equipment Turnover Package (ETP) provided on a USB drive, shipped separately

2.2. Site preparation

2.2.1. Electrical connections for units with an electrical control panel

S.U.F. hardware with AC motors cannot be used on circuits equipped with GFCI circuit protection due to the potential for nuisance tripping. The electrical plug on the S.U.F. 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 serves to provide electrical ground prior to power connection. The supplied electrical receptacle should be hard-wired into the facility by a qualified electrical technician; for US 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 hard-wired directly into the facility. **Note:** The yellow plug and receptacle are for 120 VAC and the blue are for 240 VAC S.U.F.s.

2.2.2. Outer support container preparation

Each outer support container is shipped from the manufacturer and arrives with various safety mechanisms in place. Please follow the guidelines below to set up the S.U.F. upon arrival.



WARNING: Any procedures that require the electrical control panel (E-Box) to be opened should be performed with the main electrical disconnect in the locked out position, and all power sources removed. For operator safety, secure the location of the S.U.F. unit by disabling the swivel casters before servicing.

2.2.3. Electrical preparation for systems with electrical control panels

1. Before beginning, refer to electrical schematics included with the ETP, which is shipped on a USB drive.
2. Make sure the unit is disconnected from any power source, and use standard lockout safety procedures.
3. Open the E-Box using a flat-head screwdriver. Verify that the three-way motor controller switch is in the middle position (Figure 2.1).

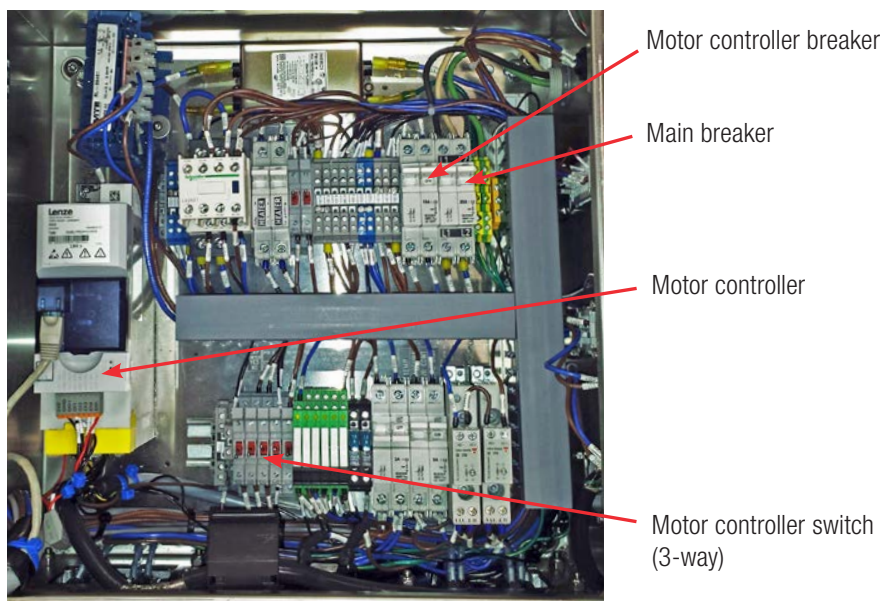


Figure 2.1. Internal view of typical S.U.F. E-Box.

4. Fermentor units are shipped with the main electrical breaker in the off position. Turn the main breaker on.
5. Close the E-Box and lock the panel.

2.2.4. Load cell preparation

1. For S.U.F. units purchased with factory-installed load cells, the load cells are shipped in the locked position (threaded up) for equipment protection. To unlock the load cells, remove and discard the delrin slip ring if it is present (Figure 2.2). Remove the tri-clamp. Loosen the lockout nut, using the small end of the supplied tool (Figure 2.3), until the nut is tight against the base or leg of the tank. Repeat this process for each load cell until all lockout nuts are disengaged from the lockout posts. Do not reinstall the tri-clamp.

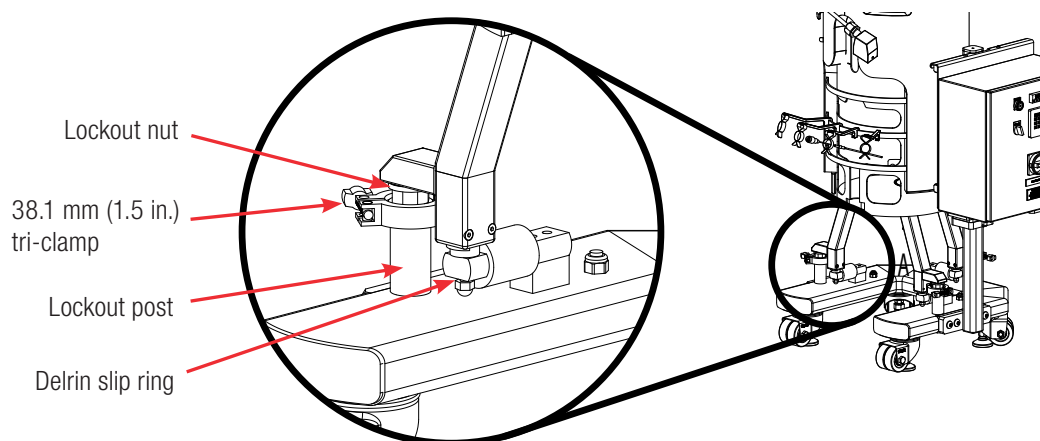


Figure 2.2. Load cells.



Figure 2.3. Supplied wrench.

2. At this point, the S.U.F. hardware is ready to prepare for a cell culture run. **CAUTION:** Do not move unit, especially when filled, while load cells are unlocked, as this can damage the load cells.
3. For systems with load cell display screens, refer to Appendix C for information about how to calibrate the tools.
4. To lock load cells that have been unlocked, hand-tighten the lockout nut onto the post. Use the supplied tool to turn the nut an extra 1/4 turn.



WARNING: 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. Complete this process for all load cells.

2.3. Installation

300 L S.U.F. systems are shipped with motors detached. Depending on doorway height, you may need to wait to install the motor until the S.U.F. is in place. See the specifications for the outer support container in Chapter 4 and the S.U.F. Packing and Unpacking Guide for more information.

All manual movements of mobile S.U.F. hardware should be over smooth surfaces, with the S.U.F. 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.F. 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 S.U.F. and ancillary components such as controllers or pumps.
2. Locate the outer support container in the area for the cell culture run.
3. If monitoring the volume, the unit may be located on a scale if load cells are not utilized. Other applications may measure all liquids going in and coming out.
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 cable/tubing lengths are satisfactory.



WARNING: Electrical shock is possible.

6. Verify that the main power is off and the emergency stop is pulled out.

Note: The emergency stop disconnects all power to the system. An alarm buzzer will sound when the emergency stop is activated.

7. Verify that the main motor power switch is in the off position.
8. Connect all electrical plugs to facility power. **Note:** 120 VAC S.U.F. should be connected to a dedicated 10 A circuit. Refer to hardware/electrical labels and schematics to ensure proper electrical voltage is connected to the S.U.F. The main power switch can now be turned on.
9. Connect the water inlet and outlet lines from the temperature control unit (TCU) to the S.U.F. (Figure 2.4). The inlet is typically on the left side when you are facing the connectors. The inlet and outlet ports on the S.U.F. water jacket are labeled.



Figure 2.4. Attaching a TCU hose to the water jacket port.

2.3.1. Exhaust filter bracket setup

To install the exhaust filter bracket, clamp it onto the rim of the S.U.F. tank. Push the red handles down to lock it into place (Figure 2.5). The exhaust filter post will slide into the hole in the bracket. The center red handle locks the post in place. This may need to be adjusted during initial BPC loading. **Note:** The pinch clamp for 30 L systems must be installed onto the exhaust filter post before it is mounted to the tank. See section 2.3.4 for instructions.



Figure 2.5. Clamping the exhaust filter bracket to 30 L S.U.F. tank.

2.3.2. Condenser unit setup (when present)

If your system includes an optional condenser, the assembled condenser will need to be installed. Condensers for 30 L units are clamped onto the exhaust filter pole (Figure 2.6). Condensers for 300 L units are bolted onto the exhaust filter bracket (Figure 2.7).

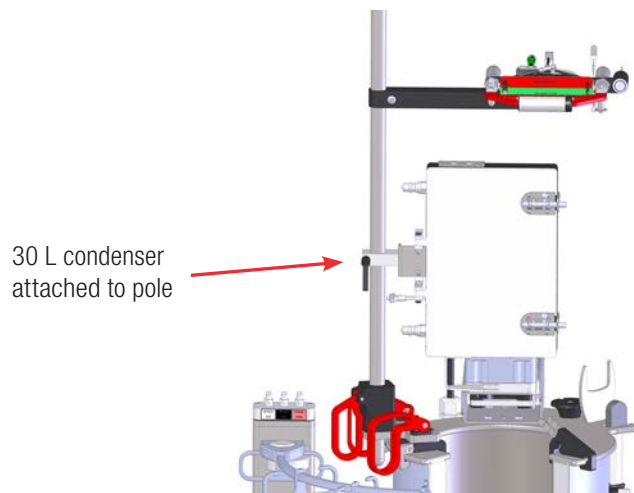


Figure 2.6. Condenser installed on a 30 L system.

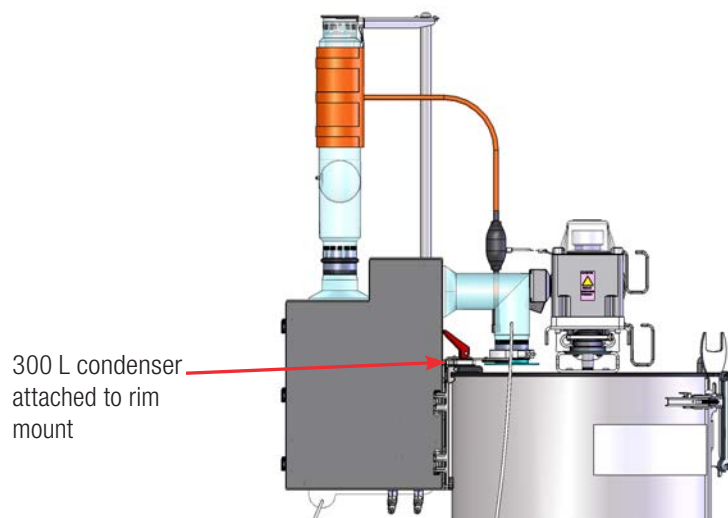


Figure 2.7. Condenser installed on a 300 L system.

2.3.3. TCU/chiller connection to condenser unit (optional)

Use the following steps to connect a TCU or chiller to the S.U.F. condenser unit, if present.

1. Connect inlet and outlet hoses to the TCU (Figure 2.10). You may need to attach the valves to the TCU, if necessary.
 - a. Use the clear supplied washers and tri-clamps to attach the fitting and then the hoses to both the inlet and the outlet port on the TCU (Figures 2.8 and 2.9).



Figure 2.8. Attaching line to a TCU unit.



Figure 2.9. Attaching a clamp to a line.

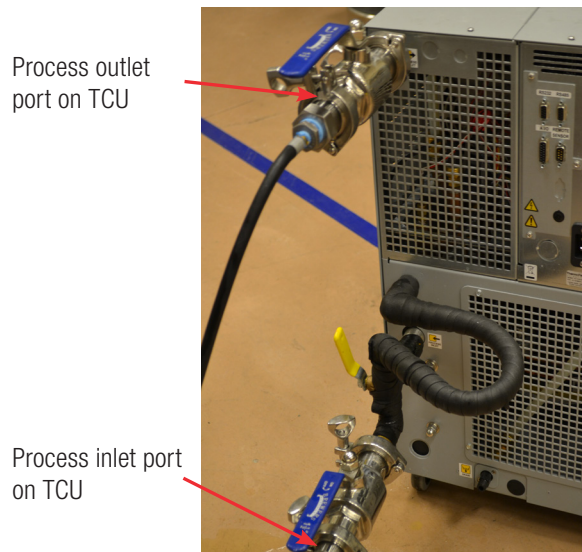


Figure 2.10. TCU ports with lines connected for S.U.F. condenser.

2. Connect the remaining end(s) to inlet port(s) on the condenser
On 300 L systems the inlet ports are the ports *closer* to the tank (shown in Figure 2.11)—On 30 L systems the inlet port is the *upper* port on the condenser (can be seen in Figure 2.6).
3. Connect the remaining end(s) to outlet port(s) on the condenser
On 300 L systems the outlet ports are the ports *farther from* to the tank (shown in Figure 2.11)—On 30 L systems the outlet port is the *lower* port on the condenser (can be seen in Figure 2.6).

Note: The inlet and outlet hoses for 300 L systems include a Y-splitter to make the connections on the condenser plates.



Figure 2.11. Attaching TCU lines to a condenser on a 300 L S.U.F. unit.

4. Fill the TCU and prepare it for operation as specified in the user's guide provided with the TCU.

2.3.4. Exhaust filter pinch clamp setup (when present)

Some systems include an exhaust filter pinch clamp (Figure 2.12), which is used to temporarily keep exhaust from flowing through redundant exhaust filters.

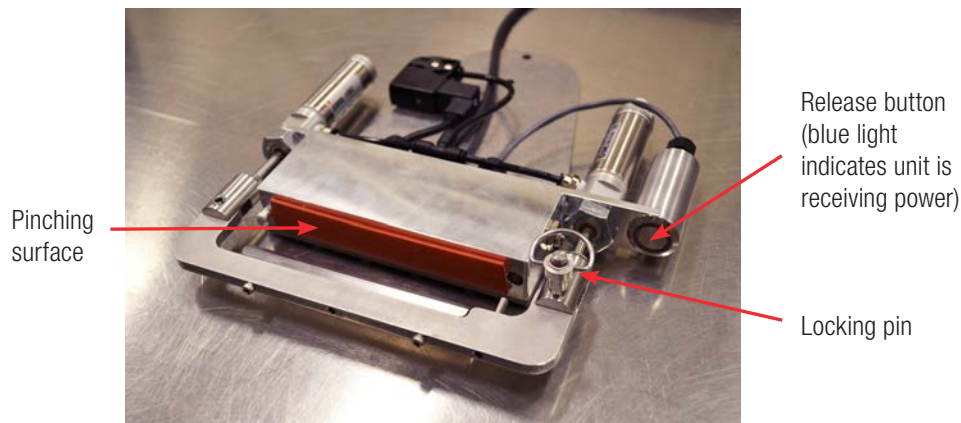


Figure 2.12. Exhaust filter pinch clamp.

Use the following steps to install the exhaust filter pinch clamp.

1. Mount the pinch clamp to the exhaust filter post (Figure 2.13) using the supplied C bracket. If the exhaust filter post is not already installed on the system, mount it onto the exhaust system bracket.



WARNING: Pinch hazard. Keep hands away from the pinching surface. Close and use locking pin when pinch clamp is not in use.



Figure 2.13. Pinch clamp installed on a 300 L S.U.F.

2. Lift the center red handle of the exhaust bracket. Slide the exhaust filter holder post into the bracket and lock the center handle down.
3. Plug the wire attached to the pinch clamp unit into the controller. A blue light on the pinch clamp's release button indicates that unit is receiving power and the unit is ready for manual initiation of the clamp.
4. Refer to the BPC loading instructions in section 3.1 for more information about how to use the pinch clamp with the BPC.

2.3.5. Optional cable management system setup

If your system includes the optional cable management system, the arm of the cable management system may be removed for shipping and must be reattached, using an Allen wrench (Figure 2.14).



Figure 2.14. Attaching arm to cable management system.

Use of the cable management system is covered in detail in the BPC loading instructions in Chapter 3 of this guide.

2.3.6. Air line preparation

See Table 3.2 and Table 3.3 (later in this guide) for recommended air flow rates. The operating pressures at the level of the S.U.F. are of primary importance and these values must be adhered to. Please note that flow rates in the graphics include both half and full volume applications.



WARNING: The S.U.F. BPC is not rated as a pressure vessel. The BPC should not be allowed to become tight during inflation or operation. Gas pressure in the BPC should not exceed 0.03 bar (0.5 psi) at any time. Conditions of over pressure may result in BPC damage or personal injury. For reference the BPC will appear to be tight at 0.007 bar (0.1 psi). The tubing after the inlet filter should be easy to compress with two fingers. When testing, be sure NOT to pinch off the air inlet line completely.

2.3.7. Drilled hole sparger line(s)

Manually orient the sparge line vertically for maximum effectiveness.

3

Operating information

Chapter contents

- 3.1 General system operating information
- 3.2 BPC and drive shaft loading instructions for 30 L units
- 3.3 BPC and drive shaft loading instructions for 300 L units
- 3.4 Exhaust system
- 3.5 Probe assembly
- 3.6 Microbial cell culture operating instructions
- 3.7 BPC sampling
- 3.8 Verification procedures

3.1. General system operating information

3.1.1. BPC preparation and loading

Each outer support container is designed for a specific S.U.F. BPC. Confirm that the correct volume BPC is being used for the corresponding volume outer support container. This section outlines the installation and setup of the different volume S.U.F. BPCs. Please follow these instructions in the order in which they are presented.

3.1.2. BPC handling instructions

Use caution when using sharp objects to open outer polybags, in order to avoid causing damage to the BPC. Do not drag containers over corners or sharp objects. Do not lift the container by the corners or top seams. Carefully coil tubing on top of the BPC to prevent puncturing the container with cable ties or clamps. Use cushioning between tubing and container in storage and transport.

3.1.3. BPC operating information

Aseptic line connection

The most commonly recommended process for making connections to the tubing lines is with an aseptic tubing fuser. **Note:** Other connection options are available as a custom BPC assembly.

Following the recommended tubing welder operating instructions, successful connections can be obtained for filling, supplementing, sampling, or dispensing from the BPC as needed.

Working volume

Each S.U.F. is designed for a working volume range. The minimum working volume and the rated working volume are listed in the specifications tables in Chapter 4. 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%. In addition, working volumes less than 20% of the rated volume can result in damage to the BPC and hardware.

Exhaust system

The exhaust vent filter(s) and condenser used on the 30 L and 300 L S.U.F.s include ZenPure™ polyethylene or Meissner™ PVDF filters. Condensate must be managed by use of the condenser system or vent filter heater(s).

Sampling

The S.U.F. is equipped with a small volume sample port that is part of the BPC thermowell. This small diameter (1.59 x 4.76 mm [1/16 x 3/16 in.]) silicone dip tube of 152.4 mm (6 in.) length allows low void volume samples to be taken for cell viability and density, as well as analyte analysis. This dip tube is supplied with an aseptic 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 (3.18 x 6.35 mm [1/8 x 1/4 in.]) by tubing welder. For recommended systems for fluid transfer, contact your sales representative.

Operating pressure

The BPC is not rated as a pressure vessel. All gas supplied to the fermentor controller must be regulated to a pressure not to exceed manufacturer's recommendations, typically 1.034–4.137 bar (15–60 psi), depending on vessel scale and use. Gas pressure in the BPC headspace should not exceed 0.03 bar (0.5 psi) at any time.



WARNING: Conditions of overpressure may result in BPC damage or personal injury. The maximum pressure in the tubing after the inlet filter should be about 0.344 bar (5 psi). The section of tubing after the inlet filter should be easy to compress with two fingers.

The BPC is not operated as a closed system. It has both inlet and exhaust filters that are utilized to maintain a sterile environment for cells to grow without concern for contamination. However, conditions can be encountered when gas inlet flow rate may exceed exhaust flow rate. This may be encountered in the unlikely event of the failure of a pressure regulator on a gas feed, or when excessive foam within the S.U.F. creates conditions of vent blockage. The S.U.F. BPC is not rated as a pressure vessel. All gas supplied to the fermentor controller must be regulated to a pressure not to exceed manufacturer's recommendations, typically 2.06–4.13 bar (30–60 psi). Gas pressure in the BPC headspace should not exceed 0.03 bar (0.5 psi) at any time.

- Demanding applications may warrant an optional exhaust vent heater.
- If foaming is excessive in your cell culture process, use a foam sensor.
- Single-use pressure transducers are available with the S.U.F. This technology combined with high-level control systems common with industrial applications can regulate gas pressure within the confines of the S.U.F.

Extensive testing has not found an occurrence of overpressure sufficient to create a containment breach. Development testing of the BPC system has shown that in conditions of excessive pressure the polymer container will fail at the upper regions of the chamber where it is unsupported by the outer support container, minimizing the likelihood of the loss of bulk liquid.

Agitation

The agitator should not be operated at volumes less than the stated minimum volume. Stirring speed may be adjusted by using the keypad interface on the controller. At low volumes, the chamber should be inflated to prevent the film of the BPC from contacting the agitators.

Agitation control interface for units with electrical control panels

The agitation control interface utilizes an LED digital display to indicate stirring speed in units of revolution 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 up and down arrows on the agitation keypad adjust the stirring speed. Due to the auto-restart capabilities of the S.U.F., 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.

Dispense and harvest

The S.U.F. 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 aseptic connection of 6.35–9.53 mm (1/4–3/8 in.) quick connect that is provided. Manipulation of the S.U.F. BPC as the last few liters of media drain will minimize liquid hold-up within the S.U.F.

3.1.4. Hardware operating information

Temperature

Temperature setpoints can be adjusted via the temperature control unit (TCU). These setpoints should be between 5°C and 55°C. The process temperature is measured by means of a supplied resistance temperature detector (RTD) (pt-100) that is inserted into the thermowell of the S.U.F. BPC. The temperature measured by the RTD is not displayed, but is passed through the 16-pin cable as a raw PT100 signal.

Heating performance

Heating times for the S.U.F. system vary based upon liquid volume and temperature, ambient or heating liquid temperature, sparge rate, and mixing rate. Users should adjust process liquid staging and seeding strategies to the unique aspects of the S.U.F. Process controllers and heaters are designed to provide optimum heat transfer and minimize heat up times, while maintaining the material integrity of the polymer film construction of the BPC (Table 3.1).

Do not operate the heater if the BPC is not at minimum liquid, 5:1 (20%) volume or greater. Care must be taken not to melt or damage the container or other components. Heaters should not be used to warm liquid above 45°C. The main power disconnect should be in the off position unless the S.U.F. hardware system is in active use.

Table 3.1. Heating times for S.U.F. systems (Ambient temperature of 25°C).

System	Liquid batch volume (half/full)	Initial liquid	Liquid target	Time (half/full)
30 L	15 L/30 L	5°C	37°C	1 hr/1.16 hr
300 L	150 L/300 L	5°C	37°C	1.3 hr/1.8 hr

General temperature mapping has been performed for S.U.F. systems by tracking thermal profiles within the liquid confines of the fermentor. Testing conditions were analyzed using chilled media and low agitation rates. Gradients within the liquid did not exceed 0.5°C during heat-up. Testing has also shown that temperature measurements in the S.U.F. when using the standard silicone thermowell with 3.18 mm (1/8 in.) diameter temperature probes properly represent fermentor content temperatures. Users desiring exact temperature calibrations can order a S.U.F. temperature/sample port. Using this port will allow users to simulate the temperatures seen by the RTD when used with the BPC.

Protective earth grounding

Protective earth grounding for the S.U.F. 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 tank, and must be tied to the controller before operation.

Resettable breakers

Electrical components of the S.U.F. are equipped with circuit protection. The variable frequency drive (VFD) used to power the mixer motor is protected by the use of 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. The breakers can be reset once the fault condition is resolved.

Breaker notes:

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

Scales and weighing systems

Monitoring liquid volume within the S.U.F. during operation can be critical in fermentation applications that involve nutrient media feeds. This can also be a useful method for increasing the scalability of the S.U.F. 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 fermentor is increased to rated working volume during the process run.

A load cell kit for weight/volume measurement is available as an option. Load cell kits 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. For more information, refer to the Specifications and parts information in Chapter 4 of this guide. Refer to section 2.1 for information about unlocking the load cells, and Appendix B for load cell display calibration instructions. **Note: Ensure that load cells are locked down before moving the S.U.F. unit.**

Use the following steps to lock the load cells before transporting a S.U.F., and refer to Figures 2.3 and 2.4 in section 2.2.4 (earlier in this guide).

1. Hand-tighten the load cell lockout nut onto the load cell lockout post. You may need to use the small end of the supplied wrench to loosen the load cell lockout nut from the bottom of the base.
2. After you hand-tighten the nut against the post, use the small end of the supplied wrench to turn it an extra 1/4 turn.
CAUTION: To avoid damaging the load cell, do not over-tighten the nut.
3. Assemble a standard stainless 28.6 mm (1.5 in.) tri-clamp around the flanges.
4. Repeat all three steps listed above for each load cell attached to the tank.

External data logging and control

Optional 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 S.U.F., floor scales can be used to measure the fluid content within the S.U.F. This is accomplished by rolling the S.U.F. onto the scale platform and leveling the S.U.F. skid once it is in position.

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

3.2. BPC and drive shaft loading for 30 L units

3.2.1. Initial installation steps for 30 L units

Each outer support container is designed for a specific S.U.F. BPC. Confirm that the correct volume BPC is being used for the corresponding volume outer support container. The following section outlines the installation and setup of the BPC.

Before beginning to load the BPC, verify that the S.U.F. hardware is stationary, with the casters locked into place.

1. Remove the irradiated BPC from the protective double polybags. Open the S.U.F. door and load the BPC into the stainless steel outer support container (Figures 3.1 and 3.2).



Figure 3.1. Opening the S.U.F. door latch.



Figure 3.2. Interior of the outer support container.

2. Orient the BPC with the bearing port up and toward the motor drive, with the connector probe ports facing the bottom access cutout.
3. Remove the cap on the BPC bearing port, and place the bearing port into the bearing port receiver (Figure 3.3). Close the door and the clamp.



Figure 3.3. Inserting the bearing port.

4. Route the bottom ports through the opening in the bottom of the outer support container (Figure 3.4).



Figure 3.4. Routing the bottom ports through the bottom of the outer support container.

5. Route the sparge line and bottom drain line through the bottom access opening (Figure 3.5).



Figure 3.5. Routing the sparge and bottom drain lines.

6. Open the door of the condenser unit, if present, and feed the condenser portion of the bag through the condenser.
7. Insert the vent filter(s) into the filter bracket (Figure 3.6).



Figure 3.6. Inserting a vent filter into the filter bracket.

8. If present, straighten and smooth the condenser bag in the condenser unit and close and latch the door of the condenser (Figure 3.7). Ensure that the condenser BPC is not too tight or too loose in the condenser hardware unit.



Figure 3.7. Loading of an optional condenser bag.

9. Secure filter heater(s) on the filter(s) (Figure 3.8). Connect the heater to the controller, and verify that it is plugged into an appropriate 120 or 240 VAC outlet. Then connect the power cord to the controller or the E-Box.

Filter notes:

- The vent filter heater controller is preset to 55°C.
- 30 L BPCs may have one or two exhaust filters.



Figure 3.8. Installing an exhaust filter heater.

10. If a cable management system is available, attach the lines to the appropriate inlet ports (Figures 3.9, 3.10, and 3.11).



Figure 3.9. Line setup on the cable management system.



Figure 3.10. Incoming line connection.



Figure 3.11. Incoming line connection to a direct sparger filter.

11. Connect incoming gas feed line to the sparger filter. Inflate the BPC with air through the sparger. Inflation time is approximately one to five minutes. Do not exceed 25 slpm or 0.034 bar (0.5 psi) internal pressure for 30 L BPCs. As the BPC inflates, ensure it is properly oriented in the support container (port alignment, drain, and sparger).



WARNING: DO NOT EXCEED 0.034 bar (0.5 psi) within the BPC or the BPC could fail. The BPC will appear to be tight at 0.007 bar (0.1 psi). The pressure in the tubing after the inlet filter should be about 0.34 bar (5 psi) and should be easy to compress with two fingers.

12. As the container fills with air, manipulate the container to align the sparge line in the slot.

Note: While a check valve is provided for the sparge line on 30 L units, it is not uncommon for some fluid to bypass check valves during typical use. Elevate the filter above the liquid level in the S.U.F. and secure it to prevent exposing the filter to liquid.

13. Use the bottom cutouts located at the base of the support container as a reference to align the hanging tabs on the BPC.
14. Attach the two hanging tabs on the bottom of the BPC to the tab holders (pins) on the S.U.F. (Figure 3.12).



Figure 3.12. Aligning a hanging tab with the pin.

15. Align the row of connector ports and probes, and then close the S.U.F. door (Figure 3.13). **Note:** Verify that all port clamps are closed and located as close as possible to the body of the BPC.



Figure 3.13. Aligning the connector ports and probes.

16. To allow for drive shaft insertion, fill the BPC with air for approximately 10–20 minutes (times will vary based on flow rate, inlet pressure, and container volume).



WARNING: To prevent damaging the BPC, the BPC must be partially inflated before you begin to insert the drive shaft. You must close and latch the access door of the S.U.F. before fully inflating the BPC.

17. Connect the media ground clip to the stainless steel insert in the sample line of the BPC. This grounds the media inside the BPC and helps to eliminate electrostatic charge (Figure 3.14).



Media ground clip connection

Figure 3.14. Media ground clip connection.

Use of exhaust filter pinch clamp (when present)

If your system includes a pinch clamp, follow the instructions below to close off redundant exhaust filters on the BPC.

1. Install the exhaust filter pinch clamp on the vent filter post.
2. Check to ensure that the blue light on the release button is illuminated, which indicates that power to the unit is enabled. The clamp will be manually closed to a 0.159 cm (1/16 in.) clearance. The clamp will then automatically close the remaining gap to shut off the exhaust filter(s).
3. Remove the locking pin and open the clamp.

4. Position the alignment cutout on the exhaust filter BPC, over the pin on the left side of the clamping surface for 30 L units (Figure 3.15). **Note:** On 300 L units, this pin is at the top of pinch clamps.



Figure 3.15. Positioning the BPC cutout over the alignment pin in a pinch clamp.



WARNING: Pinch hazard. When using the pinch clamp, keep hands away from the pinching surface.

5. Close the front of the clamp (Figure 3.16) and replace the locking pin (Figure 3.17).

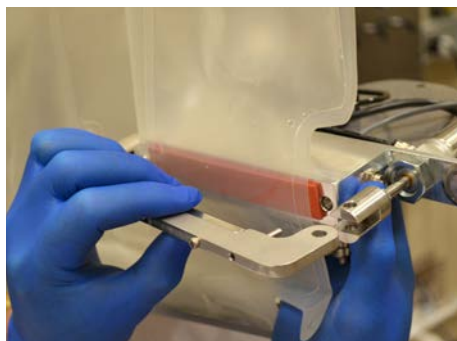


Figure 3.16. Closing the front of the clamp.

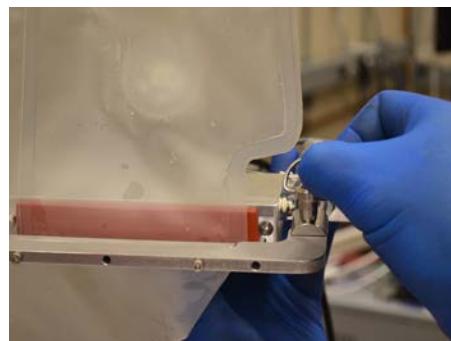


Figure 3.17. Replacing the locking pin.

6. Verify that the blue light is on.
7. Push the front of the clamp toward the pinching surface until it almost touches the BPC (Figure 3.18). The clamp will automatically close completely.

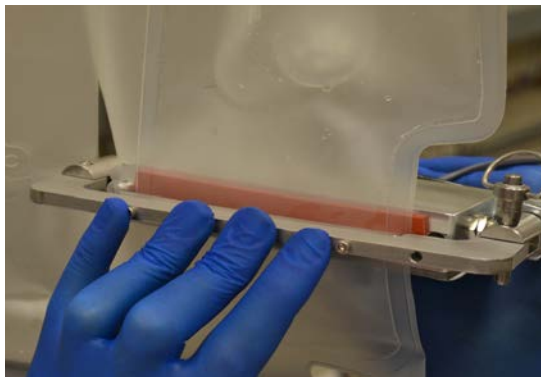


Figure 3.18. Pushing the pinch clamp closed.

8. When using the system, if the first set of filters become fouled, the pinch clamp can be manually opened to enable the backup filter. This should only be done when the pressure in the BPC is 0.034 (0.5 psi) or 0.041 bar (0.6 psi), and no foam is detected in the headspace. To manually open the clamp, push the illuminated blue button.
9. If the pinch clamp has been integrated into a controller, it can also be released using a button on the controller's touchscreen.

3.2.2. Drive shaft insertion for 30 L units



WARNING: To prevent damage to the BPC, the BPC must be partially inflated before beginning to insert the drive shaft.

1. Remove the latch pin from the motor assembly (Figure 3.19).



Figure 3.19. Removing the latch pin from the motor assembly.

2. Unscrew the threaded cap covering the pass-through of the motor.
3. Use the following steps to insert the drive shaft through the pass-through of the motor (Figures 3.20 and 3.21).
 - Use two hands to load the drive shaft through the top of the motor assembly; a slight back and forth twisting motion will aid in insertion, and prevent stretching of the impeller tubing.
 - When approximately 30 cm (12 in.) of shaft remains, twist back and forth slightly to engage the impeller.
 - When approximately 25–50 mm (1–2 in.) of shaft remains, twist back and forth slightly to engage the bearing assembly.
 - When approximately 6 mm (0.25 in.) of shaft remains, twist to align the motor drive keyway with one of the four outer slots on the drive shaft head.



Figure 3.20. Using two hands to load the drive shaft.



Figure 3.21. Aligning the motor drive keyway.

4. Use the following steps to directly couple the drive shaft to the motor drive (Figures 3.22–3.24).
 - Place the threaded cap on the hollow pass-through and hand-tighten in a clockwise direction (Figure 3.22).
 - Tighten the cap by placing the spanner wrench on the hollow pass-through and tighten the cap using the supplied torque wrench (Figure 3.23). **Note:** The torque wrench is a standard 10 mm (3/8 in.) square drive, and is calibrated at the factory at 16.9 Nm (150 in-lb.)
 - Verify that the wrenches have been removed from the system and placed in storage holders.
 - Close the safety access cover and insert the latch pin (Figure 3.24).



Figure 3.22. Replacing the cap.



Figure 3.23. Tightening the cap.



Figure 3.24. Replacing and latching the cover.

5. The air supply may be turned off once the drive shaft has been inserted.

3.2.3. Final installation steps for 30 L units

1. Position and close a bar clamp on the bottom drain line as close as possible to the BPC port (Figure 3.25).



Figure 3.25. Closing bar clamp on drain line.

2. Remove the plastic insert (if present) located in the thermowell.
3. Use the following steps to insert the RTD or selected temperature sensor into the thermowell (Figures 3.26 and 3.27).
 - Place a small amount (0.5 mL) of conductive glycerol in the thermowell to aid in heat transfer.
 - Insert the sensor until the base of the probe meets the mouth of the thermowell (Figure 3.26).
 - Secure by twisting the luer lock collar, if provided. The thermowell will stretch slightly when the RTD is seated (Figure 3.27).



Figure 3.26. Inserting the RTD into the thermowell.



Figure 3.27. Securing the RTD by twisting the luer lock collar.

- Optional: Connect the pressure sensor to the monitoring device.



WARNING: Do not over-inflate the BPC, as it could rupture. An automatic high-pressure gas shutoff device is recommended.

- Refer to section 3.5.3 for probe insertion instructions.
- Plug the optional foam sensor wire into the port in the top of the BPC (Figure 3.28), and attach the ground clip to the stainless steel insert in the RTD/sampling port (Figure 3.29).



Figure 3.28. Foam sensor wire plugged in.

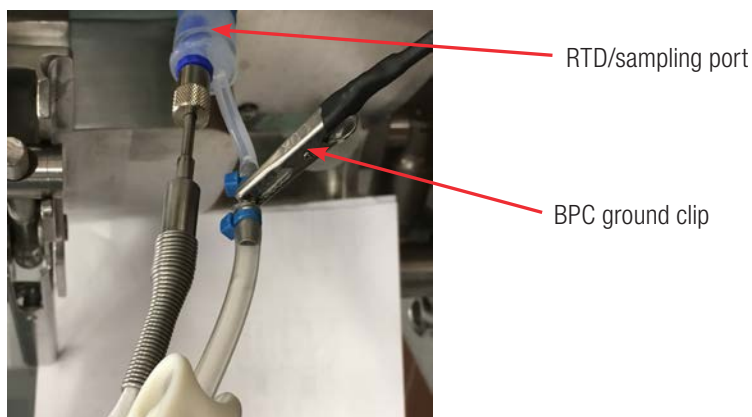


Figure 3.29. Vessel to media ground clip.

3.3. BPC and drive shaft loading for 300 L units

3.3.1. Initial installation steps for 300 L units

Before beginning to load the BPC, verify that the S.U.F. hardware is stationary with casters locked into place. BPC loading may require operators to step inside the fermentor, and the unit must be stationary for the safety of both the operator and the equipment. For ease in BPC loading, two operators may be required. For drive shaft insertion and exhaust filter positioning, a ladder or other means of elevation is required.

1. Open the door of the S.U.F. outer support container (Figure 3.30).



Figure 3.30. Opening the fermentor door.

2. Release (pull down) the latch that locks the motor in place, and slide the motor away from the center of the tank.
3. Remove the irradiated BPC from its protective packaging and double polybags (Figure 3.31). Do not remove polybags from the line sets at this stage, as the BPC may become difficult to manage. Do not allow the BPC or line sets to touch the floor.



Figure 3.31. BPC in protective polybags.

4. Reach into the outer support container with the front face (bearing port side) of the BPC oriented towards the motor (Figure 3.32).



Figure 3.32. Bearing port orientation.

Note: These steps may also be performed from the top of the unit. Be sure to use caution when using a ladder. Maintain three points of contact, and ensure that the steps are clean.

5. Place the top line sets (still in polybags) over the top edge of the tank (Figure 3.33). This will keep the container from being restricted during the air inflation step.



Figure 3.33. Preparing to place bagged lineset over edge of container.

6. From inside the tank or from an elevated position, slide the exhaust port into the exhaust port bracket at the top of the outer support container (Figure 3.34). Slide the black lever to lock the exhaust port into the bracket (Figure 3.35 and 3.36). It should click into place.



Figure 3.34. Inserting the condenser into the exhaust port in a holder at the top of the tank.



Figure 3.35. Exhaust port sliding latch (removed from the tank).

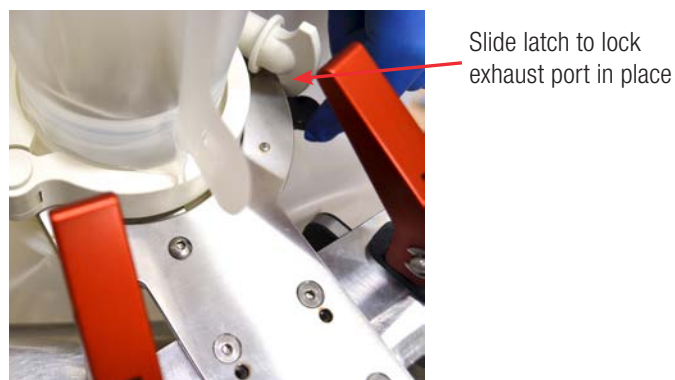


Figure 3.36. Locking the exhaust port.

7. Remove the cap from the bearing port in the BPC and load the bearing port into the receiver (Figure 3.37). The motor may be locked into position, or unlocked to facilitate bearing port insertion, if preferred. Close the bearing port door and latch it (Figure 3.38).

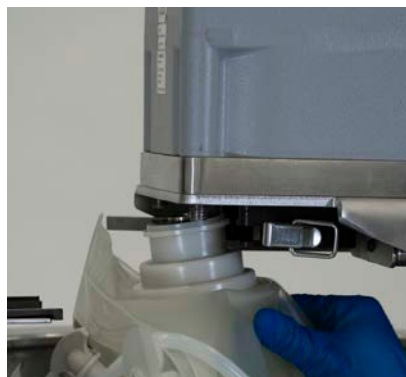


Figure 3.37. Bearing port in the receiver.

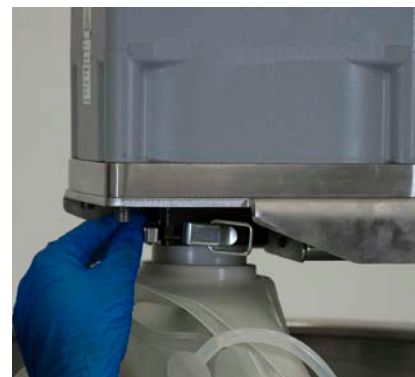


Figure 3.38. Latching the bearing port.

8. If the motor was unlocked to facilitate insertion of the bearing port, lock the motor back into position.



WARNING: Failing to lock the motor into position may cause harm to personnel or damage the BPC.

9. If your unit has one, open the door of the condenser. Feed the condenser bag through the condenser, and attach the exhaust filter bags into the filter bracket (Figure 3.39). Then close and lock the condenser door (Figure 3.40) and adjust the height of the filter bracket so there are no wrinkles or slack in the exhaust system.



Figure 3.39. Exhaust filter and condenser setup.



Figure 3.40. Closing the condenser door.

10. Remove the white plastic guide plate from the bottom of the outer support container (Figure 3.41) and guide the sparge inlet line, filter, and the drain line through the bottom cutout in the outer support container. Replace the plastic guide plate (Figure 3.42).

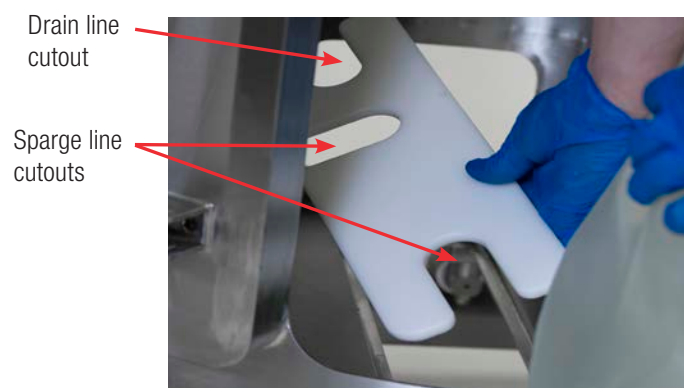


Figure 3.41. Removing the guide plate.



Figure 3.42. Replacing the guide plate.

11. Extend the tubing through the bottom of the outer support container. Ensure that the tubing isn't pinched or kinked under the container (Figure 3.43).



Figure 3.43. Sparge and drain line extension.

12. Pull the temperature/sampling port through the large opening in the front of the outer support container.

Optional: If you are using the optional exhaust filter pinch clamp to control airflow to redundant filters, follow the steps listed under the “Use of exhaust filter pinch clamp (when present)” section, which is located in section 3.2.1—Initial installation steps for 30 L units. The same pinch clamp is used for both S.U.F. sizes. However, the clamp is oriented vertically on the 300 L system (Figure 3.44), and horizontally on the 30 L system.

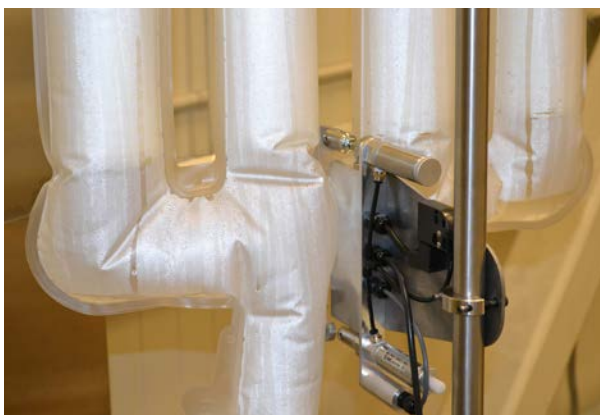


Figure 3.44. Pinch clamp installed on a 300 L BPC.

13. Connect a pressure sensor to the monitor (or the third-party controller, if used). After the display has stabilized, allow it to warm up for 30 minutes, and then tare the monitor. Verify that the monitor reads zero. **Note:** Filter input air pressure can be up to about 3.103 bar (60 psi) for the 300 L S.U.F. The maximum pressure in the tubing after the inlet filter should be less than 0.334 bar (3 psi), and that section of tubing should be easy to compress with two fingers.



WARNING: DO NOT EXCEED 0.34 bar (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. When inflating the BPC, ensure that the tubing isn't pinched or kinked under the outer support container.

Note: Filling the BPC with air takes approximately 15–20 minutes before drive shaft insertion can begin. Times will vary based upon flow rate and inlet pressure.

14. Remove the bubble wrap from the inlet filter and sparge line (Figure 3.45), connect to gas supply, and partially inflate the BPC. This will allow for proper insertion of the drive shaft and aid in aligning the BPC in the outer support container.



Figure 3.45. Sparge line and filter.

15. As the BPC fills with gas, attach the hanging tabs on the BPC to the hooks (pins) on the S.U.F. hardware at the top and bottom of the unit (Figure 3.46).



Figure 3.46. Attaching hanging tabs.

3.3.2. Drive shaft insertion for 300 L units

The motor and mixing assembly in Figure 3.47 serves as a reference for drive shaft assembly and insertion. The drive shaft is constructed using three pieces, which must be assembled and inserted piece by piece. Operators should be elevated (i.e. ladder) to effectively assemble and insert the drive shaft.



WARNING: Review ceiling height requirements in Table 4.2 in section 4.2 before trying to insert the drive shaft. Use caution when on a ladder or elevated platform. Ensure that it is stable, the steps are clean, and maintain three points of contact.

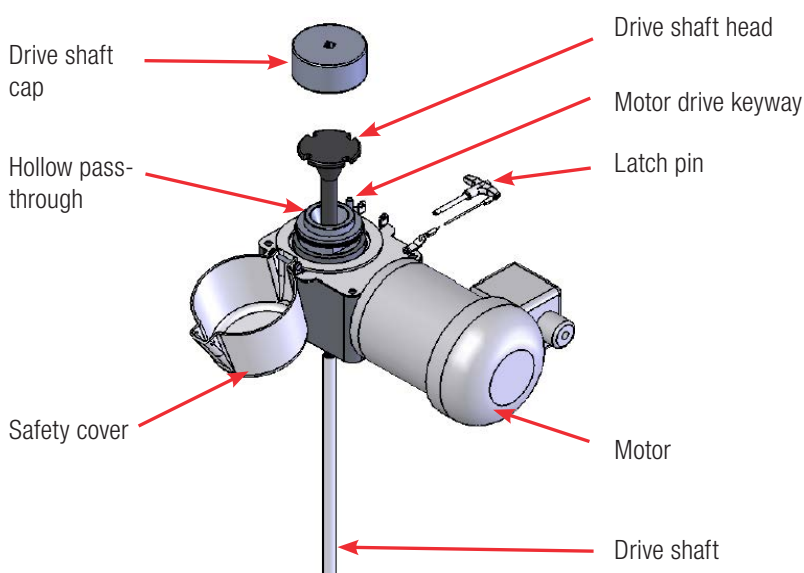


Figure 3.47. Motor and mixing assembly.

1. Prepare the hollow pass-through by first removing the latch pin on the safety cover (Figure 3.48), opening the safety cover, and removing (by turning counter-clockwise) the threaded drive shaft cap of the mixing assembly (Figures 3.49 and 3.50).

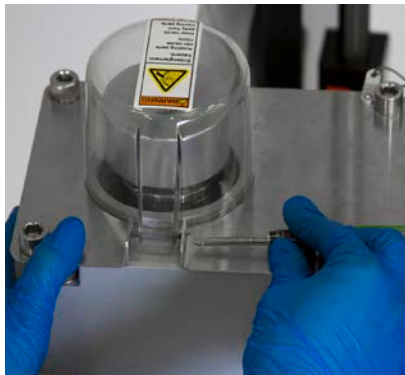


Figure 3.48. Removing the latch pin.

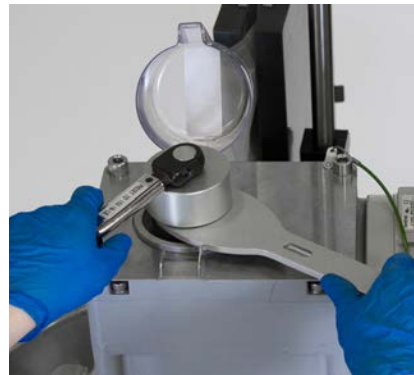


Figure 3.49. Opening the drive shaft cap.



Figure 3.50. Removing the drive shaft cap.

2. Verify that the three sections of the drive shaft are located in the drive shaft holders on the side of the outer support container. The sections will be referred to as the upper (section with the drive shaft head), middle (section with external threads on each end), and lower (section with the hexagonal end). Lubricate the threaded ends with a light coat of food grade anti-seize with each use.

3. First, insert the lower section through the hollow pass-through of the motor drive. Slide the latch pin from the motor assembly into the shaft to prevent it from falling into the tube (Figure 3.51). Assemble the middle and lower sections of the drive shaft by joining the segments with a twisting motion, fastening the two sections together (Figure 3.52).

Locate one wrench on the flat area in the middle drive shaft section, another wrench on the lower section, and tighten the connection using a counter-clockwise rotation (Figures 3.53 and 3.54). The shafts are left-threaded (reverse-threaded) to avoid loosening during operation. Once the sections are secure, return the wrenches to the tool holder. **CAUTION:** Do not over-tighten; a snug fit is sufficient. Remove the latch pin.



Figure 3.51. Inserting the lower section and securing it with a latch pin.



Figure 3.52. Connecting the middle section of the drive shaft.



Figure 3.53. Tightening the drive shaft connections.



Figure 3.54. Connecting the upper drive shaft segment.

4. Load the partially assembled drive shaft through the hollow pass-through and hold it in position with the latch pin. Obtain the upper section of the drive shaft and assemble it to the middle segment in the manner described previously.
5. Using two hands, carefully guide the completed drive shaft into the BPC using a slight back and forth twisting motion (Figure 3.55). **Note:** It may be necessary for another operator to assist with drive shaft insertion. As one operator inserts the drive shaft, another operator should carefully manipulate the impeller when the end of the drive shaft begins to couple with the impeller.
 - When 50.8 cm (20 in.) of shaft remains, twist slightly to engage the impeller.
 - When 25–50 mm (1–2 in.) of shaft remains, twist slightly to engage the bearing assembly.
 - When 6–12 mm (0.25–0.5 in.) of shaft remains, twist to align the motor drive keyway with one of the four outer slots on the drive shaft head.

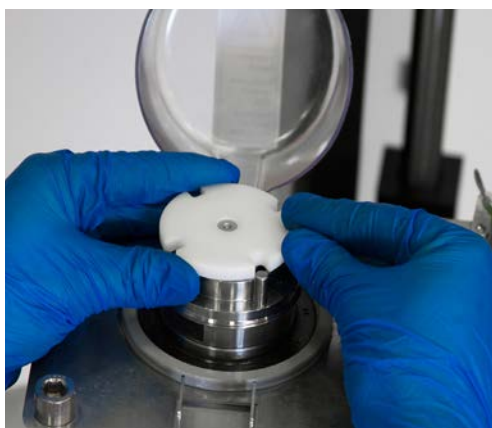


Figure 3.55. Aligning the motor drive keyway with the drive shaft head slots.

6. Directly couple the drive shaft to the motor by placing the threaded cap back on the hollow pass-through and tighten (Figure 3.56).

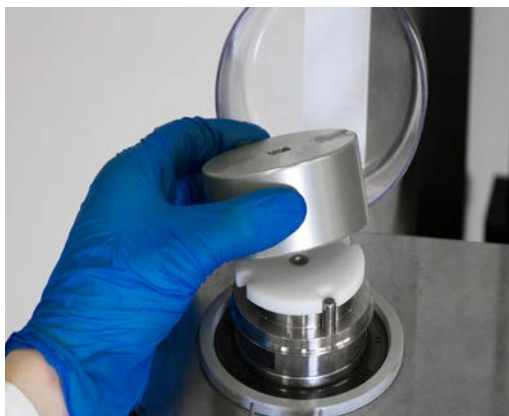


Figure 3.56. Replacing the drive shaft cap.

7. Tighten the cap by placing a spanner wrench counterclockwise on the hollow pass-through. Tighten using the supplied torque wrench (Figure 3.57). **Note:** The torque wrench is a standard 10 mm (3/8 in.) square drive, and it is calibrated at the factory at 16.9 Nm (150 in-lb.).



Figure 3.57. Tightening the cap with wrenches.

8. Remove the wrenches from the system and return them to the storage holders.
9. Close the safety access cover and insert the latch pin.

3.3.3. Final installation steps for 300 L units

1. Fully extend the ports through the front cutout of the outer support container, and attach the probe clips (Figure 3.58).



Figure 3.58. Attaching a probe clip.

2. Remove the drain line set from the polybag (Figure 3.59), position the line clamp as close as possible to the BPC port, and close the clamp (Figure 3.60). Use a cable tie around the clamp to ensure that it cannot be accidentally opened.



Figure 3.59. Removing the drain line set from a polybag.



Figure 3.60. Placing a clamp on the drain line.

3. If present, remove the plastic insert located in the thermowell.

4. Use the following steps to insert the RTD or selected temperature sensor into the thermowell (Figure 3.61).
 - Place a small amount of glycerol (0.5 mL) in the well to aid in heat transfer.
 - Insert the sensor until the base of the RTD meets the mouth of the thermowell.
 - Secure by twisting the luer lock collar, if provided. The thermowell will stretch slightly when the RTD is seated.



Figure 3.61. Inserting a sensor into the thermowell.

5. Verify that all of the port clamps are closed and located as close as possible to the body of the BPC.
6. If your BPC is equipped with a foam sensor, connect the foam sensor wire to the port at the top of the BPC (Figure 3.62).



Figure 3.62. Foam sensor wire connected in port.

7. Attach the ground clip to the stainless steel insert in the RTD/sampling port (Figure 3.63).



Figure 3.63. Foam sensor ground clip on the RTD.

8. If your system includes a cable management system, refer to the instructions for setting up the cable management system in the Optional cable management system setup in section 2.3.5 of this guide.

Note: Since there is no check valve on the inlet gas line for the 300 L S.U.F., position inlet filters well above the liquid level to prevent fouling of the filters.

3.4. Exhaust system

3.4.1. Exhaust system functional overview

The condenser is intended to be used as an accessory to the S.U.F. in conjunction with vent filter heaters, which are necessary with or without the condenser. The condenser's purpose is to prevent liquids and solids from condensing and collecting inside of the vent filters of the S.U.F.

The condenser cools the exhaust gases leaving the S.U.F. chamber, condensing the moisture out of the saturated gases coming from the S.U.F. The liquid condensate that is stripped from the exhaust gases is then returned to the bioprocessing container chamber, creating a sterile loop and significantly reducing liquid loss due to evaporation. The condenser plate is chilled by a closed bath recirculating chiller. Figure 3.64 is a functional diagram of the exhaust system on a 300 L S.U.F.

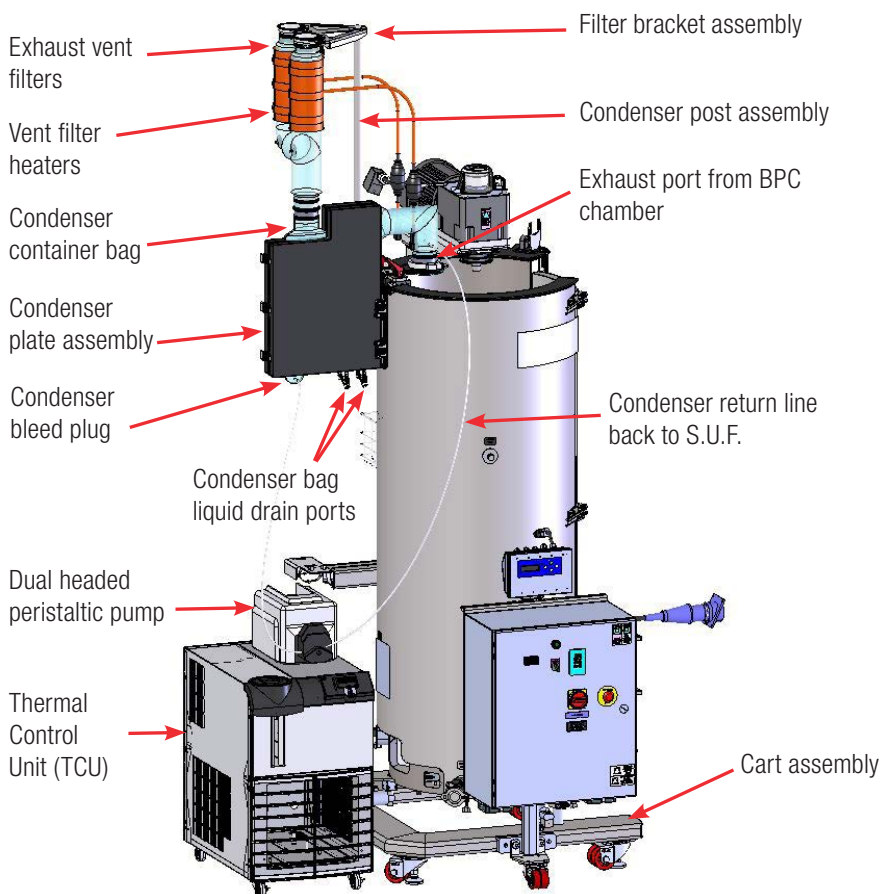


Figure 3.64. Complete exhaust system on a 300 L S.U.F.

3.4.2. When to use the condenser

Large 254 mm (10 in.) hydrophobic polyethylene vent filters with a nominal 0.2 micron pore size increase the available surface area for off-gassing. In addition, the standard 30–300 L S.U.F. is designed for use with an optional condenser. This allows the S.U.F. to improve exhaust vent protection and reliability because it strips condensate and atomized materials that may be present from the off-gas stream of the S.U.F. This system has been shown to significantly reduce the “fouling” load on the vent filters that may also increase operating back pressure as the cell culture run progresses. See the S.U.F. Validation Guide for specific details.

Some end users may prefer to omit the condenser under the expectation that this will allow for a more uniform installation or will reduce system complexity and cost. The use of exhaust vent heaters and 254 mm (10 in.) filters will provide some impressive flow capacity over short periods. However, the high sparge rates required may eventually create conditions of increased operating back pressure, usually due in part to blocking of the filter media. Depending on the application, the user may use both filters in parallel or initiate the run with a single filter, temporarily clamping off the line to the other filter, and reserve it for use as redundant back-up.

Various vent filter configurations are available on the S.U.F., depending on the process scale and intended application. In all cases, using a vent filter heater will reduce the chance of condensate blocking the filter. Over time, suspended solids carried in the exhaust stream will impede the flow of exhaust gas, resulting in increased back pressure. In addition, it is good practice to monitor the amount of foam present in the head space. S.U.F. BPCs may be equipped with foam sensors that monitor foam in the head space and can be used to automatically trigger the addition of an anti-foaming agent. A vent filter heater has very little tolerance for handling the presence of foam in the exhaust stream. A small feed of antifoaming agent added directly to the liquid surface of the head space typically provides excellent foam control.

3.4.3. Condensers and reserve vent filters

All systems, especially large systems, benefit from the use of a condenser. The condenser increases system reliability at high flow rates beyond 1 vvm (or 30 slpm for 30 L vessels, and 300 slpm for 300 L vessels), and warrants strong consideration when performing batch runs beyond one day at 1 vvm (or three days at lower vvm). Results will vary. However, it is strongly recommended that end users select a vent filter configuration providing reserve capacity where possible. For example, on 30 L units, dual vent configurations can be used independently, with the second filter serving as a backup (providing a quick reserve in case issues arise in-process). For 300 L S.U.F.s, a single vent filter may be used at 300 slpm (1 vvm), but a second filter may be added to serve as a backup. At 600 slpm (2 vvm), two filters are required, but two additional filters may be added as backups.

3.4.4. Exhaust system setup

1. Remove and assemble the vent filter holder and condenser from the crate or shipping box. Assembly instructions are included in the S.U.F. Packing and Unpacking Instructions document.

Note: For safety, two people should assemble the 300 L condenser onto the S.U.F.

2. If your system includes a condenser, connect the TCU hoses to the ports on the condenser unit.
3. Remove the reservoir cap of the TCU and add the appropriate type and volume of fluid, as specified in the TCU user's guide.
4. Verify that the peristaltic pump, if used, and TCU power cords are connected to power.
5. Turn on power to the TCU. This will allow the TCU to prime.
6. Use the processes in the TCU user's guide to set the pressure, between 1.37–2.06 bar (20–30 psi). Normally, this is controlled by a valve on the back of the unit, and displayed on an LCD display on the front of the unit.
7. Add fluid to the reservoir in the TCU as needed, in order to maintain the minimum level.
8. Purge the condenser plate by loosening the bleed plug on top of the plate. This is accessed using an open-end wrench. Loosen the plug only enough to allow trapped air to escape, then re-tighten.

9. Check the indicator or window on the front of the TCU to ensure that the reservoir is still at least at the minimum level.
10. The settings for the TCU and peristaltic pump are preset at the factory. These settings allow for the system to resume at the setpoint if the power is temporarily disrupted. Verify that the TCU and pump setpoints are at the recommended levels (5°C and 12 rpm).

3.4.5. Loading the condenser BPC

1. Remove the BPC with the condenser container (if ordered) and vent filters from the polybag packaging, being careful not to puncture the container.
2. For 30 L units, load the BPC into the bearing hub as described in section 3.2 of this guide. For 300 L units, it is best not to load the BPC into the bearing hub until the condenser has been loaded, but place the BPC into the main S.U.F. tank.
3. For 300 L units with condensers, first insert the exhaust port of the BPC into the exhaust port holder, which is attached to the bracket used to clamp the exhaust system onto of the outer support container (hardware). It may be helpful to slide the motor back out of the way for this step.
4. Open the door of the condenser unit, if present (Figure 3.65). Position the rectangular container inside the condenser unit, being careful not to pull the container out of shape. The vent filter can hang freely. Leave the condenser door open.



Figure 3.65. Opening the condenser door (300 L S.U.F. unit).

5. Place the top(s) of the filter(s) into the filter bracket(s) (Figure 3.66). Adjust the height of the filter bracket, as needed. Make sure that the position of the filter is not pulling the BPC condenser too tight, pinching off the air flow. It should also not be too loose, causing it to kink.



Figure 3.66. Positioning the condenser BPC and vent filter in bracket.

6. For units with condensers, ensure that there are no kinks or wrinkles in the container. Then, close and latch the condenser door (Figure 3.67).



Figure 3.67. Closing and latching the condenser door.

7. Place the vent filter heater(s) around the filter(s), looping the top strap of the heater around the metal bar on the filter bracket, and using the snap to secure them in place (Figures 3.68 and 3.69).



Figure 3.68. Snapping a vent filter heater onto the filter.



Figure 3.69. Using the snaps to secure the vent filter heater.

8. For 300 L units with condensers, load the tubing into the peristaltic pump, ensuring that there is sufficient slack at each end of the pump tubing. Align the tubing in the pump channel, and close the pump ramp (Figure 3.70). Verify that the flow direction returns condensate to the vessel. Consult the pump user's guide for more information about operating the peristaltic pump.

30 L note: For 30 L units, a peristaltic pump is not needed, as condensate drips back into the main BPC chamber.

Tubing note: Ensure that the tubing size is correct for the pump head. PharMed™ tubing is recommended for the condensate line. Standard tubing is silicon, which should be sufficient for 24 hours.



Figure 3.70. Loading pump tubing.

9. Verify that both the pump and TCU or chiller are enabled and running at the proper settings. We recommend a pump setting of 12–30 rpm, and a TCU/chiller setting of 5°C. Condensate flow should be verified at the maximum gas flow settings.
10. After setting up the 300 L unit, verify that the pump union is loose on both ends of the pump, and running smoothly in the peristaltic rollers.

Specific performance questions can be answered by reviewing the condenser section of the S.U.F. Validation Guide, or by contacting technical support.

3.5. Probe assembly

3.5.1. Preparation and sterilization

1. Select the appropriate probe. Verify the presence of a Teflon™ support ring and O-ring on the probe and visually inspect them for damage.
2. Perform any required probe maintenance, and calibrate the pH probe (see the probe calibration topic in section 3.5.4 of this user's guide).
3. Insert the probe into the probe assembly through the threaded adaptor.
4. Verify that the probe tip is not touching the membrane of the aseptic connector (more than 6.35 mm [1/4 in.] gap) before threading it into the probe adaptor.
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 3.71).

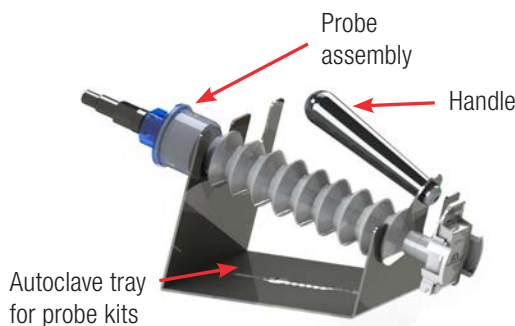


Figure 3.71. Probe and autoclave tray.

7. Autoclave the probe assembly using a validated sterilization cycle, approximately 30 minutes at 122°C. 30-minute sterilization cycles are 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 probe assemblies to cool completely before connecting to the BPC for probe insertion.
9. When stored properly, the autoclaved probe assemblies can be stored dry for short periods of time (less than 24 hours) without loss of sensor longevity, performance, or sterility.

3.5.2. Making CPC AseptiQuik connections

CPC AseptiQuik G genderless connector components

Figures 3.72 and 3.73 below 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 at <http://cpcworldwide.com> for more information.

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



Figure 3.72. CPC AseptiQuik G connector (closed).

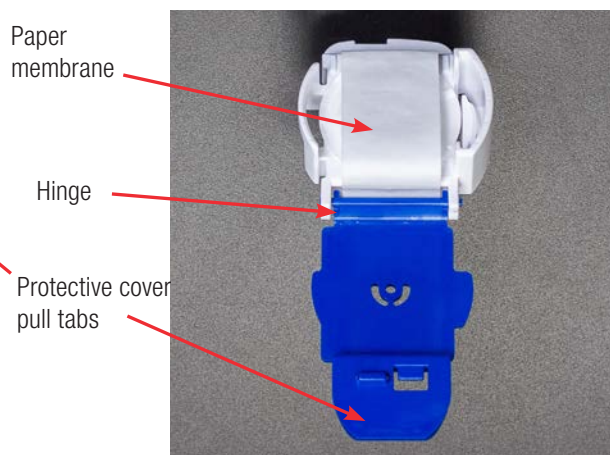


Figure 3.73. CPC AseptiQuik G connector (open).

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 3.74 and 3.75).



Figure 3.74. Pulling the tear strip.



Figure 3.75. Removing the plastic covering from the connector.

2. Unsnap and flip open the protective cover pull tabs on both connectors (Figures 3.76 and 3.77).



Figure 3.76. Opening the protective cover pull tab on the port.



Figure 3.77. Opening the protective cover pull tab on the line set.

3. Align the two connectors and push them together.
4. Squeeze each side of the connectors until you hear a click (Figure 3.78).



Figure 3.78. Squeezing connectors together.

5. Grab the joined pull tabs and pull upward to remove the paper membranes from the connectors (Figure 3.79). The pull tabs will also be removed.



Figure 3.79. Pulling tabs to remove the paper membranes.

3.5.3. Probe insertion

Before beginning probe insertion, please become familiar with the CPC AseptiQuik connector procedure outlined in section 3.5.2. If you are using Kleenpak connectors instead, refer to section 3.5.5.

1. Attach probe clips onto the outer support container above the probe assembly (Figure 3.80). Plastic probe clips slide on with firm pressure.



Figure 3.80. Attaching a probe clip.

2. Install the pre-sterilized sensor and probe kit using aseptic connection methods, as described in section 3.5.2. The aseptic connection is completed prior to the bellows being collapsed (Figure 3.81).



Figure 3.81. Installing the pre-sterilized sensor.

3. Insert the probe by collapsing the bellows (Figure 3.82).

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 3.82. Collapsed bellows.

4. Position the probe clip in the desired horizontal location. Lift the probe and set it into the probe clip (Figure 3.83).



Figure 3.83. Lifting the probe upward into the spring.

5. Verify that the probe remains at the proper insertion depth and angle as the bellows expand to rest freely in the probe clip.

3.5.4. Probe calibration

Probe calibration is controller-specific. However, the following general rules apply:

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

3.5.5. Kleenpak connection instructions

Use the following instructions to make Pall Kleenpak connections. This product is not sold sterile. For use in making sterile connections, each connector must be fitted in a closed, single-use assembly that has been subjected to a validated sterilized process. It is very important that all instructions are carefully followed and where appropriate should be incorporated into the user's standard operating procedures. If some of the procedures do not suit your needs, please consult Pall or your local distributor before finalizing your system.

Specifications

The Kleenpak connector has a maximum working pressure of 3 bar (43.5 psi) at 40°C in compatible fluids.



WARNING: Operation outside the above specifications and/or with fluids incompatible with construction materials may cause personal injury and result in damage to the device.

Receipt of equipment

The male and female Kleenpak connectors are supplied in separate packages. There are several types of end fittings in order to match different tubing size requirements and to allow for different attachment possibilities to flexible tubing. See the Pall website for more information.

Ensure the following upon receipt of equipment.

- Male and female connectors are supplied protected by an inner and outer bag. Ensure that the packaging is undamaged.
- Store the male and female Kleenpak connectors in clean, dry conditions and wherever practical in the external packaging as delivered.

- DO NOT remove from the inner device bag packaging until just before installation.
- The assembly aid is provided non sterile and can be reused multiple times. It needs to be stored in clean and dry conditions between each use. The assembly aid is supplied separately and is available for purchase from your local Pall representative.

Installation

Before installation, it is essential to verify that the connector is suitable for the liquid that it will be in contact with for the application and to follow the appropriate instructions listed below.

- Install the male and female connectors using compatible connections. Ensure that the tubing is attached firmly to the hose barb to prevent leakage during operation using cable ties or other methods. During tubing assembly, premature actuation of the male plunger is prevented by the anti-actuation ring. The anti-actuation ring needs to remain in place until actual connection takes place. The presence of valves on the tubing before the connector is recommended to prevent liquid contact with the connectors prior to use.
- If the connectors are to be autoclaved, orient them with peel strips facing upwards to prevent peel strip blockage by condensate.



WARNING: The device must remain dry prior to connection of the male and female connectors. If there is fluid present in the line or around the devices, do not use. If the protective cap has been removed, do not use.

Sterilization



WARNING: These disposable connectors must not be in-line steam sterilized. Material design limitations will be exceeded when these devices are exposed to pressurized steam and they will be ruptured.

- Connect the male or female connector to the single use system to be sterilized. A valve or clamp needs to be installed close to the connector to prevent accidental wetting after the system is filled with liquid.
- Ensure that the protective cap is firmly in place. Autoclave paper or other radiation resistant material can be used to ensure that the cap does not become dislodged during handling.

Autoclave sterilization

- Install the male or female connector to the equipment to be sterilized. If the connector is attached to a tank, the tank should be vented appropriately with a vent filter.
- Ensure that the protective cap of the connector is firmly in place. Autoclave paper or other autoclavable and air/steam permeable material can be used to cover the cap loosely to ensure that the cap does not become dislodged during handling.
- The connectors should be allowed to vent during autoclaving. The venting strip should be orientated upwards to prevent blockage by condensates.

CAUTION: To avoid collection of condensate within the connectors, do not place the venting strip downwards during autoclaving.

- The connectors should not be covered with heavy objects during the autoclave cycle.

Note: The maximum temperature is 121°C for ACD part numbers and 130°C for KPCHT part numbers and the maximum exposure time is 75 minutes. Do not autoclave at a higher temperature or for a longer time. A slow exhaust cycle is recommended.



WARNING: Do not autoclave the male and female connectors in the bags that they are shipped in.

Important: Pall recommends that the efficiency of the sterilization cycle is validated using an appropriate method.

Making the connection



WARNING: Do not use if fluid is in contact with the connector. Do not use if protective caps are loose or displaced.

Making the connection using the connector assembly aid

See the next section of this guide for instruction about making the connection without using the connector assembly aid.

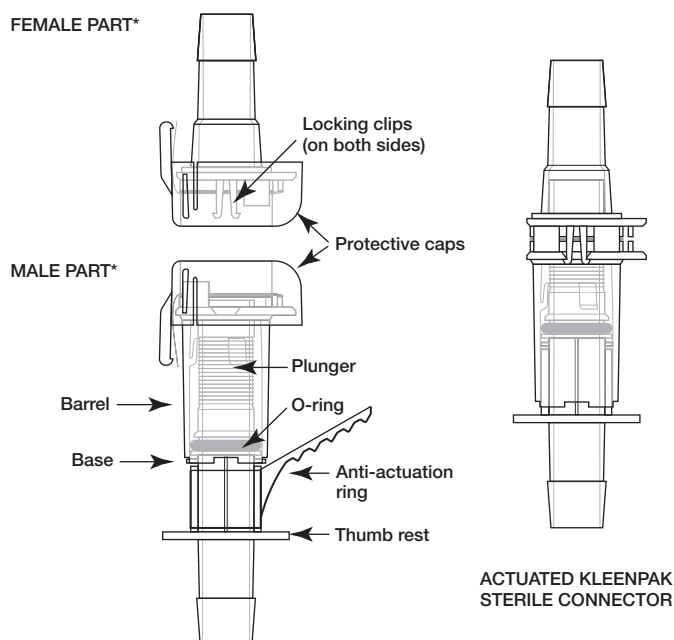


Figure 3.84. Kleenpak connector schematic.

1. Lift and pull tab off protective caps to remove caps from the connectors (Figure 3.85).

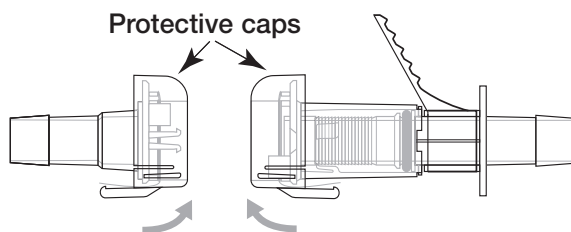


Figure 3.85. Removing caps from connectors.

2. Hold the barrel of the larger (male) connector above the base.
 - Align the smaller (female) connector with the larger (male) connector.
 - Flat sides should be aligned.
 - Both peel away strips need to remain folded (Figure 3.86).

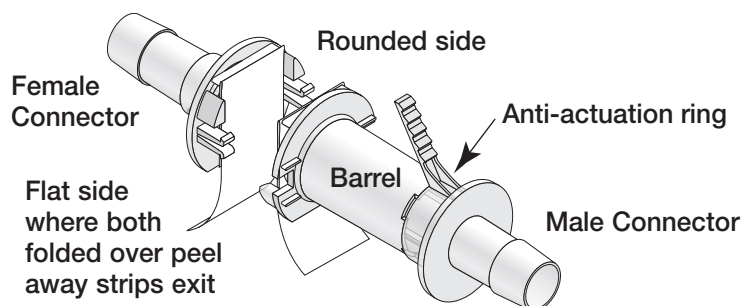


Figure 3.86. Aligning male and female connectors.

Note: If the connectors are not aligned properly, the connection cannot be made.

3. Once aligned correctly, press the two connectors together firmly until both locking clips snap together tightly (Figure 3.87).

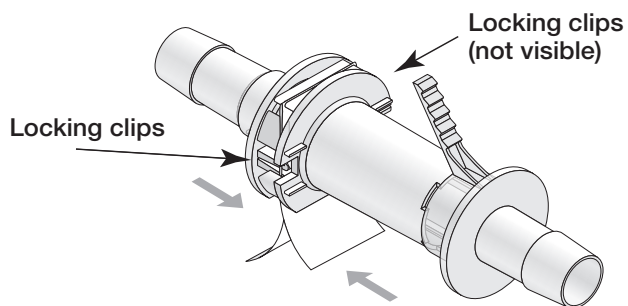


Figure 3.87. Pressing connectors together.

4. Support both the male and female connectors, and remove the anti-actuation ring from the male connector by pulling the tab towards the barbed end of the male connector (Figure 3.88).

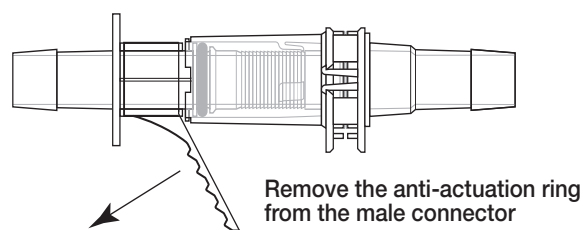


Figure 3.88. Removing anti-actuation ring.

Note: Connector should stay securely in the assembly aid when properly installed.

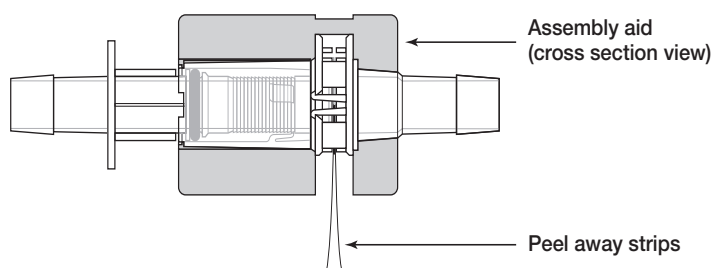


Figure 3.89. Cross-section view of assembly aid.

5. Hold assembly aid in the palm of the hand with the connector facing outwards, and thumb supporting the connector in the assembly aid. Using the other hand, firmly grasp both peel away strips as close as possible to the body of the assembly aid to ensure a secure grip and pull both peel away strips simultaneously in a smooth continuous motion. Ensure that the connector is perpendicular to the peel away strips (Figure 3.90 and Figure 3.91).

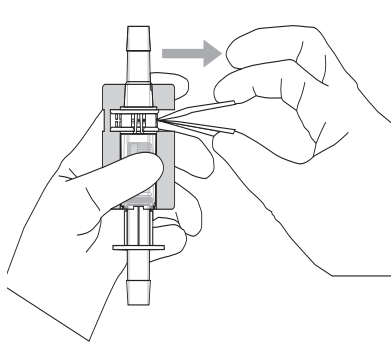


Figure 3.90. Holding assembly aid with thumb supporting connector.

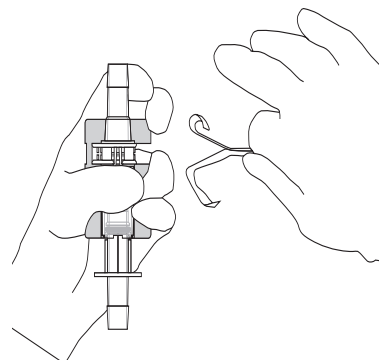


Figure 3.91. Pulling peel away strips.



WARNING: Do not use if only one peel away strip is removed accidentally instead of two, this will affect the sterility of the pathway.

6. With the connector still secured in the assembly aid, push the thumb rest of the male connector down towards the base of the barrel (Figures 3.92 and 3.93).

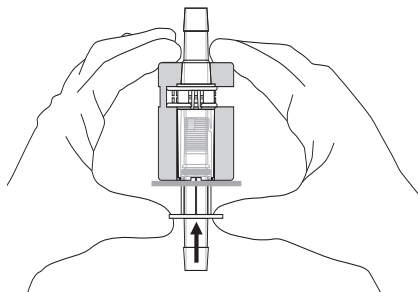


Figure 3.92. Pushing down thumb rest of male connector.

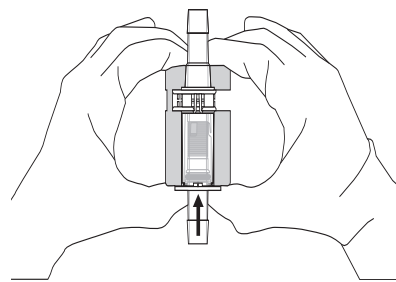


Figure 3.93. Male connector pushed down.

Note that in order to establish a proper connection, the plunger inside the male connector must be fully inserted into the female connector. As a verification, repeat actuation until a hard stop is reached.

If necessary, the connector may be removed from the assembly aid to complete the plunger movement.

7. Once the connector assembly is complete, the assembly aid may be removed. When assembly aid is removed, verify actuation until a hard stop is reached.
8. Start the fluid transfer (Figure 3.94).

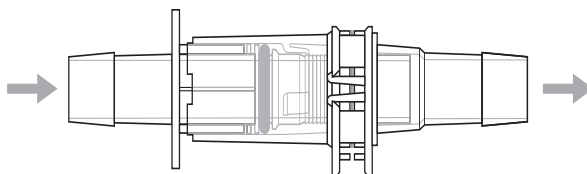


Figure 3.94. Starting fluid transfer.

Making the connection without using the connector assembly aid

1. Lift and pull tab off protective caps to remove caps from connectors (Figure 3.95).

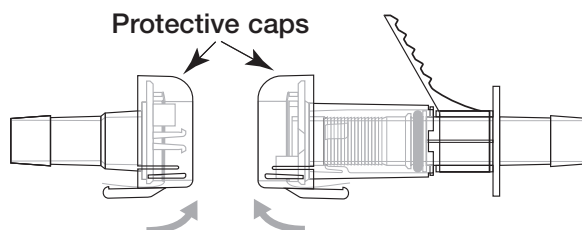


Figure 3.95. Removing caps from connectors.

2. Hold the barrel of the larger (male) connector above the base.
 - Align the smaller (female) connector with the larger (male) connector.
 - Flat sides should be aligned
 - Both peel away strips need to remain folded (Figure 3.96).

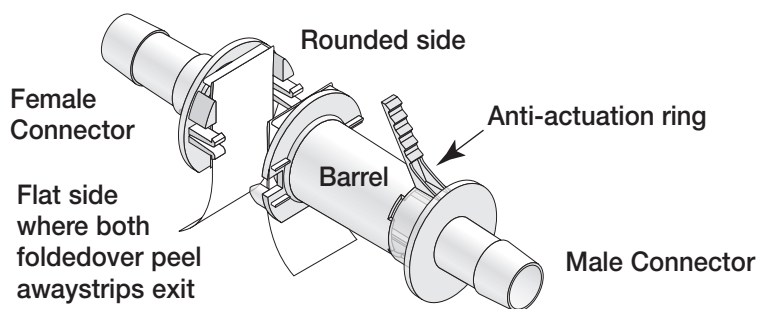


Figure 3.96. Aligning male and female connectors.

Note: If the connectors are not aligned properly, the connection cannot be made.

3. Once aligned correctly, press the two connectors together firmly until both locking clips snap together tightly (Figure 3.97).

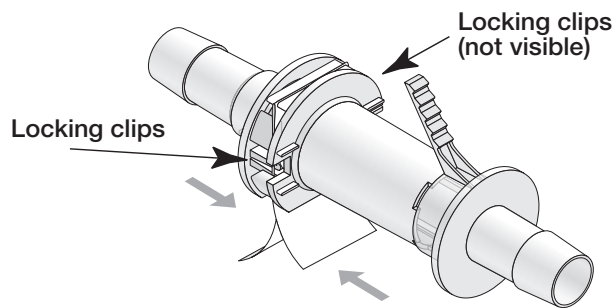


Figure 3.97. Pressing connectors together.

4. Support both the male and female connectors, and remove the anti-actuation ring from the male connector by pulling the tab towards the barbed end of the male connector (Figure 3.98).

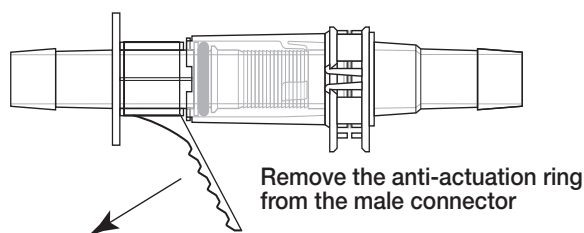


Figure 3.98. Removing anti-actuation ring.

5. With one hand, support the male and female sides of the Kleenpak connector by wrapping fingers around both sides of the connector, next to the flange. Using the other hand, grasp both white peel away strips as close as possible to the flat side of connector to ensure a good grip and pull them out simultaneously in a smooth continuous motion. Ensure that the connector is perpendicular to the peel away strips shown in shown in Figures 3.99 and 3.100. The perpendicular orientation must be maintained while the two strips are pulled simultaneously.

Note: Do not impart perpendicular forces on the connector, as it can cause the connector to break. If a perpendicular force is present due to items attached to the connector, then the connector must be properly supported.

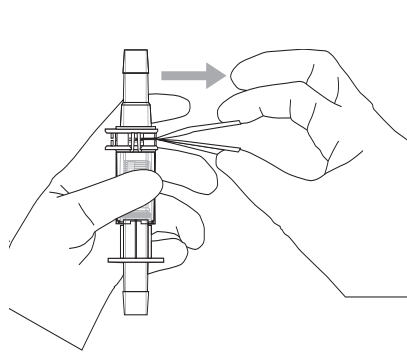


Figure 3.99. Holding assembly aid with thumb supporting connector.

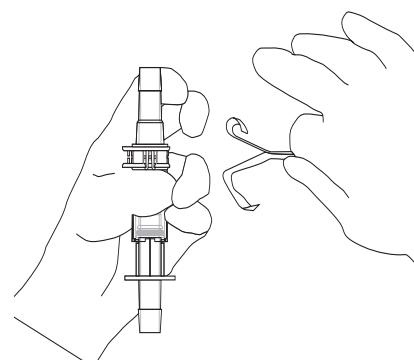


Figure 3.100. Pulling peel away strips.



WARNING: Do not use if only one peel away strip is removed accidentally instead of two, this will affect the sterility of the pathway.

6. Push the thumb rest of the male Kleenpak connector down towards the base of the barrel until they meet (Figures 3.101 and 3.102).

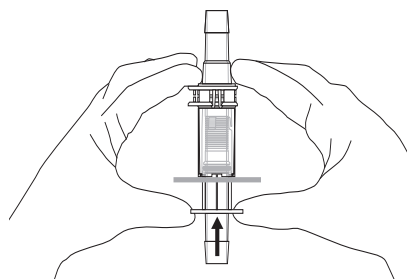


Figure 3.101. Pushing down thumb rest of male connector.

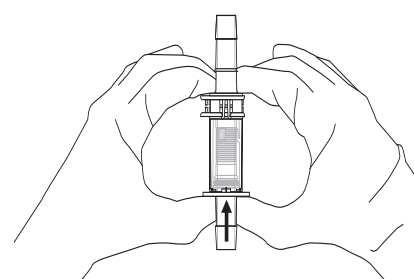


Figure 3.102. Male connector pushed down.

Note: In order to establish a proper connection, the plunger inside the male connector must be fully inserted into the female connector. As a verification, repeat actuation until a hard stop is reached.

7. Start the fluid transfer (Figure 3.103).

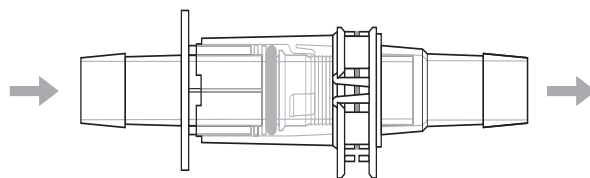


Figure 3.103. Starting fluid transfer.

3.6. Microbial cell culture operating instructions

Before beginning your fermentation run, please refer to the checklist in Appendix D to ensure that all necessary steps have been completed.

3.6.1. Operating conditions for microbial cell culture applications

Optimal operating parameters for microbial cell culture vary greatly between cell lines and media formulations. Tables are provided as a reference for establishing upper operating control limits with the standard BPC design. 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.

Table 3.2 lists values for both sizes of S.U.F.s. This data may be used in specifying maximum gas flow rates for mass flow controllers or rotameters. In optimal conditions (no condensation or fouling) the exhaust filters have a flow capacity of at least 60 and 600 standard liters per minute (slpm) at 0–0.5 psig for the small and large standard equipped filter types, respectively. The total flow rate of gas into system must be less than the sum flow rate capacity of active exhaust filters. The values listed take into account the number and type of exhaust filters that are standard on each size of S.U.F. (one small filter installed in the 30 L, one large filter installed in the 300 L). These values are not absolute requirements. They are also not intended to be process gas flow settings. The process gas flow settings should be adjusted as discussed below with starting conditions not exceeding 25% of the listed maximum values to prevent unnecessary reduction of exhaust filter life span and foam generation.

If sparging seems to lose efficiency disproportionate to the cell culture density increase, more filters may be required or the oxygen to air ratio of the gas flow may need to be increased.

Table 3.2. S.U.F. range of operating parameters (based on the ZenPure filter option; using Meissner filters may lower operating parameters).

	30 L	300 L
Temperature (°C)	2–45°C ± 0.1	
Operating volume (L)	6–30	60–300
Agitation rate (rpm)	55–600	35–375
Recommended maximum gas flow rates (slpm)	60	600*
Exhaust load (slpm)	60	600

*For maximum best $k_L a$ with air, use 510 slpm (1.7 vvm). The impeller may flood above this air flow rate, which decreases $k_L a$. With pure oxygen use, the dissolved oxygen % control continues to deliver up to, or past, 2 vvm.

3.6.2. Manual operation of drilled hole spargers

Table 3.3 provides guidelines for operating a BPC equipped with standard drilled hole sparger(s) when the user must manually set flow rates. Recommendations assume three manual flow rate adjustments of the drilled hole sparger during the course of a batch run. **Note:** Recommendation is based on a drilled hole sparger operated by a controller. End users should always verify performance in their specific operating environment.



WARNING: Operating caution must be taken when manually setting drilled hole sparge gas flow rates if the drilled hole sparge is left inactive for any length of time. For 30 L systems, it is possible for liquid to flow between the drilled hole sparger and flow check valve if it is left idle. Never set an idle drilled hole sparger directly to values higher than 10% of their maximum recommended flow rate; pushing the water through the drilled hole sparge pores at higher flow rates may result in a damaging pressure spike. After the drilled hole sparger has been purged, it can be safely set to the target gas flow rate.

Table 3.3. Manual drilled hole sparger flow rate operation recommendation in standard BPC configuration.

	30 L	300 L
Stage 1: Seed to 1/2 log growth	0.1–0.5 vvm	0.1–0.5 vvm
Stage 2: 1/2 log growth to 4th quarter log growth	0.5–2 vvm	0.5–2 vvm*
Stage 3: Stationary phase	0.1–0.5 vvm	0.1–0.5 vvm

*For maximum best $k_L a$ with air, use 1.7 vvm. The impeller may flood above this air flow rate, which decreases $k_L a$. With pure oxygen use, the dissolved oxygen % control continues to deliver up to or past 2 vvm.

For more information on the growth of specific cell lines in the S.U.F. system, please contact technical support (see Chapter 6).

3.6.3. Checkpoints prior to media fill

Verify the following before proceeding to liquid fill.

- ✓ The BPC (30 L or 300 L, respectively) has been loaded into the outer support container following the instructions provided in section 3.2 or 3.3.
- ✓ All aseptic connector port heavy-duty clamps are closed and located as close as possible to the BPC. **Note:** Clamps are normally left open during BPC manufacturing and shipping.
- ✓ The exhaust filter is upright and secured using the holder.
- ✓ The clamp on the drain tube is closed and located as close as possible to the BPC.
- ✓ The RTD is completely seated in the thermowell, and secured with the ground clip attached to the RTD shaft.
- ✓ The air-filled BPC is properly oriented in the outer support container, and the BPC bottom and top hanging tabs are secured.
- ✓ The inlet gas filter(s) are positioned above the projected liquid fill level.
- ✓ The dip tubes are held in position so that addition solution drips into the vessel volume, and doesn't pool in the port. The cable management system can be used to maintain the proper position.

3.6.4. Media fill

1. Fill the BPC with a small amount of air to help place it properly in the outer support container. Align the ports and lower tabs of the BPC in the S.U.F. tank.
2. Select the desired line set from the BPC for fluid introduction.
3. Make an aseptic connection (either tubing welder, quick connect, or tri-clamp), and begin the liquid fill.
4. After approximately 10% of the projected volume has been added, check the position of the BPC in the outer support container, particularly the sparger and the drain line. Adjust the position if necessary for a proper fit.
5. Pull the top corners of the 300 L BPC upward to reduce wrinkles in the BPC during filling. **Note:** The BPC must be pulled at the top corners. If the BPC is not pulled from the top to remove wrinkles, film tensioning below the bearing port will result.

6. Fill to the desired liquid volume—20–100% of the rated volume is recommended.
7. If employing 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.

3.6.5. Agitation for units with E-Boxes

1. After the media has reached half of the S.U.F.s total volume, the agitation control can be turned on via the motor controller power switch on the E-Box (Figure 3.104).

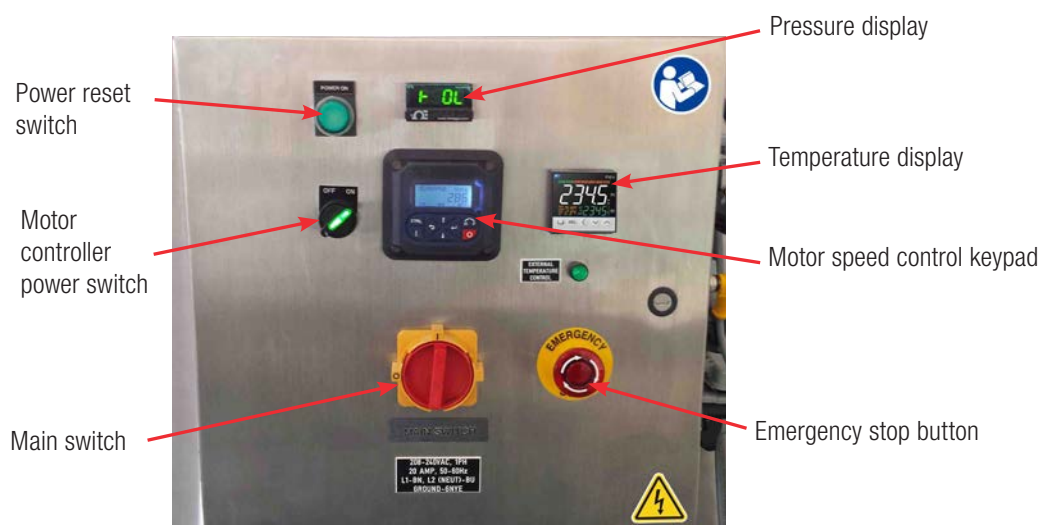


Figure 3.104. Front view of typical S.U.F. E-Box.

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 is done in Hz, and the display reverts back to displaying rpm after 2–3 seconds of inactivity. Adjust the desired agitation rate within the recommended range per Table 3.4.



WARNING: Agitation must not exceed the maximum rpm listed in Table 3.4, otherwise damage to the hardware or BPC may result.

Table 3.4. Recommended operation for selected liquid volumes (maximum rpm).

Liquid volume	Maximum rpm in 30 L unit	Maximum rpm in 300 L unit
6 L	275 rpm	--
15 L	350 rpm	--
30 L	598 rpm	--
60 L	--	120 rpm
150 L	--	240 rpm
300 L	--	375 rpm

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

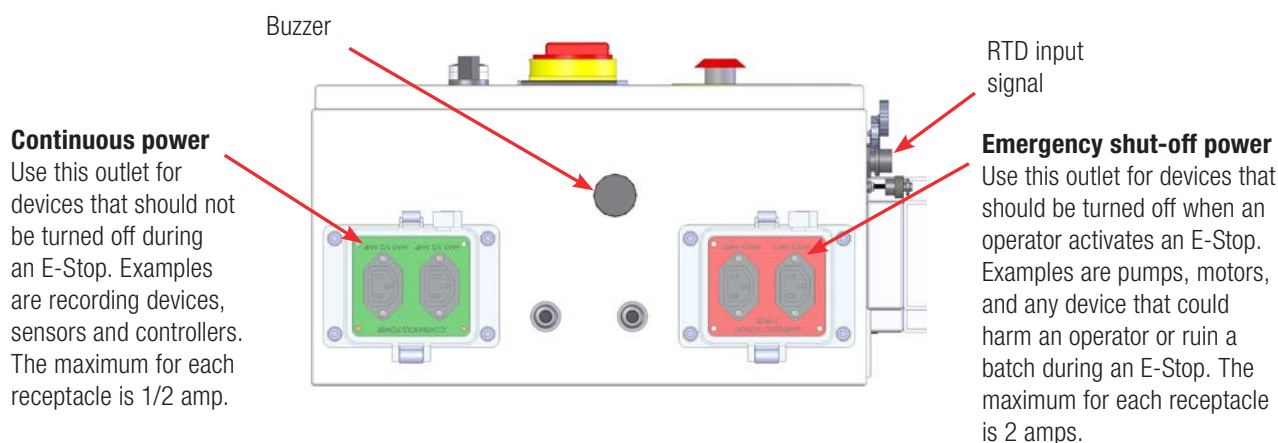


Figure 3.105. Bottom view of electrical control box.

3.6.6. Temperature control

1. Connection to an external TCU is made via the large tri-clamp couplings located on the vessel jacket. Ensure that the inlet/outlet ports are connected properly. Improper installation may result in poor heating/cooling performance.
2. Purge the jacket of air any time the vessel jacket lines are reconnected.

3. Temperature setpoints should be between 5°C and 55°C. These setpoints are controlled by the TCU. Refer to the TCU manufacturer's guidelines for setup and operating instructions.

3.6.7. pH probe calibration

In general, the pH probe calibration (post-autoclave) can be verified by pulling a sample and analyzing the pH on another calibrated pH meter.

3.6.8. DO probe calibration

After polarizing for six to eight hours, the DO probe can be calibrated in the S.U.F. using standard protocols. In general, turn on full air sparging (do not exceed 60 slpm in the 30 L S.U.F., or 600 slpm in the 300 L S.U.F.) until the DO reading stabilizes; this is the 100% DO setpoint for the controller. A zero percent dissolved oxygen setpoint can be achieved by sparging with nitrogen or by unplugging the DO probe momentarily.

3.6.9. Checkpoints prior to inoculation

Verify the following before inoculation.

- ✓ The temperature and agitation are at the desired setpoints.
- ✓ The pH probe is calibrated, autoclaved, and connected with an aseptic connector port if the single-use probe is not used. Take a sample of the media and measure the pH offline. Offset the controller setpoints according to the difference of the offline to online reading, or perform single point calibration if desired.
- ✓ If a single-use probe is not used, the DO probe is autoclaved, connected via a connector port, polarized (six to eight hours), and calibrated. If using a single-use probe, the probe only needs to be polarized and calibrated to 100% saturation.
- ✓ The temperature RTD is completely seated in the thermowell and secured.
- ✓ A method for making aseptic tubing connections is available.

3.6.10. Cell inoculation

Once the S.U.F. is operating at the targeted steady equilibrated state and has achieved temperature, the S.U.F. 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.F. Typically this is done with the tubing connection process (aseptic luer lock connection or tube welding) and peristaltic pump. Pump the desired volume of seed cells into the S.U.F.

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. Custom line sets can be supplied with dip tubes, which shorten the distance between the point of inoculum introduction and the bulk fluid level.

3.6.11. 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 not operating under pressure exceeding the recommended maximum. The pressure should not exceed 0.034 bar (0.5 psi) within the BPC. The tubing after the inlet filter should be easy to compress with two fingers. **Caution:** Do not pinch off the air inlet completely.
- ✓ The cap is tight on the drive shaft.
- ✓ The temperature RTD is completely seated and secured.
- ✓ No condensate accumulates in exhaust filter housing. If condensate has accumulated, this indicates that the use of a filter heater or a condenser system is required.

Note: Noise may be emitted from the mixer 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.

3.6.12. 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 by using the peristaltic pump.
4. When approximately three to five liters remain in the BPC, lift the BPC at the top hanging tabs located opposite of the bottom drain (this will pool media towards the drain).
5. Hold the bottom drain line near the floor while lifting the exhaust filter side of the BPC. This will facilitate draining the final liter of harvest media.

3.6.13. S.U.F. shutdown and post-use BPC disposal

1. Once a run is complete and the contents have been harvested (drained), turn off the motor controller power switch on the E-Box. Check to make sure the motor is off and the drive shaft is not rotating.
2. Remove the drive shaft by reversing the procedure described in sections 3.2 and 3.3 of this guide.
3. If the S.U.F. hardware has come in contact with caustic materials during the course of a run, rinse affected areas with a light water rinse, followed by normal routine cleaning described in section 3.6.14 of this guide.
4. Return loose items such as the drive shaft, tools and RTD probes to their storage locations to prevent accidental damage. Filters can be removed and integrity tested as needed, following your site's standard procedures.
5. Close all hose clamps on BPC line sets.
6. Disconnect and plug all additional lines.
7. Coil line sets and secure with quick ties.
8. Remove air from the BPC by pressing the air out.
9. Remove the BPC from the S.U.F. hardware.
10. Choose a sterilization method, or dispose of the BPC as dictated by your site's standard hazardous waste procedures. Sterilization methods could include heat/pressure treatment or chemical treatment.
11. When using the heat/pressure treatment for sterilization, fold the BPC into an autoclave tray, making sure that the BPC and tubing do not touch the walls of the autoclave. Then autoclave the BPC using your site's recommended settings.
12. When using a chemical treatment for sterilization, add an amount of decontamination chemical sufficient to cover all surfaces. If the bag is deflated, less decontamination chemical will be required. Let the BPC stand for the allotted time with the active chemical. Then discard treatment chemicals using your site's standard procedures.
13. Dispose of the BPC following your site's treated waste procedures.

3.6.14. Preparation for the next run

Between runs, the S.U.F. hardware (outer support container, probe shelf, drive shaft, mixer drive, etc.) can be wiped down with a sanitary wipe. Store the drive shaft in the storage holder located near the top of the outer support container.

The S.U.F. hardware can be cleaned using standard laboratory cleaning procedures. Take care to ensure that electrical connections have been disconnected and that all electrical enclosures are closed tightly. Excess water should not be introduced under the heat shield or over the E-Box. A wipe-down with normal disinfectant solutions is sufficient. Consult information provided with the cleaning product to ensure compatibility. Avoid using excessive amounts of liquid. The unit must be allowed to fully dry prior to being brought back into operation.

The S.U.F Validation Guide includes more specific information about the results of tests performed with various cleaning agents.

3.7. BPC sampling

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

3.7.1. Aseptic sampling

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

1. Remove the dust cover from the SmartSite (Figure 3.106).



Figure 3.106. Removing the dust cover.

2. Clean the SmartSite with a sanitary wipe.
3. Connect the sanitary luer lock type syringe (Figure 3.107).



Figure 3.107. Connecting the syringe.

4. Apply a small amount of vacuum pressure by pulling out the syringe plunger slightly.
5. Open the pinch clamp and pull a sample (approximately 30–60 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. Apply a small amount of vacuum pressure using the syringe.
10. Open the pinch clamp and pull the desired sample volume (approximately 10–20 mL), using 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.

3.7.2. Sampling with 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 clamps on the manifold lines.
3. Use a sterile tubing welder to connect the manifold to the sample line (Figure 3.108).



Figure 3.108. Tubing welder.

4. Inspect the welds and open the 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 this container (recommended 30–60 mL).
7. Close the clamp that is closest to the purge container.
8. Open the clamp to the sample container (50 mL sterile sample container) (Figure 3.109).



Figure 3.109. 50 mL manifold.

9. Allow the container to fill with liquid by the force of gravity (recommended 10–20 mL).
10. Close the clamps at the sample manifold inlet.
11. Close the clamp that is closest to the sample container.
12. Remove the filled manifold from the S.U.F. by welding the new manifold onto the sample line (this will be used for taking the next sample).

3.8. Verification procedures

3.8.1. Mixer speed verification

To verify the mixer speed, use a calibrated tachometer. Expect accuracy of $\pm 0.75\%$ of full scale. Speed scaling can be modified if the calibration needs to be adjusted. Please refer to Appendix B for details.

3.8.2. Temperature controller verification

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

3.8.3. Pressure monitor verification (when present)

To verify the calibration of the pressure monitor, use a calibrated pressure standard. Pressures can be verified by capping the exhaust filter and supplying gas through the gas inlet. Expect accuracy of ± 0.1 psi. The monitor can be calibrated manually by referencing the monitor user's guide supplied in the ETP.

3.8.4. Load cell verification (when present)

It is recommended that the load cell manufacturer or a qualified technician verify the load cells on site. Refer to Appendix C for load cell calibration instructions. Expect an accuracy of ± 0.5 kg. Basic load cell default parameters are listed in the electrical schematic included with the ETP.

4

Specifications and parts information

Chapter contents

- 4.1 Hardware features and dimensions
- 4.2 BPC specifications
- 4.3 Made-to-order hardware

4.1. Hardware features and dimensions

4.1.1. 30 L S.U.F. design features

Figures 4.1 and 4.2 below illustrate the features of the 30 L Single-Use Fermentor (S.U.F.).

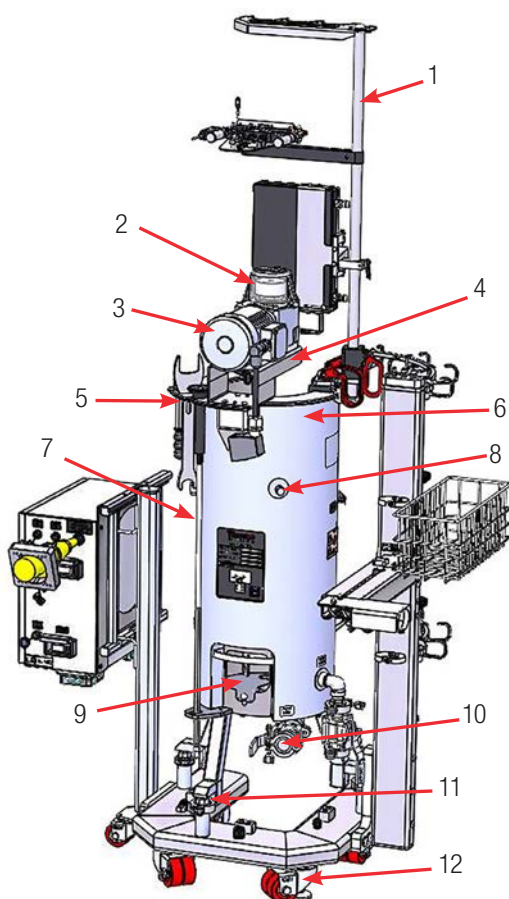


Figure 4.1. Back view of 30 L S.U.F.

1. Exhaust vent filter holder
2. Motor assembly with shield
3. Mixer motor
4. Sliding motor assembly
5. Standard tool set: 10 mm (3/8 in.) x 16.9 Nm (150 in.-lb.) square torque wrench, load cell, and motor cap lockout wrench
6. Stainless steel (304) outer support container
7. Drive shaft (stored)
8. Bleed cap
9. Bottom cutouts/pins for BPC attachment and alignment
10. Tri-clamp water inlet/outlet ports
11. Load cells (3—optional)

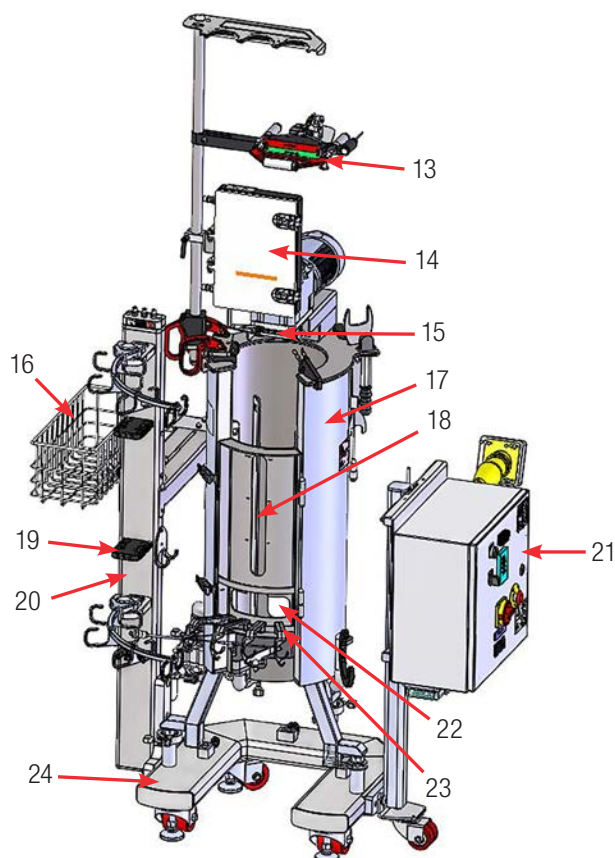


Figure 4.2. Front view of 30 L S.U.F.

12. Leveling casters
13. Exhaust filter pinch clamp (optional)
14. Condenser (optional)
15. Bearing port receiver with clamp
16. Bottle management basket (optional)
17. Water jacket (10 mm [3/8 in.] dimpled)
18. BPC loading door and liquid sight window
19. Feed bag management hook (optional)
20. Cable management system (optional)
21. E-Box (optional)
22. Probe access window
23. Probe hanger bracket
24. Cart assembly

4.1.2. 300 L S.U.F. design features

Figures 4.3 and 4.4 below illustrate the features of the 300 L S.U.F.

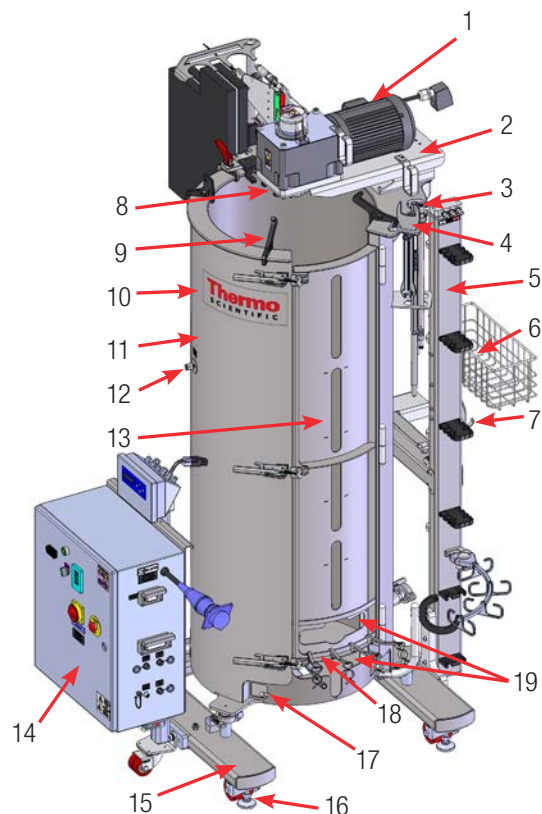


Figure 4.3. Front/top view of 300 L S.U.F.

1. Mixer motor
2. Sliding motor assembly
3. Drive shaft (stored)
4. Standard tool set: 10 mm (3/8 in.) x 16.9 Nm (150 in.-lb.) square torque wrench, load cell, and motor cap lockout wrench
5. Cable management system (optional)
6. Bottle management basket (optional)
7. Feed bag management hook (optional)
8. Bearing port receiver with clamp
9. Top hanging tab plates (optional)
10. Stainless steel (304) outer support container
11. Water jacket (10 mm [3/8 in.] dimpled)
12. Bleed cap

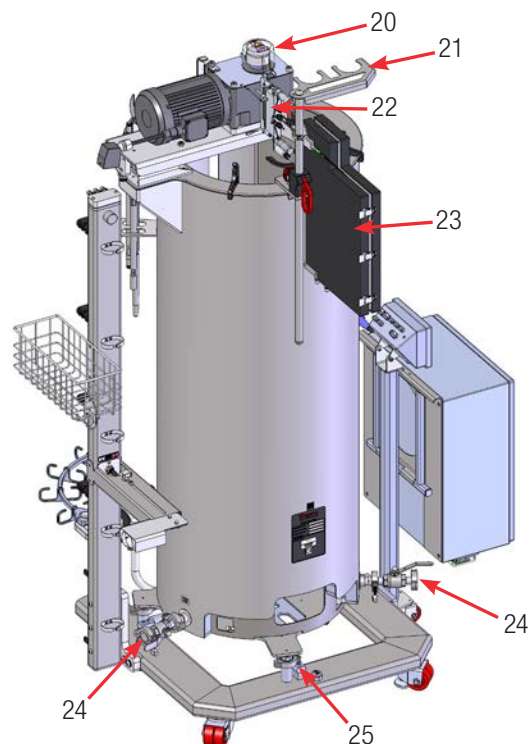


Figure 4.4. Back view of 300 L S.U.F.

13. BPC loading door and liquid sight windows
14. E-Box (optional)
15. Cart assembly
16. Leveling casters
17. Bottom cutouts/pins for BPC attachment and alignment
18. Probe hanger bracket
19. Probe access windows
20. Motor assembly with shield
21. Exhaust vent filter holder
22. Exhaust filter pinch clamp (optional)
23. Condenser (optional)
24. Tri-clamp water inlet/outlet ports
25. Load cells (3—optional)

4.1.3. 30 L S.U.F. dimensions

Figure 4.5 below illustrates the dimensions of the 30 L S.U.F. Measurements are listed in (centimeters [inches]).

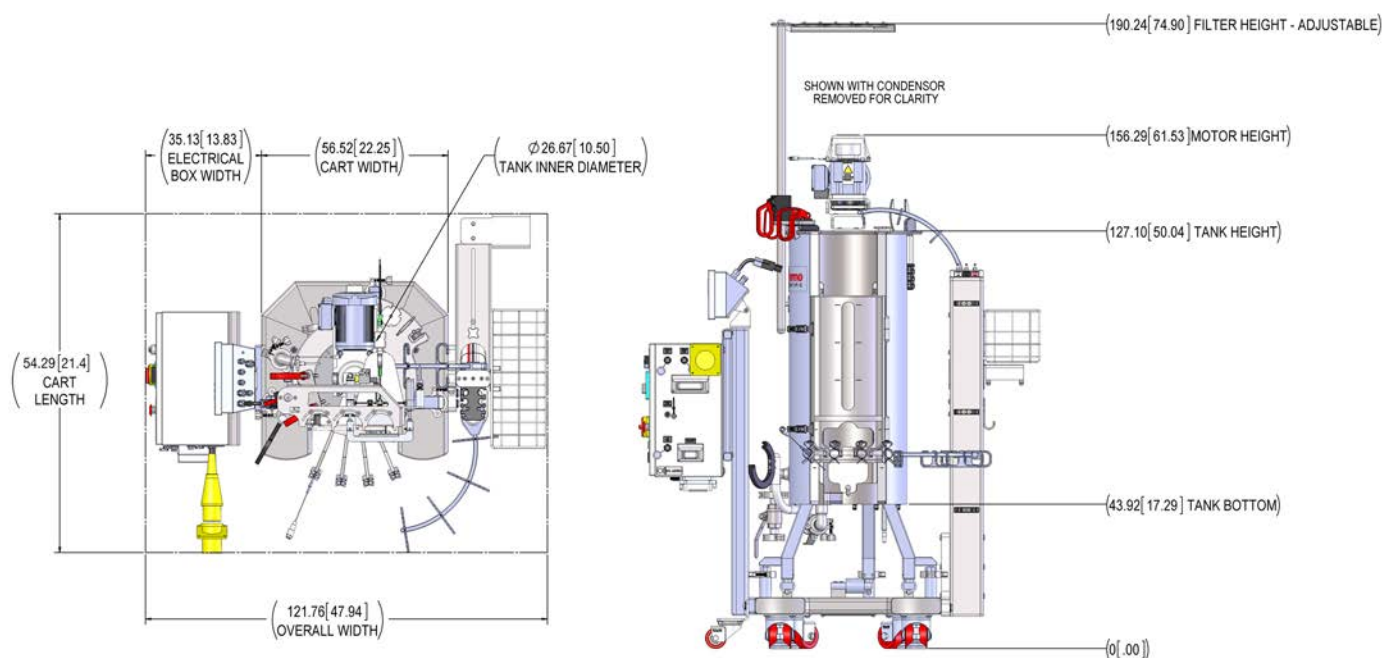


Figure 4.5. 30 L S.U.F. dimensions.

All units come standard with four probe hangers, a drive shaft, and a resistance temperature device (RTD). Other features are available, such as condensers, load cells, and cable management systems. For more information, see the Configurable hardware options topic in section 4.3 of this guide.

4.1.4. 300 L S.U.F. dimensions

Figure 4.6 below illustrates the dimensions of the 300 L S.U.F. Measurements are listed in (centimeters [inches]).

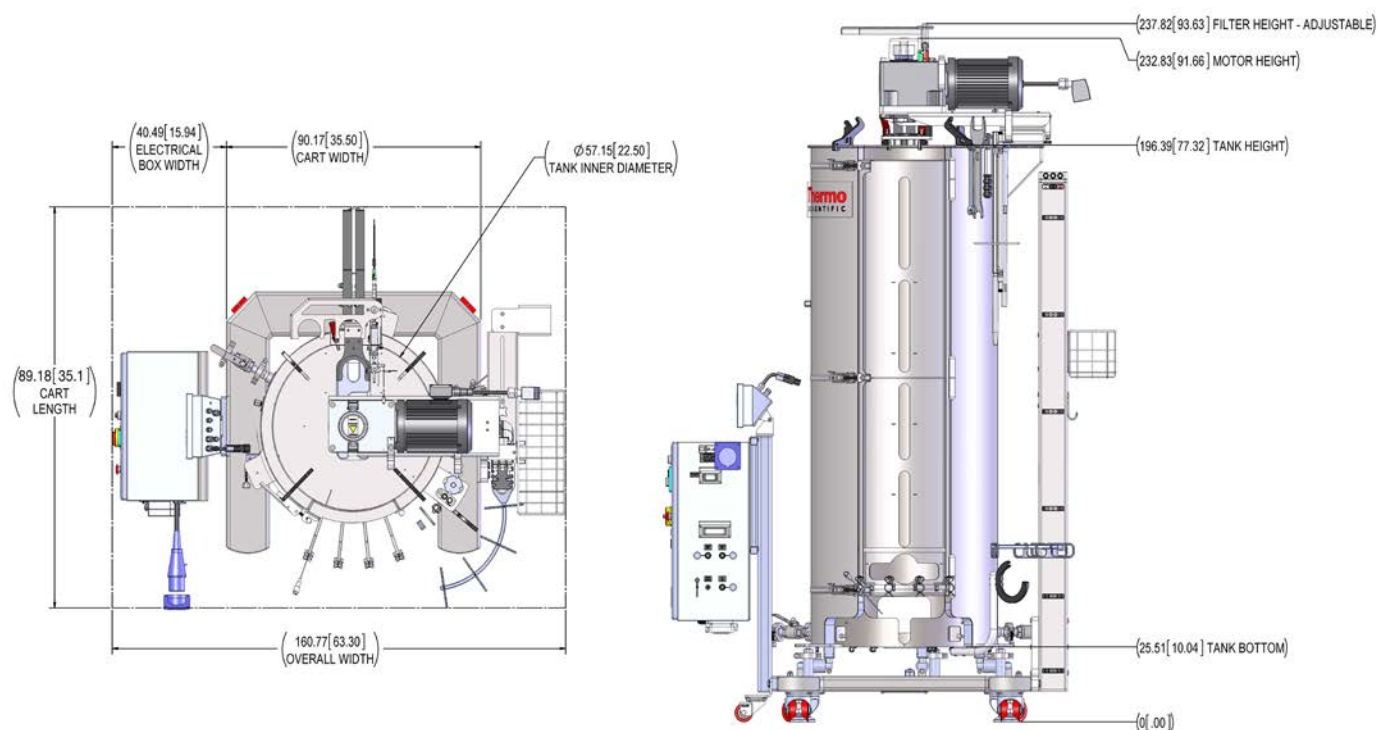


Figure 4.6. 300 L S.U.F. dimensions.

All units come standard with four probe hangers, a drive shaft, and an RTD. Other features are available, such as condensers, load cells, and cable management systems. For more information, see the Configurable hardware options topic in section 4.3 of this guide.

4.2. 30 L and 300 L S.U.F. hardware specifications

Tables 4.1 and 4.2 provide specifications for the 30 L and 300 L S.U.F. systems.

Table 4.1. 30 L and 300 L S.U.F. specifications.

		30 L	300 L
Reactor geometry	Rated liquid working volume	30 L	300 L
	Minimum liquid working volume	6 L	60 L
	Total reactor volume (liquid & gas)	43 L	435 L
	Vessel diameter	26.6 cm (10.50 in.)	57.2 cm (22.5 in.)
	BPC chamber diameter	29.7 cm (11.7 in.)	68.8 cm (27.06 in.)
	BPC chamber shoulder height	85.1 cm (33.5 in.)	169.8 cm (66.85 in.)
	Liquid height at rated working volume	57.1 cm (22.5 in.)	123.2 cm (48.5 in.)
	Fluid geometry at working volume (height/diameter) ratio	~2:1	
	Hold-up volume	> 0.5 liters	> 1.0 liters
	Overall reactor geometry (height/diameter ratio)	3:1	
Impeller	Tank baffles	4	
	Impeller (quantity x blade count)	3 x 6	
	Impeller scaling (impeller diameter/tank diameter)	1/3	
	Impeller type	Rushton	
	Impeller diameter	8.89 cm (3.5 in.)	18.79 cm (7.4 in.)
Agitation	Impeller calculated power number (N), averaged between 20 and 100% of rpm range	5.0	4.1
	Maximum rotational speed	596 rpm	375 rpm
	Power/volume ratio at maximum rotational speed	2270.5 W/1000 L (11.5 hp/1000 gal)	2164.1 W/1000 L (11 hp/1000 gal)
	Nominal agitation for best kLa value	596 rpm	375 rpm
	Nominal tip speed	279 cm/s	369 cm/s
	Mixing flow direction	Radial flow	
	Agitation shaft orientation	Vertical	
	Overall drive shaft length	96.26 cm (37.9 in.)	173.1 cm (68.14 in.)
	Operational drive shaft length	77.36 cm (30.46 in.)	152.1 cm (59.90 in.)
	Drive shaft diameter	1.27 cm (0.5 in.)	1.9 cm (0.75 in.)
	Drive shaft poly-sheath outside diameter	2.54 cm (1 in.)	3.5 cm (1.375 in.)
	Impeller clearance from tank bottom (measured at midplane of impeller)	8.9 cm (3.5 in.)	18.8 cm (7.4 in.)

Table 4.2. 30 L and 300 L S.U.F. specifications (continued).

		30 L	300 L
Motor	Agitation motor drive (type, voltage, phase) AC motor only	Induction, 208 VAC, 3 phase	
	Motor power rating (AC motor)	372.85 W (0.5 hp)	1,491.4 W (2 hp)
	Motor torque rating	4.6 Nm (40.7 in.-lb.)	34 Nm (301 in.-lb.)
	Gear reduction	5:1	
	Programmable VFD, remote panel interface, power faults auto restart	Standard	
	Motor communication methods (for external controller)	0–10 V, 4–20 mA, ModBus	
Fluid jacket / temperature control	Jacket area: half/full volume	0.14 / 0.31 m ² (1.60 / 3.35 ft ²)	0.72 / 1.46 m ² (7.77 / 15.8 ft ²)
	Jacket volume	2.53 L	10.85 L
	Jacket flow rate	4.4 GPM at 1.82 bar (26.5 psi)	16.9 GPM at 2.27 bar (33 psi)
	Process connection	1 in. Sanitary tri-clamp	
	Nominal heating/cooling load (W)	2300 heating; 2500 cooling	6100 heating; 10000 cooling
	Approx. liquid heat-up time (2–37°C)—hr / half volume	1 hr	1.3 hr
	Approx. liquid heat-up time (5–37°C)—hr / full volume	1.16 hr	1.8 hr
	TCU temperature setpoints	5°C to 55°C	
	RTD or thermocouple, 3.18 mm (1/8 in.) OD	RTD: Pt-100 SV50999.04	RTD: Pt-100 SV50999.05
Outer support container (tank)	Overall width	91.6 cm (36.08 in.) with E-Box	130.7 cm (51.44 in.) with E-Box
	Overall length	59.436 cm (23.4 in.) with E-Box	89.2 cm (35.11 in.) with E-Box
	Height to top of vent filter bracket	218.44 cm (86 in.) with condenser	280.97 cm (110.62 in.) with condenser
	Height to top of motor	157.0 cm (61.83 in.)	232.9 cm (91.7 in.)
	Dry skid weight (mass)	238 kg (524 lb.)	555 kg (1223 lb.)
	Wet skid weight—rated working volume (mass)	241 kg (531 lb.)	570 kg (1257 lb.)
Miscellaneous	Electrical power supply requirement (voltage, phase, amp)	120/240 VAC, single, 20/10 A	240 VAC, single, 20 A
	Validated system reliability (minimum)	0.9 at 90%	
	pH & DO probe—autoclavable type (Applisens, Broadley James, Mettler Toledo)	12 mm diameter x 215–235 mm insertion length x 13.5 PG thread	
	RTD or thermocouple, 3.18 mm (1/8 in.) OD	RTD: Pt-100 (standard)	
	Minimum ceiling height required	238.76 cm (94 in.)	295.91 cm (116.5 in.)
	Noise level	< 70 dB at 1.5 m	
Recommended operating parameters	Operating temperature range	Ambient to 40 +/- 0.1°C (104 +/- 0.2°F)	
	Motor speed	55–598 rpm +/- 5 rpm	35–375 rpm +/- 5 rpm
	Volume range	6–30 L	60–300 L
	Maximum rated bag pressure	0.03 bar (0.5 psi)	
	Continuous operating time (at nominal volume only)	14 days	

4.3. Configurable hardware options

Made-to-order part numbers will be generated from customer-selected configurable items shown below.

Table 4.3. Configurable hardware options.

Category	Options/capability	Notes
E-Box	120 VAC or 240 VAC with basic controls for motor rpm, pressure, and basic I/O	Supports 50–60 Hz power
Cable management system	Includes cable management tree, bag management hook, and bottle management holder bracket, and drain line holder	N/A
RTD	A single or dual element RTD is available	PT 100 signal
Load cells	Equipment is available with or without load cells	Analog, Profibus, Devicenet, Modbus & AB Rio communication
Condenser	Equipment is available with or without a condenser	N/A
Vent filter bracket	Equipment is available without a bracket or with a 2-position bracket for 30 L units; a 2 or 4 position bracket is available for 300 L units	N/A
Exhaust filter pinch clamp	Equipment is available with or without a pinch clamp	Operates on 24 VDC
Top hanging tabs	300 L unit is available with or without top hanging tabs	N/A

4.4. BPC features and specifications

4.4.1. Standard 30 L S.U.F. BPC

Figures 4.7, 4.8, and 4.9 below illustrate the standard 30 L S.U.F. BioProcess Container (BPC), which includes a condenser, foam sensor, single-use DO and pH sensors, and two vent filters. For more information, see Table 4.4.

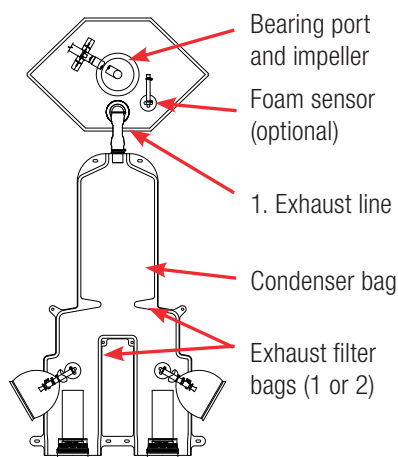


Figure 4.7. Top view of 30 L BPC.

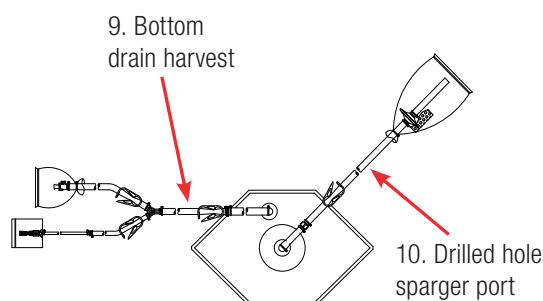


Figure 4.8. Bottom view of 30 L BPC.

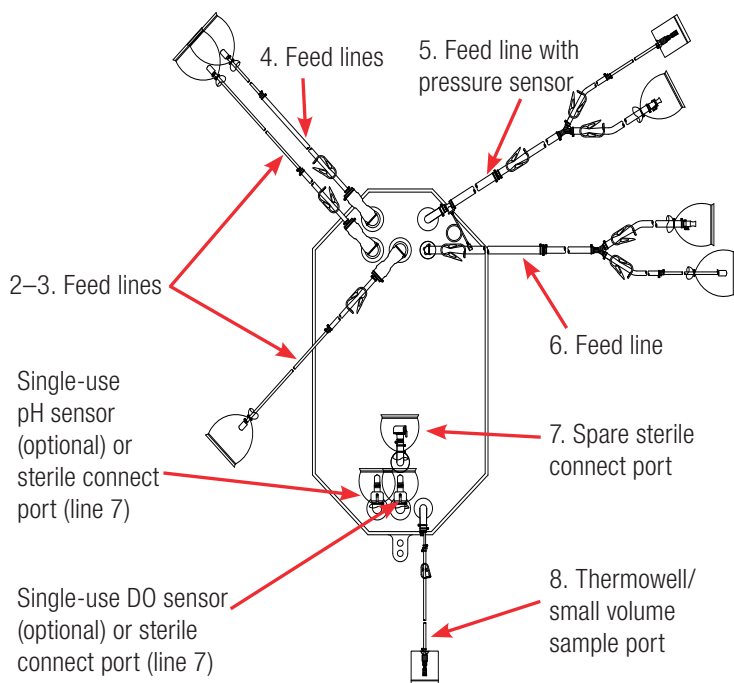


Figure 4.9. Front view of 30 L BPC.

Table 4.4. 30 L BPC specifications.

Line	Description	Tubing set (ID x OD x length)	End treatment
1.	Exhaust line	22.2 mm (7/8 in.) ID x 28.6 mm (1 1/8 in.) OD P.C. silicone x 10 cm (4 in.)	1 or 2 12.7 cm (5 in.) Meissner or 7.62 cm (3 in.) or 12.7 cm (5 in.) ZenPure exhaust filters, optional condenser bag
2–3.	Feed lines	6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) OD C-Flex tubing x 15 cm (6 in.) reduced to 3.2 mm (1/8 in.) ID x 6.4 mm (1/4 in.) OD C-Flex tubing x 152 cm (60 in.)	Female luer
4.	Feed line	6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) OD C-Flex tubing x 152 cm (60 in.) reduced to 3.2 mm (1/8 in.) ID x 6.4 mm (1/4 in.) OD C-Flex tubing x 30 cm (12 in.)	Female luer
5.	Feed line with pressure sensor	12.7 mm (1/2 in.) ID x 19.1 mm (3/4 in.) OD C-Flex tubing x 8 cm (3 in.) reduced to 9.5 mm (3/8 in.) ID x 15.9 mm (5/8 in.) OD C-Flex tubing x 152 cm (60 in.) split to 6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) OD C-Flex tubing x 30 cm (12 in.) reduced 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.)	SterilEnz pouch with injection site assembly and 9.5 mm (3/8 in.) MPC body
6.	Feed line	12.7 mm (1/2 in.) ID x 19.1 mm (3/4 in.) OD C-Flex tubing x 152 cm (60 in.) reduced to 9.5 mm (3/8 in.) ID x 15.9 mm (5/8 in.) OD C-Flex tubing x 30 cm (12 in.) split to 6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) OD C-Flex tubing x 30 cm (12 in.) reduced 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.)	Female luer 9.5 mm (3/8 in.) MPC insert
7.	Spare sterile connect port	12.7 mm (1/2 in.) tube port	Pall Kleenpak aseptic connectors—KPCHT series (female)
8.	Thermowell/ small volume sample port	Thermowell adapter for 6.4 mm (1/4 in.) diameter. 3.2 mm (1/8 in.) ID x 6.4 mm (1/4 in.) OD C-Flex tubing x 46 cm (18 in.)	SterilEnz pouch with injection site assembly
9.	Bottom drain harvest	12.7 mm (1/2 in.) ID x 19.1 mm (3/4 in.) OD C-Flex tubing x 8 cm (3 in.) reduced to 9.5 mm (3/8 in.) ID x 15.9 mm (5/8 in.) OD C-Flex tubing x 152 cm (60 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.) reduced 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 15.9 mm (3/8 in.) ID x 15.9 mm (5/8 in.) OD C-Flex tubing x 30 cm (12 in.)	SterilEnz pouch with injection site assembly 9.5 mm (3/8 in.) MPC body
10.	Drilled hole sparger port with check valve	9.5 mm (3/8 in.) ID x 15.9 mm (5/8 in.) OD C-Flex tubing x 122 cm (48 in.)	65 mm ZenPure filter, 0.2 µm 9.5 mm (3/8 in.)—12.7 mm (1/2 in.) HB feeds to 9.5 mm (3/8 in.) ID x 15.9 mm (5/8 in.) OD x 30 cm (12 in.) C-Flex tubing

4.4.2. Standard 300 L S.U.F. BPC

Figures 4.10 and 4.11 illustrate the standard 300 L S.U.F. BPC, which includes a condenser, foam sensor, single-use DO and pH sensors, and two vent filters. For more information, see Table 4.5.

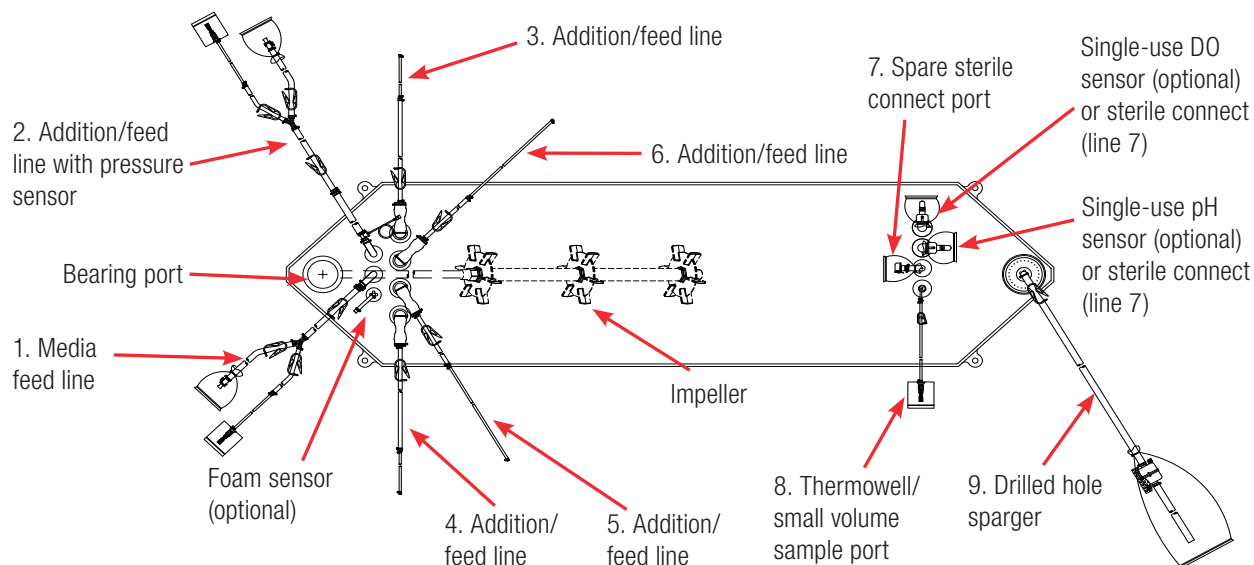


Figure 4.10. Front view of 300 L BPC.

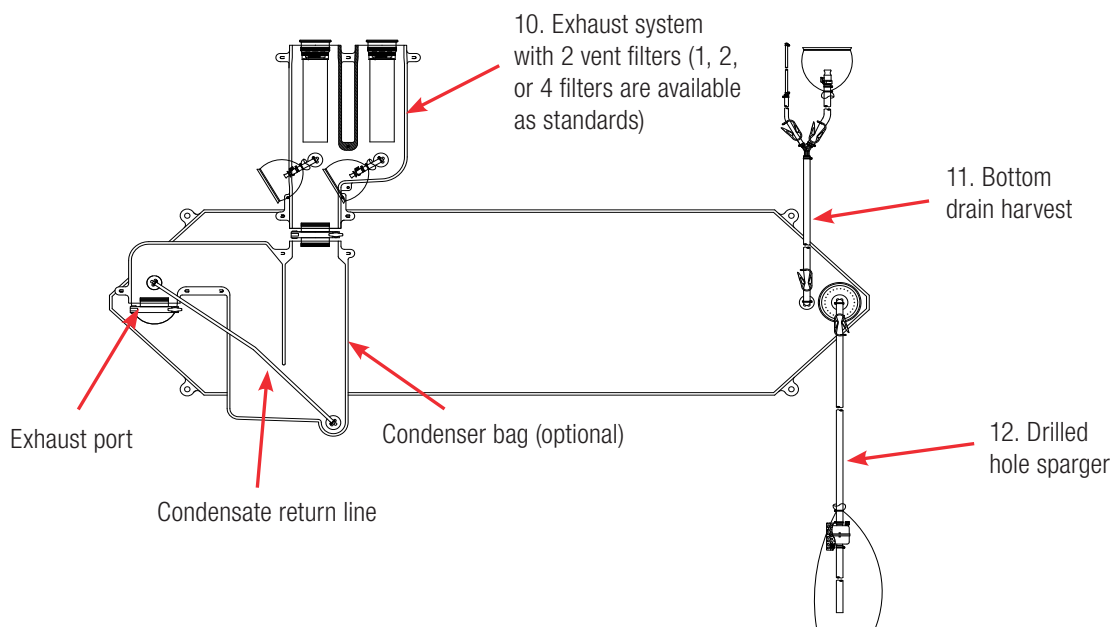


Figure 4.11. Back view of 300 L BPC.

Table 4.5. 300 L BPC specifications.

Line	Description	Tubing set (ID x OD x length)	End treatment
1.	Media feed line	9.5 mm (3/8 in.) ID x 15.9 mm (5/8 in.) OD C-Flex tubing x 213 cm (84 in.) splits to 6.4 mm (1/4 in.) ID x 12.7 mm (1/2 in.) OD C-Flex tubing x 30 cm (12 in.) reduced 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.)	SterilEnz pouch with injection site assembly 9.5 mm (3/8 in.) MPC body
2.	Addition/ feed line with pressure sensor	12.7 mm (1/2 in.) ID x 19.1 mm (3/4 in.) OD C-Flex tubing x 8 cm (3 in.) reduced to 9.5 mm (3/8 in.) ID x 15.9 mm (5/8 in.) OD C-Flex tubing x 213 cm (84 in.) splits to 6.4 mm (1/4 in.) ID x 12.7 mm (1/2 in.) OD C-Flex tubing x 30 cm (12 in.) reduced 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.)	SterilEnz pouch with injection site assembly 9.5 mm (3/8 in.) MPC body
3–4.	Feed lines	6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) OD C-Flex tubing x 213 cm (84 in.) reduced to 3.2 mm (1/8 in.) ID x 6.4 mm (1/4 in.) OD C-Flex tubing x 30 cm (12 in.)	Plugged
5–6.	Addition/feed lines	6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) OD C-Flex tubing x 15 cm (6 in.) reduced to 3.2 mm (1/8 in.) ID x 6.4 mm (1/4 in.) OD C-Flex tubing x 213 cm (84 in.)	Plugged
7.	Spare sterile connect port	12.7 mm (1/2 in.) tube port	Pall Kleenpak aseptic connectors – KPCHT series (Female)
8.	Thermowell/ small volume sample port	Thermowell adapter for 6.4 mm (1/4 in.) diameter. 3.2 mm (1/8 in.) ID x 6.4 mm (1/4 in.) OD C-Flex tubing x 46 cm (18 in.)	SterilEnz pouch with injection site assembly
9.	Drilled hole sparger port	12.7 mm (1/2 in.) ID x 19.1 mm (3/4 in.) OD C-Flex tubing x 305 cm (120 in.)	Meissner Steridyne 0.2 micron hydrophobic filter or ZenPure filter, 0.2 micron 15.9 mm (5/8 in.) HB— 15.9 mm (5/8 in.) HB with 12.7 mm (1/2 in.) ID x 19.1 mm (3/4 in.) OD C-Flex x 41 cm (16 in.)
10.	Exhaust system	1,2, or 4 vent filters, optional condenser bag with condensate return line (for use with peristaltic pump)	1, 2, or 4 Meissner or ZenPure exhaust filters, optional condenser bag
11.	Bottom drain harvest	12.7 mm (1/2 in.) ID x 19.1 mm (3/4 in.) OD C-Flex tubing x 183 cm (72 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.) reduced 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 12.7 mm (1/2 in.) ID x 19.1 mm (3/4 in.) OD C-Flex tubing x 30 cm (12 in.)	Plugged 12.7 mm (1/2 in.) MPX insert
12.	Drilled hole sparger port	12.7 mm (1/2 in.) ID x 19.1 mm (3/4 in.) OD C-Flex tubing x 305 cm (120 in.)	Meissner Steridyne 0.2 micron hydrophobic filter or ZenPure filter, 0.2 micron 15.9 mm (5/8 in.) HB—15.9 mm (5/8 in.) HB with 12.7 mm (1/2 in.) ID x 19.1 mm (3/4 in.) OD C-Flex tubing x 41 cm (16 in.)

4.5. BPC options and packaging information

See Tables 4.6–4.8 for configurable and custom options for BPCs, as well as standard BPC packaging information.

Table 4.6. Configurable BPC options.

Category	Options/capability
Condenser	BPCs are available with or without a condenser
Film	CX 5-14 or Aegis 5-14
Foam sensor	Optional head space foam sensor
Single-use sensors	Pressure sensor: PendoTECH (standard) or Finesse solutions DO and pH sensors: Mettler Toledo
Sparge line filters	ZenPure or Meissner
Vent filters	ZenPure or Meissner SterilEnz 0.2 micron exhaust vent filters; 30 L S.U.F. may be ordered with 1 or 2 vent filters; 300 L S.U.F. may have 1, 2, or 4 vent filters

Table 4.7. Custom BPC options.

Category	Options/capability	Notes
Tubing type	C Flex, platinum cured silicone, PVC, PharMed, PharmaPure	More information is available in the Tubing Selection Guide
Tubing size	Ranges from 1/8 in. ID to 1 in. ID in various lengths	More information is available in the Tubing Selection Guide
Connectors	Luers, CPC Quick Connects, SIP connectors, tri-clamp, Kleenpak, Lynx, SmartSite, Clave, Lynx steam thru, CPC steam thru, Gore steam valve, Gore Mini TC, BioQuate, SterilEnz, end plug, etc.	More information is available in the Connection System Selection Guide
Probe ports	Additional ports: second row of 3 ports for 30 L S.U.F.; second row of four for ports for 300 L S.U.F.	The reusable probe port connection use a Kleenpak connector
Addition of ports/lines (other than second row of probe ports)	Limited engineer-to-order customization only	Dependent on location in bag and compatibility with hardware
Port sizes	Limited engineer-to-order customization only	Dependent on location in bag and fit with hardware (e.g., 1 in. ID port on harvest line)
Rearrangement of lines on existing ports	Limited customization possible, e.g., moving sample/thermowell port to a probe tube port	Dependent on location in bag and fit with hardware
Dip tube lines	Limited customization possible	Length cannot interfere with impeller and shaft
Filters on media and supplement inlets	Limited engineer-to-order customization only. Choice of filters used to sterilize incoming media or supplements are available.	N/A

Note: Not all options are available for all ports. No customization of port type and location, chamber dimensions or mixing assembly is possible. For additional information, please see the Selection Guides in the BPC Catalog.

Table 4.8. BPC packaging for all sizes (as dry BPC systems).

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 to 40 kGy) inside outer packaging
Shipping container	Durable cardboard carton
Documentation	Certificate of Analysis provided with each lot for each delivery

4.6. Accessories and options specifications

4.6.1. Load cells

Load cells operate as a mechanical suspension and weighing system on the Thermo Scientific HyPerforma S.U.F.

Load cells may be purchased either at the time of equipment sale or as retro-fit kits for existing S.U.F. units. Load cell systems include three load cells, a summing block, a display, and wiring (Figures 4.12–4.14).

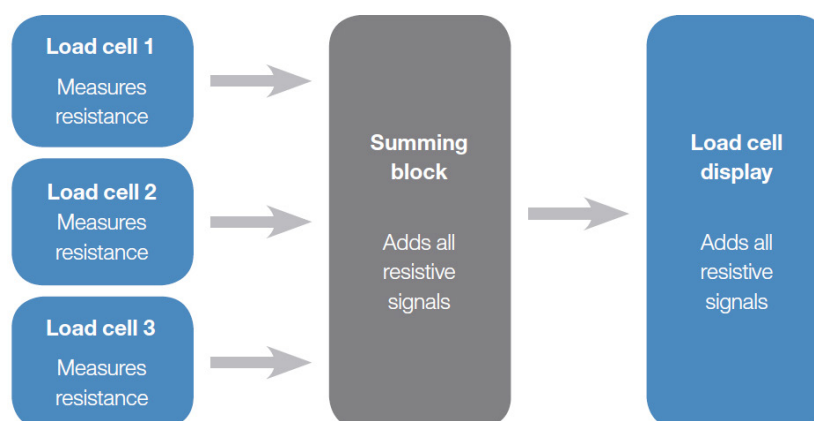


Figure 4.12. Load cell system overview.

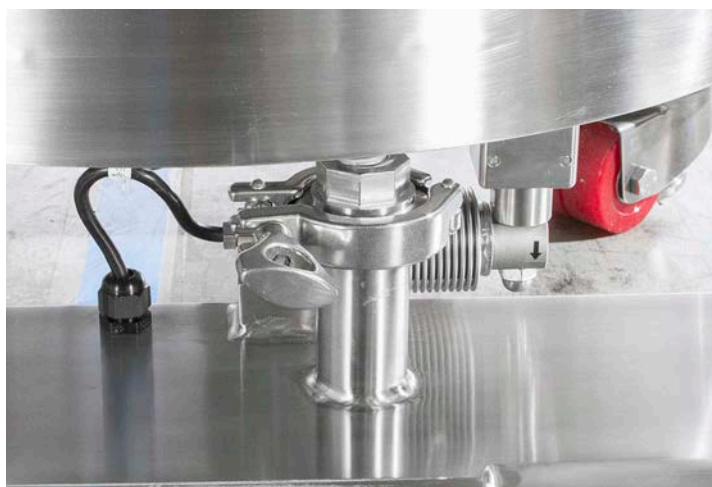


Figure 4.13. Mettler Toledo MTB load cell.

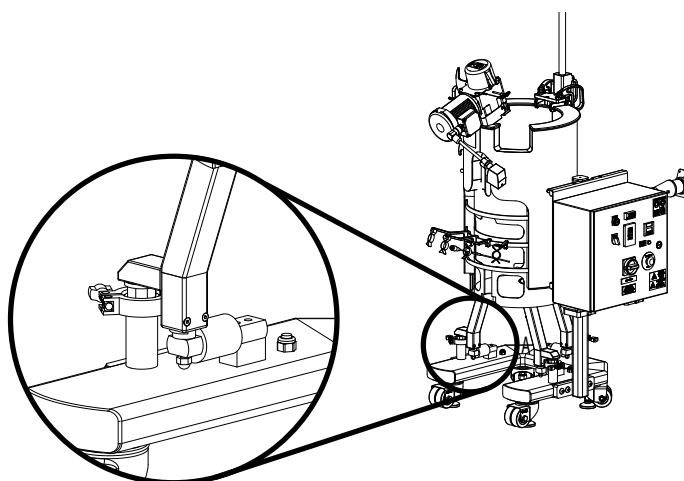


Figure 4.14. Load cell location.

Load cells are typically radial mounted in sets of three. The mounting location varies slightly for each size in order to allow easy access to the bottom drain or sparging mechanisms and tubing.

Table 4.9. Load cell specifications.

Weight module parameter	S.U.F. specification	
	30 L	300 L
Model number	MTB-100	MTB-200
Rated capacity per load cell	100 kg (220 lb.)	200 kg (441 lb.)
Load limit, safe	See specification	
Maximum horizontal force	0.98 kN (220 lb.)	1.96 kN (441 lb.)
Maximum top plate travel	Not applicable	
Maximum uplift force	Not applicable	
Safe dynamic load	70% of rated capacity	
Weight (including load cell), nominal	0.6 kg (1.3 lb.)	
Material	304 stainless steel	

Table 4.10. Ordering information for Mettler Toledo load cell kit.

Size	Description	Part number
30 L	3x load cell with summing box, no display	SV50988.04
300 L	3x load cell with summing box, no display	SV50988.03

Load cell displays

Table 4.11 lists ordering information for Mettler Toledo harsh mount displays (Figure 4.15) for 30 L and 300 L S.U.F. systems.



Figure 4.15. Load cell display.

Table 4.11. Ordering information for Mettler Toledo harsh mount load cell displays.

Description	Part number
IND331 display, harsh mount style with analog interface (STD), 120 VAC US line cord/plug	SV50177.306
IND331 display, harsh mount style with Allen-Bradley RIO interface, 120 VAC US line cord/plug	SV50177.307
IND331 display, harsh mount style with Device Net interface, 120 VAC US line cord/plug	SV50177.308
IND331 display, harsh mount style with Ethernet/IP & Modbus TCP interface, 120 VAC US line cord/plug	SV50177.309
IND331 display, harsh mount style with Profibus interface, 120 VAC US line cord/plug	SV50177.310

4.6.2. Cable management system

The cable management system includes the following components (Figure 4.16):

- Internal channel for sparge lines
- External channels for feed and base addition lines
- Harvest line hook
- Feed bag management hook
- Adjustable arm for external control power cable management (Figure 4.17)

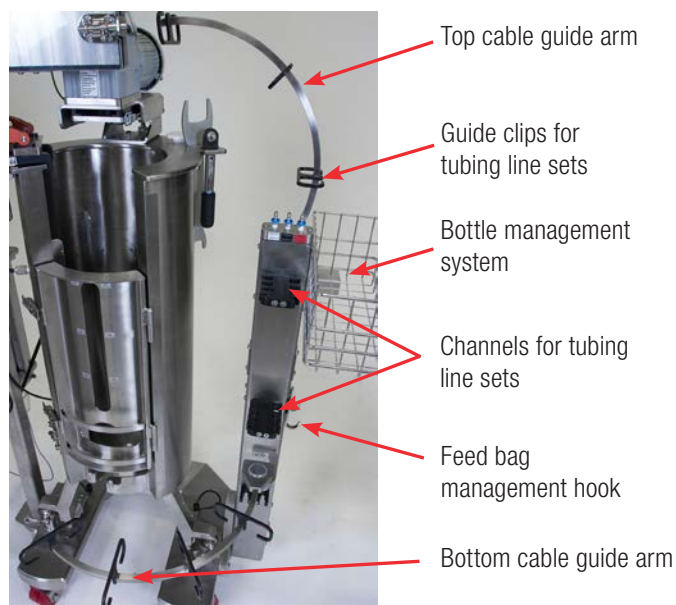


Figure 4.16. 30 L S.U.F. with cable management system.

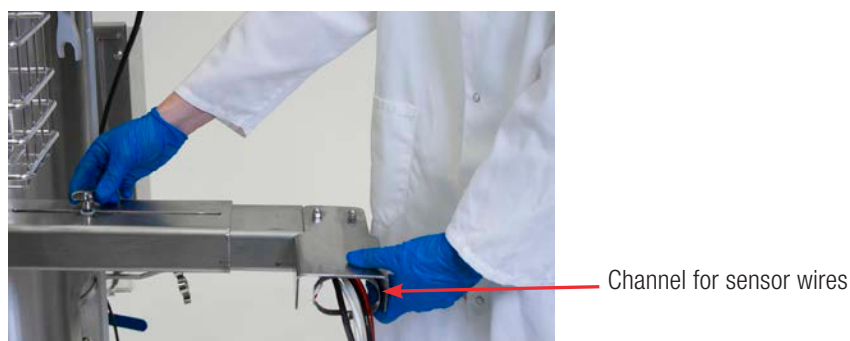


Figure 4.17. Adjustable arm and channel for sensor wires (back view).

Table 4.12. Cable management system ordering information.

Size	Description	Part number
30 L	Cable management system	SV51006.01
300 L	Cable management system, left hand configuration	SV51006.02
300 L	Cable management system, right hand configuration	SV51006.03
--	Bottle management system	SV50992.10

4.6.3. Vent filter heaters

The vent filter heater system (Figure 4.18) consists of the following components:

- Heater
- Controller (optional)
- Power cord

It includes a fully insulated resistive heating element with molded silicone foam. It is secured around the filter by use of snap retainers and fully encapsulates the exhaust filters for consistent temperature regulation. The temperature controller is preset for the S.U.F. at 55°C. The filter heater plug is a standard IEC C14 connector and plugs into a 208 volt outlet in the bottom of the E-Box.

The vent filter heater system stands alone and does not integrate with the control system of the S.U.F. Refer to the vent filter heater user's guide included in the S.U.F. ETP for more information.

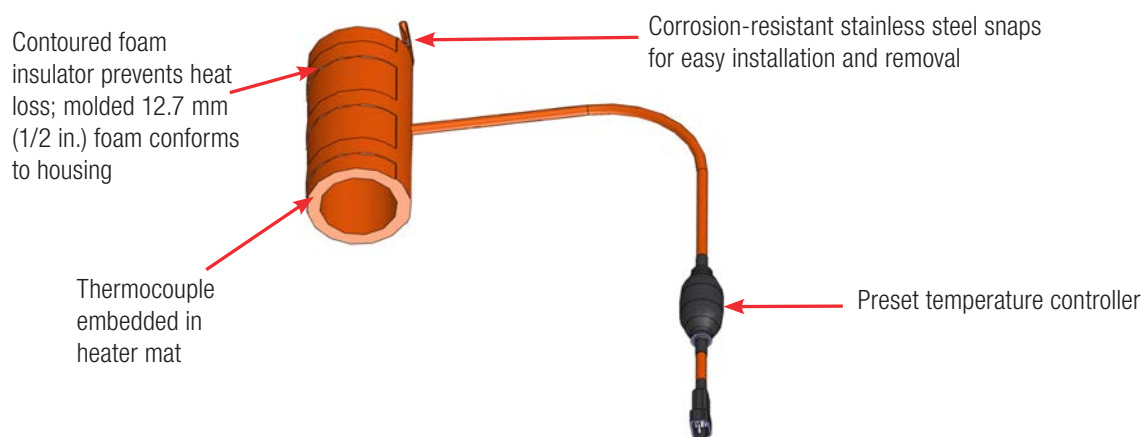


Figure 4.18. Vent filter heater.

Vent filter heaters are sold as a kit which includes vent filter heater, controller with a water-tight closure and an installation power cord.

Table 4.13. Ordering information for filter heater kits.

Description	Additional information	Part number
NEMA rated 120 VAC vent filter heater with a thermal couple	Includes preset temperature of 55°C and a turck connector	SV50191.41
NEMA rated 240 VAC vent filter heater with a thermal couple	Includes preset temperature of 55°C and a turck connector	SV50191.42
NEMA rated 120 VAC vent filter heater with controller	Includes preset temperature of 55°C and includes a standard IEC C14 plug	SV50191.35
NEMA rated 240 VAC vent filter heater with controller	Includes preset temperature of 55°C and includes a standard IEC C14 plug	SV50191.36

4.6.4. Exhaust system

The exhaust system supports the effective use of the S.U.F. A condenser is available as an optional product for both S.U.F. sizes. The condenser efficiently condenses exhaust gases and transfers condensate back into the unit, preventing potential vent filter blockage and reducing fluid loss due to evaporation. It is offered in a single chill-plate format for the 30 L S.U.F. and a double chill-plate format for the 300 L S.U.F.

The condenser protects against filter blockage by condensing out moisture prior to exhaust gases reaching the vent filters. BPCs are not intended to operate under pressure, and fouled (blocked) exhaust filters lead to bag pressurization. While vent filter heaters may prevent condensate build-up in many instances, with larger fermentors, this becomes less effective, whereas condensing out the moisture first is a more reliable method for preventing liquid from reaching the filters.

The S.U.F. exhaust system (Figure 4.19) consists of the following components:

- Condenser (chill) plate—accommodates a single-use condenser bag which is secured to the condenser plate to cool exhaust gases. Two plates are used for 300 L S.U.F. systems and a single plate is used for 30 L systems.
- Temperature control unit (TCU)—circulates water and glycol to cool the condenser plate.
- Peristaltic pump for 300 L S.U.F. units only—returns condensate to fermentor.
- Optional exhaust filter pinch clamp (not shown—see Miscellaneous items [section 4.6.5] of these specifications for more information)
- Condenser disposables—the BPC, tubing, and exhaust filters though which the exhaust gases flow and are chilled, and in which the condensate collects and is returned to the fermentor.

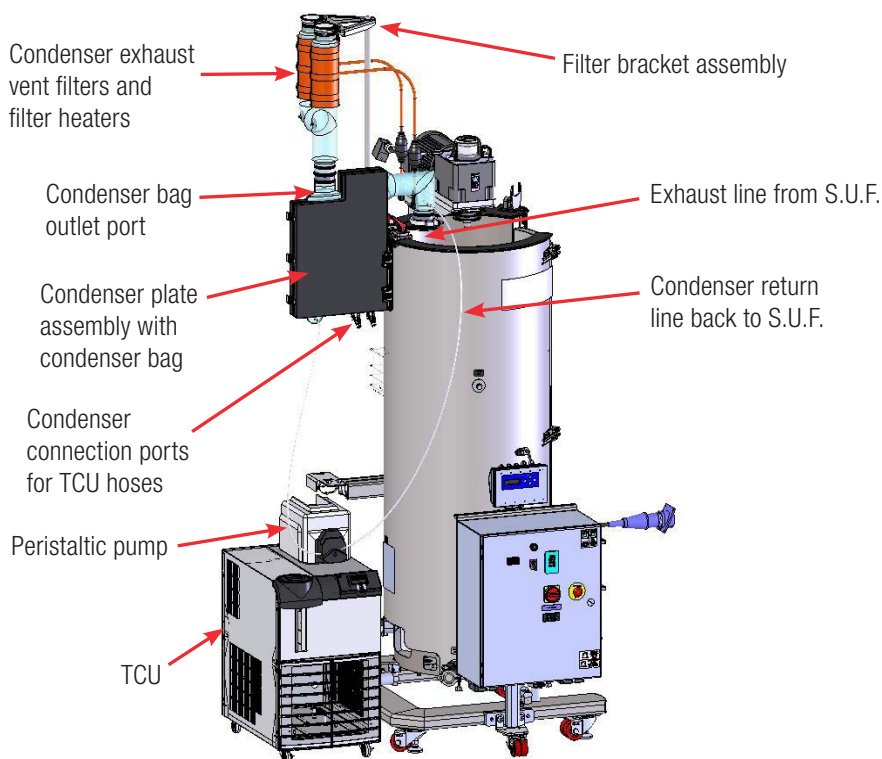


Figure 4.19. 300 L S.U.F. exhaust system.

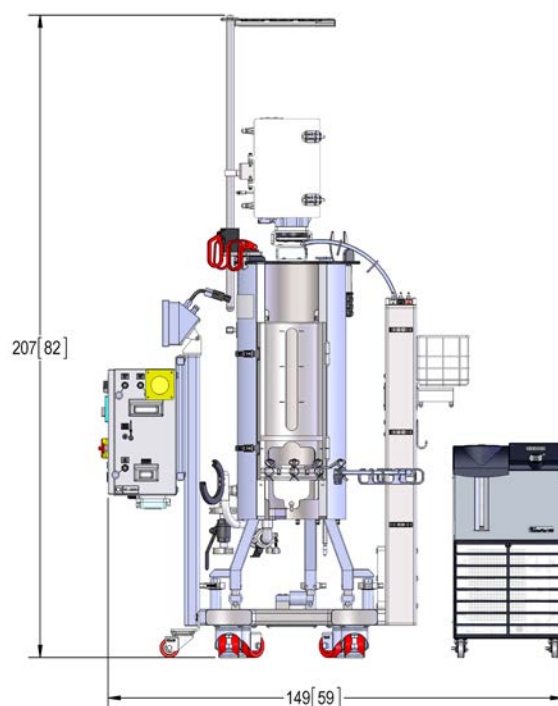


Figure 4.20. Dimensions for 30 L S.U.F. units with condenser (measurements shown in centimeters [inches]).

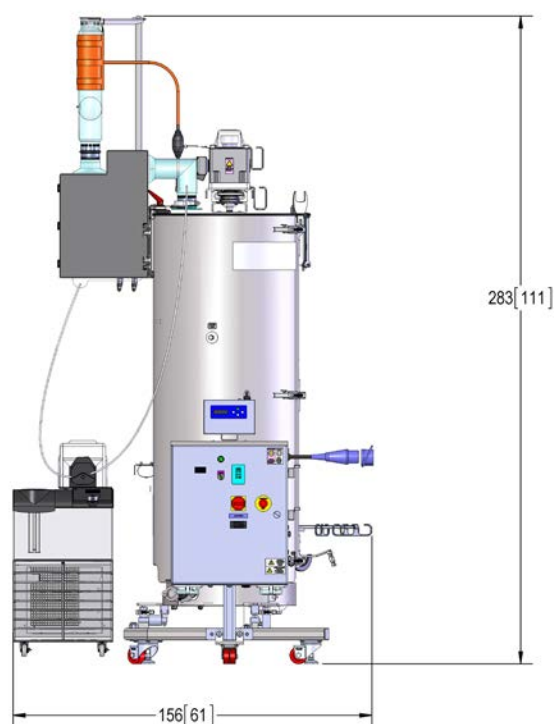


Figure 4.21. Dimensions for 300 L S.U.F. units with condenser (measurements shown in centimeters [inches]).

Table 4.14. Condenser system ordering information.

Description	Part number
Complete condenser system with 120 VAC for 30 L S.U.F. unit (TCU for condenser is included)	SV51016.02
Complete condenser system with 240 VAC for 30 L S.U.F. unit (TCU for condenser is included)	SV51016.03
Complete condenser system with 240 VAC for 300 L S.U.F. unit (TCU for condenser is included)	SV51016.01
Thermo Scientific MasterFlex pump (115 VAC/50 or 60 Hz or 230 VAC/50 or 60 Hz) for 300 L systems	SV50241.02

See section 4.6.5 for information about exhaust filter pinch clamps.

4.6.5. Miscellaneous items

The miscellaneous items in this section are ancillary components that support the sterile operation of the S.U.F. for microbial cell culture production and enhance the overall performance of the complete system.

Autoclave tray and probe assembly

The autoclave tray (Figures 4.22 and 4.23) holds the electrochemical probes and bellows in place during the autoclave sterilization process. Design elements include the following.

- Fabricated from stainless steel
- Plastic handle provides 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
- Probe holder accommodates two probes

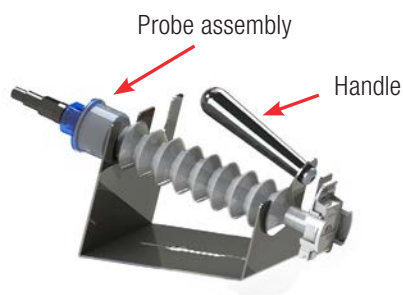


Figure 4.22. Autoclave tray.

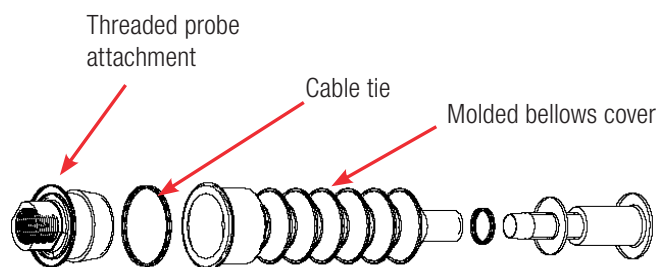


Figure 4.23. Probe assembly.

Exhaust filter pinch clamp

The exhaust filter pinch clamp may be used to temporarily stop air flow to redundant exhaust filters (Figure 4.24). It is mounted to the exhaust filter pole and is closed with a pneumatic mechanism that is activated through the controller. The pinch clamp is mounted horizontally on 30 L systems, and vertically on 300 L systems.

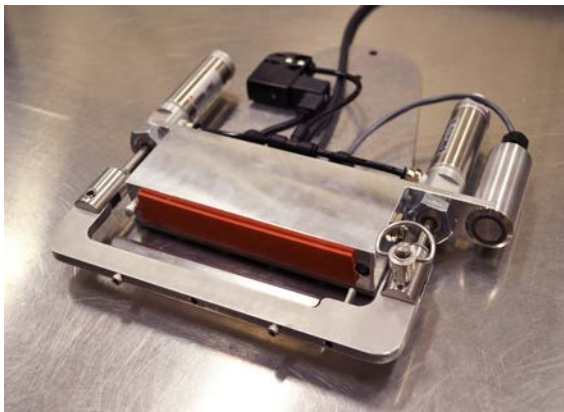


Figure 4.24. Exhaust filter pinch clamp.

Heavy-duty tubing clamps

Heavy-duty clamps are used for pinching off line sets that are not in use in order to prevent process fluids from escaping (Figure 4.25). Prior to sterile probe insertion, tubing clamps must be in place to close off probe ports. See Chapters 2 and 3 of this guide for more information.



Figure 4.25. Heavy-duty tubing clamp.

Table 4.15. Miscellaneous items ordering information.

Description	Part number
Autoclave tray	SV50177.01
Probe assembly (non-sterile for use in autoclave)	SH30720.01
Exhaust filter pinch clamp for 300 L system	SV50177E.15
Exhaust filter pinch clamp for 30 L system	SV50177E.16
Heavy duty tubing clamp (single)	SV20664.01
Heavy duty tubing clamps (10 pack)	SV20664.03

Spare parts ordering information

For spare part numbers for items such as drive shafts or RTDs, please see the hardware drawings supplied with the ETP.

5

Maintenance and troubleshooting

Chapter contents

- 5.1 Maintenance
- 5.2 Troubleshooting and frequently asked questions

5.1. Maintenance

5.1.1. Routine maintenance

Environmental conditions, operating parameters, and the ability of the user to adhere to standard operating procedures as outlined in this user's guide can have significant impact upon the useful life of the S.U.F. hardware system. The following guidelines are based upon standard operating conditions as outlined in this guide. High wear items such as bearings, seals, O-rings, and sterilization valves common to conventional fermentor systems have been purposefully considered in the design of the construction of the S.U.F.

The S.U.F. system is inherently robust, and requires low levels of routine maintenance. Taking time between runs to clean the exterior of the hardware is certain to improve the appearance and overall longevity of the system. The drive motor is an industrial grade induction motor with permanently sealed and lubricated gear box. The drive shaft is constructed to wear slightly with use, and should be visually inspected after each run. The vent filter heaters are designed to operate well within manufacturer's design limits, and will provide years of consistent performance. Visual inspection of wear components and following the guidelines listed below will be sufficient to ensure years of dependable service. Replacement parts are available.

5.1.2. Preventive maintenance schedule

Under normal operating conditions, replace the drive shaft assembly after one year of service, or refer to the drive shaft head wear specifications in Table 5.1, below.

Table 5.1. Drive shaft head dimensions.

Size	New hex diameter	Minimum hex diameter
30 L	14.9 mm (0.58 in.) +/- 0.127 mm	14.4 mm (0.56 in.)
300 L	21.3 mm (0.83 in.) +/- 0.127 mm	20.8 mm (0.82 in.)

Replace worn drive shaft head assembly when the hex diameter at its widest location measures equal to or less across the points (Figure 5.1). Diameters are measured at widest location across the points.

- Lightly coat drive cap threads with food-grade anti-seize if the motor cap becomes difficult to turn.
- If using a multiple-segment drive shaft, lightly coat the threads with food-grade anti-seize during assembly.
- Replacement of the drive motor is recommended every five years, or as needed.
- Replacement of the S.U.F. drive shaft is recommended after one year of use.

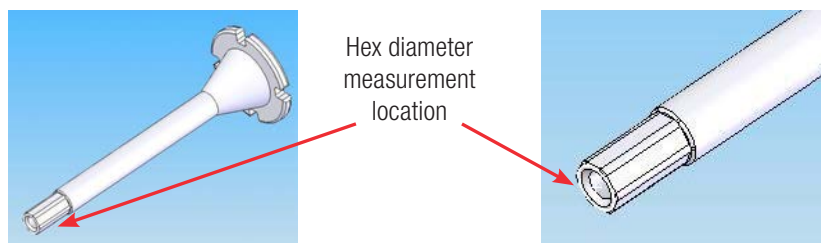


Figure 5.1. Drive shaft head assembly.

5.2. Troubleshooting and frequently asked questions

5.2.1. Hardware operation issues

Issue: **The S.U.F. will not operate.**

Solution: **Check the power supply.**

- Verify the main electrical plug connection at wall outlet, the position of main power disconnect, and the position of the emergency stop switch.
- Verify the condition of the main electrical circuit breaker of 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 S.U.F. system should be placed on its own electrical circuit.
- Disconnect the main power cord. Inspect the electrical circuit breakers and fuses inside the electrical enclosure of the S.U.F. controller. Determine the fault condition by visual inspection. If the fault condition can not be determined by visual inspection, contact the manufacturer.

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

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

Verify the following:

- The temperature probe (or RTD) is not loose and has been fully inserted into the thermowell on the BPC.
- The TCU has been filled with sufficient glycerol to aid in heat transfer.
- The TCU is working correctly; look for TCU faults and warnings.
- The control scheme of the TCU is set correctly (external control or internal control).
- The TCU PID heating and cooling values are correct.
- The system is filled with a sufficient amount of fluid. There must be enough volume of media (minimum volume of 5:1) in the BPC to provide contact with the bottom of the impeller. Add more media if the liquid level is below 5:1 (20%) volume.
- The motor is agitating the process batch.
- The tank jacket has been sufficiently purged of air.
- The BPC has been loaded correctly and is making good contact with the side walls of the tank.

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

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

- Rapidly adjusting speed control in an excessive manner may require several seconds for speed stabilization.
- Wait ten seconds and then attempt to adjust 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.
- Verify that the motor power cable is fully searched on both ends.

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

Solution: **No action is required.**

- The bearing port assembly supplied with the S.U.F. is an important component in maintaining a sterile environment during cell growth. The special seals used in the S.U.F. 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 the performance or overall durability of the BPC during the intended life of the product.
- Secure the clear protective safety access cover to prevent it from vibrating at the hinge.

Issue: **The vibration of the system seems excessive.**

Solution: **Check to make sure the system is set up properly.**

Verify the following:

- The drive shaft has not been bent.
- The motor is locked at end of stroke, centered above the tank.
- All motor bracket bolts are secure and tight.
- All 4 leveling feet are down and tightened against the floor.
- The tank is sitting horizontally level, adjust with leveling feet.

Issue: **Motor rpms are inaccurate.**

Solution: **Verify that the VFD parameters have been set correctly per the Thermo Fisher schematic.**

Issue: **The load cells are reading incorrectly**

- Solution:** **Verify that the load cells and display are set up correctly.**
- Verify that the load cell lock outs have been released, and that the tri-clamps have been removed.
 - Verify that the load cell lock outs are not contacting the mating boss extending from the cart.
 - Verify that the “capacity” parameter in the Mettler Toledo load cell display has been configured correctly.
 - Re-calibrate load cells once the above steps have been verified.

Issue: **During loading, the first foot or the last inch of the drive shaft cannot be inserted.**

Solution: **Rotate the shaft while inserting it. This rotation typically resolves the slight misalignment that can occur during drive shaft and bearing port setup.**

If needed, carefully press the film up to the shaft sleeve below the bearing port and grab the shaft sleeve tube. Gently twist the tube slightly in the opposite direction of the shaft until the shaft fully inserts. Secure the shaft following the instructions in sections 3.2 and 3.3 of this guide.

Note: On the first use of a 300 L system, if the first foot or the last inch of the drive shaft is difficult to insert, slightly loosen the four motor mounting bolts, insert the shaft, and then retighten the bolts.



WARNING: Motor mounting bolts must be retightened after initial drive shaft loading to prevent damaging the system.

5.2.2. Cell culture operation issues

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

- Solution:** **Check the physical condition of the DO probe, calibration of the DO probe, and flow rate of gas into the S.U.F.**
- DO probes require routine maintenance; replace damaged probe or membrane.
 - Verify that the cable is properly connected to the probe and controller. If using a single-use DO sensor, verify connections for the optical transmitter’s power supply, optical connections, and transmitter to the controller cable.
 - Verify DO probe calibration relative to setpoints of zero and span.
 - Inspect line sets connected to direct spargers for restriction (closed tubing clamp, pinched line, and low supply pressure).

Issue: **DO readings are erratic or unstable.**

Solution: **Adjust the controller to suit the volume of the S.U.F. system.**

- Many different parameters can effect the ability of a fermentor controller to effectively maintain a target setpoint during process control. Modern controllers utilize computer algorithms to adjust targeted parameters, the most common technique is that of tunable controller that uses variables of proportional integral derivative (PID). Tuning these PID values to the specific characteristics of the system dynamics will in most cases stabilize process parameters to an acceptable level. It is recommended that S.U.F. users consult the user's guide of the particular fermentor controller being used.
- Verify that the probe is fully inserted and that the contacts are grounding the plug. A backup 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 on the sample line of the BPC.

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

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

- pH levels can be managed in a similar manner to conventional fermentors once calibration of the probe is verified by use of an off-line sample. Ion levels in the media, and the addition of liquid titrant solutions serve to manage the pH balance of the fermentor environment. See the probe assembly instructions in section 3.5 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 on the sample line of the BPC.
- Check to make sure the pH control solution tubing is loaded correctly into the pump.
- Make sure the tubing is not leaking. Use PharMed™ tubing if the tubing is wearing out.

Issue: We are having difficulty controlling the volume and feed rate or supplement during a fermentor run.

Solution: Use load cells or a scale to control volumes based upon weight. The S.U.F. is not equipped with level sensors, other than the maximum foam level sensor that is available as an option and measures foam in the head space of the BPC. However, the S.U.F. can be set up to allow supplement feeds and volumes to be managed by weight. Please refer to the specifications in Chapter 4 for skid dimensions for sizing of scales.

Issue: We are not achieving the cell growth we expected in the S.U.F. while running under our normal fermentor agitation and sparging rates.

Solution: Reduce agitation and sparging rates. Often low cell viability and cell growth can be attributed to excessive sparging or agitation. It is recommended that users reduce their sparge rate compared to what they might use in a conventional fermentor. 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, increase agitation. Media formulation can also have a large effect on cell culture growth. Thermo Scientific can offer custom media especially for the S.U.F. and customer's specific cell line(s) via the Life Technologies division.

Issue: The mixing performance is poor.

Solution: Make sure the BPC is installed correctly. Verify the following:

- The BPC has been loaded correctly, and the hanging tabs of the BPC are attached to the pins on the tank.
- The baffles are present and well defined by the BPC.
- The drive shaft is correctly installed and engaged in the motor.
- All drive shaft joints are tight.

5.2.3. Probe and connector issues

Issue: **The pH and DO probes were not introduced prior to media fill. Can a sterile connection still be made under these conditions?**

Solution: **If you are using standard probes, as long as the clamps were closed on the aseptic connector probe ports before liquid fill, you can make a sterile connection after the media fill.**
(If you are using single-use probes, they are integrated into the BPC, and just need to be connected to the controller).

The aseptic connectors must be dry to make the connection of the probe assemblies. When media is already present in the S.U.F., follow the probe insertion procedures as outlined in section 3.5. Some fluid may enter the bellows when the probe is inserted into a BPC already filled with media.

Issue: **We are not familiar with the use of Pall Kleenpak connectors and are concerned about making connections. How can we ensure a successful connection using this system?**

Solution: **Familiarize yourself with the sterile connector instructions found in section 3.5.5 before beginning.**

- When a connection is being made, visually evaluate the status of the four locking external clips and verify they are tightly secured (the snap should be audible for all four clips when pressing the connectors together). Always make sure the four locking clips are fully engaged for the male/female connection before removing the paper strips.
- A common cause for a leaky connector is an error in the final step of seating the tapered barrels of the male/female connector. There are a series of concentric rings inside the male connector (7.72 mm [0.3 in.] in front of the black O-ring). Visually verify that the four internal clips are on the last set of rings. Using both hands place connector flanges between index fingers and thumbs and squeeze until properly seated.

5.2.4. BPC and sparging issues

Issue: **The S.U.F. BPC seems overly tight.**

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

- Reduce inlet gas flow rate of the sparger.
- Inspect exhaust filter and/or condenser 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 S.U.F. This may cause product failure and impending burst of the BPC.
- Use the backup filter option and open additional filter(s) as needed.

Issue: **There is excessive foam in the fermentor 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 S.U.F. 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 dramatic reduction of foam in the headspace.

If you are using a foam sensor, follow the steps below to make sure it is operating properly.

- Verify that the connection of the sensor wire from the controller to the single-use foam probe. Test the connection of the wire with an ohm meter by placing the lead on the ends of wire.
- Verify that the antifoam solution is available, the tubing is unrestricted and the fluid flows in the correct direction.
- Verify that the pump tubing selection is correct. Pharmed pump tubing or similar durable tubing is recommended.
- On the controller, verify that foam sensing and the actuator are turned on.
- Make sure the wire connected to the foam sensor on the BPC is connected to the level sensor port on the controller.
- Make sure the ground wire connected to the RTD at the bottom of the BPC is connected to the ground port on the controller.
- Make sure the foam sensor is perpendicular to the BPC, in a vertical position, and not grounding on the metal S.U.F. tank.
- Make sure the foam sensor port is draining properly so that condensation doesn't build up in the tubing.
- On the controller, adjust the sensor response as needed.
- Verify that the solution in the BPC is conductive.

6

General ordering information

Chapter contents

- 6.1 Ordering instructions
- 6.2 Ordering/support contact information
- 6.3 Technical support

6.1. Ordering instructions

BPCs and hardware components for the Single-Use Fermentor (S.U.F.) can be ordered directly from Thermo Fisher Scientific. These items include all components that have part numbers beginning with the following characters:

- SH
- SV
- SUF

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 (0) 670 734 093

Fax: +44 (0) 670 732 537

Email: customerservice.bioprocessing@thermofisher.com

6.3. Technical support

Technical support for the S.U.F. 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 (0) 670 734 093 (Europe, U.K.) for direct and immediate response to overall product questions, and product technical information (Technical Support). You can also contact Tech Support by emailing:
techsupport.bioprocessing@thermofisher.com

Initial setup and operation

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

Training

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

Appendix A—Installation of female electrical receptacle for units with AC motors and electrical control panels

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 panel 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.

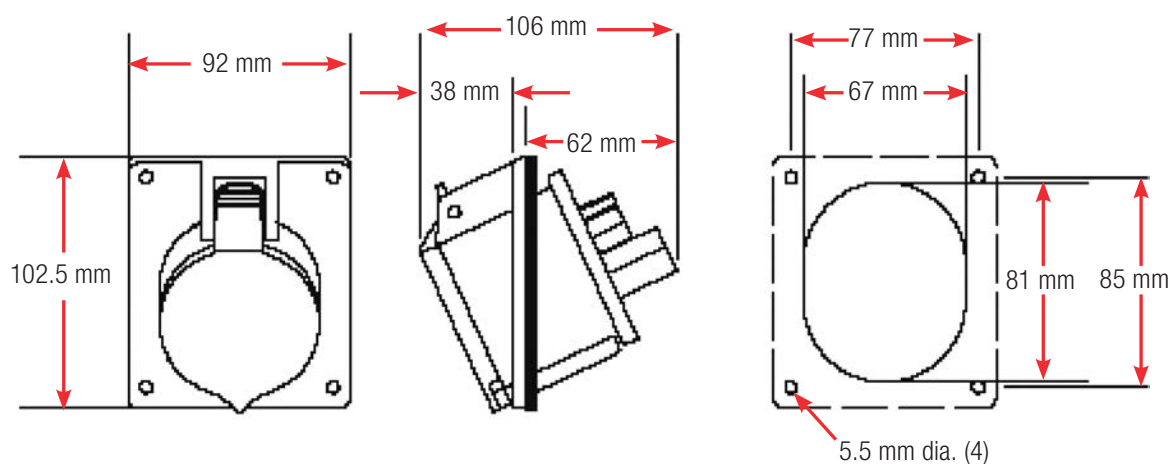


Figure A.1. Panel cutout.

4. Check the condition of the three exposed wire leads, and strip them back to expose a new wire, if needed.
5. Connect the wire leads on the receptacle (Figure A.2) 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)

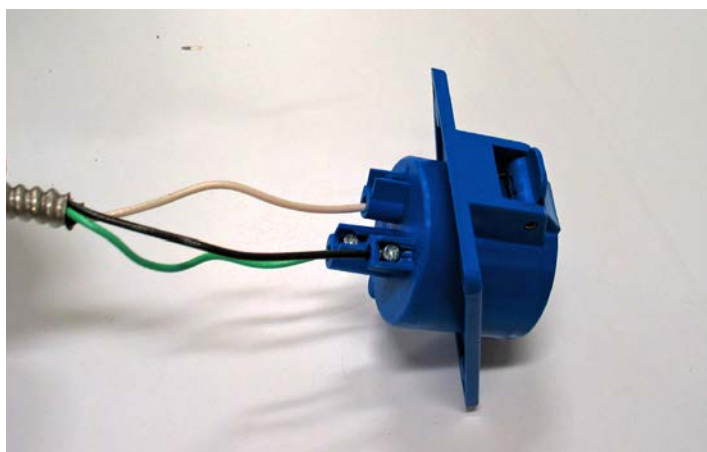


Figure A.2. Female receptacle (blue for 240 VAC; yellow for 110 VAC).

6. If 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 four supplied screw fasteners.
8. Connect power back to the electrical circuit.
9. Test the circuit with multi-meter prior to making any connections to the electrical receptacle.

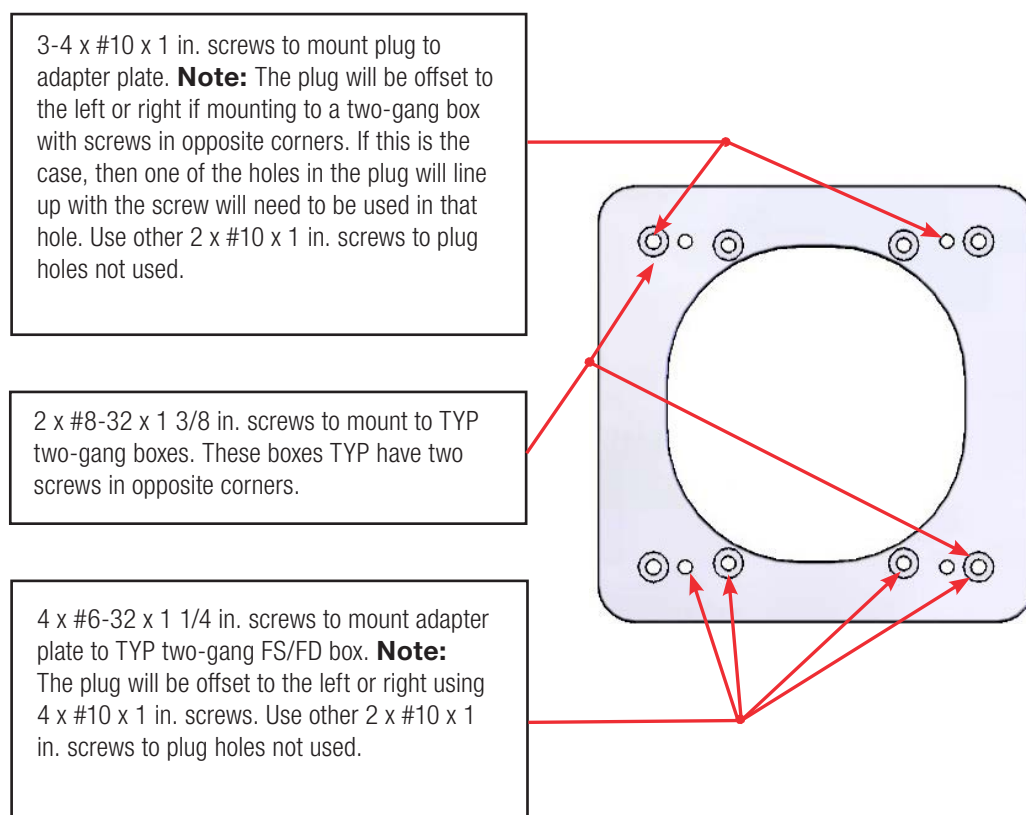


Figure A.3. Adapter mounting plate.

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 (the 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 Chapter 2 of 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.F. 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>

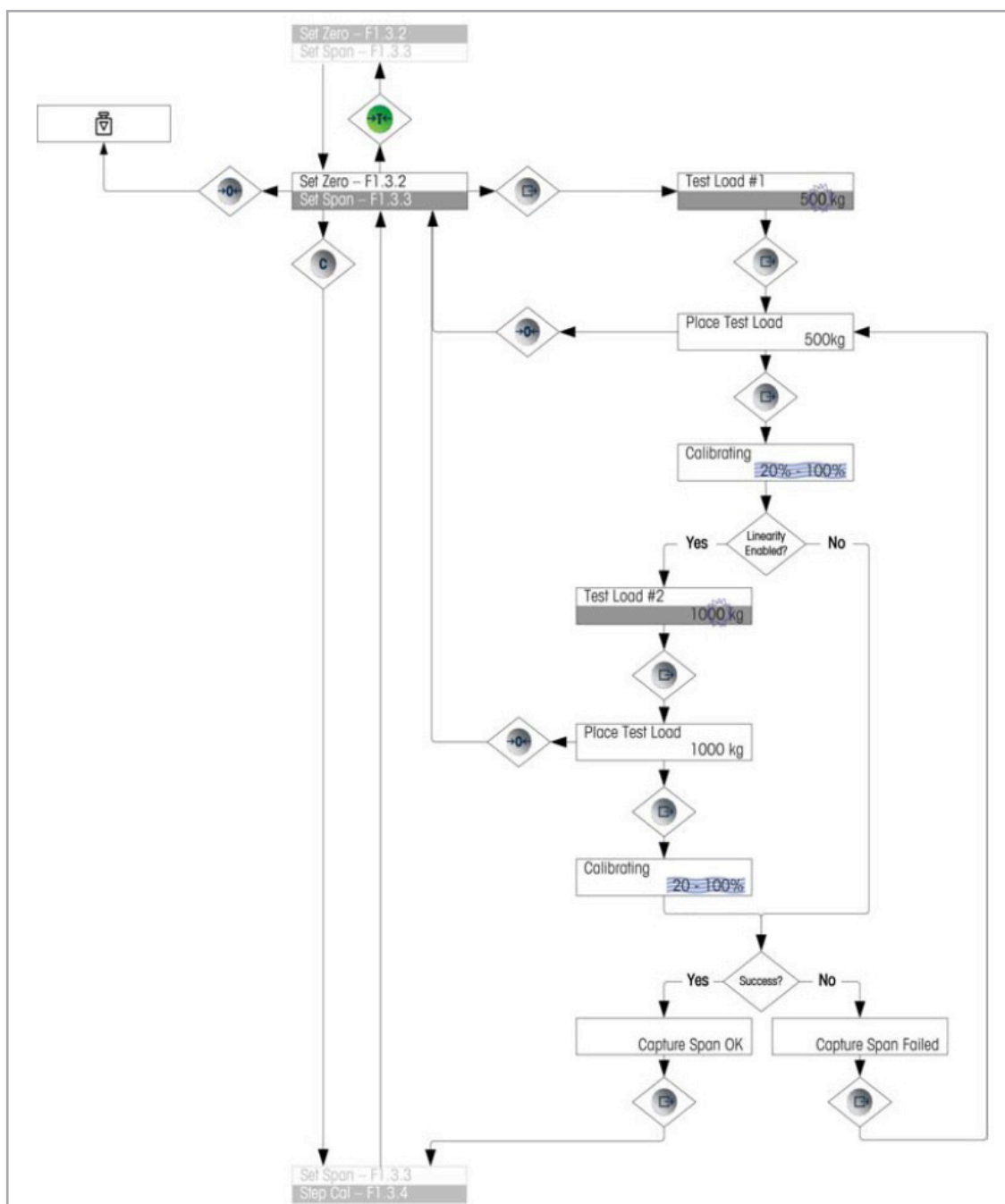


Figure B.1. Span calibration.

Appendix C—Pre-fermentation run checklist

Verify that the following steps are completed before beginning your cell culture run.

Loading the BPC

- ✓ All sharp objects are out of installation path.
- ✓ There is no blockage in the exhaust filter. Verify that a clear plug is not installed in the 3 in. exhaust port by inserting a finger in the filter exit hole.
- ✓ There is a proper exhaust air flow path through the condenser and filter. Verify that the BPC is not folded over or twisted in the condenser or in the exhaust path.
- ✓ The BPC is inflated about half-way.
- ✓ The BPC is installed with the bottom and top hanging tabs connected to the hanging tab knobs.

Filling the vessel

- ✓ Unused tubing lines are clamped off.
- ✓ Each of the four vertical seams of the 300 L BPC is aligned with one of the four baffles on the bottom hanging tab side of the baffle. Align manually by pulling the seam up along the baffle as it fills.
- ✓ The drain and sparge lines are properly aligned and flush with the bottom plate.

Checking the pressure sensor

- ✓ The pressure sensor is connected to the pressure cable.
- ✓ The pressure control loop is turned on and settings have been verified.
- ✓ Pressure sensor tubing is unobstructed through to the vessel.

Checking the foam sensor

- ✓ The foam sensor is connected to the pressure cable.
- ✓ The vessel ground clip is connected to the sample port metal tubing ground connection.
- ✓ The foam control loop is turned on and settings have been verified.
- ✓ The gas sparge, acid, base, antifoam and feed lines have been unclamped before priming the lines or beginning inoculation.

Sampling

- ✓ The cap is removed and sprayed with an ethanol solution (70–85% as per site recommendations).
- ✓ The luer lock syringe is inserted into the SmartSite port luer lock fitting.
- ✓ The sample line clamp is unclamped.
- ✓ Volume is pulled to flush the sample line.
- ✓ The sample line is clamped and flush volume is discarded.
- ✓ After sampling, clamp the tubing line, spray the sample port with isopropyl alcohol or ethanol solution (70–85%) and replace the cap.

Find out more at thermofisher.com/suf

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